Instructor's Guide:

How to manage a CT
Notifications, Ad hoc assessment, Corrective measures and Trial results

CTIS Training Programme – Module 05
Version 1.2– October 2021

What you will find

- Overview of the audiences targeted in training module 5
- Overview of the training materials included in this module
- Guidelines to disseminate the knowledge
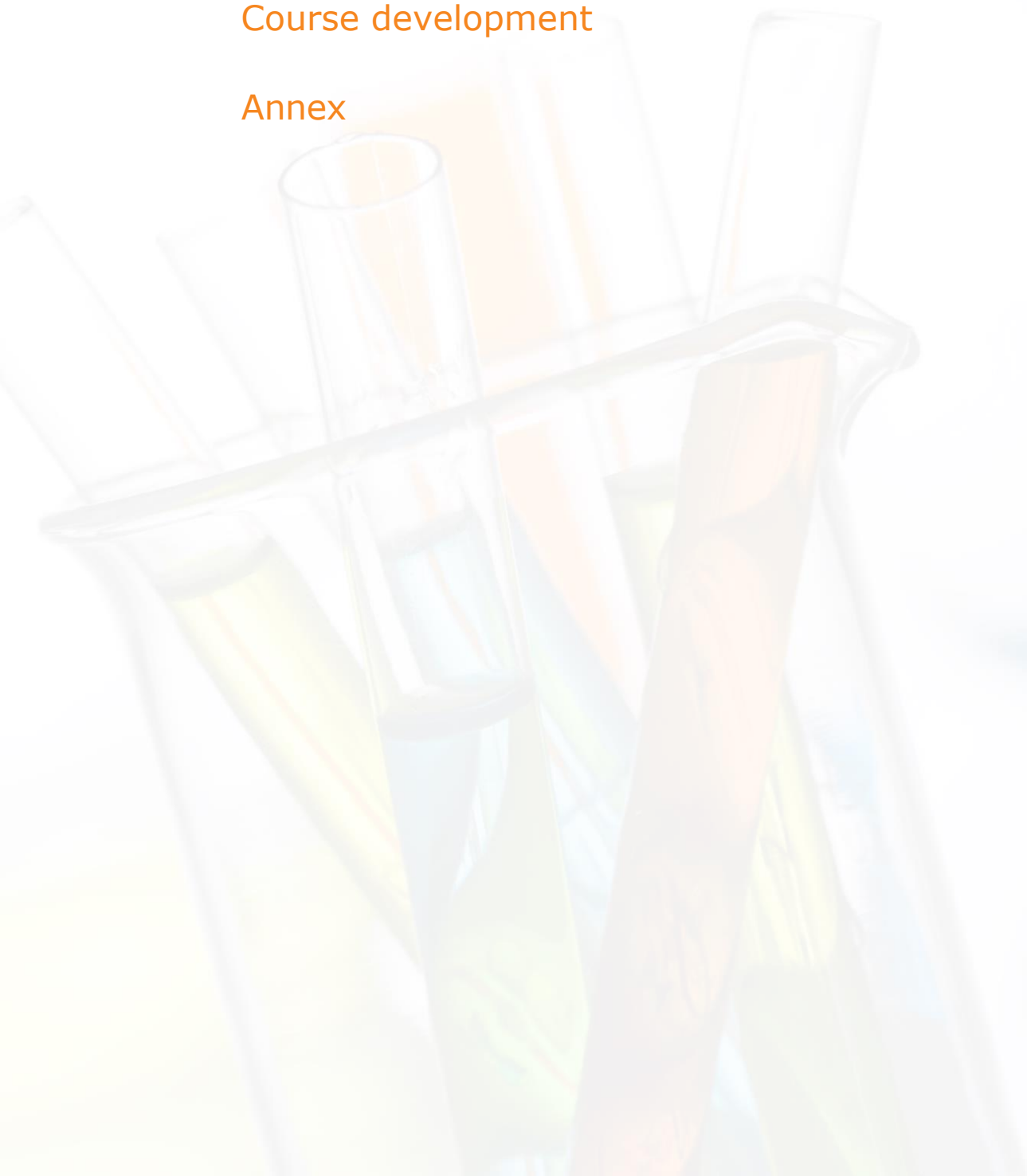- Recommendations on how to prepare and develop the training

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 **fifth Module of the CTIS Training Programme** (hereafter referred to as 'CTTM05'). This module provides an introduction to the responsibilities of the sponsors from the submission of a Clinical Trial Application (CTA) until the submission of the Clinical Trial (CT) summary of results. In addition, CTTM05 provides detailed information on several processes and functionalities in CTIS that help sponsor users to manage an authorised clinical trial, in line with their responsibilities set out in Regulation (EU) No 536/2014 on Clinical Trials (CT Regulation). This module covers in particular the following: how to use Notifications to report relevant events occurred when conducting a clinical trial to MSC; how to address requests for information/for opinion submitted as part of ad hoc assessments and intended corrective measures, and how to prepare and submit CT results at the end of a trial. **This guide provides** an overview of the audiences targeted with CTTM05, the training materials available, and a suggested methodology for disseminating the materials to end-users.

The training activities proposed in this instructor guide are available in English and have been designed for people with reading and hearing abilities. 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

CTTM05 targets **sponsor users**, including commercial and non-commercial. Depending on the audience, the users will be disseminating the material presented in this guide to one or more of these groups.

CTTM05 learning objectives

The learning objectives of CTTM05 are:

- Remember the responsibilities of the sponsors from the submission of a CTA until the submission of the CT summary of results.
- Understand the use of Notifications.
- Understand the processes of ad hoc assessments and corrective measures and how to address requests for information regarding them.
- Understand how to prepare and submit CT results.

Materials available

- **CTTM05 eLearning presentation:** One interactive presentation to familiarise users with the sponsors' responsibilities throughout the CT life-cycle and an overview of the related system functionalities concerning the use of notifications, the processes of ad hoc assessments and corrective measures and how to address requests for information regarding them.

- **CTTM05 Quick guide:** Practical and simple quick reference guide with images to prepare users on the preparation and submission of CT results.

- **CTTM05 video-clips:** Two video clips providing a practical demo of the use of the notification's functionality:

  o Clip 1: Notifications – Trial & Recruitment periods (4 minutes 58 seconds)
  o Clip 2: Notifications – Other Notifications (4 minutes 10 seconds)

- **CTTM05 Frequently Asked Questions (FAQs):** List of common questions and answers regarding the contents covered in this module.

03

Course preparation

To ensure that the learning objectives of CTTM05 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, 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 propose you to **share the relevant CTTM05 eLearning presentation and Quick guide** with the participants ahead of the training session. This will allow them to absorb the contents of the presentation on their own and reflect on questions they may have.

- Second, we propose that you organise **a webinar** around one week after having shared the eLearning presentation and Quick guide with the participants. This will allow you to check participants' knowledge absorption, address any question 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 Quick guide. As opposed to the self-assessment quiz at the end of the eLearning material, 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. It is recommended to always include one or two test questions to allow participants to test the tool before starting the quiz.

- **Send the eLearning presentation and Quick guide** to the training participants one week in advance. Remind them in the email how much time it will take them approximately to complete the materials, so that they can plan accordingly.

- **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 Clinical Trials Regulation[1], which establishes the different types of notifications and processes (e.g. respond to RFIs and submit trial results) that allow sponsors to fulfil their obligations regarding the supervision of clinical trials. Concretely, we recommend you to read at least the following articles, which are related to aspects covered in this module:

    - Chapter VI (Start, End, Temporary Halt, And Early Termination Of A Clinical Trial)

    - Article 52 (Reporting of serious breaches)

    - Article 53 (Other reporting obligations relevant for subject safety, including unexpected events and third country authorities' inspection reports)

    - Articles 54 (Urgent safety measures)

    - Articles 78 (Member State inspections)

    - Annex IV (Content of the summary of the results of a clinical trial)

    - Annex V (Content of the summary of results of a clinical trial for laypersons)

    - We also recommend you to take a look at the latest version of the European Commission's Clinical Trials Regulation Q&A,[2] concretely at section 10 (start, end, temporary halt, and early termination of a CT).

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

- **Limit participation** to a maximum of 20 participants and up to a maximum of two hours whenever possible, to maintain optimal interaction and keep the participants focused. This is applicable in the case of online events. The number of participants and the session duration may be longer in a face-to-face environment.

---

[1] European Commission, *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*, EU Official Journal L158. 16 of April 2014. 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 2.4, July 2020. 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: Completion of the eLearning presentation individually

Time: One week before the webinar

Material: CTTM05 eLearning presentation and Quick guide

Objective:

This activity consists in the completion by participants of the CTTM05 eLearning presentation and Quick guide. Due to the interactive design of this material, which is specially conceived for self-learning, it is recommended that participants complete it autonomously prior to the webinar/session to get acquainted with the content of the materials at their own pace and identify questions that are not clear to them.

Steps:

1. Send the eLearning presentation and Quick guide to the participants and ask them to complete them by a given date. Remember to indicate an approximate time for completing the materials to enable adequate planning by the participants.

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: CTTM05 eLearning presentation, CTTM05 Quick guide, CTTM05 video-clips, CTTM05 FAQs, and password-protected feedback form built by the CTIS Training Programme team with the EU survey tool to collect participant's feedback on their satisfaction with the training

experience.

Objective:

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

- Assess if participants have understood the knowledge presented in the CTTM05 eLearning presentation and Quick guide;

- Present the additional materials for the CTTM05, with a focus on notifications;

- Answer any questions regarding the content of the CTTM05;

- 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 (i.e. how to ask for the floor, mute/unmute themselves, use the chat, etc.).

   b. Explain the aim of the webinar and describe briefly the materials that will be used for the session.

   c. Open a roundtable to allow participants to introduce themselves briefly.

2. **Part 2**: Questions on the materials reviewed and interactive knowledge check (*approximately 25 minutes*).

   a. Ask if participants have any questions regarding the CTTM05 eLearning presentation and Quick guide.

   b. As an 'icebreaker', launch an online quiz to check if participants understood the key concepts from the eLearning and Quick guide for CTTM05. Make sure to explain how the tool works and allow at least for one or two test questions before starting the quiz.

3. **Part 3:** Screening of CTTM05 video-clips (*approximately 25 minutes*).

   a. Make a brief introduction of the CTTM05 video-clips, so that participants have an initial understanding of the content they are about to watch. You may want to prepare a short slide deck with key concepts to display on the screen while you are presenting (e.g. responsibilities of the sponsors from the submission of a CT application until the submission of trial results, brief description of the use and purpose of notifications and the types that there exist). This supports knowledge transfer in an online environment by keeping participants' attention. If you use a slide deck, make sure not to have too much text; use keywords and short sentences instead, as well as visual

representations. Workflows and diagrams are particularly suitable for presenting complex processes (e.g. implications of temporary halt notifications, types of trial and recruitment periods notifications, etc.).

b. Display each CTTM05 video-clip at the webinar.

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.

Break: (10 minutes)

---

4. **Part 4**: Trial and recruitment periods notifications activity (*approximately 30 minutes*).

a. Before the break, share the text document (see Annex) with the participants explaining the activity. On the communication, you should indicate the time they have to read and solve the activity. There are five cases described and five possible scenarios that match each of them. Please refer to the exercise document in the Annex of this document for more information.

b. *We suggest that, after participants come back from the break, you give them 20 minutes to read the document and complete the solution table on the second page of the document with the solution that best suits each case description.*

c. Use the remaining 10 minutes estimated for this activity to discuss the scenarios that participants have selected for each case and address any question or incorrect answer.

d. Key for the instructor: the table below outlines the correct scenarios for each of the cases.

Case ID	Correct solution ID
1	E
2	B
3	D
4	C
5	A

5. **Part 5:** Questions and answers (*approximately 15 minutes*).

a. Give some time to the participants to think and ask the questions they have on the material.

b. Note the questions of the participants. Allow them to ask them orally or via the chat. *We suggest gathering all questions at the beginning of this exercise*

*to make sure that all questions are captured without time constraints.*

    c.   Answer the questions using the CTTM05 FAQs as a support and take this opportunity to show participants this material. *We suggest that you note the questions of the participants that you are not able to answer surely. After the training session, you can send the unanswered questions, 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 10 minutes).

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

    b.   Give them 10 minutes to complete it. *If you are running out of time, you may decide to share the link to the survey with the participants via email and ask them to complete it after the webinar.*

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

    a.   Conclude the webinar and reference for future training modules and/or training sessions.
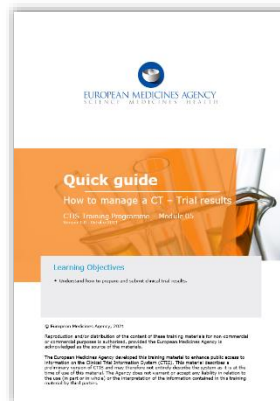
    b.   Allow participants to ask final questions.

05

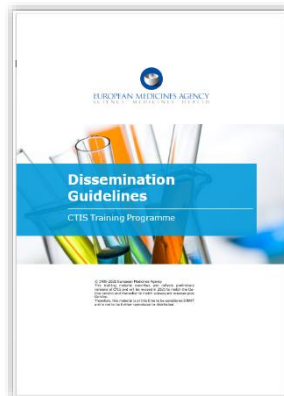## Annex

eLearning presentation
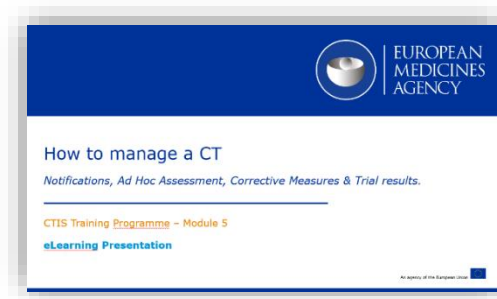
Quick guide

FAQs

Video-clips

Dissemination guidelines

Notifications activity

Read carefully the cases and solutions described in the table below regarding Notifications. Your task will be to identify which solution best matches the task to be performed by a sponsor in each case, or the effect that such case will have on the Clinical Trial (CT).

Case ID	Case description	Solution ID	Solution description
1	The sponsor Medicalical Pharmaceuticals is performing a CT with Paracetamol. For **reasons that will not have an impact** on subject safety and/or benefit-risk balance, they need to create a temporary halt notification to inform the MSC regarding the CT status. **Let's consider that the CT will be resumed within 2 years, what will happen?**	A	The trial will end after 2 years, unless the sponsor **submits a substantial modification (SM)** application, selecting the reason "extension to start trial recruitment beyond 2 years", and that **SM is authorised before the end of the initial 2-yearperiod**.
2	The sponsor Romstel Pharmaceuticals is performing a CT with Salbutamol. For **reasons that will not have an impact** on subject safety and/or benefit-risk balance, they need to create a temporary halt notification to inform the MSC regarding the CT status. **Let's consider that the CT will not be resumed within 2 years, what will happen?**	B	The trial will end after 2 years, unless the sponsor **submits a substantial modification** application **before the end of the 2-year period**, selecting the reason "extension to restart trial beyond 2 years". After the SM is authorised by the MSC, the sponsor can restart the trial also beyond the initial 2-year period.
3	The sponsor Sainz Pharmaceuticals is performing a CT with Amylinx. For **reasons that will have an impact** on subject safety and/or benefit-risk balance, they need to create a temporary halt notification to inform the MSC regarding the CT status. **Let's consider that the CT will not be resumed within 2 years, what will happen?**	C	The **sponsor must submit a substantial modification** application, selecting the reason "restart trial". After the SM has been authorised by the MSC, **the sponsor can restart the trial.**
4	The sponsor Alfabetha Pharmaceuticals is performing a CT with Acetanilide. For **reasons that will have an impact** on subject safety and/or benefit-risk balance, they need to create a temporary halt notification to the MSC regarding the CT status. **Let's consider that the CT will be resumed within 2 years, what will happen?**	D	The **sponsor cannot submit a substantial modification,** as the CT is deemed as ended. The sponsor can submit a new CTA.
5	The sponsor Ioxiox Pharmaceuticals has an **authorised CT** to be performed with Benzylpenicillin. Let's consider that for corporate reasons, **the sponsor will not start the recruitment of subjects within 2 years from its authorisation, what will happen?**	E	The **CT can be restarted.** The **sponsor does not have to submit a substantial modification** application.

Clinical Trials Information System

Solution table

Please indicate your answers in the solution ID column.

Case ID	Solution ID
1	
2	
3	
4	
5	

Clinical Trials Information System (CTIS)

Instructor's guide: How to search, view and download a CT and a CTA (Authority).