EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Instructor's Guide:

How to evaluate a clinical trial application

CTIS Training Programme – Module 06

Version 1.2 – January 2022

What you will find

- Overview of the audiences targeted in training module 06.
- Overview of the training materials included in this module.
- Guidelines to disseminate the knowledge.
- Recommendations on how to prepare and develop the training.

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.

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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(s) in your Member State or organisation.

More specifically, this guide is focused on the **sixth Module of the CTIS Training Programme** (hereafter referred to as 'CTTM06'). This module provides a general introduction to the evaluation process of a clinical trial application and the types of applications foreseen in Regulation (EU) No 536/2014 (CT Regulation). In addition, this module presents in detail the two first steps of this process, which include the selection of the Reporting Member State (RMS) and the Validation phase. **This guide provides** an overview of the audiences targeted with CTTM06, 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.

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Course elements

Target audiences

CTTM06 targets **authority users**, including Member States' national competent authorities and Member States' ethics committees.

CTTM06 learning objectives

The learning objectives of CTTM06 are:

- Understand the different types of Clinical Trial Applications (CTAs).
- Understand the evaluation process of a CTA and the common aspects of the different types of CTAs.
- Understand the RMS selection process for a multinational initial CTA.
- Understand the validation phase for an initial CTA.

Materials available

- **CTTM06 eLearning presentation:** One interactive presentation to familiarise users with the main types of CTAs, the process of evaluation, with a focus on the process of RMS selection and the process of validation of an initial CTA.
- **CTTM06 Step-by-step guide:** Short step by step document of the basic processes described in the module.
- **CTTM06 video-clips:** Three video clips providing a practical demonstration of the RMS selection process and the validation (with RFI) phase:
    - **Clip 1**: The RMS selection process (5 minutes 16 seconds).
    - **Clip 2**: Validation phase: How MSCs can raise their considerations and how the RMS consolidates those (5 minutes 24 seconds).
    - **Clip 3**: Validation phase: How RMS creates RFIs associated to the MSCs considerations, how RFI responses are assessed, and how RMS issues the validation decision (3 minutes 10 seconds).
- **CTTM06 Frequently Asked Questions (FAQs):** List of common questions and answers regarding the contents covered in this module.

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Course preparation

To ensure that the learning objectives of CTTM06 are met and that the training materials of CTTM06 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 propose you to **share the relevant CTTM06 eLearning presentation** 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 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. You may choose to adapt it to your needs and preferences.

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 eLearning presentation. 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** to the training participants one week in advance. Remind them in the email how much time it will take them approximately to complete the material, 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 applications and the principles and processes for assessment. Concretely, we recommend you to read at least the following articles, which are related to aspects covered in this module:
    - Article 2 (Definitions).
    - Article 3 (General principle for conducting CTs).
    - Article 5 (Submission of an application, validation of an initial application and selection of RMS).
    - Article 6 (Assessment report — Aspects covered by Part I). See in particular paragraph 5 on Multinational applications and phases included in the assessment process.
    - Article 7 (Assessment report – Aspects covered by Part II).
    - Articles 14 (Subsequent addition of a Member State concerned).
    - Chapter III (Authorisation procedure for a Substantial Modification of a CT).
    - Article 25 (Data submitted in the application dossier).
    - Article 44 (Assessment by Member States).
    - Annex I (Application dossier for the initial application).
    - Annex II (Application dossier for substantial modification).
    - We also recommend you take a look at the latest version of the European Commission's Clinical Trials Regulation Q&A,[2] concretely sections 2 (measures related to the application procedure) and 3 (substantial modifications).

  Additionally, it is also advised to take a look at Regulation 1182/71 of the Council determining the rules applicable to periods, dates, and time limits[3] to understand how deadlines established in the CT Regulation are calculated in practice in the system.

- **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] 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 L 158/1. 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

I Regulation (EEC, EURATOM) No 1182/71 of the Council of 3 June 1971 determining the rules applicable to periods, dates and time limits, *Official Journal of the European Communities*, No L 124/1. Available at:https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31971R1182&from=EN

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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: CTTM06 eLearning presentation

Objective:

This activity consists in the completion by participants of the CTTM06 eLearning presentation. 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 presentation at their own pace and identify questions that are not clear to them.

Steps:

1. Send the eLearning presentation to the participants and ask them to complete it by a given date.

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: CTTM06 eLearning presentation, CTTM06 video-clips, CTTM06 FAQs, CTTM06 Step-by-step guide, 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 CTTM06 eLearning presentation.
- Present the additional materials for the CTTM06, with a focus on the RMS selection and validation processes.
- Answer any questions regarding the content of the CTTM06/
- Receive feedback regarding the learning materials and the training delivery methodology.

We propose to structure this activity in eight 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.
    b. Explain the aim of the webinar and briefly describe 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 material reviewed and interactive knowledge check (*approximately 25 minutes*).
    a. Ask if participants have any questions regarding the CTTM06 eLearning presentation.
    b. As an 'icebreaker', launch an online quiz to check if participants understood the key concepts from the eLearning presentation for CTTM06. Make sure to explain how the tool works and allow at least a test question before starting the quiz.
3. **Part 3:** Screening of CTTM06 video-clips (*approximately 30 minutes*).
    a. Make a brief introduction of the CTTM06 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. proposed RMS, assignor, workshare, candidate RMS, RFI, considerations, etc.). 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. RMS selection

scenarios).

b. Display each CTTM06 video-clip at the webinar. For the RMS selection, you can user the Step-by-step guide to review possible scenarios.

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:** RMS selection role-play exercise (*approximately 25 minutes).*

   a. Divide the group into sub-groups of 5 people (*use break rooms within the webinar if allowed by the online tool chosen, or suggest that the group organises an internal chat among the sub-group members).*

   b. Provide them with the role cards prepared and explain the exercise. There is a case description and four possible scenarios. Make sure each group gets a different scenario (*please refer to the exercise document in Annex of this document for more information*).

   c. Screen the exercise explanation on the webinar main screen.

   d. Give them 25 minutes to complete the exercise and ask them to nominate a reporter to represent the group.

   e. Support them whenever necessary.

   ➢ *Key for the instructor:*

      - ***Scenario 1:*** *If the assignor does not choose any candidate from the pool of MSC willing, the proposed RMS will become the RMS.*

      - ***Scenario 2:*** *If MSCs agree with the candidate RMS proposed by the assignor, then the candidate becomes the RMS.*

      - ***Scenario 3:*** *If an MSC issues a disagreement with the candidate RMS, the proposed RMS will become the RMS. The MSC who disagrees needs to provide a justification for this.*

      - ***Scenario 4:*** *If several or all MSC issue a disagreement with the candidate RMS, the proposed RMS will become the RMS. The MSCs who disagree need to provide a justification for this.*

5. **Part 5:** Role play exercise solutions (*approximately 20 minutes*).

   a. Invite the reporter from each group to present their scenario and summarise their solution before the others in maximum 5 minutes. This will allow each participant to learn about other possible scenarios.

6. **Part 6:** Questions and answers (*approximately 15 minutes*).

    a. Give some time to the participants to think and pose 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 CTTM06 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.*

7. **Part 7:** 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.*

8. **Part 8:** 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.

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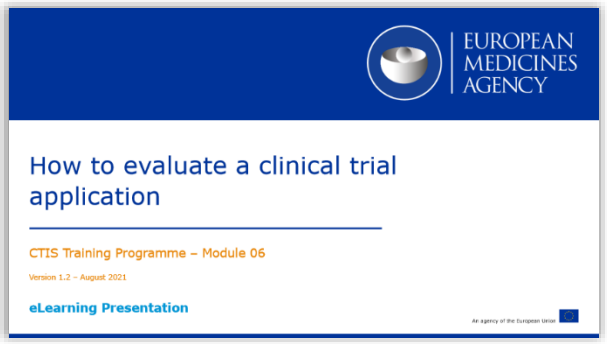
Annex

eLearning presentation

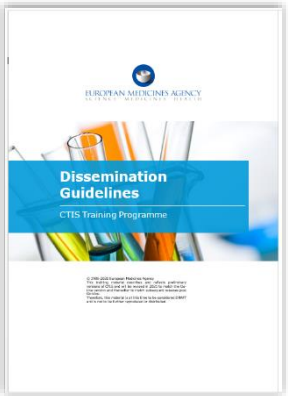


FAQs

Video-clips

Step-by-step guide

Dissemination guidelines



Role-play exercise

Case description

The company Sainz Pharmaceuticals has submitted an initial application for a clinical trial to Austria, Germany, Belgium, the Netherlands, and France to perform clinical trials with Amylinx in those countries. Sainz Pharmaceuticals has established that the proposed Reporting Member State (RMS) should be Germany, where 35% of the potential patients of the clinical trials are based.

Three days after the application dossier has been submitted, all MSCs, including Germany, are willing to become the RMS (i.e. have expressed their willingness to become the RMS by day 3 from the application submission).

Exercise

Perform the steps of the RMS selection process until the RMS is selected to solve the existing tie. Each of you has a justification to become the RMS (you will need to come up with it and present it during the discussion). Remember, you only have 3 days left (25 minutes) to agree on the RMS.

There are four possible scenarios (the Instructor will assign one to each group):

SCENARIO 1:

1. *Designate the Assignor (in CTIS, the assignor will be automatically selected by the system. The assignor will be the willing MSC with the lowest workshare. To identify the lowest workshare the following formula is applied: number of multinational CT where the MS acts as RMS/total of number of multinational CT where the MS participates *100). You need to figure out who would be the Assignor based on the information provided in your role cards.*

2. *Discuss among the MSCs who should become RMS. Each MSC has to expose its justifications.*

3. *By day 6 since the application submission, the Assignor has not chosen any candidate out of the pool of MSC who are willing. Please indicate the consequences of this inactivity.*

SCENARIO 2:

1. *Designate the Assignor (in CTIS, the assignor will be automatically selected by the system. The assignor will be the willing MSC with the lowest workshare). You need to figure out who would be the Assignor based on the information provided in your role cards.*

2. *Discuss among the MSCs who should become RMS. Each MSC has to expose its justifications.*

3. *The assignor selects a candidate RMS after the discussion, taking into account the discussion among the MSC.*

4. *MSCs agree to the candidate RMS indicated by the Assignor. Please indicate the consequences of this scenario in terms of who will be the RMS.*

SCENARIO 3:

1. *Designate the Assignor (in CTIS, the assignor will be automatically selected by the system. The assignor will be the willing MSC with the lowest workshare). You need to figure out who would be the Assignor based on the information provided in your role cards.*

2. *Discuss among the MSCs who should become RMS. Each MSC has to expose its justifications.*

3. *The assignor selects a candidate RMS after the discussion, taking into account the discussion among the MSC.*

4. *One MSC issues a disagreement with the candidate RMS indicated by the Assignor. Please indicate the consequences of this scenario in terms of who will be the RMS.*

SCENARIO 4:

1. *Designate the Assignor (in CTIS, the assignor will be automatically selected by the system. The assignor will be the willing MSC with the lowest workshare). You need to figure out who would be the Assignor based on the information provided in your role cards.*

2. *Discuss among the MSCs who should become RMS. Each MSC has to expose its justifications.*

3. *The assignor selects a candidate RMS after the discussion, taking into account the discussion among the MSC.*

4. *Several or all MSC issue a disagreement with the candidate RMS indicated by the Assignor. Please indicate the consequences of this scenario in terms of who will be the RMS.*

Austria

Condition: Willing

Workshare: 68%

Status: MSC

Germany

Condition: Willing

Workshare: 83%

Status: MSC (proposed RMS)

Belgium

Condition: Willing

Workshare: 81%

Status: MSC

Netherlands

Condition: Willing

Workshare: 75%

Status: MSC

France

Condition: Willing

Workshare: 93%

Status: MSC

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Clinical trials information system (CTIS)

Instructor's guide: How to evaluate a CT application: Types of applications, evaluation process, RMS selection, and validation.