Step-by-step guide

How to evaluate an Additional MSC clinical trial application

CTIS Training Programme – Module 08
Version 1.0 – October 2021

Learning Objectives

• Understand the process involved in the Assessment of an Additional Member State Concerned Clinical Trial Application (Add MSC CTA).

• Remember the workload management functionalities in CTIS that allow users to monitor their tasks during the evaluation of an Add MSC CTA.

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Additional MSC CTA evaluation

An **Additional Member State Concerned Clinical Trial Application (Add MSC CTA)** is an application for extending a previously authorised Clinical Trial (CT) to the territory of another Member State(s). The subsequent addition of an MSC to a CT can be for both mononational and multinational trials.

The evaluation process of adding a subsequent MSC is established in Article 14 of the Regulation (EU) No 536/2014 on Clinical Trials (CT Regulation). This process includes an **assessment of Part II** and the **decision**, as there has already been a positive conclusion on part I.

The additional MSC will have access to Part I of the application and will be able to create considerations, which can lead the Reporting Member State (RMS) to raise a Request for Information (RFI). However, the assessment of the additional MSC on Part I will not change the decision made on this part of the application.

This Step-by-step guide includes:

1. **Evaluation of a Clinical Trial Application (CTA)**
   - This section outlines an overview of the evaluation of a clinical trial application process.

2. **Assessment of Add MSC CTA**
   - This section outlines the steps that the added MSC, to which the CTA has been extended, has to follow to evaluate the Part II of the CTA, and the specificities in case the added MSC wants to create considerations for Part I.

3. **Decision of Add MSC CTA**
   - This section outlines the steps that the added MSC, to which the CTA has been extended, has to follow to submit a decision regarding the Add MSC CTA (i.e. whether the trial is ‘Authorised’, ‘Authorised with conditions’, or ‘Not authorised’).
The evaluation process starts **once the sponsor has submitted an initial Clinical Trial Application (CTA)**. The MSCs can **evaluate the documentation** provided by the sponsor to ensure the compliance with the CT Regulation. The evaluation is performed for the following types of CTAs: **Initial CTA**, **Substantial Modification (SM)** and **Additional MSC CTA (Add MSC)**.

### EVALUATION OF A CLINICAL TRIAL APPLICATION

**Initial CTA**
- RMS selection
- Validation
- Assess Part I
- Assess Part II*
- Decision

**Substantial Modification CTA**
- Validation
- Assess Part I
- And/or
- Assess Part II
- Decision

**Additional MSC CTA**
- Assess Part I
- Assess Part II
- Decision

*The MSC has 52 days to complete the evaluation + 31 days if requests for information are raised.*

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**Focus of this document.**

- Content included in module 06 eLearning | Step-by-step guide RMS selection.
- Content included in module 08 Quick guide | Step-by-step guide SM | Step-by-step guide Add MSC.

**Step in the process that may occur depending on the CTA submitted.** An SM CTA can include Part I and Part II, Part I only or Part II only. For an Add MSC CTA users may raise considerations for Part I, but the conclusion cannot be modified.

*In case of applications limited to Part I, the sponsor has two years from the notification of the conclusion of Part I to submit an application limited to Part II.*
1. Similar to other types of CTAs, the subsequently added MSC receives a notice informing that an Add MSC CTA has been submitted. Users can access the tasks through the notice received, the ‘Task’ tab or the evaluation section.

2. On the ‘Tasks’ tab, added MSCs will receive a series of tasks related to the assessment. MSCs can start by assigning the “Document Considerations” tasks.

3. Users perform the evaluation of the Add MSC CTA in the ‘Evaluation’ section of the CTA; regardless of the way they accessed the application (i.e. via ‘Notice & alert’ or ‘Task’ tabs).

The evaluation of an Add MSC CTA mainly consists in the assessment of the Part II of the CTA by the MSC to which the CTA is being extended to. The additional MSC can create considerations regarding Part I. However, the assessment of the additional MSC on Part I will not change the conclusion on Part I.
Assess Part I: create considerations

1. To create considerations regarding the Part I of an Add MSC CTA, the added MSC can access the ‘Tasks’ tab. Then, click on the ‘Assign to me’ button from the ‘Document Considerations Additional MSC’ task to go to the CTA Evaluation section.

2. The added MSC can review the Part I documentation (e.g. Translations) and add considerations on the conclusion from the application, including Part I, by clicking on the ‘+ New’ button, filling in the pop-up form, and clicking on the ‘Save’ button.

3. Then, users can select the considerations created with the checkbox, and share the consideration(s) with the other MSC(s) using the ‘Share’ button. The assessment of the additional MSC on Part I will not change the conclusion on Part I.

Only the RMS will be able to consolidate the considerations created by the additional MSC on Part I.

The assessment of the additional MSC on Part I will not change the conclusion made on this part of the application.
Assess Part II: create considerations

1. Users can start the assessment of the Add MSC CTA by completing the task to create considerations assigned to them. They can click on the task to access the ‘Evaluation’ section.

Considerations are comments/corrections or questions that the additional MSCs may have while reviewing the regulatory documentation of the CTA.

2. MSCs can create considerations regarding the Add MSC CTA (e.g. Part II) by clicking on the ‘+ New’ button, filling in the pop-up form, and clicking on the ‘Save’ button.

MSCs can edit a consideration that has not been shared.

3. Then, users can select the considerations created with the checkbox, and share the consideration(s) using the ‘Share’ button. The process to create and share considerations is the same for the Part I of the CTA.

After the considerations have been shared, they need to be consolidated by the added MSC. The consolidated considerations are the basis of the RFI.

#CTIS insights
4. To consolidate considerations, the added MSC can access the ‘Tasks’ tab and select the ‘Assign to me’ button from the ‘Consolidate considerations’ task. Users can click on it to access the ‘Evaluation’ section.

5. The added MSC can select the considerations via the checkbox, and click one of the four buttons to consolidate them (i.e. ‘Not Included’, ‘Adapt’, ‘Merge’, ‘Accept’).

6. Users can view the results of the consolidation on the ‘Consolidated considerations’ sub-tab.

7. On the ‘Consolidated considerations’ sub-tab, the added MSC can share the consolidated considerations.

The purpose of consolidating considerations is to ensure that all the relevant information is included, by using the four functionalities (‘Not Included’, ‘Adapt’, ‘Merge’, ‘Accept’) to avoid repetition and duplicate considerations, or to clarify some descriptions.
1. After reviewing the considerations, **the newly added MSC can create a Request For Information (RFI)** to the sponsor. To do so, users can click on the checkboxes of the related considerations and on the ‘+ Create RFI’ button.

2. Then the added MSC can populate the pop-up window establishing the **due date**, uploading **supporting document**, selecting the **considerations**, and clicking on the ‘Submit’ button. Once the RFI is submitted, users can view it in the ‘Evaluation’ section.

3. The added MSC can assess the response to the RFI submitted by the sponsor by selecting the ‘Response to RFI Submitted’ alert or the ‘Assess RFI response’ task and the **assign to me** button. This will redirect the MSC to the dedicated RFI section of the evaluation on the application page.

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**#CTIS insights**

After reviewing and consolidating all the considerations, if there is an error in the CTA documentation, as there is no validation step, **the newly added MSC can send a request for information** for the sponsor to clarify or correct based on the considerations.
Assess RFI response

1. MSCs can open the RFI and **scroll down to review the details**. Then, they can **share assessment comments** at the end of the RFI.

Submit Part II conclusion

1. On the **Tasks** tab, users can assign the **Submit Part II Conclusion** task.

2. On the **evaluation page**, MSCs can click on the **padlock** button to be able to upload the **assessment report**.
3. The added MSCs can click on the ‘Add document’ button to add a Draft (as applicable) and Final Assessment Report documents.

Below, users can share comments to generate a discussion within the MSC regarding the assessment reports of the CTA. To do so, they can type a comment on the text field and click on the ‘Share comment’ button.

5. Then, MSCs can select the final conclusion out of the drop-down list, among the options: ‘Acceptable’, ‘Acceptable with conditions’, or ‘Not acceptable’ and click on the ‘Submit’ button. Finally, they can click on the ‘Confirm’ button.

The Final Assessment Report is the final assessment of the regulatory documentation of the application dossier for Part II. The MSC can engage in an internal discussion regarding the Assessment Report and the conclusion of Part II by sharing comments on the section Discussion within the MSC.
1. After the final assessment report has been submitted and Part II assessment has been concluded, MSCs can access ‘Tasks’ tab and click on the ‘Assign to me’ button from the ‘Authorise’ task. So that a decision on the authorisation of the CT can be issued by the added MSC.

2. On the Decision page, via a drop-down list, users are able to select whether the trial is ‘Authorised’, ‘Authorised with conditions’, or ‘Not authorised’.

3. Finally, users can add supporting documentation to the decision and can click on the ‘Complete’ and ‘Confirm’ buttons.

The added MSC can decide on the deferral of the Assessment report Part II set by the sponsor.

#CTIS insights

The decision consists of the notification to the sponsor of the authorisation, the authorisation with conditions, or the refusal to conduct a given trial. If the decision outcome is ‘authorised with conditions’, the MSC must indicate the conditions.
Clinical Trials Information System (CTIS)
Step-by-step guide: How to evaluate an Additional MSC clinical trial application: Assessment and Decision