Quick guide
How to evaluate a Clinical Trial Application: Assessment and Decision

CTIS Training Programme – Module 08
Version 1.2 – December 2021

Learning Objectives

• Remember the phases and associated timelines for evaluating an initial Clinical trial application (CTA).
• Understand the process and the user roles involved in the Assessment of Part I of an initial CTA as a Reporting Member State (RMS) and as a Member State Concerned (MSC).
• Understand the process and the user roles involved in the Assessment of Part II of an initial CTA as a MSC.
• Understand the process and the user roles involved in the Decision regarding the authorisation of an initial CTA.
• Remember the workload management functionalities in CTIS that allow users to monitor their tasks during the evaluation of an initial CTA.
Overview of Assessment Part II

The assessment of Part II consists in the evaluation of the application by each MSC, for its territory, regarding the following aspects set out in Article 7 of the CT Regulation¹ and the General Data Protection Regulation²:

- Requirements for gathering the informed consent of the subjects.
- Arrangements for rewarding or compensating subjects and investigators.
- Arrangements for the recruitment of subjects.
- Protection of personal data.
- Suitability of individuals involved.
- Suitability of clinical trial sites.
- Damage compensation.
- Collection, storage, and future use of biological samples of the subject.

These aspects are to be reflected in the documents of the application dossier, which are evaluated as part of the Assessment of Part II (see figure on the right).

The sponsor can submit a partial application dossier including only Part I to launch the evaluation process, and may leave the submission of Part II for a later stage. However, if the sponsor does not submit Part II to an MSC within two years after the notification of the conclusion of Part I, the application will lapse.

If Part II is submitted to an MSC, that MSC shall complete its assessment and submit, through CTIS, an assessment report for Part II, including its conclusion, to the sponsor.

Timelines

The assessment of Part II can run in parallel to the assessment of Part I and can take up to 45 days, and up to 76 days if RFIs are submitted (from the validation of the Initial CTA).

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² Regulation (EU) 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, EU Official Journal, L 119/1. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679&from=EN
The main dates shown in the figure above (see Annex) correspond to the evaluation of an initial CTA. If the tasks are completed earlier, the maximum timeframes between the end of a task and the end of the subsequent one will be respected, but the overall deadlines will be recalculated.

The maximum deadlines foreseen for the tasks related to the assessment of Part II are:

- For hard tasks (mandatory tasks):
  - Submit Final Assessment Report Part II and conclusion Part II – up to 45 days or 76 days (if RFIs are raised), from the Validation of the initial CTA. *Performed by the RMS.*

- For soft tasks (non-mandatory tasks):
  - Document considerations (application documents) – up to 45 days from the Validation of the initial CTA.
  - Consolidate considerations – up to 45 days after the validation of the initial CTA. *This task must be performed right after the considerations have been documented and before submitting an RFI to the sponsor.*
  - Submit RFI (if applicable) – up to 45 days from the validation of the Initial CTA. *This task will be performed after the considerations have been consolidated.*
  - Assess RFI response (if applicable) – up to 19 days after the response is sent by the sponsor.

### Process to assess Part II

The assessment of Part II starts after the Validation has been submitted by the RMS, and can be performed in parallel to the assessment of Part I. The process is very similar to the one for Part I, but it is performed individually by each MSC. The MSC will receive the following notice:

<table>
<thead>
<tr>
<th>Referencenumber</th>
<th>Evaluationprocess</th>
<th>Received</th>
<th>IMP</th>
<th>RMS</th>
<th>Sponsor</th>
<th>Textorganisationname</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020-500376-29-00</td>
<td>Validation</td>
<td>16/10/2020</td>
<td>Paracetamol</td>
<td>Austria</td>
<td>Test Organisation Demo</td>
<td></td>
</tr>
</tbody>
</table>

The validation conclusion of Valid has been recorded for the 2020-500376-29-00 Initial application.

From the moment the application has been validated, each MSCs can document their considerations for Part II of the application dossier.

To perform this task MSC users with appropriate permissions (*see section Roles and Permissions*) need to follow these steps:

1. Access the Tasks tab and click on the ‘Document Considerations Assess Part II’ task. The task can be assigned to him/her by a CT Coordinator or if the user has the appropriate role, the user can select ‘Assign to myself’.
2. The system will redirect them to the relevant Evaluation section where they can document considerations.

3. Select the ‘+ New’ button and fill in the pop-up form.

4. Select the application section (see figure 1, page 1) and document in which they have the consideration. Describe the consideration in the form of free text and finally click on ‘Save’.

5. After saving the consideration the user can still work on it and edit it as needed. For Part II, all MSC users with the appropriate permissions can view draft considerations. They are shared to indicate it is ‘finished’.

After the considerations have been shared, they need to be consolidated by the submitter or preparer role (see section Roles and Permissions). This task must be completed by day 45 from the validation of the initial application, in order to be able to raise an RFI.

To perform this task MSC users with appropriate permissions need to follow these steps:

1. Access the Tasks tab and click on the ‘Consolidate Considerations’ task. The task can be assigned to him/her by a CT Coordinator or if the user has the appropriate role, the user can select ‘Assign to myself’.

2. The system will redirect the user automatically to the relevant Evaluation section where the document considerations are stored.

3. To consolidate the considerations, the MSC should first select the considerations via the checkbox on the left of each of them.
4. Select one of the four following buttons:

- **Not included**: allows the user to reject a consideration deemed not applicable.
- **Adapt**: allows the user to adapt a consideration shared by a MSC. In this case, the MSC must include the final wording of the consideration.
- **Merge**: allows the user to merge similar or identical considerations. In this case, the MSC must include the final wording of the consideration.
- **Accept**: allows the user to accept a specific consideration as it is.

5. View the result by clicking on the tab ‘Consolidated considerations’.

After reviewing and consolidating all the considerations, if the MSC deems that certain information from the application is missing, or that a document needs clarification, the MSC can **raise an RFI** to the sponsor.

To perform this task MSC users with appropriate permissions (see section Roles and Permissions) need to follow these steps:

1. Create an RFI by selecting the relevant considerations and click on the button ‘+Create an RFI’ on the top-right corner of the consolidated considerations section.

2. Establish the date by which the RFI response should be provided (a maximum period of 12 days can be selected).

3. MSC can assess the response to the RFI submitted by the sponsor by selecting the alert ‘Response to RFI Submitted’ or the task ‘Assess response to RFI’. This will redirect the MSC to the dedicated RFI section of the evaluation on the application page. There the MSC can assess the response and submit comments.

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3 The process of assessing a response to an RFI is similar in all phases of the evaluation. To view how this task is performed please refer to video-clip CTTM06_Clip 3\_Validation - RFI and issue validation decision in Module 6.
After the RFI has been assessed, each MSC needs to submit the **Part II Final Assessment Report (FAR) and Part II conclusion**.

To perform this task MSC users with appropriate permissions (see section Roles and Permissions) need to follow these steps:

1. **Access the Tasks tab and click on the ‘Submit Part II Conclusion’ task.** The task can be assigned to him/her by a CT Coordinator or if the user has the appropriate role, the user can select ‘Assign to myself’.

2. **Once in the Evaluation section of the assessment of Part II corresponding to the Conclusion, the MSC needs to upload the Part II FAR.**

3. **MSC users can discuss amongst themselves before submitting the Part II FAR and conclusion, by using a discussion functionality.**

4. **Select the conclusion in the drop-down menu among the options: ‘acceptable’, ‘acceptable with conditions’, or ‘not acceptable’**.

"Assess a clinical trial application (RMS selection and Validation)."
Roles and permissions

Two roles are involved in the Assessment of Part II: Assessor Part II preparer and Assessor Part II submitter. Both take part in all the tasks related to the Assessment of Part II, except for the following two: send an RFI and submit the Final assessment report and conclusion of Part II. These tasks can only be performed by the Assessor Part II Submitter.

Assessment Part II - Roles

There are two roles in each MSC that take part in the Assessment of Part II of the application dossier:
1) Assessor Part II Preparer.
2) Assessor Part II Submitter.

#CTIS insights

Since Part II is assessed individually by each MSC, the DAR cannot be circulated with other MSC and hence no task is displayed in the Tasks tab, as opposed to Part I. However, it is important that each MSC creates the DAR and discusses it among the users of that MSC, before raising considerations on the Part II documentation of the application.
Assessment Part II

- Initial application with Part I and Part II or Part I (only) validated
- Day 26: Circulate draft assessment Part I report
- Day 38: Consolidate considerations
- Day 45: Submit RFI
- Day 69: Assess RFI response
- Day 76: Submit Final Assessment Report Part I and conclusion Part I

MSC:
- Document Considerations: DAR must be circulated by day 26
- Circulate draft assessment Part I report
- Functionality and task trigger once a consideration has been shared
- Functionality and task trigger once an accepted, adopted or merged consideration has been shared

RMS:
- Triggered once a Part I application has been validated

Due date: Sponsor response date + 12 days (up to Day 69) for the MSC and + 19 days (up to Day 76) for the RMS
Clinical Trials Information System (CTIS).
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