Learning Objectives

- Understand the Reporting Member State (RMS) selection process for a multinational CTA.
Selection of the Reporting Member State

The main purpose of the Reporting Member State (RMS) selection process is to select a Member State Concerned (MSC) for the trial life cycle that will play a leading role during the evaluation. The RMS leads the evaluation, raises and consolidates considerations during the validation and Part I assessment phases, and issues the conclusion on part I.

There are two main actors involved in the RMS selection process:

- **Sponsors:** Propose an MSC to be the RMS in the application dossier.
- **MSCs:** Express willingness/unwillingness to become the RMS and discuss amongst them which MSC should be the RMS.

In the case of multinational trials, the RMS is proposed by the sponsor at the time of submission of an initial application dossier and is finally assigned to an MSC after the completion of the RMS selection tasks by all MSCs. In a mononational trial, the RMS is assigned to the only MSC selected by the sponsor in the application.

The RMS selection process **is triggered as soon as the initial application dossier is submitted** by the sponsor. This process runs in parallel to the validation phase. However, an RMS needs to be selected to be able to complete this phase, as the RMS is responsible for consolidating the considerations made by the MSCs and submitting the validation conclusion. The selection of the RMS can occur within **6 days after the submission** of the application dossier by the sponsor, in line with Article 5(1) of the Regulation (EU) No 536/2014 on Clinical Trials (CT Regulation).

This step-by-step guide outlines the different scenarios within the RMS selection process and examples of possible scenarios.
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).

**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 rise considerations.

*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.*
RMS selection overview

The different scenarios within the RMS selection process for multinational and mononational clinical trials are shown below:

### RMS selection Mononational clinical trials

The MSC is appointed RMS

### RMS selection Multinational clinical trials

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>RMS Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Express Willingness/Unwillingness" /> 1 MSC express Willingness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RMS</td>
</tr>
<tr>
<td><img src="image" alt="Express Willingness/Unwillingness" /> &gt;1 MSCs express Willingness</td>
<td><img src="image" alt="Agree RMS" /> 2.1. Assignor selects a candidate RMS (pool of willing)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RMS</td>
</tr>
<tr>
<td><img src="image" alt="Express Willingness/Unwillingness" /> 0 MSC express Willingness</td>
<td><img src="image" alt="Agree RMS" /> 3.1. MSCs re-express willingness</td>
<td><img src="image" alt="Re-express Willingness/Unwillingness and agree RMS" /></td>
<td></td>
<td></td>
<td></td>
<td>RMS</td>
</tr>
<tr>
<td><img src="image" alt="Express Willingness/Unwillingness" /> 0 MSC express Willingness</td>
<td><img src="image" alt="Agree RMS" /> 2.2. MSCs issue a disagreement (page 5,6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RMS</td>
</tr>
<tr>
<td><img src="image" alt="Express Willingness/Unwillingness" /> 0 MSC express Willingness</td>
<td><img src="image" alt="Agree RMS" /> 3.2. Assignor selects a candidate RMS (page 9, 10, 11)</td>
<td><img src="image" alt="Re-express Willingness/Unwillingness and agree RMS" /></td>
<td></td>
<td></td>
<td></td>
<td>RMS</td>
</tr>
<tr>
<td><img src="image" alt="Express Willingness/Unwillingness" /> 0 MSC express Willingness</td>
<td><img src="image" alt="Agree RMS" /> 3.3. MSCs issue a disagreement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RMS</td>
</tr>
<tr>
<td><img src="image" alt="Express Willingness/Unwillingness" /> 0 MSC express Willingness</td>
<td><img src="image" alt="Agree RMS" /> 3.4. Assignor doesn’t select a candidate RMS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RMS</td>
</tr>
</tbody>
</table>

Legend:
- **Tasks**
- **RMS** Willing RMS
- **RMS** Candidate RMS
- **RMS** Sponsor proposed RMS
Scenario 2.2: Issue disagreement with the candidate RMS

Example of an RMS selection process with 3 MSCs (Austria, Germany, and Greece).

1. All MSCs can view the 'Express Willingness/Unwillingness' task in the 'Task' tab by entering the EU CT ID or using the 'Advance search'. Then, they can assign the task to users, using the appropriate button on the right side of the task.

2. Once in the Express willingness page, all MSCs can click on the blue 'Pending' label to express willingness or unwillingness.

3. The MSCs can select one of the radio buttons 'Willing' or 'Unwilling' and then they can select the 'Share' button in order to enable the 'Complete' button. Once the task is completed, it will be visible for the other MSCs. In this example there are 2 willing MSCs and 1 unwilling MSC.

In case an MSC (including the Proposed RMS) does not express willingness or unwillingness in the system, the default value at the end of day 3 will be set for as 'Unwilling'.

If the proposed RMS selects 'Unwilling' a justification must be included.

If more than one MSC are simultaneously working on the same process, they will have to refresh the page to see the latest updates.
### RMS selection scenarios

#### Scenario 2.2: Issue disagreement with the candidate RMS

4. If by the end of day 3 or earlier there is more than one MSC willing to be the RMS, the MSC with the lowest workshare out of those willing to be the RMS will become the **assignor**.

<table>
<thead>
<tr>
<th>MSC</th>
<th>Willing at end of day 3</th>
<th>Justification</th>
<th>Number of trials (MSC)</th>
<th>Number of trials (RMS)</th>
<th>Workshare % (YTD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GERMANY</td>
<td>willing</td>
<td>-</td>
<td>206</td>
<td>110</td>
<td>53.396 %</td>
</tr>
<tr>
<td>GREECE</td>
<td>unwilling</td>
<td>-</td>
<td>365</td>
<td>78</td>
<td>21.370 %</td>
</tr>
<tr>
<td>AUSTRIA</td>
<td>proposed RMS</td>
<td>-</td>
<td>90</td>
<td>57</td>
<td>63.333 %</td>
</tr>
</tbody>
</table>

5. The MSCs can find the ‘Agree RMS’ task available on the ‘Tasks’ tab and assign it to a user.

6. The MSCs are encouraged to express their comments prior to the election of the candidate RMS in the ‘Discussion with MSCs’ section and then they can click on the ‘Share comment’ button.

7. The assignor (i.e. Germany) can **select the candidate RMS** among the willing MSCs. *In this example, the assignor has selected Germany as the candidate RMS.*

8. The users can **disagree with the candidate RMS** selected by the assignor by including a justification and clicking on the ‘Issue disagreement’ button.

9. If there is a disagreement on the choice of the candidate RMS, the **proposed RMS** (i.e. Austria) **will become the RMS**.

#CTIS insights

If the MSCs (including the candidate RMS) do **not express their agreement/disagreement,** the candidate RMS selected by the assignor will be appointed.

The disagreement is **not possible before assignor has made an active selection.**

The assignor cannot issue disagreement with its own selection.
RMS selection scenarios

Scenario 2.3: Assignor doesn’t select a candidate RMS

Example of an RMS selection process with 3 MSCs (Austria, Germany and Greece).

1. All MSCs can view the ‘Express Willingness/Unwillingness’ task in the ‘Task’ tab by entering the EU CT ID or using the ‘Advance search’. Then, they can assign the task to users, using the appropriate button on the right side of the task.

2. Once in the Express willingness page, all MSCs can click on the blue ‘Pending’ label to express willingness or unwillingness.

3. The MSCs can select one of the radio buttons ‘Willing’ or ‘Unwilling’ and then they select the ‘Share’ button in order to enable the ‘Complete’ button. In this example there are 2 willing MSCs and 1 unwilling MSC.

In case an MSC (including the Proposed RMS) does not express willingness or unwillingness in the system, the default value at the end of day 3 will be set as ‘Unwilling’.
Scenario 2.3: Assignor doesn’t select a candidate RMS

4. If by the end of day 3 or earlier there is more than one MSC willing to be the RMS, the MSC with the lowest workshare out of those willing to be the RMS will become the assignor.

<table>
<thead>
<tr>
<th>MSC</th>
<th>MSC willing at end of day 3</th>
<th>Justification</th>
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<td>57</td>
<td>61.333 %</td>
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</table>

Assignor selected by the system

Proposed RMS by the sponsor

5. The MSCs can find the ‘Agree RMS’ task available on the ‘Tasks’ tab and then they can select the ‘Assign to me’ button.

6. The MSCs are encouraged to express their comments prior to the election of the candidate RMS in the ‘Discussion with MSCs’ section and then they can click on the ‘Share comment’ button.

7. If the assignor (i.e. Germany) does not select a candidate RMS among the willing MSC, the proposed RMS (i.e. Austria) will become the RMS at the end of day 6.
**Scenario 3.1:** Assignor selects a candidate RMS after MSCs re-express willingness/unwillingness

Example of how to re-express willingness or unwillingness and agree on the RMS with 3 MSCs (Austria, Germany and Greece).

1. All MSCs can view the ‘Express Willingness/Unwillingness’ task in the ‘Task’ tab by entering the EU CT ID or using the ‘Advance search’. Then, they can assign the task to users, using the appropriate button on the right side of the task.

2. Once in the Express willingness page, all MSCs can click on the blue ‘Pending’ label to express willingness or unwillingness. In this example, none of the MSCs express willing or unwilling.

3. If no MSC is willing to be the RMS by the end of day 3, all MSCs can re-express willingness or unwillingness until day 5. They can select the ‘Assign to me’ button on the right side of the ‘Re-express willingness/unwillingness and agree RMS’ task.

In case an MSC (including the Proposed RMS) **does not express willingness or unwillingness** in the system, the default value at the end of day 3 will be set as ‘Unwilling’.
Scenario 3.1: Assignor selects a candidate RMS after MSCs re-express willingness/unwillingness

4. Once in the re-express willingness/unwillingness and agree RMS page, all MSCs can click on the blue ‘Pending’ label to re-express willingness or unwillingness.

5. The MSCs can select one of the radio buttons ‘Willing’ or ‘Unwilling’ and then they can select the ‘Share’ button in order to enable the ‘Complete’ button. In this example there are 2 willing MSCs and 1 unwilling MSC.
**Scenario 3.1: Assignor selects a candidate RMS after MSCs re-express willingness/unwillingness**

6. If by the end of day 5 or earlier there is more than one MSC willing to be the RMS, the MSC with the lowest workshare out of those willing to be the RMS will become the assignor.

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7. The MSCs can find the ‘Agree RMS’ task available on the ‘Tasks’ tab and then they can assign the task to users, using the appropriate button on the right side of the task.

8. The MSCs can express their comments regarding the candidate RMS in the ‘Discussion with MSCs’ section.

9. Then the assignor (i.e. Germany) can select the candidate RMS among the willing MSC. In this example, the assignor has selected Germany as the candidate RMS.

10. If there isn’t a disagreement on the choice of the candidate RMS, the candidate RMS (i.e. Germany) will become the RMS at the end of day 6.
Clinical Trials Information System (CTIS)
Step-by-step guide: How to evaluate a CTA - RMS selection

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