



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Step-by-step guide

How to evaluate an Initial CTA - RMS selection

CTIS Training Programme – Module 06
Version 1.1 – November 2021

Learning Objectives

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

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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 withing the RMS selection process and examples of possible scenarios.



Evaluation of a Clinical Trial Application (CTA)

This section outlines an overview of the evaluation of a clinical trial application process.



RMS selection flowchart

This section outlines an overview of the RMS selection process for multinational and mononational clinical trials.



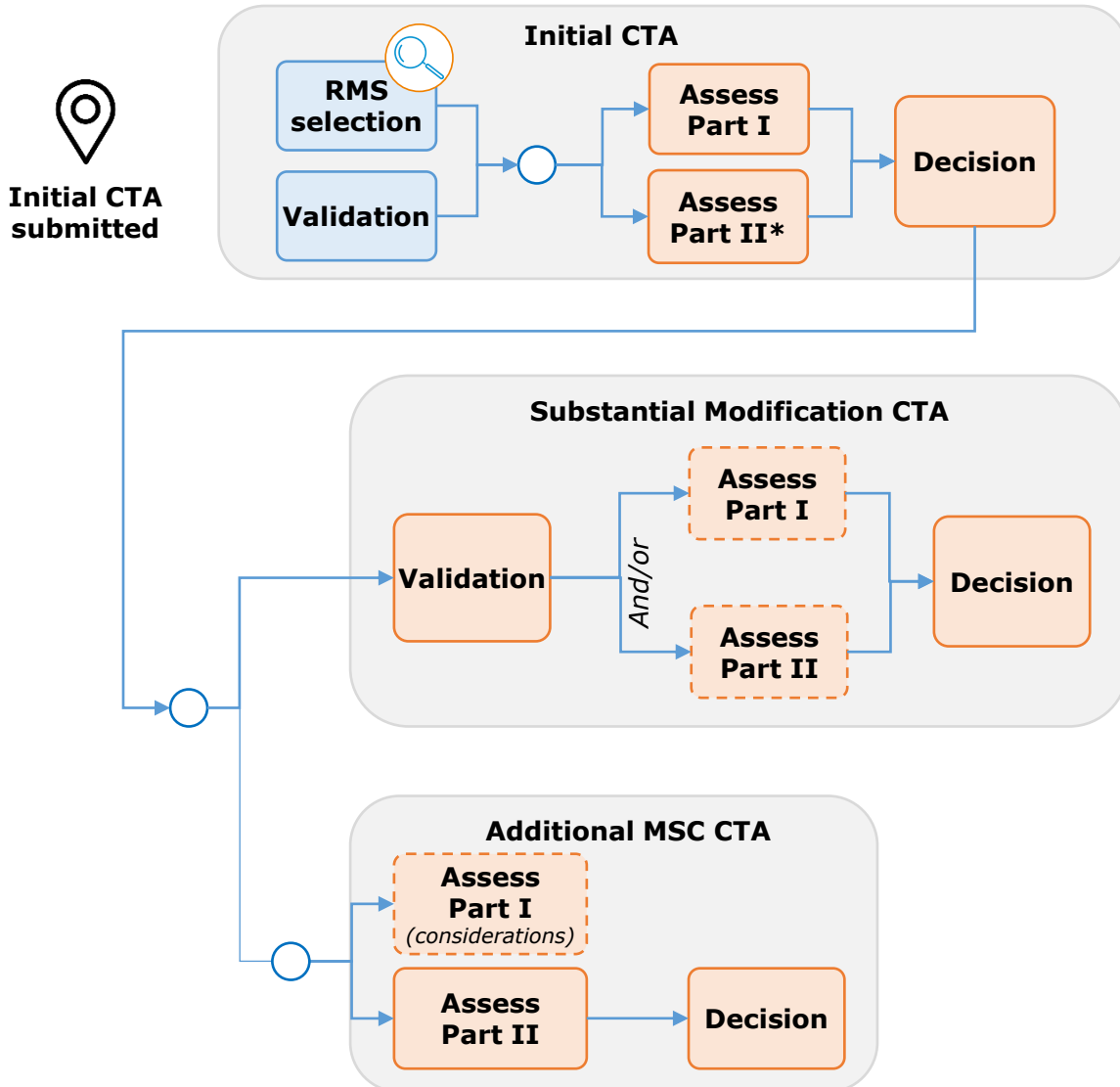
RMS selection scenarios

This section outlines the steps that MSCs should follow in some of the possible scenarios of the RMS selection process.

Evaluation of a CTA

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



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 flowchart

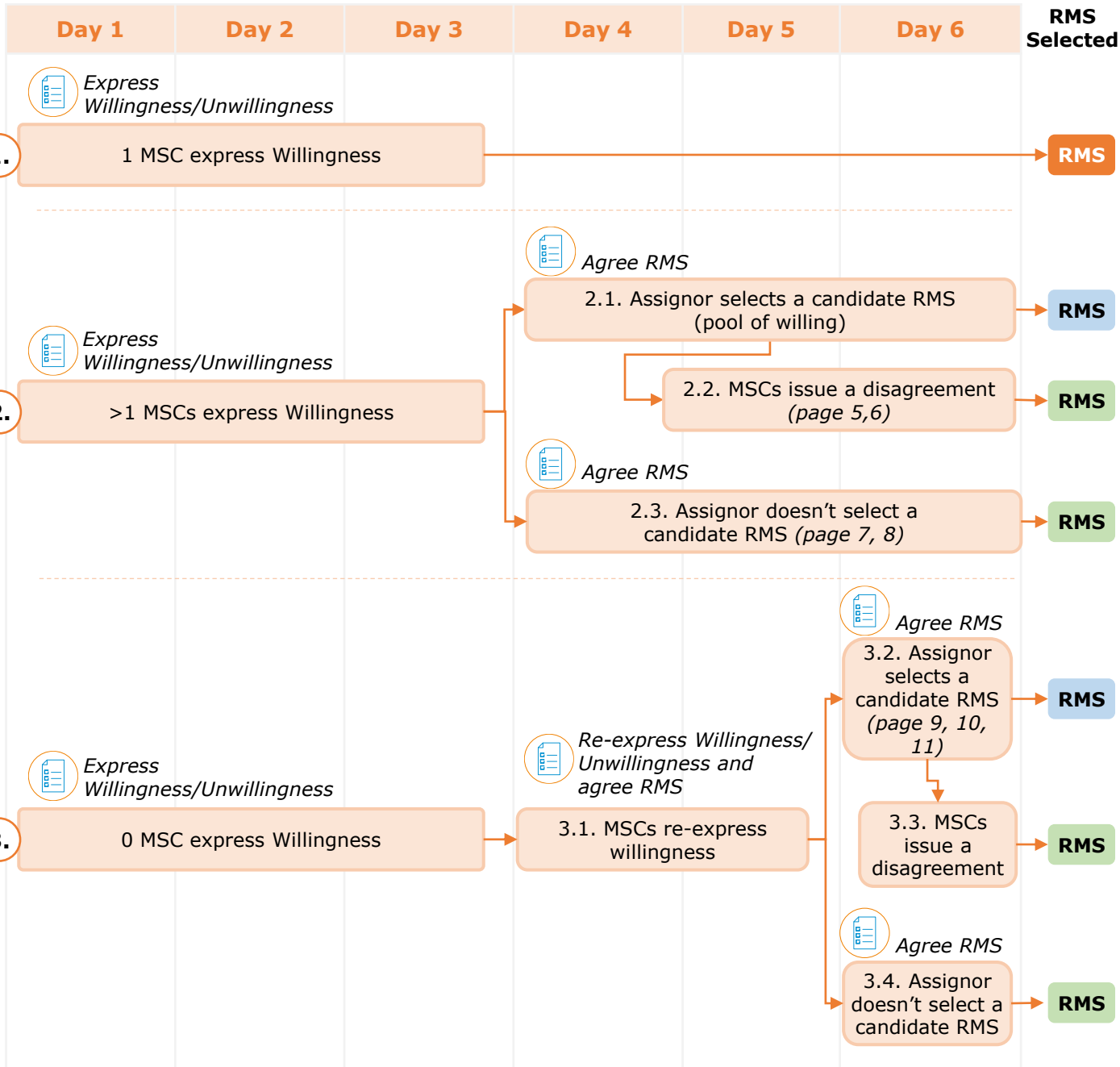
RMS selection overview

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



Legend:

- Tasks
- Willing RMS
- Candidate RMS
- Sponsor proposed RMS

RMS selection scenarios

Scenario 2.2: Issue disagreement with the candidate RMS

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

- 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.

The screenshot shows the 'Tasks' tab selected in the top navigation bar. Below it is a search bar with a 'SEARCH' button. The main content area displays a table of tasks. The first task is 'Express willingness/unwillingness' with a 'Pending' status and ID '2021-501395-28-00'. The table includes columns for 'RMS', 'Application and Non-SM type', 'Sponsor/Co-sponsors', 'Evaluation process', 'Created', 'Due', 'Remaining days', and 'Assignee'. The 'Assignee' column for this task shows a blue user icon button.

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

The screenshot shows the 'Express willingness' page for 'CTIS Training'. It features a 'Due date: 09/09/2021' and a 'View trial details' link. Below this is a table of MSCs with their current willingness status. The 'Pending' status for each MSC is highlighted with a red box.

MSC	Current willing	Justification	Number of trials (MSC)	Number of trials (RMS)	Workshare % (YTD)
AUSTRIA Proposed RMS	Pending	-	90	57	63.333 %
GERMANY	Pending	-	206	110	53.398 %
GREECE	Pending	-	365	78	21.370 %

- 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.*

The screenshots show three dialog boxes for MSCs to express their willingness. Each dialog has a title (e.g., 'MSC 1 AUSTRIA:'), a section for 'Express willingness to be RMS' with 'Willing' and 'Unwilling' radio buttons, a 'Justification' text area, and 'CANCEL' and 'Share' buttons. The 'Share' button is highlighted in red in each dialog. Below the third dialog, there is a '+ Create subtask' button and a 'Complete' button with a checkmark, also highlighted in red.

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**.

Summary					
MSC	MSC willing at end of day 3	Justification	Number of trials (MSC)	Number of trials (RMS)	Workshare % (YTD)
GERMANY Assignor	willing	-	206	110	53.398 %
GREECE	unwilling	-	365	78	21.370 %
AUSTRIA Proposed RMS	willing	-	90	57	63.333 %

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 assign it to a user.

Agree RMS		RMS:	Application and Non-SM type:	Sponsor/Co-sponsors:	Evaluation process:	Created:	Due:	Remaining days:	Assignee:
Pending	2021-501396-84-00		INITIAL	Test Organisation	Validation	31/08/2021	07/09/2021	7	

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.

Discussion with MSCs

Greece

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.*

RMS selection

Proposed RMS AUSTRIA

Assignor GERMANY

Candidate RMS by assignor **GERMANY**

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.

Issue disagreement

Issue disagreement

Candidate RMS GERMANY

Date of disagreement

Justification is mandatory for disagreement

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

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).

- 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.

Tasks

SEARCH

Express willingness/unwillingness	RMS:	Application and Non-SM type:	Sponsor/Co-sponsors:	Evaluation process:	Created:	Due:	Remaining days:	Assignee:
Pending 2021-501395-28-00		INITIAL	Test Organisation	Validation	31/08/2021	03/09/2021	3	Assign

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

CTIS Training

Express willingness Assigned

Under evaluation Due date: 09/09/2021 View trial details

Sponsor : Test Organisation

Product being tested: IMP1 Irbesartan 300 mg tablets
Marketing Authorisation: Yes
Active substance name: Irbesartan

MSC	Current willing	Justification	Number of trials (MSC)	Number of trials (RMS)	Workshare % (YTD)
AUSTRIA Proposed RMS	Pending	-	90	57	63.333 %
GERMANY	Pending	-	206	110	53.398 %
GREECE	Pending	-	365	78	21.370 %

- 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.

MSC 1 AUSTRIA:

Express willingness to be RMS Willing Unwilling

Justification

CANCEL Share

MSC 2 GERMANY:

Express willingness to be RMS Willing Unwilling

Justification

CANCEL Share

MSC 3 GREECE:

Express willingness to be RMS Willing Unwilling

Justification

CANCEL Share

+ Create subtask Complete

RMS selection scenarios

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**.

Summary					
MSC	MSC willing at end of day 3	Justification	Number of trials (MSC)	Number of trials (RMS)	Workshare % (YTD)
GERMANY Assignor	willing	-	206	110	53.398 %
GREECE	unwilling	-	365	78	21.370 %
AUSTRIA Proposed RMS	willing	-	90	57	63.333 %

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.

Agree RMS		RMS:	Application and Non-SM type:	Sponsor/Co-sponsors:	Evaluation process:	Created:	Due:	Remaining days:	Assignee:
Pending	2021-501396-84-00		INITIAL	Test Organisation	Validation	31/08/2021	07/09/2021	7	

IMP1: Irbesartan 300 mg tablets · IRBESARTAN

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.

Discussion with MSCs

Greece



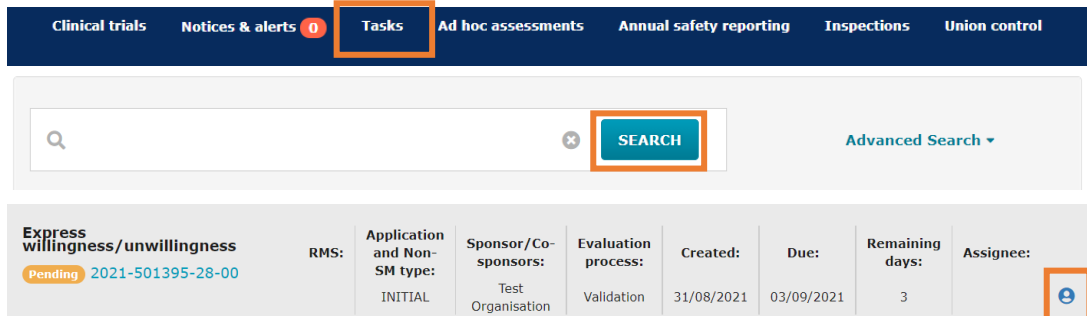
7. If the assignor (i.e. Germany) **does not select a candidate RMS** among the willing MSC, the **proposed RMS** (i.e. Austria) **will become the RMS** at the end of day 6.


RMS selection scenarios

Scenario 3.1: Assignor selects a candidate RMS after MSCs re-express willingness/unwillingness

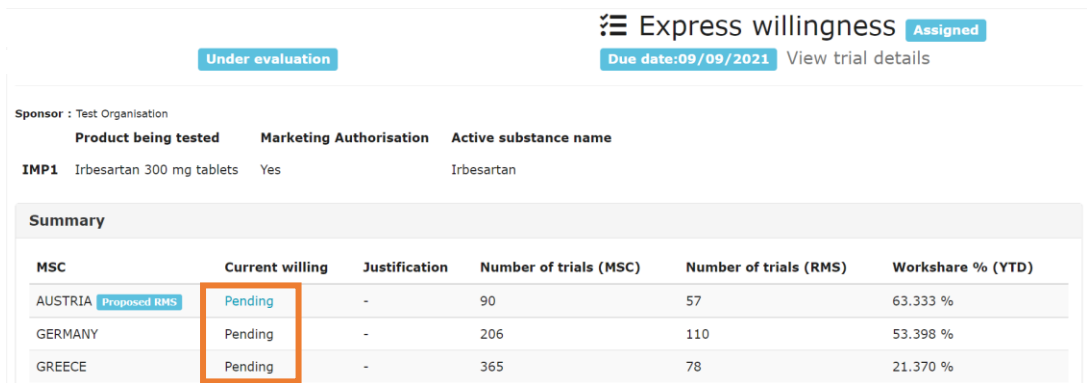
Example of how to re-express willingness or unwillingness and agree on the RMS with 3 MSCs (Austria, Germany and Greece).

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.



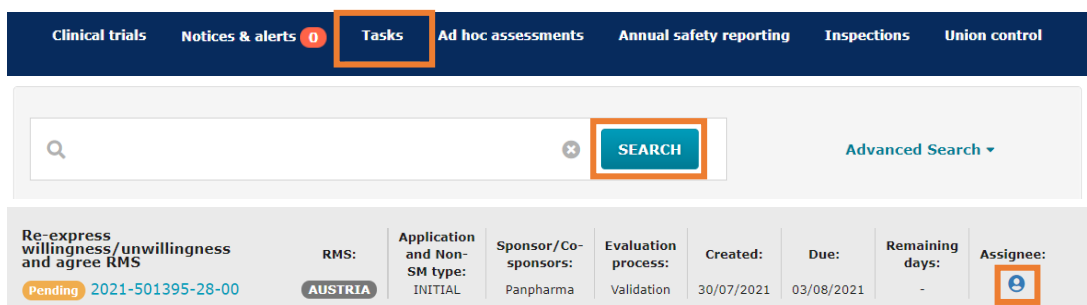
Express willingness/unwillingness	RMS:	Application and Non-SM type:	Sponsor/Co-sponsors:	Evaluation process:	Created:	Due:	Remaining days:	Assignee:
Pending 2021-501395-28-00	INITIAL	INITIAL	Test Organisation	Validation	31/08/2021	03/09/2021	3	


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.*



MSC	Current willing	Justification	Number of trials (MSC)	Number of trials (RMS)	Workshare % (YTD)
AUSTRIA Proposed RMS	Pending	-	90	57	63.333 %
GERMANY	Pending	-	206	110	53.398 %
GREECE	Pending	-	365	78	21.370 %

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.



Re-express willingness/unwillingness and agree RMS	RMS:	Application and Non-SM type:	Sponsor/Co-sponsors:	Evaluation process:	Created:	Due:	Remaining days:	Assignee:
Pending 2021-501395-28-00	AUSTRIA	INITIAL	Panpharma	Validation	30/07/2021	03/08/2021	-	

RMS selection scenarios

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.

CTIS Training ☰ Re-express willingness/unwillingness and agree RMS

Under evaluation Assigned Due date: 06/08/2021 [View trial details](#)

Sponsor : Test Organisation

Product being tested	Marketing Authorisation	Active substance name
IMP1 Irbesartan 300 mg tablets	Yes	Irbesartan

Summary

MSC	Re-Express Willing	Justification	Number of trials (MSC)	Number of trials (RMS)	Workshare % (YTD)
AUSTRIA Assignor	Pending. It is only possible to re-express willingness until...	-	90	57	63.333 %
GERMANY	Pending	-	206	110	53.398 %
GREECE	Pending	-	365	78	21.370 %

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.*

MSC 1 AUSTRIA: ✕

Express willingness to be RMS **Willing** Unwilling

Justification

CANCEL ✓ Share

MSC 2 GERMANY: ✕

Express willingness to be RMS **Willing** Unwilling

Justification

CANCEL ✓ Share

MSC 3 GREECE: ✕

Express willingness to be RMS Willing **Unwilling**

Justification

CANCEL ✓ Share

+ Create subtask ✓ Complete



RMS selection scenarios

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**.

Summary					
MSC	MSC willing at end of day 3	Justification	Number of trials (MSC)	Number of trials (RMS)	Workshare % (YTD)
GERMANY Assignor	willing	-	206	110	53.398 %
GREECE	unwilling	-	365	78	21.370 %
AUSTRIA Proposed RMS	willing	-	90	57	63.333 %

Assignor selected by the system

Proposed RMS by the sponsor

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.

Agree RMS		RMS:	Application and Non-SM type:	Sponsor/Co-sponsors:	Evaluation process:	Created:	Due:	Remaining days:	Assignee:
Pending	2021-501396-84-00		INITIAL	Test Organisation	Validation	31/08/2021	07/09/2021	7	

IMP1: Irbesartan 300 mg tablets · IRBESARTAN

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

RMS selection

Proposed RMS AUSTRIA

Assignor GERMANY

Candidate RMS by assignor

RMS --

Discussion with MSCs

Greece

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.*

RMS selection

Proposed RMS AUSTRIA

Assignor GERMANY

Candidate RMS by assignor **GERMANY**

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.

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Clinical Trials Information System (CTIS)

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