



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

## Changes done to an application via NON SM and RFI responses

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SME and academia Clinical Trials Information System (CTIS) two-part training webinar

Presented by Laura Pioppo on 04 March 2021





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- Non Substantial modifications are mentioned in Article 81(9) of the Regulation
- These are any changes to the clinical trials which are not substantial modifications but are relevant for the supervision of the clinical trial by the Member States concerned
- It is a functionality implemented in the system to enable sponsors to keep the dossier up to date
- Once submitted, non substantial modification do not require Member States assessment (differently from substantial modifications)

- Non SM can be applied to each part of the clinical trial application (part I and/or part II). A description of the changes made has to be provided by the sponsor.
- There are business rules implemented in CTIS to 'control' what can be modified by the sponsors with a NON SM mechanism , so not all the fields are editable
- Examples:
  - Translation of data and documents in the application dossier
  - A change in the number of clinical trial participants for the trial
  - Any change of persons/entities and contact details to whom the sponsor delegated tasks
  - Extension of validity of insurance certificate

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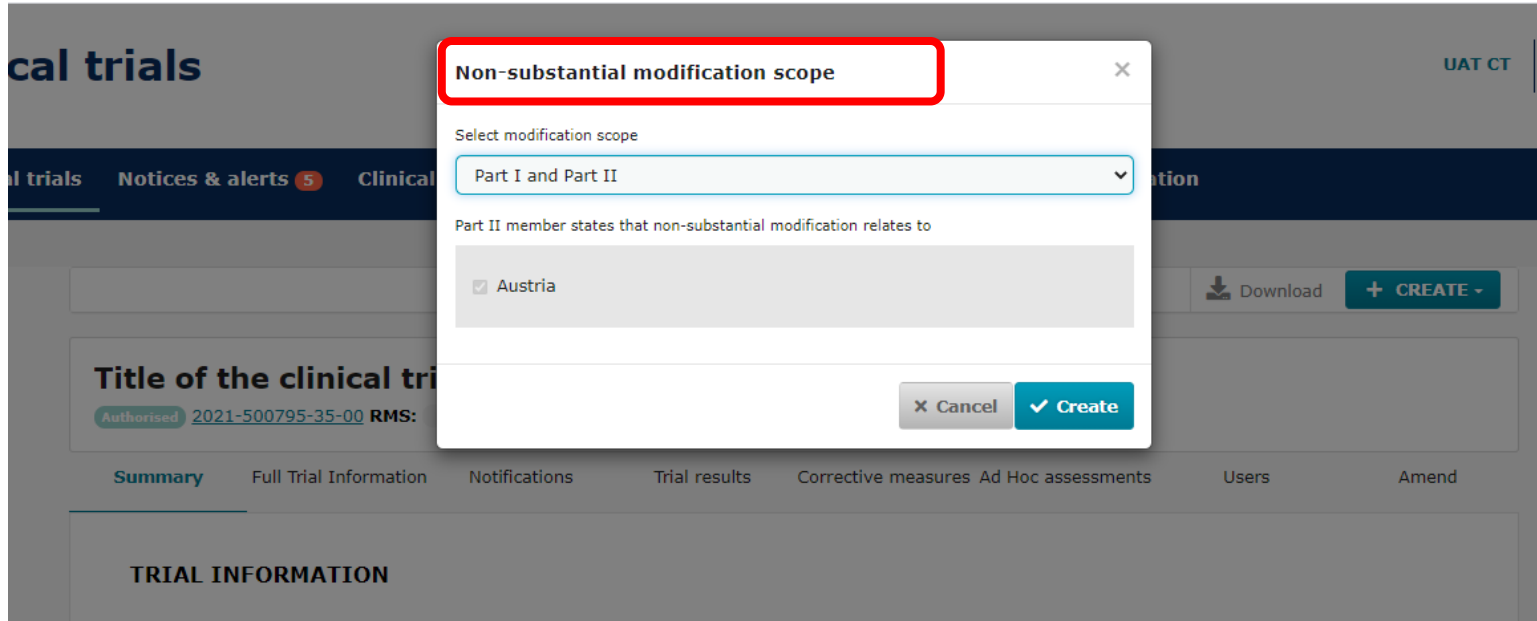
Download **+ CREATE**

**Title of the clinical trial**

Authorised [2021-500795-35-00](#) RMS: Austria

Summary Full Trial Information Notifications Trial results Corrective measures Ad Hoc assessment

- Single trial substantial modification
- Multi trial substantial modification
- Non-substantial modification**
- Additional MSC



The screenshot displays a web interface for clinical trials with a modal dialog box open. The dialog box is titled "Non-substantial modification scope" and contains the following elements:

- A dropdown menu labeled "Select modification scope" with the selected option "Part I and Part II".
- A section titled "Part II member states that non-substantial modification relates to" containing a list with one item: "Austria" (checked).
- Buttons for "Cancel" and "Create".

The background interface shows a clinical trial entry with the title "Title of the clinical trial", an "Authorised" status, and the reference number "2021-500795-35-00 RMS:". Navigation tabs include "Summary", "Full Trial Information", "Notifications", "Trial results", "Corrective measures", "Ad Hoc assessments", "Users", and "Amend". A "Download" button and a "+ CREATE" button are also visible.

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**i** Please note that data and documents provided in the EU Database are subject to publication rules (including the protection of personal data and commercially confidential information), as per Regulation (EU) 536/2014, Article 81(4).

Title of the clinical trial 2021-500795-35-00  
/ Non-substantial modification ID: NSM-1 [Draft](#) [New version draft Non-SM-1](#) [View submitted application](#) / RMS: Austria

[✓ Check](#) [📁 Save](#) [⌛ Cancel](#) [📤 Submit](#)

- Form
- MSCs
- Part I
- Part II

### Trial specific information (Part I)

Trial details 

Trial identifiers 



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Title of the clinical trial 2021-500795-35-00  
/ Non-substantial modification ID: NSM-1 **Draft** **New version draft Non-SM-1** **View submitted application** / RMS: Austria

**Form** | **Form details**

**MSCs**

**Part I** | **Non-substantial modification details**

**Part II** | **Non-substantial modification description \***

Sponsor to provide here a description of the changes made|



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### OVERALL TRIAL STATUS

Member State	Overall Trial Status	First decision date	Start of trial	End of trial	Recruitment start date
AT	Authorised <sup>Ⓞ</sup>	09/02/2021			

### APPLICATION AND NON-SUBSTANTIAL MODIFICATION

Type	ID	Parts	MSCs	Submission date	Decision date	
Non-substantial modification	<a href="#">NSM-1</a>	Part I & Part II	AT(Authorised)	09/02/2021		
Initial	<a href="#">IN</a>	Part I & Part II	AT(Authorised)	09/02/2021	09/02/2021	+ INFO



## RFI updates across applications

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Updates to clinical trial applications via the means of request for information (RFI)

- During the evaluation of an application (initial, substantial modification of any type and addition of a new MSC), the MSC can raise a request for information (RFI) to be addressed by the sponsor of the trial
- The RFI can be raised at the time of validation, assessment of part I, assessment of part II or both, as applicable
- The RFI have to be addressed by the sponsor within the deadline imposed by the RMS/MSA, otherwise the application will lapse
- Raising an RFI automatically leads to an extension of the timelines for evaluation, as foreseen in the Regulation
- Regardless of the number of RFI raised, the extension occurs once



*Note*: the same request for information (RFI) mechanism it is also implemented in CTIS to enable the sponsors to provide responses to request for information raised by the MSC **outside of the evaluation process**, namely:

- In case of an *ad hoc assessment* initiated by the MSC following submission of a notification (e.g. serious breach, unexpected events, etc..)
- In case the sponsor is requested to provide an opinion in the context of a *corrective measure* (Article 77 of Regulation)
- Modification of the application dossier is not allowed via these RFI responses

# EMA CTIS training programme Module 11: How to respond to RFIs received during the evaluation of a Clinical Trial Application



Training materials related to this module will be released on the EMA website in 2021.

See Module 04 Support with workload management [here](#) for an overview of the RFI list functionality.



# Any questions?

## Further information

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[CT.Sponsortraining@ema.europa.eu](mailto:CT.Sponsortraining@ema.europa.eu)

**Official address** Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands

**Telephone** +31 (0)88 781 6000

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