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SCIENCE MEDICINES HEALTH

Changes done to an application via NON SM and RFI responses

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

Presented by Laura Pioppo on 04 March 2021

The European Medicines Agency developed this training material to enhance public access to information on the Clinical Trial Information System (CTIS). This material describes a preliminary version of CTIS and may therefore not entirely describe the system as it is at the time of use of this material. The Agency does not warrant or accept any liability in relation to the use (in part or in whole) or the interpretation of the information contained in this training material by third parties.

Changes introduced to the dossier via NON SM

- 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)

Changes introduced to the dossier via NON SM

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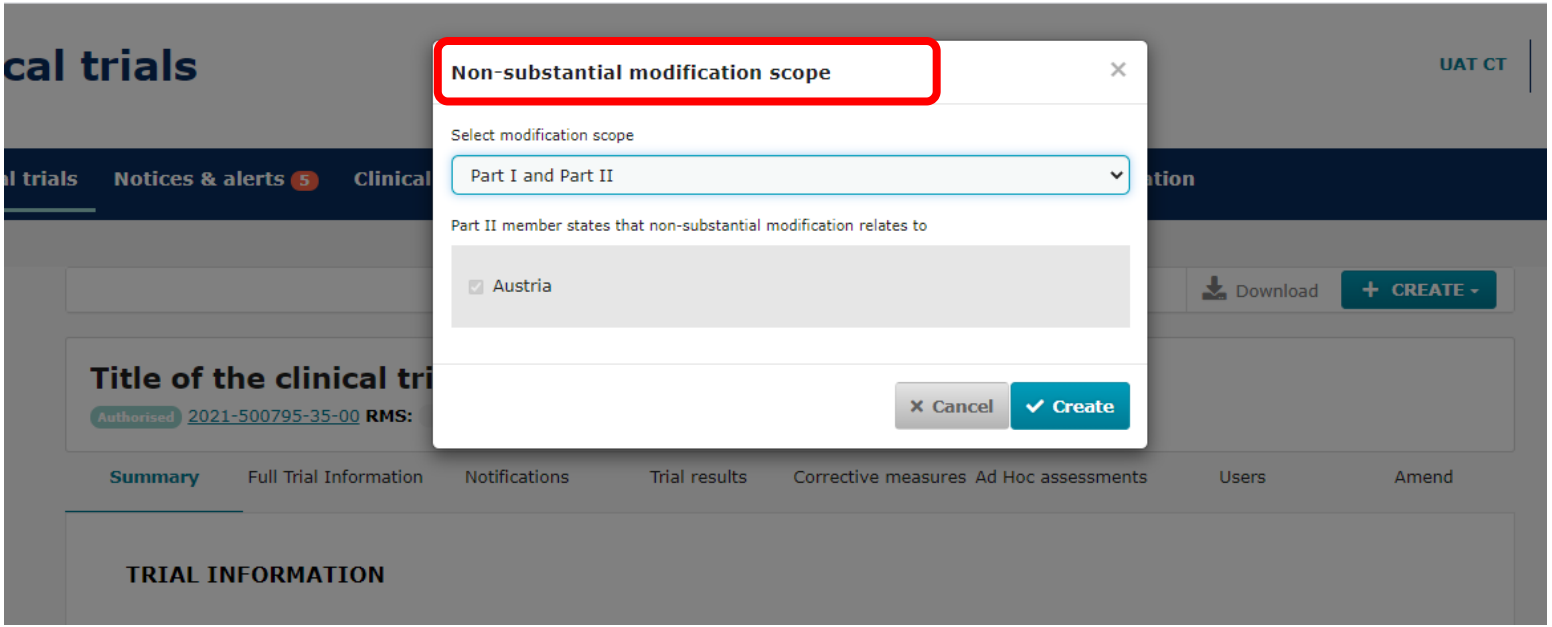
- Non SM can be applied to each part of the clinical trial application (part I and/or part II). A description of the changes made has to be provided by the sponsor.
- There are business rules implemented in CTIS to 'control' what can be modified by the sponsors with a NON SM mechanism , so not all the 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

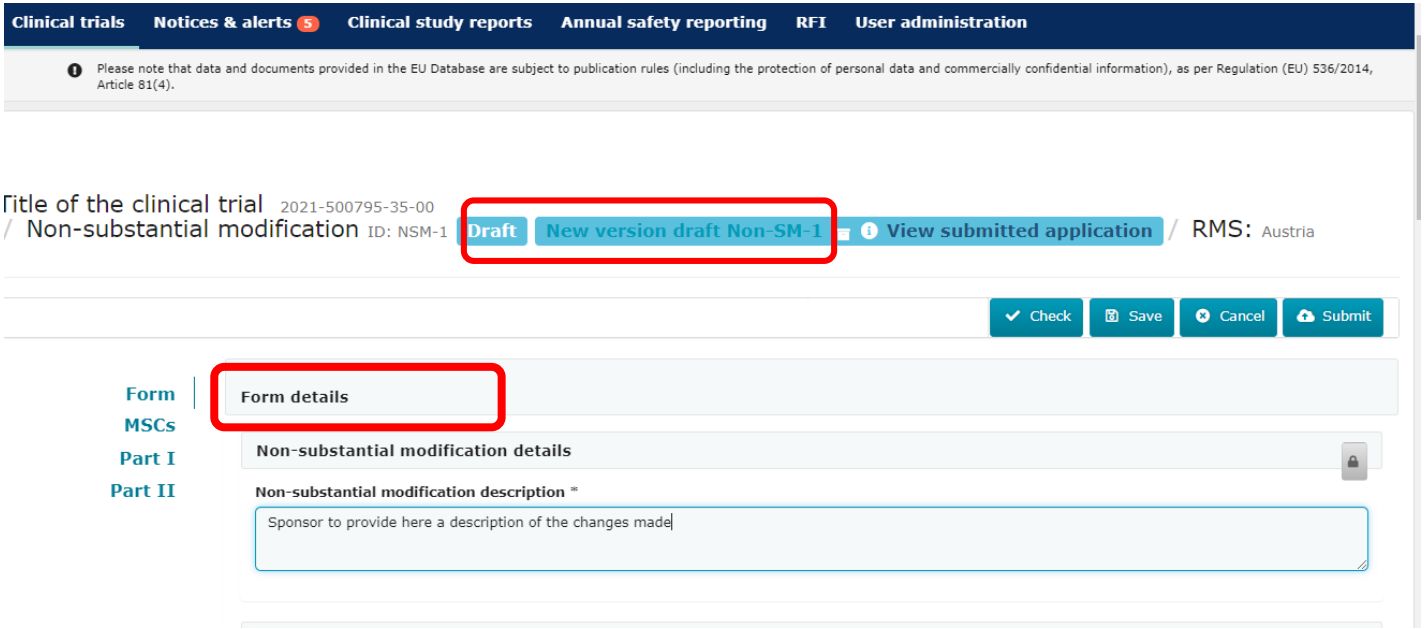
Creation of NON SM

Creation of NON SM

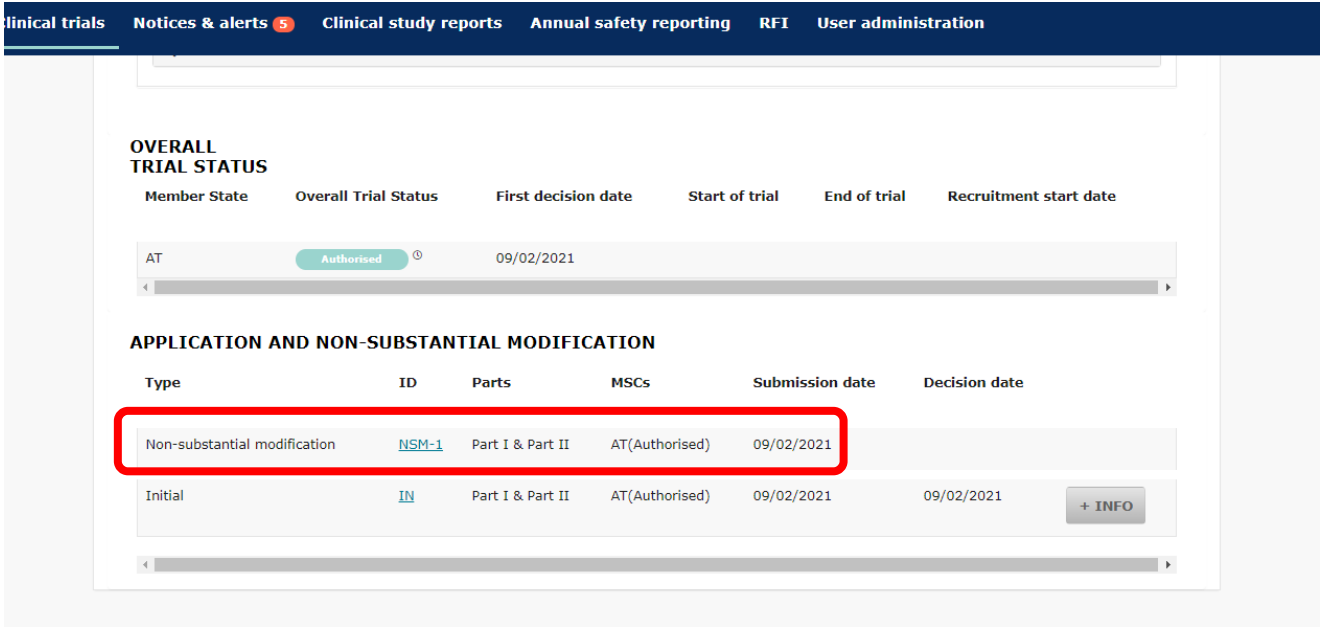


Creation of NON SM

Creation of NON SM



Submission of NON SM



RFI updates across applications

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

Key concepts on 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/MSC, 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

RFI mechanism in ad hoc assessment and opinion for CM

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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

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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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