

# **GCP | ENHEDERNE**

God klinisk forskning ✓✓✓

**The Danish GCP Units guide to the Clinical Trials Information  
System (CTIS)**

## Content

1	Introduction .....	4
1.1	What is CTIS? .....	4
1.2	Sponsor is responsible for the application via sponsors workspace .....	5
2	How to Create, Submit and Withdraw an initial Clinical Trial Application (CTA) .....	6
2.1	Application dossier for the initial application .....	6
2.2	Sponsor registration in OMS .....	9
2.3	Fill in the trial title and sponsor organisation in CTIS.....	9
2.4	Fill in the Form and Member states concerned (MSCs) section .....	11
2.5	Fill in the Part I section .....	13
2.6	Fill in the Part II section .....	17
2.7	Site and third party registration directly in CTIS .....	20
2.8	How to submit an additional member state concerned (MSC) application (add a new country) ..	20
2.9	Withdrawal of an application .....	21
2.10	Resubmission of an application.....	22
3	Validation, Request for Further Information (RFI) and Authorisation.....	22
3.1	How to access and view a request for further information (RFI).....	22
3.2	How to upload documents into CTIS in response to an RFI: change application.....	25
3.3	How to change a Clinical Trial Application as part of a RFI response (Sponsors).....	26
3.4	How to respond to RFI considerations and submit an RFI response.....	27
3.5	Timetable.....	28
3.6	Authorisation .....	29
3.7	How to find the “Report for the Application Evaluation Decision” in CTIS:.....	31
4	15 days notifications from start to end of trial.....	32
5	How to create and submit a Substantial Modification (SM) .....	35
6	Summary of Results and Summary for Layperson.....	39
7	Changes log.....	41

## Abbreviations

AR = Assessment report

AxMP = Auxiliary medicinal product

CT = Clinical Trial

CTA = Clinical Trial Application

CTIS = Clinical Trial information System

CTR= Clinical Trial Regulation

EMA =European Medicines Agency

GCP =Good Clinical Practice

IMPD=Investigational Medicinal Product Dossier

MSC = Member states concerned

OMS = Organisation Management System

RFI = Request for information

RMS = Reporting member states

RSI= Reference Safety Information

SM = Substantial modification

SmPC= Summary of Product Characteristics

SAE=Serious Adverse Event

SAR=Serious Adverse Reaction

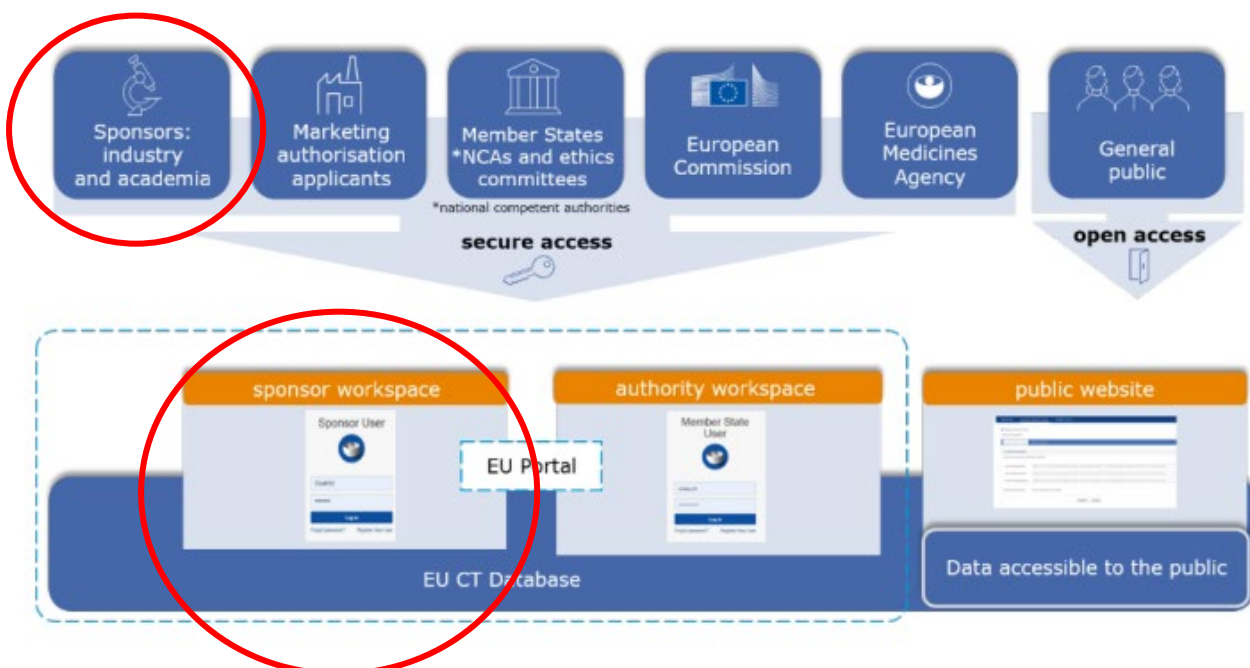
# 1 Introduction

## 1.1 What is CTIS?

The [Clinical Trials Regulation, CTR \(Regulation \(EU\) No 536/2014\)](#) came into force on 31 January 2022 and submission of clinical trials with medicinal products shall no longer be submitted directly to the Health Authorities and Ethics Committees, but instead the submission will take place via a **Clinical Trial Information System (CTIS)**. CTIS is the **single entry point** for submitting clinical trial information in the EU. All communication including final decision from the authorities will be received via CTIS. With CTIS, sponsors can apply for clinical trial authorisation in multiple EU/EEA countries with a single application.

CTIS is structured in two **restricted** and **secured** workspaces, only accessible to registered EMA account users, and a website with open access to the general public:

- The **sponsor workspace**, accessible to commercial and non-commercial sponsors. It supports the preparation, compilation and submission of clinical trial data for its assessment by Member States. [Link for sponsors workspace in CTIS](#)
- The **authority workspace**, accessible to national competent authorities, ethics committees, the European Commission, and the European Medicines Agency (EMA). It supports the activities of Member States and the European Commission in assessing and overseeing clinical trials.
- The **public website**, accessible to patients, healthcare professionals, scientists, clinical research associations, media, and members of the public. It supports the open access to clinical trials' data in the European Union, in line with the transparency goal set out in Regulation (EU) No 536/2014 (Clinical Trials Regulation, CTR).



This guidance covers the process on how to submit, complete and maintain a clinical trial application (CTA) in Denmark or in EU as a sponsor, using the **trial-centric approach**, as well as management of relevant notifications and information throughout the life-cycle of clinical trials.

**Any feedback and questions to the Danish GCP unit's Guidances is welcome:**

GCP unit at Aalborg and Aarhus University hospitals: [gcp-unit@clin.au.dk](mailto:gcp-unit@clin.au.dk)

GCP unit at Odense University hospital: [GCP-enheden@rsyd.dk](mailto:GCP-enheden@rsyd.dk)

GCP unit at Copenhagen University hospital: [gcp-enheden.bispebjerg-frederiksberg-hospitaler@regionh.dk](mailto:gcp-enheden.bispebjerg-frederiksberg-hospitaler@regionh.dk)

This guidance is based on and can be used as a supplement to the following:

**CTIS training guides:**

- [Clinical Trials Information System \(CTIS\): online modular training programme | European Medicines Agency \(europa.eu\)](#) - How to create a CTA – see module 10
- Clinical Trial Information System (CTIS) – [Sponsors Handbook](#)
- How to access CTIS: [Step by step guide to access CTIS](#)
- How to search and create organisations in CTIS: [Step by step guideline](#)
- Guide for [CTIS common features](#)
- EMAs help desk for CTIS: [Service Now](#) - *Before submitting a ticket to Service Desk, please check information available on the EMA CTIS Support page*
- [EMA CTIS Support page](#)

**Q&As for CTR and CTIS:**

- [Regulation CTR Q&A](#) (Question and answer document – Regulation Eudralex vol. 10, Chapter V - Additional documents)
- [EMA Q&A](#)
- [Danish Medicines Agency Q&A and general information from DMA](#)
- [Danish Ethics Committee Q&A](#)

**1.2 Sponsor is responsible for the application via sponsors workspace**

The sponsor workspace provides clinical trial sponsors with functionalities for submission of CTA's, notifications and clinical trial results to Member states authorities and the public and management of information throughout the life cycle of clinical trials.

## 2 How to Create, Submit and Withdraw an initial Clinical Trial Application (CTA)

### 2.1 Application dossier for the initial application

[Link to the CTIS database](#). For first time log-in see section 3.2 in the The Danish GCP Units guide – User access, roles and responsibilities in CTIS

The documents for the Clinical Trial Application dossier is described in [Annex I of the CTR](#).

**Info box:**

Templates for some documents can be found in [EudraLex - Volume 10 - Clinical trials guidelines](#)  
GO TO: Chapter I - Application and application documents

### EudraLex - Volume 10 - Clinical trials guidelines

#### Chapter I - Application and application documents

- **Templates documents for FORM section of the CTIS**
  - Template statement on compliance Regulation (EU) 2016/679: [PDF](#) {EN | ...} / [Word](#) {EN | ...}
- **Part II application document templates**
  - Compensation for trial participants - Template: [PDF](#) {EN | ...} / [Word](#) {EN | ...}
  - Harmonisation guidance: [PDF](#) {EN | ...}
  - Investigator Curriculum Vitae template: [PDF](#) {EN | ...} / [Word](#) {EN | ...}
  - Declaration of interest template: [PDF](#) {EN | ...} / [Word](#) {EN | ...}
  - Site suitability form: [PDF](#) {EN | ...} / [Word](#) {EN | ...}
  - Informed consent and patient recruitment procedure template: [PDF](#) {EN | ...} / [Word](#) {EN | ...}
  - Compliance with applicable rules for biological samples: [PDF](#) {EN | ...} / [Word](#) {EN | ...}

**Info box:**

Please avoid any kind of signatures, both digital and wet ink signatures, in all documents, as they can be copied, when the documents are made public. Be aware not to include personal information (e.g. CPR numbers, private addresses and telephone numbers) in investigators CV.

Overview of documents and information that are made public in CTIS public database: [Transparency – publication of clinical trial](#)

**Info box:**

**Language requirements** (Part I): [CTR Q&A Annex II](#)  
**National requirements** (Part II) [CTR Q&A Annex III](#) (CTR Q&A: *Eudralex Vol. 10: Chapter V*)  
**List of all documents:** [CTR ANNEX I - APPLICATION DOSSIER FOR THE INITIAL APPLICATION](#)

The asterisk \* in CTIS indicates mandatory fields. Some separate documents (e.g. recruitment) must be uploaded even though the same text is already mentioned in other documents e.g. the protocol.

**Documents can be in Danish for trials running in Denmark only.**

Part I	Part II
<ul style="list-style-type: none"> <li>➤ Cover letter (for content, please go to Annex 1, section B in the <a href="#">Regulation</a>) – cover letter must be uploaded in the section “Form” in CTIS</li> <li>➤ EU Application form (structured data entered directly in CTIS)</li> <li>➤ Protocol and protocol synopsis (synopsis can be part of protocol or separate document) (CTR Q&amp;A, section 5.8 for synopsis guidance)</li> <li>➤ Patient facing documents (questionnaires, diary) that are <u>linked to the endpoints</u> of the clinical trial shall be uploaded with the protocol in Part I - <i>you can upload several documents with the protocol</i></li> <li>➤ Investigators Brochure (IB)/SmPC</li> <li>➤ IMPD quality, safety and efficacy/ Simplified IMPD with reference to the valid SmPC</li> <li>➤ Content of labelling of IMPD</li> <li>➤ Template statement on compliance with Regulation (EU) 2016/679 (GDPR) (<a href="#">template in Volume 10</a>) – must be uploaded in the section “Form” in CTIS</li> </ul>	<ul style="list-style-type: none"> <li>➤ Informed consent and patient recruitment procedure template (<a href="#">template in Volume 10</a>)</li> <li>➤ Subject information and informed consent form</li> <li>➤ Patient facing documents (e.g. recruitment)</li> <li>➤ Investigator CV (<a href="#">template in Volume 10</a>) – it is not mandatory to use this template</li> <li>➤ Site suitability form (<a href="#">template in Volume 10</a>) - one form per site</li> <li>➤ Proof of insurance cover or indemnification (Insurance: non-commercial sponsors can upload a document stating that the trial sites in DK are covered by “Patienterstatningen”)</li> <li>➤ Financial and other arrangements</li> <li>➤ Proof of payment of fee (not applicable for Denmark for non-commercial trials)</li> <li>➤ Compliance with applicable rules for biological samples (<a href="#">template in Volume 10</a>)</li> </ul>

**Info box:**

Documents in CTIS **must not contain DATE and VERSION in the file name** as this will be transferred to the “Title field” in CTIS and that “Title” will be the same during the entire life cycle of the clinical trial , also in case of substantial modifications. Or you can rename your documents in CTIS after upload.

## 1. Uploading documents into CTIS: filename, CTIS title, version number and date

The **Title** of the document in CTIS. The filename as it was uploaded is pre-filled here, this should be changed to match the requirements for document coding and titles (see next slide). Always remove version and date from the Title, because the Title cannot be changed when uploading a newer version later.

The filename of the uploaded file. The uploaded files can have any name, except for some forbidden characters:  
The filename provided is not valid. No special characters (/ . : ; |) allowed.

Change the default version (1) and default date (today) to the actual date and version of the document (in this example: version 4, date 12/02/2022).

Please note: the version field is free text: e.g. a zero of N/A can be filled in for documents that do not have a version number.

The CTIS System version of a document, always starting at 1.00 for the first version of a document uploaded into CTIS, and increasing when using the Update functionality. Cannot be edited. System Version therefore does not necessarily match the true version.

### Document codes and titles in CTIS (version 1.4, dd 7 September 2022)

Please adhere to the structure of CTR Annex I for document codes and titles when uploading files in CTIS, as shown below (Part I: section B-J; Part II: section K-S). Please fill in the requested information in the marked grey fields. Make sure that all documents have self-explanatory titles including relevant identification when applicable as mentioned below and include “redacted” in the file name in case a separate document for publication is uploaded. Please note that the files uploaded into CTIS can have any filename, but do not include special characters ((),.,:;|). The coding and naming applies to the document name in CTIS (the field ‘Title’ in the upload window). The original filename is pre-filled in the field ‘Title’ but can be adapted. Version number and date should not be in the document title, instead indicate the correct version number and date in the corresponding fields in the upload window.

#### B. Cover letter

B1\_ Cover letter EU CT number

#### D. Protocol

D1\_ Protocol EU CT number

D1\_ Protocol synopsis\_ENG EU CT number

D1\_ Protocol synopsis\_NL EU CT number (include MS in title, example is for NL)

D2\_ Protocol modification nr number EU CT number (in case of SM as separate doc.)

D3\_ DSMB Charter EU CT number

D4\_ Patient facing documents e.g. questionnaire or diary (if applicable)

D5\_ Master protocol EU CT number and name and sub-protocol name and specific number/ID (applicable for complex CT)

#### E. Investigator’s Brochure

E1\_ IB product name

#### F. Documents GMP compliance (if applicable)

F1\_ GMP declaration abbreviated name manufacturer/importer

F2\_ QP declaration abbreviated name manufacturer/importer

F3\_ Other statements/licences (e.g. import license) abbreviated name manufacturer/importer

#### G. Investigational Medicinal Product Dossier

G1\_ IMPD\_Q product name

G1\_ IMPD\_E-S product name

G2\_ SmPC product name

#### H. Auxiliary Medicinal Product Dossier

H1\_ AxMPD product name

#### I. Scientific advice and pediatric investigational plan (PIP)

I1\_ Scientific advice name organization

I2\_ PedCo opinion

I3\_ PIP decision name agency

#### J. Labeling

J1\_ Label IMP\_NL product name (include MS in title, example is for NL)

J1\_ Label IMP\_ENG product name

J2\_ Label AxMP\_NL product name (include MS in title, example is for NL)

J2\_ Label AxMP\_ENG product name

#### K. Recruitment arrangement

K1\_ Recruitment arrangements

K2\_ Recruitment material description

#### L. Subject information sheet, informed consent form, other subject information material

L1\_ SIS and ICF description (e.g. SIS and ICF adults, SIS and ICF 12-16 yr)

L2\_ Other subject information material description (e.g. information leaflet adults)

#### M. Suitability investigator

M1\_ CV Investigator name investigator and clinical trial site (use abbreviations)

M2\_ DoI Investigator name investigator and clinical trial site (use abbreviations)

#### N. Suitability facilities

N1\_ Site suitability form name clinical trial site

#### O. Proof of Insurance or indemnification

O1\_ Trial participant insurance certificate

O2\_ Proof of coverage sponsor or investigator name sponsor/trial site (if not covered by O1)

#### P. Financial and other arrangements

P1\_ Compensation trial participants, investigator, funding and other arrangements

#### R. Compliance GDPR

R1\_ Compliance on the collection and use of personal data

#### S. Biological samples

S1\_ Compliance on the collection, use and storage of biological samples




## 2.2 Sponsor registration in OMS

Any Sponsor can register in the Organisation Management Service (OMS). In their request to OMS, Sponsors should attach a **CT registration headed letter** available in the [OMS portal](#).

Please consult E - Change request document available in [SPOR portal under the documents section](#) for further clarification on the process.

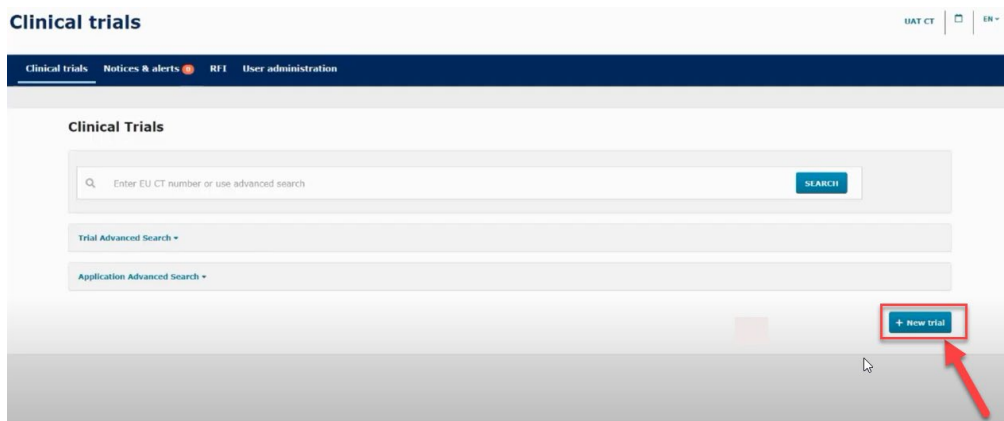
## 2.3 Fill in the trial title and sponsor organisation in CTIS

**Info box:**

The padlock  needs to be **locked** to enter data. Remember to unlock after uploading data in each tab. Save the data before going to the next tab.

CTIS should be completed in English. Remember to click **Save** on the top of the page. This should be done often as there will be no automatic savings.

When you are logged into CTIS, click on the tab “New Trial”:

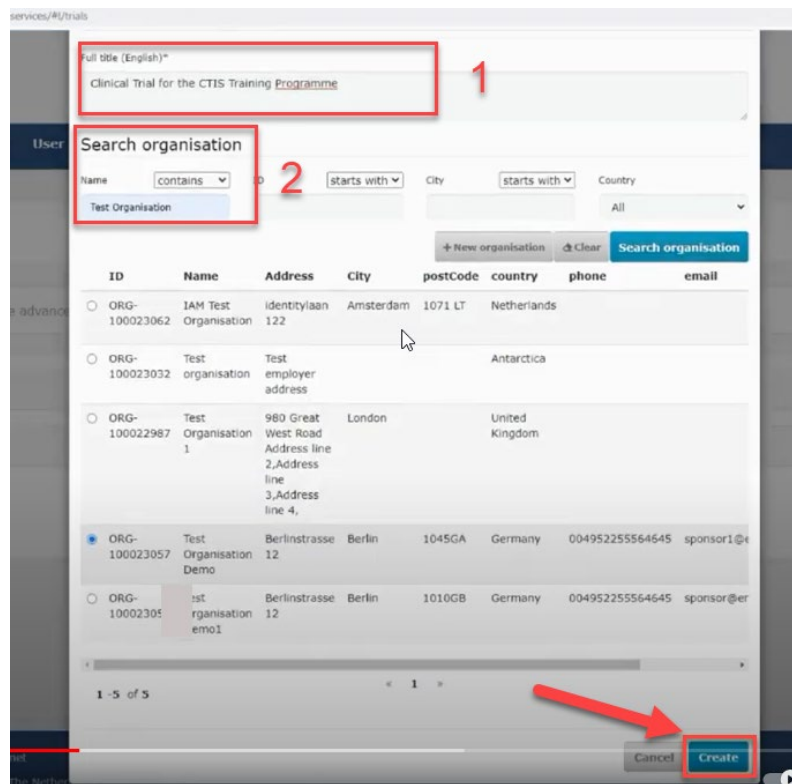
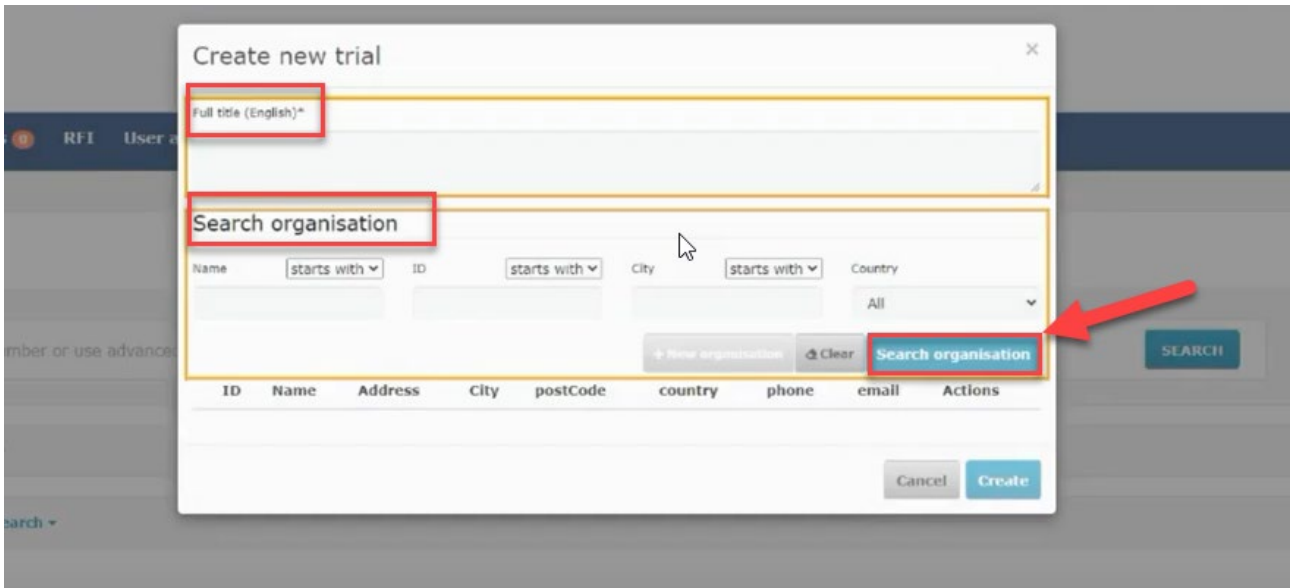


Type the full title of the trial.

Click on the “Search organisation” to search for the sponsor which must be registered in the Organisation Management System (OMS) before the CTA is created. It is important to choose the organisation where sponsor is located if it is different from where you are located. It is not possible to correct afterwards.

Be sure you choose the right address for the specific organisation. This can be the address of the hospital, university etc., where sponsor is located.

If the specific address of sponsor location, is not registered in OMS, then you must choose the overall address of the hospital/university or register the correct location in OMS – please refer to section 2.2.





When the two fields are filled in, click on the create button and the draft of the CTA will be created. On the following picture on the top right side there are four buttons:

1. Check: Identifies the mandatory fields in the sections which have not been filled in.
2. Save: Save the data which have been filled in up to that moment.
3. Cancel: To cancel your application. This can only be done while your trial is an “draft” mode.
4. Submit: Submit the application when all information is entered and it is completely ready.

The four different sections of the application which needs to be filled in with data and documents are:  
Form, MSCs, Part I and Part II.

The screenshot shows the CTIS application form interface. At the top, there is a navigation bar with 'Clinical trials', 'Notices & alerts', 'RFI', and 'User administration'. Below this is a disclaimer: '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)'. The main form area is titled 'Form details' and contains several sections: 'Initial Application details', 'Cover letter', 'Deferral publication dates', and 'Publish dates of trial information'. The 'Cover letter' section has a red box pointing to an asterisk with the text 'the asterisk \* = mandatory fields'. The 'Deferral publication dates' section has a red box pointing to a lock icon with the text 'Click on the "lock button" to be able to enter data in the form'. At the top right of the form, there is a 'Check' button. At the bottom right, there is an 'Add document' button. On the left side, there is a vertical menu with 'Form', 'MSCs', 'Part I', and 'Part II' highlighted in red, with a red box below it stating 'The four sections that need to be filled in'. At the top right of the form, there is a row of buttons: 'Check', 'Save', 'Cancel', and 'Submit'.

**Info box:**

 The "Check" button  can as well be used to validate for missing sections at all times during completion.

The asterisk \* in CTIS indicates mandatory fields to be filled in and/or mandatory upload of documents.

See also check list of required fields/documents:  
[List of required fields per CTA \(europa.eu\)](https://europea.eu).

## 2.4 Fill in the Form and Member states concerned (MSCs) section

**Video on this topic in EMA training module 10:**  
[Training video: Fill in the Form and the MSC sections](#)

Form: Add the cover letter and category of the trial. To select the trial category you must use the drop down menu. The category can be from 1- 3.

Category 1: Pharmaceutical development clinical trials.

Category 2: Therapeutic exploratory and confirmatory trials.

Category 3: Therapeutic use clinical trials.

Thereafter you need to add the “justification for the trial category”.

	Category 1 clinical trials (pharmaceutical development clinical trials):	Category 2 clinical trials (therapeutic exploratory and confirmatory clinical trials):	Category 3 clinical trials (therapeutic use clinical trials)
<ul style="list-style-type: none"> <li>• Protocol</li> <li>• Investigator’s brochure</li> <li>• Responses from sponsor in relation to any aspect of the trial</li> </ul>	Sponsor may opt to defer this up to the time of MA using this trial or up to <b>7 years</b> after the end of the trial whichever is earlier.	Sponsor may opt to defer this up to the time of MA using this trial or up to <b>5 years</b> after the end of the trial whichever is earlier.	Time of decision on the trial. Sponsor may opt to up to the time when the summary of results is made public usually <b>12 months</b> after the end of the trial in the EU.

**Info box:**

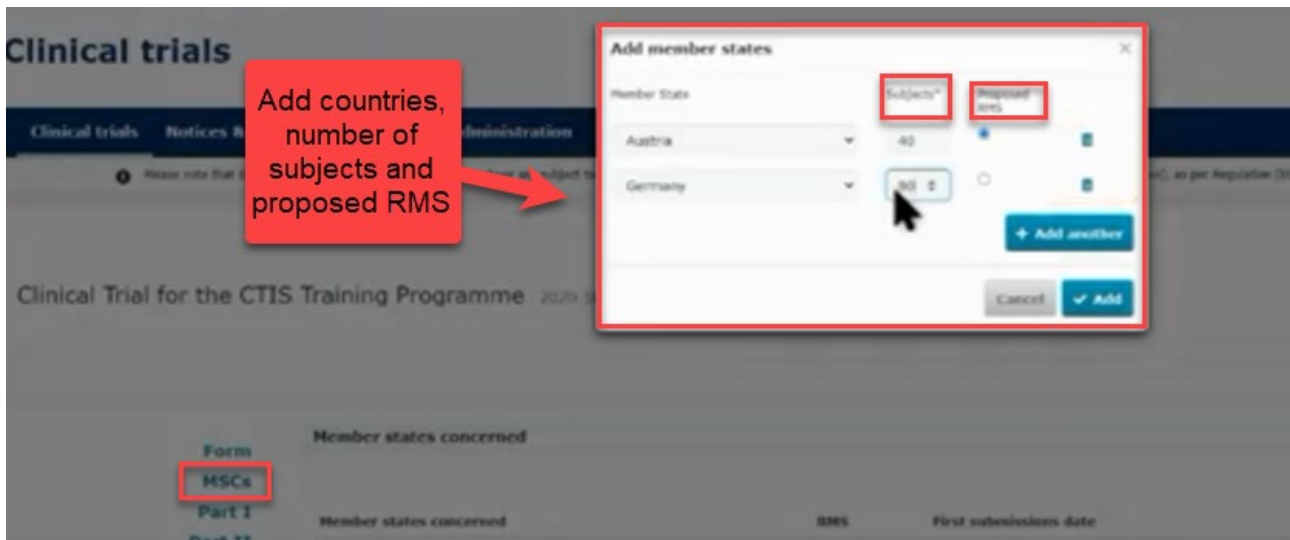
The protocol will automatically be accessible in the public workspace. In case of sensitive information in the protocol according to GDPR, it is also possible to upload a second edition of the protocol not for publication. The first document you upload is always for publication so be sure to choose the document without sensitive information first.

If you afterwards want to upload a document not for publication click on the ‘Add’ button (+) and upload a second protocol (not for publication)



The “deferral publication dates” must only be filled in if the sponsor has applied for a deferral date of the publication of the documents in the application.

MSCs: Member states concerned. Add the countries (member states) where the trial application should be submitted. Add the number of subjects that are expected to participate in each country. If there are more than one country participating in the trial, you can suggest a country as RMS (reference member state) which is the country that are responsible for the overall scientific assessment.



## 2.5 Fill in the Part I section

### Videos on this topic in EMA training module 10:

[Training video: Fill in the Part I section](#)

[Training video: Fill in the trial details of Part I section](#)

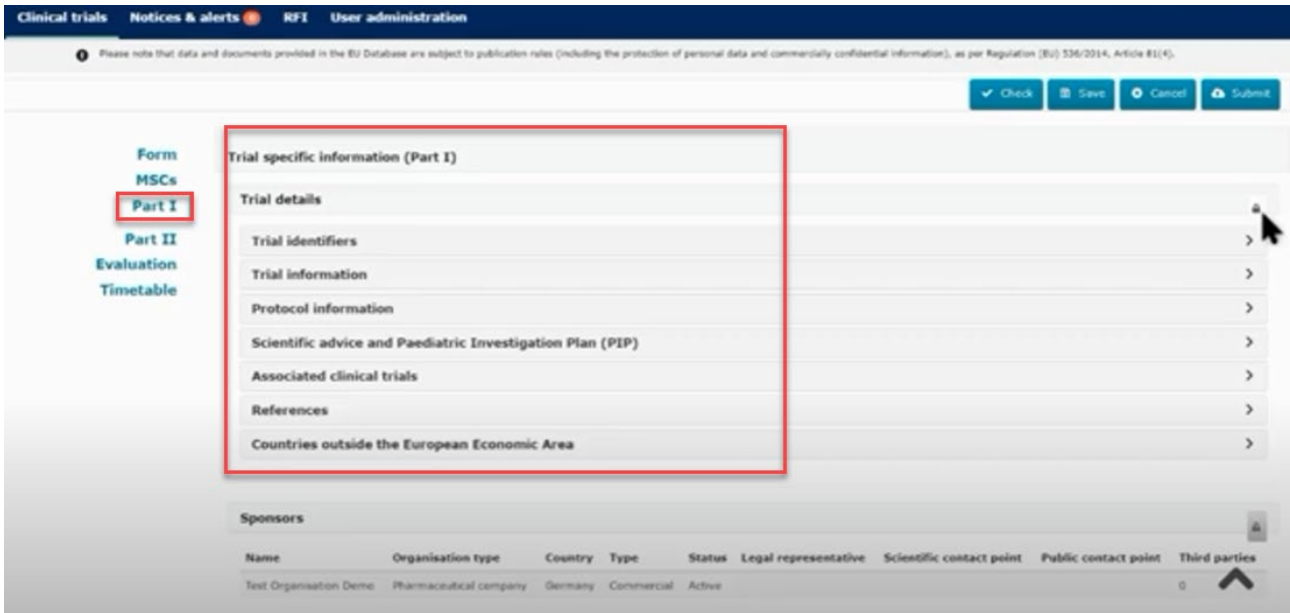
[Training video: Fill in the Sponsor details of Part I section](#)

[Training video: Fill in the Product details of Part I section](#)

**Part I:** This section contains information mainly to be assessed by the Medicines Health Authorities in each country.

### Trial details

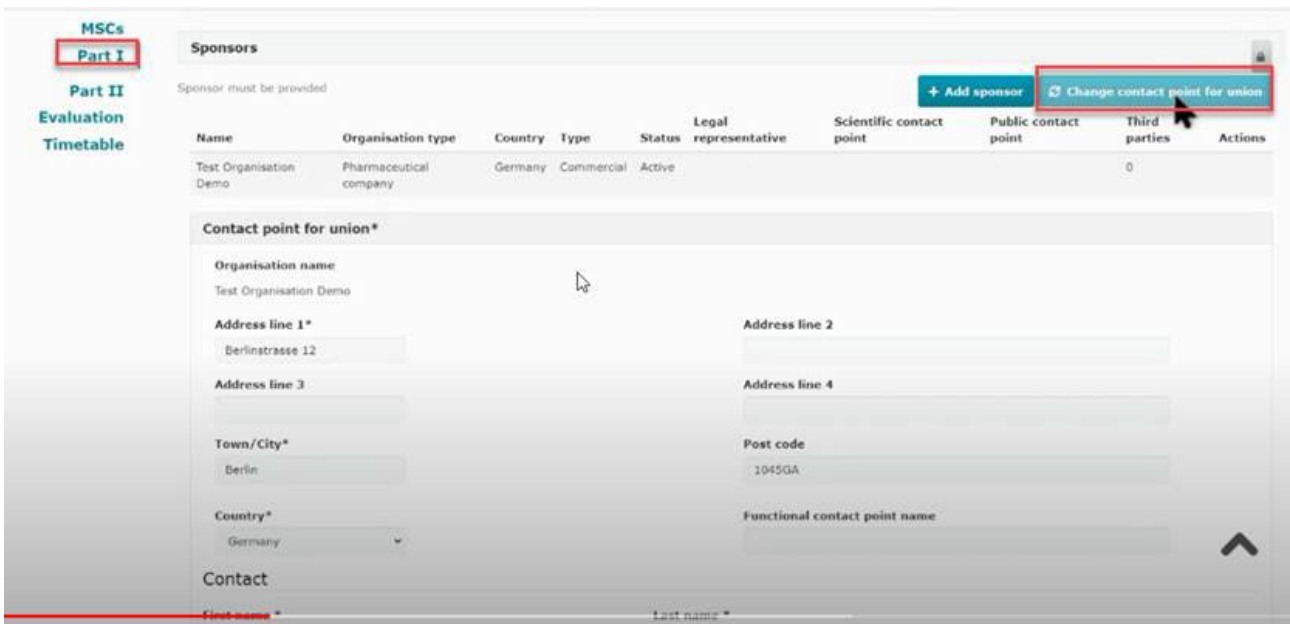
Medical condition, trial objective, inclusion- and exclusion criteria, end points, trial duration, population of trial subjects and upload of protocol.



For the main objective you can choose several “trial scopes” that are relevant for the trial.

Sponsor details

Includes sponsor information which was added when the application was first created.



The screenshot shows the 'Contact point for union' form in the CTIS system. The form is divided into two main sections: 'Contact point for union\*' and 'Contact'. The 'Contact point for union\*' section includes fields for Organisation name, Address line 1-4, Town/City, Country, Post code, and Functional contact point name. The 'Contact' section includes fields for First name, Last name, Phone, and Email. A red box highlights the 'Contact' section.

Click on the sponsor line and add:

- The legal representative (an EU contact that only need to be added if sponsor is located outside EU),
- Scientific contact point and public contact point (must be added for all trials and can be the same person) – The organization (including its email address) where the general public may obtain information about the clinical trial - in academic/non-commercial trials this person will often be the sponsor contact point (the contact point for union).
- Contact point for union – this is the **sponsor representative from the sponsor organisation**. This contact is used by the Union in case of required **contact to the sponsor** - in academic/non-commercial trials this person will often be the same as the scientific contact point.
- Third party (only if tasks or functions in the trial have been delegated to third parties). This is e.g. monitoring (the GCP unit) or laboratory facilities. If the third parties are not already registered in OMS, they can also be registered directly in CTIS without the need to register them in OMS (please refer to section 2.7).
- **To search for a third party in OMS you need to use the organization number (ORG) or location number (LOC) – it is not possible to search for the GCP-unit or a specific laboratory facility.**

**Only the coordinating GCP unit in Denmark needs to be added as third party.**

The organisation numbers (ORG) and location numbers (LOC) for the three Danish GCP units are:

GCP-enheden ved Københavns Universitetshospital:

ORG-100028217

Frederiksberg Hospital

**LOC-100045259**

GCP-enheden ved Odense Universitetshospital

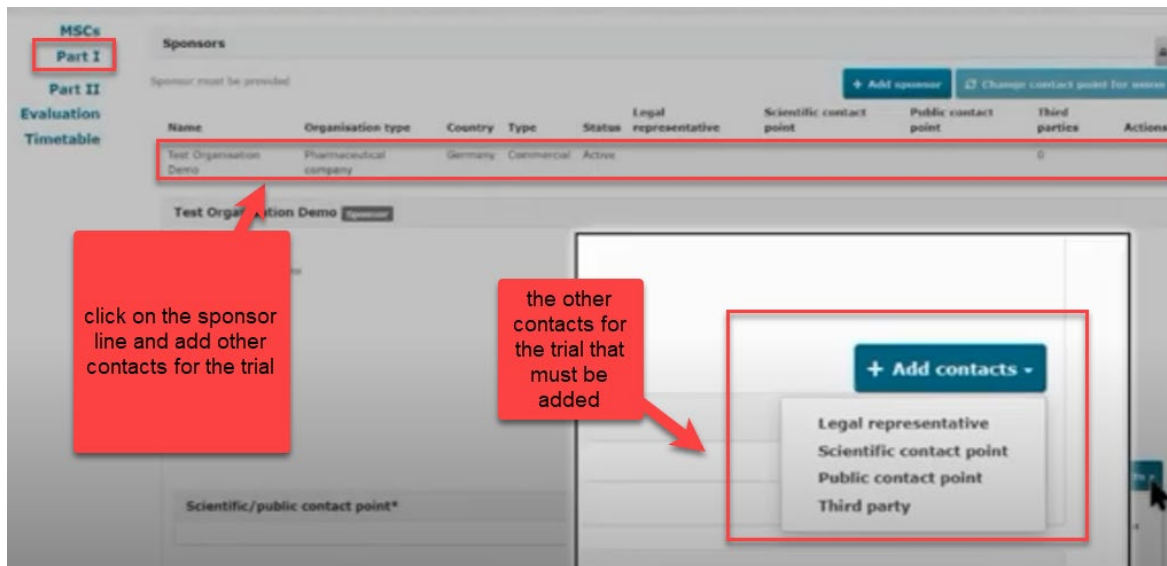
ORG-100007716

Odense University Hospital

**LOC-100053630**

GCP-enheden ved Aalborg og Aarhus Universitetshospitaler  
ORG-100028380  
Aarhus Universitet  
Institut for Klinisk Medicin  
Palle Juul-Jensens Boulevard 11  
**LOC-100079923**

**When adding a third party remember to update information about the third party (duties, phone number and email) using the pencil.**



### Product details

Information on the medicinal products used in the trial must be added. If the products has a marketing authorisation you need to click on “Add”. Select the role (e.g. test/comparator) of the product. It is mandatory to have at least one test product (investigational medicinal product (IMP)) in the application.

An authorised product or active substance can be added by searching per product details, active substance, or ATC code, as applicable.

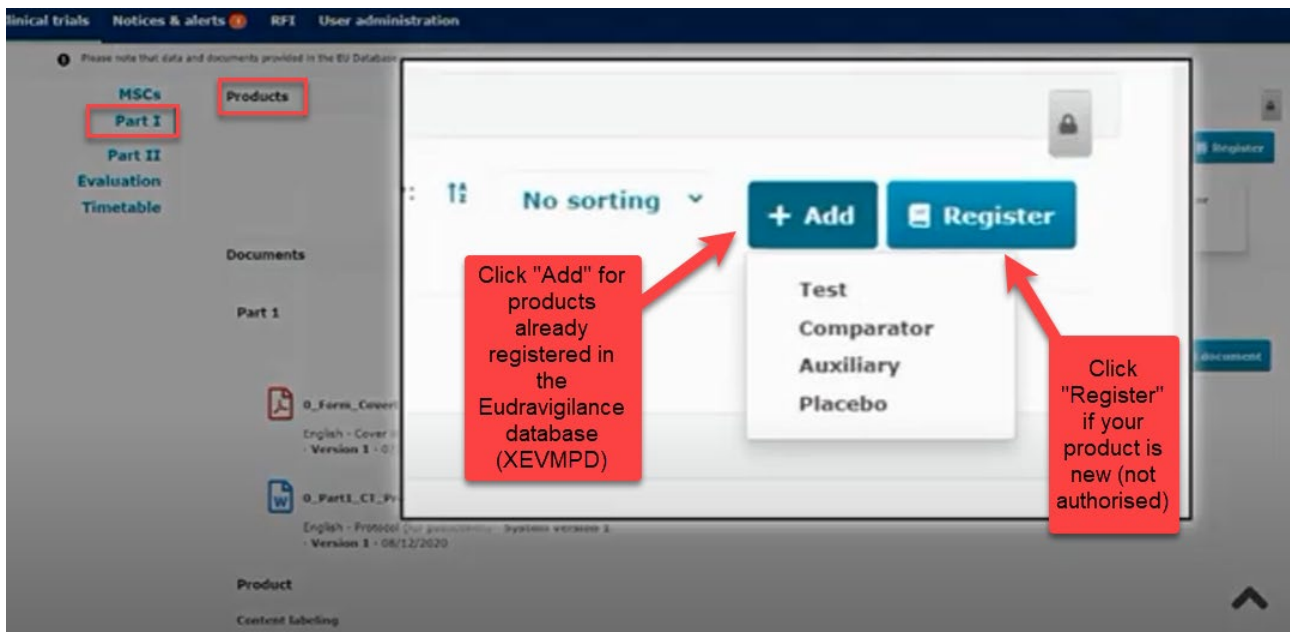
Non authorised medicinal products must now be registered in the Extended Eudravigilance Medicinal Product Dictionary (XEVMPPD), if not already done. For IMPs not registered in XEVMPPD there is no EU MP number. Please contact the manufacturer (e.g. pharmacy) regarding registration of the product in the XEVMPPD database.

All medicinal products that are marketed in EU are registered in XEVMPPD and can therefore be found in CTIS. Blinding, including re-encapsulation and re-packaging, of a marketed medicinal product does not need to be re-registered in XEVMPPD. You can also read more about the registration in XEVMPPD at the [DKMA homepage](#) (in Danish only).

### Placebo

If the IMP is a placebo, the information requirements shall be limited to quality data. No additional documentation is required if the placebo has the same composition as the tested IMP (except the active substance), is manufactured by the same manufacturer, and is not sterile.





In the section “Investigator brochure for the medicinal product” either the Investigators Brochure (IB) or the SmPC must be uploaded. The labelling must only be uploaded if the IMP has a special label.

If you scroll down to the end you see all the uploaded documents for Part I.

## 2.6 Fill in the Part II section

**Video on this topic in EMA training module 10:**

[Training video: Fill in the Part II section](#)

Part II: Individual information for each country, mainly to be assessed by the Ethics Committees in each country. Local documents from each country needs to be uploaded.

The screenshot shows the 'User administration' section of the CTIS interface. The 'Trial sites' table is highlighted with a red box. A red callout box points to the '+ Add site' button, stating 'Trial sites for each country can be added'. Another red callout box points to the 'Part II' menu item, stating 'In this section you need to upload the documents for part II'. A third red callout box points to the 'All documents' section in the 'Documents' list, stating 'It is possible to upload all documents for part II in the section "All documents"'. The table below shows a single trial site entry.

Organisation ID	Organisation name	Site location	Site street address	Site city	Site post code	Site country	Title	First name	Last name	Department	Phone	Email	Actions
8285	Medizinische Universität Innsbruck	Schopfstrase 41, Wilten	Schopfstrase 41	Innsbruck	6020	Austria	Dr.	First	Last	Chest Clinic	42342424	flast@email.com	[Edit] [Delete]

Documents listed and uploaded in chronological order is recommended in the section "All documents".

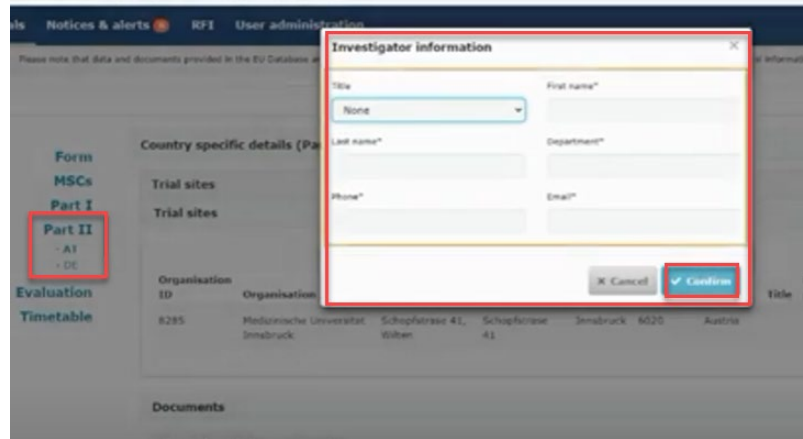
Trial sites must be added: Name, address and e-mail of trial sites and principal investigators at the trial sites.

*Please note: The first Danish site (Investigator) listed will be appointed National Coordinating Investigator in the Danish database "Nationalt Forsøgsoverblik" and so be responsible for validation and enrichment of source data in the database from the approving bodies.*

Be aware not to include personal information (e.g. CPR numbers, private addresses and telephone numbers) in investigators CV.

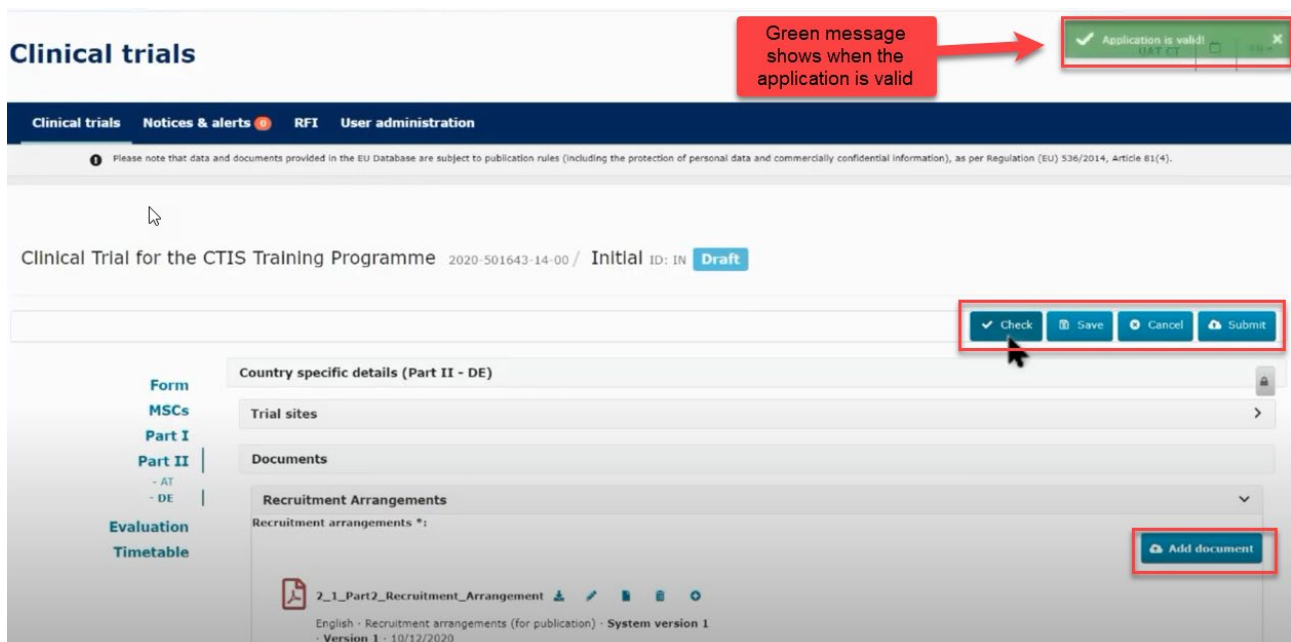
The name and address of the university/hospital organisation must be registered in OMS/CTIS before you can search and add the organisation (site) to the application form. If the specific address of investigator location, is not already registered in OMS or CTIS you can add the site – please refer to section 2.7.

When the organisation is found or registered in CTIS, the details of the principal investigator at each site must be added (first and last name, department, email address, phone).

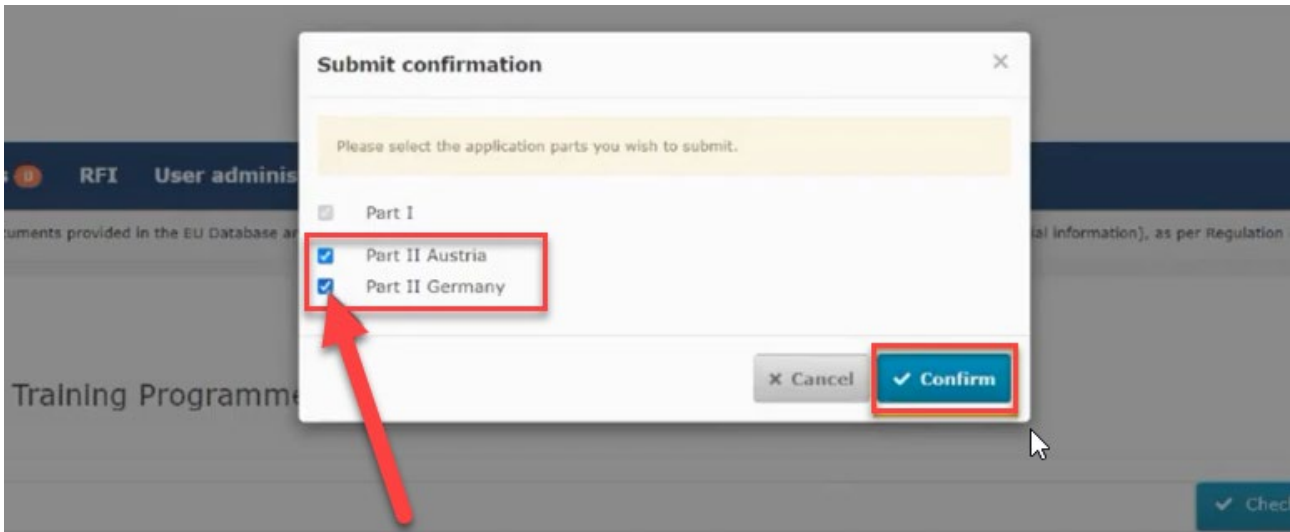


Supporting documents: Upload documents in each separate section or upload all the documents in the section “All documents” and specify in the document title what the document contains.

Click on the “Save” button to save all uploaded documents and click on the “Check” to see if any documents or information are missing. The green message shows when the application is valid.



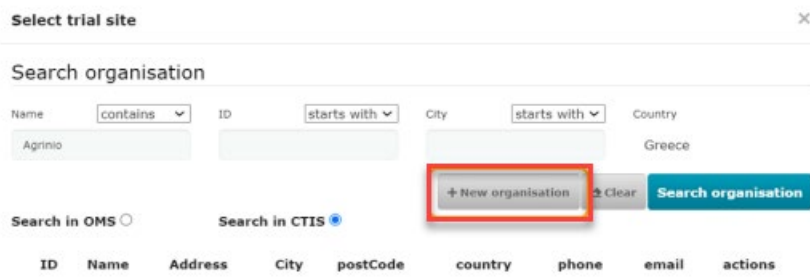
Remember to upload the Part II information relevant for each country. Part I is always included by default in the submission for all countries.



## 2.7 Site and third party registration directly in CTIS

Sites and third parties can also be registered directly in CTIS without the need to register them in OMS.

Organisations created locally in CTIS behave and function in the same way as the ones sourced from OMS and can be searched and selected once they have been registered in CTIS.



If users do not find the site in CTIS (red message will be displayed on the upper right corner), or if it is not listed in the search results, they can create the site in CTIS by clicking the button 'New Organisation', which will now appear enabled.

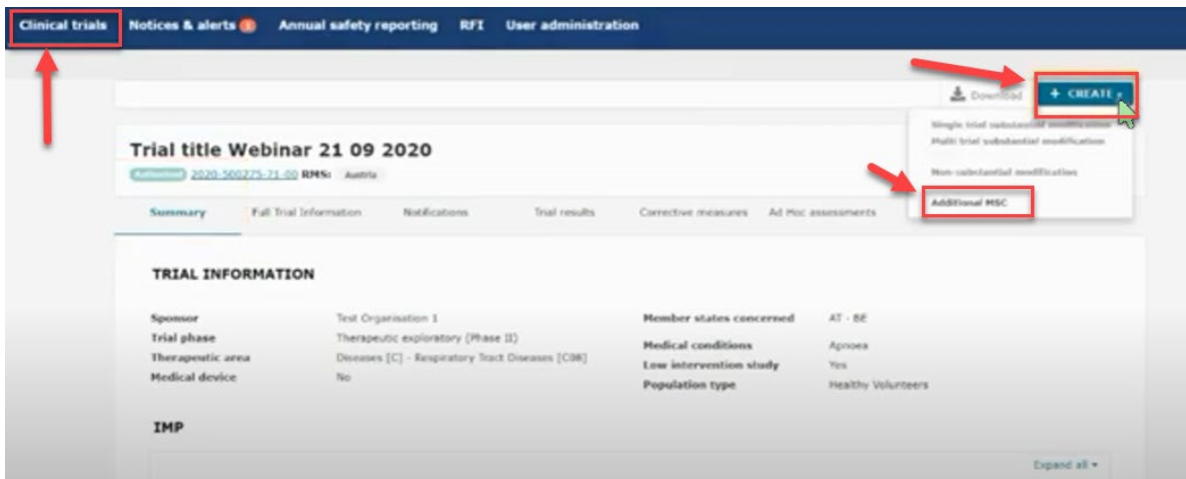
For more details of site registration in CTIS, please refer to [EMA module 03 step by step guide](#).

## 2.8 How to submit an additional member state concerned (MSC) application (add a new country)

**Video on this topic in EMA training module 10:**

[Training Video: How to submit an additional MSC application in the CTIS Sponsor workspace](#)

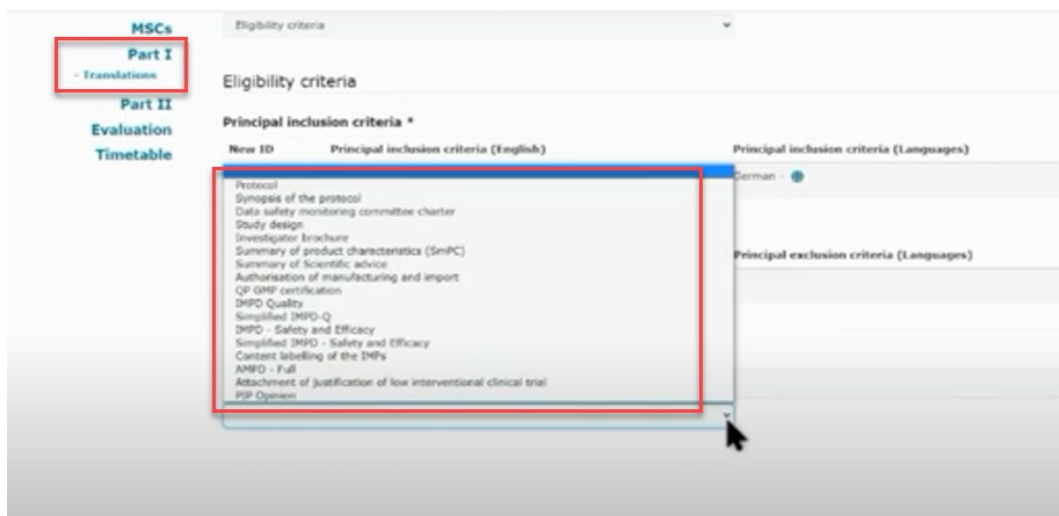
To add a new member state (MSC) to an already approved application. In the page of the authorised clinical trial click on the "create" button and choose "Additional MSC".



In the next pop-up window you can select one or several MSCs to add on the same time and specify for each country the number of subjects. Each application will be assessed individually by the country that has received the new application.

In the Form section a new cover letter must be uploaded for each added MSC.

In the Part I section you can provide translations if required by the new MSC. If you need to upload translations for documents you can choose the document type on a list and thereafter upload the new document and add the language.



In the Part II you can add the site details for the new MSC.

## 2.9 Withdrawal of an application

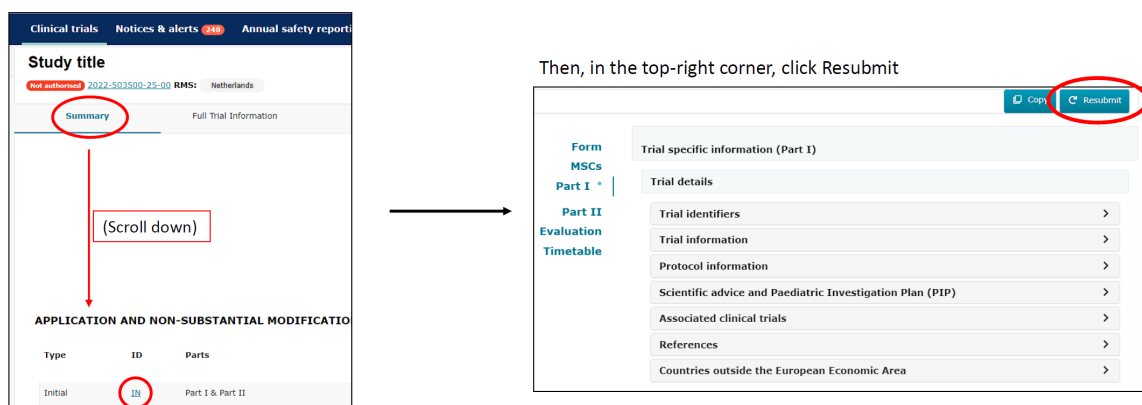
After opening the initial trial application which is under evaluation, select the “withdraw” button. A justification for the withdrawal should be provided.



## 2.10 Resubmission of an application

### Resubmission of a trial

CT applications can lapse (e.g. when the sponsor misses a response due date), be withdrawn by the sponsor, or rejected by the authorities. Lapsed, withdrawn and rejected CT applications can be resubmitted.  
On the CT page, in the Summary tab, scroll down to the application section. Click the application you want to resubmit: IN = initial application



The documents of the original submission will be copied to the resubmission. Documents can be replaced if necessary (e.g. cover letter). Please note: the version and date of all documents is reset to v1 and today, so click Edit (pencil icon) to enter the correct version and date for all documents. The resubmission will keep the original CT-number, but ending with -01.

## 3 Validation, Request for Further Information (RFI) and Authorisation

### 3.1 How to access and view a request for further information (RFI)

**Videos on this topic in EMA training module 11:**

[Training Video: How to access and view a request for further information \(RFI\) in CTIS \(Sponsors\)](#)

**Info box:**

Please be aware to regularly check for Request for Information (RFI) from the authorities **in CTIS**. It is not possible to receive any mails or reminders in your mail box.

RFI: Questions from authorities to sponsor.

Sponsor must check for Request for Information (RFI) from the authorities during both validation and assessment. As some RFIs can have a very short deadline for responding, the GCP units recommend that sponsors or delegated personal check for RFI on a daily basis.

**Info box:**

In case the sponsor does not respond to a RFI before the given deadline, it will cause the lapse of the application - there is no second change. RFI must be answered within the specified deadline for each RFI. Sponsors do only have one change to answer each RFI. When sponsor submits the answer to RFI, all questions from the authorities must be answered.

If the application is rejected, use the “re-submission”.

**If in doubt about anything – call the Danish Medicines Agency or EC before submitting the answer to the RFI.**

A timetable (see section 3.4) for estimated timelines will be generated and available in CTIS for each CTA, but it is important for sponsors to notice that the workflow in CTIS is dynamic. This means that the timelines shown in CTIS correspond to the maximum deadlines foreseen for each task/action. If a task/action is completed before its deadline, the corresponding deadlines for the following tasks/actions are recalculated.

In the sponsors workspace you will be able to see incoming RFIs in the “Notices and alerts” tab.

You can access the RFI by clicking on each of the alerts. The RFI can also be accessed from the RFI tab next to the “Notices and alerts” tab, this is a more direct path to respond to each RFI.

It is possible to download the RFI’s – see section 3.7

The screenshot shows the CTIS interface with the following elements:

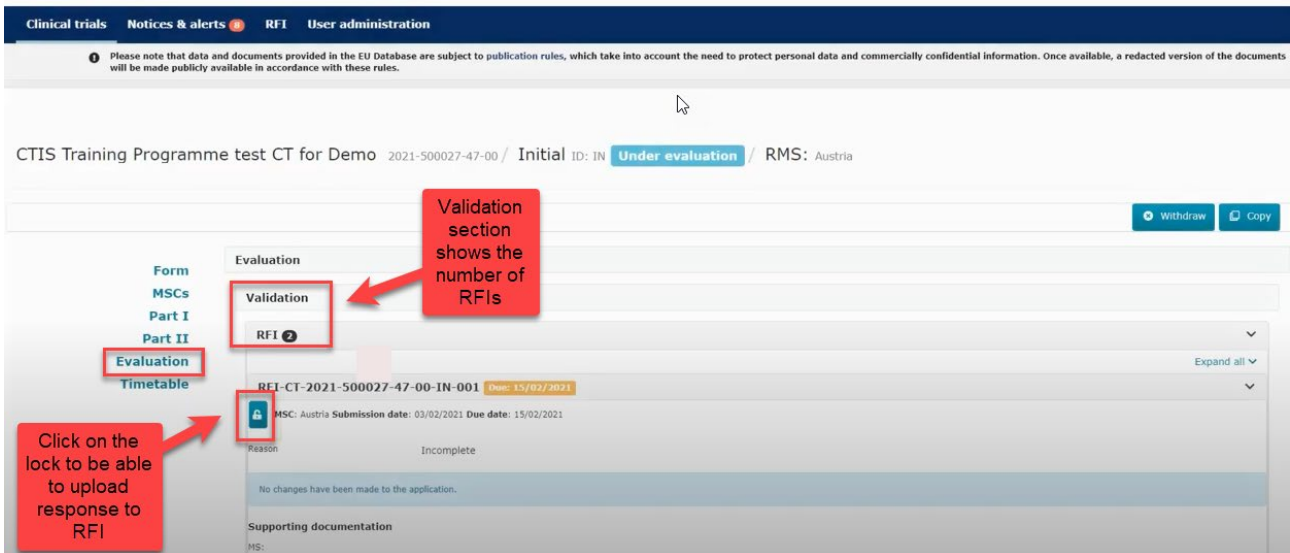
- Navigation tabs: Clinical trials, Notices & alerts (with a notification icon), RFI, and User administration.
- Search bar: "Enter EU CT ID or ASR ID (Business Keys) or use advanced search." with a SEARCH button and an Advanced Search dropdown.
- Table of alerts:

Alert	RFI sent to sponsor	Ref number	Source type	Evaluation process	Received	IMP	RMS	Sponsor
An RFI has been sent by Austria for the Initial application, Validation .		2021-500027-47-00	Initial	Validation	03/02/2021	Paracetamol Tablets 500mg	Austria	Test Organisation Demo
An RFI has been sent by Austria for the Initial application, Validation .		2021-500027-47-00	Initial	Validation	03/02/2021	Paracetamol Tablets 500mg	Austria	Test Organisation Demo

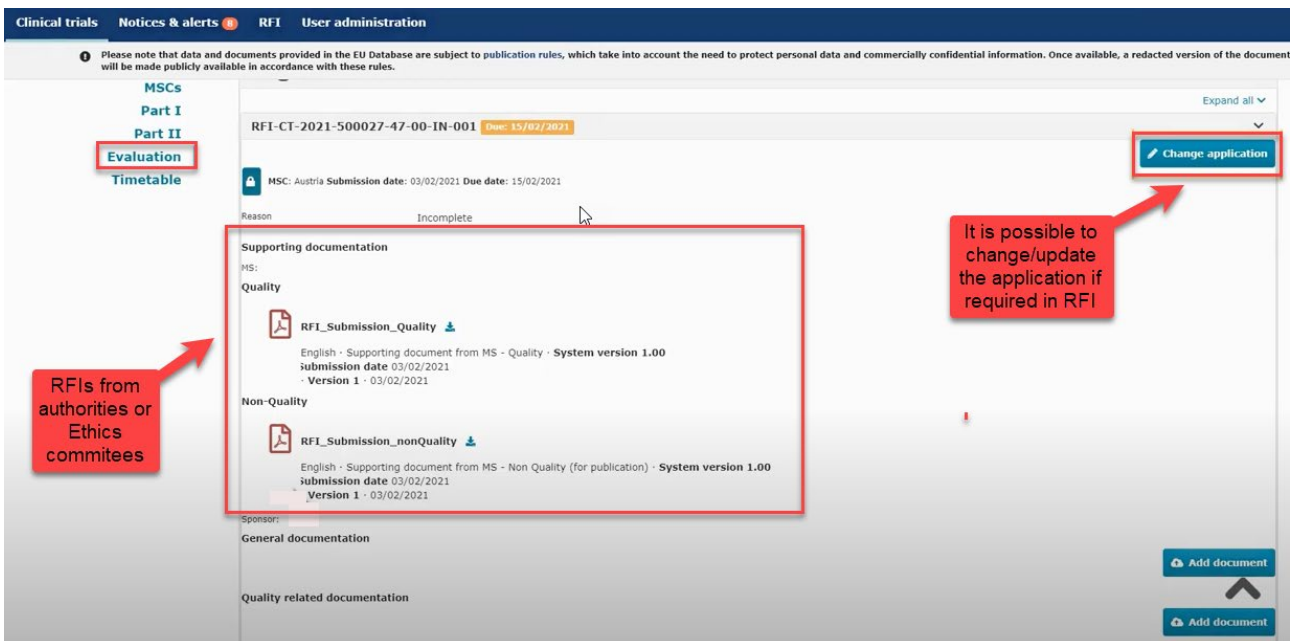
Every single RFI must be opened by clicking on ‘RFI- CT-xxxx-xxxxxx-xx-xx-IN-001 IN’ (black text):

In most cases there will be several RFIs and often in both Part I and Part II. The due date for responding to each RFI is stated in “Due” column in the RFI tab.

Click on the RFI and you will be redirected to the “Evaluation” section where the Request for further information (RFI) is shown.



When you have clicked on the padlock button you can see the documents that the authorities have attached to the RFI. The RFI can be related to “quality” or “non quality”.



In the “Add document” tab you can upload supporting documentation to the RFI. If the RFI requires, you must as well click on the “Change application” and then change information in documents that have previously been uploaded or entered for the CTA. Be aware that besides responding to each RFI, changes to



the CTA is most often required as revised documents like for example an edited protocol with a new version must be uploaded.

Please remember to upload a protocol with track changes, please refer to the info-box in section 2.4 to see how to upload a document “not for publication”.

### 3.2 How to upload documents into CTIS in response to an RFI: change application

For any changes to the application (documents or data) requested in the RFI. E.g. missing documents requested during validation, requests to modify document title/date/version during validation, or a new protocol version requested during assessment.

Optional, only for documents containing the response to this specific consideration. If the consideration requests a missing or updated document, do not upload it here, but instead use “Change application”!

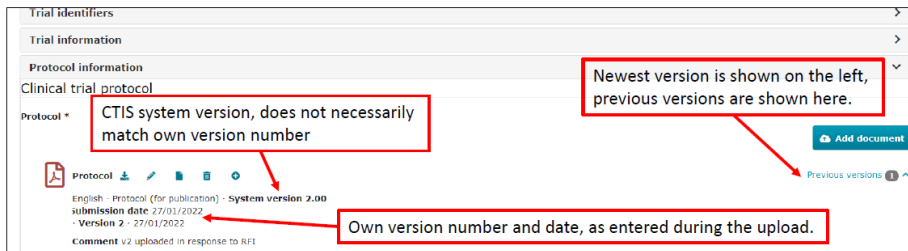
Clicking ‘Change application’ and confirming it, leads you back to the dossier, where documents can be added similarly to the initial submission. Click the lock and navigate to the location of the dossier where the change should be made.

**Update:** for uploading a new version of an existing document, e.g. protocol v2 with changes requested by the MS. You are asked to enter the version number and date, but the document title in CTIS cannot be changed!

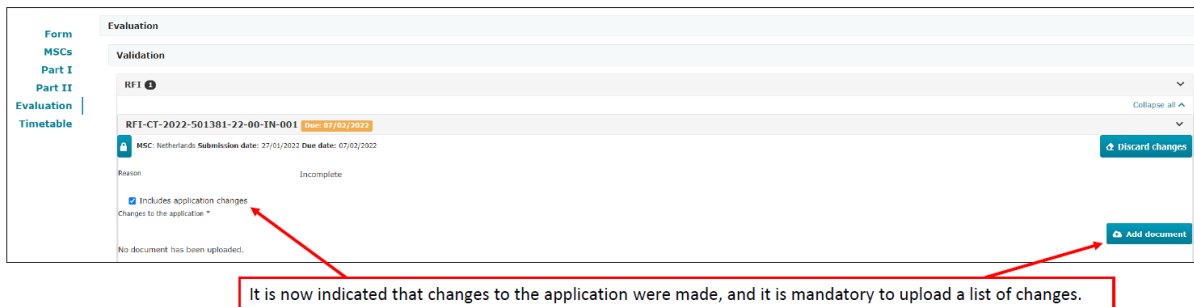
**Add document:** for adding fully new documents, e.g. missing documents requested by the MS during validation. The System version will be 1.00. Please use document codes and titles as explained earlier.

**Edit:** for changing the title, version or date of an existing document. If by mistake an uploaded document contained a version or date in its title, or the indicated version and/or date do not match the documents, then you will likely be asked to correct this in the Validation RFI.

Uploading a new version of an existing document using the Update-button, creates System Version 2.00



When finished adding new/changed documents to the application, navigate back to the RFI response.



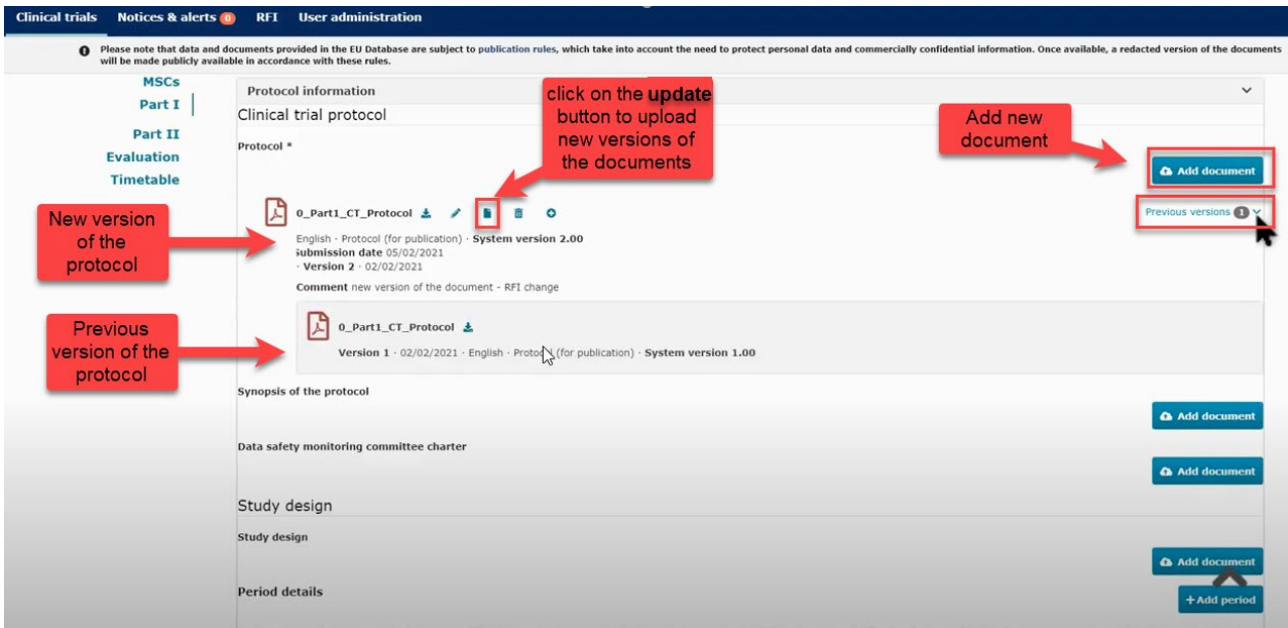
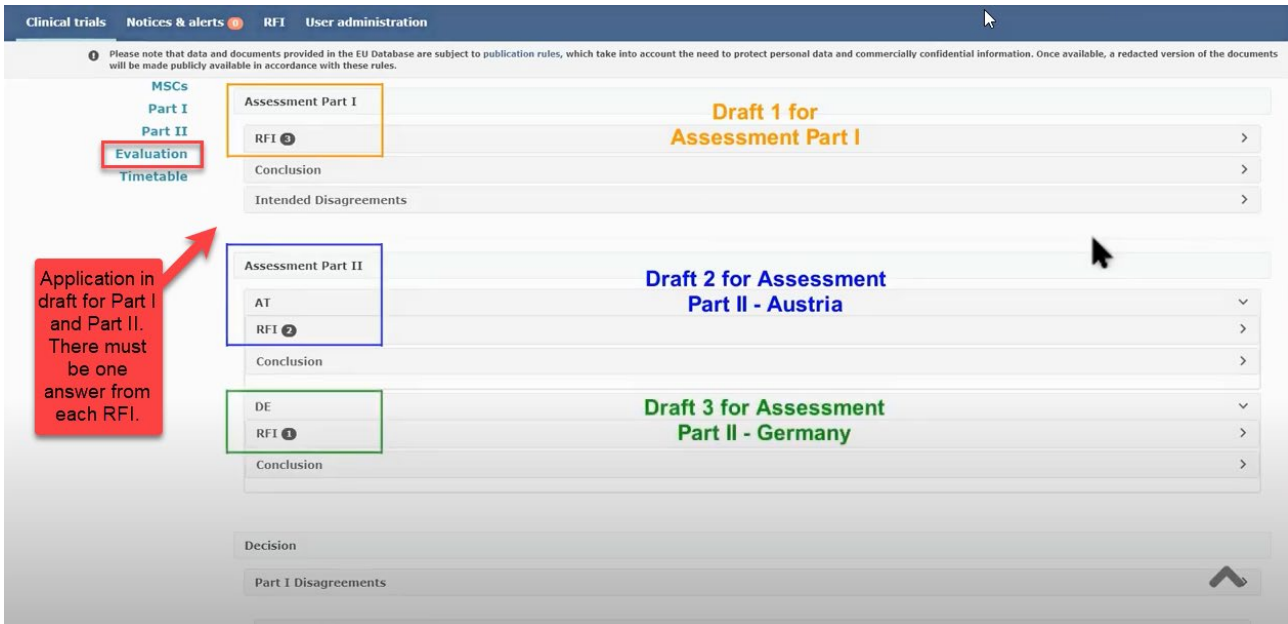
### 3.3 How to change a Clinical Trial Application as part of a RFI response (Sponsors)

**Videos on this topic in EMA training module 11:**

[Training Video: How to change a Clinical Trial Application as part of an RFI response \(Sponsors\)](#)

If the RFI requires changes to the application you must click on the change application button. Then a new version of the application has been drafted. Each RFI must be answered separately. You can make changes in the sections Form, Part I and Part II.

If there are RFIs from different countries it is necessary to make a draft application for each RFI. There can for example be one RFI for Part I and one RFI for Part II from each member state.

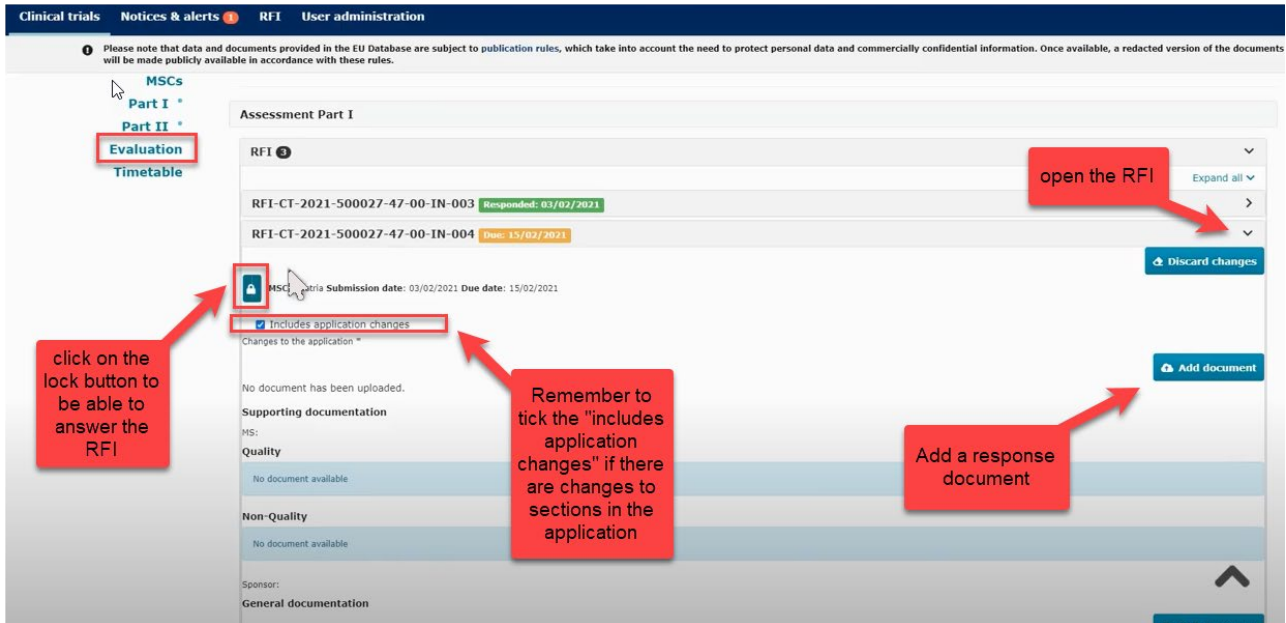


Remember to unlock each section when you are done answering the RFI and uploading new documents.

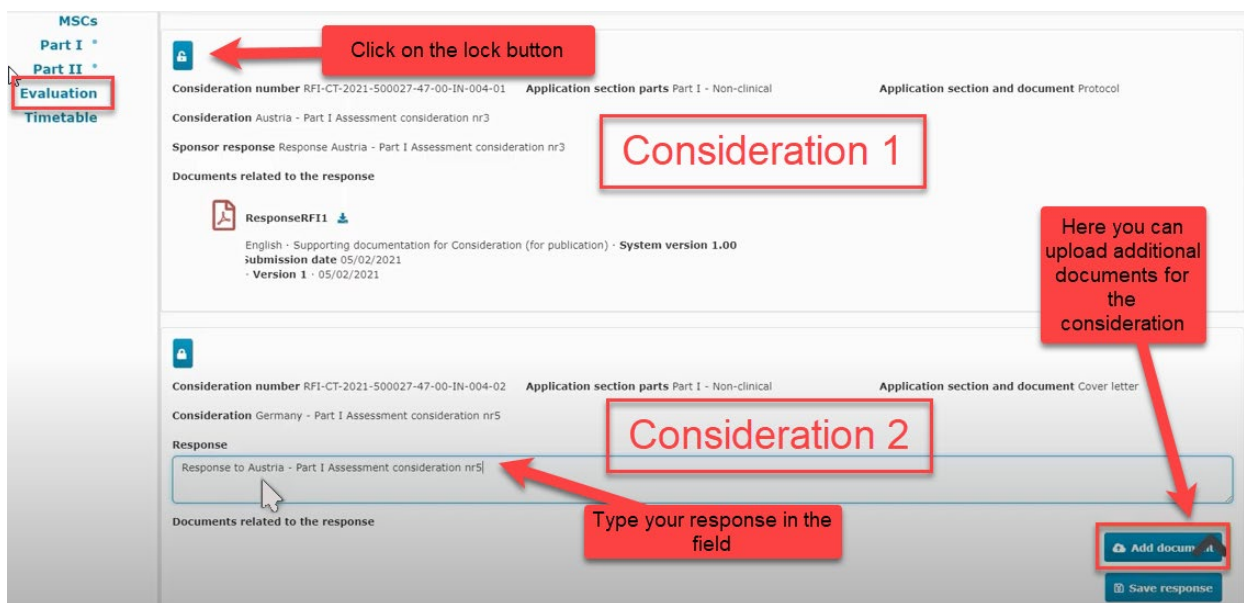
### 3.4 How to respond to RFI considerations and submit an RFI response

**Videos on this topic in EMA training module 11:**  
[Training Video: How to respond to RFI considerations and submit an RFI response \(Sponsors\)](#)

Sponsor must reply to each of the RFI received from the authorities. You can upload a response document that describes the changes to the application.



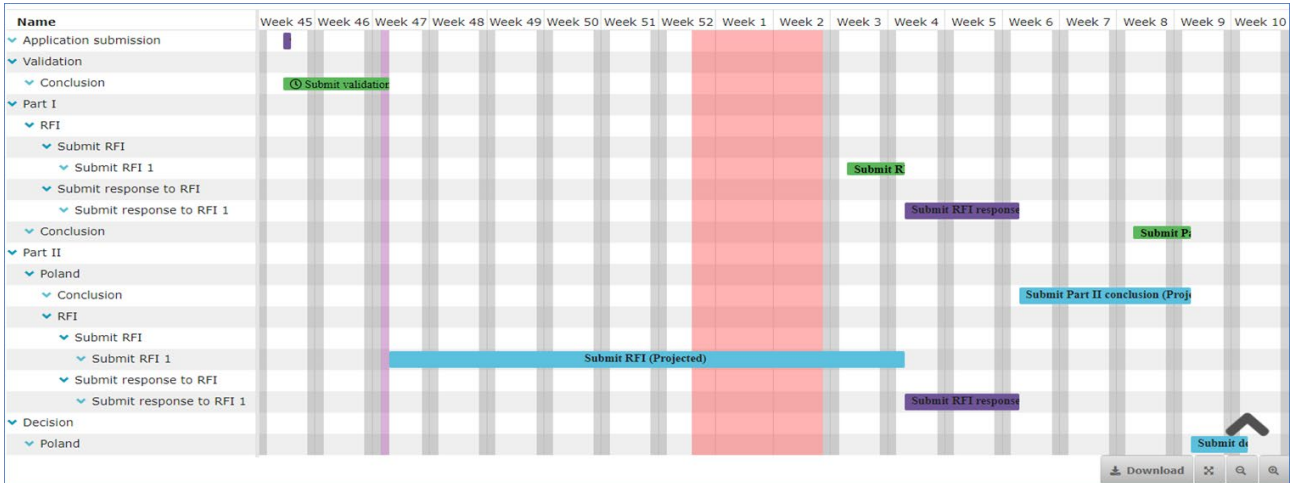
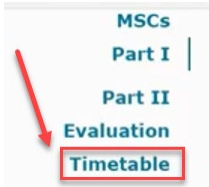
Below the RFI, there can be considerations which also must be answered. You can respond separately to each consideration.



The "Submit response" button will be active when the changes have been saved on "save response".

### 3.5 Timetable

In the timetable tab on the left side of the page in CTIS it shows the dates for the assessment schedule. All timelines will be in calendar days, however the due dates must never fall on a weekend or official holiday. A time period will not be shorter than two consecutive working days. It is important for sponsors to notice that the workflow in CTIS is **dynamic** which means that timelines can be changed.



The figure below shows an overview of the general timetable and deadlines for authorities and sponsors.

[CTIS Evaluation Timelines](#)

Process	Task	Timers for an initial application	Shorten the due date of the next workflow if completed earlier?
Validate Application	Submit validation conclusion	Day 10 + 15	Yes
Assess Part I	Submit part I conclusion	Day 45 + 31	Yes, if the assess part II is also completed earlier
Assess Part II	Submit part II conclusion	Day 45 + 31	Yes, if the assess part I is also completed earlier
Submit Decision	Submit decision	Day 5	-

**3.6 Authorisation**

**Info box:**  
The trial must include patients in the member state within 2 years from authorisation date in order to keep the trial authorised in that member state.

In the assessment overview at the “Evaluation” page it is shown which countries have authorised the trial.

The screenshot shows the CTIS interface with a navigation menu on the left containing 'MSCs', 'Part I', 'Part II', 'Evaluation' (highlighted with a red box), and 'Timetable'. The main content area is titled 'DECISION' and includes a 'Part I Disagreements' section. Below this is an 'ASSESSMENT OVERVIEW' table with columns for 'MSCs', 'Validation', 'Assessment Part I', 'Assessment Part II', 'Decision', and '+All'. A red arrow points to the 'Decision' column, which is also highlighted with a red box. The 'Decision' column shows 'Authorised (05/11/2020)' for both Austria and Germany.

MSCs	Validation	Assessment Part I	Assessment Part II	Decision	+All
AUSTRIA IMS	Valid (30/10/2020)	Acceptable (04/11/2020)	Acceptable (04/11/2020)	Authorised (05/11/2020)	+
GERMANY			Acceptable (05/11/2020)	Authorised (05/11/2020)	+

An overview of all documents and the approval date is shown at the end of "full trial information". Some countries do send "approval letters" but Denmark is not, and the approval date can only be seen in CTIS "Decision – authorised".

#### ALL DOCUMENTS

Section	Document type	Document Title	Document Version	Document Comment	Document Submission Date	System version	Language	Authorisation date	Application	Download
Part I	Cover letter (for publication)	Cover letter	1		17/01/2022	1.00	English	17/01/2022	INITIAL - IN	
Part I	Protocol (for publication)	Protocol for publication	1		17/01/2022	1.00	English	17/01/2022	INITIAL - IN	
Roles: Test Name: DENUBIL 250 mg/180 mg solución oral	Summary of Product Characteristics (SmPC) (for publication)	SmPC - NaCl 09 - Braun Melsungen DE	1		17/01/2022	1.00	English	17/01/2022	INITIAL - IN	
Part I	Content labelling of the IMPs (for publication)	Labelling	1		17/01/2022	1.00	English	17/01/2022	INITIAL - IN	
Part I	Compliance with Regulation (EU) 2016/679 (for publication)	Compliance with Reg 2016_679	1		17/01/2022	1.00	English	17/01/2022	INITIAL - IN	

### 3.7 How to find the “Report for the Application Evaluation Decision” in CTIS:

Go to front page -> ”Summary” -> 1 (”Download”) -> “Applications” -> mark "Initial" -> mark “Form, MSC, Part 1, Part 2 and Evaluation” select all -> mark “structured data in PDF”

Click the Start download button. Will be downloaded as a ZIP file.

Go to evaluation and then decision

The screenshot shows the CTIS interface for a trial named "TEST Poseidon". At the top right, there is a "Download" button with a red circle around it and a red arrow pointing to it. Below the trial name, there are tabs for "Summary", "Full Trial Information", "Notifications", "Trial results", "Corrective measures", "Ad Hoc assessments", and "Users". In the "Applications" table, the "Applications" header is circled in red. The table has columns for "Application type", "Application ID", "Member states concerned", "Application Part", "Submission date", and "Decision date". Below the table, there is a "Start Download" button. The "Contents for Download" section has two main areas: "Contents for Download:" and "Include the following:". Under "Contents for Download:", there are checkboxes for "Form", "MSC", "Part I", "Part II", "Select all", and "Denmark". Under "Include the following:", there are checkboxes for "Structured data in PDF\*" (checked) and "Documents\*" (unchecked). A note below says "\* these only include the latest version related to the application".

### How to find the “Report for the Application Evaluation Decision” in public space in CTIS:

Go to front page -> ”Summary” -> ”Download CT” -> Full Trial Information -> mark application type "Initial" -> Click download clinical trial -> Export file.

Will be downloaded as a ZIP file

About ▾ Search clinical trials and reports ▾ CTIS for sponsors CTIS for authorities Support ▾

🏠 Search clinical trials and reports > Search for clinical trials

Please select information you would like to download for clinical trial with EUCT Number: 2022-502250-14-00

▾ Trial Summary

Trial Summary will be included in the downloaded file

▾ Full Trial Information

Full Applications Information will be included in the downloaded file

Application type	Status	Member states concerned	Submission date	Decision date
▸ <input checked="" type="checkbox"/> INITIAL	Authorised	DK:Authorised, not started	13/01/2023	22/03/2023

▾ Attached documents

All attached documents will be included in the downloaded file

Zip file has been created. Click here to download: [Export file](#)

**How to see in CTIS how long the trial is approved:** Go to "Full trial information" -> "Trial details" -> "Trial information" -> "Trial duration".

In case of increased trial duration, the sponsor is expected to update the 'estimated end of trial date' field.

This is a non-substantial modification and require no approval from the authorities.

## Trial duration \*

**Estimated  
recruitment  
start date in  
EEA**

01/09/2022

**Estimated  
end of trial  
date in EEA**

01/09/2028

## 4 15 days notifications from start to end of trial

**Video on this topic in EMA training module 5:**

[Training Video: How to manage a CT in the CTIS sponsors workspace – Trial and recruitment periods notifications](#)

The **notification tab** can be found in each clinical trial in the sponsor workspace. Sponsors use the notification tab to inform each member state of important milestones in the clinical trial:



**Notifications that need to be submitted for every clinical trial:**

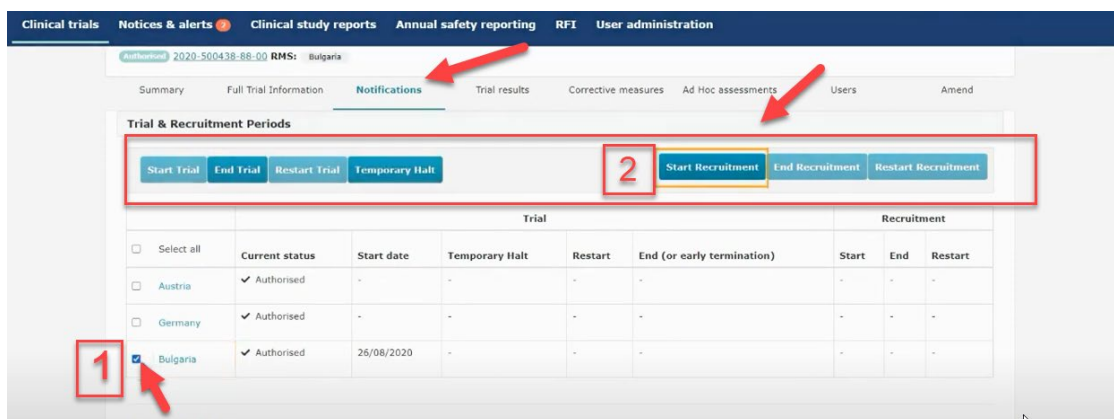
- **Start trial:** the first act of recruitment of a potential subject for a specific CT, unless defined differently in the protocol.
- **Start recruitment:** the first visit of the first subject. The date could be the same one as for start trial.
- **End recruitment:** act of not recruiting subjects anymore in an MSC.
- **End trial:** last visit of the last subject, or a later point in time as defined in the protocol.

**Notifications that need to be submitted only when the sponsor needs to interrupt a CT on specific grounds with a view to resuming it afterwards:**

- **Temporary halt:** An interruption not provided in the protocol of the conduct of a CT with the intention of the sponsor to resume it.
- **Restart trial:** The act of restarting the trial, after a temporary halt or after a suspension of the CT as part of a corrective measure by an MSC.
- **Restart recruitment:** The act of restarting the recruitment of subjects. The trial must have been restarted to be able to restart the recruitment.

The **deadline** for reporting these notifications in CTIS is **15 days**. The notifications should be made for each member state where the clinical trial is approved. The specific country must be selected and then click on the notification tab you want to enter.

All buttons found in the notification tab will be active once the clinical trial is authorized.

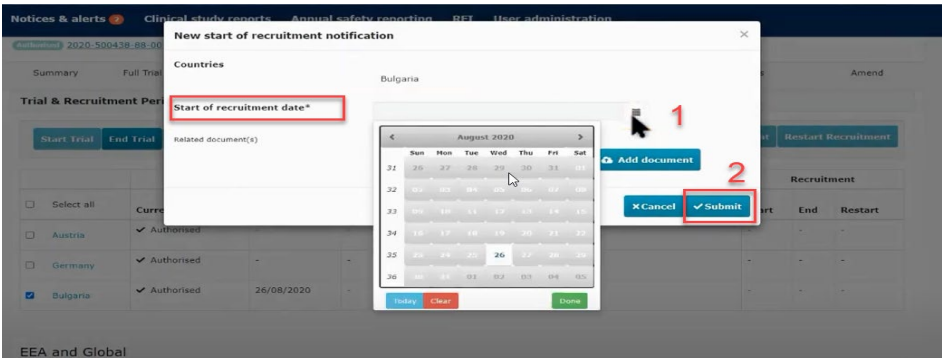


Select the specific country where you want to make a notification

Click on the notification tab you want to enter either **Start Trial, End Trial, Restart trial, Temporary Halt, Start recruitment, End recruitment or Restart recruitment.**

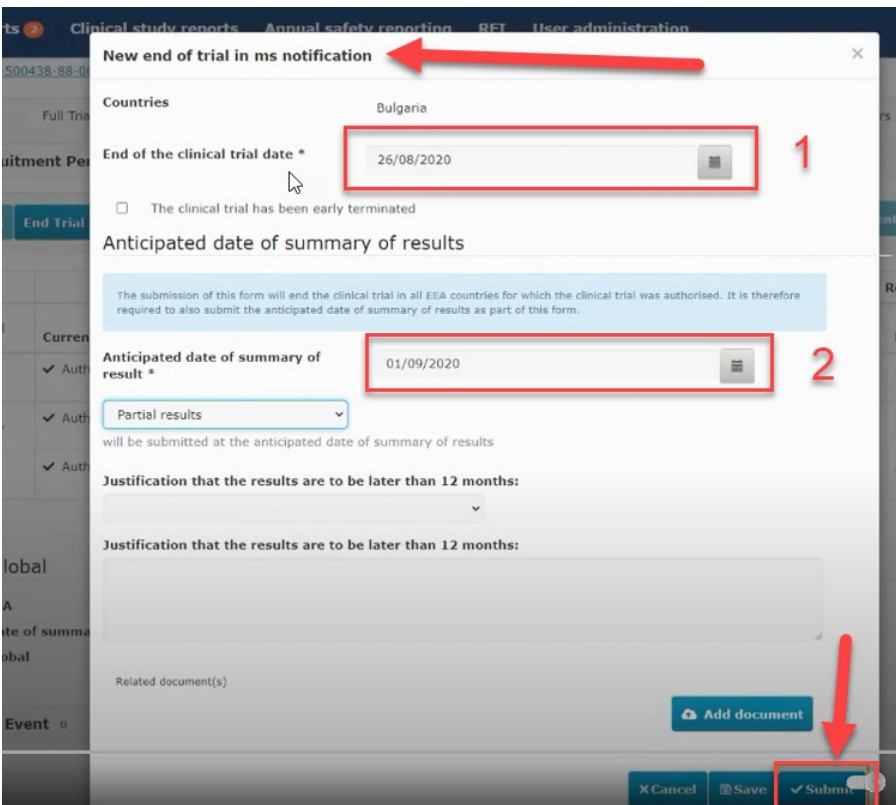
**Examples:**

**Start of recruitment notification at the latest 15 days after start:**



Choose the country where you want to notify about recruitment start. Enter the date where the recruitment will start and then click submit.

**End of trial notification at the latest 15 days after the trial ended:**



Enter the date where the clinical trial ended according to the protocol or if it was terminated early.

Enter the anticipated date of where the summary of results will be available.

By clicking on the country link you can go to the notification history for that specific country.

Each time you submit a notification a notice is created on the “notices & alerts” tab.

Ref number	Source type	Evaluation process	Received	IMP	RMS	Sponsor
2020-500438-88-00			26/08/2020	Paracetamol Tablets 500mg	Bulgaria	Test Organisation 1
2020-500438-88-00			26/08/2020	Paracetamol Tablets 500mg	Bulgaria	Test Organisation 1
2020-500438-88-00			26/08/2020	Paracetamol Tablets 500mg	Bulgaria	Test Organisation 1
2020-500438-88-00			26/08/2020	Paracetamol Tablets 500mg	Bulgaria	Test Organisation 1

**Info box:**

To be able to see the “**Annual safety reporting tab**” and to perform ASR related activities, the CT administrator should assign the “**ASR submitter role**” to him/herself.

Please refer to [The Danish GCP Units guide - Submission of Annual Safety Report \(ASR\) in CTIS](#) for more information.

## 5 How to create and submit a Substantial Modification (SM)

**Video on this topic in EMA training module 10:**

[Training Video: How to submit a substantial modification in the CTIS sponsor workspace](#)

There are three types of changes to a clinical trial:

1. Substantial Modification (SM)
2. Non Substantial Modifications (NSM)
3. 81.9 Non Substantial Modification (81.9 NSM)

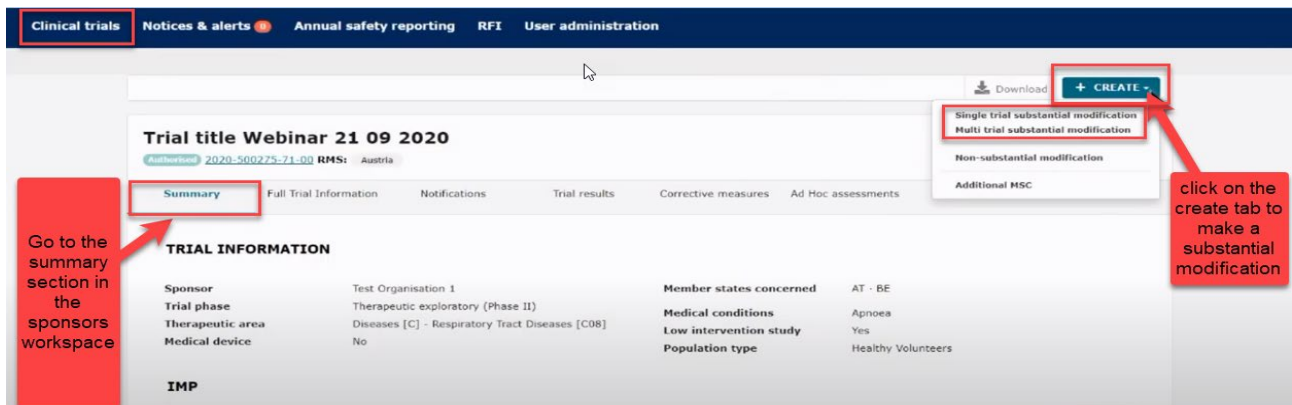
Classification of changes to ongoing trials can be found in [CTR Q&A, Annex IV](#): “Classification of changes to ongoing clinical trial”.

All non substantial changes, both 81.9 NSM and NSM, do not require an approval before implementation.

The 81.9 NSMs must be updated by sponsor regularly in CTIS during the trial period. These are changes that are relevant to the member states concerned.

Other NSMs must be updated in CTIS with next SM or latest at end of trial, if no SMs have been submitted meantime.

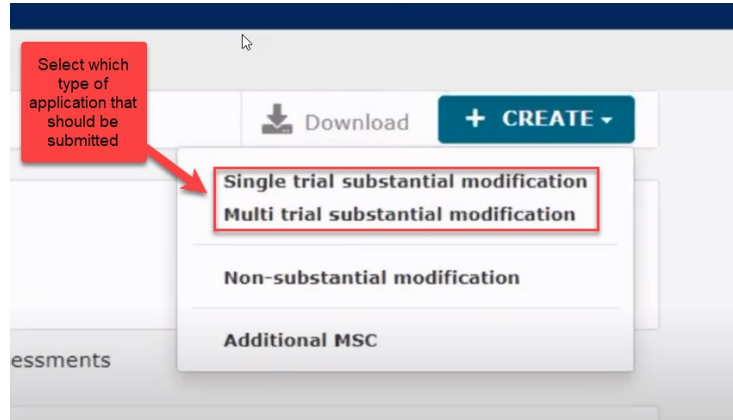
To create and submit a substantial modification after the clinical trial has been authorised, users can select the '+ CREATE' button in the sponsors workspace at the top-right corner of the Clinical Trial page.

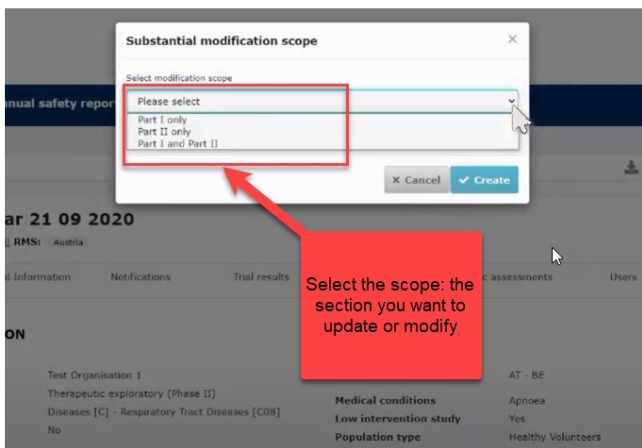


This will enable you to select which type of modification you want to submit:

Single trial substantial modification: to update information for *only one trial*.

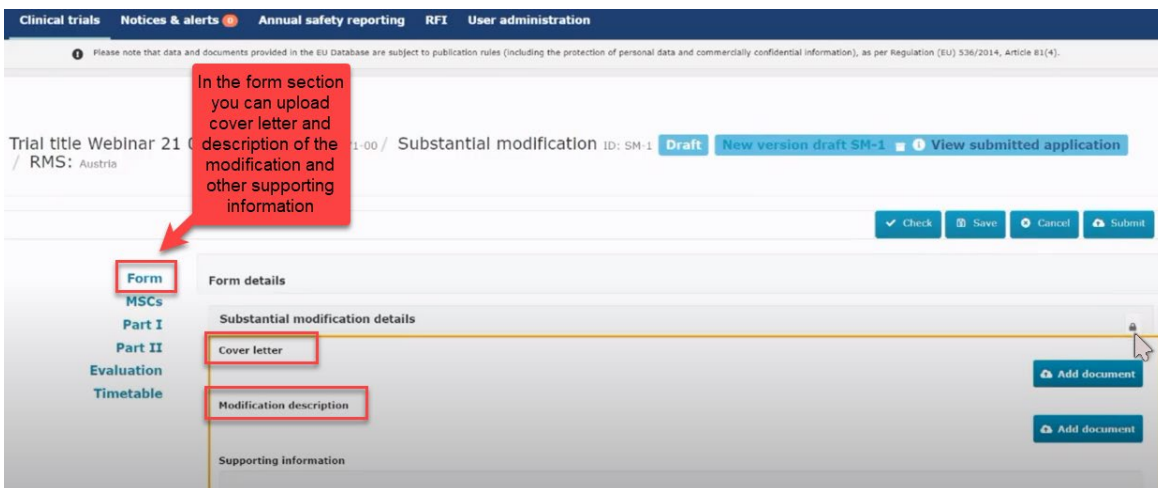
Multi trial substantial modification: to update information for trials that have the same investigational medicinal product (IMP) and the same sponsor. In this case it is possible to submit *a single application covering several trials*.



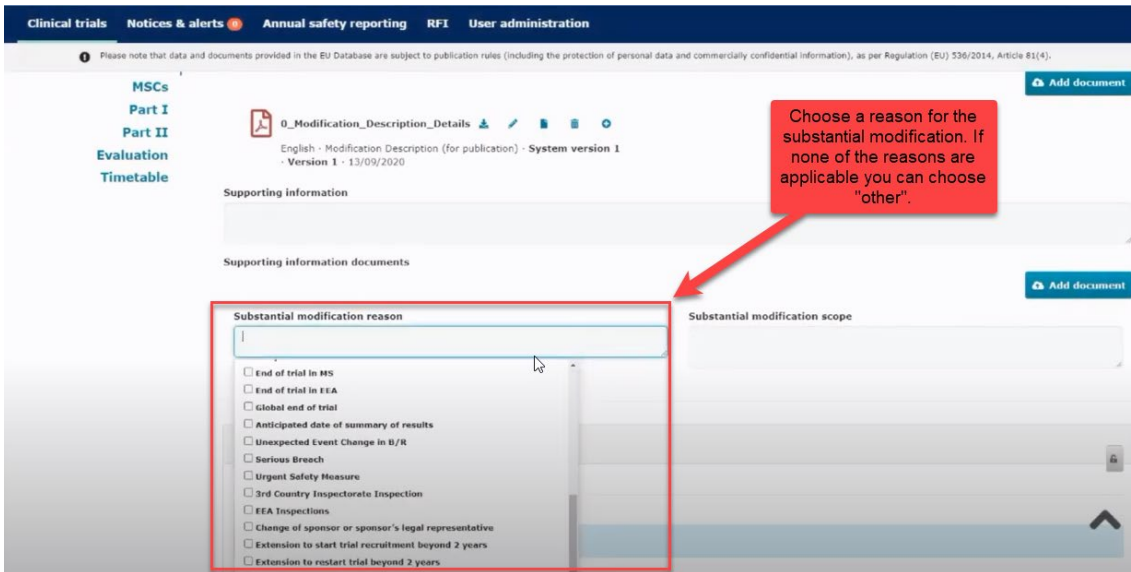


If you click on the **“Single trial substantial modification”** you will be redirected to a window where you need to enter the scope of the substantial modification. Thereby you will define the part which will be modified (Part I and/or II).

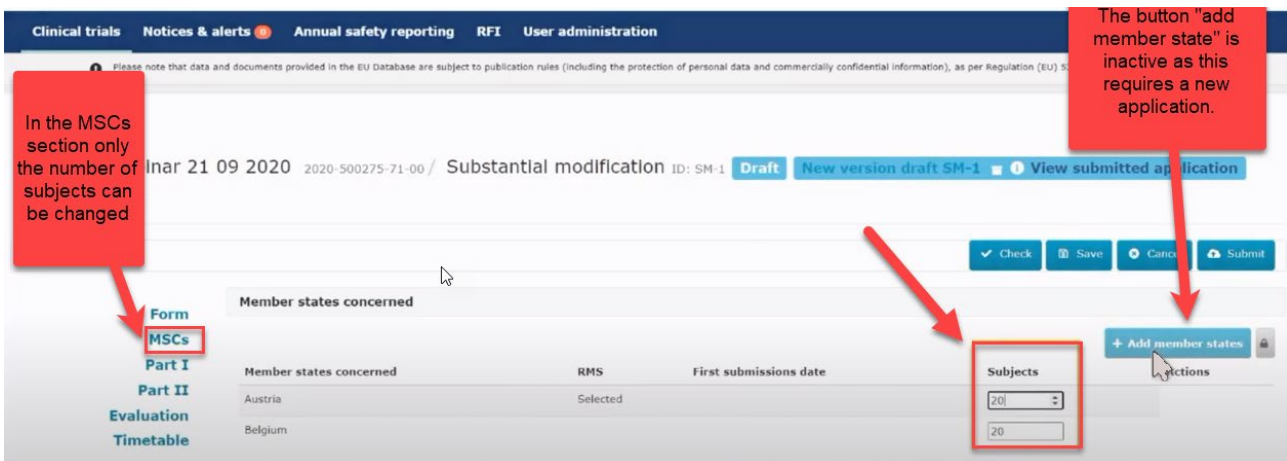
In the **“Form”** section, cover letter etc. should be uploaded and you can add details about the substantial modification.



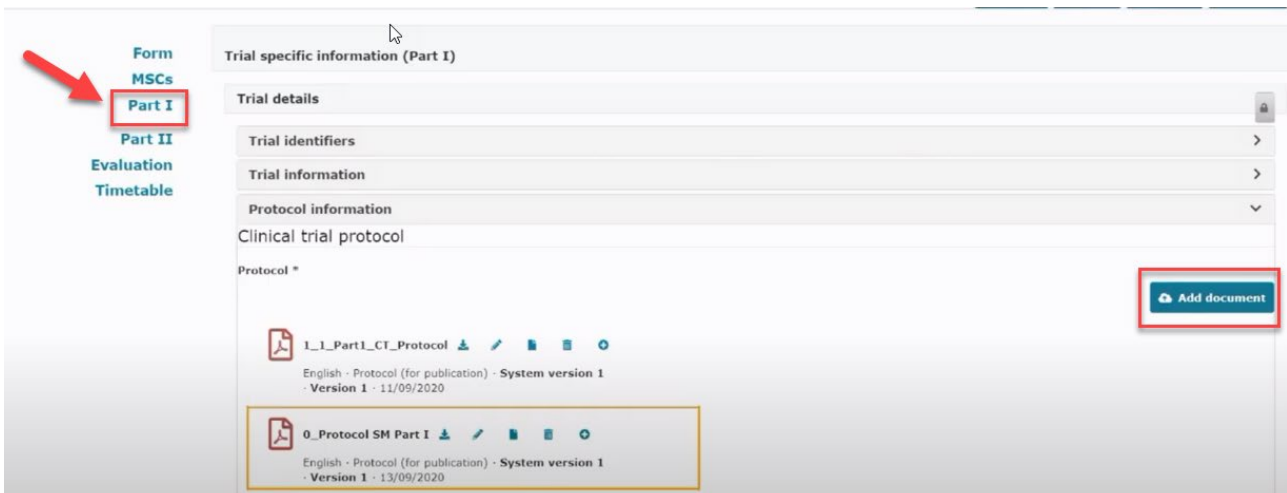
If you scroll down, the reason for the substantial modification must be added here.



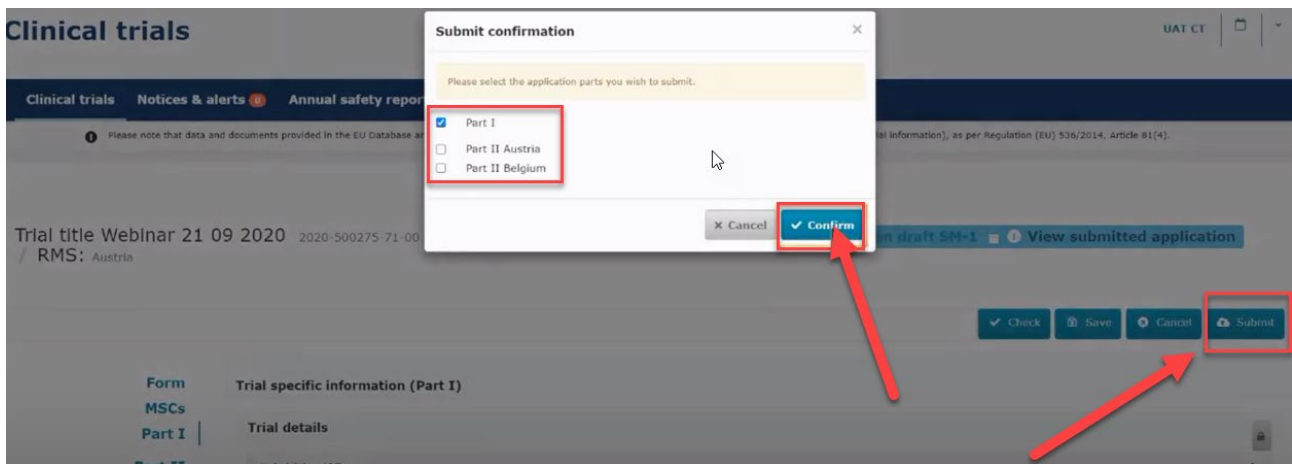
In the “MSCs section” only subject numbers (number of planned trial subject) can be modified.



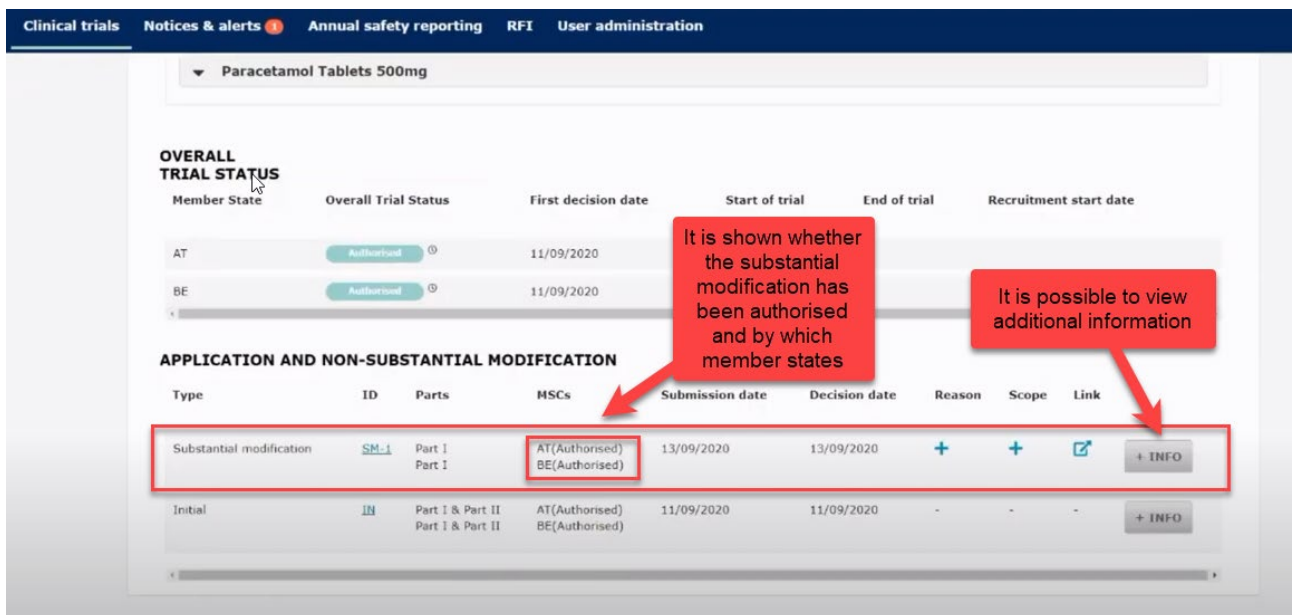
In the “Part I or Part II” section you can upload the relevant documents with changes.



When all data and documents have been modified and uploaded, click on “Submit”. Then select the parts of the application you want to submit and click on the “confirm” button.



In the Summary page you can scroll down and see the status of the substantial modification.



## 6 Summary of Results and Summary for Layperson

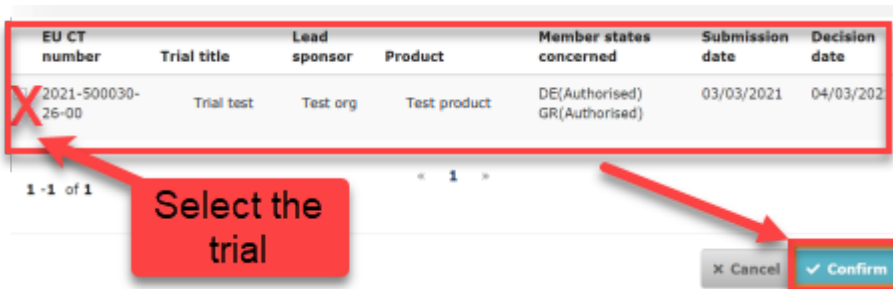
The sponsor shall submit a summary of the results of the Clinical Trial. The deadline for uploading the results in CTIS is 1 year after end of trial.

The content of the summary of results is set out in [Annex IV of the regulation](#). It shall be accompanied by a summary written in a manner that is understandable to laypersons. The content of lay person summary of results is described in [Annex V of Regulation](#).

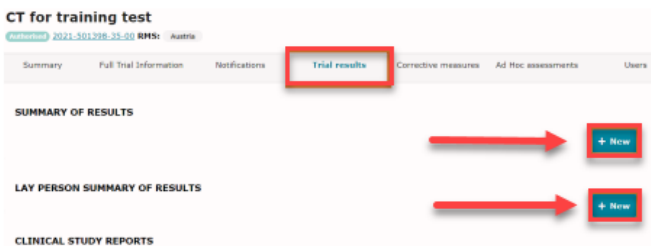
To submit the summary of results go to Clinical Trial page and search for the clinical trial by entering the “EU CT number” or use advanced search.



Select the trial from the results page and click on the 'Confirm' button.

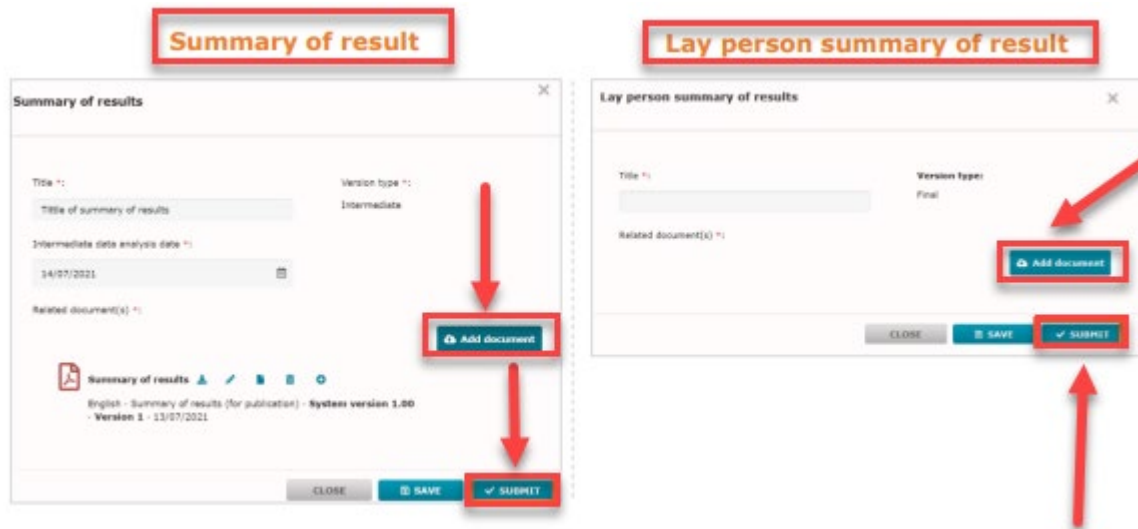


When the trial is selected a window will show where the “summary of results” and “layperson summary of results” can be uploaded.



Select the “Add document”. Then “Save” and “Submit”.





## 7 Changes log

Version 1.0

Version 1.2 Links corrected.

Version 1.3 Updated according to comments from users.

Version 1.4 Updated with new experiences from authorities and users and links corrected.

Version 1.5 Updated with information of resubmission and other small corrections.

Version 2.0 Updated section on how to respond to RFI, removal of section on how to create an EMA account, roles and responsibilities and ASR.

Version 2.1 Updated with information of sponsor, third party and site registration directly in CTIS, updated list of documents and templates and new links.

Version 2.2 Updated according to comments from users and how to find and download Report for evaluation decision in CTIS and in public space. Location number is updated for the GCP-unit in Aalborg and Aarhus.

Version 2.3 Added comment from Trial Nation regarding the first mentioned investigator in CTIS will be named "coordinating investigator" in the database Danish National Trial Overview (Nationalt Forsøgsoverblik).

Version 2.4 Further explanation about log in to CTIS