The guide to the Clinical Trials Information System (CTIS)

based on the guide made by Danish GCP-unit

29.12.2023

Content

Abbreviations

ASR = Annual Safety Report

AR = Assessment report

CT = Clinical Trial

CTA = Clinical Trial Application

CTIS = Clinical Trial information System

CTR= Clinical Trial Regulation

DLP=Data Lock Point

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 = Reference member states

RSI= Reference Safety Information

SM = Substantial modification

SmPC= Summary of Product Characteristics

SAE=Serious Adverse Event

SAR=Serious Adverse Reaction

Pictures used in the document are copied from EMA's materials and are publicly available.

1 Introduction

1.1 What is CTIS?

The Clinical Trials Regulation (Regulation (EU) No 536/2014) came into application 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 is taking place via a **Clinical Trial Information System (CTIS)**. CTIS is the **single entry point** for submitting clinical trial information in the EU, which is stored in the system. All communication including final decision from the authorities is 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.

- 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 start up, complete and maintain a clinical trial application (CTA) 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.

For more specific questions you are welcome to contact the Clinicaltrials at fimea.fi or EMA helpdesk or Fimea´s webpage.

This guidance is based on and can be used as a supplement to the following CTIS training guides from EMA:

- Clinical Trials Information System (CTIS): online modular training programme | European Medicines Agency (europa.eu)
    - How to create a CTA – see module 10 – 8 videos
- Clinical Trial Information System (CTIS) – Sponsor Handbook
- How to access CTIS: Step by step guide to access CTIS
- European Medicine Agency (EMA) QUESTIONS & ANSWERS (see section 2, 3 and 5)

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.

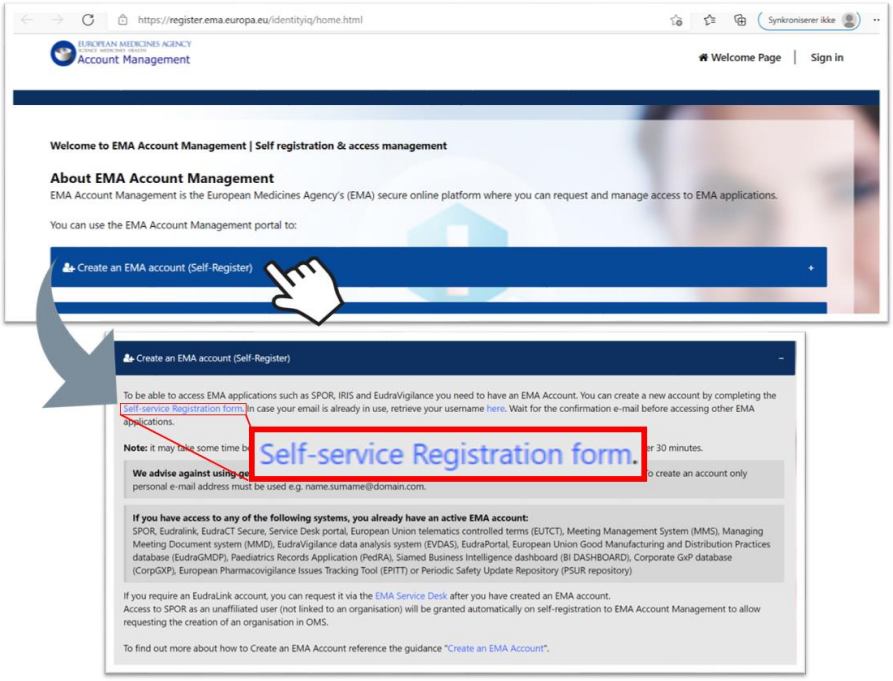
1.3 What is needed to work in the CTIS? How to get started

If you already have an EMA account and the address of sponsor is registered in OMS – please go to section 4 in this guideline.

In order to access the CTIS Sponsor workspace, a user will need to have an active EMA Account. If the user already uses other EMA applications (e.g. Eudralink, SPOR, IRIS, EudraVigilance, OMS or the EU Clinical Trials Database), the user already has an EMA Account and could access the CTIS Sponsor workspace using his/her existing EMA Account credentials. If the user does not have an active EMA Account, (s)he needs to create one, by self-registration. In addition, organisations must be registered in EMA's Organisation Management System (OMS).

2 How to create a new EMA Account

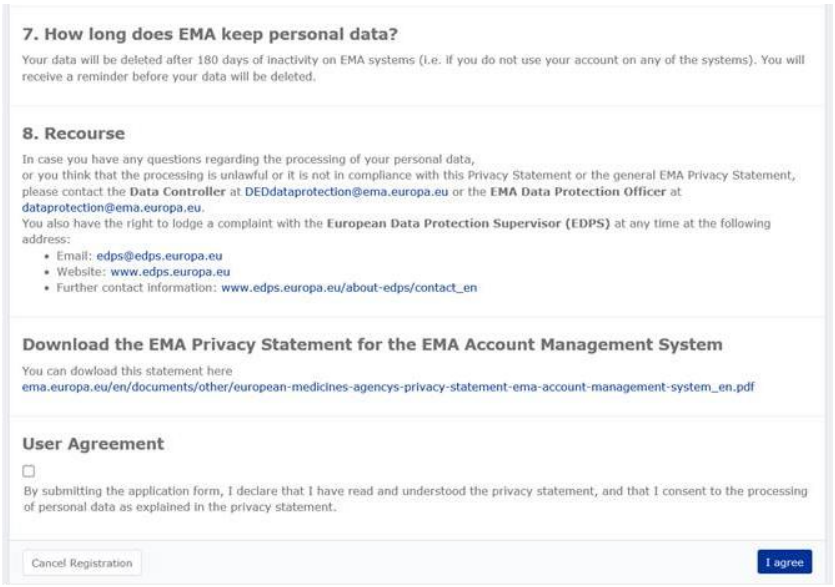
Go to [EMA's Account Management portal]



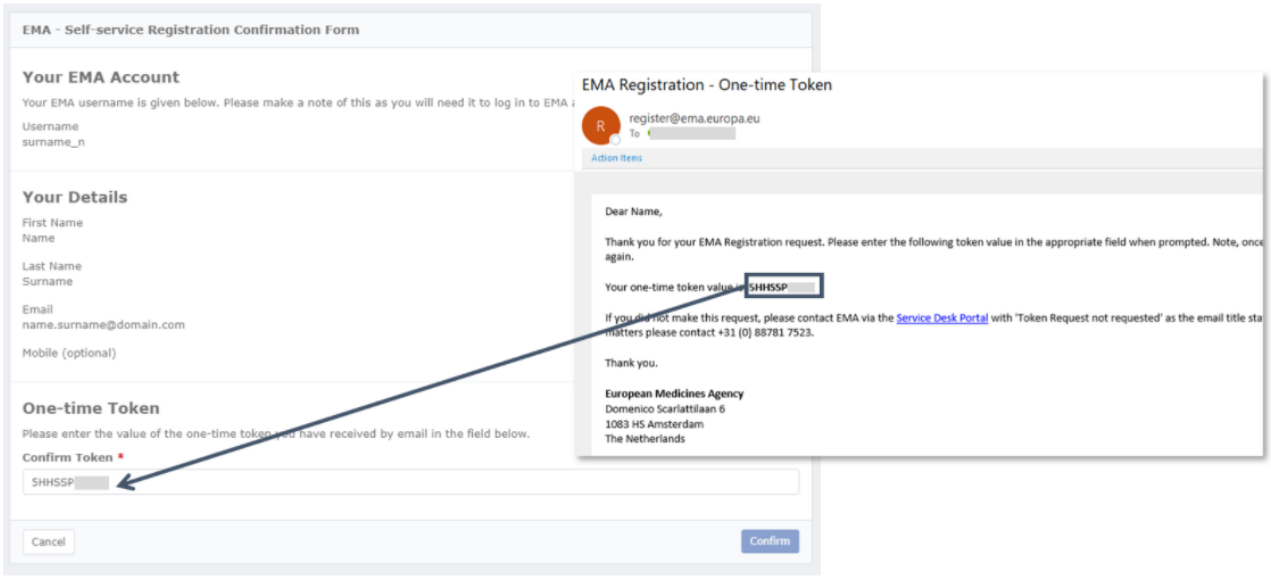
Click on "Create an EMA account (Self Register)" and open the "Self-service Registration form".

Complete the "Self-service Registration Form" with the relevant information. Fields marked with red asterisks (*) are mandatory. Password is case sensitive and must be at least 8 characters long and contain 4 different character types. Now you can download and read the EMA Privacy Statement.

Tick the "**User Agreement**" checkbox and then click on the "I agree" button.



Set up "**Security Questions**", answer the captcha (Completely Automated Public Turing test to tell Computers and Humans Apart) question and click the "Next" button. A "**Self-service Registration Confirmation Form**" will appear:



Complete the one-time Token received by mail and click Confirm. An automatic notification will be sent to the email address that you provided to confirm your account registration. It is recommended to save this confirmation-email.

It may take up to 30 minutes before the access is granted.

3 User access, roles and responsibilities in CTIS – Trial-centric approach

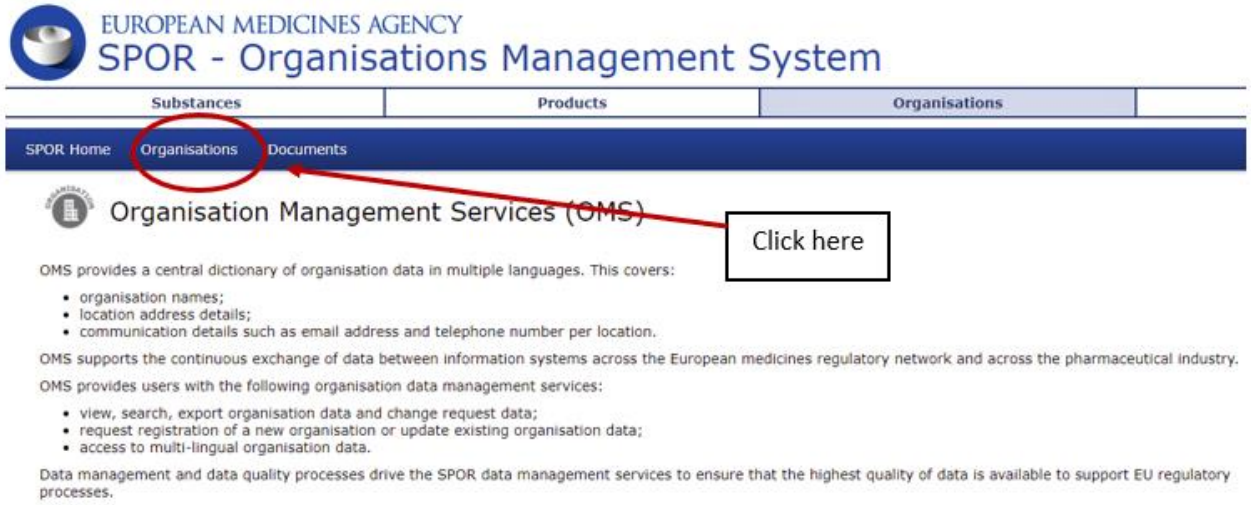
There are two general approaches to user management in CTIS: The organisation-centric approach and the trial-centric approach.

The focus of this guide is the trial-centric approach.

Trial-centric approach - Is intended to serve the needs of small organisations and specifically ***academic sponsors***, which may initiate trials on an ad hoc basis. It allows for the management of a smaller number of users and one or very limited numbers of clinical trials. This approach allows a faster process (no need for registration of a high-level sponsor administrator) when submitting a first initial, and subsequent application. Further allocation of other CT Administrator (CT Admin) roles or business roles is assigned to users at the clinical trial level. The CT Admin can manage users only for the particular trial(s) of his/her concern and can perform all sponsor business activities in CTIS related only to the particular trial.

3.1 How to check for registration of the sponsor organisation in OMS

You can search The Organisation Management System (OMS) without an EMA account.

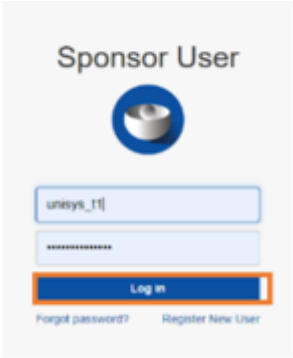


Each organisation (University Hospital, Hospital or University) has **one** Organisation ID, but can have several location ID's. Be sure you choose the right address for the specific organisation.

The sponsor details from OMS must first be added when you have logged into the CTIS database, please refer to section 4.2 in this guideline.

3.2 Access to CTIS

When "EMA account *Sponsor User"* log into the system and initiates a new CTA in CTIS, the system will automatically check if a high-level sponsor administrator has been appointed for the sponsor organisation selected.



If that is not the case, the user will be able to proceed becoming the clinical trial administrator (CT Admin) for that particular trial and can then assign other roles in the particular trial to other users also holding an EMA account.

Video on this topic in EMA training module 7:

How to request roles and how to assign roles to register users in CTIS

3.3 Considerations of which roles to assign to users within the organisation

For consideration of which roles to assign in CTIS the document CTIS User Personas can be used. On pages 6-8 this guide describe typical tasks each person in an academic institution, a hospital department or a clinical trial unit may complete in CTIS and the possible user roles they could be assigned.

The CT Administrator role is as mentioned assigned automatically to the person that initiates a new CTA, but it is recommended that at least one back up CT Admin is assigned as well. Users can also be given one of the business roles; Viewer, Preparer or Submitter.

Viewer role:

- Allows user to view structured data, documents, and includes download of document.

Preparer role (the Preparers also have Viewers permissions):

- Create permission: allows the user to edit, upload documents, save, update saved drafts. It also allows users to copy from an existing CTA to create a new one.
- Delete permission: delete refers only to eliminate/cancel draft items.

Submitter role (the Submitters also have the Viewers and Preparers permissions):

- Submit permission: allows the user to submit data/documents from their respective workspace to CTIS
- Update permission: allows updating submitted information
- Withdraw permission: refers to the withdrawal of submitted items

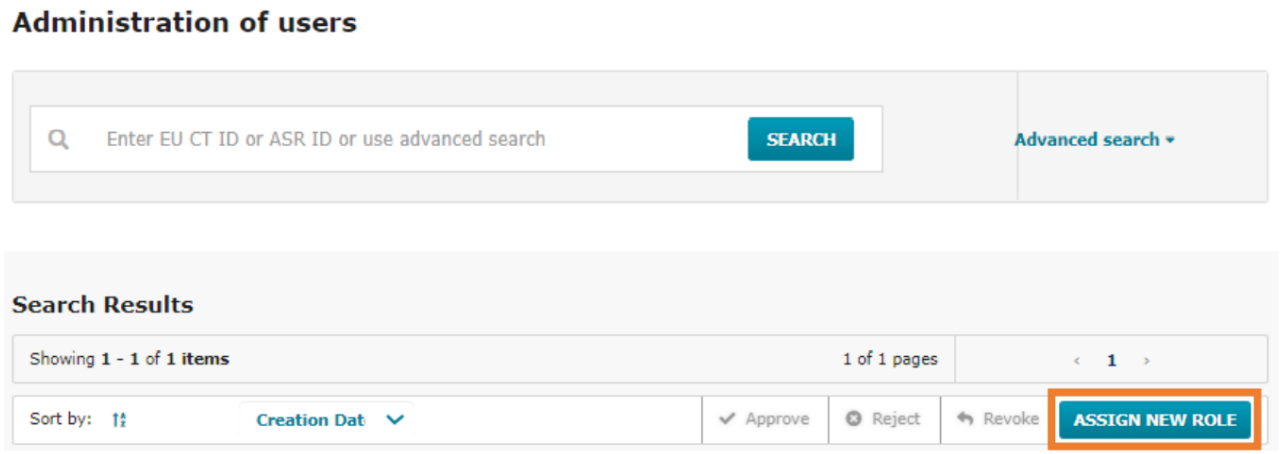
3.4 How to assign business role to users within the organisation

After a new CTA is created (See section 4.1), the CT Admin can assign business roles for that specific trial

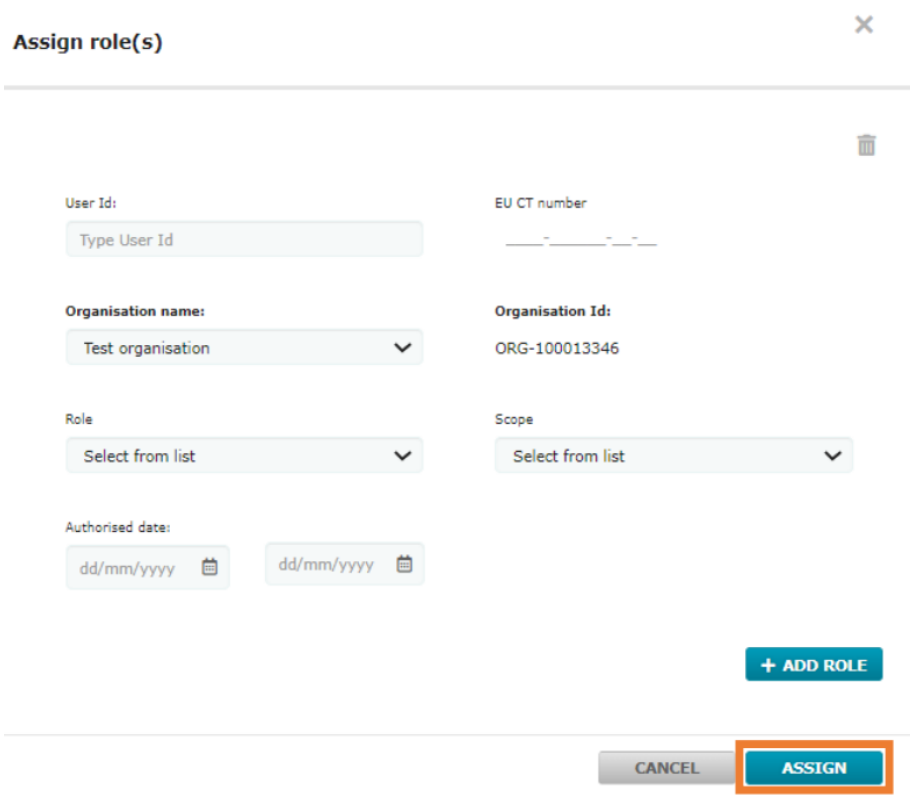
1. After the CT Admin is approved, users can log in to CTIS and click the User administration tab.

Info box:
For more detailed information please refer to Module19 - Step-by-step guide - User access management and user administration (europa.eu)

2. Click on the 'Assign new role' button.



3. Fill in the information about the business role to be assigned to users within the organisation and click on the 'Assign' button.

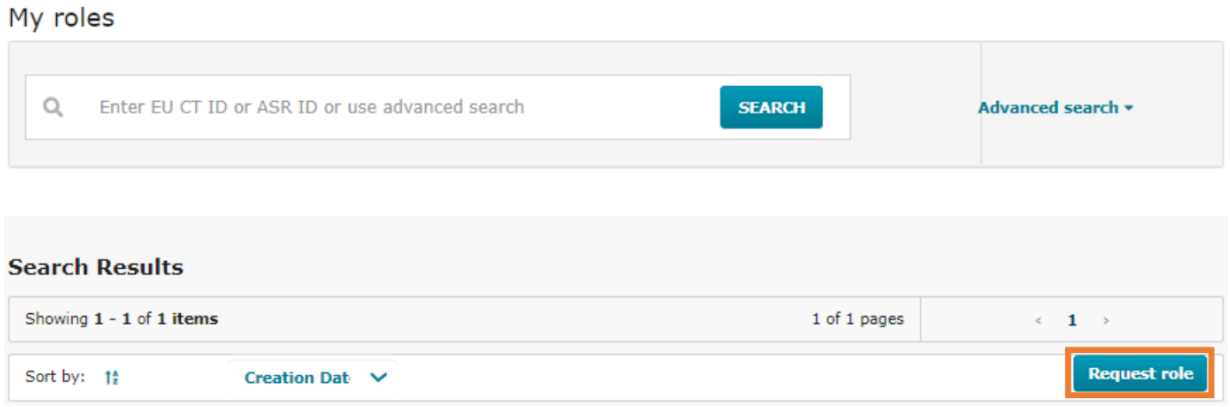


3.5 How to request a role

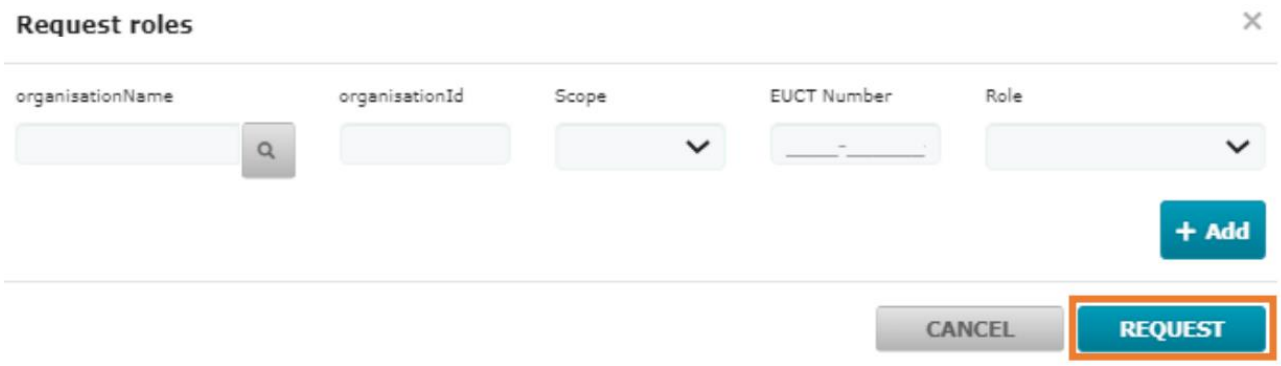
1. Users can instead choose to request a role. This is done by log in to CTIS and click the username button at the top-right corner of the CTIS start page.

2. Click on the ‘My roles’ button.

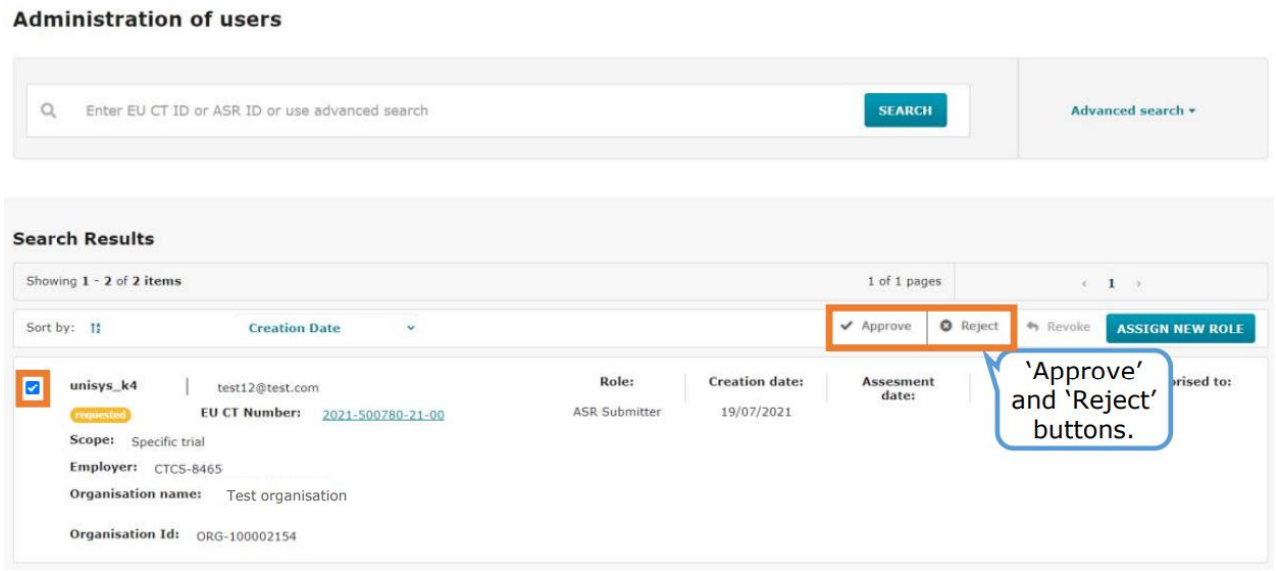
3. Click on the ‘Request role’ button.



4. Populate the information from the pop-up window and click the ‘Request’ button.



5. Once users request a role, the CT admin clicks the checkbox next to the role and clicks on the 'Approve' or 'Reject' buttons. Role requests will appear in the User administration tab. No notice or alert will be generated. Therefore, CT administrators are encouraged to check the User administration tab regularly.



When a role is assigned, users must log out and log in again, in order to have the role assigned to them in the system.

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

Transitio:

In accordance with the Directive clinical trials with at least one active site after 30 January 2025 must be transferred as a transitional trial to the CTIS portal in accordance with the EU Regulation. If there are no active sites in Finland in the clinical trial, no transfer will be needed for Finland.

More information on transition can be found on Fimea´s webside, and more detailed instructions.

Fimean sivuilta löytyy tietoa transitiotutkimuksista ja tarkempi ohje.

4.1 Application dossier for the initial application

Link to the CTIS database: https://euclinicaltrials.eu/ctis-for-sponsors

The Clinical Trial Application dossier is contained in Annex I of the EU Regulation.

Templates for some of the documents can be found in Eudralex Volume 10.

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. You may send a public and non-public version at the same time.

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

Info box:
Language requirements for Part I documents can be found in Section 2 in EMAs Q&A (updated April 2022). Documents can be in Finnish, Swedish or English for trials running only in Finland.

The asterisk * in CTIS indicates mandatory fields to be filled in and/or mandatory upload of documents. Some separate documents (e.g. recruitment arrangements) must be uploaded even though the same text is already mentioned in other documents e.g. the protocol.

Template for the the document “Proof that data will be processed in compliance with EU law on data protection (GDPR)” can be found in Volume 10.

On Fimea's website, you can find information on the instructiotrns for trilas in accordance with the regulation.

Fimean sivuilta löytyy lisätietoa asetuksen mukaisiin käytäntöihin

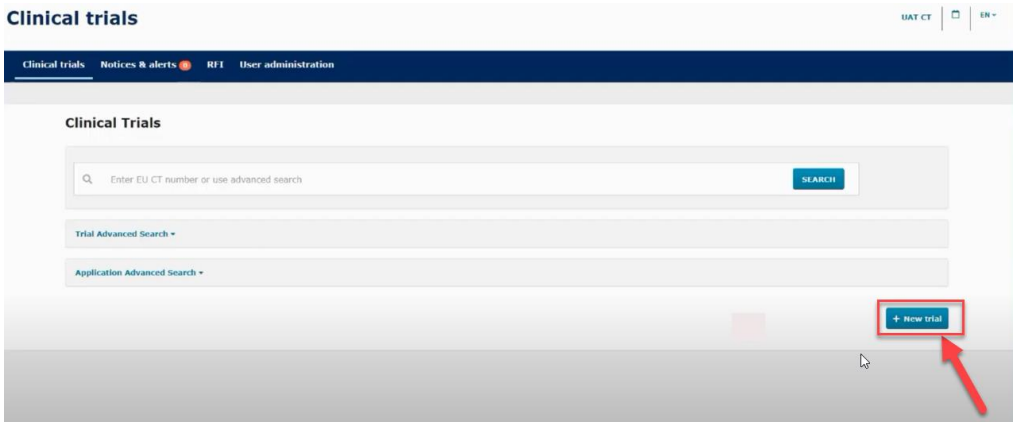
Part I	Part II
➢ Cover letter ➢ EU Application form (data entered directly in CTIS) ➢ Protocol and protocol synopsis (synopsis can be part of protocol or separate document) ➢ Investigators Brochure (IB)/SmPC ➢ IMPD quality, safety and efficacy/ Simplified IMPD with reference to the valid SmPC ➢ Content of labelling of IMPs ➢ Proof of payment of fee (invoicing details or a request for exemption from payment, laskutettavan tiedot tai maksuvapausanomus)	➢ Recruitment arrangements (template in Volume 10) ➢ Subject information and informed consent form, National Committee on Medical Research Ethics (Tukija´s) template ➢ Investigator suitability and CV (template in Volume 10) ➢ Suitability of the facilities (template in Volume 10) ➢ Proof of insurance cover or indemnification ➢ Financial and other arrangements, Tukija´s template ➢ Proof that data will be processed in compliance with EU law on data protection (GDPR)

Info box:
When uploading documents in CTIS be aware not to use date and version in the file name on your documents 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 even if there comes substantial modification updates. Otherwise you can rename your documents in CTIS after upload.

4.2 Fill in the trial title and sponsor organisation in CTIS

Info box:
CTIS should be completed in English. Remember to click Save on the top of the page.

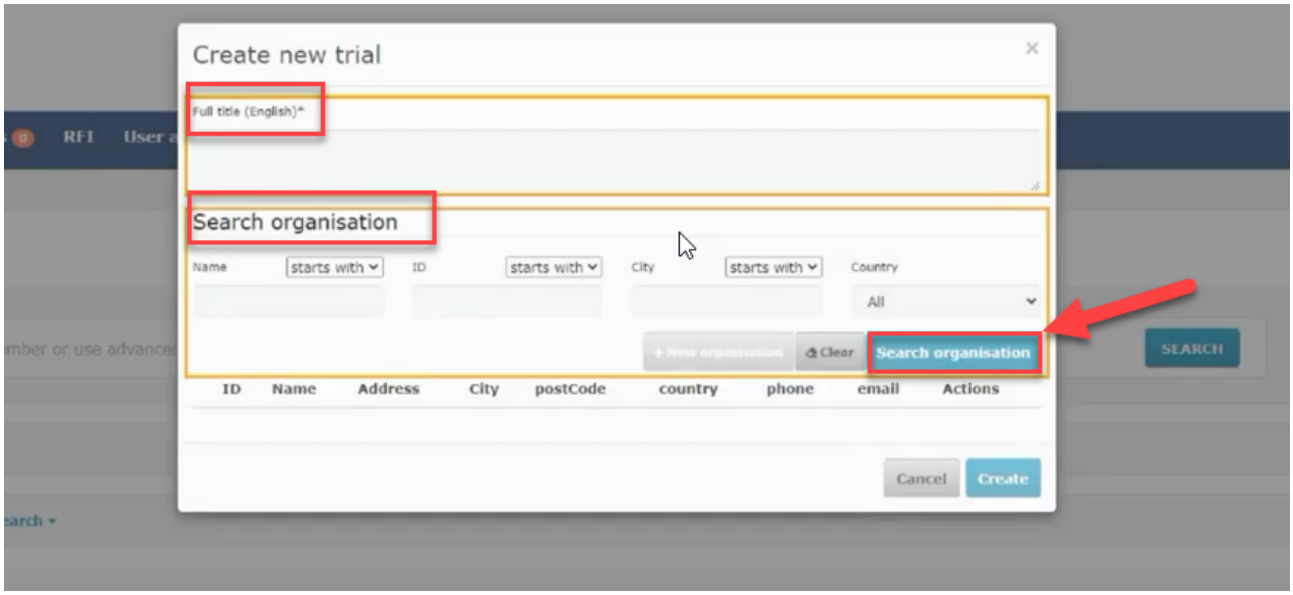
When you are logged in to the CTIS, click on the tab “New Trial”:

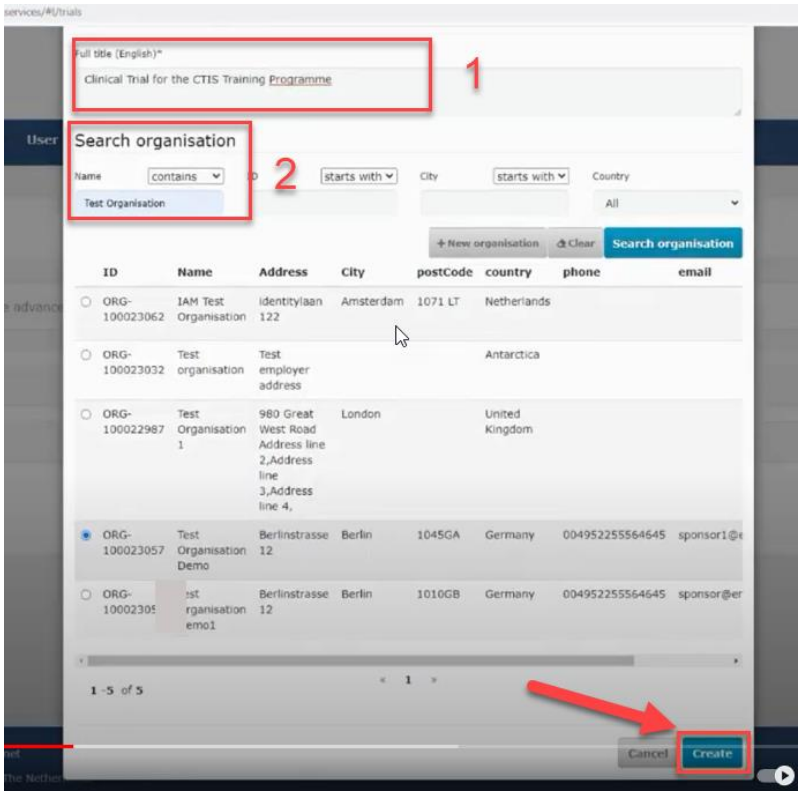


Type the full title of the trial.

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. 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.





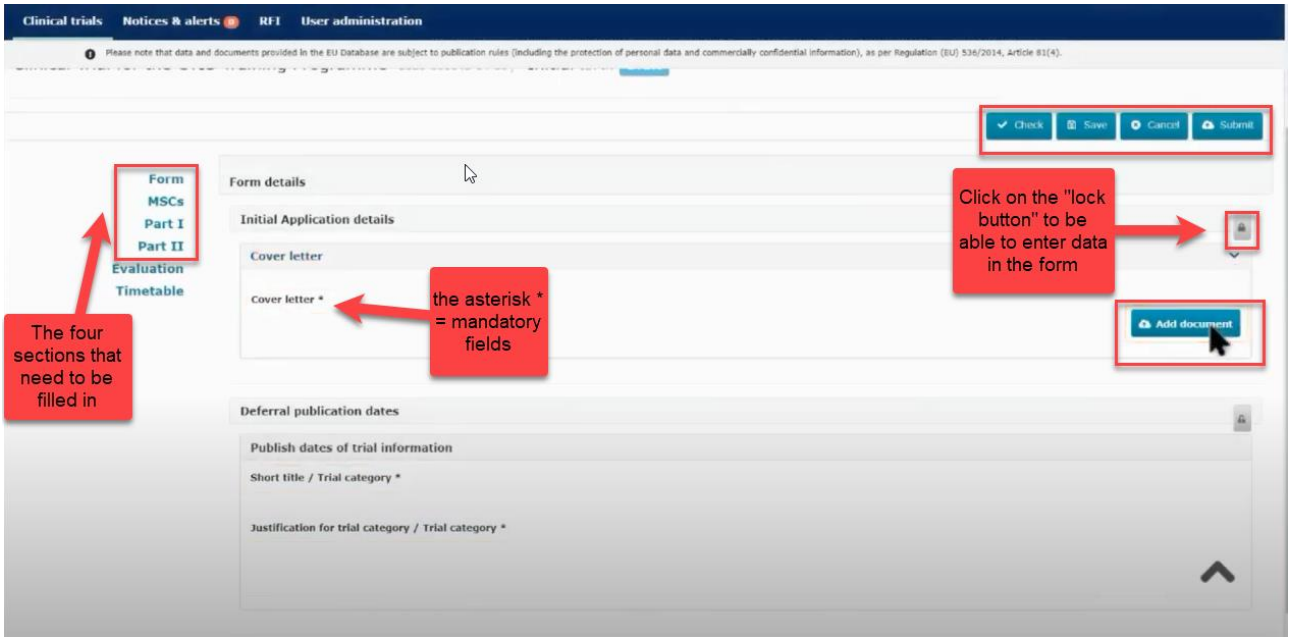
When the two fields are filled in, click on the create button and the draft of the CTA will be created.

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 on “draft” mode.
4. Submit: Submit the application when all information is entered and it is completely ready.

Info box:
The lock button needs to be **locked** to enter data. Remember to unlock after uploading data in each section. Save the data before going to the next section.

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.



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).

4.3 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.

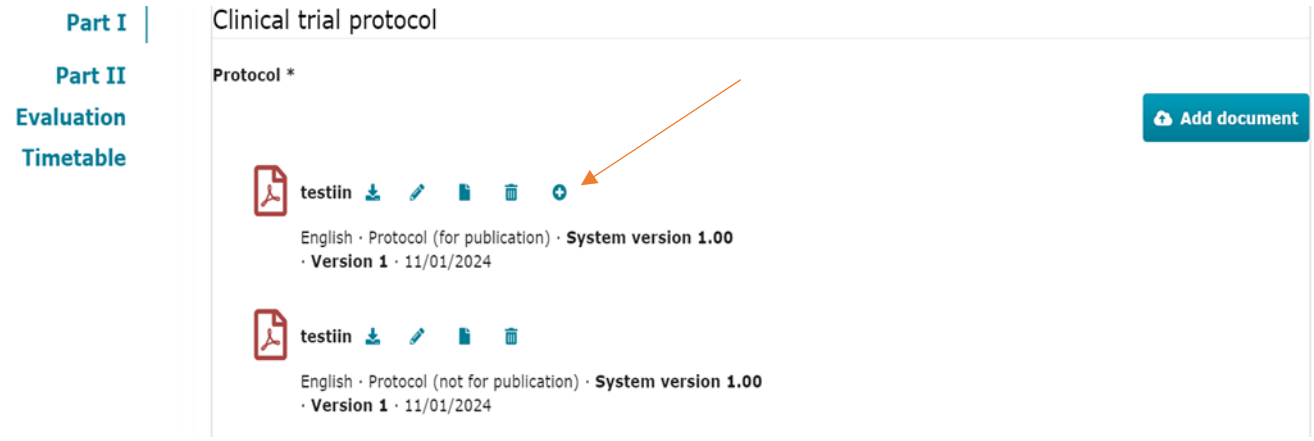
Thereafter you need to add the "justification for the trial category".

Info box:
The protocol will automatically be accessible in the public workspace after the authorisation. 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.

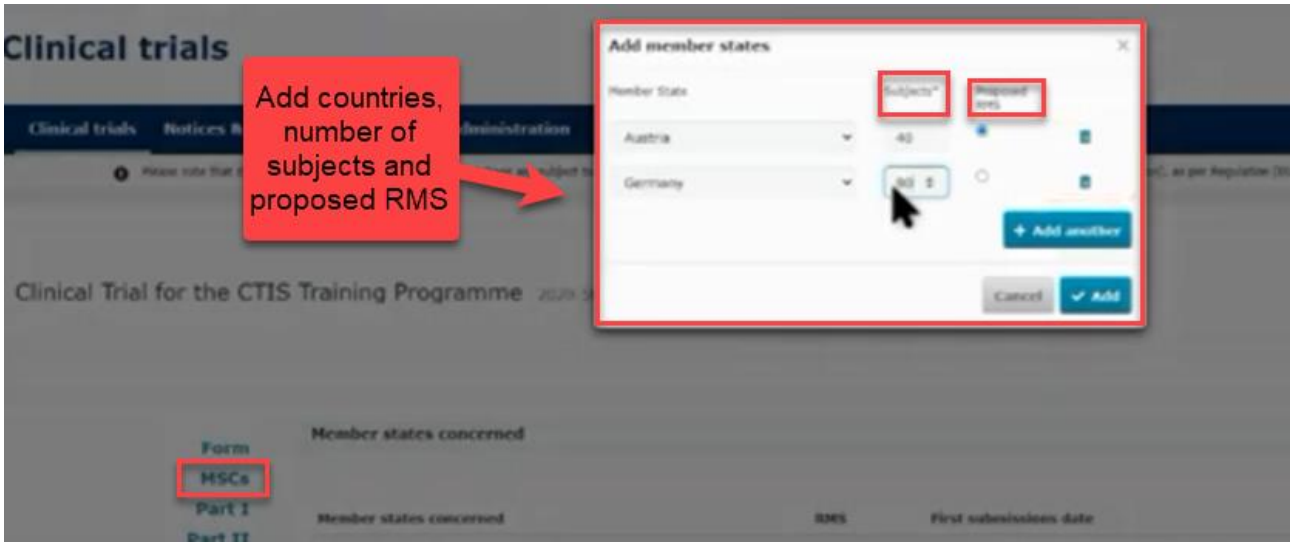
	Category 1 clinical trials (pharmaceutical development clinical trials):	Category 2 clinical trials (therapeutic exploratory and confirmatory clinical trials):	Category 3 clinical trials (therapeutic use clinical trials)
• **Protocol** • **Investigator's brochure** • **Responses from sponsor in relation to any aspect of the trial**	Sponsor may opt to defer this up to the time of MA using this trial or up to **7 years** 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 5 years** 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 **12 months** after the end of the trial in the EU.

Revised CTIS transparency rules were adopted on 5.10.2023, main differences: publication focused on keydocuments of interest, removal of deferral functionality, documents are published earlier in time, use of redaction as the method to protect commercially confidential information and protection of personal data, if included in those key documents.

Documents can be put into the CTIS program either as for publication-versions or not for publication-versions by adding the not for publication version via plus:



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.



4.4 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

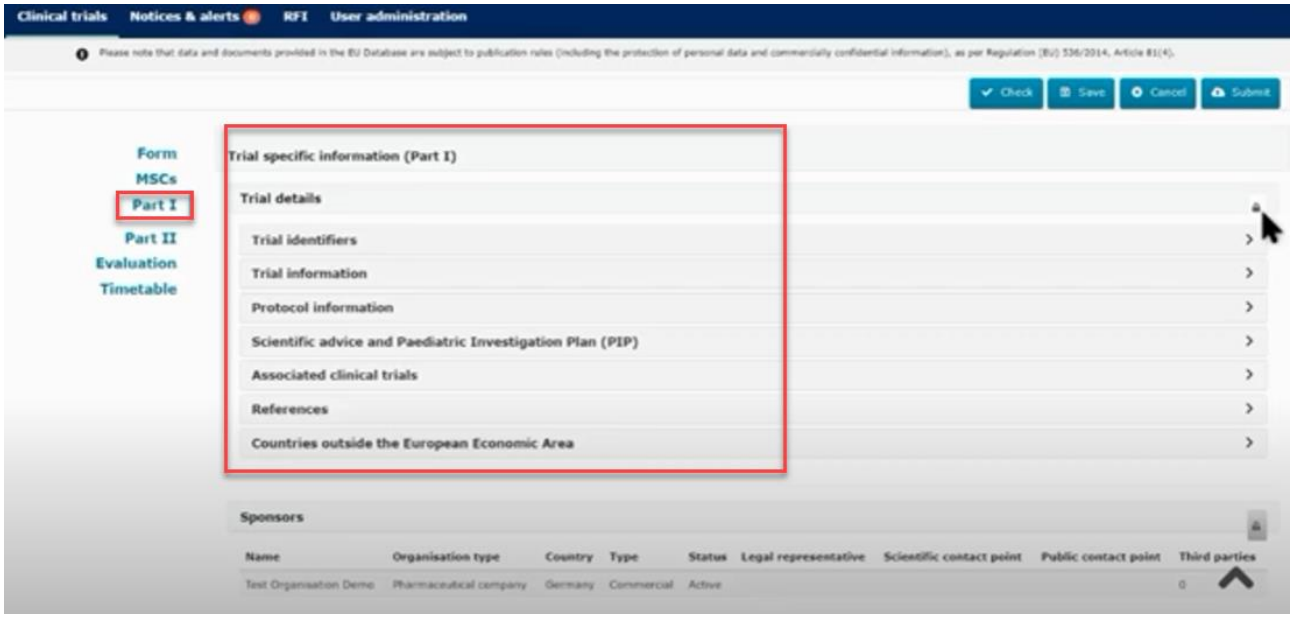
Training video: Fill in the Sponsor details of Part I section

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. Model for the protocol can be found in Fimea´s webpage.

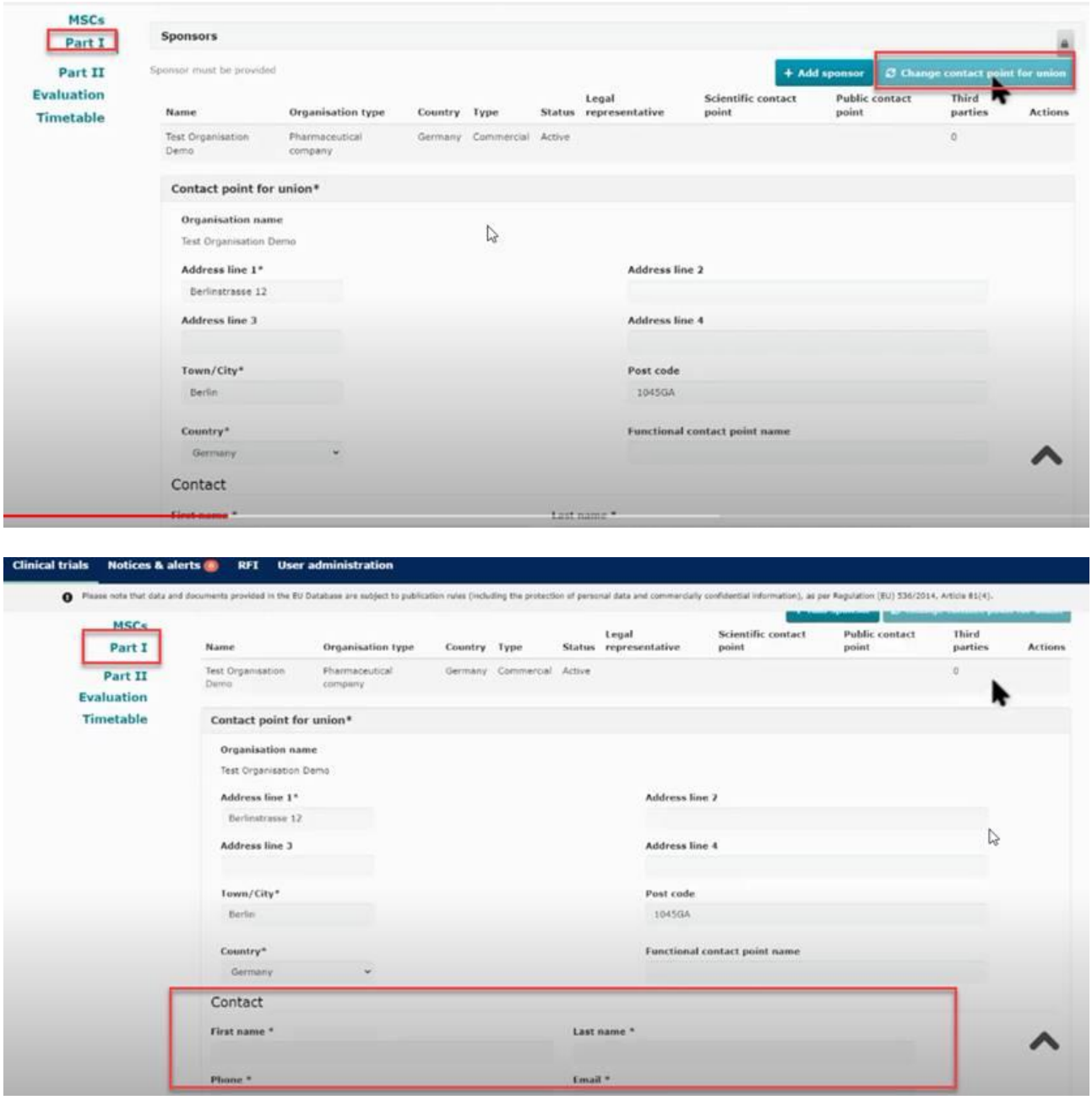


For the main objective you can choose several “trial scopes” that are relevant for the trial.

Sponsor details

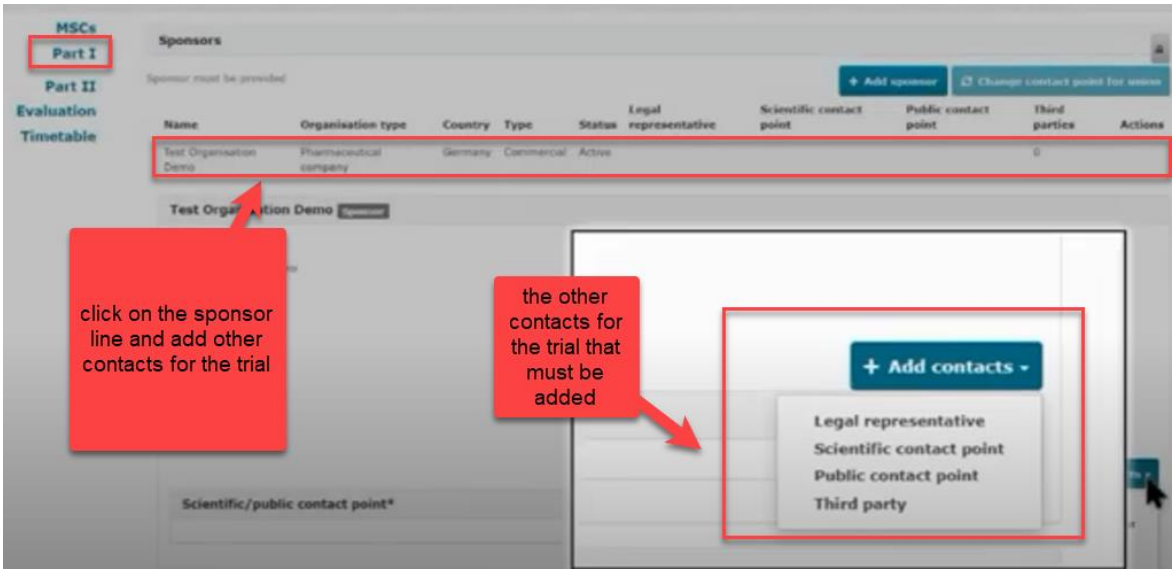
Includes sponsor information which was added when the application was first created.
All these contacts must also be registered in OMS.

The first contact point for union must be added. This person will be the contact point for sponsor.



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) – in academic/non-commercial trials this person will often be the sponsor contact point (the contact point for union).
- 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. All third parties must be registered in OMS.

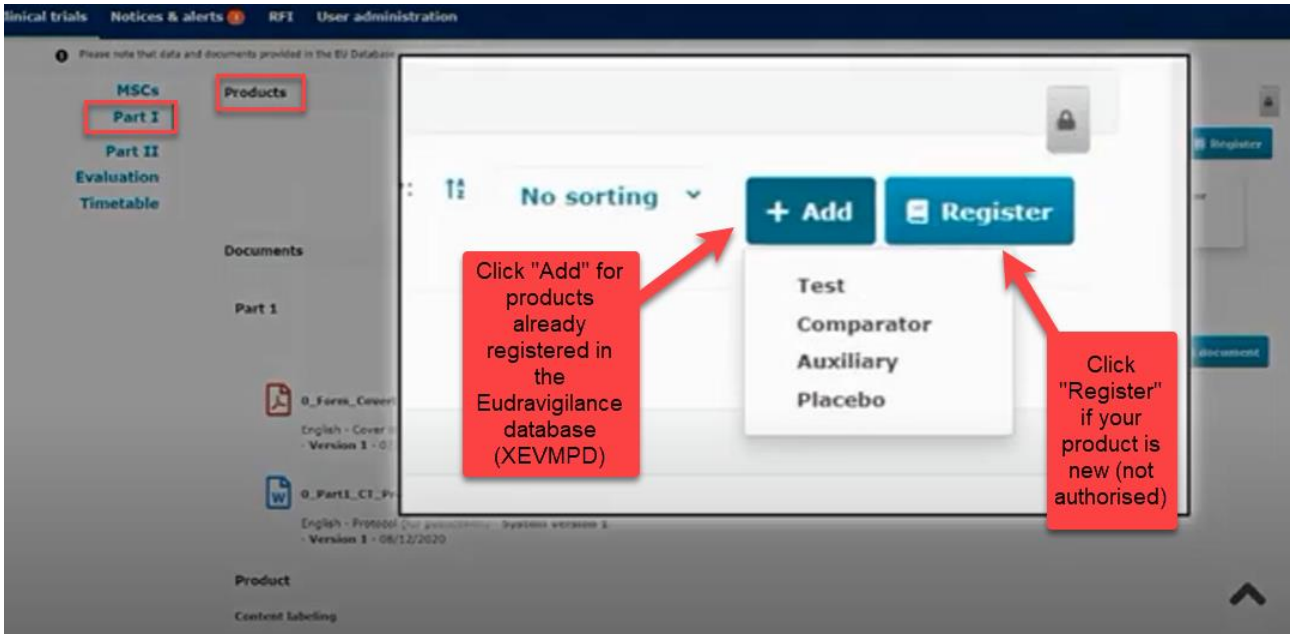

MSCs
Part I
Part II
Evaluation
Timetable
Sponsors
Name
Organisation type
Country
Type
Status
Legal representative
Scientific contact point
Public contact point
Third parties
Actions
click on the sponsor line and add other contacts for the trial
the other contacts for the trial that must be added
+ Add contacts
Legal representative
Scientific contact point
Public contact point
Third party
Scientific/public contact point*

Product details

Information on the medicinal products used in the trial must be added. If the products have 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.

Non authorised medicinal products must now be registered to the Extended Eudravigilance Medicinal Product Dictionary (XEVMPD) if this is not already done.

EMA´s handbook item 6 tells how to enter not authorised product into the XEVMPD system.



The reference safety information (RSI) which can be either the Investigators Brochure (IB) or the SmPC must also be uploaded. The labelling must also be uploaded.

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

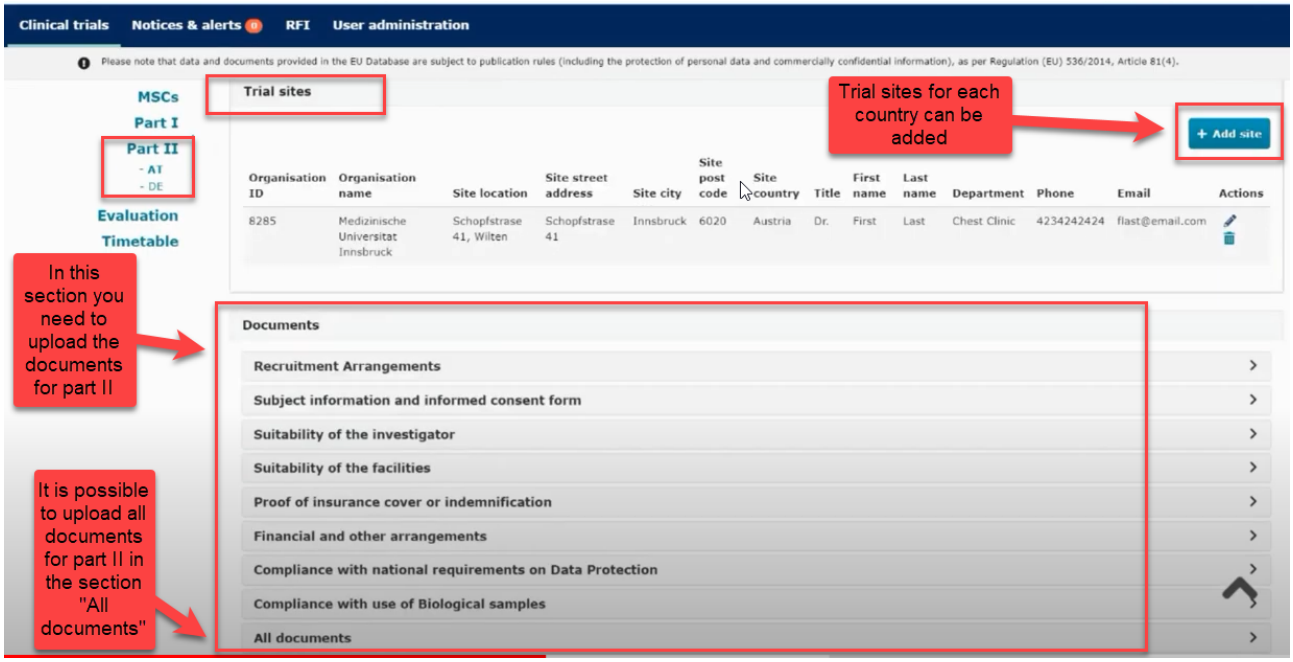
4.5 Fill in the Part II section

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.

Finnish EC requirements: Local documents from each country needs to be uploaded.
Tukijan sivulta löytyvät ohjeet paikallisesti toimitettaviin asiakirjoihin.

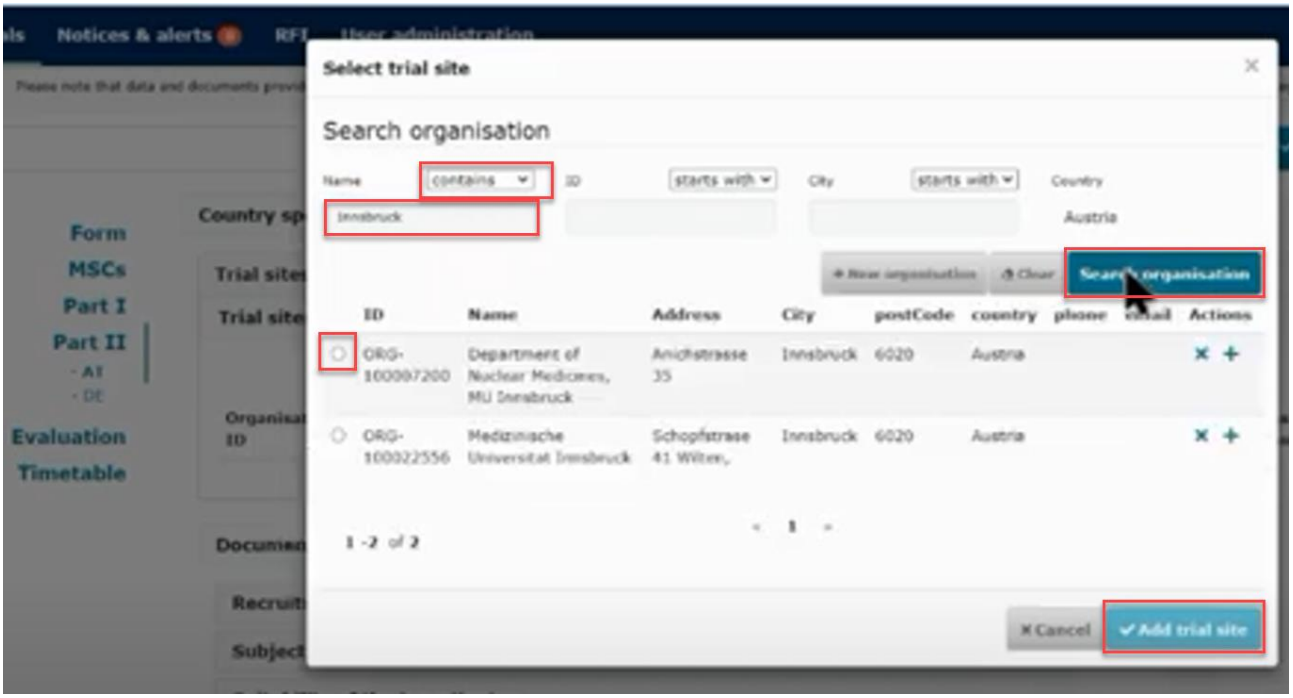


Documents listed and uploaded in chronological order is recommended in the section “All documents”.

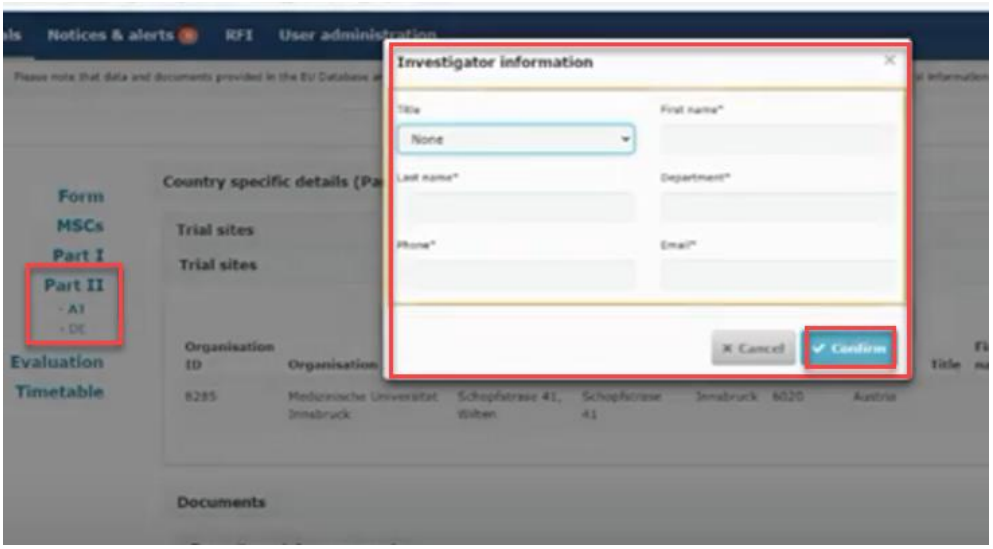
Trial sites must be added: Name and address of trial sites and primary investigators at the trial sites.

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

The name and address of the university/hospital organisation must be registered in OMS before you can search and add the organisation to the application form. If the organisation is not already part of the OMS system, the organisation must be added to OMS (see section 3.1). This must be done by sponsor or the organisation itself.

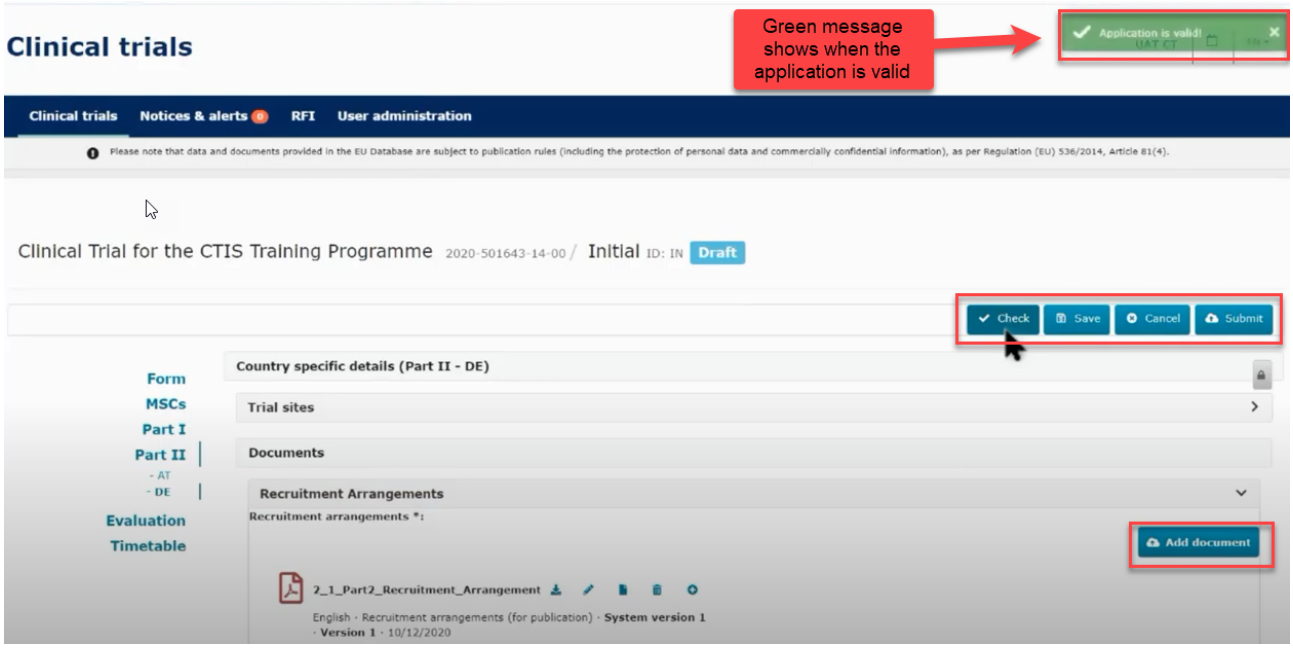


When the organisation is found via the search function, the details of the investigators must be added (first and last name, department, email address, phone).

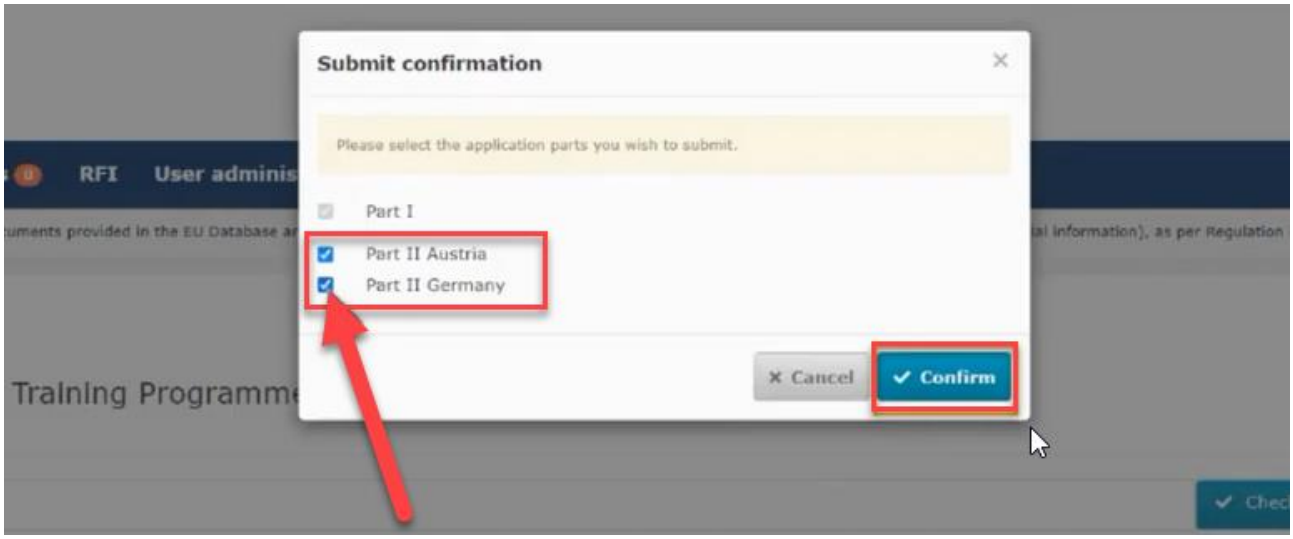


Supporting documents: Upload documents in each separate section or upload all the documents in the section “All documents” and specify in the document title what the document contains.

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.

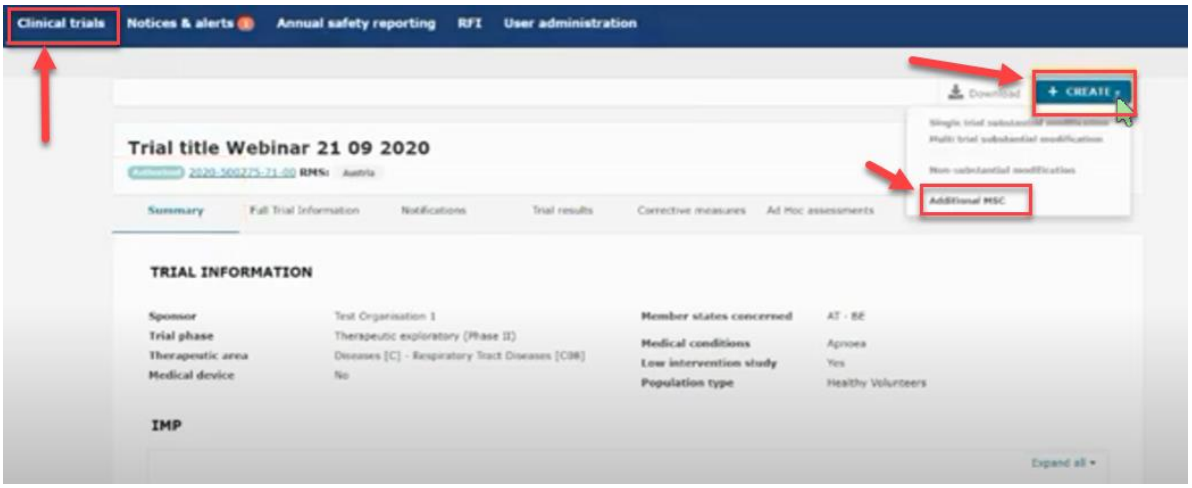


4.6 How to submit an additional member states concerned (MSC) application (add a new country)

Video on this topic in EMA training module 10:

Training Video: How to submit an additional MSC application in the CTIS Sponsor workspace

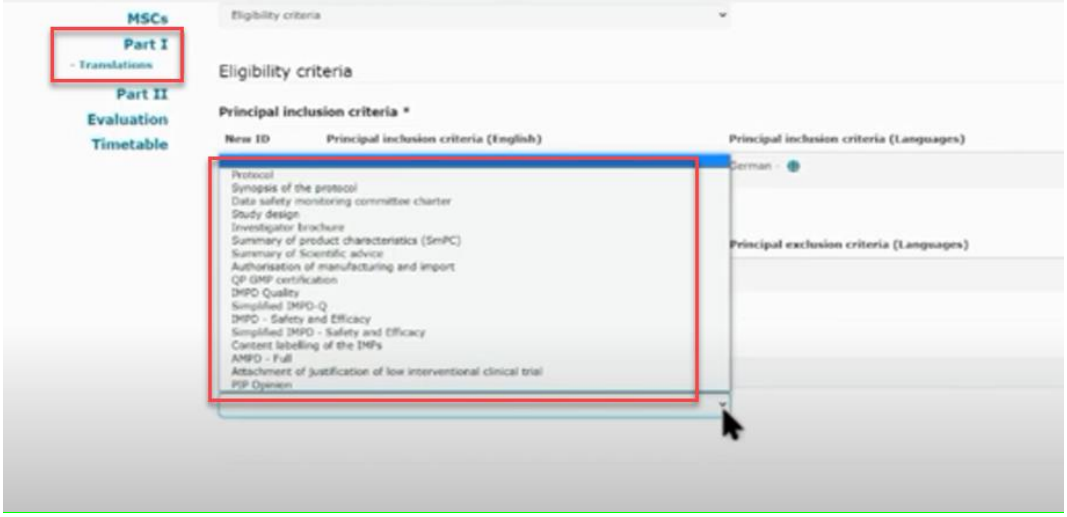
To add a new member state (MSC) to an already approved application. In the page of the authorised clinical trial click on the “create” button and choose “Additional MSC”.



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.

4.7 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.

5 Validation, Request for Further Information (RFI) and Authorisation

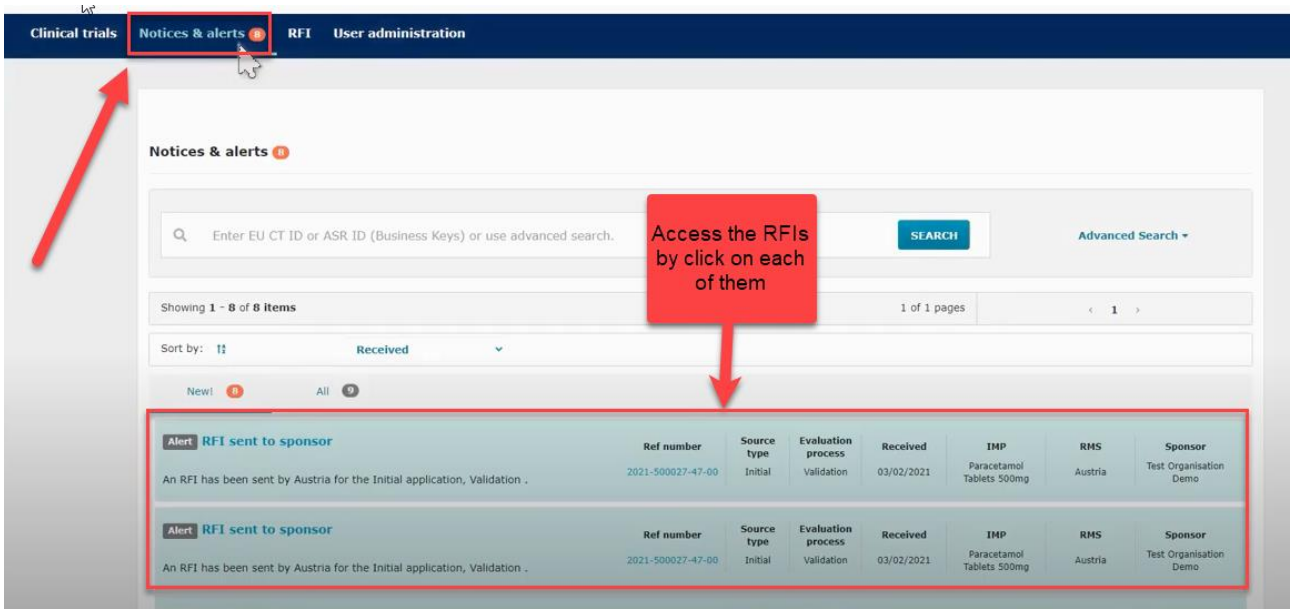
5.1 How to access and view a request for further information (RFI)

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)

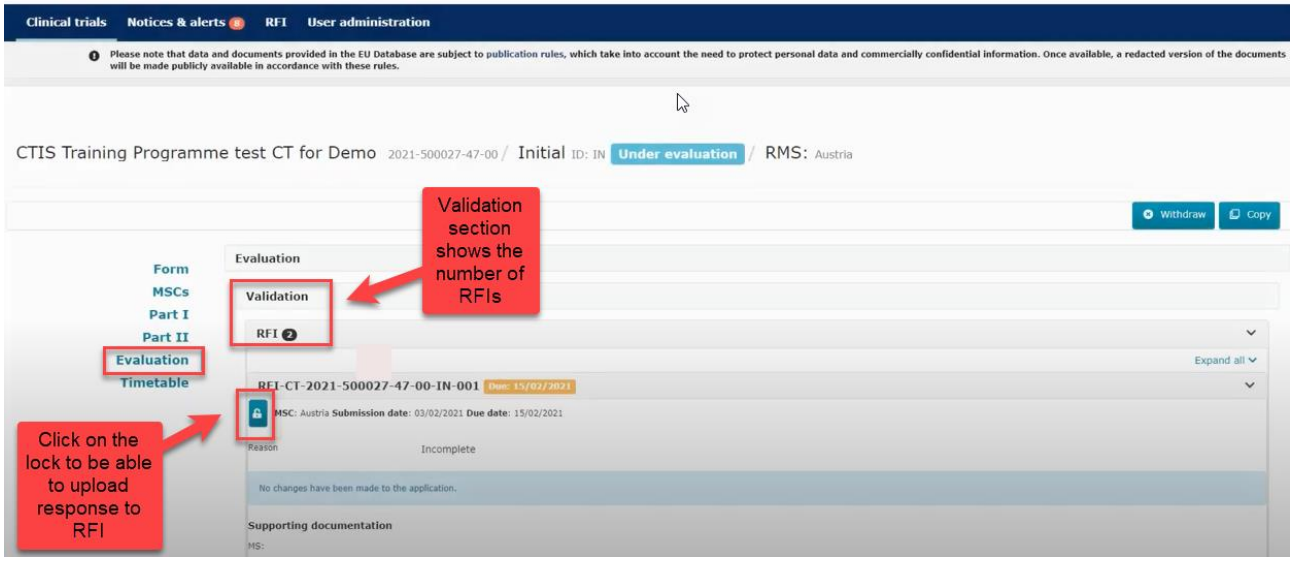
RFI: Questions from authorities to sponsor.

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

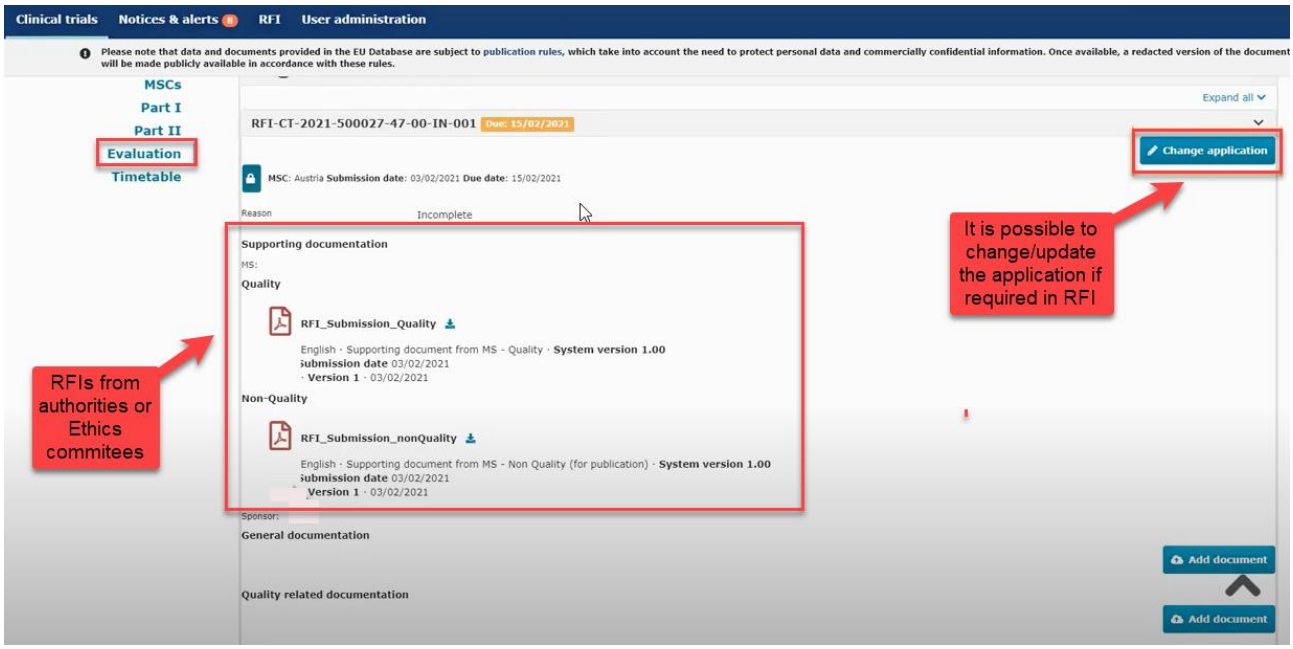


You can access the RFI by clicking on each of the alerts. They can also be accessed from the RFI tab next the “Notices and alerts” tab.

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



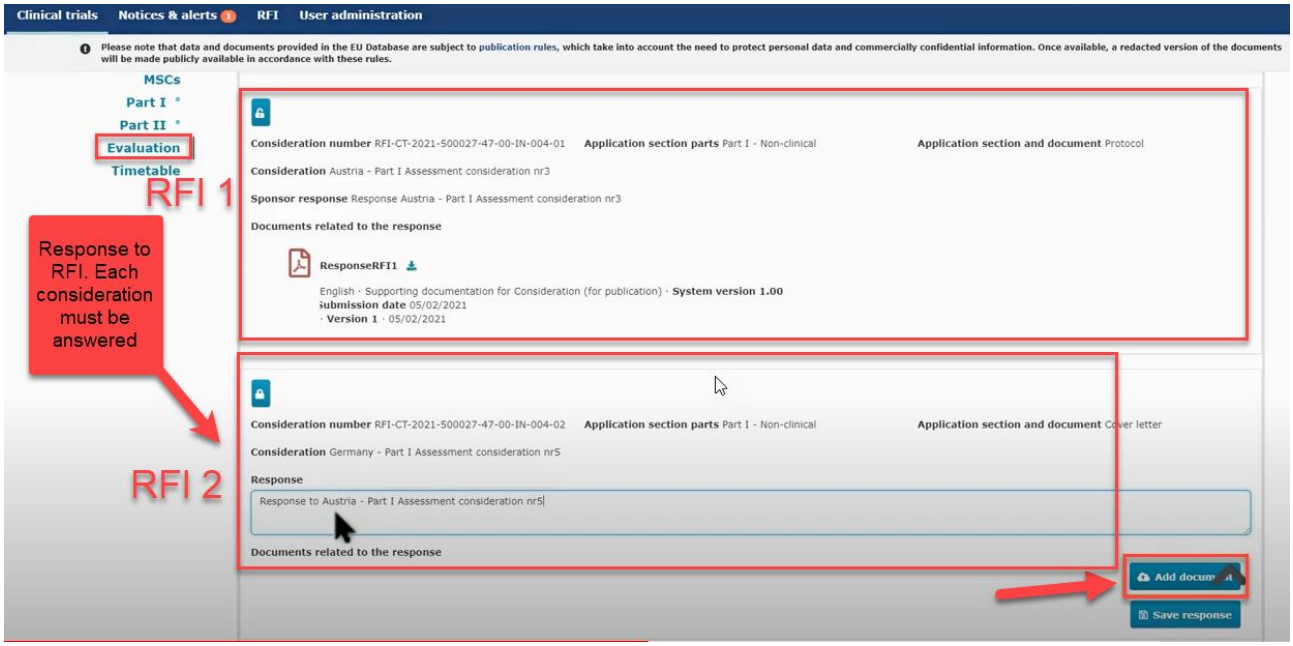
In the “Add document” tab you can upload supporting documentation. If the RFI requires, you can click on the “Change application” and then change information which is previously uploaded or entered for the CTA.

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

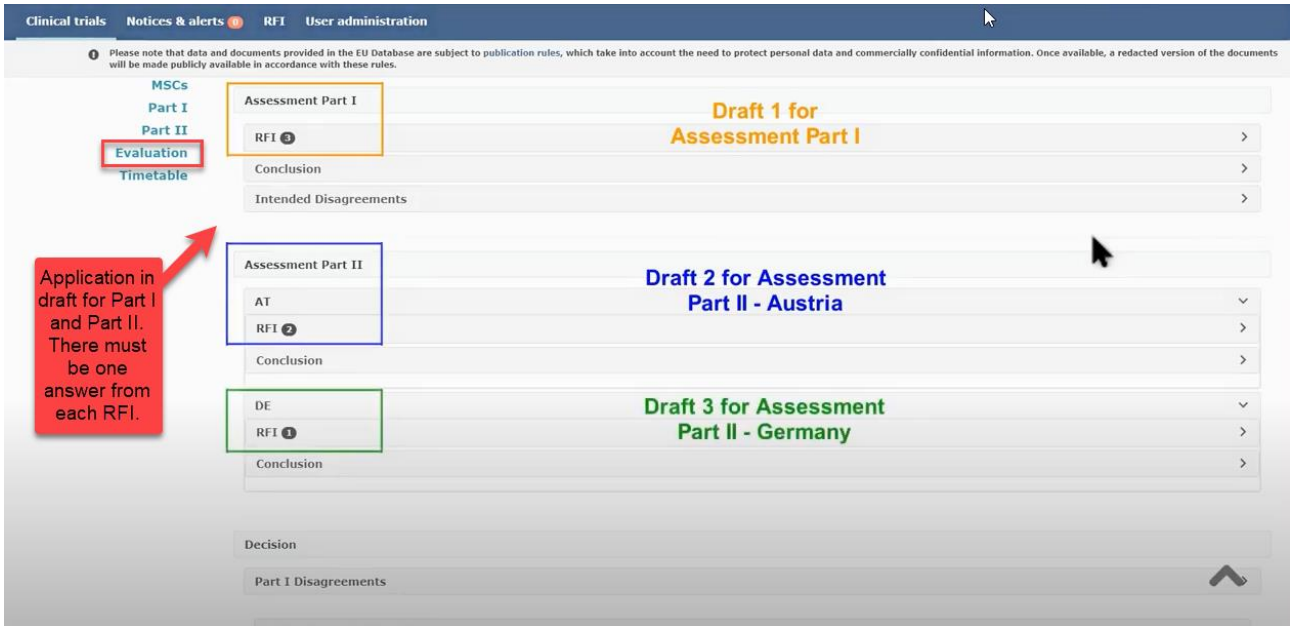
Videos on this topic in EMA training module 11:

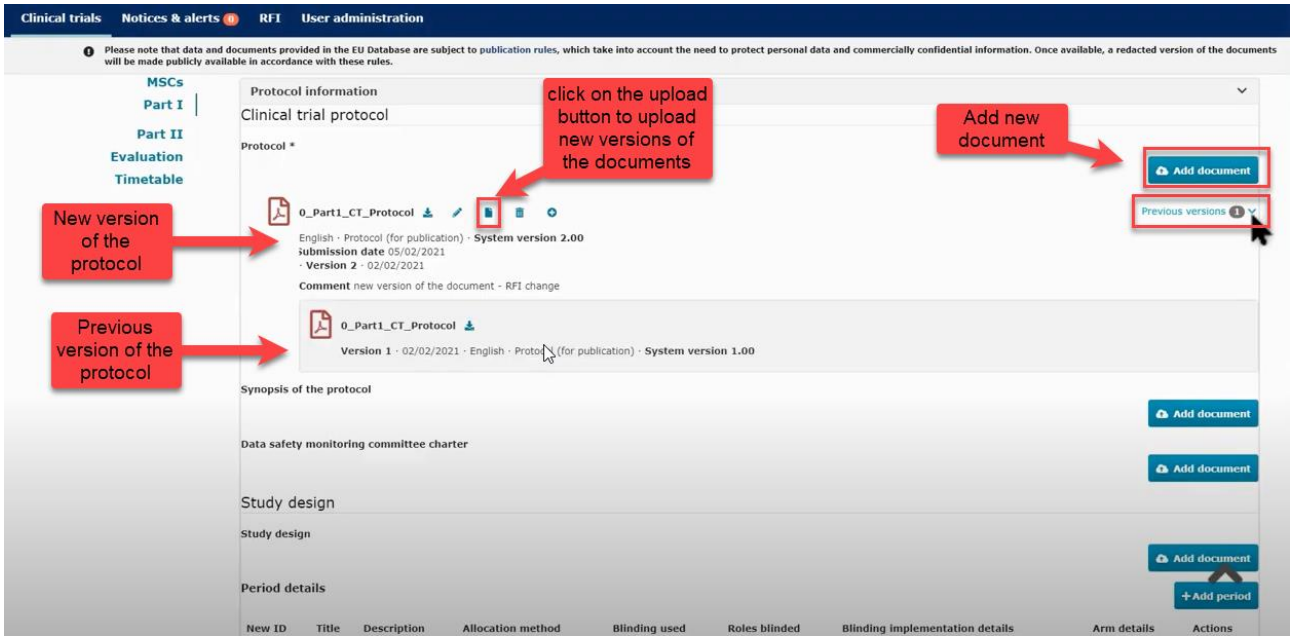
Training Video: How to change a Clinical Trial Application as part of an RFI response (Sponsors)

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.





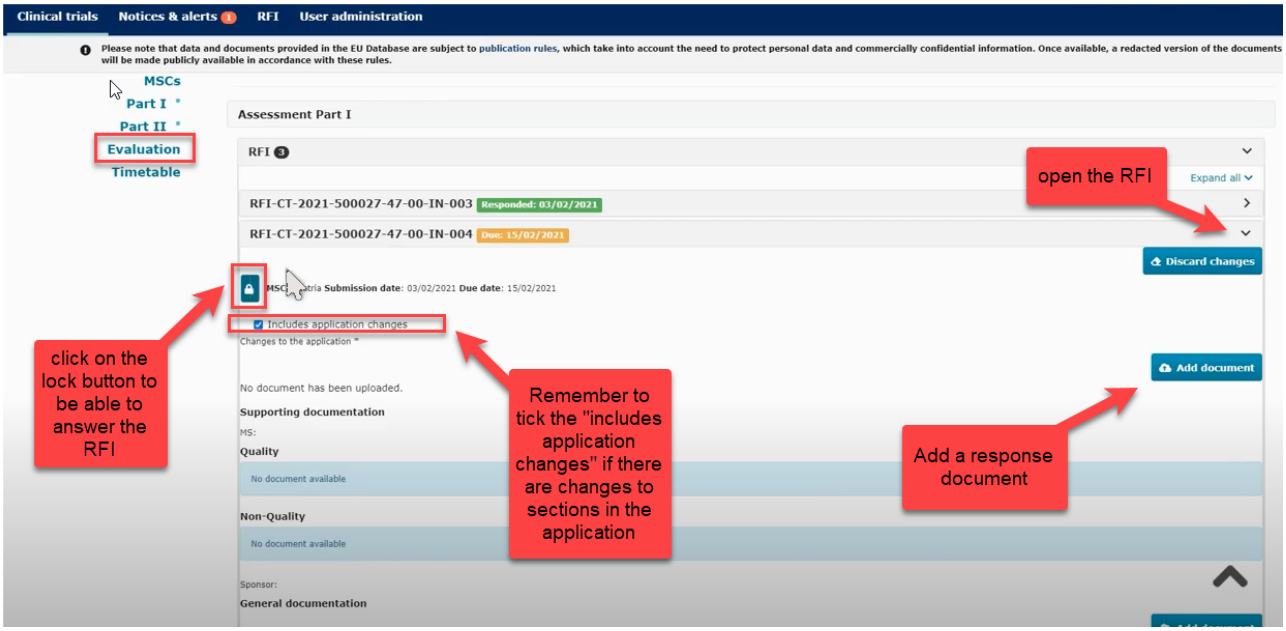
Remember to unlock each section when you are done answering the RFI and uploading new documents.

5.3 How to respond to RFI considerations and submit an RFI response

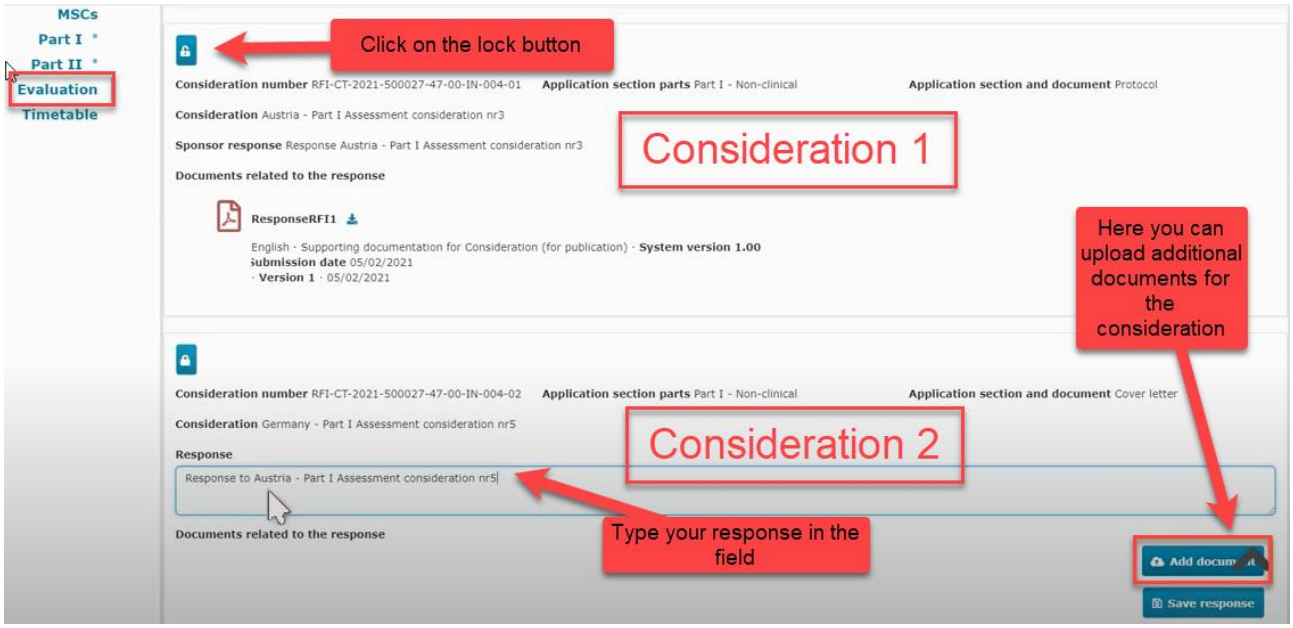
Videos on this topic in EMA training module 11:

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.



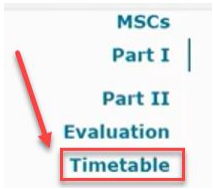
Below the RFI, there can be considerations which also must be answered. You can respond separately to each consideration.

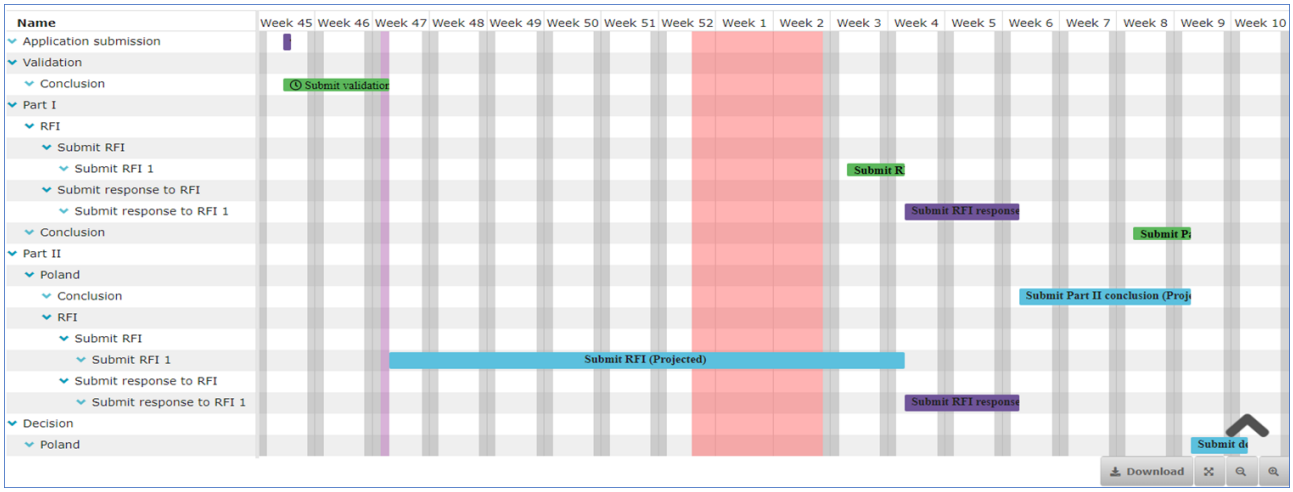


The “Submit response” button will be active when the changes have been saved on “save response”. Please check that the top lock is open and the other locks are closed, then the “submit response” button is available. It is advisable to include the track changes document if there are many changes (in protocol, ICF etc.)

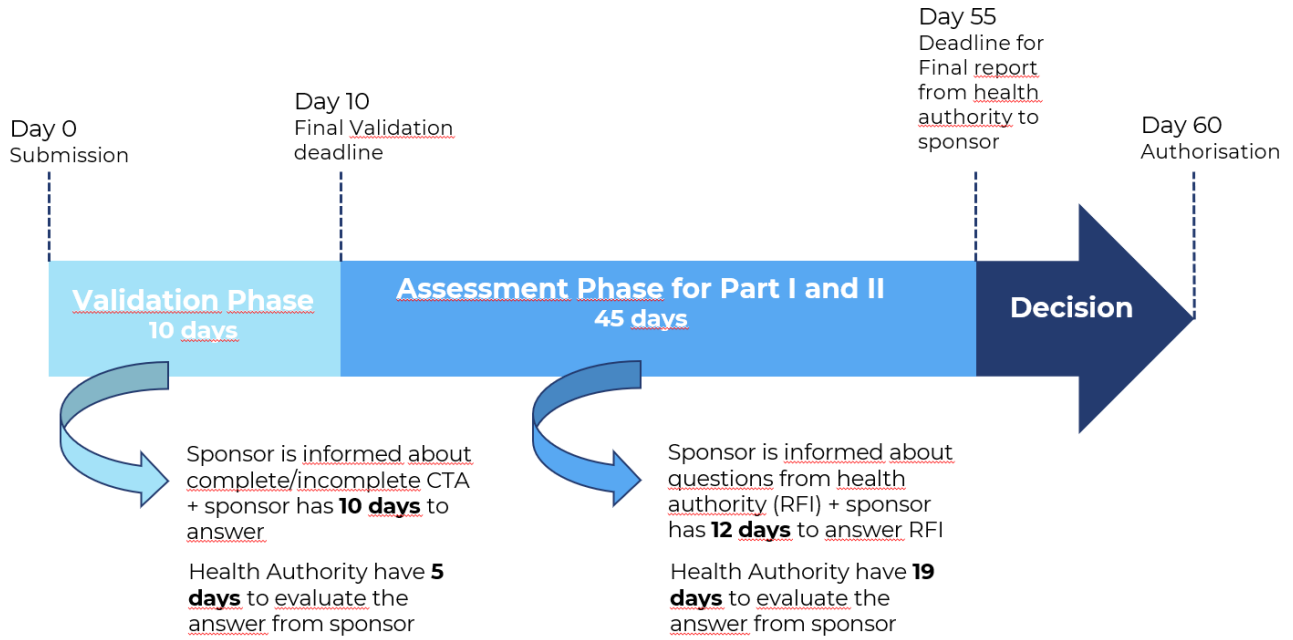
T5.3 Timetable

In the timetable tab on the left side of the page in CTIS it shows the dates for the assessment schedule.





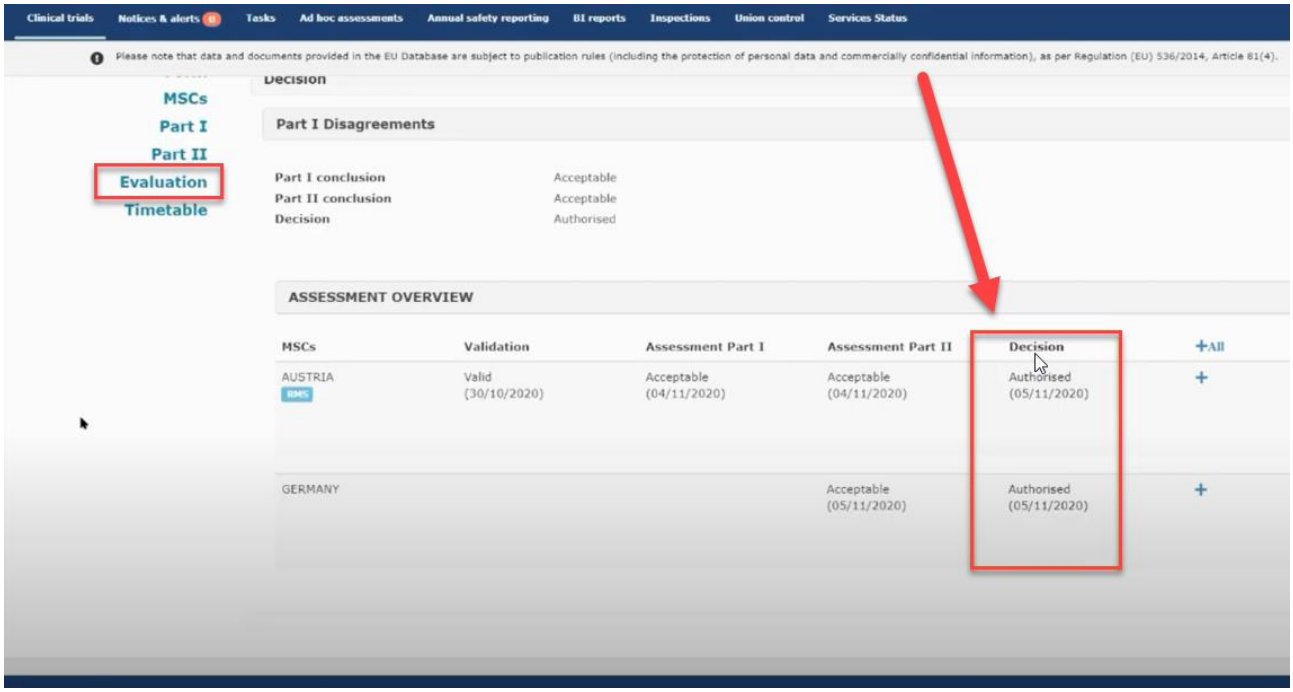
The figure below shows an overview of the general timetable and deadlines for authorities and sponsors.



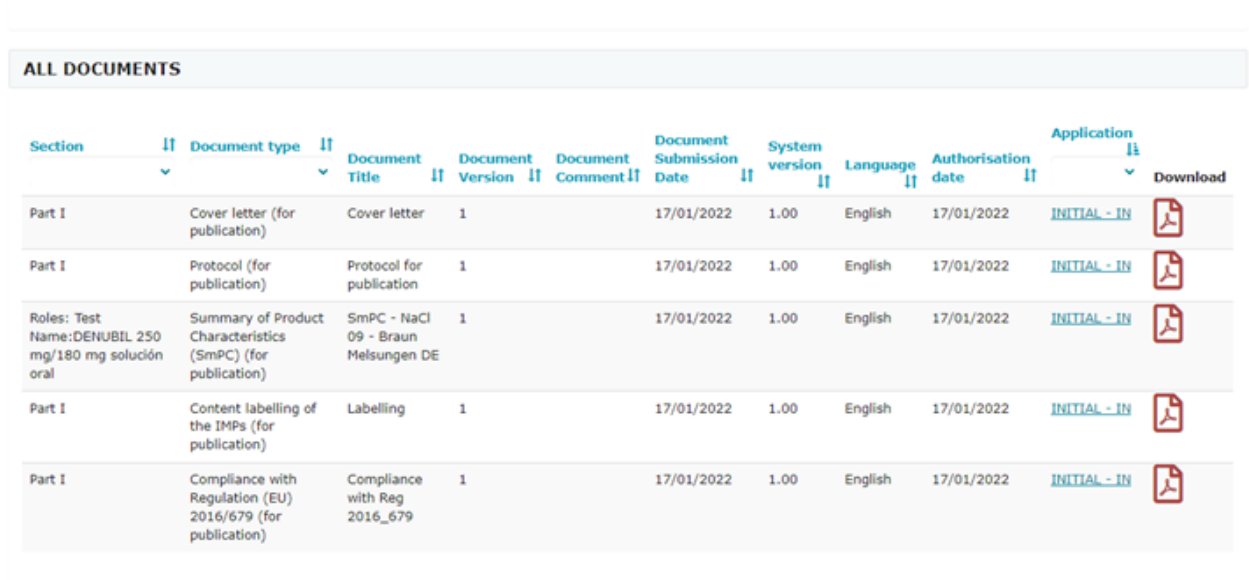
5.4 Authorisation

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.



An overview of all documents and the approval date is shown at the end of ”full trial information”.



6 15 days Notifications after Authorisation

Video on this topic in EMA training module 5:

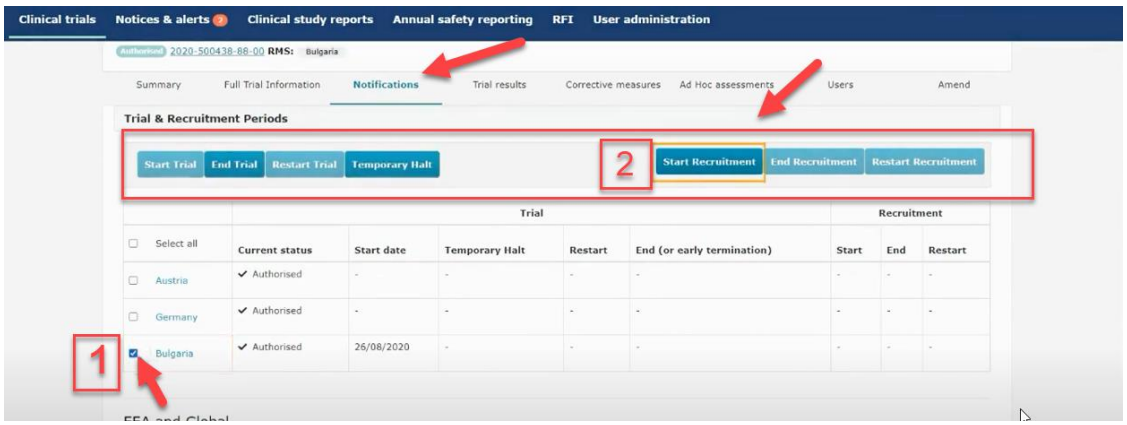
Training Video: How to manage a CT in the CTIS sponsors workspace – Trial and recruitment periods notifications

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:

- Start of recruitment
- Start of inclusion
- Temporary halt of the clinical trial
- Temporarily halted clinical trial is resumed
- End of recruitment
- End of inclusion
- End of trial

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.

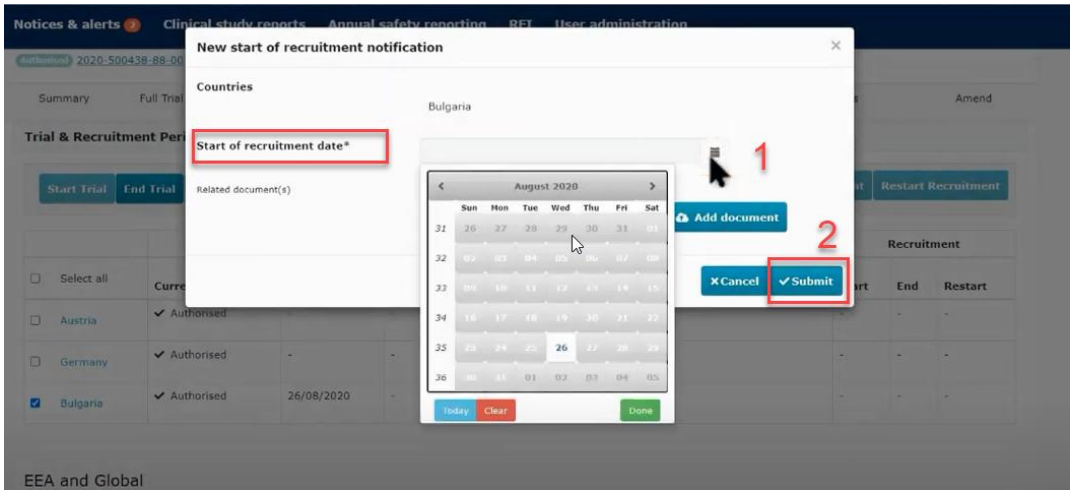


Select the specific country where you want to make a notification

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.**

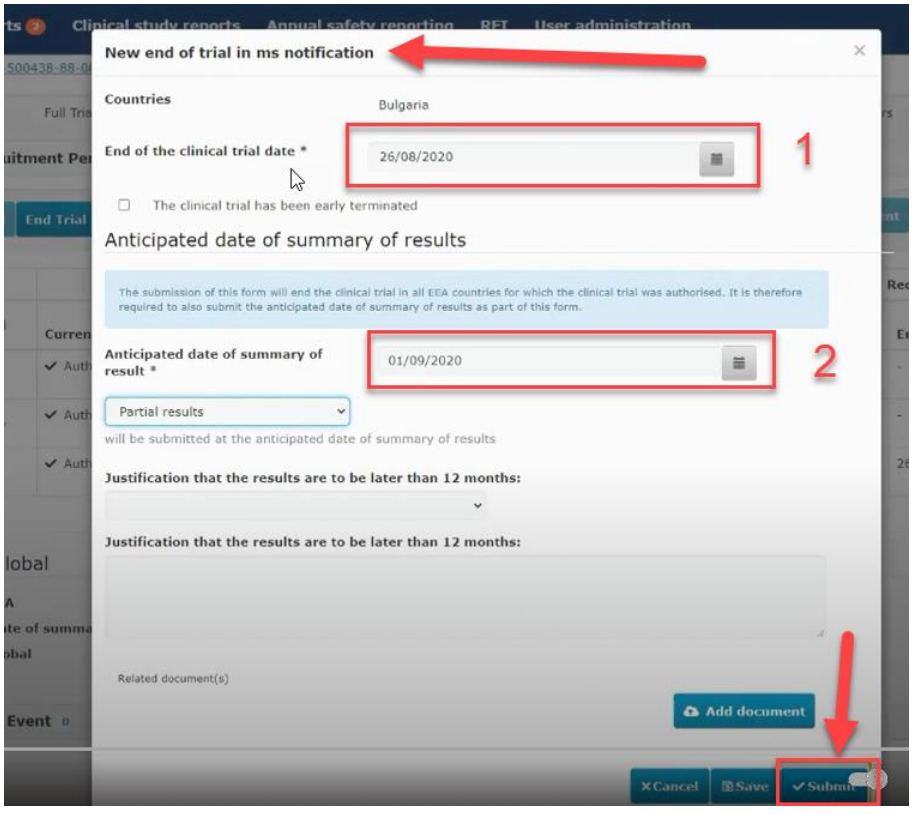
Examples:

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:

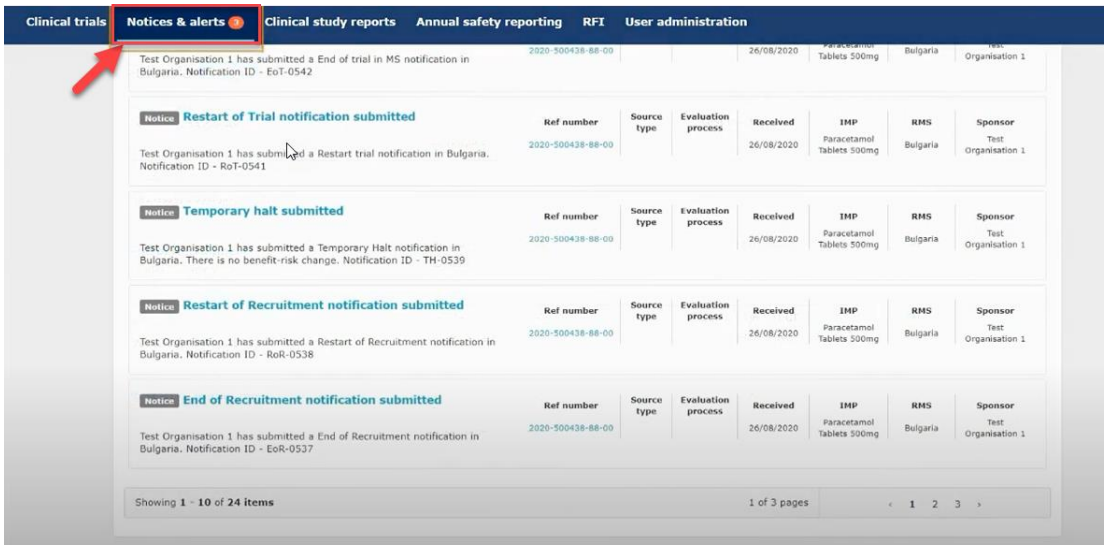


Enter the date where the clinical trial ended according to the protocol or if it was terminated early.

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.



7 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)

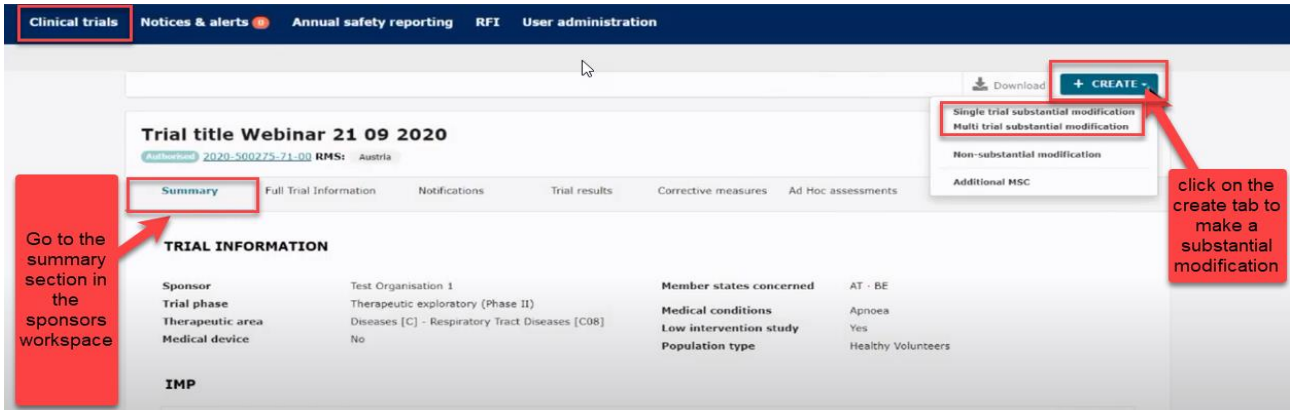
Classification of changes to ongoing trials can be found in EMA Q&A Annex IV “Classification of changes to ongoing clinical trial”.

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

The CTR´s 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.

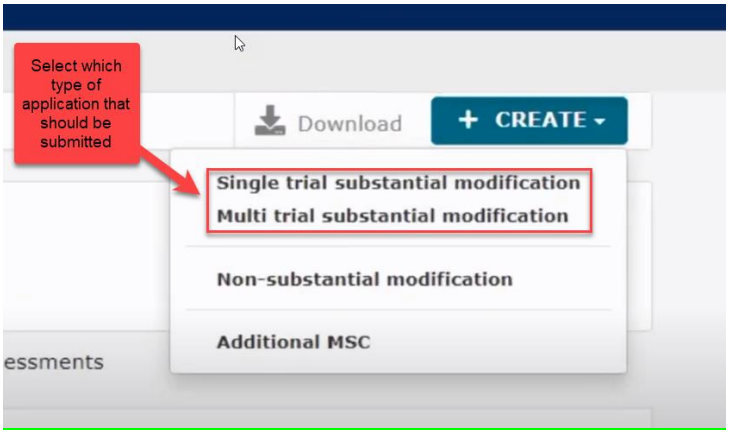
To create and submit a substantial modification after the clinical trial has been authorised, users can select the ‘+ CREATE’ button in the sponsors workspace at the top-right corner of the Clinical Trail page.

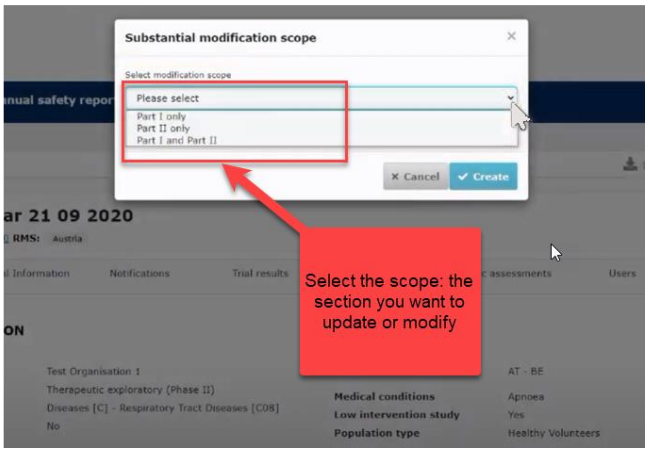


This will enable you to select which type of modification you want to submit:

<u>Single trial substantial modification:</u> to update information for *only one trial*.

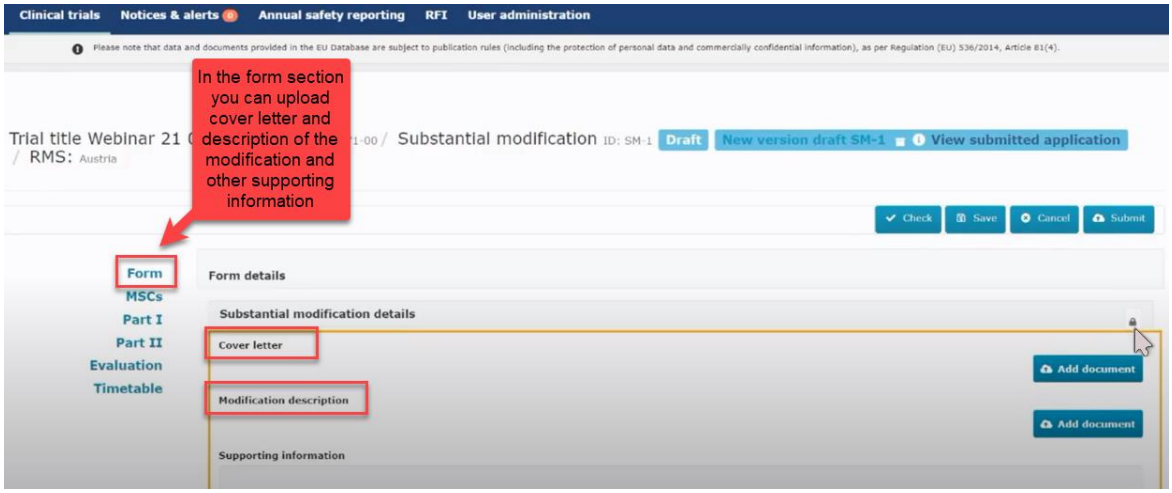
<u>Multi trial substantial modification:</u> to update information for trials that have the same investigational medicinal product (IMP) and the same sponsor. In this case it is possible to submit *a single application covering several trials.*



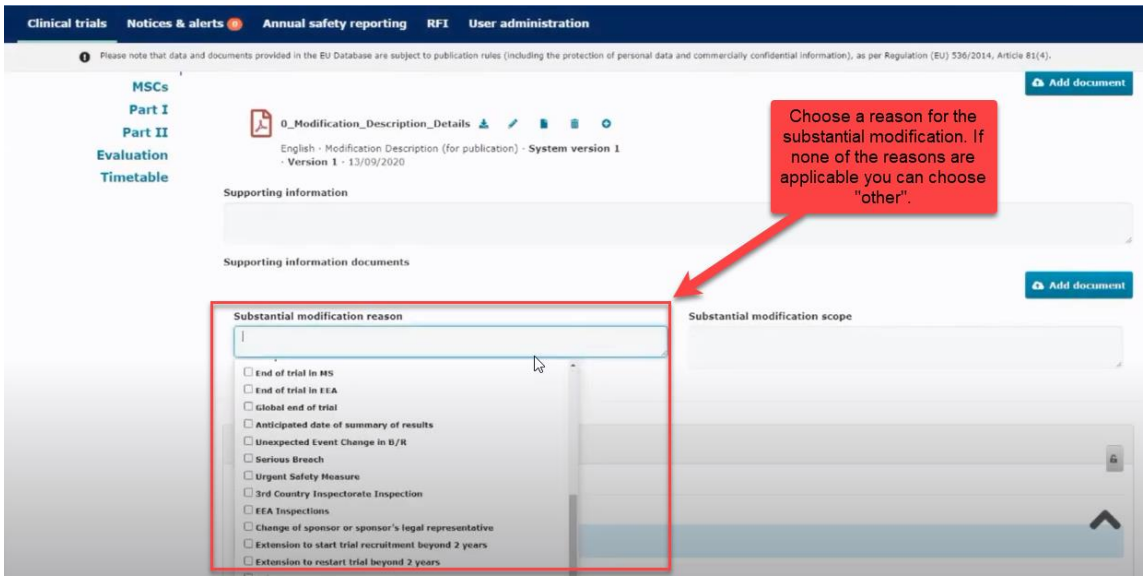


If you click on the **"Single trial substantial modification"** you will be redirected to a window where you need to enter the scope of the substantial modification. Thereby you will define the part which will be modified (Part I and/or II).

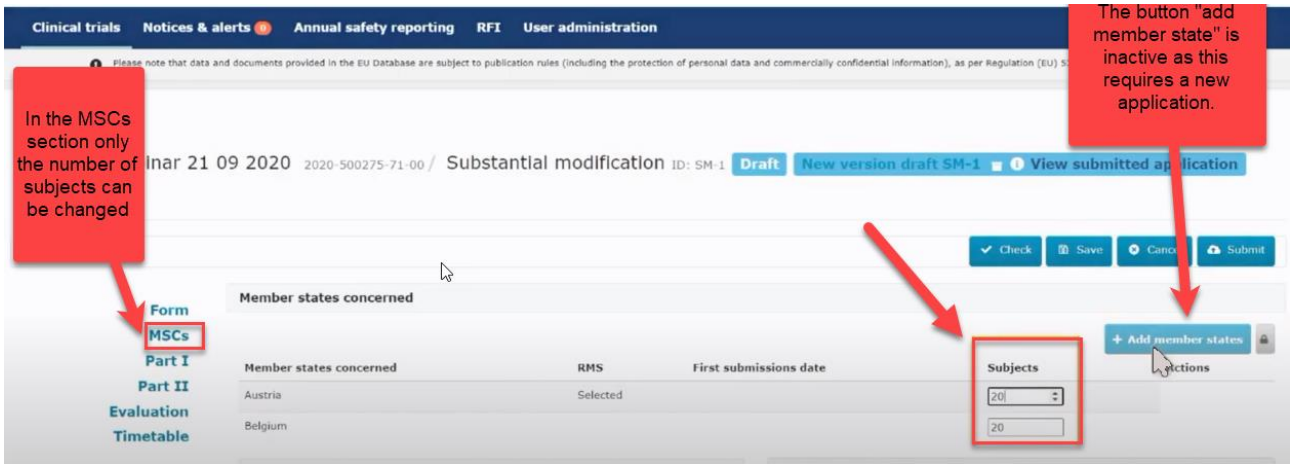
In the **"Form" section**, cover letter etc. should be uploaded and you can add details about the substantial modification.



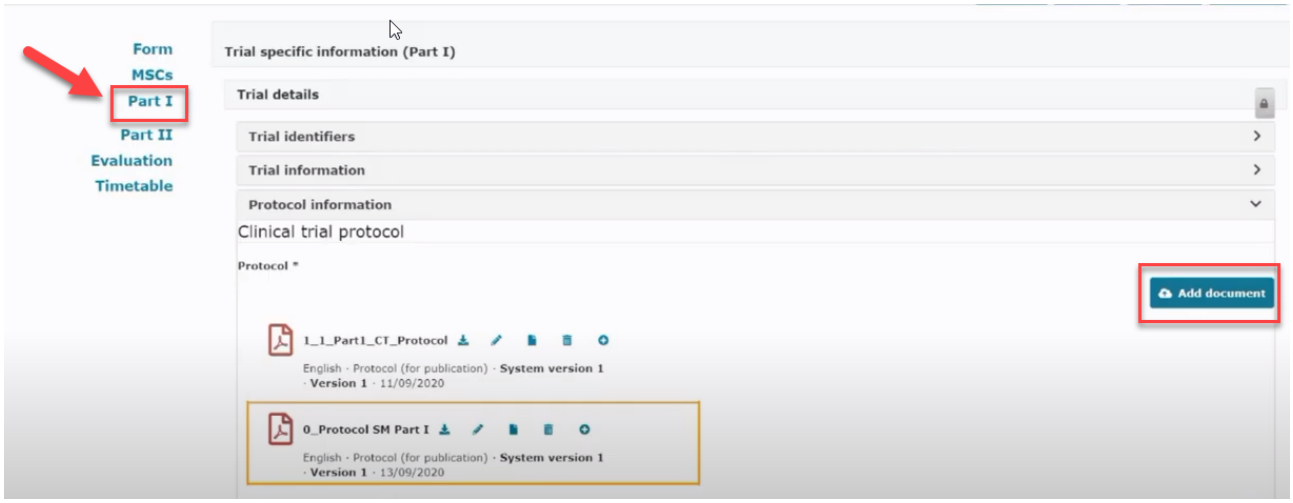
If you scroll down, the reason for the substantial modification must be added here.



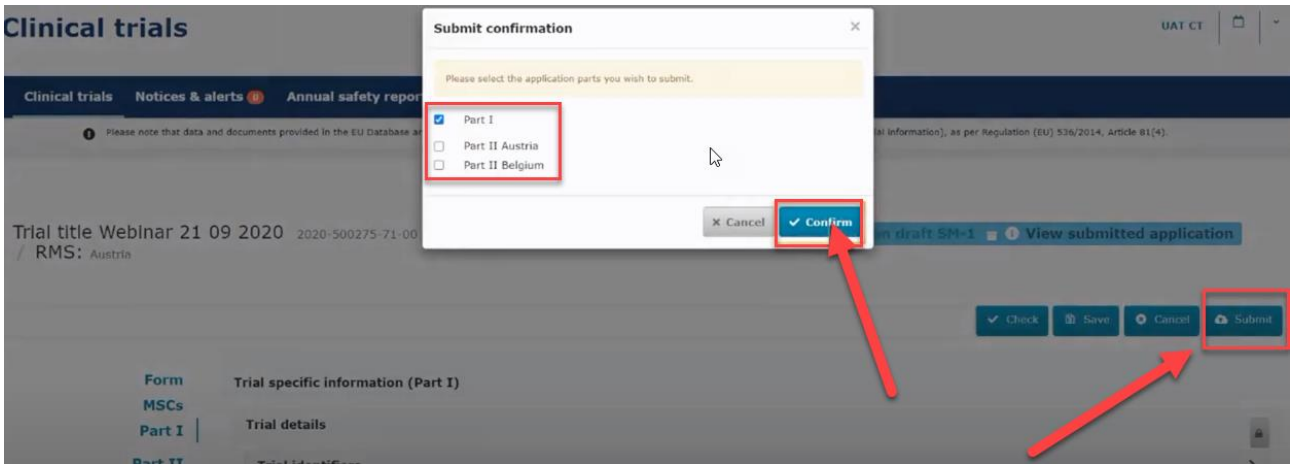
In the "**MSCs section"** only subject numbers (number of planned trial subject) can be modified.



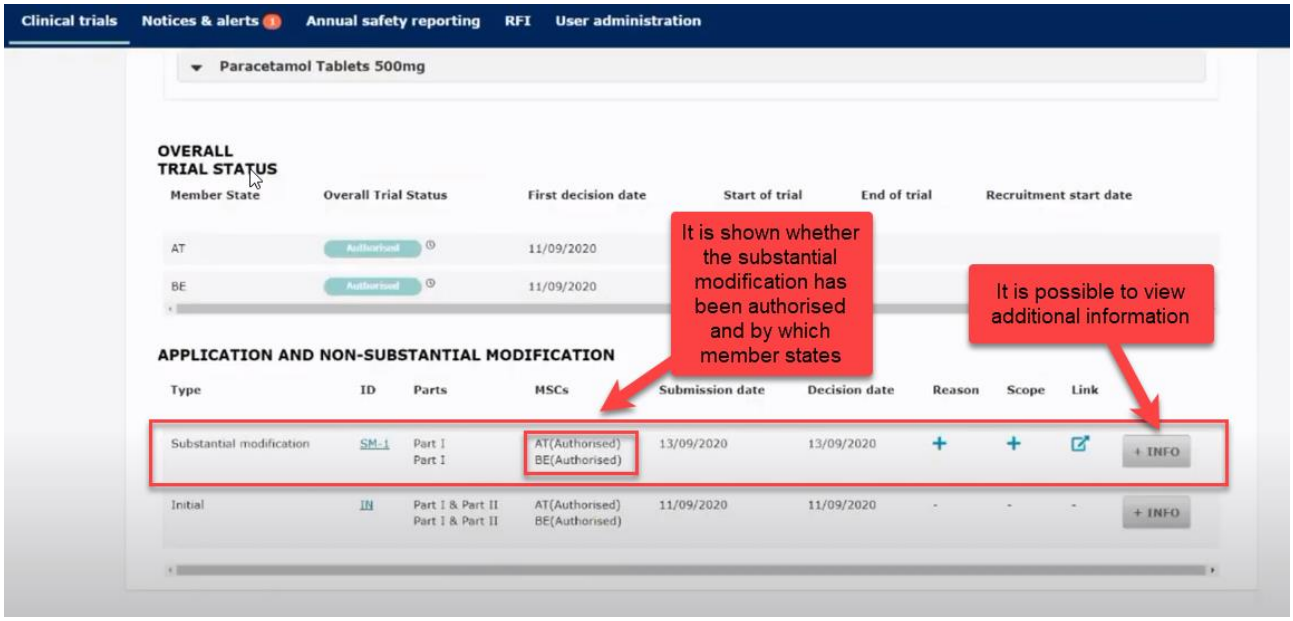
In the “**Part I or Part II” section** you can upload the relevant documents with changes.



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.



8 Create and submit an Annual Safety Report (ASR)

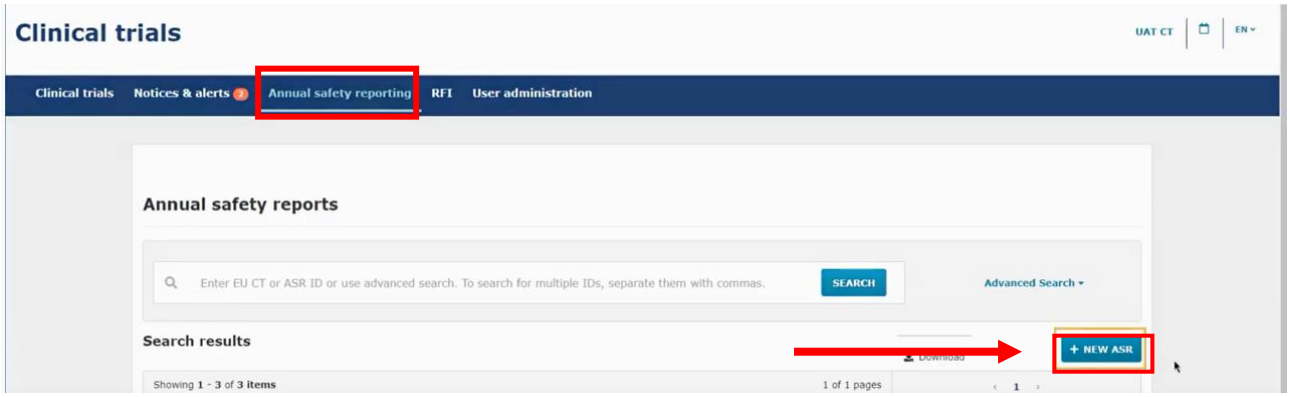
Video on this topic in EMA training module 18:

Training Video: How to create, cancel or clear and submit an Annual Safety Report

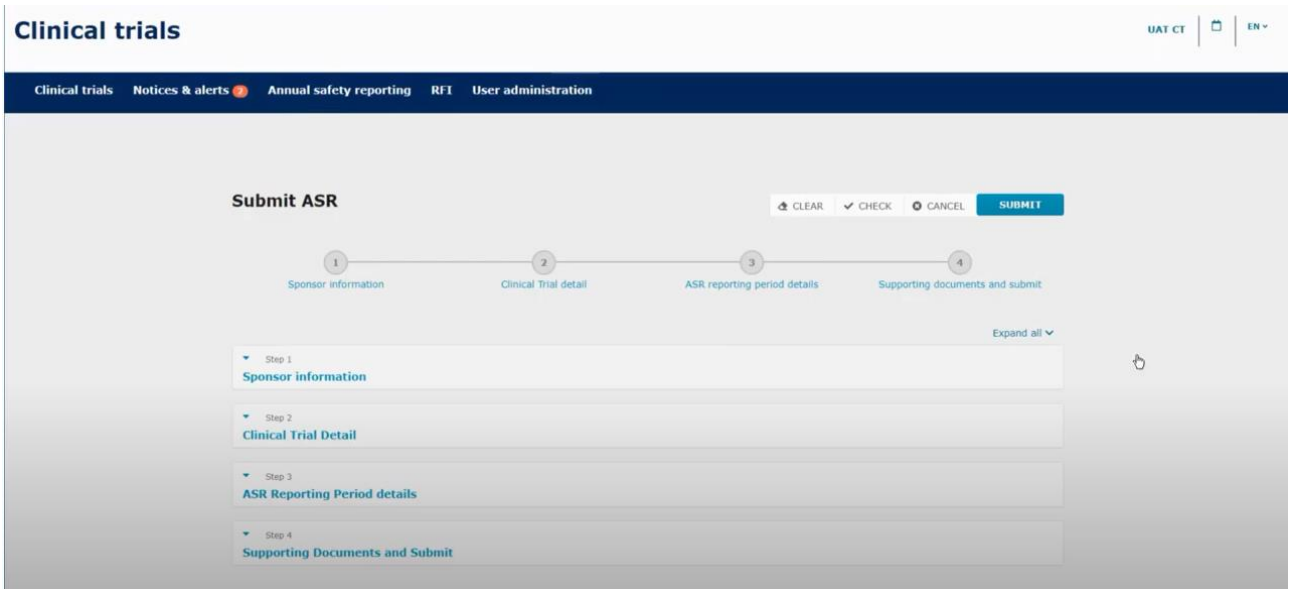
Info box:

Make sure to have the ASR document in PDF prepared.
You also need to have all the relevant information ready (e.g. Investigational medicinal products, relevant events that occurred, reporting period, etc) before you start.

To create and submit an Annual Safety Report users can open “the Annual Safety Reporting form” by clicking on the ‘+New ASR’ button in the sponsor’s workspace.

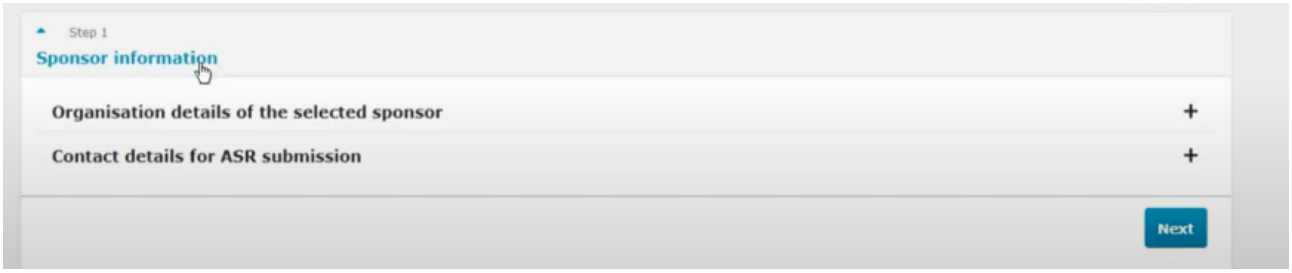


An ASR form opens:



Fill in the information for the four steps (**Sponsor information**, **Clinical trial details**, **ASR reporting period details** and **supporting documents**) and submit on the "Submit" button. The ASR form has to be filled in and submitted in one go. You need to have all information ready because it cannot be saved.

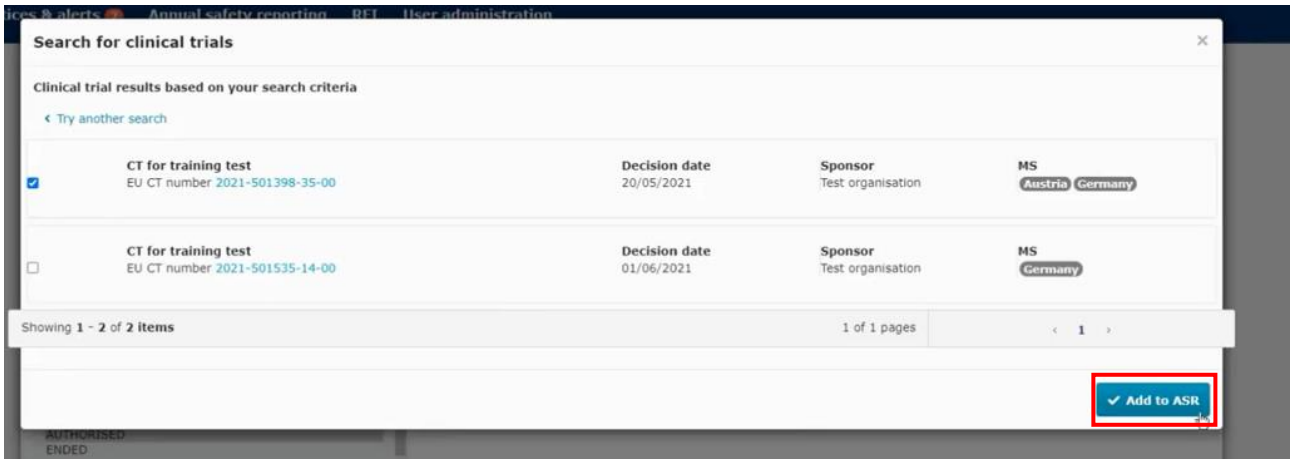
Step 1: Sponsor information



Fill in Organisation details of the selected sponsor and the contact details for the person who is responsible for the submission and can be contacted with an email address and / or phone number.

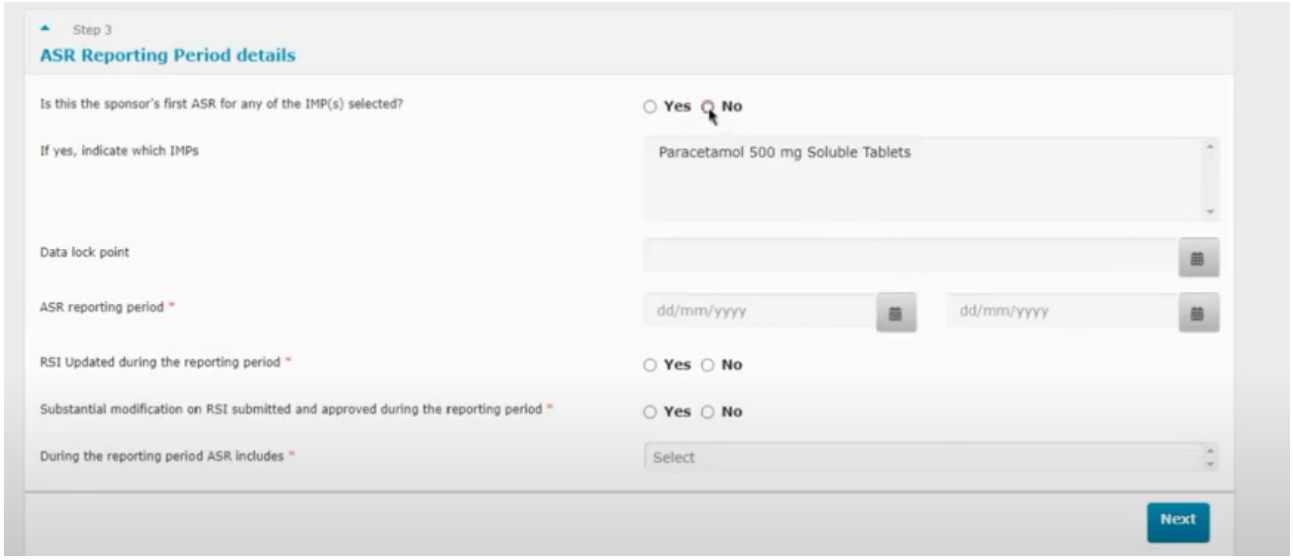
Step 2: Clinical trial details

Search for the Clinical Trial (CT) to which you want to submit an ASR. You search for clinical trials that are authorised for the selected sponsor organisation and select the trial(s) for which you want to submit an ASR.



When the form opens you click on the related IMP or IMP's for the clinical trial you want to submit an ASR.

Step 3: ASR reporting period details



In this section you need to select and fill in the **data lock point (DLP).** That is the cut-off date of selecting data for the ASR. The DLP must be as close as possible to the approval date.

If this is the first ASR in the clinical trial the **ASR reporting period** starts with the date where the clinical trial is first authorised and ends with the selected DLP (approximately after one year).

The deadline for submission of ASR is every year 60 calendar days after the DLP.

The following should also be answered:

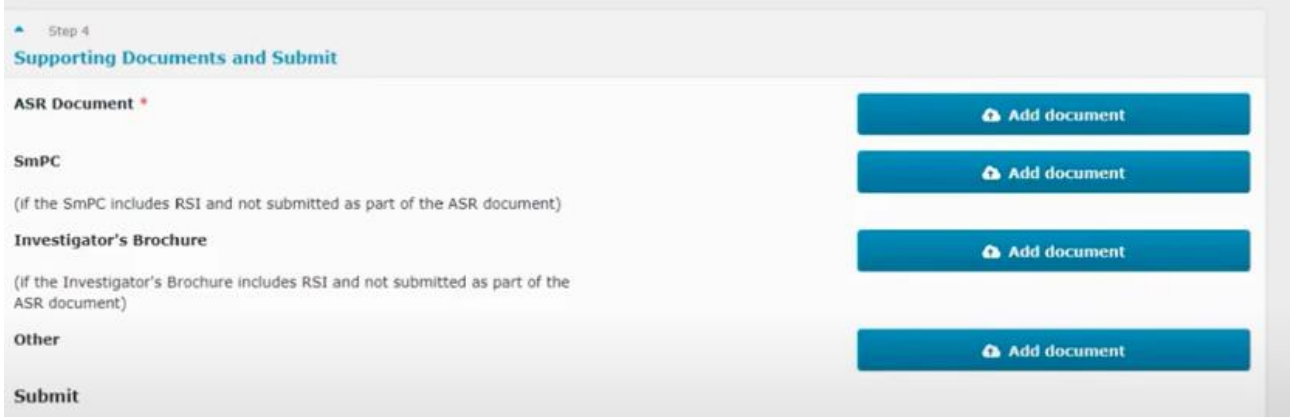
- Has the RSI (reference safety information) been updated during the reporting period?

- Has a Substantial modification on the RSI been submitted and approved during the reporting period?

In most cases the answer would be no.

From the drop down menu it is possible to choose what the ASR includes.

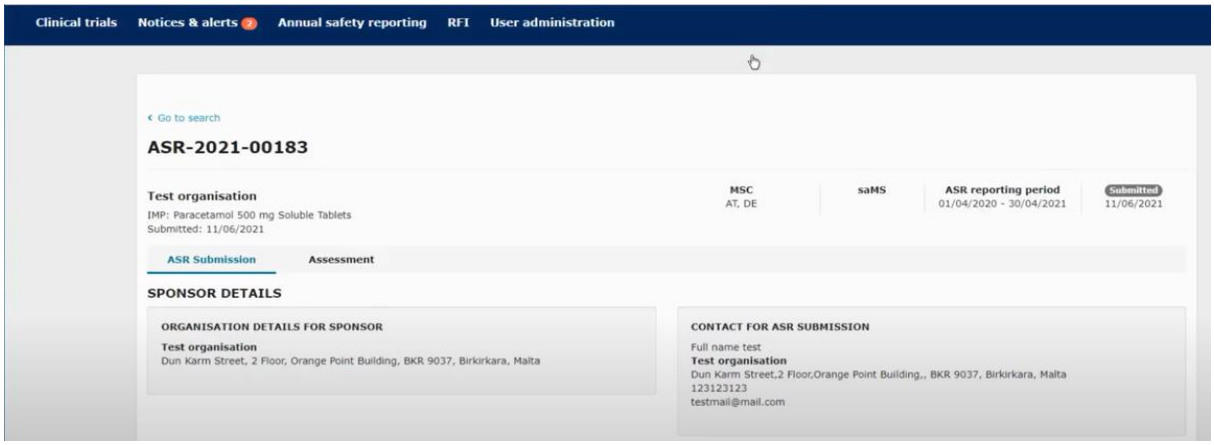
Step 4: Supporting documents and submit



In step 4 you add the ASR report document and you can also add other supporting documents. The ASR report should be uploaded as a PDF.

Then you can check if all information is valid or anything is missing by using the **check button** and then you can submit.

Once submitted you see this page where all the information that was populated will appear.

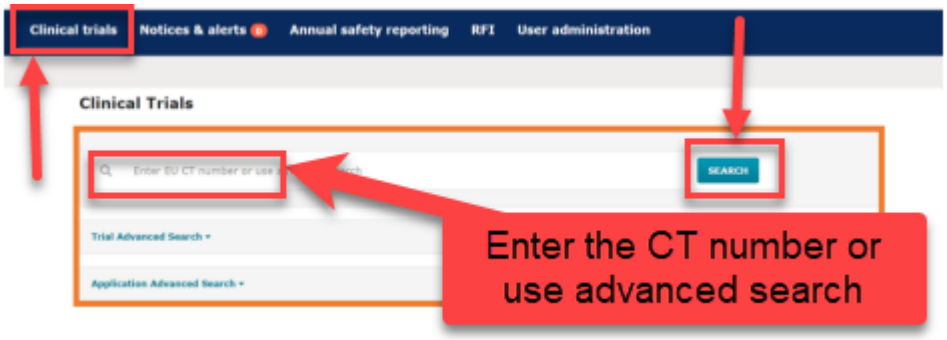


9 Summary of Results and Summary for Layperson

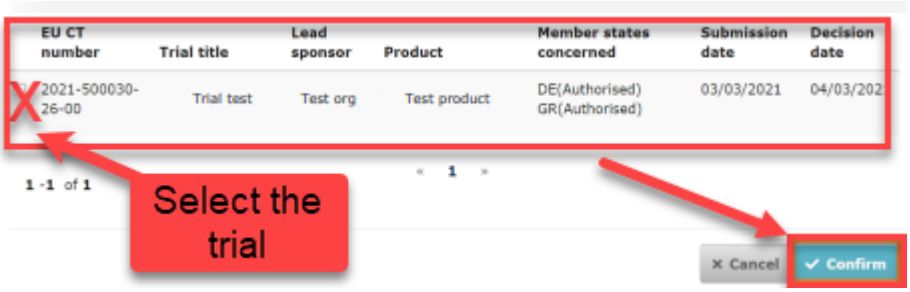
The sponsor shall submit a summary of the results of the Clinical Trial. The deadline for uploading the results in CTIS is 1 year after end of trial.

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.

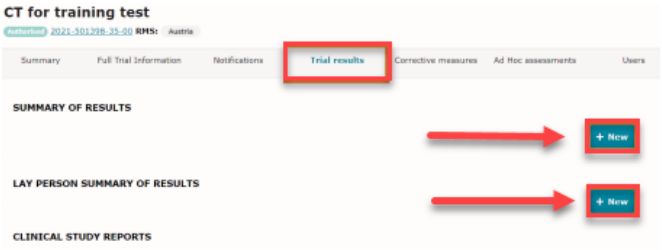
To submit the summary of results go to Clinical Trial page and search for the clinical trial by entering the "EU CT number" or use advanced search.



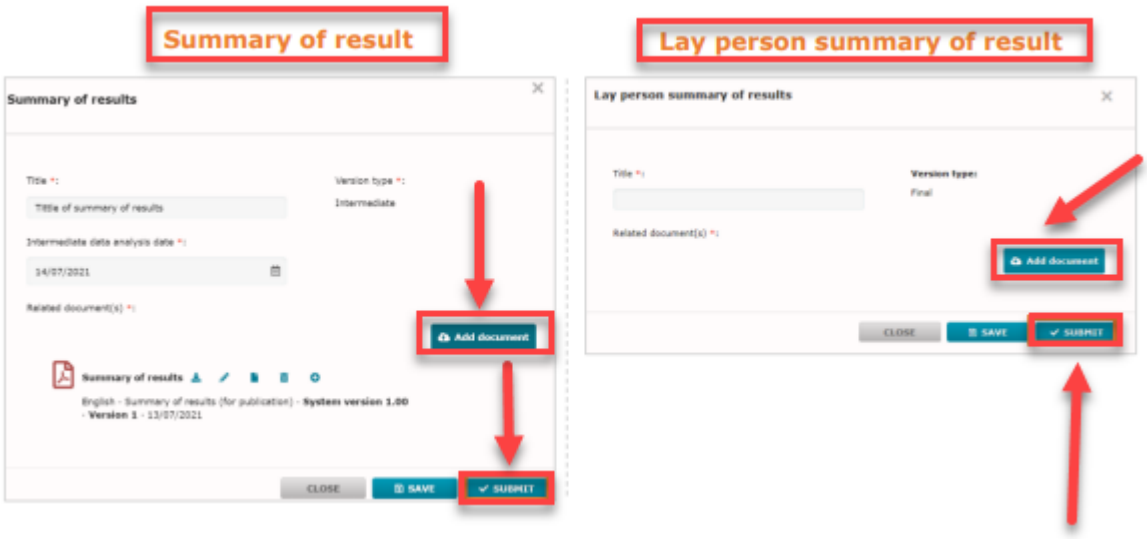
Select the trial from the results page and click on the 'Confirm' button.



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".



10 Changes log

Version 1.0

Version 1.2 Links corrected

Version 1.3 Updated according to comments from users

Version 1.4 updated modifications of Finland, 03.05.2022

Version 1.5 updated modifications of Finland 29.12.2023