



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

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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

(s)IMPD = (simplified) 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

XEVMPD =Extended Eudravigilance Medicinal Product Dictionary

1 Introduction

1.1 What is CTIS?

Clinical Trial Information System (CTIS) is the **single entry point** for submitting clinical trial information in the EU. All communication, including final decisions 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 **secure** 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
[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).
- The **public website**, accessible to patients, healthcare professionals, scientists, clinical research associations, media, and members of the public: [CTIS](#)

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.

Important for users from Odense University Hospital and the Capital Region of Denmark

This guidance has been developed based on the **trial-centric approach** in CTIS and therefore assumes that users create a new clinical trial record themselves and obtain an EU CT number as part of the application process.

However, Odense University Hospital (OUH) and the Capital Region of Denmark use the **organisation-centric approach** for the registration of clinical trials in CTIS. Researchers from these organisations must therefore contact the relevant local CTIS support function before initiating a new CTIS application.

[Link to information for Odense University Hospital and the Capital Region of Denmark](#)

Through the organisation-centric process, the trial will be registered within the organisation's CTIS account and an **EU CT number** will be assigned before work on the application begins.

Consequently, researchers from OUH and the Capital Region of Denmark may disregard the instructions in section 2.2. concerning trial creation, provided that an EU CT number has already been assigned through the local organisation-centric process.

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

GCP unit at Aalborg University hospital: gcp@rn.dk

GCP unit at Aarhus University hospital: gcp-unit@clin.au.dk

GCP unit at Odense University hospital: GCP-enheden@rsyd.dk

GCP unit at Copenhagen University hospital: 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 \(CTIS\): training and support | European Medicines Agency \(europa.eu\)](https://european-medicines-agency.europa.eu)
- **Clinical Trial Information System (CTIS) – [Sponsors Handbook](#) and [CTIS Sponsor FAQs](#)– covers all training material**
- [Quick guide for sponsors – Regulation 536/2014 in practice](#)
- How to search and create organisations in CTIS: [Step by step guideline](#)
- Guide for [CTIS common features](#)
- EMAs help desk for CTIS: [CTIS Service Desk](#) - *Before submitting a ticket to Service Desk, please check information available on the EMA CTIS Support page [EMA CTIS Support page](#)*
Help desk: Non-commercial sponsors can submit their question now by raising a ticket and indicating their status as a “Non-commercial Sponsor” in the mandatory field “User affiliation”

Q&As for CTR and CTIS:

- [Regulation CTR Q&A](#) (Regulation Eudralex vol. 10 – Question and answer document.)
- [Frequently asked questions related to Clinical trials submitted under the Regulation EU 536/2014 - this document addresses practical challenges and offers operational solutions.](#)
- [Danish Medicines Agency Q&A and general information from DMA](#)
- [CTR and CTIS Q&A | Danish Research Ethics Committees](#)

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 the first time log-in to the CTIS Sponsor Workspace we refer to the “The Danish GCP Units guide – User access, roles and responsibilities in CTIS”

Info box:

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

On the HMA homepage templates for cover letters, SM and RFI are found
[Heads of Medicines Agencies: GO TO: Key documents list](#)

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

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, neither digital nor wet ink signatures, in all documents, as they can be copied, when the documents are made publicly available. 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 will be accessible from the public domain of CTIS: [Revised CTIS Transparency Rules](#)

Info box:

Language requirements (Part I) and National requirements (Part II):

See [CTR Q&A Annex II and Annex III](#)

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
➤ Cover letter (content, Annex 1, section B in the Regulation) – cover letter must be uploaded in the section “Form” in CTIS. Template: Clinical Trials Coordination Group (hma.eu) , CTCG “Key documents list”) ➤ EU Application form (structured data entered directly in CTIS) ➤ Protocol and protocol synopsis (synopsis can be part of protocol or separate document) (CTR Q&A, section 5.8 for synopsis guidance) ➤ 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. Translations should be uploaded in part II.</i> ➤ Investigators Brochure (IB)/SmPC ➤ IMPD quality, safety and efficacy/ Simplified IMPD with reference to the valid SmPC ➤ Content of labelling of IMPD ➤ Template statement on compliance with Regulation (EU) 2016/679 (GDPR) (template in Volume 10) – must be uploaded in the section “Form” in CTIS	➤ Informed consent and patient recruitment procedure template (template in Volume 10) ➤ Subject information and informed consent form ➤ Patient facing documents (e.g. recruitment) ➤ Investigator CV (template in Volume 10) – it is not mandatory to use this template ➤ Declaration of interest, only for principal investigator (PI) (template in Volume 10) ➤ Site suitability form (template in Volume 10) - one form per site ➤ 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”) ➤ Financial and other arrangements ➤ Proof of payment of fee ➤ Compliance with applicable rules for biological samples (template in Volume 10) ➤ Statement on compliance with Danish Data Protection Act (Databeskyttelsesloven) (see example on the gcp-unit homepage) or refer to other relevant national requirements on data protection in the applied member states. Patient-facing documents e.g. questionnaire or diary in MS language* (if applicable)

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. It is possible to rename your documents in CTIS after upload.

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

Document upload

Place documents here or click to upload
Protocol ABC123 v4 12Feb2022.pdf

Title* Protocol ABC123 v4 12Feb2022 **Type*** Protocol (for publication)

Language English **Version*** 1 **System version** 1.00

Date* 29/03/2022

Comment (optional)

The above document(s) will be published.

Annotations:

- 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

[CTCG best practice guide naming of documents, version 3.0 February 2026](#)

2.2 Create a new trial

When you are logged into CTIS, click on the tab **“New Trial”**. Type the full title of the trial.

+ New 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.

Some hospitals are mentioned in OMS as the **“Region”** e.g. **“Region Hovedstaden”** and **“Region Midtjylland”** and others with the name of the hospital. Be aware to choose the right location ID (street address) of the hospital.

“Region Midtjylland”: use ORG-100009397 when you search for an organisation in CTIS. Then you will be able to find the location of each hospital in the Region.

The screenshot shows the 'Create new trial' modal window. The 'Full title (English)*' field is highlighted with a red box. Below it, the 'Search organisation' section is also highlighted with a red box. This section contains four dropdown menus for 'Name', 'ID', 'City', and 'Country', each with a 'starts with' filter. Below the dropdowns are three buttons: '+ New organisation', 'Clear', and 'Search organisation'. A red arrow points to the 'Search organisation' button. At the bottom of the modal, there is a table with the following columns: ID, Name, Address, City, postCode, country, phone, email, and Actions. The table is currently empty. At the bottom right of the modal are 'Cancel' and 'Create' buttons.

The screenshot shows the GCP CTIS interface. At the top, the 'Full title (English)*' field is highlighted with a red box and labeled '1'. Below it, the 'Search organisation' dropdown is highlighted with a red box and labeled '2'. The dropdown menu is open, showing a list of organisations. At the bottom right, the 'Create' button is highlighted with a red box and a red arrow points to it.

ID	Name	Address	City	postCode	country	phone	email
ORG-100023062	IAM Test Organisation	identitylaan 122	Amsterdam	1071 LT	Netherlands		
ORG-100023032	Test organisation	Test employer address			Antarctica		
ORG-100022987	Test Organisation 1	980 Great West Road Address line 2,Address line 3,Address line 4,	London		United Kingdom		
ORG-100023057	Test Organisation Demo	Berlinstrasse 12	Berlin	1045GA	Germany	004952255564645	sponsor1@e
ORG-10002305	Test Organisation Demo	Berlinstrasse 12	Berlin	1010GB	Germany	004952255564645	sponsor@er

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

2.3 How to complete the clinical trial application (CTA)

At the following picture in the top right corner there are four buttons:

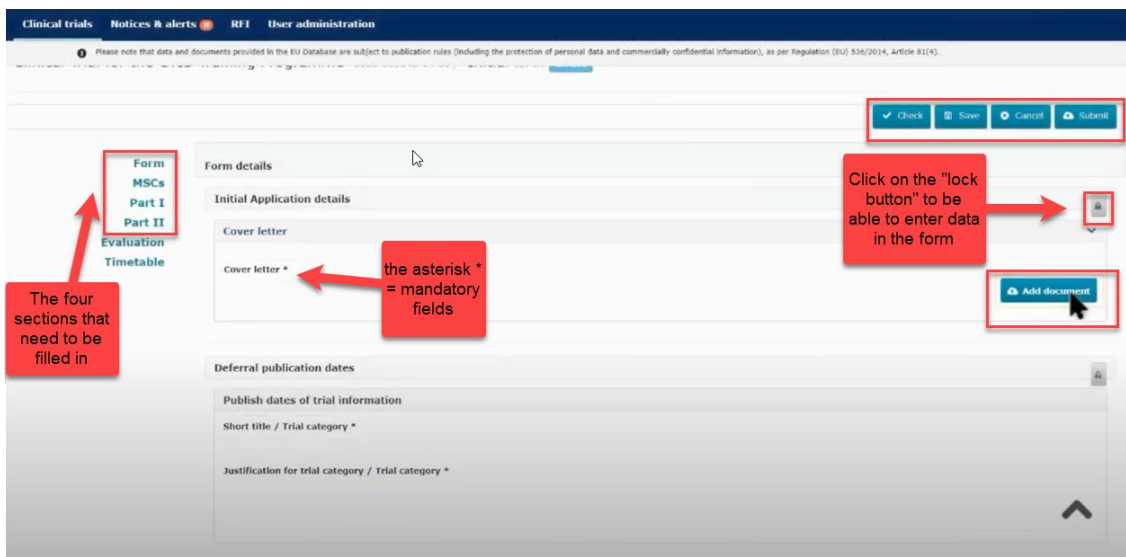
1. Check: Identifies the mandatory fields in the sections which have not yet been completed.
2. Save: Save the data provided in the CTA up to that moment.
3. Cancel: To cancel your application. This can only be done while your CTA is still in “draft” mode.
4. Submit: Submit the final application when all information is entered, and the CTA is complete.

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

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 or Danish for trials only running in Denmark. Remember to click **Save** on the top of the page. This should be done frequently as there will be no automatic savings.



The screenshot shows the 'Form details' page in the CTIS system. The page has a dark blue header with navigation links: 'Clinical trials', 'Notices & alerts', 'RFI', and 'User administration'. Below the header is a warning message about data and document publication rules. The main content area is divided into sections: 'Initial Application details', 'Deferral publication dates', and 'Publish dates of trial information'. The 'Initial Application details' section includes a 'Cover letter' field with an asterisk, indicating it is mandatory. A red box with an arrow points to this asterisk with the text 'the asterisk * = mandatory fields'. Another red box with an arrow points to the 'Add document' button with the text 'Click on the "lock button" to be able to enter data in the form'. A third red box with an arrow points to the 'Form', 'MSCs', 'Part I', 'Part II', 'Evaluation', and 'Timetable' tabs with the text 'The four sections that need to be filled in'. At the top right of the form, there are buttons for '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 [Sponsors Handbook section 2.2](#) and Detailed fields descriptions in the document [CTIS applications fields](#).

2.4 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](#)

The screenshot shows the 'Form details' section of the EMA application form. On the left, a sidebar contains links: 'Form' (highlighted with a red box), 'MSCs', 'Part I', 'Part II', 'Evaluation', and 'Timetable'. The main content area is divided into two sections. The first section, 'Initial Application details', contains a 'Cover letter' field with a text input area and an 'Add document' button (highlighted with a red box and an arrow from a red callout box labeled 'Add the cover letter'). The second section, 'Deferral publication dates', contains a 'Publish dates of trial information' field with a text input area and an 'Add document' button (highlighted with a red box and an arrow from a red callout box labeled 'Add the trial category and justification for the category').

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:

First trials conducted with new medicines or new pharmaceutical forms or routes of administration of existing medicines as well as generic or biosimilar medicines. Includes **phase 0 and I clinical** trials in healthy volunteers or patients. **Bioequivalence and bioavailability trials** are also in this category 1.

Category 2: Therapeutic exploratory and confirmatory trials:

Carried out for treatment, diagnosis or prevention. Include the **phase II and III and phase I+II (integrated)** trials carried out during clinical development of a new product or during exploration of new indications, pharmaceutical forms, strengths and routes of administration for an existing product that already has a marketing authorisation.

Category 3: Therapeutic use clinical trials:

The study drug is in routine use in medical practice. Includes **phase IV trials and phase III+IV (integrated)** that are post marketing studies to delineate additional information including the risk, benefits, and optimal use of the study drug. They are carried out in accordance with the terms of the marketing authorisation (indication, route of administration and pharmaceutical form and strength).

Low-intervention clinical trial is also a category 3 trial.

More information about categories, see guideline: [Revised transparency rules](#), Annex 1

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

Info box:

The protocol will automatically be accessible in the public workspace (Category 2 and 3 trials).

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)



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 more than one country is participating in the trial, you can suggest a country as RMS (reference member state) which is the country that is responsible for the overall scientific assessment.

2.5 Adding Countries outside the European Economic Area

Go to part I and scroll down – see screen shot below.

Trial specific information (Part I)

Trial details

Trial identifiers >

Trial information >

Protocol information >

Scientific advice and Paediatric Investigation Plan (PIP) >

Associated clinical trials >

References >

Countries outside the European Economic Area

+ Add non-EEA country

Rest of the world subjects*

0

2.6 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.

Clinical trials Notices & alerts RFI User administration

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).

Check Save Cancel Submit

Form
MSCs
Part I
Part II
Evaluation
Timetable

Trial specific information (Part I)

Trial details

- Trial identifiers
- Trial information
- Protocol information
- Scientific advice and Paediatric Investigation Plan (PIP)
- Associated clinical trials
- References
- Countries outside the European Economic Area

Sponsors

Name	Organisation type	Country	Type	Status	Legal representative	Scientific contact point	Public contact point	Third parties
Test Organisation Demo	Pharmaceutical company	Germany	Commercial	Active				

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

Trial Information

The field ‘Individual Participant Data (IPD) Sharing Statement’ collects information on how data will be made available to other researchers. Sponsor users in CTIS can now record in a structured way how IPD will be shared in the future. ‘Plan to share IPD’, is mandatory. Users need to select a response from a drop-down list of pre-defined values (Yes/No/Undefined). We recommend that sponsor users select “Yes” or “No”, to meet the requirements of the International Committee of Medical Journals Editors (ICJME).

The second field, ‘Plan description’, is optional. It allows users to describe the plan in detail, in free text, using up to 1000 characters.

Estimated recruitment start date in EEA *

01/06/2024

Estimated end of trial date in EEA *

31/08/2024

Estimated global end date of the trial *

15/09/2024

Source of monetary support or material support

+ Add source

Organisation name	Actions
Individual Participant Data (IPD) Sharing Statement	
Plan to share IPD *	
Yes	
Plan description	
free text field to type description for the plan	

Population of trial subjects

If the trial is to be listed in a PIP or to include paediatric subjects, then Main Characteristics, Notifications and Summary of Results associated with this trial will be published at the date of decision on the trial.

Age range *

18-65 years

Age range secondary identifier

Sponsor details

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

Sponsors

Sponsor must be provided

[+ Add sponsor](#) [Change contact point for union](#)

Name	Organisation type	Country	Type	Status	Legal representative	Scientific contact point	Public contact point	Third parties	Actions
Test Organisation Demo	Pharmaceutical company	Germany	Commercial	Active				0	

Contact point for union*

Organisation name
Test Organisation Demo

Address line 1*
Berlinstrasse 12

Address line 2

Address line 3

Address line 4

Town/City*
Berlin

Post code
1045GA

Country*
Germany

Functional contact point name

Contact

First name *

Last name *

Phone *

Email *

Clinical trials **Notices & alerts** **RFI** **User administration**

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).

Sponsors

[+ Add sponsor](#) [Change contact point for union](#)

Name	Organisation type	Country	Type	Status	Legal representative	Scientific contact point	Public contact point	Third parties	Actions
Test Organisation Demo	Pharmaceutical company	Germany	Commercial	Active				0	

Contact point for union*

Organisation name
Test Organisation Demo

Address line 1*
Berlinstrasse 12

Address line 2

Address line 3

Address line 4

Town/City*
Berlin

Post code
1045GA

Country*
Germany

Functional contact point name

Contact

First name *

Last name *

Phone *

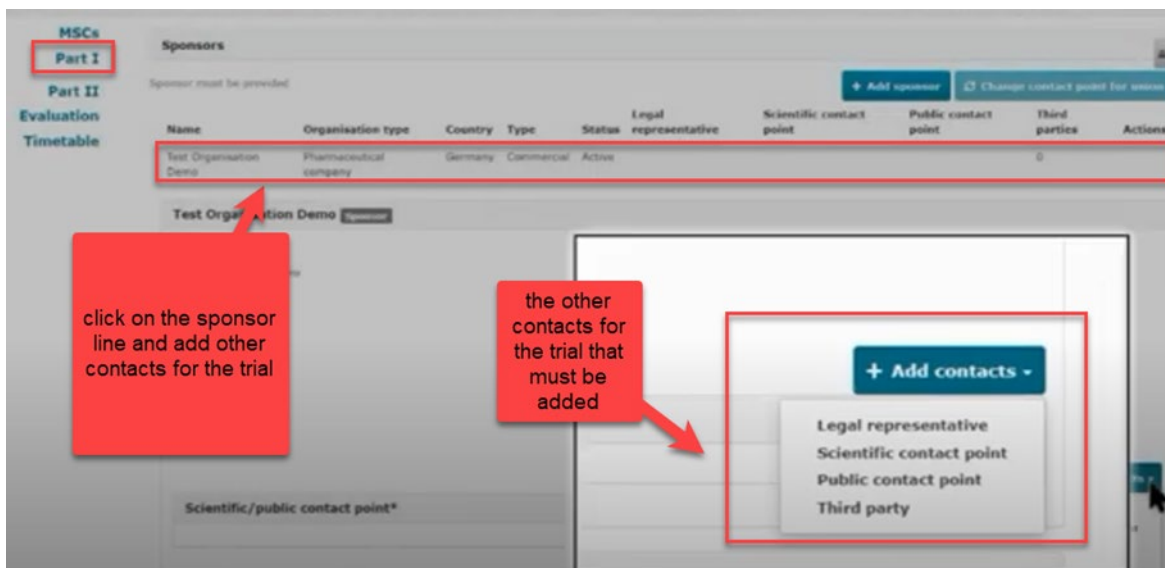
Email *

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 organisation (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/public contact point. The given email address should be one that is monitored regularly and is independent of a specific person, in case the authorities urgently needs to get in touch with the sponsor.

- Third party (only if tasks or functions in the trial have been delegated to third parties). This is e.g. On-site monitoring, Safety reporting, E-data capture (for example, if agreed with the GCP units) 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 2.6).
- **To search for a third party in OMS you need to use the organisation number (ORG) or location number (LOC) – it is not possible to search for the GCP unit or a specific laboratory facility.**
- To add a Third party - See screenshot below.



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

The organisation numbers (ORG) and location numbers (LOC) for the four Danish GCP units are mentioned below.

It is important that you choose the right ORG and LOC number. Each GCP unit is registered only with their organisations (hospital or university) addresses and the name "GCP unit" is not mentioned.

Phone no. and Email are mandatory fields and must also be added in CTIS.

Info box:

Please remember to contact the GCP unit in your Region
to inform about the trial
when you submit a CTIS application
in which the GCP unit was added as third party.

<https://gcp-enhederne.dk/kontakt/>

GCP-enheden ved Københavns Universitetshospital:

ORG-100002431

Organisation name: Region Hovedstaden

(Please be aware to choose the right address and LOC-ID as there are many addresses called "Region Hovedstaden")

Address: Nordre Fasanvej 57

Location ID: LOC-100045259

Tel. phone: +45 38 63 56 20

E-mail: gcp-enheden.bispebjerg-frederiksberg-hospitaler@regionh.dk

GCP-enheden ved Odense Universitetshospital:

ORG-100007716

Organisation name: Region Syddanmark

(Please be aware to choose the right address and Location ID as there are many addresses called "Region Syddanmark")

Address: J B Winsloews Vej 4

Location ID: LOC-100053630

Tel. phone: +45 51 25 14 13

E-mail: OPEN@rsyd.dk

GCP-enheden ved Aarhus Universitetshospital:

ORG-100028380

Organisation name: Aarhus Universitet

Address: Palle Juul-Jensens Boulevard 11

Location ID: LOC-100079923

Tel. phone: +45 78 41 39 50

E-mail: gcp@clin.au.dk

GCP-enheden ved Aalborg Universitetshospital:

ORG-100022335

Organisation name: Region Nordjylland

Address: Søndre Skovvej 15 (in OMS the address is "Sdr")

Location ID: LOC-100047716

Tel. phone: +45 21 53 13 49

E-mail: gcp@rn.dk

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

Product details

All medicinal products that are marketed in EU are registered in the Extended Eudravigilance Medicinal Product Dictionary (XEVMPD) 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 XEVMPD. You can also read more about the registration in XEVMPD at The DKMA homepage: [Registration of new investigational medicinal products in the EudraVigilance database \(XEVMPD\)](#)

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

When a substance is added further information must be entered. Be aware that if you tick the selected substance, there will reveal further sub-sections that contain mandatory fields to be populated.

It is important that the protocol and CTIS are consistent with regard to whether the investigational medicinal product is identified by active substance/generic name or by a specific medicinal product. In case of any discrepancies, the protocol shall take precedence.

Dosage and administration details	
Route of administration*	Maximum duration of treatment* Week(s)
Maximum daily dose allowed*	Daily dose unit of measure*
Maximum total dose allowed*	Total dose unit of measure*

It is mandatory to fill in “Information about the modification of the Medicinal Product” and “Dosage and administration details” for each product in CTIS. Dosage and administration details must be thoroughly and correctly described in the protocol, this is very important. Therefore, when you fill in “Dosage and administration” in CTIS you must use a safety perspective. If you don’t know maximum daily dose allowed (e.g. because the product is administrated on a weekly basis) then you can estimate or calculate maximum daily dose.

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

For sponsors in Region Hovedstaden and Region Sjælland: Please contact “Reg H Sygehusapotek Herlev” to get your product registered in XEVMPD, mail: kliniskeforsoeg.region-hovedstadens-apotek@regionh.dk or Tel: 44577803.

For sponsors in Region Nordjylland: Please contact “Sygehusapoteket region Nordjylland” to get your product registered in XEVMPD, mail to farmaceut: kirsten.lykke.vorbeck@rn.dk or phone: +45 30361382

For sponsors in Region Midtjylland: Please contact “Sygehusapoteket region Midtjylland” to get your product registered in XEVMPD, mail to farmaceut Lisbet Emmery Jørgensen, lisjoe@auh.rm.dk or phone +45 2155 4581

For sponsors in Region Syddanmark: Please contact the GCP unit at Odense University hospital to register a medicinal product that is not authorised in XEVMPD: gcp-enheden@rsyd.dk

For IMPs that are not authorised in the EU and do not have a marketing authorisation from a third country that is party to ICH, and are not manufactured in the EU, an authorisation referred to in article 61(1) and a QP declaration of GMP equivalence is required. In the latter case, if a Mutual recognition Agreement (MRA) covering also clinical trials is in place with the particular country, the latter declaration is not required if the MRA provides for GMP equivalence already.

In case IMP is still under development and the sponsor of a clinical trial is not the product owner (PO) of the IMP and should not have access to the quality IMPD (IMPD-Q) or associated considerations/RFI in order to protect commercially confidential information, the PO can submit the IMPD-Q to CTIS via an initial application for Part I only ("IMPD-Q-only application"). The "IMPD-Q-only application" must be submitted at the same time as the initial application of the trial for which the IMP is intended ("sponsor trial"). It is recommended that both submissions are not more than 24 hours apart.

The Part I-only application must be prepared by the PO according to question 2.15 in [CLINICAL TRIALS - REGULATION \(EU\) NO 536/2014 - QUESTIONS & ANSWERS](#).

Mandatory fields that are not relevant should be completed with "IMPD-Q-only" for text fields or "0" for numeric fields. In the final step when submission of the Part I-only application is confirmed, it is by selecting only the Part I tick-box, confirmed that only Part I should be assessed by the selected RMS.

For investigational advanced therapy medicinal products (ATMP) in clinical trials you can get more information in the [DKMA ATMP Q&A](#)

The field "Excluded MSC"

This field is only relevant for multinational trials and should not be used for national trials. It must only be used if it is described in the protocol (and cover letter), that some products (Test, Auxilliary, Comparators), drug forms or strengths, *will not be used* in all Member States concerned.

Example: A multinational trial with MSCs Denmark, France and Netherlands with paracetamol as the test product. In France and Netherlands their sites will be using specifically Paracetamol Zentiva and in Denmark their sites will use Pamol. Hence, DK is added as "Excluded MSC" in the Paracetamol Zentiva tab, and FR and NL in the Pamol tab.

Role: Test Name: Paracetamol "Zentiva", tabletter

+ Add

Product authorisation	Product name	Pharmaceutical form	Strength	Sponsors product code	Active substance name	EU substance number	ATC Name	ATC Code	ATC Level	Sponsors substance code	Active substance other descriptive name	Type	Excluded MSC	Action
Authorised	Paracetamol "Zentiva", tabletter	Tablet	Paracetamol 500mg	-	Paracetamol	SUB09611MIG	PARACETAMOL	N02BE01	5	-	-	Product	Denmark	

Role: Test Name: Pamol, filmovertrukne tabletter

+ Add

Product authorisation	Product name	Pharmaceutical form	Strength	Sponsors product code	Active substance name	EU substance number	ATC Name	ATC Code	ATC Level	Sponsors substance code	Active substance other descriptive name	Type	Excluded MSC	Acti
Authorised	Pamol, filmovertrukne tabletter	Film-coated tablet	Paracetamol 500mg	-	Paracetamol	SUB09611MIG	PARACETAMOL	N02BE01	5	-	-	Product	France Netherlands	

Placebo

If the IMP is a placebo, the information requirements shall be limited to quality data, a simplified IMPD (sIMPD) must be submitted. 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 this case placebo must be added as an "Authorised Substance" followed by a search for *placebo*, remember to give the correct pharmaceutical form and route of administration as given for the test product. The strength for placebo must be "0 mg" and the pharmaceutical form must be added.

Clinical trials Notices & alerts RFI User administration

Please note that data and documents provided in the EU Database

MSCs Products

Part I Part II Evaluation Timetable

Documents

Part 1

0_Forms_Cover English - Cover Version 1 - 01/12/2020

0_Part1_CT_P English - Protocol (for submission) Version 1 - 08/12/2020

Product Content labeling

No sorting

+ Add Register

Test Comparator Auxiliary Placebo

Click "Add" for products already registered in the Eudravigilance database (XEVMPD)

Click "Register" if your product is new (not authorised)

Documentation requirements in the application dossier

As a general rule, the documentation requirements in the application dossier for IMPs also apply to non-authorised AxMPs and authorised AxMPs which are modified while such modification is not covered by the marketing authorisation. Regulation (EU) No 536/2014 Annexes I and II set out the requirements of the application dossier for initial applications and substantial modifications, respectively. Registration in CTIS is only mandatory for non- authorised AxMPs and for authorised AxMPs for which such modification is not covered by the marketing authorisation. It is not a requirement for marketed unmodified AxMP to be registered in CTIS. However, they must be listed in the cover letter or protocol for the trial.

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 trial specific label.

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

2.7 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 need to be uploaded.

We advise not to state or describe part II aspects of the clinical trial in the protocol, as this can lead to an unnecessary number of updates to the protocol through substantial modifications (SM). Instead, a reference to the part II document or CTIS, where the information is to be provided, should be made, and/or added to the structured data under Part II in CTIS. Otherwise, sponsor must update both Part I and Part II of the trial, when there are changes to part II aspects of the trial that are described in the protocol. It is strongly recommended to carefully read the [guidance given on the MREC website](#).

MSCs
Part I
Part II
- AT
- DE
Evaluation
Timetable

Trial sites

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).

Trial sites for each country can be added

+ Add site

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	Schopfstrasse 41, Wilten	Schopfstrasse 41	Innsbruck	6020	Austria	Dr.	First	Last	Chest Clinic	4234242424	flast@email.com	

Documents

- Recruitment Arrangements
- Subject information and informed consent form
- Suitability of the investigator
- Suitability of the facilities
- Proof of insurance cover or indemnification
- Financial and other arrangements
- Compliance with national requirements on Data Protection
- Compliance with use of Biological samples
- All documents

In this section you need to upload the documents for part II

It is possible to upload all documents for part II in the section "All documents"

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.

Info box:

Please be aware not to include personal information (e.g. CPR numbers, private addresses and tel. numbers) in investigators CV or in the structured data in CTIS. The investigator name, mail and phone no. will be public available in “CTIS Public”, when the trial is approved.
It is recommended to use a mail address and tel. phone no., created for the specific trial or for the department (site).

Please note: Trials running in Denmark will as well be extracted from CTIS and listed in the Danish database “Nationalt Forsøgsoverblik”. The website is driven by the Danish Region Zealand, and the GCP-units are not involved in this website.

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 2.6.

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

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.

Clinical trials

Clinical Trial for the CTIS Training Programme 2020-501643-14-00 / Initial ID: IN **Draft**

Country specific details (Part II - DE)

Trial sites

Documents

Recruitment Arrangements

Recruitment arrangements *:

2_1_Part2_Recruitment_Arrangement

English - Recruitment arrangements (for publication) - System version 1

Version 1 - 10/12/2020

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

Submit confirmation

Please select the application parts you wish to submit.

☐ Part I

☒ Part II Austria

☒ Part II Germany

2.8 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](#).

2.9 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 at 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.

2.10 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.

2.11 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

Then, in the top-right corner, click Resubmit

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.

Click on the 'Resubmit' button: a new draft application is created. The new draft will include all of the most recent information in the structured data and the documents that were submitted in the previous application, even if they were updated by responding to an RFI. Only the most recent information is shown, not the historical one(s). Note: in case the 'Resubmit' button does not appear, it could be that the application was already resubmitted, or the trial has a status that is different from the ones stated above. Modify the new application as needed. Note that once the resubmission version is created, all metadata, including the documents dates are reset as it is considered a new submission. You would need to modify the relevant metadata as appropriate.

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. You may set up e-mail notifications in your CTIS profile as described below. However, the sponsor remains responsible for monitoring CTIS, irrespective of whether notifications are received.

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 may have very short response deadlines, the GCP Units recommend that sponsor, or delegated personnel with administrative user rights, check CTIS for RFIs on a daily basis.

CTIS offers an optional e-mail notification service. When enabled, notifications related to notices and alerts in CTIS are sent to the user's registered e-mail address in a daily consolidated message. However, e-mail notifications should be considered a supplementary reminder only and do not replace the requirement to actively monitor CTIS on a regular basis, particularly for time-sensitive requests such as RFIs.

To activate e-mail notifications in CTIS:

1. Log in to CTIS.
2. Open your personal user profile.
3. Locate the e-mail notification setting.
4. Enable the notification slider to subscribe to CTIS notices and alerts.
5. Save the updated settings.

Once activated, e-mail notifications will apply to all notices and alerts associated with the user's CTIS role(s). By default, this feature is disabled for all users.

Personal profile

User ID: [REDACTED]

My info

First name:

Email:

[Password reset](#)

My employer

Employer name:

Contact details / Employer address:

Receive notices and alerts via email: ☐ Off

Last name:

Phone:

[Update personal information](#)

[Update employer information](#)

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 chance 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”.

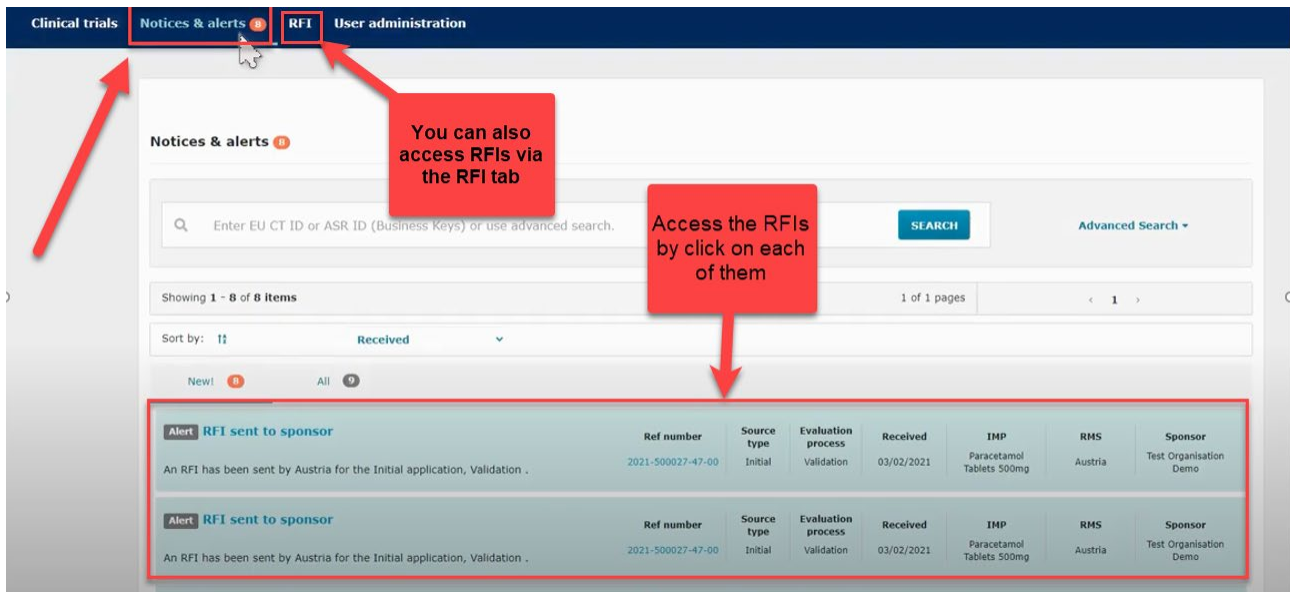
If in doubt about anything – call the Danish Medicines Agency or EC before submitting the answer to the RFI.

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.

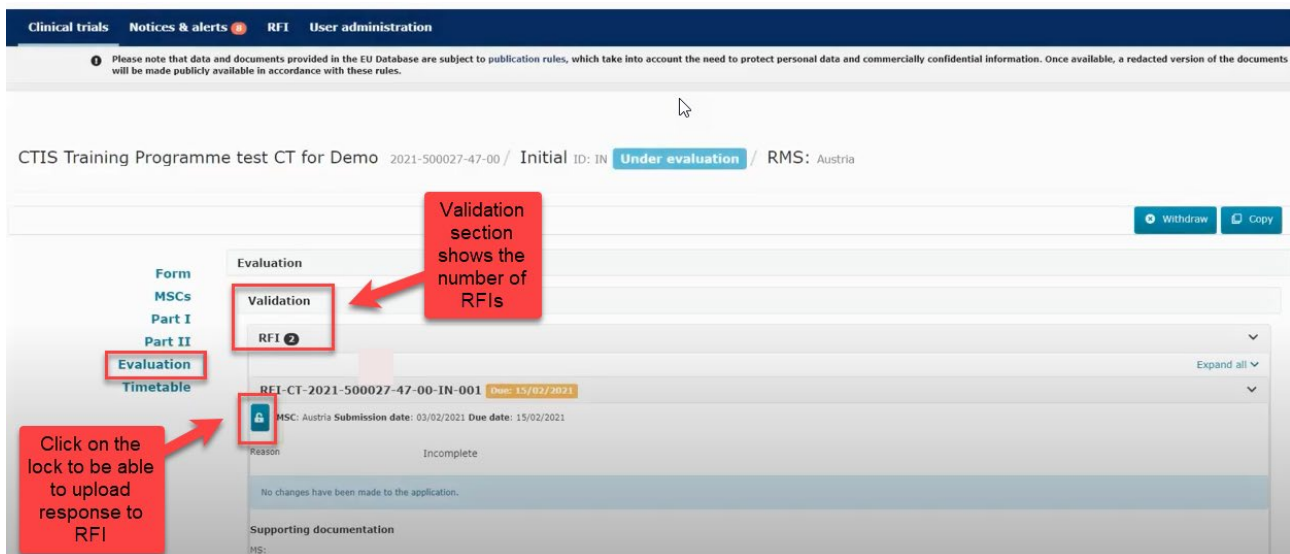
It is possible to download the RFI’s – see section 3.6



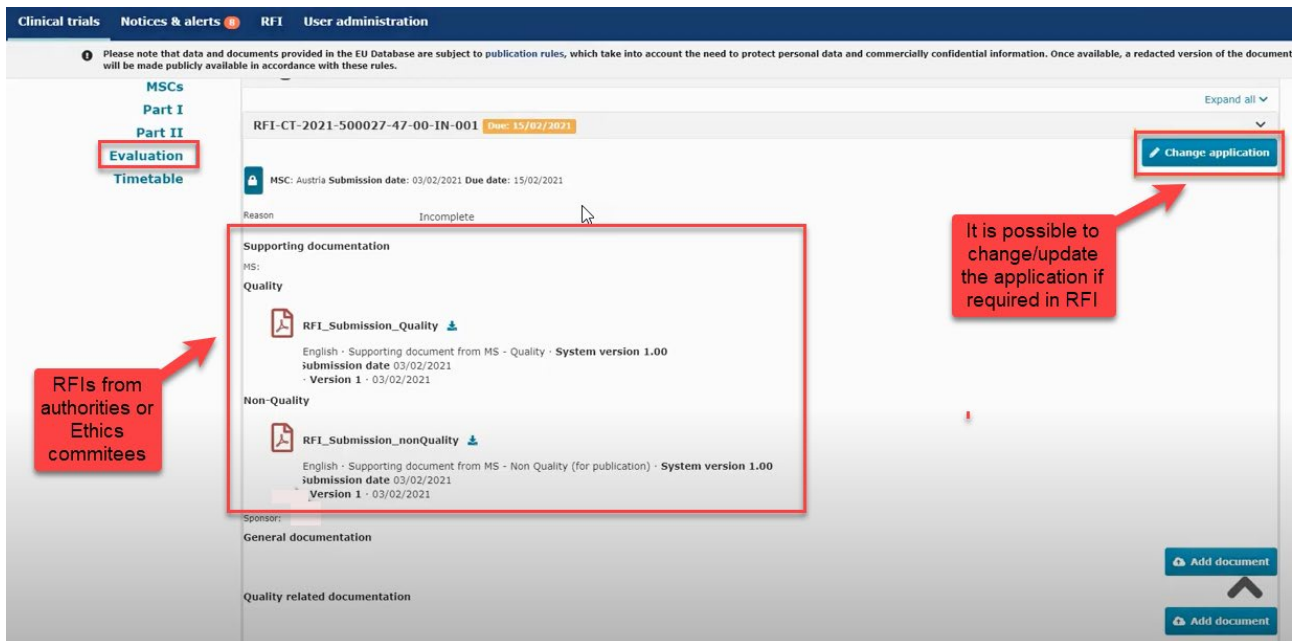
Every single RFI must be opened by clicking on 'RFI- CT-xxxx-xxxxxx-xx-xx-IN-001 IN' (black text):

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. You must as well click on the “Change application” and then change information in the 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.

Remember to upload both a **clean protocol** (as an updated version of the current document in trial dossier in part I in CTIS) and a **protocol with track changes**, (as supportive documentation to the RFI response in CTIS). Please refer to the info-box in section 2.3 to see how to upload a document “not for publication”.

3.2 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.

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

Validation

RFI

RFI-CT-2022-501381-22-00-IN-001 Due date: 07/02/2022

MSC: Netherlands Submission date: 27/01/2022 Due date: 07/02/2022

Reason: Incomplete

Supporting documentation

MSD:

Quality

No document available

Non-Quality

No document available

Sponsor:

General documentation

Quality related documentation

Please notice that in this section only supporting documentation to the response should be uploaded. If a new version of any of the documents included in the Annex I of Regulation (EU) 326/2014 needs to be provided, should be uploaded on the respective section of the application dossier and NOT here

Response to consideration

Consideration number RFI-CT-2022-501381-22-00-IN-001-01 Application section parts Part 1 - Clinical Application section end document Protocol

Consideration Please submit

Response

Textual response

Documents related to the response

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'!

The “add document” button next to the response to RFI, should only be used in case you have supportive documentation to justify your response.

In the new draft of the application:

Protocol information

Clinical trial protocol

Protocol *

0_Part1_CT_Protocol English - Protocol (for publication) - System version 2.00
submission date 05/02/2021
Version 2 - 02/02/2021
Comment new version of the document - RFI change

0_Part1_CT_Protocol English - Protocol (for publication) - System version 1.00
Version 1 - 02/02/2021 - English - Protocol (for publication) - System version 1.00

Synopsis of the protocol

Data safety monitoring committee charter

Study design

Study design

Period details

New version of the protocol

Previous version of the protocol

click on the update button to upload new versions of the documents

Add new document

Previous versions

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!

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.

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.

If a document (e.g. protocol) needs to be changed, this should be done from the correct placeholder (by the original document) by using the “update” button. This will ensure correct versioning of approved documents and publication in accordance with deferral/transparency rules.

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

Newest version is shown on the left, previous versions are shown here.

CTIS system version, does not necessarily match own version number

Own version number and date, as entered during the upload.

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

It is now indicated that changes to the application were made, and it is mandatory to upload a list of changes.

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.

3.3 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.

In order to address an RFI, the sponsor has to provide a response in the free text displayed after each consideration raised by the RMS/MS as part of the RFI, that can be complemented by supporting documents. RFI responses can be saved as drafts before submission.

The sponsor also has the possibility to apply changes to the dossier, both structure data and documents, depending on the nature of the request raised. If changes to the dossier are applied, the sponsor should also provide a document containing a description of the changes made. See link for template: [RFI response List of Changes to the application](#)

click on the lock button to be able to answer the RFI

Remember to tick the "includes application changes" if there are changes to sections in the application

open the RFI

Add a response document

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

Click on the lock button

Consideration 1

Here you can upload additional documents for the consideration

Consideration 2

Type your response in the field

Add document

Save response

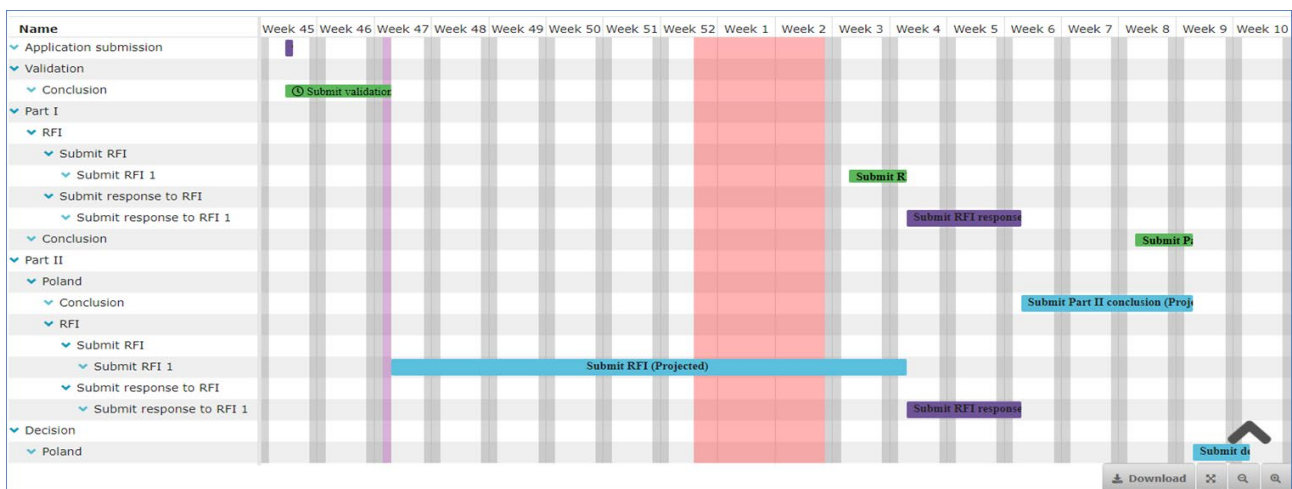
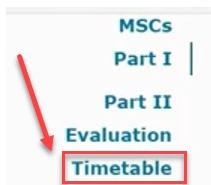
Remember to save response for each consideration with the “save response” button. When the response is saved, unlock the padlock for each consideration.

Important to remember to be able to click on “submit response”:

- All response fields should be answered
- It is mandatory to upload a list of changes
- Pad locks to each consideration should be unlocked and the pad lock to the RFI should be locked.

3.4 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.

According to the mentioned evaluation timelines, the maximum days for an application is 106 days for initial applications and 95 days for substantial modifications.

3.5 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.

There must be a conclusion and a final assessment report (FAR) from both Health Authority and Etichs Committee. If you receive a “No conclusion” it means that the authorities have not answered within the deadline (60 days), which is a mistake.

Decision

Part I Disagreements

Part I conclusion: Acceptable
Part II conclusion: Acceptable
Decision: Authorised

ASSESSMENT OVERVIEW

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 does 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	

3.6 “Report for the Application Evaluation Decision” and “Assessment reports” 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 assessment reports are only available in “CTIS sponsor workspace” for roles with permission. They are not available in CTIS Public.

TEST Poseidon
Under evaluation 2023-502710-24-00 RMS: Denmark

Summary Full Trial Information Notifications Trial results Corrective measures Ad Hoc assessments Users

Start Download Cancel

Applications

Application type	Application ID	Member states concerned	Application Part	Submission date	Decision date
INITIAL IN	3662	DK (Under evaluation)	Part I Part II	21 Mar 2023	

Contents for Download:

- ☒ Form
- ☒ MSC
- ☒ Part I
- ☒ Part II
- ☒ Select all
 - ☒ Denmark
- ☒ Evaluation
 - ☒ Validation
 - ☒ Assessment Part I
 - ☒ Assessment Part II
 - ☒ Decision

Include the following :

- ☒ Structured data in PDF*
- ☐ Documents*

* these only include the latest version related to the application

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
▸ ☒ INITIAL	Authorised	DK:Authorised, not started	13/01/2023	22/03/2023

▾ Attached documents

☐ All attached documents will be included in the downloaded file

Download clinical trial

Cancel

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

3.7 Date for Trial Duration

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

The extension of trial duration is a non-substantial modification and requires no approval from the authorities.

The sponsor can when creating a Non substantial modification (NSM) in CTIS change the date manually in Part I and thereafter submit the change.

Date for "estimated end of trial" is the expected date for last patient last visit (LPLV). EEA: European Economic Area.

Trial duration *	
Estimated recruitment start date in EEA	Estimated end of trial date in EEA
01/09/2022	01/09/2028

3.8 Annual safety report

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.

3.9 Serious breach notification

This guideline gives examples of what could be a serious breach and show the template form for reporting a serious breach in CTIS and what information that needs to be submitted together with the notification.

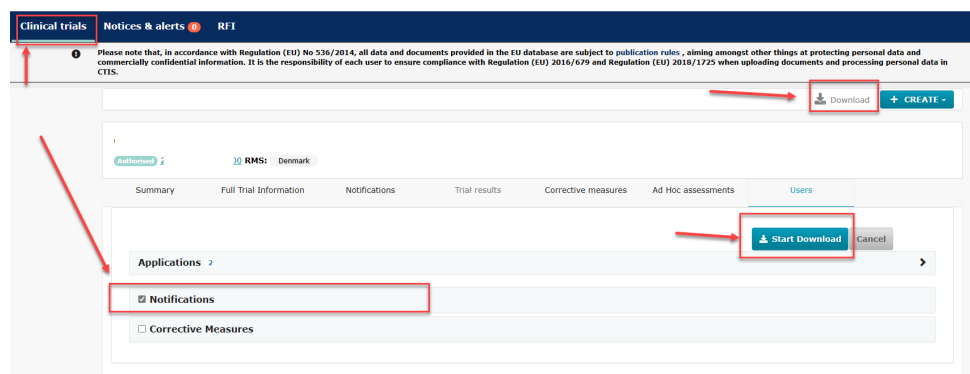
[Guideline for the notification of serious breaches of Regulation \(EU\) No 536/2014 or the clinical trial protocol](#)

3.10 End of Trial

The notification “End trial” must be entered in CTIS not later than 15 days after end of trial. The date for “End trial” is defined as the last visit of the last subject (LPLV), or a later point in time as defined in the protocol.

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

The “End Trial” can be documented by “Report for General Notifications”, which can be downloaded from CTIS and archived in sponsors TMF.



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](#)

Info box:

After initial approval, the sponsor must enter dates in CTIS for
“start trial” and **“start recruitment”**
for each country.

If the dates are not entered, the approval of the trial in CTIS will
expire after 2 years, unless an extension, on request of the sponsor,
has been approved.

Sponsors can request an extension to start the recruitment beyond 2 years via a Substantial Modification (SM) Part I & II or via SM Part II. *Note, that an SM Part I-only cannot be used to request the extension of start of recruitment.*

In the ‘Form’ section of this SM sponsors must **select “Extension to start trial recruitment beyond 2 years” as the reason for the SM** and must **enter the anticipated extended deadline in the field “Recruitment start date”**.

According to the CTR, the SM must be authorised or authorised with conditions in that MSC within the 2 year timeline. The trial will remain ‘Authorised’ in that MSC allowing the sponsor to submit the ‘First visit of first subject’ with the ‘Start recruitment’ notification. The ‘Start of recruitment date’ entered in this notification must be within the extended recruitment start timeline authorised in the SM, while the notification can be submitted within the extension period granted plus additional 15 days.

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.

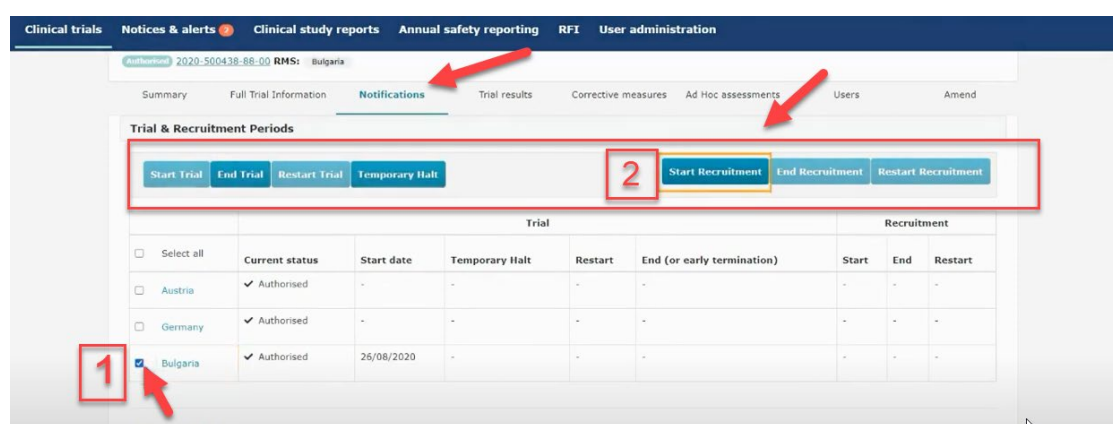
- **Restart trial:** The act of restarting the trial, after a temporary halt or after a suspension of the CT as part of a corrective measure by an MSC.

- **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** after the date of the specific event has taken place.

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 authorised.



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**.

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.

4.1 For trials transitioned to CTIS

When submitting a notification (i.e. Start of Trial, Start of Recruitment, ...) for a transition trial, it is not possible to select a date earlier than the initial authorization data recorded in CTIS. The authorities recommend selecting the date that is closest to the actual date and submitting a supporting document explaining the issue and specifying the correct date.

See also: [CTIS List of known issues for Sponsors - v1.0.62.0.pdf](#)

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

[See CTG key document list](#) for templates to use when submitting a SM

Video on this topic in EMA training module 10:

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

Classification of changes to ongoing trials can be found in [“Questions and Answers Document - Regulation \(EU\) 536/2014, Annex IV: “Classification of changes to ongoing clinical trial”](#)

Before creating a draft application, ensure there are no other draft applications or applications under assessment for the same part of application.

Sponsors are advised to avoid creating draft applications for Substantial Modifications (SM), Non-Substantial Modifications, or Additional Member State Concerned not only while previous application is still under evaluation (as currently indicated in system warning messages) but also when a draft already exists, unless the sponsor understands that these drafts are mutually exclusive. This is because when a draft application is created, it copies the documents and data from the last authorised application. For example, if a draft SM Part I is created when an Additional Member State (AMS) application is already in draft, the AMS application will not include the Part I SM changes. As a consequence, if this AMS is submitted and under evaluation after the SM Part I is authorised, the sponsor will have to withdraw the AMS application, as it will not contain the latest version of Part I introduced with the SM Part I.

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.

Clinical trials Notices & alerts Annual safety reporting RFI User administration

Download **+ CREATE**

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

click on the create tab to make a substantial modification

Trial title Webinar 21 09 2020
Authorised 2020-500275-71-00 RMS: Austria

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

TRIAL INFORMATION

Sponsor	Test Organisation 1	Member states concerned	AT · BE
Trial phase	Therapeutic exploratory (Phase II)	Medical conditions	Apnoea
Therapeutic area	Diseases [C] - Respiratory Tract Diseases [C08]	Low intervention study	Yes
Medical device	No	Population type	Healthy Volunteers

IMP

Go to the summary section in the sponsors workspace

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*.

A screenshot of a web application interface. At the top right, there is a blue button labeled '+ CREATE'. A red arrow points from a red text box 'Select which type of application that should be submitted' to a dropdown menu that has appeared. The dropdown menu contains four options: 'Single trial substantial modification' (highlighted with a red box), 'Multi trial substantial modification' (highlighted with a red box), 'Non-substantial modification', and 'Additional MSC'. Below the dropdown, the word 'essments' is partially visible.

A screenshot of a web application interface showing a dialog box titled 'Substantial modification scope'. The dialog box has a close button (X) in the top right corner. Inside, there is a section 'Select modification scope' with a dropdown menu labeled 'Please select'. The dropdown menu is open, showing three options: 'Part I only', 'Part II only', and 'Part I and Part II'. A red arrow points from a red text box 'Select the scope: the section you want to update or modify' to the dropdown menu. Below the dialog box, there is a table with columns for 'Test Organisation 1', 'Therapeutic exploratory (Phase II)', 'Diseases [C] - Respiratory Tract Diseases [C08]', 'Medical conditions', 'Low intervention study', 'Population type', 'AT - BE', 'Apnoea', 'Yes', and 'Healthy Volunteers'. The table contains several rows of data.

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. Billing information must be provided again for the SM in the "proof of payment" section in CTIS. For public entities, the EAN number must be provided. If invoices need to include specific information, such as references like PO numbers or contact persons, this should be indicated in the billing information.

A screenshot of a web application interface showing the 'Form' section for a Substantial modification. The top navigation bar includes 'Clinical trials', 'Notices & alerts', 'Annual safety reporting', 'RFI', and 'User administration'. Below the navigation bar, there is a message: '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 content area shows 'Trial title Webinar 21' and 'RMS: Austria'. Below this, there is a section for 'Substantial modification' with ID 'SM-1' and a status of 'Draft'. There are buttons for 'Check', 'Save', 'Cancel', and 'Submit'. A red arrow points from a red text box 'In the form section you can upload cover letter and description of the modification and other supporting information' to the 'Form' section. The 'Form' section is highlighted with a red box. Below it, there is a section for 'Form details' with a sub-section 'Substantial modification details'. This section contains two items: 'Cover letter' and 'Modification description', each with an 'Add document' button. The 'Form' section also includes a sidebar with links for 'Form', 'MSCs', 'Part I', 'Part II', 'Evaluation', and 'Timetable'.

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

Choose a reason for the substantial modification. If none of the reasons are applicable you can choose "other".

Substantial modification reason

- ☐ End of trial in MS
- ☐ End of trial in EEA
- ☐ Global end of trial
- ☐ Anticipated date of summary of results
- ☐ Unexpected Event Change in B/R
- ☐ Serious Breach
- ☐ Urgent Safety Measure
- ☐ 3rd Country Inspectorate Inspection
- ☐ EEA Inspections
- ☐ Change of sponsor or sponsor's legal representative
- ☐ Extension to start trial recruitment beyond 2 years
- ☐ Extension to restart trial beyond 2 years

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

In the MSCs section only the number of subjects can be changed

The button "add member state" is inactive as this requires a new application.

Member states concerned

Member states concerned	RMS	First submissions date	Subjects
Austria	Selected		20
Belgium			20

+ Add member states

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

Form
MSCs
Part I
Part II
Evaluation
Timetable

Trial specific information (Part I)

Trial details

Trial identifiers

Trial information

Protocol information

Clinical trial protocol

Protocol *

1_1_Part I_CT_Protocol

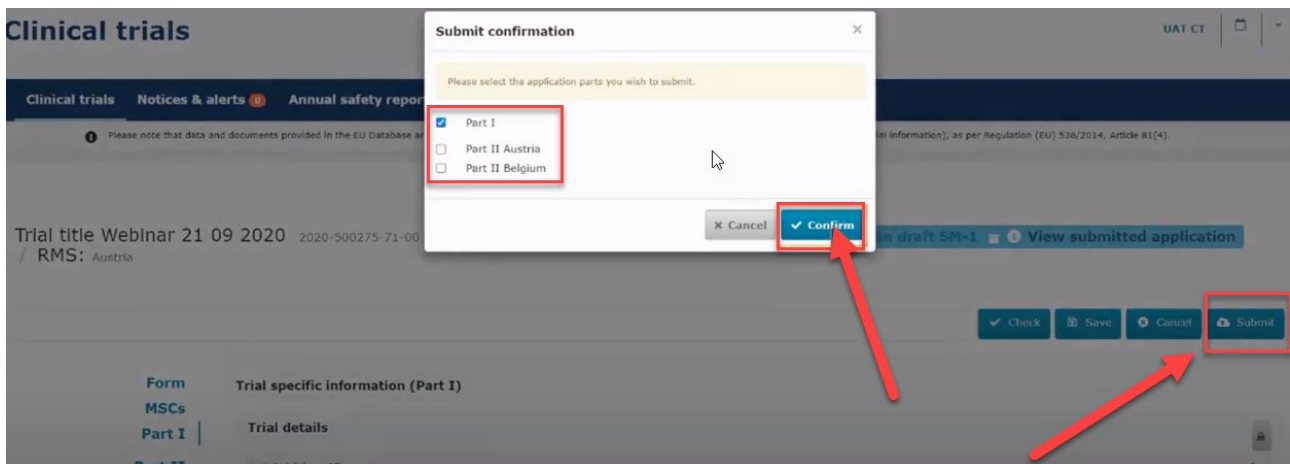
English - Protocol (for publication) - System version 1
Version 1 - 11/09/2020

0_Protocol SM Part I

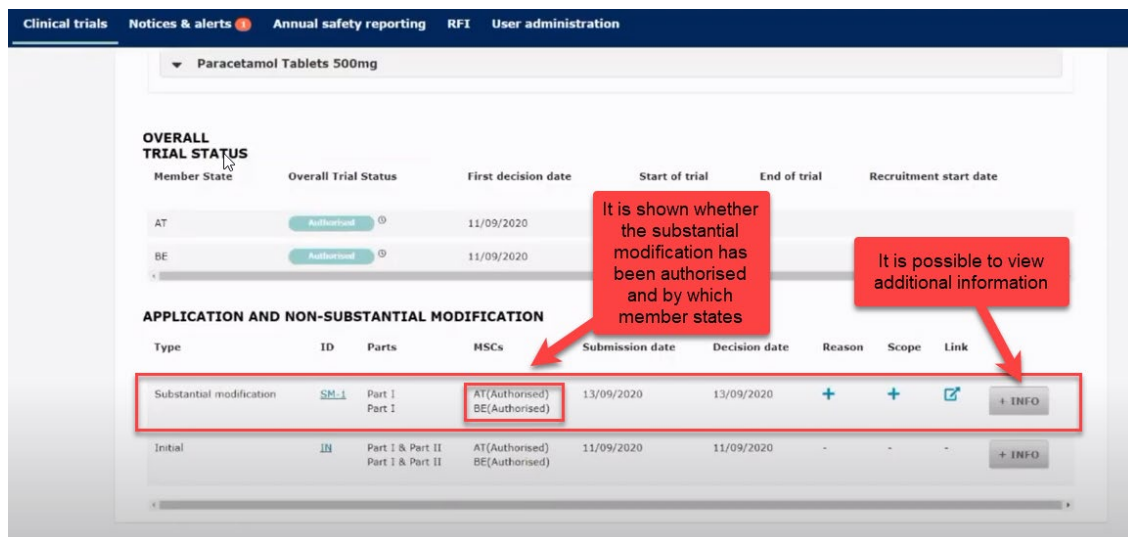
English - Protocol (for publication) - System version 1
Version 1 - 13/09/2020

Add document

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 Substantial modification to change of sponsor

See guide from: [CTCG Guide for change of trial sponsor](#)

Sponsor users can submit an SM Part I to request the change of the **sponsor ORG-ID**, in order to transfer the ownership of the trial to a different sponsor with a different legal entity. This type of SM is the ‘Part I only – change of sponsor’ SM and is different from the ‘Part I only’ SM, where this change is not permitted. Also, in case the change regards only an address change, but the legal entity remains the same, the sponsor can submit a NSM.

In the ‘Summary’ subtab of the CT page, select the ‘+ CREATE’ at the top right corner and choose “Single trial Substantial Modification”.

Select '**Part I only – Change of Sponsor**' from the dropdown menu. A red warning message appears. Note: the tick in box regarding the change of dossier appears checked by default and cannot be unticked, since the structured data for Part I/sponsor section will be modified).

Modify those sections where you will find a padlock (Form: 'SM details' and Part I: 'Sponsors' sections) and upload the **relevant documents** ('Cover letter' and 'Modification description' are mandatory: see details above).

In the 'Sponsors' section, after having made sure that the new sponsor has an ORG-ID in OMS, click on the padlock at the top right. An edit button (pencil icon) appears on the right side of the ribbon that includes the main sponsor details.

Click on the pencil icon and search for the new sponsor's organisation in the pop-up menu. Once found, **select the correct organisation** from the search results, by using the radio button on the left side. The 'Add sponsor' button is activated.

Click on the '**Add sponsor**' button: now the details of the initial sponsor were overwritten with those of the new selected organisation, intended to be the new sponsor of the trial after the authorisation of this SM by all MSC(s). Details of the new selected sponsor are displayed in the structured data of the 'Sponsor' section in Part I.

If the new sponsor organisation follows the **CT-centric approach**, the initial sponsor user roles will be all revoked once the SM is approved. **CT Admin users of the initial sponsor** (those ones that were holding the CT Admin role before the authorised change of sponsor) need to contact the EMA CTIS Service Desk and request that the CT Admin role is assigned to a user that represents the new sponsor organisation, otherwise the ticket does not pass the EMA validation. The new sponsor's users cannot open this Service Desk ticket.

7 How to create and submit a Non Substantial Modification (NSM)

There are two types of non substantial changes:

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

Classification of changes to ongoing trials can be found in ["Questions and Answers Document - Regulation \(EU\) 536/2014, Annex IV: "Classification of changes to ongoing clinical trial"](#)

All non-substantial changes, both 81.9 NSM and NSM, do not require 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 the next Substantial modification (SM), if one is submitted during the trial. There is no requirement to submit a SM solely for the purpose of updating NSMs upon trial completion. NSMs may be submitted upon trial completion if no Substantial Modification (SM) has been submitted in the meantime; however, there is no requirement to do so.

To submit a NSM the sponsor can update documents (e.g. protocol and participant information).

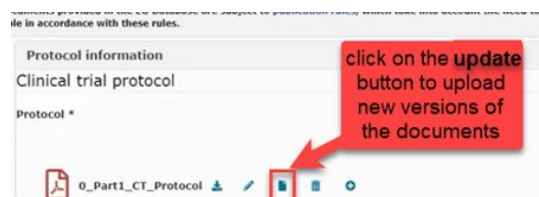
Documents that belong to Part I can be modified with limitations and documents in Part II can be changed by using the "update" icon. Only the relevant documents must be uploaded, a cover letter is not required.

Structured data and documents that are modified through a NSM are all **published in line with the CTIS Publication rules**. When a NSM is submitted on a trial submitted before 18 June 2024 ('historical trial'), all documents that are subject to publication as per publication rules are published, see Table IV of [Annex I to Guidance document on how to approach the protection of personal data and CCI while using the CTIS](#).

This means that the sponsor needs to make sure that all documents uploaded in the 'for publication' placeholders are redacted of commercially confidential information (CCI) and that their personal data are anonymised, including those documents that are not strictly in scope of the NSM.

The detailed **list of structured data and documents that can or cannot be modified through a NSM** can be seen in column P (see worksheet tabs "Part I" and "Part II") of the [CTIS application fields document](#). The scope can be Part I only, Part II only, or Part I and Part II (see more details below). After selecting the scope of the NSM, users need to add/edit the required information as applicable throughout the dossier.

The "81.9" change cannot be selected specifically in CTIS, but the tab "NSM" must be used.



It is also described in ["Sponsor handbook"](#)

8 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 Annex V of the regulation and in [Summaries of Clinical Trial Results for Laypersons](#).

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.

Clinical trials Notices & alerts Annual safety reporting RFI User administration

Clinical Trials

Enter EU CT number or use

Trial Advanced Search +

Application Advanced Search +

Enter the CT number or use advanced search

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

EU CT number	Trial title	Lead sponsor	Product	Member states concerned	Submission date	Decision date
2021-500030-26-00	Trial test	Test org	Test product	DE(Authorised) GR(Authorised)	03/03/2021	04/03/2021

1 - 1 of 1

Select the trial

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

CT for training test
Authorised 2021-501235-35-00 RMS: Austria

Summary Full Trial Information Notifications **Trial results** Corrective measures Ad Hoc assessments Users

SUMMARY OF RESULTS

LAY PERSON SUMMARY OF RESULTS

CLINICAL STUDY REPORTS

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

Summary of result

Summary of results

Title *: Version type *: Intermediate

Intermediate data analysis date *:

Related document(s) *:

Lay person summary of result

Lay person summary of results

Title *: Version type: Final

Related document(s) *:

9 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.

Version 2.5 Updated according to comments from users and new/updated guidelines.

Version 2.6 Updated according to comments from users, authorities, and new/updated guidelines.

Version 2.7 Updated and rewritten according to comments. New Section 3.7 *Date for Trial Duration* and 3.8 *End of trial*. Separated and elaborated section 6 on *How to create and submit a Non Substantial Modification (NSM)*.

Version 2.8 Changed ORG no. for GCP unit Copenhagen

Version 3.0 The following is added and updated: Section 2.9: Resubmission of an application; Section 3.7: Date for Trial Duration; Section 5 How to create and submit a SM; Section 6: Substantial modification to change a sponsor and Section 7: How to create and submit an NSM

Version 4.0 Updated and rewritten according to comments from users, authorities and new/updated guidelines. The following sections were updated: Section 1.1: Organisation centric approach at Odense University Hospital and the Capital Region of Denmark. Section 2: New headlines, information about countries outside the European economic area and updated ORG numbers. Section 3: Updated with information about the optional email notification service in CTIS, and link to guideline for notification of serious breaches. Section 4: Notification of Start of Trial, Start of Recruitment, ... in transition trials.