



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# FAQs

How to create, submit and withdraw  
a CTA

CTIS Training Programme – Module 10

Version 1.6 – August 2024

## What you will find

- Answers to questions regarding the creation and submission of Initial CTAs.
- Answers to questions regarding the creation and submission of Substantial modifications CTAs.
- Answers to questions regarding the creation and submission of Additional MSC CTAs.
- Answers to questions regarding non-substantial modifications.



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## Record of updated versions

The table below describes the updated versions after CTIS go-live (January 2022):

Version	Version description	Date
1.6	<p><b>New question:</b></p> <p>4.10 How can the sponsor information be changed in CTIS via Substantial Modification?</p>	August 2024
1.5	<p><b>New questions:</b></p> <p>2.5. Which documents are subject to publication and will be available at the CTIS public portal?</p> <p>2.7. What are the timelines for publication of documents subject to publication and which information is published?</p> <p>5.7. How can the sponsor information be changed in CTIS via Non-Substantial Modification?</p> <p><b>Removed questions:</b></p> <p>2.10. What is a 'deferral'?</p> <p>2.11. How can users request a deferral?</p> <p>2.12. For how long can the CTA data/documents be deferred?</p> <p>2.13. What is the deferral of publication for unauthorised trials?</p> <p>2.14. Can MSCs request a deferral for the CTA evaluation data/documents?</p> <p><b>Updated questions:</b></p> <p>2.4. How can users edit, update or add additional documents?</p> <p>2.6. How can users upload a document 'not for publication' version of a document subject to publication?</p> <p>2.15. Is the information in the contact points on sponsors' subsection published?</p>	June 2024
1.4	<p><b>New questions:</b></p> <p>2.31. How can a medical device be populated in a CTA under CTR?</p> <p>2.35. When can the sponsor of a partial submission application submit a substantial modification or an additional MSCs?</p> <p>6.6. Can the other types of CT applications (Substantial Modification, Additional MSC) be resubmitted?</p> <p><b>Updated questions:</b></p> <p>1.7. How can users cancel a CTA?</p> <p>1.8. How can users copy a CTA?</p> <p>1.9. What information can users find on the CTA page?</p> <p>2.29. How are Advanced Therapy Medicinal Products populated in clinical trials?</p> <p>2.34. In cases of applications limited to Part I, how should a sponsor proceed to submit an application for Part II?</p>	November 2023

	<p>4.4. What information can users include in the different sections of a Substantial Modification CTA?</p> <p>6.5. Can an Initial CTA be re-submitted?</p>	
1.3	<p><b>New questions:</b></p> <p>1.10. Is it mandatory to upload to CTIS all documents required by the Clinical Trial Directive (CTD)?</p> <p>2.4 How can users upload a document not for publication?</p> <p>2.5. How can users edit, update or add additional documents?</p> <p>2.9. Do the cover letter and financial arrangements need to be ink-signed?</p> <p>2.11. How can users request a deferral?</p> <p>2.14. Can MSCs request a deferral for the CTA evaluation data/documents?</p> <p>2.19. How can users add a Third-party contact?</p> <p>2.20. How can users populate the dose box?</p> <p>2.29. How are Advanced Therapy Medicinal Products (ATMPs) populated in clinical trials?</p> <p><b>Updated questions:</b></p> <p>2.3. How can users create and edit an Initial CTA?</p> <p>2.9. What is a deferral?</p> <p>2.11. What is the maximum publication deferral?</p> <p>6.5. Can an Initial CTA be re-submitted?</p>	September 2022
1.2	<p><b>New questions:</b></p> <p>2.8. What is the maximum publication deferral?</p> <p>2.11. What information can users include in Part I section?</p> <p>2.12. What is an Associated Clinical Trial?</p> <p>2.24. Can Initial applications be limited to Part I only?</p> <p>2.25. In cases of applications limited to Part I, how should a sponsor proceed to submit an application for Part II?</p> <p>4.6. How can users describe the changes they have made in a CTA section?</p> <p><b>Updated questions:</b></p> <p>2.15. What roles can medicinal products have in a clinical trial in CTIS?</p> <p>2.21. How can users link the placebo with other investigational medicinal products?</p> <p>2.22. What information can users include in Part II section?</p> <p>2.23. Is it mandatory to upload a recruitment arrangement document?</p>	March 2022

	4.3. How can users create a Substantial Modification CTA?	
1.1	Training material version published at CTIS go-live	January 2022

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# FAQs



In this document, we list common questions regarding *Module 10: Create, submit and withdraw a CTA*. They are categorised into: Questions of a general nature regarding Clinical Trial Applications (CTA); questions on the Initial application; questions on the Additional Member State Concerned application; questions on the Substantial Modification (SM) application; questions on Non-Substantial Modifications (Non-SMs), and questions regarding the withdrawal of any clinical trial application type. The specific learning objectives of this module are:

1. Understand the different types of clinical trial applications and Non-substantial modifications.
2. Understand the process of creating, submitting, and cancelling a clinical trial application.
3. Understand the process of withdrawing a clinical trial application.
4. Understand the roles and permissions involved in the management of a clinical trial application.

We encourage you to read these questions and answers carefully. If you have any questions which are not covered in this document, please contact us at [CT.Training@ema.europa.eu](mailto:CT.Training@ema.europa.eu) so that we can update this document accordingly. This document will be progressively enriched with the input of the experts involved in the validation of the training material, the Master Trainers disseminating the materials, and the end-users.

## 1. General information

### 1.1. What is a 'clinical trial' in the context of the Clinical Trial Regulation (EU) No 536/2014<sup>1</sup>?

According to Article 2(2) (2) of the CT Regulation<sup>2</sup>, a clinical trial (CT) is a clinical study which fulfils any of the following conditions:

The subject's assignment to a particular therapeutic strategy is decided in advance and does not fall within the normal clinical practice of the Member State Concerned (MSC).

The decision to prescribe the investigational medicinal products is taken together with the decision to include the subject in the clinical trial.

Diagnostic or monitoring procedures in addition to normal clinical practice are applied to the subjects.

### 1.2. What is a 'Clinical trial application'?

A Clinical trial application (CTA) is a request made by the sponsors to the Member States Concerned (MSCs) for the authorisation to perform an action related to CTs conducted in the EU. These actions can include the authorisation to conduct a new CT, to extend an existing CT to another MSC territory, or to perform a substantial modification (SM) to a previously authorised CTA.

### 1.3. What types of CTAs are available in CTIS?

The CT Regulation provides for three different types of application dossiers: Initial Application (Article 5 of the CT Regulation for full initial part I and part II, and Article 11 for partial submission including part I only<sup>3</sup>); SM (Chapter III of the CT Regulation<sup>4</sup>), and Additional MSC (Article 14 of the CT Regulation<sup>5</sup>).

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<sup>1</sup> Referred to as 'CT Regulation' hereafter.

<sup>2</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, *EU Official Journal* L158. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf)

<sup>3</sup> Idem<sup>2</sup>

<sup>4</sup> Idem<sup>2</sup>

<sup>5</sup> Idem<sup>2</sup>

## 1.4. How can users create and submit a CTA?

The trial life cycle starts with the creation of an initial application for a clinical trial. To do so, users need to click on the '+ New trial' button in the Clinical Trials tab. The system will trigger a pop-up form that needs to be populated by the user regarding the full title of the CT and the information of the sponsor organisation. Once this information has been filled out, users need to click on the 'create' button. With this procedure, an Initial CTA is created, with a unique EU CT number associated with it. Users can create and submit other types of CTAs only after the authorisation of the initial application. (*For more information, refer to questions 2.3, 3.3 and 4.3*).

The different CTAs linked to the same CT will be displayed in the 'Application and Non-SM' sub-section at the bottom of the CT summary page.

## 1.5. Can users submit information and documents in the CTAs in more than one language?

Yes. The information provided for a CTA can be submitted in one or more languages. Structure data and documents can be provided in all the official languages of the EU and as per MSCs requirements, as provided for in Article 26 of the CT Regulation<sup>6</sup>.

## 1.6. How can users edit a CTA?

Users can edit the application while it is in draft status (i.e. until it has not been submitted). To do so, users can access the application, from the CT summary page and select the Application ID under the column 'ID' of the 'Application and Non-SM' section. In order to populate and upload the relevant information and documentation of an application, users need to click on the padlock button of each sub-section. Afterwards, they can either save the application by clicking on the 'save' button in the upper-right corner of the page or, if all the required fields are completed, submit the application. After submitting the CTA, if users want to update the dossier, they need to create an SM CTA or a non-SM, as applicable (*refer to sections 4 and 5 for more information*).

## 1.7. How can users cancel a CTA?

Users can cancel any application while it is in draft status. To do so, users need to open the application, from the CT summary page, and click on the 'cancel' button on the upper-right corner of the page. If the sponsor cancels the application, all populated data and documents will be deleted from CTIS.

If an application is drafted but then cancelled, the EU number cannot be reused. Therefore,

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<sup>6</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, *EU Official Journal* L58. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf).

the sponsor will need to issue a new number and change it in all the corresponding CT documentation where the CT number is needed.

## 1.8. How can users copy a CTA?

Once a CTA has been authorised, users can copy it to create a similar CTA. To do so, users need to open the authorised application, from the CT summary page and click on the 'copy' button on the upper-right corner of the page. A pop-up will request the user to specify which sections of the application he/she wishes to copy - Part I (mandatory), or Part I and Part II, as well as the MSC in case there is more than one. The new CTA will have a new and unique EU CT number, will be in draft and users will be able to edit it before submitting it. The data and documents of the last submitted version of the original application will be copied and not those of previous versions. If multiple RFI responses with CTA changes had been submitted during assessment of the original application, the copied CTA draft will contain the details and documents of the last submitted application version.

## 1.9. What information can users find on the CTA page?

The CTA page is structured in six sections, which provide all the relevant information regarding a CTA submitted by a sponsor:

**Form:** Displays information on the application form details including cover letter, proof of payment if so required by the MSC, and the anticipated publication dates for data and documents, including deferrals, if applicable.

**MSC:** Displays information such as the MSCs of the application, the proposed RMS, the countries outside of the EU/EEA where the trial is intended to be conducted, an estimated total population for the trial, etc.

**Part I:** Displays trial-specific information such as protocol information, trial design, inclusion and exclusion criteria, conditions to be treated, the therapeutic area, sponsor and product details, etc.

**Part II:** Displays documents of the regulatory nature of the CTA for each of the MSC, including, for example, the template for the informed consent, the subject recruitment arrangements, compliance with national data protection requirements, etc.

**Evaluation:** Displays the different phases of the application evaluation to be performed by the MSC. By accessing this section, Member State users can perform their evaluation tasks, for example, by documenting considerations or uploading draft assessment reports.

**Timetable:** Displays a visual overview of the evaluation status and progress of the CTA. The information is displayed only after the submission of the CTA, not while the initial application is in draft.

It should be noted that depending on the application type, not all the six sections above mentioned will be completed by the sponsors. *More details on the different types of applications are provided in sections 2, 3, and 4.*

## 1.10. Is it mandatory to upload to CTIS all documents required by the Clinical Trial Directive (CTD)?

Users should comply with the Clinical Trial Regulation 536/2014<sup>7</sup>. CTIS offers several placeholders to enable the user to upload the required documentation.

## 2. Initial CTA

### 2.1. What is an Initial CTA according to the CT Regulation?

An Initial CTA provides comprehensive information about the trial to be conducted and the investigational medicinal product(s) to be used, enabling the authorities of the MSC to evaluate the acceptability of conducting the trial. The elements to be included in the application dossier for an initial application are defined in Annex I of the CT Regulation<sup>8</sup>.

### 2.2. What types of Initial CTAs can be submitted by sponsor users?

Depending on the number of Member States concerned by the application, Initial CTAs can be divided into:

**Mononational:** CTAs which concern only one Member State. These applications aim at receiving the authorisation to conduct a CT in the territory of a Member State.

**Multinational:** CTAs which concern more than one Member State. These applications aim at receiving the authorisation to conduct a CT in the territories of more than one Member State.

Additionally, Initial CTAs can be divided into those including information for Part I and Part II (full submission), and those that only include information relevant to Part I, or for Part I and Part II but only some of the MSC (partial submission). *Refer to question 2.32 for more information.*

### 2.3. How can users create and edit an Initial CTA?

Initial CTAs are created via the Clinical Trials tab by clicking on the '+ New trial' button. The system will trigger a pop-up form that needs to be populated by the user regarding the full title of the CT and the information of the organisation that will be the sponsor of the trial. Once the information is populated and users click on the 'create' button, they are redirected

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<sup>7</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, *EU Official Journal* L158. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf).

<sup>8</sup> *Idem*<sup>7</sup>

to the sections of the CTA where they can start completing the required information. By default, the section 'Part I' is displayed.

If users wish to continue filling out the required information at another moment, they need to click on the 'save' button, which allows saving a draft application without submitting it. For editing the application at a later stage, users must select the Application ID under the column 'ID' of the 'Application and Non-SM' section. In the case of Initial CTAs, the ID will be 'IN'.

To upload documents in CTIS, users are advised to consult the 'Best practice guide naming of documents in CTIS', available in the 'Key document list' section on the Clinical Trials Coordination Group page<sup>9</sup>.

## 2.4. How can users edit, update or add additional documents?

The revised CTIS transparency rules focus on the publication of clinical trial documents that are more impactful for patients and clinical researchers and are described in Annex I of the Revised CTIS Transparency Rules. These documents are the Protocol, Synopsis of the protocol, Summary information and informed consent form, Recruitment arrangements, Final summary of results, Lay person summary of results and Clinical study reports. (Refer to [Revised CTIS Transparency Rules<sup>10</sup>](#) for more information).

After uploading a document, users can edit the information ('Edit' button), submit additional documents ('Add document' button), or a new version of the same document ('Update' button).

**Edit button:** Users will be able to include comments and change the versions of the documents by clicking on the edit button.

**Update button:** Users will be able to change the document they uploaded by clicking on the update button, once the application and the documents are submitted. It is not allowed to update a new document to replace the original one when the CTA is still in draft. To update a document in a draft CTA, users need first to remove it and then add a new document.

**Add document:** After uploading a first document users can upload additional documents. The documents will appear listed below the first one uploaded. Documents subject to publication will be published in the CTIS public portal taking into consideration the CTIS revised transparency rules. It is possible to share a non-public version of a document subject to publication (more information in question 2.7).


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<sup>9</sup> Heads of Medicines Agencies: Clinical Trials Coordination Group. Best Practice Guide for Sponsors of document naming in CTIS. March 2023. Available at: [https://www.hma.eu/fileadmin/dateien/HMA\\_joint/00-About\\_HMA/03-Working\\_Groups/CTCG/2023\\_04\\_CTCG\\_Best\\_practice\\_guide\\_naming\\_of\\_documents\\_version\\_2.0.pdf](https://www.hma.eu/fileadmin/dateien/HMA_joint/00-About_HMA/03-Working_Groups/CTCG/2023_04_CTCG_Best_practice_guide_naming_of_documents_version_2.0.pdf)

<sup>10</sup> European Medicines Agency. Revised CTIS Transparency Rules. October 2023. Available at [https://www.ema.europa.eu/en/documents/other/revised-ctis-transparency-rules\\_en.pdf](https://www.ema.europa.eu/en/documents/other/revised-ctis-transparency-rules_en.pdf)






Clinical trial protocol

Protocol \*

 Add document

 Protocol     

English · Protocol (for publication) · System version 1.00  
· Version 1 · 05/06/2024

 Protocol not for publication    

English · Protocol (not for publication) · System version 1.00  
· Version 1 · 05/06/2024

## 2.5. Which documents are subject to publication and will be available at the CTIS public portal?

The Revised CTIS transparency rules brought the following main changes, compared to the previous disclosure rules:

- publication focused on key documents of interest
- removal of deferral functionality – documents are published earlier in time

use of redaction as the method to protect CCI and PD, if included in those key documents. The documents subject to publication changed with the implementation of the [CTIS revised transparency rules<sup>11</sup>](#) on 18 June 2024. The documents subject to publication are the following:

- Protocol;
- Protocol Synopsis;
- Summary of product characteristics (SmPC);
- Subject information and informed consent form;
- Recruitment arrangements;
- Final summary of results;
- Lay person summary of results;
- Clinical study reports

<sup>11</sup> European Medicines Agency. Revised CTIS Transparency Rules. October 2023. Available at [https://www.ema.europa.eu/en/documents/other/revised-ctis-transparency-rules\\_en.pdf](https://www.ema.europa.eu/en/documents/other/revised-ctis-transparency-rules_en.pdf)

## 2.6. How can users upload a document 'not for publication' of a document subject to publication?

For the documents uploaded in CTIS subject for publication (e.g. protocol, protocol synopsis, clinical study reports etc.), users should not include Commercial confidential information (CCI) and personal data. This will be indicated in the document upload pop-up window with the legend 'The above documents will be published'. For the CTA sections where documents are never published (e.g. IMPD - Quality) it is indicated in the pop-up window with the legend 'This document will not be publicly accessible'.

In cases when documents are uploaded for publication, and users need to upload a document with the redacted data from the original (personal data or CCI), they need to submit a version 'not for publication'. This enables sponsors to provide all the information to the Member States, avoiding the publication of sensitive information.

To do so, users can click on the 'Add' button (+) that appears in the document section after uploading the first version of the document intended for publication (only available in CTIS sections where the documents to be uploaded are published).

This button is a cross-system functionality available in some sections of the CTA, where applicable, in the form of an RFI response and in other sections related to the life cycle of a CT. It is also available for the Clinical Study Report of MAH users.



## 2.7. What are the timelines for publication of documents subject to publication and which information is published?

Data and documents are published according to the established timelines for the trial category, population age and trial phase. An overview of the trial categories and which structured data and documents are published in CTIS can be found in the tables below.



Trial Category	Trial type
Category 1 Pharmaceutical development clinical trials	Phase I clinical trials in healthy volunteers or patients Bioequivalence and bioavailability trials Similarity trials for biosimilars Equivalence trials for combination or topical products
Category 2 Therapeutic exploratory & confirmatory clinical trials	Phase I and phase II integrated clinical trials Phase II clinical trials Phase II and phase III integrated clinical trials Phase III clinical trials
Category 3 Therapeutic use clinical trials	Phase III and phase IV integrated clinical trials Phase IV clinical trial and low interventional trials

## Structured data – what will be published & when

Structured data	Category 1		Category 2 integrated ph1&2	Category 2 & 3 (excl. integr. ph1&2)
	Paediatrics and/or PIP	Adults		
CTA fields*	First MSC decision	First MSC decision 30 months after EU/EEA End of Trial	First MSC decision	First MSC decision
Product/AS details on strength, dose and treatment duration*	30 months after EU/EEA End of Trial			
MSC(s) conclusions and decision outcomes	That MSC decision			
Notifications on trial status and recruitment	As soon as submitted by sponsor			
Notifications on serious breaches, urgent safety measures, unexpected events	After MSC assessment	30 months after EU/EEA End of Trial & MSC assessment	After MSC assessment	
Corrective measures (suspension, revocation, modification request)	When applied by MSC(s)			*see following slide

## Structured data – what will be published & when

Structured data	Category 1		Category 2 integrated ph1&2
	Paediatrics and/or PIP	Adults	
CTA fields populated by the sponsor, including: <ul style="list-style-type: none"> <li>- Public title (= title in lay terms)</li> <li>- Trial identifiers in registers, protocol code</li> <li>- Phase, medical cond., rare disease, therap. area <ul style="list-style-type: none"> <li>- Population age, gender</li> <li>- Sponsor details</li> </ul> </li> <li>- Details of clinical investigator sites in MSC(s)</li> </ul>	First MSC decision	First MSC decision	First MSC decision
Remaining CTA fields populated by the sponsor		30 months after EU/EEA End of Trial	
Product/AS details: Strength of product & active substance, Maximum duration of treatment, Maximum daily dose allowed, Daily dose unit of measure, Maximum total dose allowed, Total dose unit of measure	30 months after EU/EEA End of Trial		

## Structured data – what will be published & when

Structured data	All categories
Sponsor legal representative details	Never
Any request for information (RFI) and RFI responses	
Validation conclusion details, assessment decision conditions (if any)	
MSC(s) assessment(s) on notifications	
3 <sup>rd</sup> country inspection details	

## 2.8. What does an Initial CTA dossier include?

As per Annex I of the CT Regulation<sup>12</sup> (letters A to R), the application dossier includes the following information:

- Introduction and General principles
- Cover letter
- Compliance with Regulation (EU) 2016/679
- EU Application form
- Protocol

<sup>12</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, *EU Official Journal* L58. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req\\_2014\\_536/req\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req_2014_536/req_2014_536_en.pdf).

- Investigator's brochure
- Documentation relating to compliance with Good manufacturing practice (GMP) for the investigational medicinal product
- Investigational medicinal product dossier (IMPD)
- Auxiliary medicinal product dossier
- Scientific advice and Paediatric Investigation Plan (PIP)
- Content of the labelling of the Investigational Medicinal Products (IMP)
- Requirements for gathering the informed consent of the subjects (information per MSC);
- Arrangements for rewarding or compensating subjects and investigators (information per MSC);
- Arrangements for the recruitment of subjects (information per MSC);
- Suitability of individuals involved (information per MSC);
- Suitability of clinical trial sites (information per MSC);
- Proof of insurance cover or indemnification (information per MSC);
- Financial and other arrangements (information per MSC);
- Proof of payment of fee (information per MSC);
- Proof that data will be processed in compliance with union law on data protection.

## 2.9. Which sections of a CTA page must users complete for an Initial CTA?

The sponsor will have to populate the following sections as part of an Initial CTA dossier:

- Form
- MSC
- Part I
- Part II

It should be noted that at the time of submission on an Initial CTA, the sponsor user can choose to submit a full dossier according to Article 5 (including Part I and Part II), or progress with a partial submission with Part I only or Part I and Part II for some of the MSC under Article 11 of the CT Regulation.

## 2.10. What information can users include in the Form section?

The information covered in the Form section of a CTA includes:

- Cover letter;
- Compliance with Regulation (EU) 2016/679;
- Proof of payment, if so required by each MSC;
- The anticipated publication dates for data and documents, including deferrals settings, if applicable.

## 2.11. Do the cover letter and financial arrangements need to be ink-signed?

The signature requirement is an aspect linked to the Member State law and therefore each user can request the CT Member State nation contact point for more information.

## 2.12. What information can users include in MSCs section?

The information covered in the MSC section of a CTA includes:

- Member States concerned (where the CT is intended to be conducted);
- Proposed RMS (in case of mono-national trials the proposed RMS will be selected by default);
- An estimated total number of subjects for the trial in each MSC;
- The MSC section also conveys a 'read-only' display of the countries outside the EU/EEA where the trial is intended to be conducted and an estimated number of subjects. This information is populated in Part I and automatically copied into the MSC section.

## 2.13. What information can users include in Part I section?

The information covered in the Part I section of a CTA includes structure data and documents covering three main sub-sections: trial details/sponsor details/product details.

Trial details include:

- Trial information, including objectives, endpoints, inclusion and exclusion criteria;
- Protocol information, including protocol synopsis, data safety monitor board chart, and trial design details;
- Scientific advice and Paediatric Investigation Plan (PIP);
- Associated CTs (if applicable). For more information on Associated CTs refer to question 2.17;
- Countries outside the EEA where the CT is planned to be conducted and number of subjects involved (if applicable).

Sponsor details include:

- Contact point in the Union;
- Scientific and public contact points;
- Legal representative in the Union – this is only required if the sponsor of the trial is not based in the EU.

Product details include:

- Details for authorised or development products extracted from XEVMPD;
- Investigator's Brochure (IB) or Summary of Product Characteristics (SmPC);
- Documentation about good manufacturing practice (GMP) for the investigational medicinal product;
- Investigational medicinal product dossier (IMPD) divided into Quality (IMPD-Q) and Safety and Efficacy (IMPD S and E);
- Auxiliary medicinal product dossier;
- Content of the labelling of the investigational medicinal products.

It should be noted that not all the fields mentioned above are mandatory to be completed prior to the submission of an initial application. Mandatory fields and documents to be completed in CTIS can be easily identified as they are marked with an asterisk (\*).

## 2.14. What is an Associated Clinical Trial?

An Associated Clinical trial is a functionality that has been implemented in CTIS in order to allow sponsors to refer to data generated in another clinical trial. Sponsors can refer to a trial authorised under the regime of CTD or CTR.

To do so, users can access the 'Associated clinical trials' tile under the 'Trial details' subsection of Part I. Then, users can click on the '+ Associated clinical trial' button and retrieve the trial number (EU CT or EUDRA CT) using the search functionality. Once the trial has been associated, in case the associated trial is owned by a different sponsor, an agreement from the sponsor owner needs to be provided. To upload this document in the dedicated placeholder, users can click on the '+' icon and then on the 'Add document' button that appears below. *For more information, please refer to Article 25(4) and (5) of Regulation (EU) No 536/2014<sup>13</sup>.*

EU CT number	Full title	Sponsor	Actions
2030-532207-24-00	Clinical trial - test - Back up	Test Organisation Spain	+ All +

Agreement from another sponsor

+ Add document

<sup>13</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, *EU Official Journal* L158. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req\\_2014\\_536/req\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req_2014_536/req_2014_536_en.pdf).

## 2.15. Is the information in the contact points on sponsors' subsection published?

The sponsor's 'Contact Point for Union' section and the contact for 'Legal Representative' are not published in the CTIS public domain allowing personal contact details can be populated. However, the functional contact details for 'Scientific Contact Point', 'Public contact point' and 'Third party' are made public, and therefore only functional contact details should be provided.

## 2.16. How can users add a Third-party contact?

If needed, users can include a Third-party contact in the trial by clicking on the '+ Add contacts' and 'Third party' buttons under the 'Sponsors' tile. Then, they can search for the corresponding organisation and click on the 'Add third party' button.

**Part I**  
**Part II**  
Evaluation  
Timetable

**Test Organisation Spain** Sponsor

<b>Name</b>	Test Organisation Spain	<b>Status</b>	Commercial
<b>Address</b>	Santiago Calle 10	<b>Town/City</b>	Madrid
<b>Post code</b>	28001	<b>Country</b>	Spain
<b>Phone</b>	0200110000	<b>Email</b>	info@testorganisation-spain.com

Scientific/public contact point\*

+ Add contacts -

- Legal representative
- Scientific contact point
- Public contact point
- Third party

Select third party

Search organisation

Name starts with ID starts with City starts with Country All

+ New organisation Clear Search organisation

ID	Name	Address	City	postCode	country	phone	email	actions
----	------	---------	------	----------	---------	-------	-------	---------

X Cancel Add third party

Once the Third party is included, users can click on the pencil icon to modify the information regarding that third party (assigned tasks and contact details).

ID	Name	Country	Address	Town/City	Post code	Phone	Email	Duties	Actions
21352	Test Organisation Spain	Spain	Santiago Calle 10	Madrid	28001				

## 2.17. What is a 'medicinal product'?

Article 1(2) of the Medicinal Products for human use Directive<sup>14</sup> defines a 'medicinal product' as follows:

- (a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings.
- (b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

The CT Regulation foresees two main types of medicinal products: Investigational medicinal products (Article 2(5)), which can be tested or used as a reference in a CT, and auxiliary products (Article 2(8)), which are used for the needs of a CT as described in the protocol.

CTIS enables users to add such medicinal products in a CTA as a test, comparator, auxiliary, or as a placebo (refer to question 2.18).

## 2.18. What roles can medicinal products have in a clinical trial in CTIS?

CTIS allows adding several roles for a medicinal product in an Initial CTA:

- **Test:** Investigational Medicinal Product (IMP) which is being tested. To be able to progress with the application submission, users need to add at least one test role.
- **Comparator:** Medicinal Product used as a reference in a CT to be compared to the substance being tested.
- **Auxiliary:** Auxiliary Medicinal product used for the needs of a CT as described in the protocol, but not as an IMP, e.g. background treatments, challenging agents, rescue medication, or to assess the endpoints<sup>15</sup>.
- **Placebo:** Product with no therapeutic effect, used as a control when testing new drugs.

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<sup>14</sup> Directive (EU) No 2001/83/EC of the European Parliament and of the council of 6 November 2001 on the Community code relating to medicinal products for human use, EU Official Journal L311. 28 of November of 2001. Available at: [https://health.ec.europa.eu/system/files/2016-11/dir\\_2001\\_83\\_cons\\_2012\\_en\\_0.pdf](https://health.ec.europa.eu/system/files/2016-11/dir_2001_83_cons_2012_en_0.pdf)

<sup>15</sup> European Commission, *Clinical Trials Regulation (EU) No 536/2014 Questions & Answers*. Available at: [https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10\\_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014)

## 2.19. What types of products can be added as a test role in CTIS?

Users can add to the Initial CTA an authorised product, an active substance, and an anatomical therapeutic chemical (ATC); or an unauthorised product. They can also add a product that has not yet received marketing authorisation, i.e. development product. Each product added to a CTA needs to be extracted from XEVMPD, the extended EudraVigilance medicinal product dictionary. Users can apply filters (i.e. 'starts with', 'equal to' and 'contains') to search for information easily. For example, 'Contains' filter is recommended in case users don't know the exact data.

Once selected from XEVMPD, each product will come with a set of information retrieved and copied from XEVMPD. The list of fields is displayed below:

Nature	Type of product	Fields
Authorised	Product	<ul style="list-style-type: none"> <li>• Medicinal product details</li> <li>• Product characteristics</li> <li>• Dosage and administration details</li> <li>• Information about the modification of the Medicinal product</li> <li>• Product classification</li> <li>• Product authorisation details</li> <li>• Orphan Designation</li> <li>• Active substance</li> <li>• Advanced Therapy Medicinal product</li> <li>• Device associated with the medicinal product</li> </ul>
	ATC	<ul style="list-style-type: none"> <li>• ATC code description</li> <li>• Product characteristics</li> <li>• Dosage and administration details</li> <li>• Information about the modification of the Medicinal product</li> <li>• Product classification</li> <li>• Orphan designation</li> <li>• Advanced therapy medicinal product</li> <li>• Device associated with the medicinal product</li> </ul>
	Substance	<ul style="list-style-type: none"> <li>• Active substance description</li> </ul>



		<ul style="list-style-type: none"> <li>• Product characteristics</li> <li>• Dosage and administration details</li> <li>• Information about the modification of the medicinal product</li> <li>• Product classification</li> <li>• Orphan designation</li> <li>• Active substance</li> <li>• Advance Therapy Medicinal product</li> <li>• Device associated with the medicinal product</li> </ul>
Unauthorised	Product	<ul style="list-style-type: none"> <li>• Medicinal product details</li> <li>• Product characteristics</li> <li>• Dosage and administration details</li> <li>• Product classification</li> <li>• Orphan Designation</li> <li>• Active substance</li> <li>• Advanced Therapy Medicinal product</li> <li>• Device associated with medicinal products</li> </ul>

Regarding the documents for the product, the following sections are common for the test role and are available once the role has been added:

- Investigator's Brochure for the Medicinal Products or SmPC;
- Compliance with (GMP) for the Medicinal Product;
- IMPD Quality;
- IMPD – Safety and Efficacy.

## 2.20. Can users add more than one IMP per test role in the CTA?

Yes, users can add several IMPs under the 'test' section in CTA. It may be that several products share common documentation (*refer to question 2.22 for more information*).

## 2.21. Is it mandatory to include the IMPD documents?

If users have already uploaded the IMPD-related documents (IMPD Quality or IMPD Safety and Efficacy) to other clinical trials, they might not need to upload any documents again. In that case, they can include an indicative text in the 'Justification for no IMPD upload' field (e.g. the exact IMPD-related documents have been already submitted via a different CTA).

If they upload one document to any of the document placeholders, the free text field disappears, and users need to upload all the mandatory documents to be able to submit their application.

The screenshot shows a user interface for uploading IMPD documents. It features three document placeholders, each with an 'Add document' button:

- IMPD Quality** (dropdown menu)
- IMPD - Safety and Efficacy** (dropdown menu)
- IMPD - Safety and Efficacy \*** (text field)
- Simplified IMPD - Safety and Efficacy \*** (text field)
- Justification for no IMPD upload \*** (text field)

## 2.22. How can users search for a product?

Users can retrieve information on medicinal products from the EudraVigilance medicinal product dictionary (xEVMPD). Users can access this information using available search fields, which are different depending on the type of product.

Authorised:

- **Product:** EU Medicinal Product number, Pharmaceutical form, Marketing authorisation number, Strength, Name of product, Active substance name, EU substance number, and/or ATC code.
- **ATC:** ATC code, Pharmaceutical form, Strength.
- **Substance:** Name, EU Substance Number, Pharmaceutical form, Strength.

Unauthorised:

- **Product:** EU Medicinal Product number and EU substance number.

For more information, refer to Module 02: Overview of CTIS workspaces and common system functionalities<sup>16</sup>.

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<sup>16</sup> European Medicines Agency, CTIS online training modules, Module 02: Overview of CTIS workspaces and common system functionalities: <https://www.ema.europa.eu/en/human-regulatory-overview/research-development/clinical-trials-human-medicines/clinical-trials-information-system-training-support/clinical-trials-information-system-ctis-online-training-modules>

## 2.23. Can users indicate that a product is applicable only to certain MSCs?

- Yes. By default, the product is applicable to all MSCs. However, sponsors can choose to exclude a product from an MSC by clicking the 'Exclude MSC' button and selecting the MSC in a drop-down list of the MSCs involved in the trial. This might be the case in case of concurrent medication for underlying disease treatment.

## 2.24. How can users link the placebo with other investigational medicinal products?

Users are able to link a placebo to other products with the role 'Test/Comparator' by clicking on the button 'Link products' displayed in the section bearing the same name.

## 2.25. How can users populate the dose box?

Under the 'Product' subsection of Part I, users can populate the dosage and administration details. Users can include a dot '.' to separate the decimals. It is possible to have two decimals behind the dot.

## 2.26. How are Advanced Therapy Medicinal Products populated in clinical trials?

According to the European Medicines Agency website<sup>17</sup>, Advanced Therapy Medicinal Products (ATMPs) are medicines for human use that are based on genes, tissues or cells. They offer ground-breaking new opportunities for the treatment of disease and injury.

Users need to populate the products of their trials in CTIS, retrieving data from xEVMPD<sup>18</sup>. The information of whether a medicinal product is classified as ATMP is not captured in xEVMPD, that attribute is captured locally in CTIS. If the selected products are considered ATMP, that information needs to be populated in the tile 'Advanced Therapy Medicinal Product'. Under each selected product, users can click on the row that includes the information of the product to view various tiles, among them, the aforementioned 'Advanced Therapy Medicinal Product'.

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<sup>17</sup> European Medicines Agency - Advanced therapy medicinal products: Overview. Available at: <https://www.ema.europa.eu/en/human-regulatory/overview/advanced-therapy-medicinal-products-overview>

<sup>18</sup> European Medicines Agency - Extended EudraVigilance medicinal product dictionary (XEVMPPD) training. Available at: <https://www.ema.europa.eu/en/human-regulatory/post-authorisation/data-medicines-iso-idmp-standards/extended-eudravigilance-medicinal-product-dictionary-xevmpd-training>

Products

Sort by: 11 No sorting + Add Register

Role: Test Name: Ibuprofeno Dermogen 400 mg suspensión oral + Add

EU MP number	Marketing authorisation number	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	Actions
PRD1160996	66.330	Authorised	Ibuprofeno dermogen 400 mg suspensión oral	Oral suspension	Ibuprofen 400mg	-	Ibuprofen	SUB08098MDG	IBUPROFEN	M01AE01	5	-	-	Product	 

Details for Product with EU MP number: PRD1160996

- Medicinal product details >
- Product characteristics >
- Dosage and administration details >
- Information about the modification of the Medicinal Product >
- Product Classification >
- Product authorisation details >
- Orphan Designation >
- Active substance >
- Advanced Therapy Medicinal Product >
- Device associated with medicinal product >

By expanding this tile, users can click on the 'Add Advanced Therapy' button. In the pop-up window, users select an option from the 'Advanced therapy classification' drop-down menu, and populate the Committee for Advanced Therapies (CAT) Reference number<sup>19</sup>, if applicable.

**Advanced Therapy Medicinal Product** ×

**Advanced therapy classification** ▼

- Somatic Cell Therapy
- Tissue Engineered Therapy
- Gene Therapy

**CAT reference number**

Cancel Save

Based on the selection of the type of therapy, relevant fields might be expanded below, that will allow users to record additional information regarding ATMP. The selection of the first fields might affect the following fields and under specific circumstances, some of them might be mandatory. Mandatory fields will be indicated with an asterisk. Your selection of the first fields affects the following fields and they might be mandatory. The available fields for each Advanced therapy classification are listed below:

- **Somatic Cell Therapy:** Somatic cell origin (Autologous; Allogenic; Xenogeneic); Somatic cell type (Stem; Differentiated; Other).
- **Tissue Engineered Therapy:** Tissue engineered cell type (Stem; Differentiated; Other); Origin of the engineered tissue (Autologous; Allogenic; Xenogeneic).
- **Gene Therapy:** Gene therapy type (In vivo; Ex vivo); Type of gene transfer product (Naked nucleic acid; Complex nucleic acid; Viral vector; Other); Genetically modified cell present (Yes; No).

After populating the relevant details, users can save the information, recorded on ATMP tile. After saving the ATMP details, users can edit the information, by using the 'pencil' icon or they can remove it and add new data, by using the respective button, 'Remove Advanced Therapy'. The 'eye' icon allows users to view all the details.

<sup>19</sup> European Medicines Agency - Committee for Advanced Therapies. Available at: <https://www.ema.europa.eu/en/human-regulatory/overview/advanced-therapy-medicinal-products-overview#committee-for-advanced-therapies-section>

**Advanced Therapy Medicinal Product**
▼

Add Advanced Therapy
Remove Advanced Therapy

		Therapy type	CAT reference number
<input checked="" type="checkbox"/>		Somatic Cell Therapy	

## 2.27. What information can users include in Part II section?

The information covered in the Part II section of a CTA includes structure data with details of the trial sites and a set of documents listed below for each of the MSCs if more than one:

Details of the trial sites, including name and address of the site and details of the principal investigator conducting the trial at the site (name of the person on the side of the sponsor organisation, department, department phone number and email address). The functional contact details for the investigator are made public.

- Recruitment arrangements;
- Subject information,
- Informed consent form and procedure;
- Suitability of the investigator;
- Suitability of the facilities;
- Proof of insurance cover or indemnification;
- Financial and other arrangements;
- National requirements for data protection, as applicable;

Use of biological samples, as applicable. Users can find some of the templates for these documents<sup>20</sup>.

## 2.28. How can a medical device be populated in a CTA under CTR?

Medical devices are products or equipment intended for a medical purpose (more details on the medical device homepage on EMA website<sup>21</sup>). The CTR Q&A document available on Eudralex vol 10<sup>22</sup> indicates under which circumstances a medical device, in combination with

<sup>20</sup> For more information, please consult [https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10\\_en](https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10_en)

<sup>21</sup> European Medicines Agency. Medical Devices section. Available at <https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices#medical-devices-legislation-section>

<sup>22</sup> European Commission, *Clinical Trials Regulation (EU) No 536/2014 Questions & Answers*. Available at: [https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10\\_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014)

a medicinal product, could have a role in a clinical trial and be assessed under CTR. If the medical device (in combination with the medicinal product, or ATC or substance) is indeed the object of the study under CTR, the details of the medical device could be populated in the details for the selected medicinal product that is combined with the device.

Users will need to click on the ribbon that hosts the overview details of the medicinal product (or ATC, or substance) that is combined with the medical device. Fields related to the selected product will be revealed below. Among them, in the end, users could see the tile 'Device associated with medicinal product'.

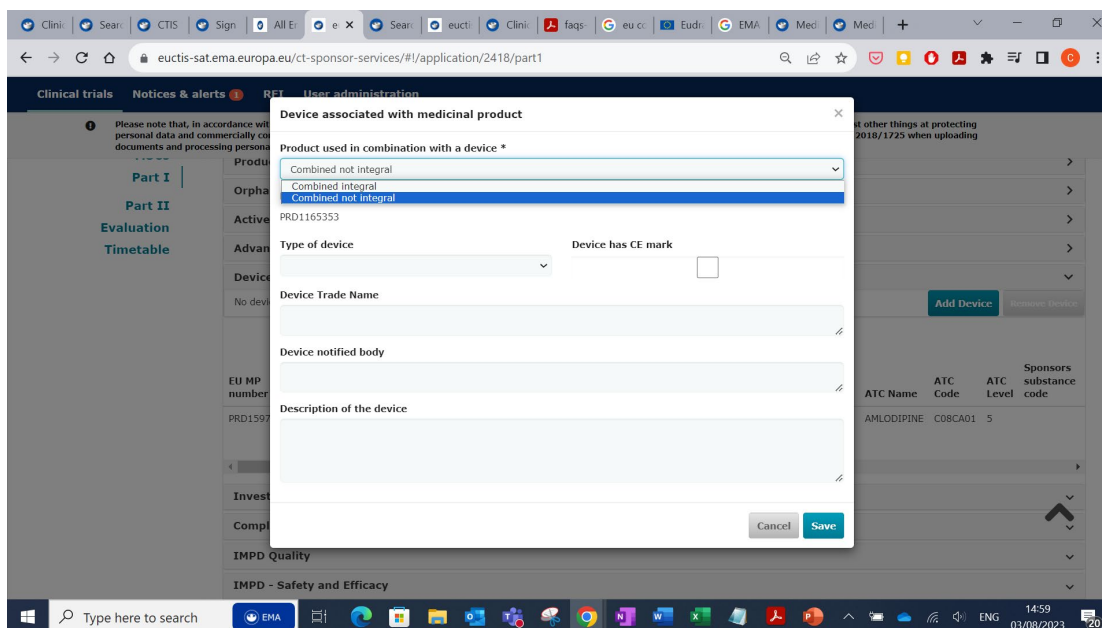
The screenshot shows a table of medicinal products. A yellow box highlights a row with the following data: PRD1165353, PL 28444/0085, Authorised, Paracetamol tablets 500mg, Tablet, Paracetamol 500mg, Paracetamol, SUB09611MIG, PARACETAMOL, N02BE01, 5. A yellow arrow points to the 'Tablet' column. Below the table, a sidebar labeled 'Revealed fields' lists various categories for the selected product (PRD1165353). The categories are: Medicinal product details, Product characteristics, Dosage and administration details, Information about the modification of the Medicinal Product, Product Classification, Product authorisation details, Orphan Designation, Active substance, Advanced Therapy Medicinal Product, and Device associated with medicinal product. The 'Device associated with medicinal product' category is highlighted with a yellow box.

Users need to open the tile and use the 'Add device' button.

The screenshot shows a detailed view of the 'Device associated with medicinal product' tile. It displays the text 'No devices combined with the product' and a blue 'Add Device' button. There is also a grey 'Remove Device' button.

A form will pop up in which the user can populate the details of the device. The first field, 'Product used in combination with a device', is a drop-down list for which, users need to indicate whether the device is combined as an integral item with the product or not. Then, users can use the following fields to indicate the type of the device (drop-down list), whether there is a CE mark<sup>23</sup> on the device (tick-in box) and to add details regarding the trade name, the notified body, and the description of the device (all three are free text fields).

<sup>23</sup> More details on the EMA's homepage on Medical Devices: <https://www.ema.europa.eu/en/human-regulatory-overview/medical-devices#medical-devices-legislation-section>



By saving all the populated details of the device, those will appear in the overview. Users may use the pencil icon to edit the details of the device or use the tick-in box on the left side of the overview and activate the 'Remove device' button in case they need to remove completely the entry.

## 2.29. Is it mandatory to upload a recruitment arrangement document?

Yes. According to the CT Regulation<sup>24</sup>, the Recruitment arrangement document is mandatory.

## 2.30. Can Initial applications be limited to Part I only?

Yes. Under Article 11 of the CT Regulation, the sponsor has the ability to initially submit part I only for assessment. They will need to wait for the RMS/MSC to submit the conclusion of the assessment to part I (reporting date) before they can submit part II. After the reporting date, the sponsor has two years to complete their application with part II to obtain a decision for the trial. Failure to do so within this period leads to the lapse of the application.

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<sup>24</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, EU Official Journal L158. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf)

## 2.31. In cases of applications limited to Part I, how should a sponsor proceed to submit an application for Part II?

Following the submission of the conclusion on Part I (reporting date), but only during the subsequent 2 years, a sponsor may submit an application limited to the aspects covered by Part II of the dossier, declaring that they are not aware of any new substantial scientific information that would change the validity of any item submitted in the application on the aspects covered by Part I of the dossier which were already assessed by the MSC. The list of the documentation and information required to be provided in Part II is set out in CT Regulation Annex I (sections K to R)<sup>25</sup>.

For more information, please consult the Clinical Trials Information System (CTIS) Bitesize talk session on Partial submitted trials: <https://www.ema.europa.eu/en/events/clinical-trials-information-system-ctis-bitesize-talk-part-i-only-applications-part-ii-requirements>

## 2.32. When can the sponsor of a partial submission application submit a substantial modification (SM) or an additional MSCs?

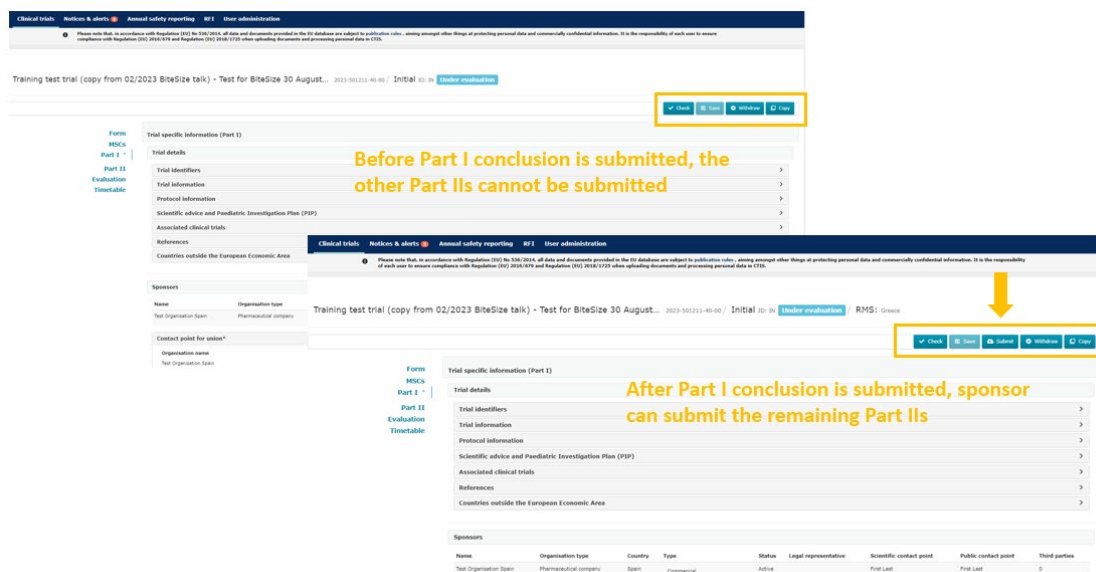
With the current CTIS functionalities and until further notice, sponsors cannot submit a substantial modification (SM) for a partial submitted initial application before Part II for all MSCs have been submitted and all MSCs have issued decisions.

In case only some MSCs have issued decisions for the initial application (those MSCs for which Part II had been already submitted by the sponsor), the sponsor cannot submit any SM. If the sponsor needs to submit an SM, it needs to wait until Part II is submitted for all MSCs and the remaining MSCs issue their decision. Alternatively, if the sponsor cannot wait for so long and needs to submit an SM as soon as possible, it can withdraw the trial for the remaining MSCs for which no decision has been issued. After withdrawal, the sponsor can submit its substantial modification. After a decision is issued on the SM, the sponsor can add additional MSC applications for the MSCs for which it withdrew the trial earlier.

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<sup>25</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, *EU Official Journal* L158. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf).





Similarly, the sponsor cannot submit any additional MSC applications, as long as no decision has been issued for at least one MSC. In addition, if the evaluation of an SM that includes Part I is ongoing, no additional MSC application can be submitted.

For more information, please consult the Clinical Trials Information System (CTIS) Bitesize talk session on Partial submitted trials: <https://www.ema.europa.eu/en/events/clinical-trials-information-system-ctis-bitesize-talk-part-i-only-applications-part-ii-requirements>

## 2.33. What happens if the sponsor does not submit Part II?

In accordance with Article 11 of the CT Regulation<sup>26</sup>, the sponsor can submit a partial application dossier, including only Part I for the start of the evaluation process. However, the sponsor needs to submit Part II before the MSC has issued a decision regarding the authorisation of the CT. If the sponsor does not submit Part II after two years from the submission of the conclusion on Part I (reporting date), the application will be expired.

<sup>26</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, *EU Official Journal* L158. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req\\_2014\\_536/req\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req_2014_536/req_2014_536_en.pdf)

## 2.34. After the receipt of the decision on the clinical trial, does the sponsor have the option to appeal against the decision?

Yes. The CT Regulation states that Member States shall provide an appeal procedure in respect of a refusal related to<sup>27</sup> :

- Article 8 (Decision on the clinical trial).
- Article 14 (Subsequent addition of a Member State concerned).
- Article 20 (Validation, assessment, and decision regarding a substantial modification of an aspect covered by Part II of the assessment report) and.
- Article 23 (Decision on the substantial modification of aspects covered by Parts I and II of the assessment report).

In this situation, the respective national laws apply to each MSC.

## 2.35. Does a sponsor have to await positive decisions from all Member States concerned before starting the trial in any of them?

No. The sponsor/investigator can start a clinical trial in an MSC if a positive decision has been issued by at least that MSC. The trial can only start in the MSC that has authorised the trial, even if the assessment is still ongoing in the rest of them.

# 3. Additional Member states concerned CTA

## 3.1. What is the purpose of the Additional MSCs application?

An additional MSC CTA is an application for extending a previously authorised CT to the territory of another Member State(s).

## 3.2. When can users submit an Additional MSC Application?

The Additional MSC application can be submitted while there are no other applications under evaluation. There are a few exceptions to this rule. It is possible to submit and Add MSC CTA if there is an assessment for SM part II ongoing in other MSC, or if there are other Additional

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<sup>27</sup> European Commission, *Clinical Trials Regulation (EU) No 536/2014 Questions & Answers*. Available at: [https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10\\_en#set-of-documents-applicable-to-clinical-trials-authorised-under-regulation-eu-no-5362014](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorised-under-regulation-eu-no-5362014)

MSC applications under evaluation, the user can submit more Additional MSC applications to other MSC.

### 3.3. How can users create an Additional MSC CTA?

From the CT summary page, users can create an Additional MSC Application, by clicking on the 'create' button on the upper-right corner of the page. On the pop-up window that appears, the sponsor can select one or more MSCs that are to be included and the estimated number of subjects in each MSC. After that, the sponsor users can populate the newly added MSC details, including the compulsory fields marked with an asterisk, such as the trial site details and the mandatory documents.

### 3.4. What information can users include in the different sections of an Additional MSC CTA?

The information that can be included in the different sections of an Additional MSC CTA is the following:

- Form
- Cover letter.
- Proof of payment.
- MSCs
- MSCs included in the CTA and the estimated total population for the CT in each MSC.
- Part I

In Part I section, users can submit documentation related to the translation of specific Part I data and documents such as the ones listed below (if so required by the MSC).

- Fields such as the CT title, the medical condition, the CT objectives, the eligibility criteria, etc.
- Documents such as the protocol, data safety monitoring committee charter, investigator brochure, etc.

#### Part II

Documentation related to aspects that concern additional MSC to which the user wants to extend the conduct of the CT. These include the following:

- Trial sites information;
- Recruitment arrangements;
- Subject information;
- Informed consent form and procedure;
- Suitability of the investigator;

- Suitability of the facilities;
- Proof of insurance cover or indemnification;
- Financial and other arrangements;
- Compliance with data protection national requirements;
- Compliance with the use of biological samples.

### 3.5. Is there a limitation to the number of MSCs in an Additional MSC Application?

No, there is no limitation. By clicking on the 'create' button on the upper-right side and 'additional MSC', a sponsor can select one or multiple MSCs to the add MSC application.

Once created, each application for each MSC will be treated separately, and sponsor users will have to provide MSC details for each MSC to be added. Once submitted, each application will be evaluated by the newly added MSC.

### 3.6. What happens if there are missing or incomplete documents in an Additional MSCs Application?

In case there are missing or incorrect documents, for instance, because of wrong information or language, a Request for Information (RFI) will be used by the MSCs to request the sponsor to submit the necessary documents and information and update the application accordingly<sup>28</sup>.

### 3.7. Can an Additional MSCs CTA be submitted whilst another one is ongoing?

Yes, this is possible, as mentioned in 3.4. However, it is advisable to combine the requests to include additional MSCs and submit those at the same time<sup>29</sup>.

## 4. Substantial Modification CTA

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<sup>28</sup> Idem<sup>27</sup>

<sup>29</sup> Idem<sup>27</sup>

## 4.1. What is a 'Substantial Modification'?

As per Article 2(13) of the CT Regulation, an SM is any change to any aspect of a CT, which is made after the notification of a decision on a previously submitted application and which is likely to either:

Have a substantial impact on the safety or rights of the subjects; or

On the reliability and robustness of the data generated in the CT.

If none of the above criteria is met, and the sponsor wants to make a change to the CT dossier that is not likely to have a substantial impact on the safety or rights of the subjects or the reliability and robustness of the data generated in the CT, but that is relevant for the supervision<sup>30</sup> then a non-SM can be filed. (Refer to question 5.1 for more information). In case of doubt about whether a change should be deemed as an SM or not, the sponsor shall consult the MSC<sup>31</sup>.

## 4.2. What types of Substantial Modification CTAs can be submitted?

Chapter III of the CT Regulation refers to three types of SMs:

- SM of Part I only (Articles 17 to 19).
- SM of Part II only (Article 20).
- SM of both Part I and II (Articles 21 to 23).

Additionally, depending on the number of trials the sponsor wants to apply an SM for Part I, SMs can be further divided into:

- **Single-trial SM:** Where an SM concerns only one CT.
- **Multi-trial SM:** Where an SM concerns more than one CT of the same sponsor and with the same investigational medicinal product. In this case, users will need to indicate the EU CT number of the concerned trials. The changes made will apply to all trials provided.

The sponsor will be able to submit the (multi-trial) SMs including Part I only for those trials that have already been authorised (or authorised with conditions) and that do not have a parallel assessment or pending notification of a decision. Multi-trial SMs for Part II can be submitted in parallel to different MSCs.

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<sup>30</sup> Article 81(9) Of Regulation (EU) No 536/2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req_2014_536/reg_2014_536_en.pdf)

<sup>31</sup> European Commission, *Clinical Trials Regulation (EU) No 536/2014 Questions & Answers*. Available at: [https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10\\_en#set-of-documents-applicable-to-clinical-trials-authorised-under-regulation-eu-no-5362014](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorised-under-regulation-eu-no-5362014)

### 4.3. How can users create a Substantial Modification CTA?

From the CT summary page, users can create two types of SMs: single-trial SMs and multi-trial SMs (see question 4.2 above). When clicking on the 'create' button on the upper-right corner of the page, the two types of SM will appear in a drop-down list.

After selecting the type of SM, a pop-up window will appear in which the user must include the scope of the SM:

- Part I only: users are able to make changes to any section of the application, except Part II.
- Part II only: users can select the MSC for which they want to submit a substantial modification. Users can select only one MSC at a time.
- Part I and Part II: users can select multiple MSCs at the same time.

After creating the SM, the user will land on the 'Form' section of the CTA page in which the SM details must be included, including a cover letter and a description of the changes made to the dossier with the SM. In the case of a multi-trial SM, users must also populate the title 'Included trials' by selecting the 'Add trial' button and specifying the EU CT Number of the additional trials included in the same SM application.

### 4.4. What information can users include in the different sections of a Substantial Modification CTA?

The information that can be included in the different fields (i.e. structured data or documents) of the sections of an SM CTA is the following:

#### Form

- Users should provide details on the nature of the SM (reason and scope). Although those fields are not considered mandatory, they should be populated. Users must upload a new cover letter and a document explaining the substantial changes related to this CTA to be able to submit the CTA.

#### MSCs

- Users can only modify the expected number of subjects to be recruited on a CT. Users cannot include any additional MSC, as this is done via an Add MSC CTA.

#### Part I

- Trial-specific information that can be modified as needed via an SM CTA. For example: protocol information, CT design, inclusion and exclusion criteria, conditions to be treated, the therapeutic area, etc.

#### Part II

- Documents of the CTA of a regulatory nature can be modified as needed via an SM CTA. e.g. informed consent form, subject recruitment arrangements, trial sites, etc.

If users need to upload new versions of documents, they can submit a clean version of the updated document, as well as the original document with track changes, to facilitate the assessment of CTAs.

The documents with track changes (as well as other intermediate versions of documents) can be uploaded in document placeholders that are **NOT** for publication.

## 4.5. When can users submit a Substantial Modification?

SM can be submitted by the sponsor if no other application is under evaluation (be it an initial application, a request to add an MSC or a request for another SM on either or both of the Parts). In other words, the SM can be submitted and assessed only after the decision on the previously submitted application is issued or authorised by tacit approval.

There are only two exceptions to this:

When there is a parallel assessment of SMs for Part II in different MSCs, i.e. an application for an SM of Part II in an MSC can be submitted while the assessment of another SM for Part II is ongoing in another MSC.

An Additional MSC CTA is possible while there is an ongoing assessment of an SM for Part II in another MSC.

An SM CTA may be required in certain circumstances during the CT lifecycle, because of new information that becomes available on the medicinal product(s) used or on the trial, or for instance in the following cases:

- A Corrective measure applied by one or more MSCs to the trial.
- In order to request an extension of time, if the recruitment of subjects has not started within two years from the CT authorisation, to avoid an application lapse.
- To restart a CT that was halted in an MSC for reasons of subject safety/benefit-risk balance.

For more information about the CT lifecycle, refer to the elearning of Module 05: How to manage a CT (Notifications, Ad hoc Assessment, Corrective measures and Trial results)<sup>32</sup>.

## 4.6. How can users describe the changes they have made in a CTA section?

Users can include a description of the changes applied in the 'Section changes description' tile of the respective section. Once they have included their comments, an exclamation mark will appear in the modified sections.

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<sup>32</sup> European Medicines Agency. CTIS online training modules. Module 05 Manage a clinical trial through CTIS. Available at: <https://www.ema.europa.eu/en/human-regulatory-overview/research-development/clinical-trials-human-medicines/clinical-trials-information-system-training-support/clinical-trials-information-system-ctis-online-training-modules>

## 4.7. When is a modification considered 'substantial'?

A non-exhaustive list of examples of modifications that should be regarded as substantial is provided in Annex III of the European Commission CT Regulation Questions & Answers document<sup>33</sup>. Some examples from the non-exhaustive list that are typically considered to be 'substantial' are listed below:

Part I		
Protocol	IMPD and IB	Others
<ul style="list-style-type: none"> <li>• A change in the definition of the end of the trial.</li> <li>• New toxicological or pharmacological data which is likely to impact on the risk/benefit assessment.</li> <li>• Changes in the number of scheduled subject trial visits.</li> <li>• Change of a diagnostic or medical monitoring procedure which is likely to have a significant impact on the safety or scientific value of the CT.</li> </ul>	<ul style="list-style-type: none"> <li>• Any change in the quality of the IMP.</li> <li>• Change in the overall risk and benefit assessment in the IMPD or IB.</li> <li>• New clinical data e.g. from previous CTs and human experience in the IMPD or IB which might have a significant impact on the risk/benefit ratio.</li> <li>• Changes to the reference safety information for the annual safety report and SUSAR reporting.</li> </ul>	<ul style="list-style-type: none"> <li>• A change of sponsor, co-sponsor or the sponsor's legal representative.</li> <li>• The revocation or suspension of the IMP's marketing authorisation.</li> </ul>
Part II		
<ul style="list-style-type: none"> <li>• Addition of a site, change in facilities, change in site suitability or change of principal investigator.</li> <li>• Change of the insurance policy, e.g. a new insurance company, changes in insurance coverage, conditions and/or insured amounts.</li> <li>• Modifications in any documents for subjects such as the subject information sheet, and informed consent form, which could include changes in safety information, trial procedures or data handling.</li> <li>• Change in access, disclosure, dissemination, alteration or loss of information and personal data processed.</li> <li>• Change in the collection, storage and future use of biological samples from CT subjects.</li> <li>• Change in financial arrangements.</li> <li>• Change in the compensation paid to subjects and/or investigator/site for participating in the trial.</li> </ul>		

## 4.8. Who is responsible for assessing whether a modification is deemed as 'substantial'?

In principle, it is the responsibility of the sponsor to assess whether a modification is to be regarded as 'substantial'. This assessment is to be made on a case-by-case basis in view of what is described in question and answer 4.2.

The sponsor should also assess whether an SM leads to changes in the CT to the extent that it has to be considered as a completely new CT. Some scenarios would require an application for a new trial authorisation to be considered instead of an SM; for example<sup>34</sup>:

- A change of the Investigational Medicinal Product (IMP).
- Significant modifications such as a change to the main objective or primary endpoint of the CT in all phases.

<sup>33</sup> European Commission, *Clinical Trials Regulation (EU) No 536/2014 Questions & Answers*. Available at: [https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10\\_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014)

<sup>34</sup> Idem<sup>33</sup>



- Unplanned and unjustified addition of a trial arm or placebo group (except in the exceptional case of a CT with a novel design, where this was already described in the protocol of the initial application).

#### 4.9. Is the addition of a new Member State considered as a Substantial Modification?

No. as explained in section 3, the subsequent addition of another MSCs to extend an authorised CT requires the submission of an Additional MSC application dossier in accordance with Article 14 of the CT Regulation<sup>35</sup>. An application dossier may only be submitted after the notification date of the initial authorisation decision (refer to question 3.2).

#### 4.10. How can the ownership of a trial be changed from a sponsor to a different sponsor (change of sponsor-entity)?

To be able to change the ownership of the trial from the original sponsor to a different sponsor, users need to **submit a Substantial Modification (SM) Part-I** (according to [Annex IV of the Q&A document on CTR](#)) to request a change of the sponsor entity.

Before requesting a change of sponsor entity in CTIS, users should ensure that the new sponsor is registered in [OMS](#), i.e. the request for OMS registration has been submitted and approved.

This type of SM can only be submitted after the initial application has been authorised by all Member States Concerned (MSCs). Also, all MSCs must authorise the SM, for the change of sponsor to come into effect.

Please note that, for historical trials that were authorised before 18 June 2024, the SM Part-I for the change of sponsor triggers the publication of part I documents. For these trials, if the part I documents 'for publication' contains commercially confidential information or personal data, please refer to slide 17 of the [quick guide on the revised CTIS transparency rules and historical trials](#).

For step-by-step guidance, Sponsors can consult instructions on [Module 10 step-by-step guide](#).

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<sup>35</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, EU Official Journal L158. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf)

## 5. Non-Substantial Modifications

### 5.1. What is a Non-Substantial Modification?

A sponsor can submit a Non-SM when it wishes to apply a change to any aspect of a CT (after the notification of a decision on a previously submitted application) which is not likely to have a substantial impact on the safety or rights of the subjects or the reliability and robustness of the data generated in the CT. However, it is still relevant for the supervision of the CT (Article 81(9))<sup>36</sup>.

### 5.2. Is a Non-Substantial Modification considered as a CTA?

A non-SM is not considered as an application as it is not subject to the evaluation and decision issued by the MSC.

### 5.3. How can Non-Substantial Modifications be created?

In CTIS, non-SM can be created from the CT summary page, listed on the 'applications and non-SM' at the bottom of a CT page.

In case of doubt about whether a change is an SM or not, the sponsor must consult the MSC.

### 5.4. When can users submit a Non-Substantial Modification?

Sponsors can submit Non-SM to keep information of the dossier up to date. However, this can be done while there are no other applications ongoing. Non-SM changes can also be provided as part of RFI responses where so required<sup>37</sup>.

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<sup>36</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, *EU Official Journal* L158. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req\\_2014\\_536/req\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/req_2014_536/req_2014_536_en.pdf)

<sup>37</sup> European Commission, *Clinical Trials Regulation (EU) No 536/2014 Questions & Answers*. Available at: [https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10\\_en#set-of-documents-applicable-to-clinical-trials-authorised-under-regulation-eu-no-5362014](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorised-under-regulation-eu-no-5362014)

## 5.5. Can a Non-Substantial Modification affect multiple trials?

No. Unlike multi-trial SMs, in case a sponsor wants to apply non-substantial changes to multiple CTs, it will need to submit one non-SM per each CT.

## 5.6. Is there a predefined list of modifications that should be regarded as Non-Substantial Modifications?

A non-exhaustive list of examples of modifications that should be regarded as non-substantial is provided in Annex III of the European Commission CT Regulation Questions & Answers document<sup>38</sup>. Some of the modifications that are typically considered not to be 'substantial' regarding specific sections of CTA are listed below (this table contains examples and is subject to suffer modifications in the future):

Part I		
Protocol	General	Non-SMs the sponsor should notify within EUPD
<ul style="list-style-type: none"> <li>• Increase in duration of the overall time of the trial, provided that specific exposure to treatment, the definition of the end of the trial, and scheduled subject trial visit arrangements remain not extended and unchanged.</li> <li>• A change in the number of CT participants per trial site, if the total number of participants in the MSC is identical or the increase/decrease is insignificant in view of the absolute number of participants.</li> <li>• A change in the documentation used by the research team for recording trial data (e.g. case report form or data collection form).</li> </ul>	<ul style="list-style-type: none"> <li>• Correction of typographical errors in any document change in the quality of the IMP.</li> </ul>	<ul style="list-style-type: none"> <li>• Review the IB at least annually. The sponsor has to verify whether the update relates to changes which are to be considered as substantial.</li> <li>• Any change of persons/entities and contact details to whom the sponsor delegated tasks, for example, the applicant, technical service providers, electronic systems providers, laboratories and clinical research organisations ('CROs').</li> </ul>
Part II		
<ul style="list-style-type: none"> <li>• Extension of validity of insurance certificate.</li> <li>• Correction of typos in any document.</li> <li>• Technical and administrative changes in subject documents including the subject information sheet or informed consent (e.g. change in phone number or typo errors).</li> <li>• A validated translation of the locally approved ICF in another language in order to be used for a potential subject who is not fluent in the local (country) language.</li> </ul>		

<sup>38</sup> European Commission, *Clinical Trials Regulation (EU) No 536/2014 Questions & Answers*. Available at: [https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10\\_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014)

## 5.7. How can the sponsor information be changed in CTIS (Via Non-Substantial Modification)?

For changes on the sponsor details that are classified as changes of 81.9 non-substantial modification (according to Annex IV of Q&A document on CTR<sup>39</sup>), sponsor users can update the sponsor details recorded on the application form with the **submission of a non-SM**. Such changes might be a change of the sponsor's name (without change of the legal entity), the contact details, or the address.

Sponsor details are captured in Part I, therefore, to change the sponsor's information users would need to submit a non-SM that affects Part I (Part I only or Part I & II).

Before recording the sponsor changes on CTIS, sponsor users **need to update the OMS data**. Users will need to submit a change request to update organisation details [in OMS](#) (see document [E - OMS Change Requests](#) in [OMS document repository](#)), wait until their change request is validated and approved by the OMS team and then apply the changes on CTIS.

For step-by-step guidance, Sponsors can consult instructions on [Module 10 step-by-step guide](#).

## 6. Withdraw a CTA

### 6.1. When can users withdraw an Initial CTA for a CT?

As per Article 12 of the CT Regulation<sup>40</sup>, a withdrawal of an initial application for all MSCs can be done until the RMS submits a conclusion on Part I (reporting date). After the reporting date and while the initial application is still under evaluation, but before the decision has been issued by each MSC, the application can be withdrawn from each MSC separately.

The CT Regulation specifically foresees the possibility for the sponsor to withdraw an application in all or individual MSCs (Article 12). Various scenarios are outlined in the European Commission CT Regulation Questions & Answers document<sup>41</sup> in the case a sponsor wishes to do so:

**Scenario 1:** The sponsor decides to withdraw an application for a CT in an MSC. This may happen at any time until the decision is made, providing a justification. However, in cases of withdrawal of an application before the conclusion of each MSC (reporting date), the withdrawal will apply to the entire application in all MSCs.

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<sup>39</sup> European Commission, *Clinical Trials Regulation (EU) No 536/2014 Questions & Answers*. Available at: [https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10\\_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorized-under-regulation-eu-no-5362014)

<sup>40</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, EU Official Journal L158. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf)

<sup>41</sup> *Idem*<sup>39</sup>

**Scenario 2:** The sponsor decides to withdraw an application in case of partial submission of a CTA (refer to questions from 2.18 to 2.19). Scenario 1 above also applies in this case. However, additionally, in the case of MSC that received only a CTA limited to Part I, a CTA could be withdrawn at any point after the reporting date even if the CT is already authorised in one or more of the other MSC that received a full application.

**Scenario 3:** The sponsor decides to terminate early an ongoing CT in one of the MSCs (i.e. after the decision is issued in that MSC). In that case, the sponsor should notify the MSC of the early termination.

Once the decision regarding an initial application is taken, a sponsor no longer has the possibility to withdraw the application. If, after authorisation of the trial, the CT does not start and the sponsor decides not to carry it out in an MSC within two years from the notification date of the decision of authorisation, the application will expire.

## 6.2. When can users withdraw a Substantial Modification CTA or an Additional MSC CTA?

Different timelines are foreseen depending on the type of application in question:

In the case of an SM of Part I or Part I and Part II, the withdrawal applies to all MSCs, before the conclusion on Part I (i.e. reporting date), and can take place until the decision is issued;

In the case of an SM of Part II only, an application can be withdrawn from one or more MSCs, at any point until the decision is issued.

## 6.3. When can users withdraw Additional of an MSC CTA?

For Additional MSCs, the withdrawal can be done separately for each MSC involved until the decision has been issued.

## 6.4. Is it compulsory to include a justification in case of withdrawal?

Yes. Sponsors must include a justification for the withdrawal of any application in CTIS.

## 6.5. Can an Initial CTA be re-submitted?

As per Article 13 of the CT Regulation<sup>42</sup>, following the refusal of authorisation or the withdrawal of an application, an initial application can be re-submitted to any intended MSC. In order to save the time of the user, CTIS offers an option to re-submit an already submitted CTA. Besides applications with status 'Withdrawn' or 'Not authorised', sponsor users can resubmit applications with status 'Lapsed' or 'Expired'.

By clicking on the 'Resubmit' button, a new draft of the application will be created. The new draft will include all the information in the structured data and the document attachments that were submitted last time for the previous application, meaning that if users had updated the dossier of the previous application by, for example, responding to an RFI, they would duplicate that most recent dossier version, to create the new draft. This new draft will have a different identifier, keeping the original EU CT number ending with incrementing digits starting from 01. Users can modify the new dossier as needed and submit it. **The resubmission will be deemed as a new CTA.**

The [Clinical Trials Coordination Group \(CTCG\)](#) provides guidelines on their webpage for naming documents required for both initial submissions and re-submissions. These guidelines are accessible under the 'Key Documents List' section.

## 6.6. Can the other types of CT applications (Substantial Modification, Additional MSC) be resubmitted?

Both substantial modification and Additional MSC applications can be resubmitted, but the restrictions below apply:

1. Status of the application (similar to initial applications) should be: 'Withdrawn', 'Lapsed', 'Expired', or 'Not authorised'.
2. The application needs to be the latest application submitted. Sponsor users cannot resubmit an application if other applications have been submitted after the application for resubmission.
3. The last submitted SM can be resubmitted if there is no other SM in draft. The same applies to the Additional MSC.

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<sup>42</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, EU Official Journal L58. 16 of April 2014. Available at: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf)

## 7. Roles and permissions

### 7.1. What user roles are involved in the submission of a CTA?

The CT admin is the only role able to create a CTA and all the subsequent applications. Five roles are involved in the editing and drafting of the CTA, and only two roles can submit or cancel a draft CTA and withdraw it after it has been submitted:

- **Submit/cancel/withdraw a CTA:** CT admin and Application submitter.
- **Edit/draft a CTA:** CT admin, Part I Preparer (excl. Q-IMPD), Part II preparer, Q-IMPD preparer, and Application submitter.
- **Create a CT and a CTA and copy a CTA:** CT admin.

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Clinical Trials Information System (CTIS)

FAQs: How to create, submit and withdraw a Clinical trial application

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