CTIS Bitesize Talk:
Part I-only applications and Part II requirements in CTIS

30 Aug 2023

Presented by Noemie Manent (EMA), Charalampos Drosos (EMA), Ann Marie Janson Lang (Swedish MPA), Monique Al (CCMO) and Marianne Lunzer (AGES)

A few housekeeping rules

Questions were collected in advance on **www.sli.do**
With event code **#bt30aug**

Tips for optimal screen viewing

- Make use of the instructions under the embedded video in the event page and connect directly to the **IBM channel** *for the full-screen experience*
- Increase the *video quality* from the **HD button** on the right bottom of the screen setting it to 720p (or 1080p).
- Have a stable internet connection

CTIS Bitesize Talk - Panellists

Noémie Manent

Principal Scientific Administrator

CTIS Expert

Monique Al

Coordinating Special Advisor

CTCG Vice-chair

Marianne Lunzer

Safety Assessor

CTCG Chair

Charalampos Drosos

CTIS Change Officer

CTIS Expert

Ann Marie Janson Lang

Expert, Clinical Assessor

CTCG member

CT Regulation 536/2014 (CTR) - Article 11

Article 11 provisions give the ability to the sponsor to submit an initial application in a sequential fashion to request for a decision to conduct the clinical trial.

Article 11

Submission and assessment of applications limited to aspects covered by Part I or Part II of the assessment report

Where the sponsor so requests, the application for authorisation of a clinical trial, its assessment and the conclusion shall be limited to the aspects covered by Part I of the assessment report.

After the notification of the conclusion on the aspects covered by Part I of the assessment report, the sponsor may within two years apply for an authorisation limited to aspects covered by Part II of the assessment report. In that application the sponsor shall declare that he is 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 assessment report. In this case, that application shall be assessed in accordance with Article 7 and the Member State concerned shall notify its decision on the clinical trial in accordance with Article 8. In those Member States where the sponsor does not apply for an authorisation limited to aspects covered by Part II of the assessment report within two years, the application on the aspects covered by Part I of the assessment report shall be deemed to have lapsed.

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Background

For a multiple member states application, the sponsor can prepare an application that includes Part I and II to some Member States concerned and limited to Part I only (on the basis of article 11) to other Member States concerned.

99. Therefore, in order to shorten the assessment and approval timelines and to avoid unnecessary rejections due to time-constraints, the submission of complete and high-quality applications is of particular importance.

European Commission Q&A – Q 2.7 (99)

Background (2)

European Commission Q&A – Q 2.14

122. The CTR foresees that an application can be limited to Part I of the assessment report. In this case:

123. The application for Part I will follow the process as laid down in art. 5, 6 and 7

124. The subsequent application for Part II will be assessed in accordance with art. 7 and notification of decision will happen in line with art. 8

Principles (1)

Considerations:

- The sponsors can submit partial initial clinical trial applications, in line with the requirements of Article 11 of the Clinical Trial Regulation (CTR), by submitting an application with Part I to all Member States Concerned (MSC) and part II to none or some MSC.

- After the **conclusion on part I** is issued, the sponsor has the option to submit the outstanding part II to the MSC, enabling the MSC to issue a decision. This will be enabled for 2 years and from the reporting date of the conclusion to part I.

- The initial application will remain **under evaluation** in a Member State from the time the Part I is submitted and until a decision is issued in that Member State or for a **period of 2 years**, after which the application will **lapse**.

For more information, please consult Q 2.2 in European Commission Q&A

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Principles (2)

Considerations:

- A decision (proactively by the Member States or tacitly*) can only be issued once Part II has been assessed and concluded.
  *Article 8.6 of the Regulation No 536/2014

> 6. Where the Member State concerned has not notified the sponsor of its decision within the relevant periods referred to in paragraph 1, the conclusion on Part I of the assessment report shall be deemed to be the decision of the Member State concerned on the application for authorisation of the clinical trial.

- When submitting the additional part II, the sponsor should declare 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 assessment report.

- The submission of further applications of any type (substantial modification, non-substantial changes), can only occur after **all MSC have issued a decision**, i.e. after all MSC have received both part I and part II of the dossier.

For more information, please consult Q 2.2 - Q 2.5 in European Commission Q&A

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Considerations:

- In cases where the sponsor needs to submit a substantial modification (SM) while some MSCs have not yet issued a decision, the sponsor has the option to withdraw the application for those MSCs.

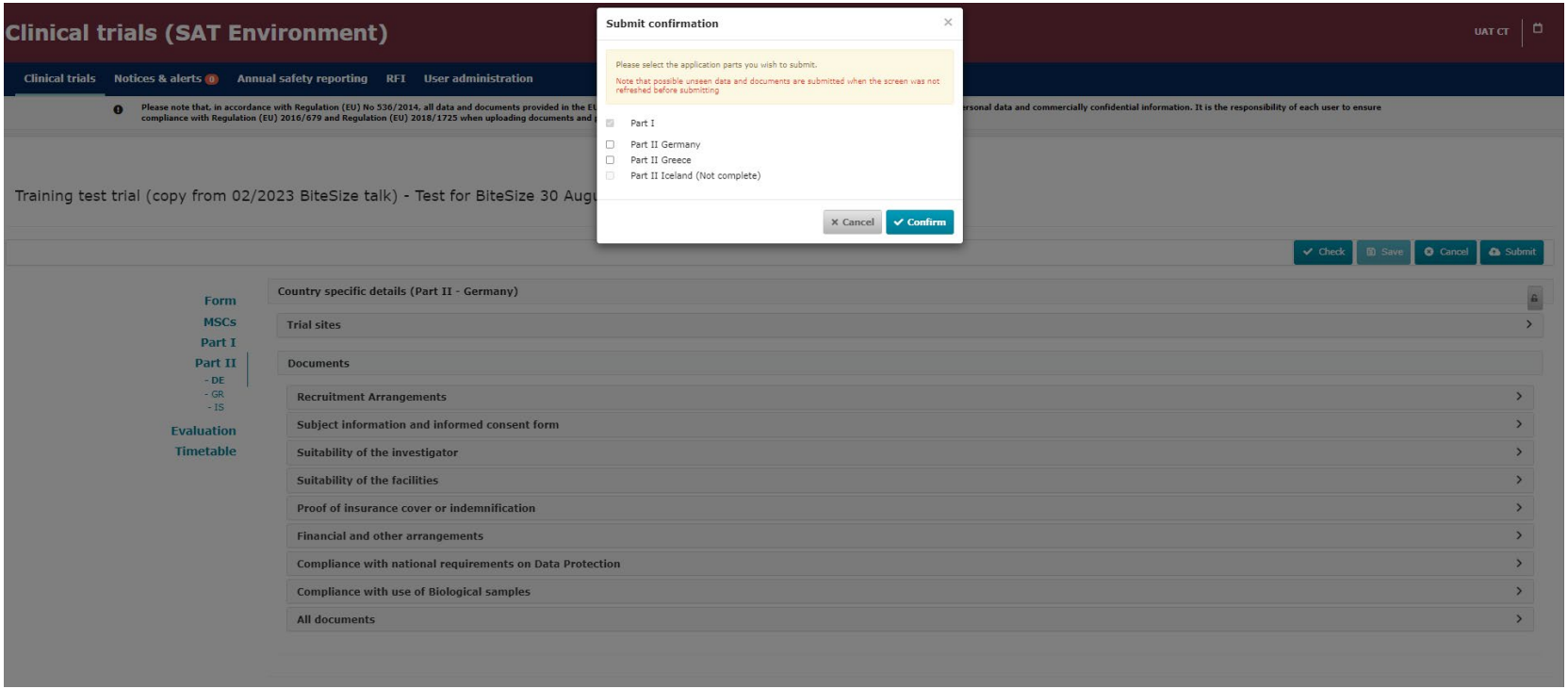
- Sponsor can start the trial in an MSC that has issued a positive decision (authorisation) the trial without waiting the authorisation of the trial to all MSCs.

- If no deferrals have been applied on CTA data, only the parts (Part I or Part II) that have been submitted and authorised are published.

For more information, please consult Q 2.2 - Q 2.5 in European Commission Q&A

How to complete the dossier in CTIS

Process



- Part I is (by default) submitted and sponsor decides which Part IIs to submit. Sponsor cannot submit the third one, as it has not been completed (tick in box is deactivated).

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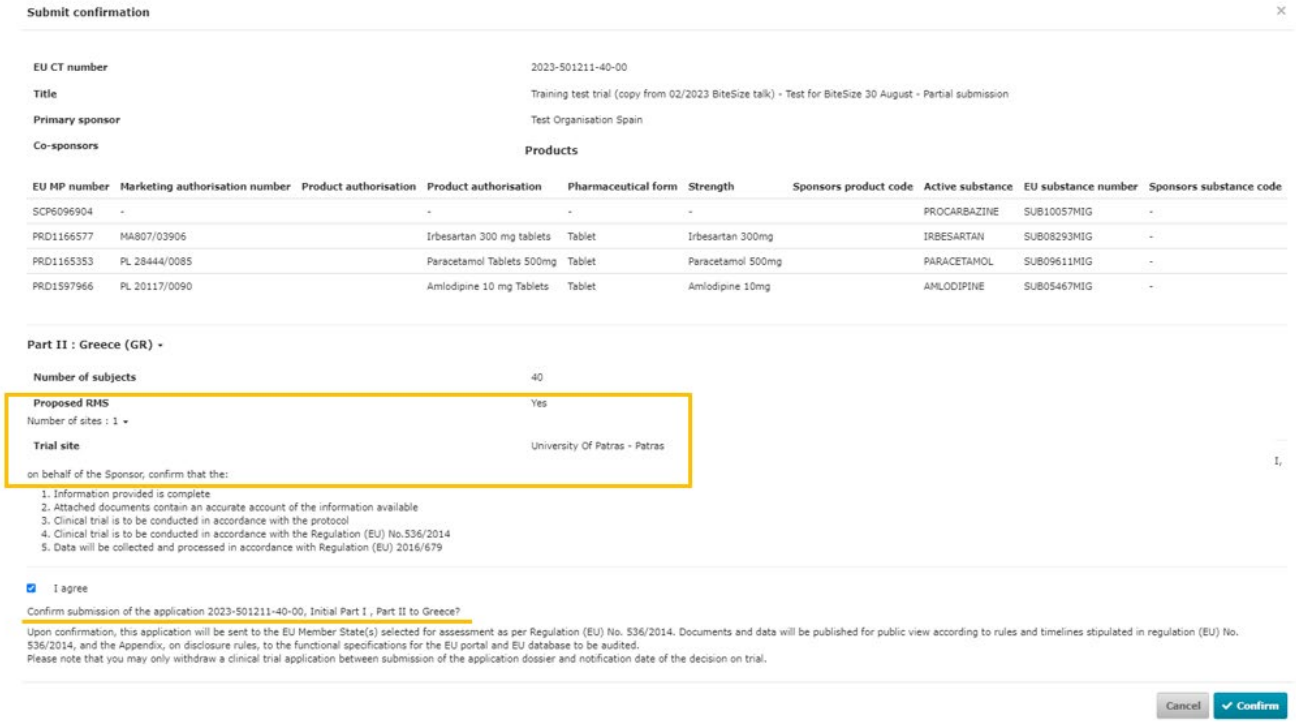
Process (2)



Submit confirmation

EU CT number	2023-501211-40-00
Title	Training test trial (copy from 02/2023 BiteSize talk) - Test for BiteSize 30 August - Partial submission
Primary sponsor	Test Organisation Spain
Co-sponsors	

Products

EU MP number	Marketing authorisation number	Product authorisation	Product authorisation	Pharmaceutical form	Strength	Sponsors product code	Active substance	EU substance number	Sponsors substance code
SCP6096904	-		-	-	-		PROCARBAZINE	SUB10057MIG	-
PRD1166577	MA807/03906		Irbesartan 300 mg tablets	Tablet	Irbesartan 300mg		IRBESARTAN	SUB08293MIG	-
PRD1165353	PL 28444/0085		Paracetamol Tablets 500mg	Tablet	Paracetamol 500mg		PARACETAMOL	SUB09611MIG	-
PRD1597966	PL 20117/0090		Amlodipine 10 mg Tablets	Tablet	Amlodipine 10mg		AMLODIPINE	SUB05467MIG	-

Part II : Greece (GR)

Number of subjects	40
Proposed RMS	Yes
Number of sites : 1	
Trial site	University Of Patras - Patras

I,

on behalf of the Sponsor, confirm that the:

1. Information provided is complete
2. Attached documents contain an accurate account of the information available
3. Clinical trial is to be conducted in accordance with the protocol
4. Clinical trial is to be conducted in accordance with the Regulation (EU) No.536/2014
5. Data will be collected and processed in accordance with Regulation (EU) 2016/679

I agree

Confirm submission of the application 2023-501211-40-00, Initial Part I , Part II to Greece?

Upon confirmation, this application will be sent to the EU Member State(s) selected for assessment as per Regulation (EU) No. 536/2014. Documents and data will be published for public view according to rules and timelines stipulated in regulation (EU) No. 536/2014, and the Appendix, on disclosure rules, to the functional specifications for the EU portal and EU database to be audited.
Please note that you may only withdraw a clinical trial application between submission of the application dossier and notification date of the decision on trial.

Cancel | Confirm

- Sponsor selects to submit the Part I and Part II just for one MSC, scheduling the submission of the other two MSCs' Part IIs for later.

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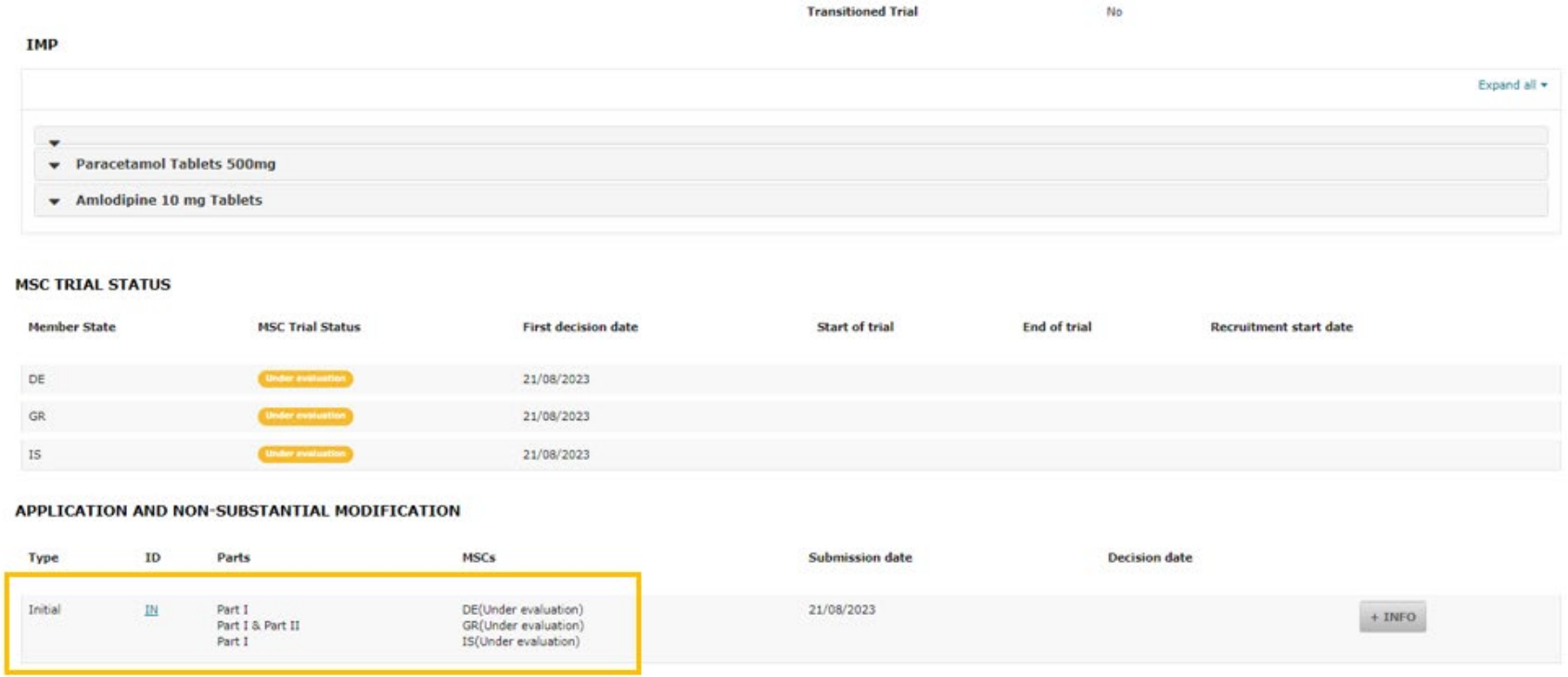
Process (3)



Transitioned Trial: No

IMP

Expand all

- Paracetamol Tablets 500mg
- Amlodipine 10 mg Tablets

MSC TRIAL STATUS

Member State	MSC Trial Status	First decision date	Start of trial	End of trial	Recruitment start date
DE	Under evaluation	21/08/2023			
GR	Under evaluation	21/08/2023			
IS	Under evaluation	21/08/2023			

APPLICATION AND NON-SUBSTANTIAL MODIFICATION

Type	ID	Parts	MSCs	Submission date	Decision date	
Initial	IN	Part I Part I & Part II Part I	DE(Under evaluation) GR(Under evaluation) IS(Under evaluation)	21/08/2023		+ INFO

- After partial submission, users can see in the overview page of the trial that Part I has been submitted for all MSCs and Part II only for one MSC

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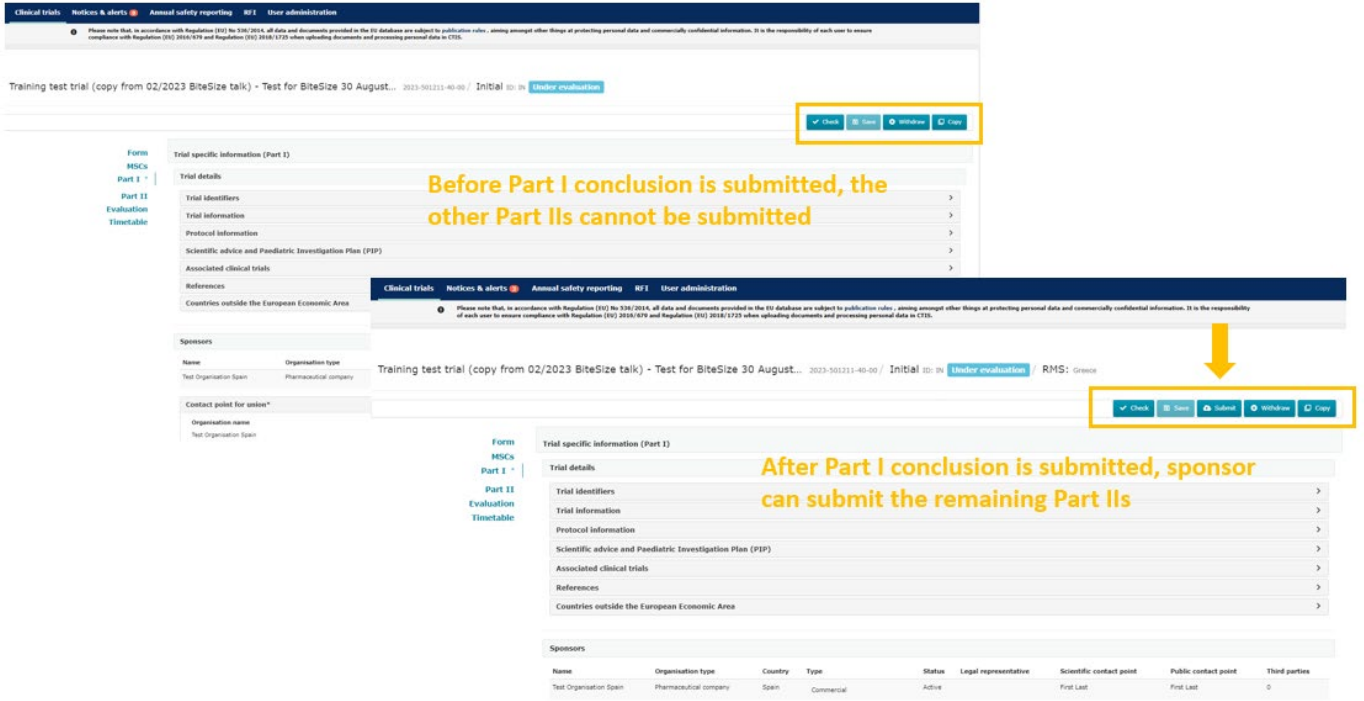
Process (4)



- Submit button appears after Part I conclusion submission and allows sponsor users to submit the remaining Part IIs.

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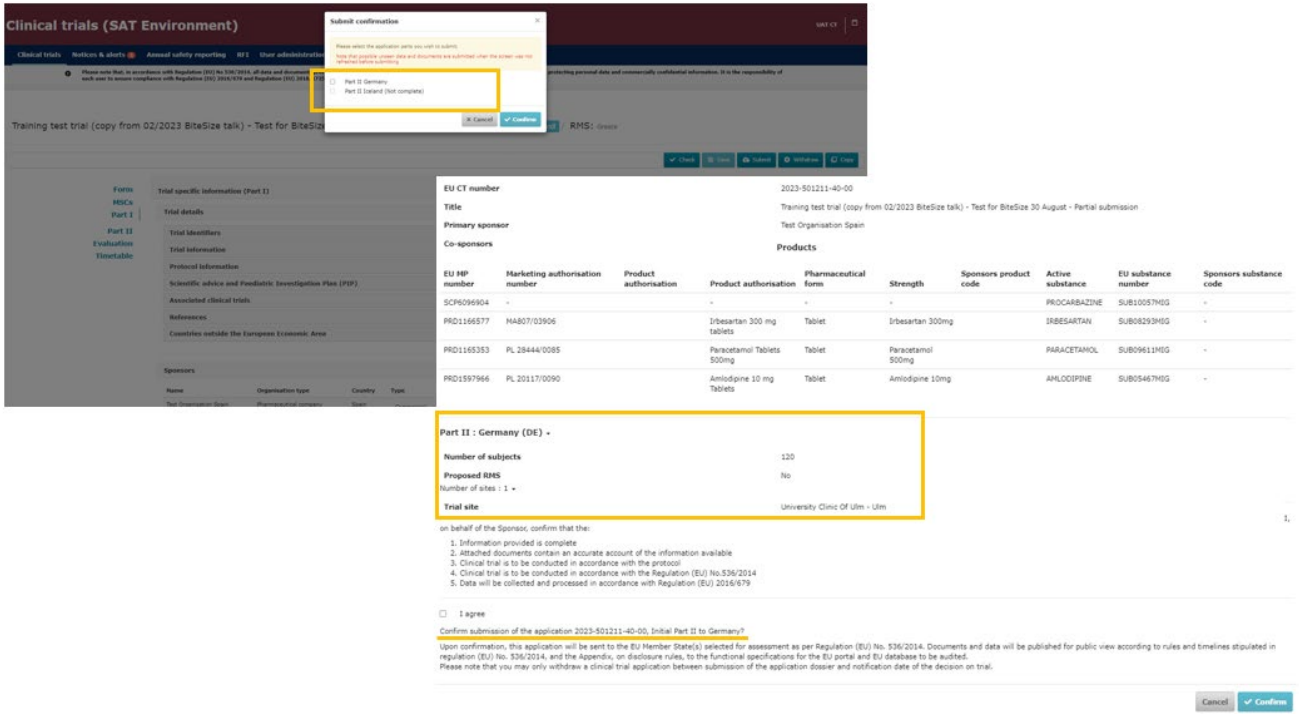
Process (5)



- Sponsor can submit the Part II for the second MSC, but not for the third MSC, as it has not been completed; documents or data might be missing (tick in box is deactivated).

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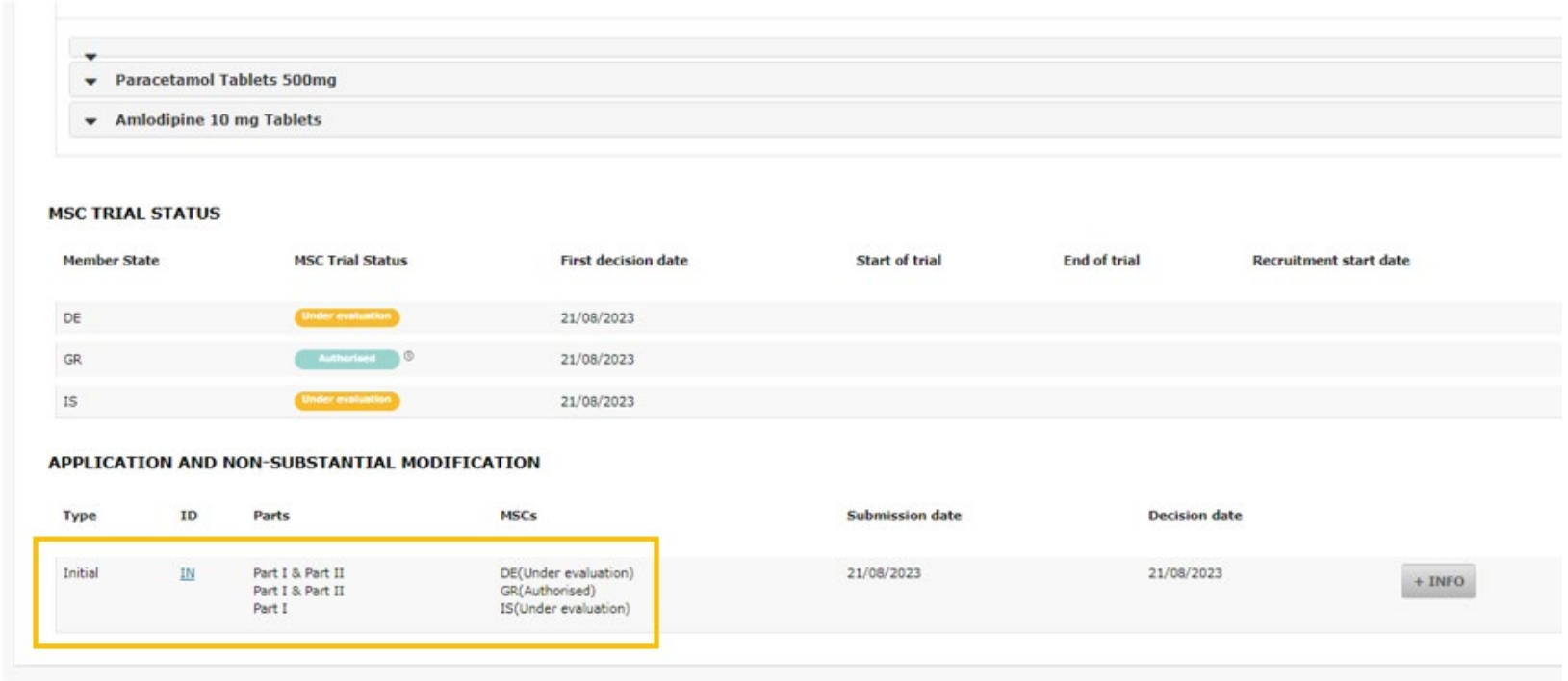
Process (6)



Paracetamol Tablets 500mg

Amlodipine 10 mg Tablets

MSC TRIAL STATUS

Member State	MSC Trial Status	First decision date	Start of trial	End of trial	Recruitment start date
DE	Under evaluation	21/08/2023			
GR	Authorised	21/08/2023			
IS	Under evaluation	21/08/2023			

APPLICATION AND NON-SUBSTANTIAL MODIFICATION

Type	ID	Parts	MSCs	Submission date	Decision date	
Initial	IN	Part I & Part II Part I & Part II Part I	DE(Under evaluation) GR(Authorised) IS(Under evaluation)	21/08/2023	21/08/2023	+ INFO

- In the CT overview, we can see the status for each Part of the application. Part I has been authorised for all MSCs. Part II has been authorised for one MSC (GR), is under evaluation for the second MSC (DE) and is pending for the third MSC (IS).

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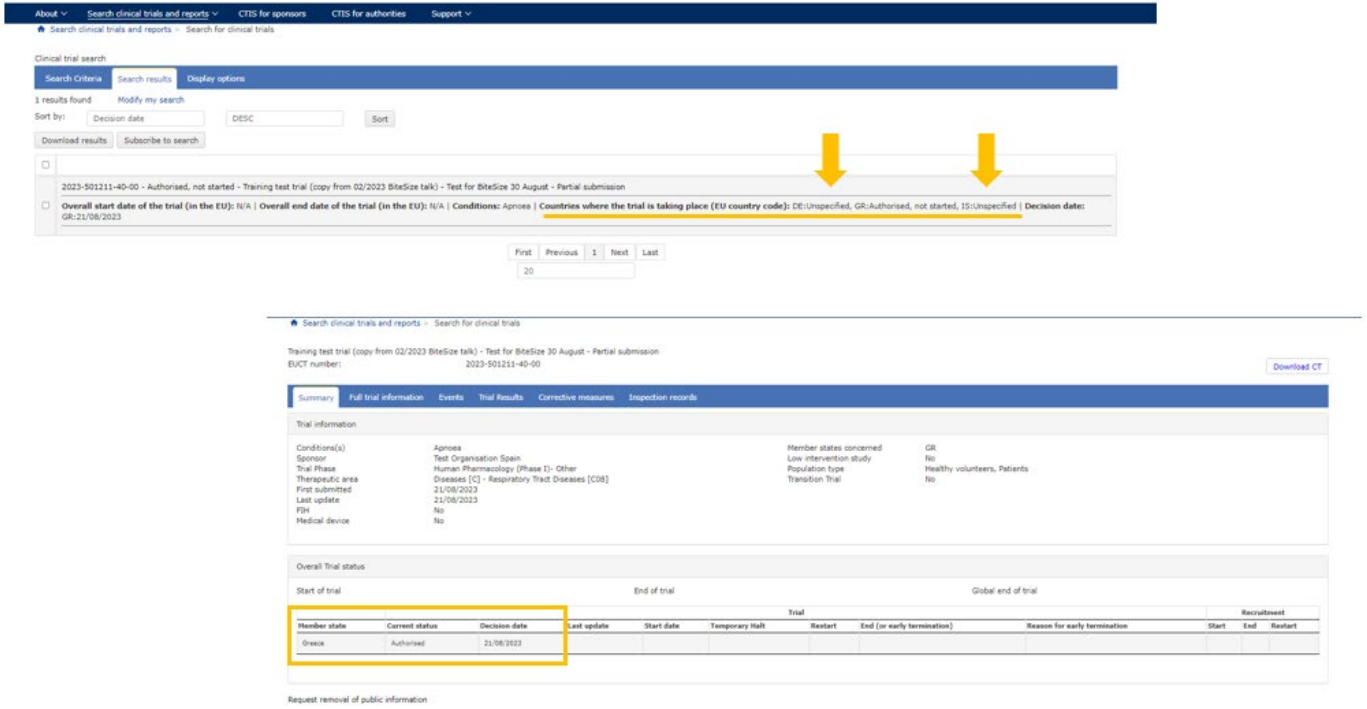
Process (7)



- No deferrals have been applied. Part I is published after one MSC (GR) authorises the trial (by submitting Part II conclusion and Decision). Pending Part IIs or Under evaluation Part IIs are not published.

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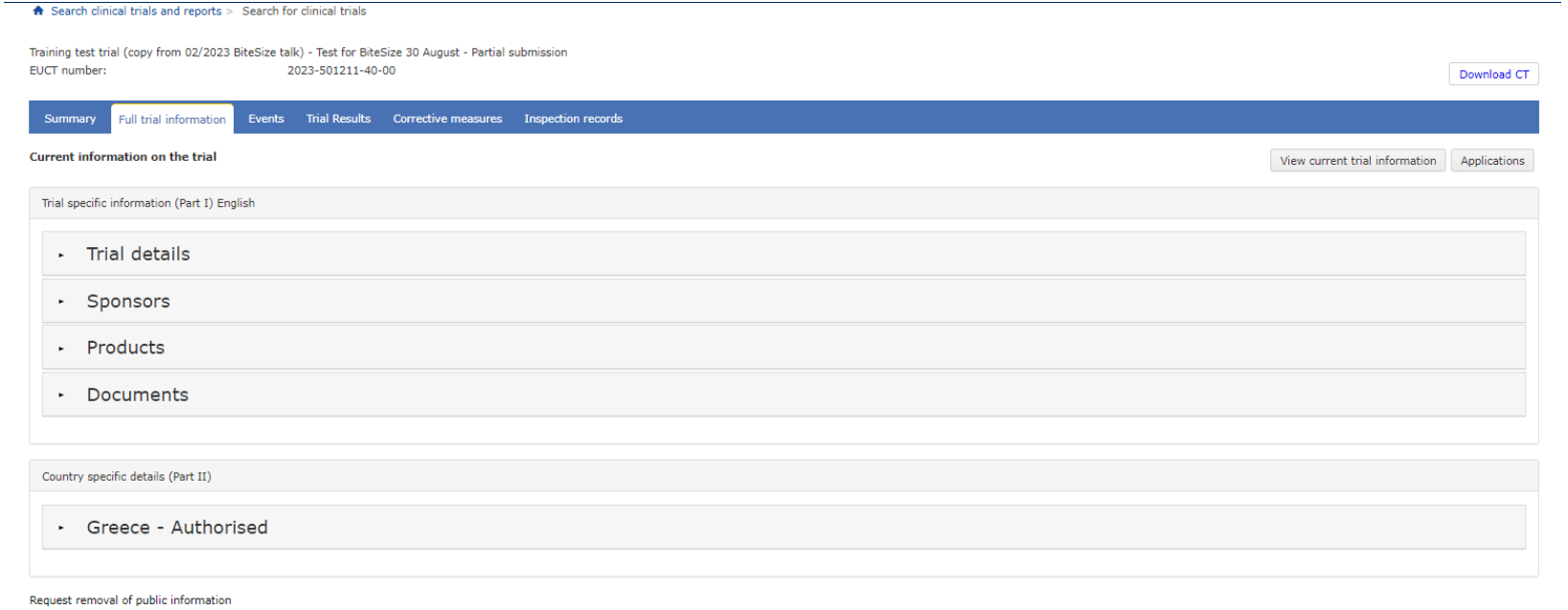
Process (8)



- In the Full trial information tab, users could access all documents and data for Part I (authorised by all MSCs) and all documents and data of the Part II for which the MSC has made a decision.
- If Part II is pending or is under evaluation (consequently, no decision has been made), their respective data and documents are not published.

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Q&A session

For questions,
*go to **www.sli.do***
& use event code
#bt30aug

We ask for *your feedback* on this event

The feedback **poll is now open** in Slido

*Go to **www.sli.do***
*& use event code **#bt30aug***
*or scan Slido **QR code:***

CTIS training environment Survey 4.0

Survey 4.0 remains open where new potential users of CTIS can express interest to access the CTIS training environment (CTIS Sandbox).

CTIS Sandbox Survey 4.0

For post-event survey, go to ***www.sli.do*** *& use event code* ***#bt30aug***

CTIS upcoming events

- **CTIS Walk-in Clinic – 20 Sep 2023 – 16:00 – 17:00 CEST**
- **CTIS Sponsor End-user Training Programme – 19-22 Sep 2023**

For post-event survey, go to ***www.sli.do*** *& use event code* ***#bt30aug***

Annex

CTIS data fields for Part I application

Part I section	Sub-sections		Required Fields
Trial Details	Trial Identifiers		• Full title • Public title
	Trial Information	*Trial Category*	• If Low intervention trial (check box) / Justification for the low intervention trial • Trial phase
		Medical condition	• Add condition (button) / Medical condition(s) • Therapeutic area
		Main objective	• Trial scope • Main objective
		Eligibility criteria	• Add inclusion criteria (button) • Add exclusion criteria (button)
		End points	• Add primary endpoint (button)
		Trial duration	• Estimated recruitment start date in EEA • Estimated end of trial date in EEA
		Population of trial subjects	• Age range • Gender • Clinical trial group • (if check box 'Vulnerable group' is clicked) Recruitment population group
	Protocol Information	*Clinical trial protocol*	• Protocol

CTIS data fields for Part I application

Part I section	Sub-sections	Required Fields
Sponsors	Contact point for Union	• Add contact point for Union (button) • Scientific Contact Point • Public Contact Point
Products	Products	• +Add (button)
	Role: Test *(example)*	• +Add (button) / Authorised product (example)
	Dosage and administration details	• Route of administration • Maximum duration of treatment • Maximum daily dose allowed • Total dose unit of measure
	Information about the modification of the medicinal product	• Has the medicinal product been modified in relation to its Marketing Authorisation? (check box)
	Investigator brochure for the medicinal product	• Investigator brochure • Summary of product characteristics (SmPC)
	IMPD Quality*	• IMPD-Q • Simplified IMPD-Q • Justification for no IMPD upload
	IMPD - Safety and efficacy*	• IMPD - Safety and Efficacy • Simplified IMPD - Safety and Efficacy • Justification for no IMPD upload
	Content labelling	• Content labelling of the IMP's

* To view the required fields per IMP please refer to question 2.12 on the Frequently Asked Questions document of Module 10 of the CTIS Online Training Modules.

For more information on the language requirements for Part I documents, please consult Annex II of the European Commission Q&A

COM Q&A – Annex 3 – Part II Docs – National reqs

Annex III: Part II documentation - where sponsors can find national requirements

Member State	Websites where sponsors can find important information to submit high quality Part II documents as part of their clinical trial applications.	Email address for enquiries related to Part I clinical trial applications	Email address for enquiries related to Part II clinical trial applications
Austria	• www.basg.gv.at	clinicaltrials@basg.gv.at	clinicaltrials@basg.gv.at
Belgium	• CTR page on the FAMHP website : https://www.famhp.be/en/eu_regulation_5362014	CTR@fagg-afmps.be	CTR@fagg-afmps.be
Bulgaria	• https://www.bda.bg/bg/62-business-info/clinical-examinations-biz	clintrialsquestions@bda.bg	clintrialsquestions@bda.bg
Croatia	• https://zdravlje.gov.hr/o-ministarstvu/djelokrug-1297/lijekovi-i-medicinski-proizvodi/1349 • https://www.halmed.hr/O-HALMED-u/Sredisnje-eticko-povjerenstvo-SEP/Naputci-podnositeljima-zahtjeva/ • https://www.halmed.hr/O-HALMED-u/Usluge-i-cjenik/Cjenik-usluga-HALMED-a/	klinicka.ispitivanja@miz.hr	klinicka.ispitivanja@miz.hr
Cyprus	• Cyprus National Bioethics Committee website: http://www.bioethics.gov.cy/moh/cnbc/cnbc.nsf/index_en/index_en?OpenDocument • Pharmaceutical Services website: https://www.moh.gov.cy/moh/phs/phs.nsf/home_en/home_en?openform	clinicaltrials@phs.moh.gov.cy	cnbc@bioethics.gov.cy
Czechia	• https://www.sukl.cz/leciva/klh-ctis-01 (Czech) • https://www.sukl.eu/medicines/klh-ctis-01 (English)	ctis-dpo@sukl.cz	eticka.komise@sukl.cz
Denmark	• https://nationaltcenterforetik.dk/ansoegerguide/ansoegninger-til-vmk/kliniske-forsoeg-med-laegemidler/anmeld-kliniske-forsoeg-efter-ctr	kf@dkma.dk	kontakt@dvmk.dk

Full list of national requirements for Part II documentation can be found here

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Additional resources

- Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation

- CTCG Best Practice Guide for sponsors of multinational clinical trials with different protocol versions approved in different Member States under the Directive 2001/20/EC that will transition to the Regulation (EU) No. 536/2014

Any questions?

Further information

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