



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Clinical Trial Information System (CTIS) Bitesize talk

Notifications (part 1)

Presented by Laura Pioppo and Ana Rodriguez on 28 September 2022
European Medicines Agency

An agency of the European Union





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CTIS Bitesize talk:

Notifications: trial and recruitment period

14:30 - 14:35 **Introduction**

14:35 – 15:55 **CTIS Demonstration Sessions followed by live Q&A Sessions**

15:55 – 16:00 **Closing remarks**

*For questions,
go to **www.sli.do**
& use event code
#bt28sep*

A few housekeeping rules

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- ❖ Have a **stable internet connection**



A few housekeeping rule

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❖ Make use
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Live broadcast - 14:30 - 16:00 Amsterdam time (CET)



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Main Session: CTIS Demo with Q&A

Notifications:
trial and recruitment period

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Laura Pioppo
CTIS Scientific Officer

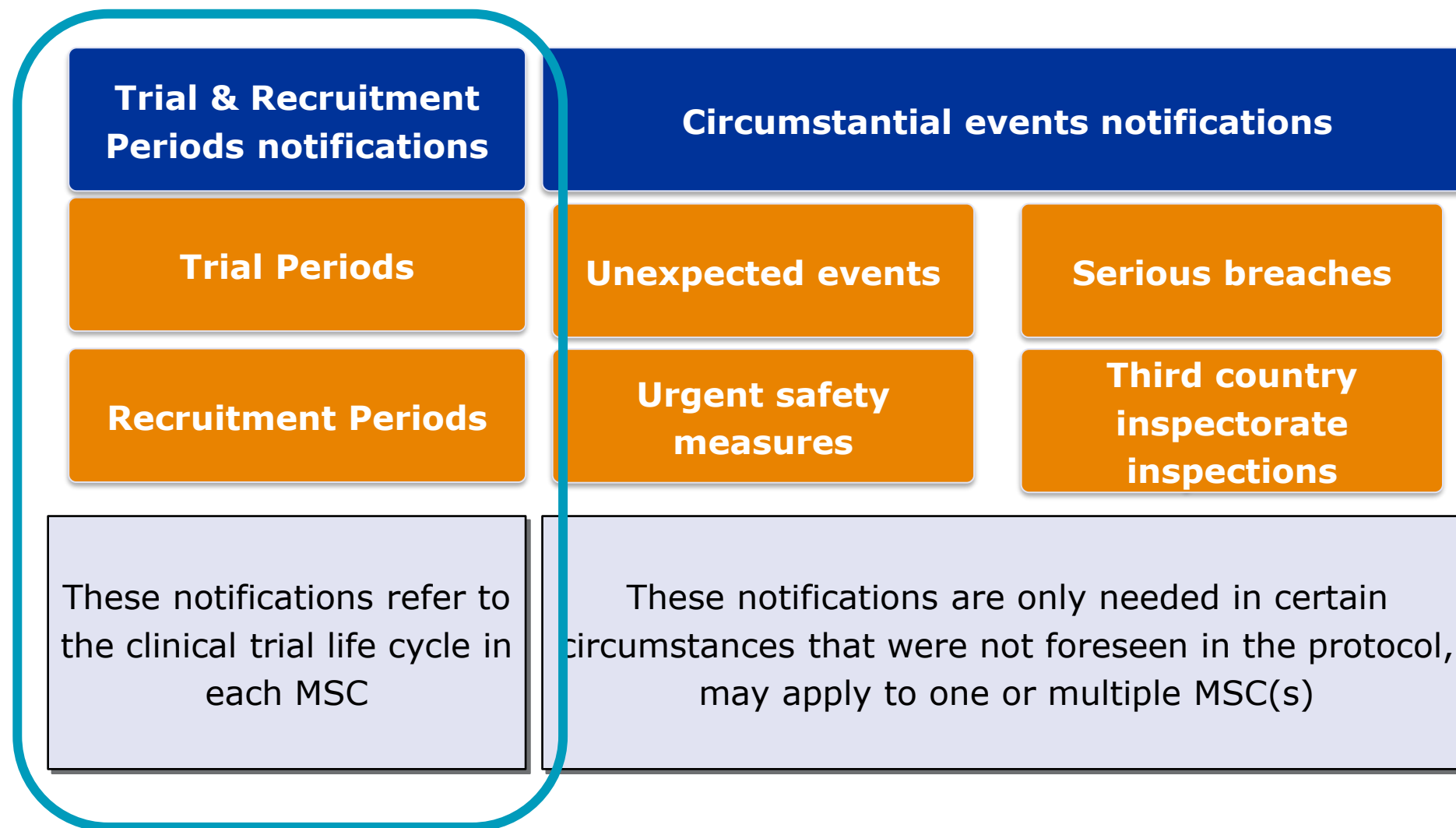


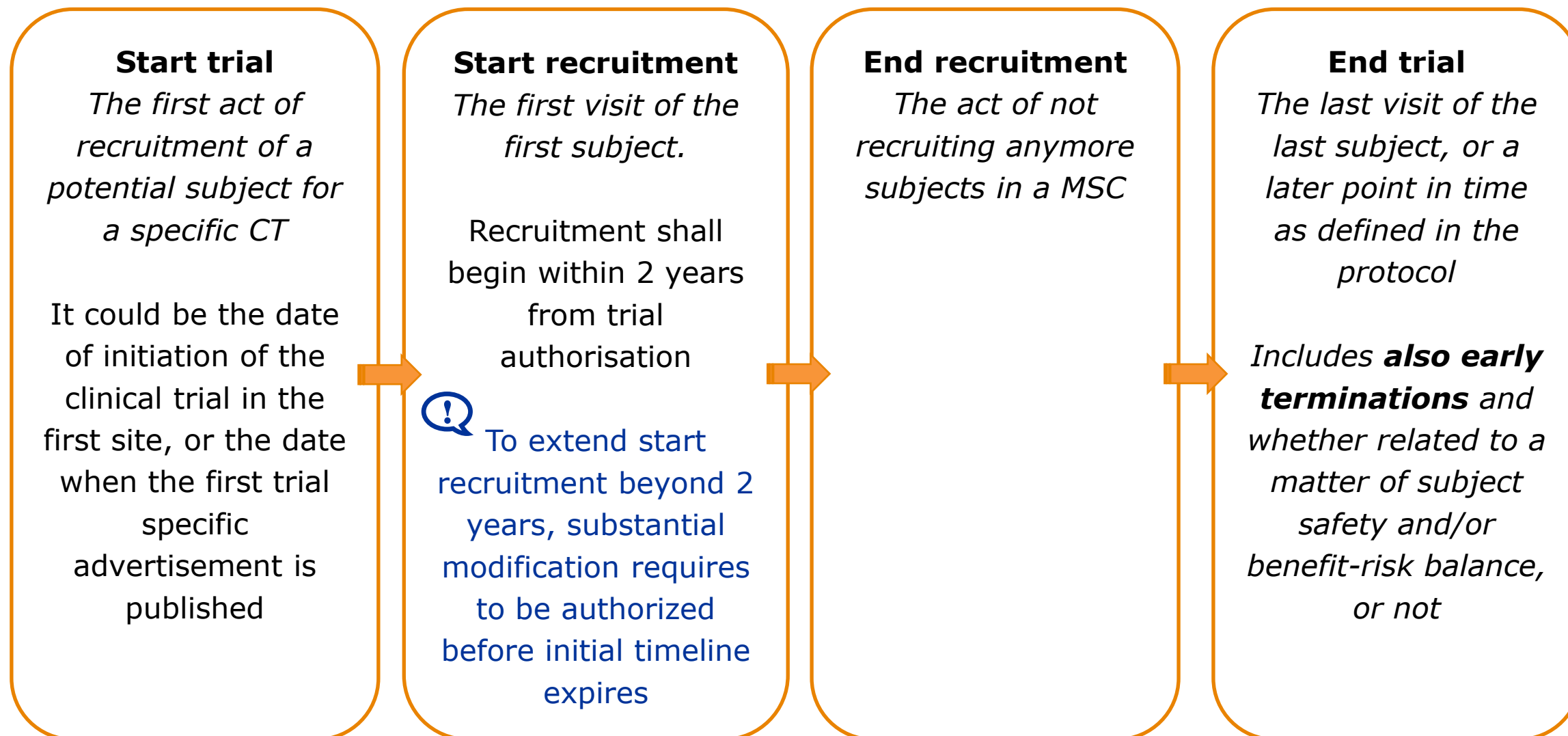
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**Ana Rodriguez
Sanchez Beato**
CTIS Delivery
Workstream Lead



Notifications





Temporary halt

An interruption not provided for in the protocol of the conduct of a trial by the sponsor with the intention to resume it

There are two types depending if the temporary halt is related to subject safety and/or benefit-risk balance (B/R), or not

A halted trial is automatically ended if not restarted within 2 years

! For an extension to restart the halted trial beyond 2 years, substantial modification requires to be authorised before initial timeline expires

Restart trial

The act of restarting the trial after a temporary halt, or after suspension of the trial by an MSC



If temporary halt is related to subject safety and/or benefit-risk balance, a **prior substantial modification must be submitted and authorised** to enable notification

Restart recruitment

The act of restarting the recruitment of subjects



The trial must be restarted to enable restart the recruitment notification

- The legal basis for notifications submission is in Article 36 and Article 37 of the Regulation (EU) No 536/2014
- The relevant training material on the topic is in Module 5 published on EMA website - online training modules: <https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-ctis-online-modular-training-programme>
- Relevant clarifications can be found also in section 10 of the COM Q&A document: https://health.ec.europa.eu/system/files/2022-09/regulation5362014_qa_en.pdf

Latest version 6.2 published in Sept 2022

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Trial & Recruitment Periods

Start Trial End Trial Restart Trial Temporary Halt

Start Recruitment End Recruitment Restart Recruitment

	Trial					Recruitment		
☐ Select all	Current status	Start date	Temporary Halt	Restart	End (or early termination)	Start	Restart	End
☐ Greece	✓ Authorised	-	-	-	-	-	-	-
☐ France	✓ Authorised	-	-	-	-	-	-	-

EEA and Global

End of trial EEA

Submitted on

Anticipated date of summary of results

Submission of results

End of trial Global

Submitted on

- Notifications to a MSC can be submitted as soon as the trial is authorised by that MSC
- The sponsor does not need to wait to have the trial authorised in all MSC before a notification can be submitted
- As soon as a trial is authorised the sponsor can submit Start of trial (SoT) or early termination notifications
- Submission of these notifications is sequential and follows predefined logic
- Notifications can be submitted to one or more MSC simultaneously with the multi select functionality
- CTR defines specific timelines for notifications submission however the system is flexible in terms of business rules to allow submission beyond due date (MS can monitor compliance though)
- Documents can be attached to the notifications – but this is optional



Demo on SoT/SoR/EoR and 1st Q&A session

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Demo includes:

- Entry point for notifications
- How to populate and submit a notification
- Document upload
- Sequential flow
- Update functionality
- Withdrawal
- Publication aspects



Temporary halt and restart of trial

Temporary halt and restart of trial

Article 2(2)(28)

Temporary halt of a clinical trial' means an interruption not provided in the protocol of the conduct of a clinical trial by the sponsor with the intention of the sponsor to resume it;

- Sponsor can stop trial activity described in the protocol (i.e., recruitment only or recruitment and treatment), due to unexpected circumstances that could (or not) affect the benefit/risk ratio
- In case of a change of the B/R the sponsor can only restart the trial if a substantial modification (part I only, part II only or part I and II) has been authorised by the MSC
- Substantial modification to restart should be submitted with 2 years since the halt started

From COM Q&A:

- In case of temporary halt that have no potential effect on the benefit/risk balance (e.g., lack of supply of IMP/shortages), the sponsor should notify in CTIS the restart of trial within 15 days from its occurrence
- If a temporarily halted CT is not resumed within **two years**, the expiry date of this period or the date of the decision of the sponsor not to resume the clinical trial, whichever is earlier, shall be deemed to be the **date of the end of the CT**.
- A sponsor can submit within the two-year period following a temporary halt a SM requesting a restart date **after** the 2-year period. This SM can only be submitted **before the expiry** of the 2-year period and applies to temporary halts for reasons of subject safety or not.

Trial and recruitment period notifications

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Trial & Recruitment Periods

Start Trial End Trial Restart Trial Temporary Halt

	Current status	Start
☐ Select all		
☒ Greece	✓ Authorised	26/09
☐ France	✓ Authorised	-

EEA and Global

End of trial EEA
Anticipated date of summary of results
End of trial Global

Unexpected Event 0

Business key	MSCs	Internal
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Serious Breach 0

Business key	Affected countries	MSCs	Internal sponsor id	Last modified	Submission date	Status	Actions
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New temporary halt notification

Countries Greece

Temporary halt date *

Planned restart of trial date

Has the trial been halted for reasons of change of subjects safety and/or change of the benefit-risk balance? * ☐ Yes ☐ No

Reason for the temporary halt *

Explanation for the temporary halt

Follow-up measures (including for subjects)

☐ Treatment has been stopped

Number of subjects still receiving treatment *

Related document(s)

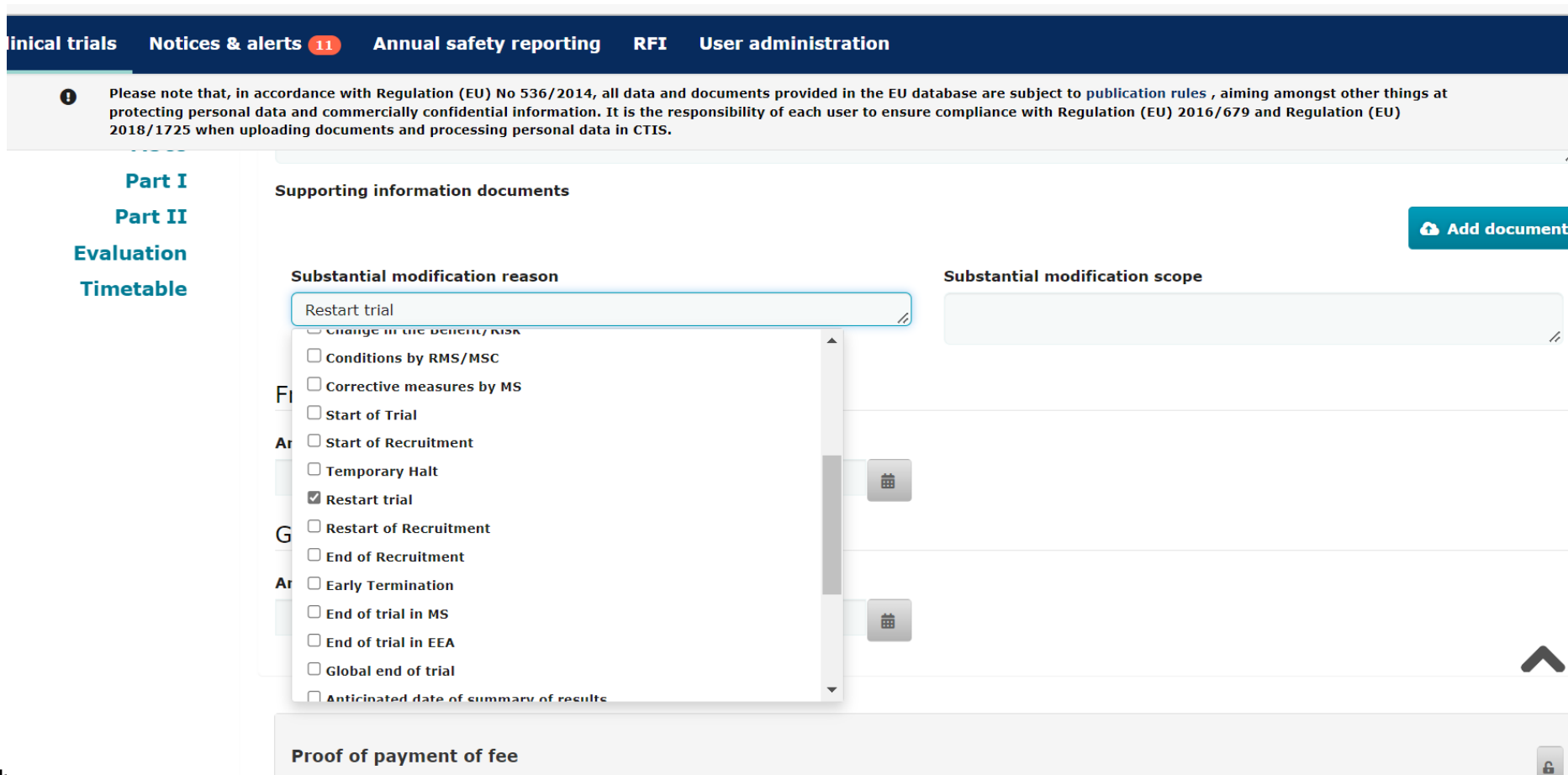
Recruitment

Start	Restart	End
26/09/2022	-	-
-	-	-

- A temporary halt (TH) not B/R related is published as soon as they are submitted
- A temporary halt B/R related is also published as soon as it is submitted with the exception of the field on reason/explanation for TH
- After an assessment is performed by the MSC the reason/explanation of the TH form is published
- Restart of trial for temporary halt not B/R related can be submitted, as applicable, when issue solved
- Restart of trial for temporary halt B/R related can only be submitted after an SM has been authorised

Trial and recruitment period notifications

- It is very important that when a substantial modification is submitted to restart a trial following a temporary halt impacting B/R (benefit/risk) the sponsor select the correct value "restart trial" from the SM form



The screenshot displays the CTIS interface for submitting a substantial modification. The top navigation bar includes links for 'Clinical trials', 'Notices & alerts' (with a red notification icon and the number 11), 'Annual safety reporting', 'RFI', and 'User administration'. A warning message is present: 'Please note that, in accordance with Regulation (EU) No 536/2014, all data and documents provided in the EU database are subject to publication rules, aiming amongst other things at protecting personal data and commercially confidential information. It is the responsibility of each user to ensure compliance with Regulation (EU) 2016/679 and Regulation (EU) 2018/1725 when uploading documents and processing personal data in CTIS.'

The main content area is divided into two columns. The left column contains a sidebar with links for 'Part I', 'Part II', 'Evaluation', and 'Timetable'. The right column contains the 'Supporting information documents' section with an 'Add document' button. Below this, the 'Substantial modification reason' dropdown menu is open, showing a list of options: 'Restart trial' (selected), 'Change in the benefit/risk', 'Conditions by RMS/MSC', 'Corrective measures by MS', 'Start of Trial', 'Start of Recruitment', 'Temporary Halt', 'Restart of Recruitment', 'End of Recruitment', 'Early Termination', 'End of trial in MS', 'End of trial in EEA', 'Global end of trial', and 'Anticipated date of summary of results'. The 'Substantial modification scope' section is also visible, with a text input field and a calendar icon. At the bottom, there is a 'Proof of payment of fee' section with a lock icon.



Demo on Temporary halt and restart 2nd Q&A session

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End of trial and summary of results

- End of trial notifications (like the other period notifications) can be submitted for individual MSC
- Last end of trial notification in a MSC is equal to end of the trial in the EU/EEA
- When completing the end of trial in the EU/EEA the sponsor is prompted to specify the anticipated date for submission of summary of results

Trial and recruitment period notifications



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Please note that, in accordance with the GDPR, you must ensure that you are protecting personal data and that you are complying with the requirements of the GDPR (2018/1725) when uploading documents.

Trial & Recruitment

Start Trial **End of trial**

☒ Select all

☒ Greece

☒ France

EEA and Global

End of trial EEA

Anticipated date of summary of results

End of trial Global

New end of trial in ms notification

Countries

France

Greece

End of the clinical trial date * 27/09/2022

☐ The clinical trial has been early terminated

Anticipated date of summary of results

The submission of this form will end the clinical trial in all EEA countries for which the clinical trial was authorised. It is therefore required to also submit the anticipated date of summary of results as part of this form.

Anticipated date of summary of result * 27/09/2023

All results

will be submitted at the anticipated date of summary of results

Justification that the results are to be later than 6 months:

Justification that the results are to be later than 6 months:

amongst other things at
and Regulation (EU)

Restart Recruitment

Recruitment

start	End
	-
	27/09/2022

Clinical trials

Notices & alerts 4

Annual safety reporting

RFI

User administration

!

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☐ Select all	Current status	Start date	Temporary Halt	Restart	End (or early termination)	Start	Restart	End
☐ Greece	✓ Ended	26/09/2022	-	-	27/09/2022	26/09/2022	-	-
☐ France	✓ Ended	26/09/2022	-	-	27/09/2022	27/09/2022	-	27/09/2022

EEA and Global

End of trial EEA 27/09/2022

Submitted on 27/09/2022

Anticipated date of summary of results 13/09/2023

Submission of results All results

End of trial Global

Submitted on

Update result date

Unexpected Event 0

+ New

Business key	MSCs	Internal sponsor id	Last modified	Submission date	Status	Actions
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Demo on end of trial and last Q&A session

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We ask for *your feedback* on this event

A brief **poll is now open** in Slido

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Info on upcoming events



Upcoming CTIS events 2022 – Save the date

*Submit your
questions in
advance!*

Date	CTIS event
<u>19 Oct</u>	OMS TroubleShooting Session for CTIS users
<u>5 Oct</u> <u>20 Nov</u>	CTIS Walk-in clinics
<u>16 Nov</u>	CTIS Webinar - 9 months on and going forward
<u>23 Nov</u>	CTIS bitesize talk: Notifications - Part 2

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Thank you for attending today's event

*Next CTIS bitesize talk
on 23 November*

Further information

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Official address Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands

Telephone +31 (0)88 781 6000

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