



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# Clinical Trials Information System (CTIS): Readiness for mandatory use of the Clinical Trials Regulation from 31 January 2023

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Virtual Event – 20 January 2023





# Etiquette for Clinical Trials Information System (CTIS): Readiness for mandatory use of the Clinical Trials Regulation from 31 January 2023



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muted**



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Event**



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received in  
advance in  
Slido**

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**#CTIS2023a**

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# Welcome and introduction

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Marianne Lunzer (AGES / CTCG chair)

Peter Arlett (Head of TDA, EMA)



# Opening Remarks

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Emer Cook (EMA)

Björn Eriksson (MPA)



# Session 1

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## Clinical Trials Regulation Implementation



# CTR Implementation and KPIs

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Laura Pioppo (EMA)



## KPI on CTR implementation

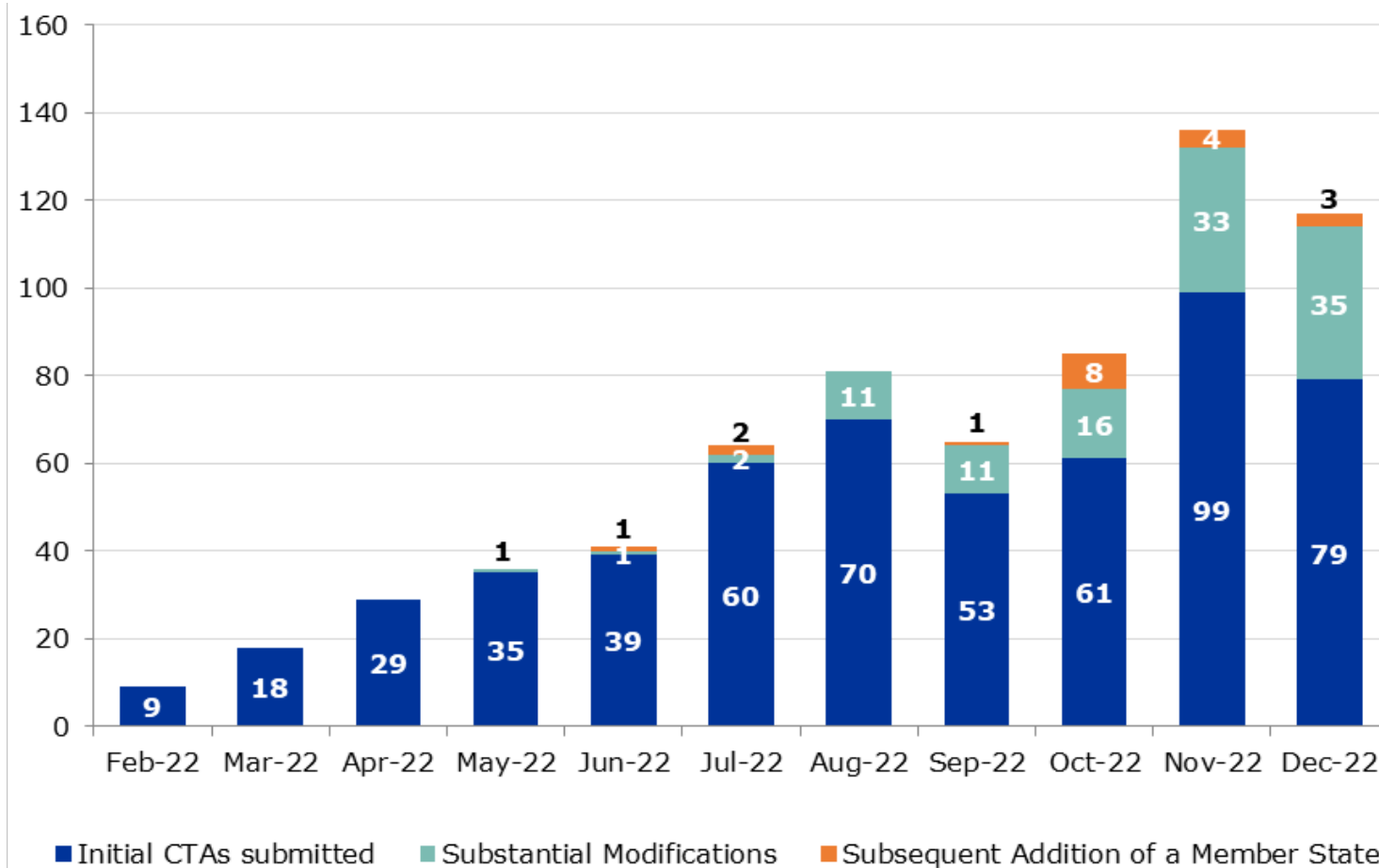
- Clinical Trials Regulation (EU) No 536/2014 (CTR) became applicable on 31 January with the launch of CTIS, a unique platform for the submission, evaluation and supervision of clinical trials in the EU/EEA
- EMA, European Commission and EU/EEA Member States are closely monitoring the progress on the implementation of the CTR and its implementing acts
- In line with Article 97 of the CTR, the European Commission shall assess the impact of the CTR on scientific and technological progress
- As part of the [ACT EU](#) business change initiative, a KPI report has been published on Key Performance Indicators (KPIs) on the measurement of the progress of the CTR
- The first publication occurred on 20 May, clinical trials day
- The latest edition of the ACT EU KPI report can be found at the linked [webpage](#)



# KPI on CTR implementation

- The report reflects measurement of KPIs agreed within the Regulatory network
- It compares data between CTIS and EudraCT (database used for clinical trial applications submitted under the Directive 2001/20/EC)
- CTIS and EudraCT differ substantially in the way clinical trial data, also on authorisation, are captured
- KPI for CTIS cover measurement of clinical trial data as well as clinical trial applications, as single CT can have one or more applications
- A regular update of the report is published on monthly basis
- Statics in this presentation cover CTIS submissions as of 31 December 2022 and will be published soon in KPI report document edition 9

# Clinical Trial Applications (CTAs) submitted per month



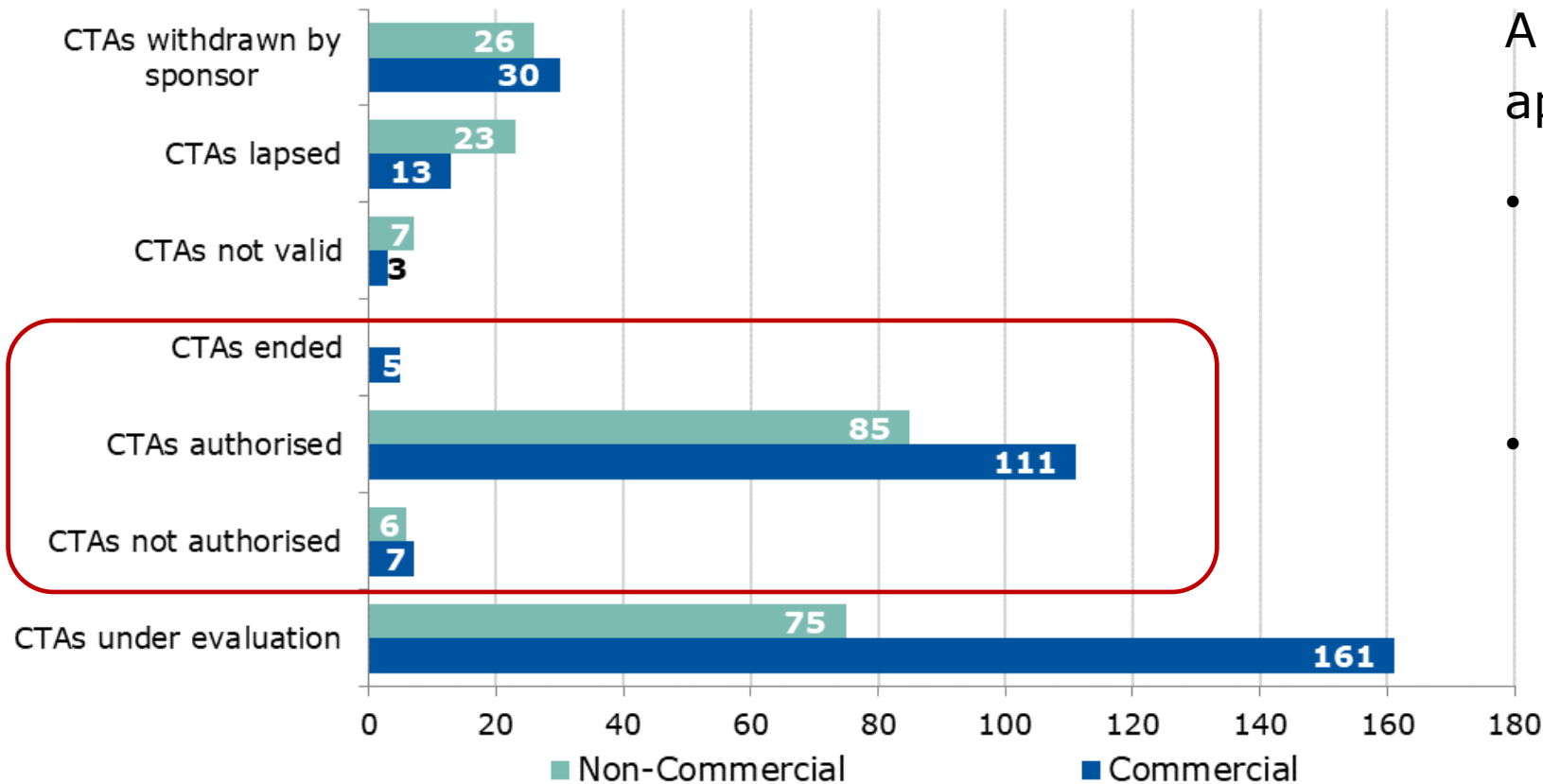
A total of **681** CTAs

- **552** *initial applications*
- **110** *substantial modifications*
- **19** *addition of a new Member State Concerned*



# CTAs per Trial Status

## Commercial versus Non-Commercial

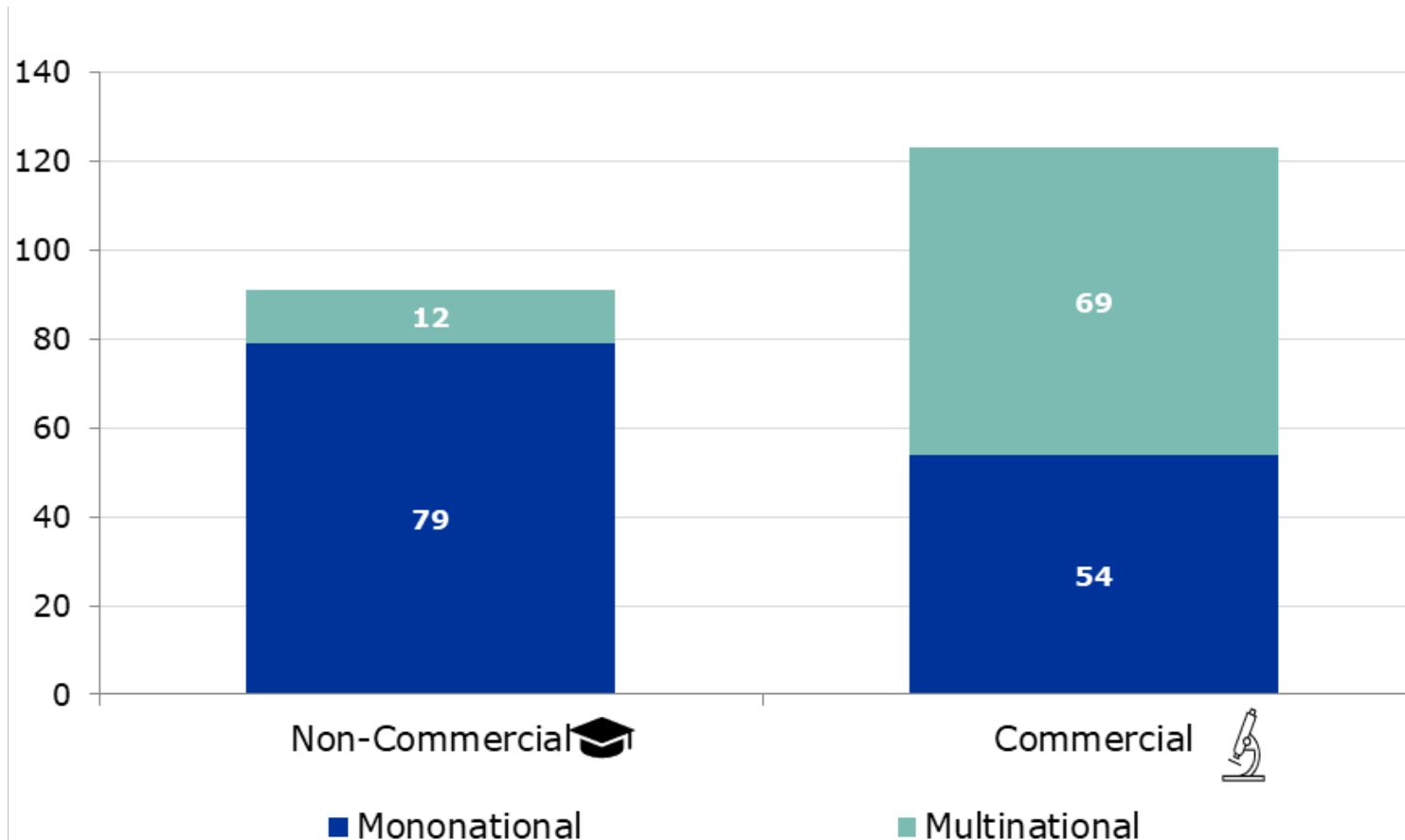


A total of 552 initial clinical trial applications

- *209 initial applications with a decision: authorised (also with conditions) or not authorised*
- *5 CTAs which have ended*

# Clinical Trials with a decision

*Split into Sponsor Type and Mono- versus Multinational*

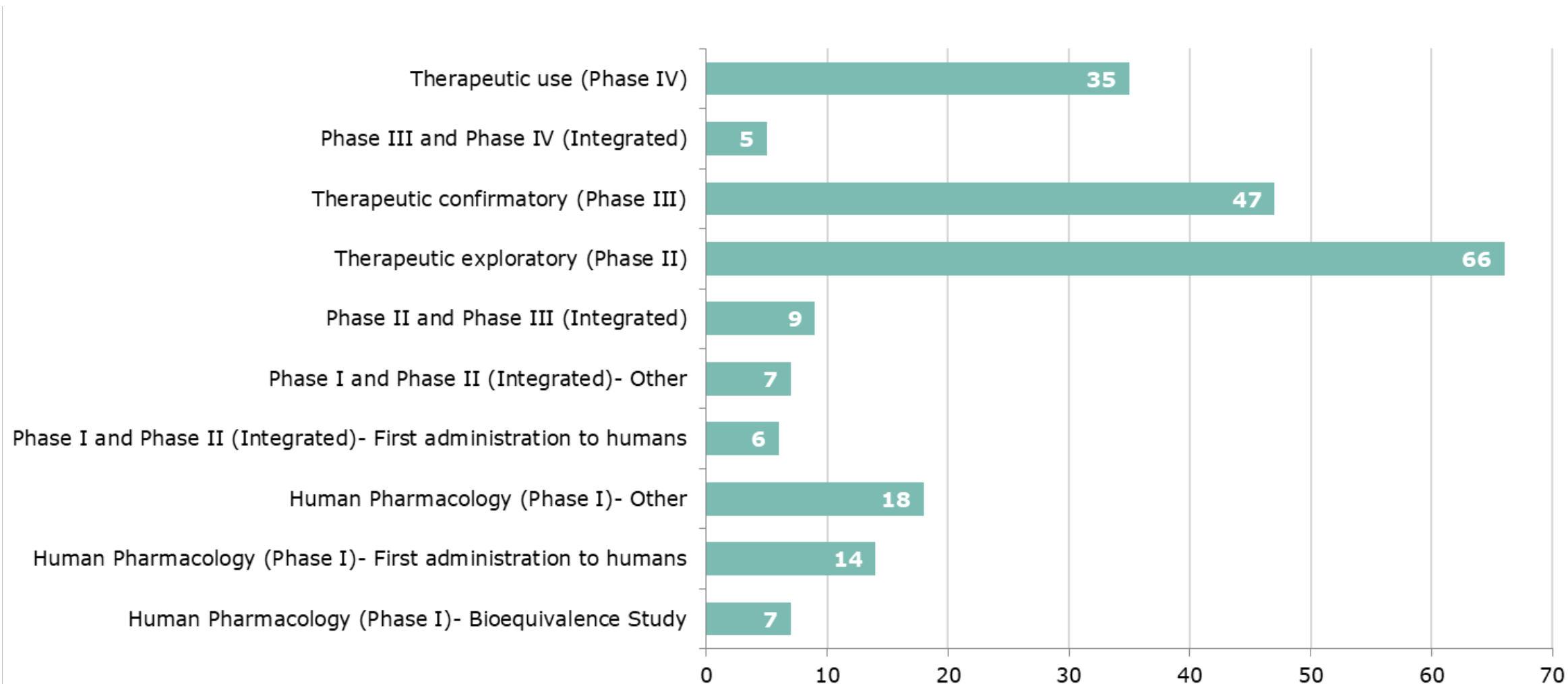


- 209 initial applications with a decision: authorised (also with conditions) or not authorised

And

- 5 trials which have ended, previously authorised

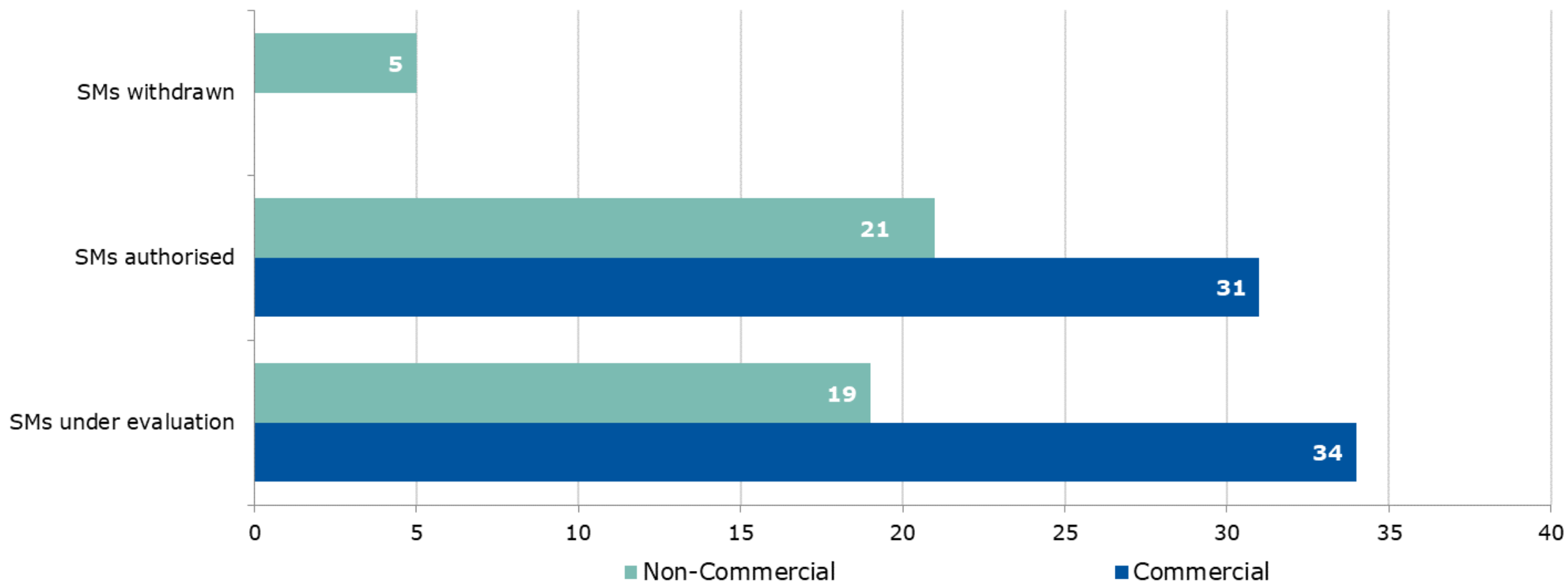
# Clinical Trials with a decision per phase





# Substantial Modifications – status'

*Split into Sponsor Type*





# Thank you for your attention

## Any questions?

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# Member States' Experience and Perspective

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Maria Elgaard Sørensen (DKMA)



LÆGEMIDDELSTYRELSEN

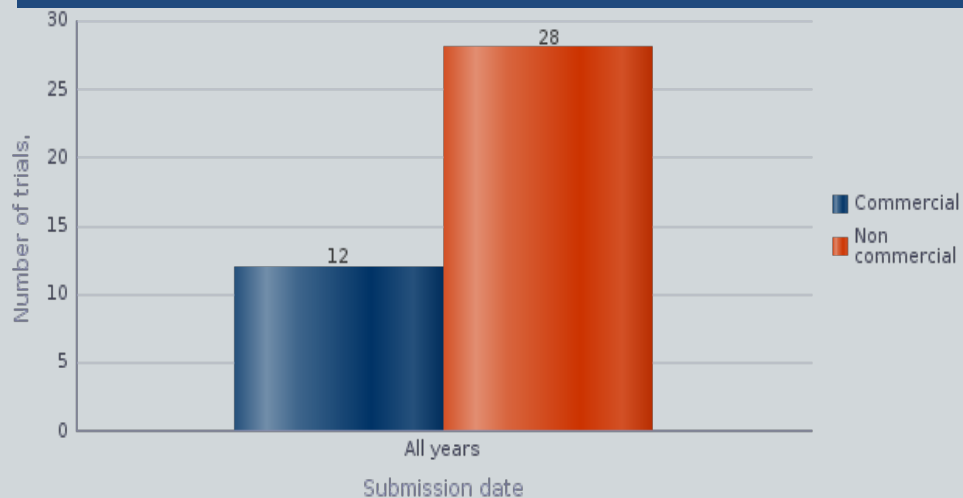
# Clinical Trials Regulation Implementation

Member States' Experience and Perspective

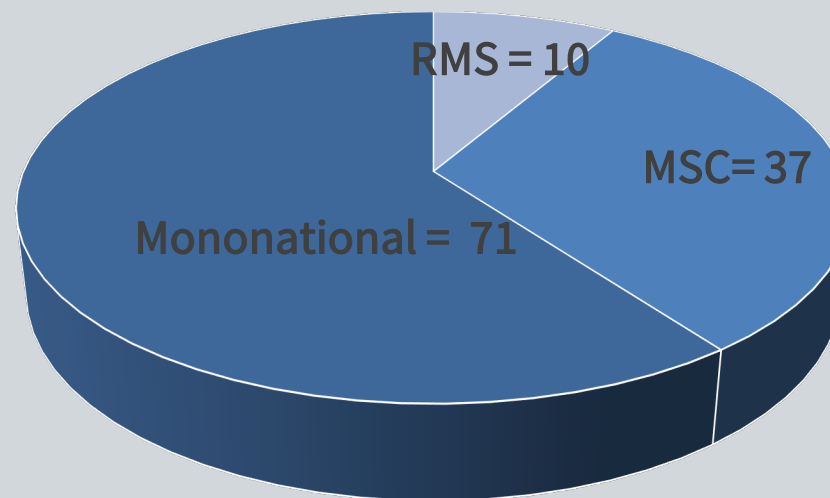


# CTAs in DK in numbers – basis for experience

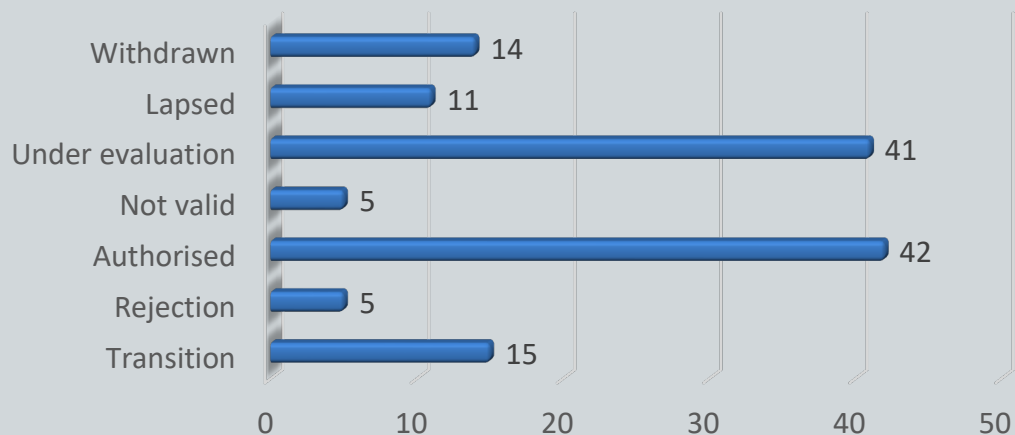
Number of authorised CTAs in DK by sponsor type



Number of CTAs divided per procedure and role of DK



Number of Initial CTAs by status





## Experiences and points for attention



● Rigid deadlines with no possibility for extension – risk of lapse and tacit authorisation.

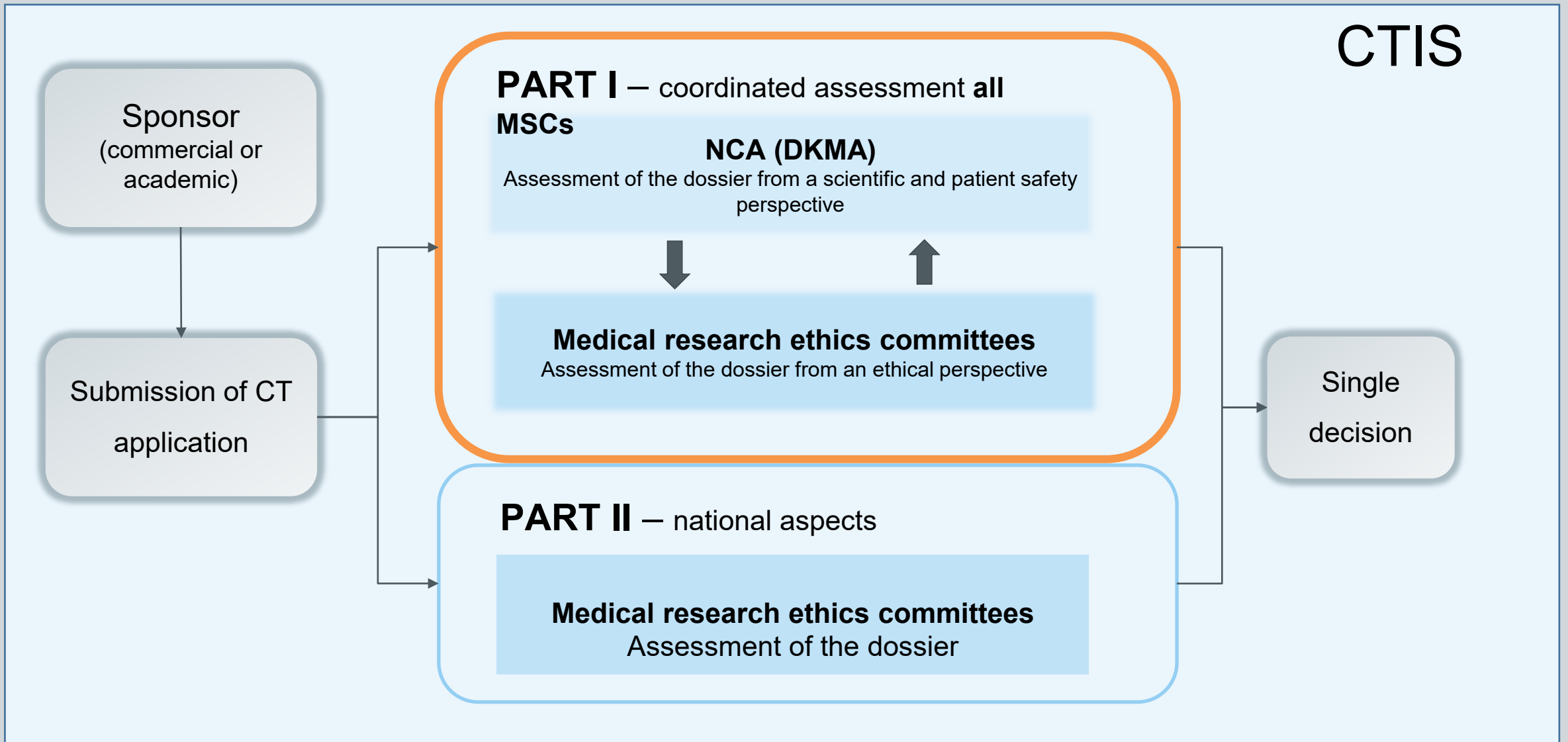
● Relatively few days to respond to authorities' RFI, requires the sponsors to be **prepared for change requests to the dossier.**

● No notifications/alerts out of the CTIS, - requires **attentive applicants** monitoring the CTIS on a daily basis.

● One round of RFI per phase, - no possibility to clarify or request administrative fixes i.e. **the considerations AND CTA needs to be very well prepared!**

● Surveillance of ongoing CTs (notifications, ASR and SUSARs) – **full benefit of the CTIS cannot be obtained until the end of the transition period.**

# CT application and assessment procedure in CTIS – national perspective



# Coordinated and harmonised assessments



## Coordination

CTIS facilitates coordinated assessment with involvement of all Member States concerned with a CT, lead by a reporting MS (RMS) concluding on part I,- ie.harmonised conclusion on the core documents that constitutes the scientific basis of the CT

- Enables circulation of assessment report (by RMS) for commenting and protects confidential communication between Member States in relation to the assessment
- Enables sharing of considerations including commenting and consolidation
- Enables transparent assessment of the response by sponsors allowing all MSCs to provide input before final conclusion

## Assessment and conclusion of part I

- RMS to *respectfully* take ownership of the assessment and the final conclusion of Part I
- Take into considerations/concerns by MSCs (ECs and NCAs)
- Consolidate scientific AND ethical opinions within a short timeframe

# Perspectives on the harmonised assessment



## Initiatives to facilitate and strengthen harmonisation (CTCG)

- **Assessors roundtables,- sharing of experiences and practices also with ethic committee representatives**
- Implementation and development of best practices
- Development of guidelines ie. complex and decentralised trials
- Centralised query management





# Good advice to facilitate the assessment



- **For all applications use the cover letter wisely!**
  - Specific concerns or information relevant to highlight for assessors
  - For transition AND new CT: Clarify (in)consistency with versions of documents/information already authorised under CTD
- **Read the sponsor handbook – use the CTIS correct and reach out to RMS/EMA before the submission (response to RFI) if something appears to be wrong (in CTIS)**
- **Monitor CTIS on a frequent basis**
- **Make sure the dossier is fit for publication rules of the CTR (guidance and QnA on the way)**
- **For safety submissions such as ASRs and SUSARs be mindful of the national requirements for the ongoing CTD trials and avoid double-reporting (as above use the cover letter!).**

# Support and guidance



- Support - EMA ([euclinicaltrials.eu](https://euclinicaltrials.eu))
- Training modules and training environment
- CTR and related guidelines (Eudralex volume 10)
- Bitesize talks and CTIS walk-in clinics
  
- CTCG
- Best practice on transition
- New QnA on protection of CCI and personal data in CTIS, expected to be published within days

## Local support and events

- DKMA website regular updates with QnA
- Do not hesitate to reach out, when in need!





# Thank you for the attention

Follow us




@laegemiddelstyrelsen



# Sponsors' Experience and Perspective – Commercial sponsor

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Karina Griffiths (EFPIA / Pfizer)



# Readiness for Mandatory CTR use from 31 January 2023

Karina Griffiths  
EFPIA  
CTIS Event  
20 January 2023



# Highlights

## January 2022 to Jan 2023 – The Transition & The Highlights



**Many of CT applications completed approval process successfully**



**Aligned timelines in EU**



**EMA Service Desk responsiveness**

Intensive work undertaken by the EMA team during the first year to address the bugs

Visibility post ticket closure would be welcome



**CTIS Timetable**



**Straightforward system when you are fully trained**

# Highlights

Relevance of supportive tools and systems

Importance of Sandbox – Request for Sandbox to remain through 2023

High-quality interactions between Sponsors & RMS/MSCs – Guidance & support provided to MSC from RMS

One single opinion

- ✓ CTD unpredictable timelines and variability by Market
  - ✓ In some markets Reduce cycle time for processing (*Providing one consolidated opinion*)
  - ✓ Allowing for “faster” start of trial in some EU countries

# CTIS System

Easy to use when fully trained – Bugs in system cause a number of workarounds

## General bugs

- Regular releases to solve the issues

## Known issues

- List regularly updated
- Workarounds published as soon as available
- Sometimes there is no workaround and need to wait for next release to solve issue

## Not possible to download list of submitted documents

- Only full documents package can be downloaded Excel
- Excel (csv or xlsx format) would be ideal

## Member states having issues with timelines

- Not in line with CTR described timelines
- Variable success on predicting approvals
- May lead to submission of responses outside of CTIS due to technical issue

# Technical issues

Adding to resource needs, complexity & timelines

## Upload issues

- Documents disappearing, becoming corrupted after upload, updates not possible and requiring a workaround

## Still a few hundreds of tickets to be resolved

- EMA technical team increased to solve most of tickets before end January 2023

## List of known issues published and regularly updated by EMA

- Workarounds not always intuitive and sometimes burdensome
- Sometimes no workaround available
  - In this case, generally sits under 'hot fix'

## Several important updates implemented

- Ex.: 50MB document size limit now implemented for all documents

# Expectations vs experience

To be Expected through learning curve

One single round of RFI

- Both validation and assessment may receive multiple rounds of RFIs
- Second round of assessment RFIs may allow to avoid conditional approval

Assessment reports displaying CCI

- Need an agreed solution
- Workaround from sponsors is to submit RFI responses under quality

Additional MS requirements not always aligned with CTR requirements and with MS publication

- e.g: additional staff documents
- CVs for sub investigators or investigator team members

Patient facing material not listed in CTR nor Q&A but in ICH-GCP

- Q& A provides some information on Pt Materials – there are additional Pt materials used that need further clarity - To submit or not to submit ?

Some MSCs asking for pre-warning about RMS selection

- Not planned in CTR but allows for much quicker RMS selection confirmation
- This is a benefit to sponsor where we can schedule pre meetings & allow for engagement with RMS

# Challenges

Process for Product registration more complex than EUdraCT

AxMPD requirements – needs further clarification

Filenames to be updated when uploaded in CTIS (to not include version & date)

Transition trials

- Not expected to be re-assessed
- Clarified in Q&A 6.3

Lack of alignment and consistency among MS

- Mainly for Part II

Part II RFIs received before Part I – Collaboration needed

- Requires SM to update Part II documents
  - Additional work for both Sponsor and MSCs and can significantly delay start of trial
  - No possibility to clarify Qs with Ethics committee

Ability to manage complex Trials limited and needs some focus

# Transparency and Disclosure challenges

## Redaction vs Deferral

- Redaction adding time and workload for documents preparation
- Redactions required within 12d RFI – adding additional challenge

## Redaction

- Non OCR documents difficult to redact
  - Need technical workarounds

## Deferrals

- Uncertainly around deferral acceptance
  - Although so far the only rejection of deferral request is linked to wrong category selection

## IMPD-Q

- Issue with access not restricted to CT-Admin from co-sponsor

# Conclusion

Transition period allowing for learning curve.

It is evident that there is more work to be done to streamline the system  
It is also evident significant amount of work has been conducted to share information through Q&A  
Respond to issues through fixes and acknowledgment of challenges

EFPIA is confident that EUCTR will deliver on promise to make EU a competitive location to conduct clinical research.

Important for EMA and the Commission to continue meeting regularly with Sponsors, MS and other Stakeholders for sharing Information, issues and respond to future needs to support favourable environment EU Clinical Trials.

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Thank you

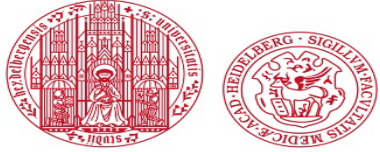




# Sponsors' Experience and Perspective - Academia

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Andrea Seidel-Glätzer (ECRIN / Universitätsklinikum Heidelberg)



**MEDIZINISCHE  
FAKULTÄT  
HEIDELBERG**



## **CTIS Event Readiness for Mandatory CTR use from 31 January 2023**

### **Sponsors' Experience and Perspective- Academia**

Andrea Seidel-Glätzer

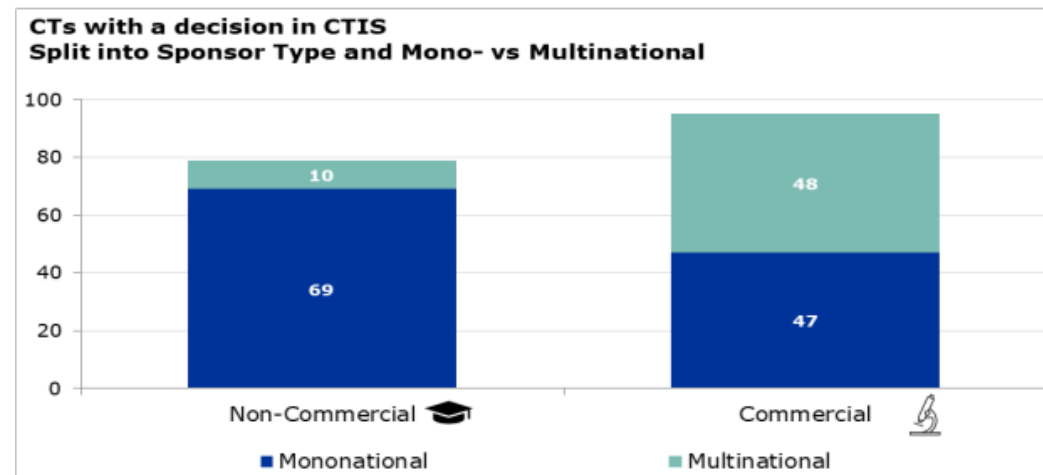
Coordination Centre for Clinical Trials at the University Hospital Heidelberg

Sponsor Product Owner for Academia-CTIS Working Group on behalf of ECRIN





- ✓ Same requirements
- ✓ Same workarounds
- ✓ Same technical issues
- ✓ Same timelimes
- ✓ Different financing
- ✓ Different problems
- ✓ Different ressources
- ✓ Different trials (?)



# Expectations

## EMA Homepage:

“The Clinical Trials Regulation **harmonises** the processes for **assessment and supervision of clinical trials** throughout the EU.”

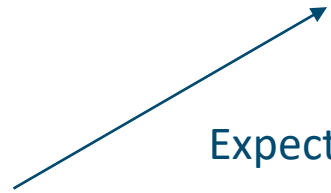
## CTR:

“Scientific development, however, suggests that future clinical trials will target more specific patient populations, such as subgroups identified through genomic information. In order to include a sufficient number of patients for such clinical trials it may be necessary to involve many, or all, Member States. **The new procedures for the authorisation of clinical trials should stimulate the inclusion of as many Member States as possible.**”

expectations

[ɛkspɛk'teɪʃ(ə)ns] noun

one of the main causes of disappointment.



Expectations

VS



Reality

Country	Topic
Ireland Germany	Part II documents: Site suitability template not accepted because the country has published specific one
Greece	Part II documents: Financial arrangements need to include signed site agreements
Luxembourg	Part II assessment required uploading the CRF
Spain	ECs located at one of the recruiting sites asked for modifications in the ICF after the document had been approved
Hungary	Protocol Signature Page by all investigators has been requested in an RFI

# What else?

- Part II documents seem to be the minimum standard plus nationally required documents

Regulation (EU) No 536/2014 Questions & Answers December 2022

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

- RFIs partially in national language, especially concerning the ICF
- RFI not being consistent

**Consideration:**

IT's indicated that a pregnancy test will be done at the beginning and at the end (visit 7). Justify why it is not done at each visit

Because of patients' safety, sponsor is asked to perform urine pregnancy test on every study visit in study centre. Sponsor is asked to amend protocol accordingly.

- No contact possible for consultation
- Misunderstandings due to language barriers
- Lapsing of application due to unforeseen national requirements
- Shortage of timelines

## Article 86 - Fees




“This Regulation shall be without prejudice to the possibility for Member States to levy a fee for the activities set out in this Regulation, provided that the level of the fee is set in a transparent manner and on the basis of cost recovery principles. **Member States may establish reduced fees for non-commercial clinical trials.**”

- some countries: **no fee payment** for any trial
- some countries: fees are **applicable to any trial**
- No consistent definition of “non-commercial”
- Budgeting the payments for grant applications is almost impossible
- Likely to cause gaps in trial financing
- Burdensome investigations upfront

# IMPD and cross-referencing

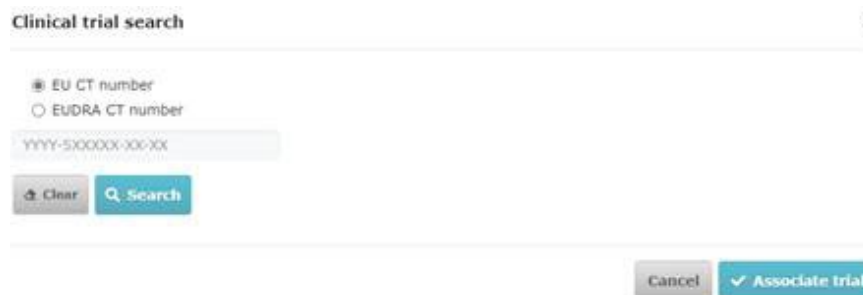
## 2.3 SPONSOR CTA PREPARER AND SUBMITTER ROLES

(Black text refers to soft tasks, and red text refers to hard tasks)



Phase	Permissions/Tasks	CT Admin	Part I preparer (excl. Q-IMPD)	Part II Preparer	Q-IMPD Preparer	Application Submitter
Create CTAs	Create a new trial (initiate)					
	Create a CTA copy or resubmit a CTA					
	Create subsequent applications (SM, AMS, non-SM)					
Create initial application	<b>Form:</b> create cover letter/Compliance Reg. 2016/679/ Deferral/ (CT Transition) <sup>1</sup>					
	<b>Form:</b> proof of payment					
	<b>MSC:</b> add MSCs involved					
	<b>Part I:</b> Populate information Part I (Q-IMPD)					
	<b>Part I:</b> Populate information Part I (excl. Q-IMPD)					
	<b>Part II:</b> Populate information for Part II					
	<b>Timetable:</b> Modify Winter clock stop					
Create substantial modification	Cancel/ <b>submit/ withdraw</b> a CTA					
	Initiate creation SM					
	<b>Form:</b> cover letter/SM description					
	<b>Form:</b> proof of payment					
	<b>MSC:</b> Modify the expected number of subjects					
	<b>Part I:</b> Modify Part I (Q-IMPD)					
	<b>Part I:</b> Modify Part I (excl. Q-IMPD)					
	<b>Part II:</b> Modify Part II					
<b>Timetable:</b> Modify Winter clock stop						
Cancel/ <b>submit/withdraw</b> SM						

- Role conception of Q-IMPD Preparer is not accepted
- Academia is receiving negative feedback from industry
- Cross-referencing still is possible, but only to documents already approved under the CTR



Clinical trial search

EU CT number  
 EUDRA CT number

YYYY-SXXXXX-XX-XX

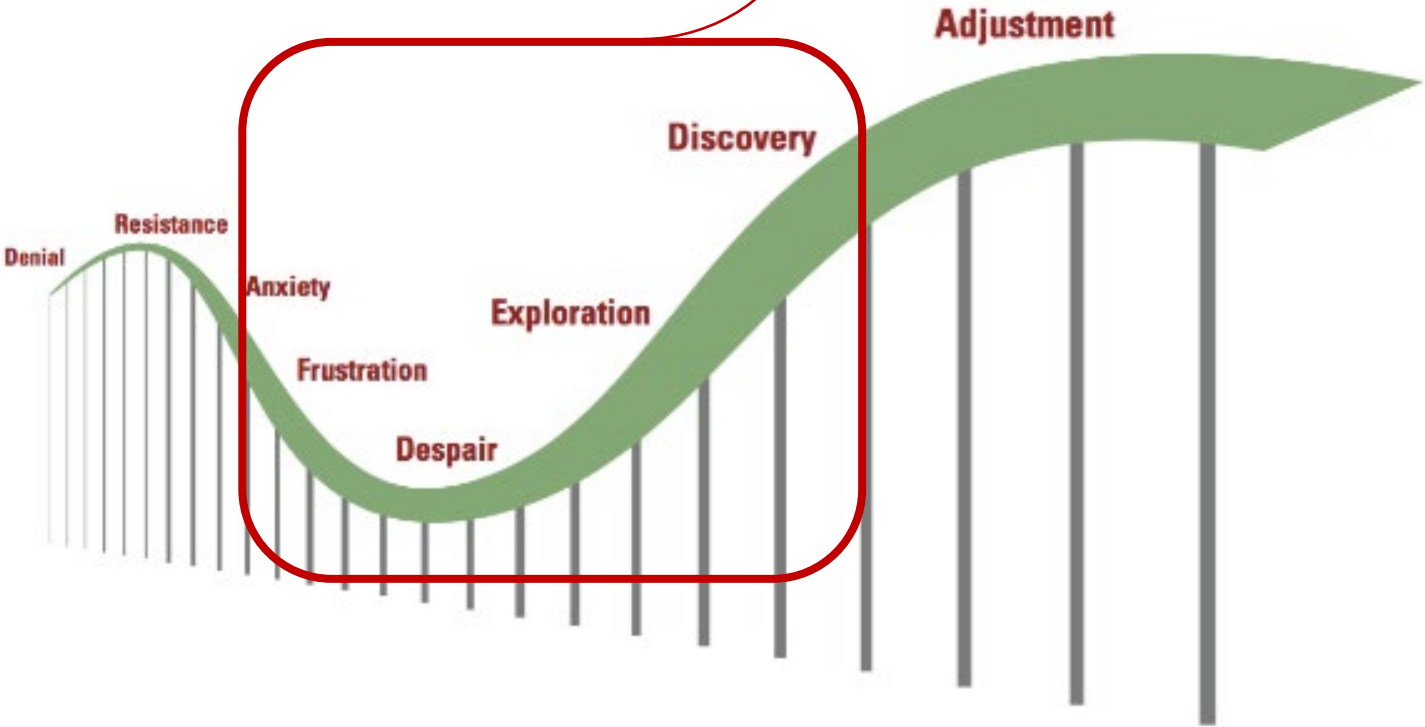
# Conclusions for Academia

- Academia is able to fulfill the requirements of the CTR and is still positive about the new CTR

**but**

- Too many Workarounds right now- but technical problems will hopefully resolve in the future
- Increase of bureaucratic burden for academic sponsors, this will increase the costs for academic trials (user management, transparency, document needs)
- Harmonization approach has not been fulfilled → disappointing for multinational academic trials
- Lapsing of trials due to unforeseen national requirements and very challenging timelines
- One solution does not fit all- Requirements should be fixed (Part II) but the system should stay flexible

Keep going!



Source: [Surviving Change: The Change Curve - Ultimate Resilience](#)



# Questions and Answers

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## Session 2

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### CTIS Governance, Update and Planning



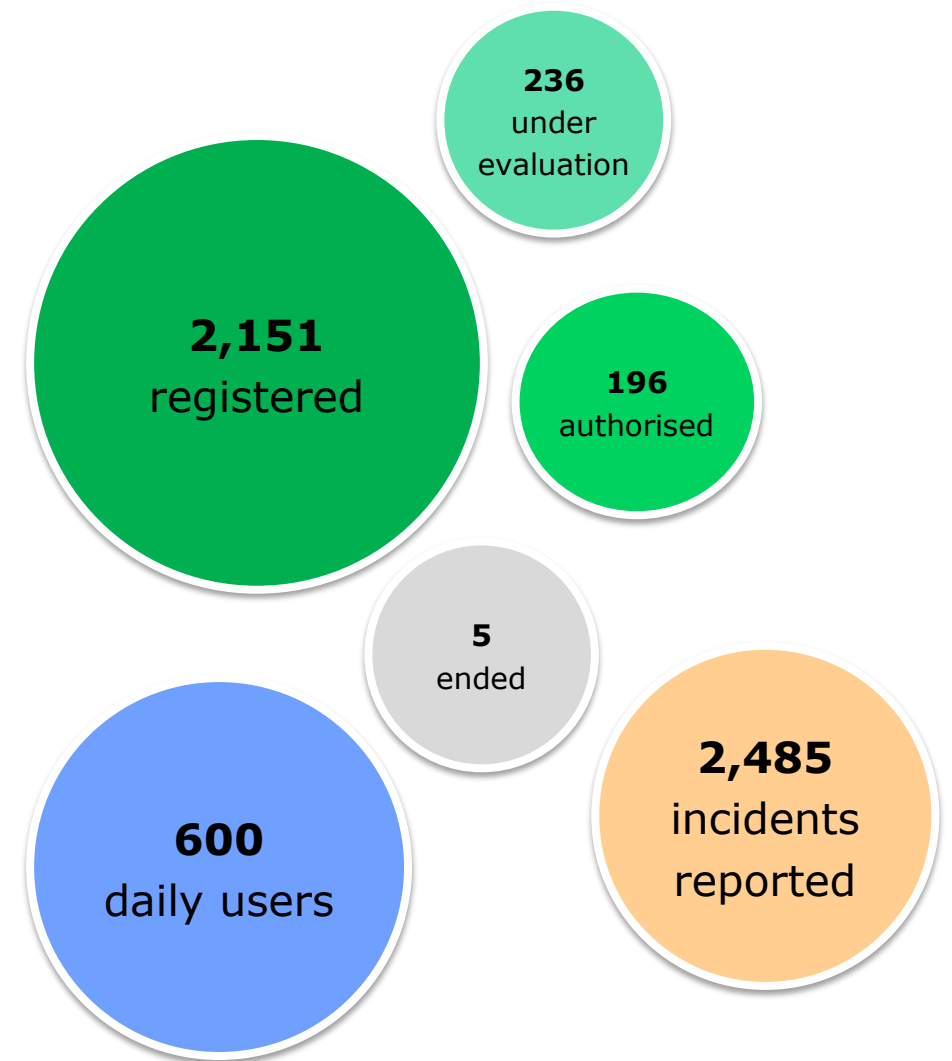
# CTIS Status Update

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Ana Rodriguez Sanchez Beato (EMA)

- AMS- Additional Member State Concerned
- AxMP- Auxiliary Medicinal Product
- AMPD- Auxiliary Medicinal Product Dossier
- API- Application programming interface
- AR- Assessment Report
- ASR- Annual Safety Report
- CT- Clinical Trial
- CTIS- Clinical Trials Information System
- IMPD- Investigational Medicinal Product Dossier
- MS- Member State
- MSC- Member State Concerned
- NOA- National Organization Administrator
- NSM- Non Substantial Modification
- OMS- Organization Management System
- PIP- Paediatric Investigational Plan
- RFI- Request for information
- RMS- Reference Member State
- SM- Substantial Modification

- Successful go-live of CTIS on 31<sup>st</sup> January 2022 with a very large scope
- Use is gradually scaling up and expected much higher after 31<sup>st</sup> January 2023
- Most trials submitted have been authorised without issues: **236 under evaluation and 196 authorised Clinical Trial applications** by 31<sup>st</sup> December 2022
- Production problems have created challenges, which are closely monitored and managed
- The CTIS delivery plan was in line with the decision at EMA Management Board to focus on bug fixing to improve the stability of the system in preparation for the 31 of January 2023



# CTIS Delivery Plan: Key Objective for the 1<sup>st</sup> year of transition period

The CTIS delivery plan has been built accordingly, to ensure the critical bugs in the system are fixed, enabling assessment and authorisation for all new trials in the EU and successfully launching the 2nd year of transition

← **1<sup>st</sup> year Transition Period** →

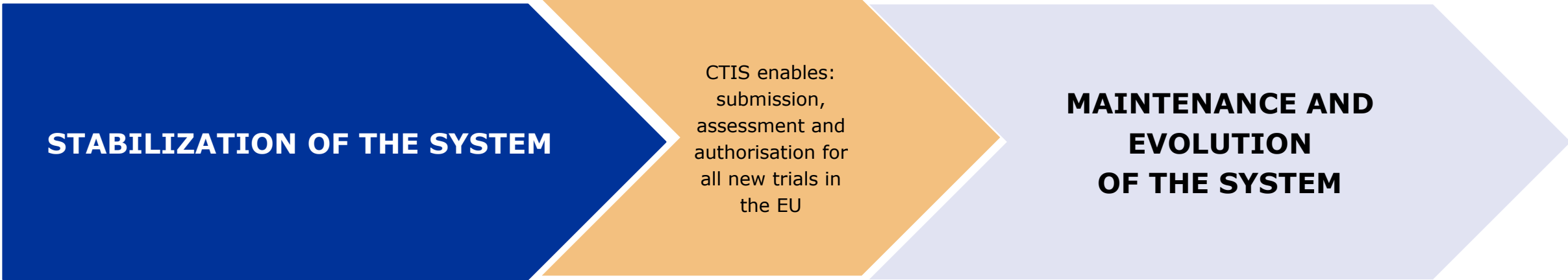
Go-Live- 31 January 2022



31st Jan 2023



February 2023 and onward



# CTIS Increment Plan: high level overview procedure

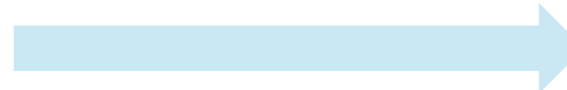
- The activities of the delivery team will come from the prioritized **backlog** and **PIRQs** in Production with higher priority
- **Member States and Sponsor Product Owners** work with EMA to **identify the priorities** to be included in the Increment Plan
- 4 Increment Plan delivered in 2022: PI1 (Feb-Apr), PI2 (May-July), PI3 (Aug-Sep) and PI4 (Oct-Dec)
- PI5 (Jan-March 2023): started

Delivery

**Backlog Prioritisation activities** (issues identified during past and ongoing testing activities)



**Backlog Prioritisation**  
(from 5 to 11)



The prioritized backlog will feed the **Increment Planning**

## **INCREMENT PLAN**

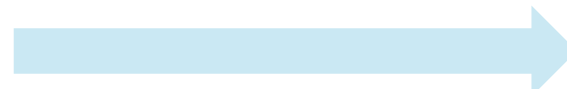
- Backlog priorities (planned work)
- Problems priorities (unplanned work):
  - By 31<sup>st</sup> January: aim to have solved critical and high problems
  - After 31<sup>st</sup> January: prioritised medium ones can be included
  - Low will go to backlog for prioritisation

Operation

**PIRQs reported to Service Desk:**  
**Problems:** root cause of one or more incidents.  
**Incidents:** unplanned interruption/reduction to an IT Service  
**Requests:** information/changes/other  
**Questions**



**Problem prioritisation**  
(critical, high, medium and low)



**Problems** to address the root cause will be prioritised and planned to be **solved during the increment.**

**Note:** The critical incidents will be resolved using a **workaround** and/or deploying an **urgent hotfix** in Production.

# Deployed Production Releases Overview



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Date	Problem Release	Status
2022-07-14	PR#1	Deployed
2022-09-27	PR#2	Deployed
2022-10-18	PR#3	Deployed
2022-11-15	PR#4	Deployed
2022-11-17	PR#5	Deployed
2022-11-23	PR#6	Deployed
2022-12-06	PR#7	Deployed
2022-12-12	PR#8	Deployed
2022-12-21	PR#9	Deployed
2023-01-12	PR#10	Deployed

## ACCESS MANAGEMENT

- Ensuring correct role assignment to users with very similar username.
- Reinforcing right role assignment by adding email address on top of the username when assigning roles to users.
- Sponsor (CT Admin)/MS users with scope specific trials have access only to Notices & Alerts for trials under their role scope.
- Preventing CT Admins with scope "Specific trial" from creating trials for sponsors following the Organization Centric approach.
- The CT "User" Tab display now only those users who have at least one role to access a particular CT.
- Ensuring Assessor Part II Preparer, being able to delete, comment and share consolidated considerations
- Only submitted RFI responses become visible from Authority and MS API and anymore the draft ones.

## USER MANAGEMENT

- Sponsor (CT Admin) and MS (NOA) Administrators only able to amend and revoke roles according to their role and scope.
- Sponsor and CT Administrators having administrator roles for different organizations (i.e. different Organisation IDs), which share the same organization name, can now assign roles to users for these organizations.
- Sponsor and MS administrators able to assign roles to a blank user, who has revoked CTIS roles previously assigned by an administrator of a different organization.
- Warning message now displayed when an administrator role tries to assign a role to a user with scope "specific trial" when the user has already this role but with scope "all trials".
- The OMS search display now correctly organisations with special characters in the User Management functionality page.
- Any user can update his Employer Name successfully and the name is displayed correctly.

## APPLICATION CREATION/SUBMISSION

### General issues:

- The closing of the CTA cancelation pop-up window does not cancel the draft CTA anymore, just close the window.
- Introduced the ability to create Organisations locally in CTIS without the need to be registered in OMS (Investigational Trial sites, Third-party organisations, site where the serious breach occurred, Third country inspection site and Inspected site).
- Lock mechanism working now properly when concurrent users are working on the same clinical trial application.
- Sponsor users are now able to delete a MSC from a draft clinical trial application.
- The deletion of the “for publication” documents is not possible, unless the linked “not for publication” document is first deleted.
- As consequence of previous fix, sponsors are now able to create an SM or NSM without a red pop-up error displayed.

### Document upload

- Documents with a maximum size of 50MB can now be uploaded in CTIS.
- The language drop-down of the document upload pop-ups, in both workspaces, is updated with a more specific list of official EU languages, sorted by alphabetic order and with an “other” option.

### Transitional trials

- Sponsor users are now able to select a date in the past for the “Estimated recruitment start date” field of the Part I- trial details.
- Sponsor user can submit an initial application only after valid EudraCT number is entered in the field for this number.

## APPLICATION CREATION/SUBMISSION

### Specific issues

- Fixed issue with products with "Excluded MSC", the user is now able to delete this product and role.
- The content labelling documents linked to a product can now be deleted.
- The "status" field in the sponsor details section is now named "sponsor type" and has a dropdown list with the options "commercial" and "non-commercial" for selection.
- The documents 'Agreement from another Sponsor' and 'PIP Opinion' uploaded by Sponsor in as submitted CTA are now visible in the Authority workspace, regardless of whether they are for publication or not for publication.
- In the IMPD Safety and Efficacy and Quality placeholders, the justification field is now hidden if a document has been previously uploaded in one of these sections
- Fixed several issues with the submission of an AMS CTA ( e.g. now possible to submit an AMS CTA for a MSC that previously issued a negative decision, was withdrawn or lapsed; or when an SM Part I or SM Part I & II or SM Part II lapses or is withdrawn; or contains more than one AMS submitted at the same time).

## NOTIFICATIONS

- The "Restart of trial" notification after a Temporary Halt due to risk/benefit reasons can be submitted once a SM has been authorised or authorised with conditions.
- The "Start of Recruitment" (with Start of Recruitment date within 2 years from the clinical trial authorization) can be submitted, during the 15 days after the 2 years from the clinical trial authorization date, without the need to provide a SM.

## RFI REQUEST/RESPONSE ISSUES

**Change of Application:** the sponsor user can now perform the “Change application” action as part of an RFI response in any evaluation phase:

- Product related documents are not mixed up/copied correctly as part of an RFI response raised in the context of AMS and SM.
- The “proof of payment” document remains in its placeholder;
- The padlock to ‘Change application’ is now enabled/present in a pending Part II RFI, regardless of the CTA status in any other MSC involved in that CTA.

## Preventing incorrect expiration of RFIs (lapsing CTAs)

- A second RFI raised in the validation or assessment Part I phase and not responded within 23 natural days of the submission of that application or 47 of the validation conclusion of that application, respectively, does not expire now.
- MS user cannot set RFI due dates in the past when manually typed after closing the calendar date picker.
- RFI response due date can never be later than the Submit Validation Conclusion or Submit Part I Conclusion task due date

## Creation of RFI

- RMS/MS, are now able to raise the first validation RFI on the due date of the “Submit Validation conclusion task (day 10 or day 6 for an initial application or SM, respectively).
- RMS/MS, they are now able to raise the first part I assessment RFI on the due date of the “Submit Part I conclusion task” (day 45, day 38 or day 47 for an initial application, SM or an AMS application, respectively).
- RMS/MS raising the first RFI, they can now add, if required, the maximum number of days (10 in validation and 12 in assessment part I, respectively) for the sponsor to respond.

## WORKFLOW, TASKS AND TIMETABLE

### Workflow

- Member States Concerned can continue their activities under the evaluation workflow in the case the CTA lapses in one of the MSC
- The due date for the task Agree RMS is now correctly calculated in one particular scenario.
- Annual Safety Report, the "Appoint saMS" task does lead now to the generation of the task "Circulate draft ASR-AR" upon expiration

### Tasks

- The notice "Response to RFI Submitted", "Consolidated Considerations" and the task "Assess RFI Response" are now generated for all application types (Full or partial initial, SM or AMSC) and during all assessment phases.
- A MS user that claims a task will always have it visible from "My task" filter.
- MS user can select now "all" considerations and shared consolidated considerations when selecting the tick-box 'select all', regardless the number of pages needed for listing those.
- Fixed issue with the Considerations and Consolidated Considerations sorting mechanism (arithmetic or alphabetic order).

### Timetable

- The tasks Submit RFI response (projected) appears now with the correct values and there is no gap between Submit RFI (projected) task and Submit RFI Response (projected).
- The submission date is shown on the same date as the clinical trial application was submitted when users are in different time zones

## MS API

- MS API searching by CT is not now retrieving an error
- In the case of a trial authorized with conditions in Part II, the conditions provided in Part II conclusion are displayed in the API.
- Fixed issue with age range between 18-64 years in the MS API, which is now present in the CT\_AGE\_RANGE table.
- The user is able to retrieve all trial sites information under Part II in the endpoint `clinicalTrials/{clinicalTrialId}/applications/{applicationId}/parts2/{part2Id}`.

## PUBLIC PORTAL

- Migration from LifeRay to Angular
- Fixed several issues with deferrals lost and set to default, preventing incorrect publication of documents

## OTHER ISSUES

- No document can be uploaded/updated in CTIS using the GDPR feature having the field Date empty.
- The GDPR feature can now be used to replace documents uploaded not only by Sponsor users but also by Authority users.

Current plan until the mid February

<b>Date</b>	<b>Problem Release</b>	<b>Status</b>
2023-01-24	Problem release #11	Business Validation
2023-01-31	Problems release #12	In development
2023-02-07	Disaster Recovery Priority 3 scenarios	In development
2023-02-14	Problems release #13	Pending

## **Problem Release 11 - 24/01/23 (planned)**

- MSC will be able to submit Part I Disagreement for SM part I only or SM part I&II in which part II was submitted only to the RMS, even if the RMS already issued a decision on the application
- The authorise task will not include the list of conditions from Part II Conclusion of another MSC.
- MSs will be able to retrieve via MS API the complete list of notifications present in a CT.
- MS API will display the page entries correctly.
- The title of a CT updated in the context of a NSM or authorised SM will be correctly displayed in all areas of the system.
- The decision date of a tacit decision will be correctly displayed with the due date of the Authorize task.
- The updated information in “number of subjects” created as a response to an RFI by clicking on the "Change application" will be displayed in authority workspace and MS API only after submission.
- The decision section of an AMS application will only include the Part I disagreement related to that application.
- The substance(s) information missing in some products will be correctly retrieved.
- The due date of the “Consolidate Considerations” and “Submit RFI tasks” will be calculated using Central European Time (CET) instead of Universal Time Coordinated (UTC)
- Improved behaviour of the pop-up cancel button in the tasks section to ensure that the user action performed is indeed canceled.
- The sponsor and Member States will be able to download documents with special characters.

## **Problem Release 12** - 31/01/23 (tentative)

- Alerts "Response to RFI due" will not be displayed after the sponsor replies to an RFI
- Alert "There are 2 days remaining to submit a decision on the trial" will not be displayed after a decision is made on the trial
- Alert "Express willingness/unwillingness task due" will not be displayed after willingness/unwillingness is expressed
- Alerts no longer applicable when a CTA is withdrawn will not be displayed
- Alert "Assess Part I. 12 days after circulating end date passed for application" will not be displayed, as it is not applicable
- Alert 'Considerations due (Validation)' will not be displayed to non-MSCs
- Medicinal Products Search will work now for products with more than 35 substances

## **Disaster Recovery Scenarios**- 07/02/23 (tentative)

- System downtime during Assess Part I phase of an initial CTA - Scenario with "Creating an RFI" afterwards
- System downtime during Assess Part I and Assess Part II phase of initial CTA, with ongoing RFIs - Expired RFIs scenario
- Extend start of recruitment date via SM
- Extension to restart of a Halted trial through a substantial modification
- Sponsor not submit Restart of Trial notification after Temporary Halt (Halted-->Expired)

## **Problem Release 13** - 15/02/23 (tentative) (final scope still not finalized)

- Each AxMP section will only display its related SMPCs instead of "all" related to all AxMPs
- Structured Data Download Document doesn't include most current CTIS entries
- AMPD Full has 'for publication' version but is not published
- Sponsor user will be able to submit 2nd RFI in Part II



# CTIS Governance, Update and Planning

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Petri Paakkonen (EMA)

CTIS went live successfully with a very large scope and its use has been scaling up gradually



Since Go-Live accumulation of production problems has been gradually solved to stabilize the core functionalities of the system and to increase performance



Based on the production experiences, an architecture study has been conducted to analyse technical areas for enhancement

2023 plan has been put together to ensure stable operations, implementation of prioritized improvements and future proofing of CTIS



Since Go-live we have been focusing on **stabilising the system**:



Addressing **bugs** identified through **incidents** raised by users or coming from the **historical backlog**

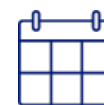


Resolving a pre-defined set of **technical fixes** and **technical improvements** from the backlog

Before the mandatory use of CTIS for new applications, the focus will be also on:

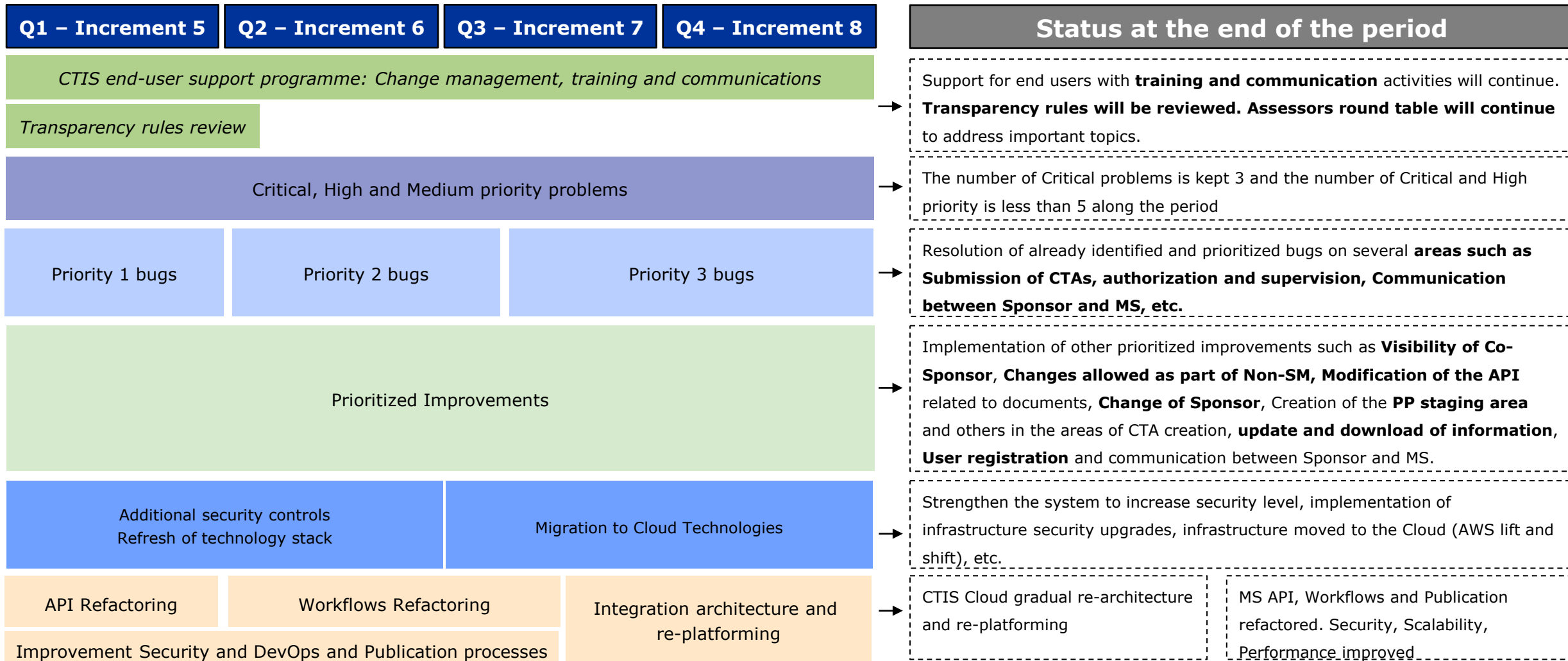


Ensuring the security of the system by enhancing the **monitoring** and **early detection tools**



Preparing for a possible downtime of the system **protecting** the **timelines** indicated by the Regulation

The below overview provides a picture on priority areas in 2023, as endorsed by the ACT EU Steering Group in 2022



CTIS will continue its evolution following **the guidance of Product Owners and the experience gained from the real use** of the CT Regulation and CTIS along the way. **The EMA agile transformation will ensure the continuous engagement of representative users** in the prioritisation and planning of future CTIS releases, adapting the system as needed.

EMA will continue providing **support to CTIS user community: MS, Sponsors, Academia.**



- Continue adapting CTIS to the use of native cloud solutions through the Refactoring activities
- Continue improving the CTIS security controls
- Continue ensuring the technological alignment with modern IT technologies and best practices



# Questions and Answers

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# Helpdesk support and how to report a priority issue

Anna Herks Vitezova (EMA)

# Clinical trials in EU – changes with 31 January 2023



CTR

Clinical Trial Regulation (EU) No  
536/2014 – ***new ways of  
working***

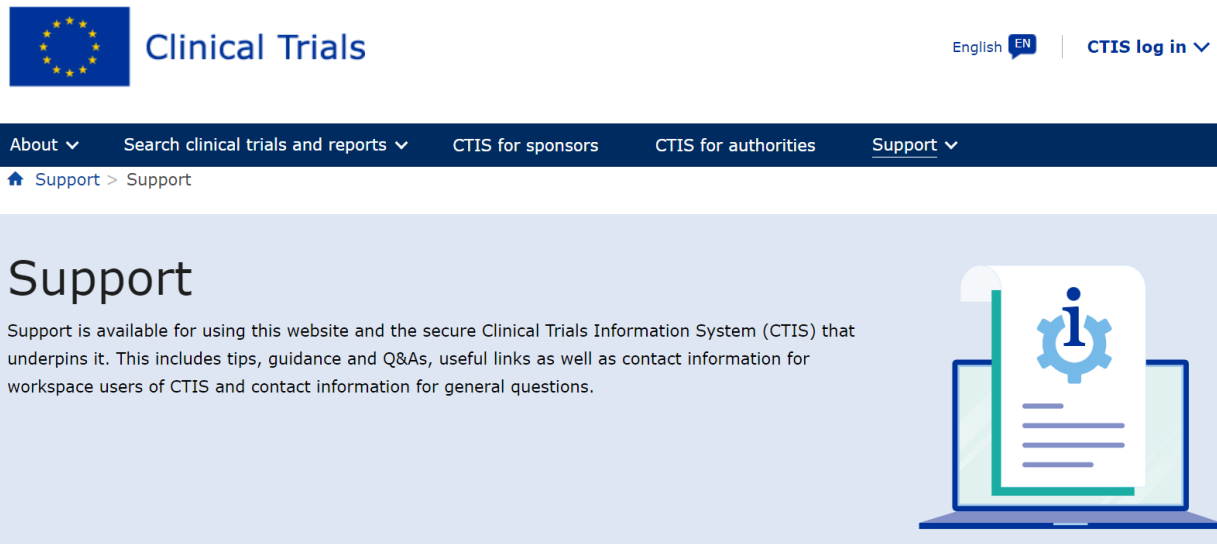
CTIS

Clinical Trial Information System –  
***new complex application***

# Different types of support to the user

- Before submitting a ticket to Service Desk please check information available on the support page:

<https://euclinicaltrials.eu/support-info/>



Legend: CTIS- Clinical Trial Information System; Q&As- Questions and Answers.

1

If you cannot find an answer to your question, please consult our training and supporting materials on how to use CTIS.

Training on  
using CTIS

2

Find questions and answers on how to use CTIS.

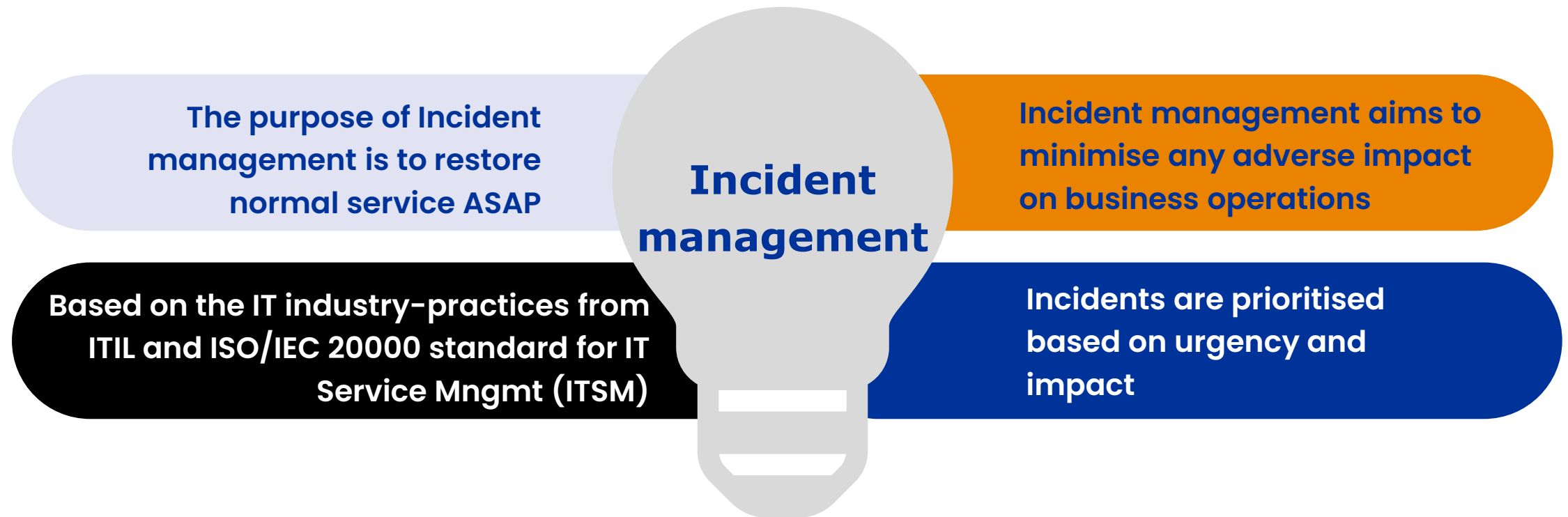
Guidance  
and Q&As

3

See when this website and CTIS will be unavailable due to maintenance and upgrades, as well as an overview of system releases

Website  
outages and  
system  
releases

***Incident*** is an interruption to a normal operation of an IT Service which prevents an end user from using that service in the manner intended



## Incident prioritisation criteria:



**P1**

A large number of users cannot use the application (usually the application is down).



**P2**

A single or a small group of users cannot use the application, or a functionality is unavailable. Important but not a blocker for users.



**P3**

Single user has an issue with one or more functionalities (the most "common" case).



**P4**

An issue of a user that is not blocking or urgent for the user.

# Incident management

## Submitting SD ticket 1

### CTIS support



#### Request a service

I need a standard service  
e.g. password reset



#### Report an issue

I'm prevented from working  
by a problem with  
software/systems



#### Ask a question

I need information about  
something

Legend: SD- Service Desk; CTIS- Clinical Trial Information System

Service Desk

## Service Desk

Welcome to the EMA Service Desk self-service portal which enables you to request the services you require from the Agency.

### Change Status Report

To see the report click here

What do you need help with?



Search help

Request a service (I need ...

**Report an issue (I'm pre...**

Ask a question (I need inf



#### Report an issue with CTIS

Issues (known as incidents) with CITS applications only



#### [Moved to ServiceNow] Audio visual, conferencing, virtual meeting, multimedia services or AV equipment

Issues (known as incidents) with audio visual meeting room equipment (e.g. projectors, voting system or audio quality)



#### Report an issue to Reprographics or the Mailroom

Issues related to Reprographics and Mailroom



#### Report an issue to Building Maintenance

Issues and faults related to the building installations and systems, e.g., air-conditioning, lighting, plumbing, lifts etc.



#### Report an issue to the Facilities Management and Security

Issues related to Security, Cleaning and Office equipment

# Incident management

## Submitting SD ticket 2

**Summary = title of the incident**

Example:

**CTIS issue**

VS

**RFI response not possible:  
deadline 23 Jan. 2023**

Service Desk / Service Desk

## Report an issue with CTIS

Raise this request on behalf of

Herks Vitezova Anna

Summary

CTIS Services (optional)

None

Description (optional)

Aa v | B I ... | ☰ v | 🔗 <> + v

Attachment (optional)

📎 Drag and drop files, paste screenshots, or browse

Create Cancel

Legend: SD- Service Desk; CTIS- Clinical Trial Information System; RFI- Request for Information

# Incident management

## Submitting SD ticket 3

### **Detailed incident description**

**Provide as much information as possible**



- Who you are: sponsor (pharmaceutical industry, CRO, academia) or Member State (NCA, ethics committee, etc.)



- Role
- Trial number/RFI number
- Location (country)



- Username
- Describe steps taken
- Attach screen shots of the issue

*Legend: CRO- Clinical Research Organisation; NCA- National Competent Authority; RFI- Request for Information*

Service Desk / Service Desk

## Report an issue with CTIS

Raise this request on behalf of

Herks Vitezova Anna

Summary

CTIS Services (optional)

None

Description (optional)

Aa v B I ... ≡ v 🔗 <> + v

Attachment (optional)

📎 Drag and drop files, paste screenshots, or browse

Create Cancel

## Incident management –final remarks

- Service Desk set up and operating according to industry standards
- Daily monitoring of incoming SD tickets
- Daily briefings between colleagues operating SD, IT and business
- Additional measures in place in preparation for 31 January 2023 and mandatory CTR use

*Legend: SD- Service Desk; IT- Information Technology; CTR- Clinical Trial Regulation*

# Any questions?

## Further information

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**EMA Service Desk for CTIS** - Questions on CTIS functionalities - for EMA account holders

**AskEMA** - Questions on CTIS functionalities - for non-EMA account holders

**EMA ServiceNow** - Assistance with information technology (IT) systems

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# Training and Change Management Activities

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Noemie Manent (EMA)



# Agenda



Communication



CTIS Training Environment



CTIS Training material production and revision



Sponsor End User Programme



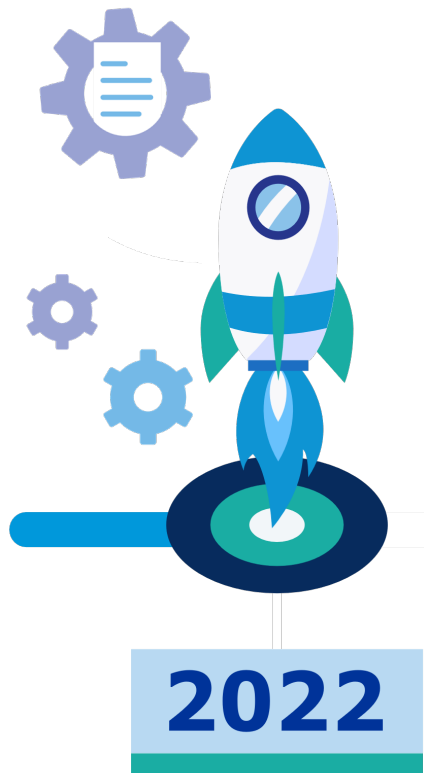
Training and Information events



# Communication

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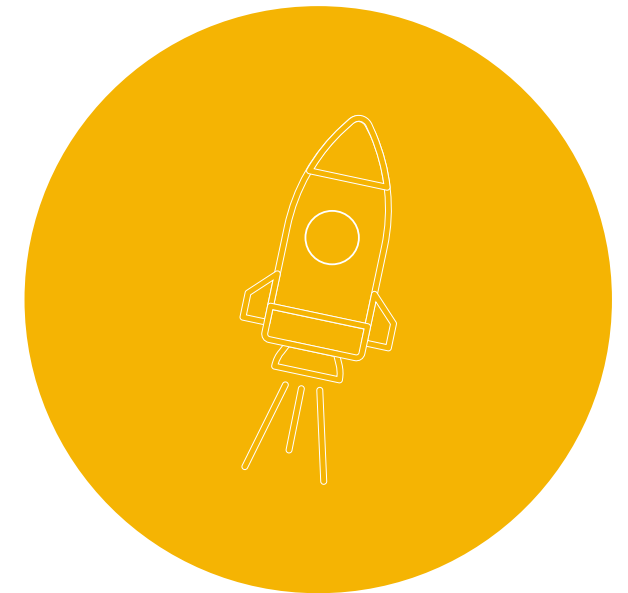
# CTIS in 2022: 1<sup>st</sup> year of transition of Clinical Trials Regulation



- CTIS went live on 31 January 2022, kicking off the 1st year of transition of the CTR
- Key **2023 objectives**:
  - Facilitating sponsors and MSs to learn and adapt to CTR
  - Detecting & resolving bugs before end of transition year
- **Nearly 200 clinical trials authorised** in CTIS
- Intensive collaboration with Sponsors, MS to resolve challenges with a small number of trials
- Focus on **getting CTIS ready for compulsory use** for submission of initial trial applications **starting 31 January 2023**

# Effective Incident Management

- Hands-on support from EMA to MS and Sponsor users in resolving incidents with specific CTAs
- Major incidents and mitigation actions escalated to CTIS Early Phase Oversight Group, which includes HMA, EC and EMA representatives
- Prioritisation of fixes with a consistent and focused release plan for 2023



## Support to MS and sponsors

- Strengthening collaboration with COM and MS via CTCG, aiming towards harmonisation in the EU
  - Support to weekly CTCG Assessors Round Table
- Survey of CTIS sponsor users on main hurdles encountered so far with CTIS use (as part of the ACT EU initiative). Concerns of sponsors: 1. MS preparedness; 2. CTIS
- Hands-on support from EMA to sponsor users (as mentioned previously)



# Support to MS and sponsors: Guidance on transparency aspects

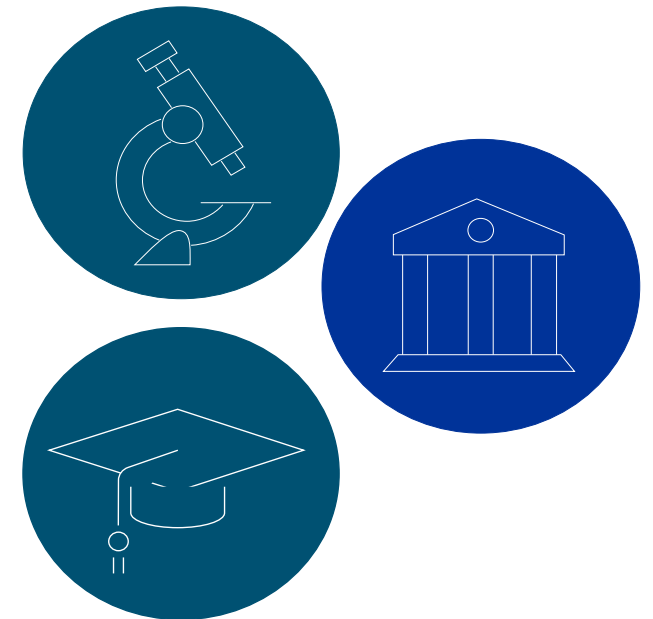
Revision and finalisation of Guidelines and Procedures related to CTIS processes:

- Draft guidance document on how to approach the **protection of personal data and commercially confidential information** in documents uploaded and published in CTIS was under open consultation until 8 September 2022
- On 14 July 2022, **workshop** held with nominated participants from sponsors and authorities to collect feedback on the topic
- Guidance is currently being finalised



# Support to MS and sponsors: Communication

- Since May 2022, **monthly clinical trials KPI reports** are published as part of the ACT EU programme ([link](#))
- Two **CTIS Webinars held** to discuss lessons learned from MS and sponsor experience in CTIS (1 July and 16 November 2022)
- Since March 2022, **monthly Walk-in clinics & Bitesize talks** offered - sponsor Q&A sessions with practical guidance on CTIS and on specific CTIS functionalities
- Launch of monthly **Organisation Management Service (OMS)** support sessions for CTIS users
- **Newsletter** (every 2 months) - **Clinical Trials Highlights** issue 12 [published](#) in December 2022
- **Newsflash** (weekly) – since December 2022



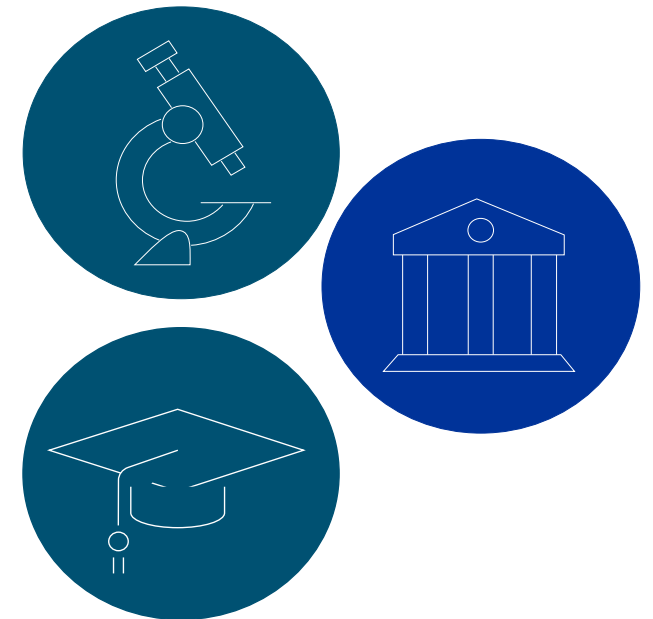
# Support to MS and sponsors: CTIS Release Communication

- January 2023 release notes and known issues documents available on the [Website outages and system releases](#) page on the Clinical Trials website
- Provides details on:
  - ✓ Maintenance windows tied to CTIS and related systems updates
  - ✓ Release notes describing updates made
  - ✓ Known issues and workarounds



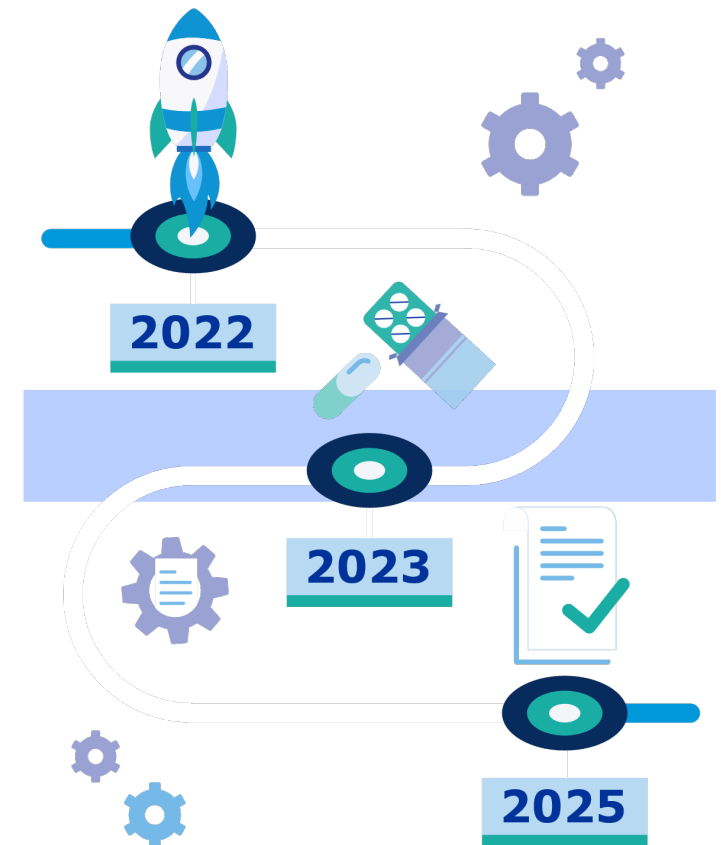
# Support to MS and sponsors: Training

- 23 online [training modules](#) published
- [New document](#) published, outlining latest updates to CTIS training materials
- Detailed [document dedicated to evaluation timelines](#) was published
- Access to **CTIS Training Environment** provided to more sponsor users, supporting efficient preparation and training in the future use of CTIS
- **Master MS Training Expert Panel** to meet on a regular basis to discuss progress in the CTIS implementation and changes to the training material



# Communication campaign – reminders re: end of Transition Year 1

- ACT EU priority action 6 (communications) developed a communication campaign to remind sponsors of the need to submit all initial clinical trial applications via CTIS starting 31 January 2023.





# CTIS Training Environment update

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# CTIS Training Environment update

The CTIS Training environment survey (Survey 4.0) is reopened:

<https://ec.europa.eu/eusurvey/runner/2abb5ba8-0ec4-9979-b692-0c63f4508b9b>

This survey collects expressions of interest in accessing the CTIS training environment ('CTIS Sandbox'), information and contact details of representative individuals, the organisations that they represent and the planning for use of CTIS of these organisations is reopened.

All details will serve to proactively identify the needs and intention of use of CTIS and grant access accordingly.





# CTIS Training material production and revision

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## Highlights



### WORK DONE:

- ✓ CTIS Training material production and revision programme is on track:
  - ✓ Training module **catalogue completeness: 100%**
  - ✓ The **revision** of training materials **started in Q3 2021**. So far 21 modules have been revised and all of them are already available on EMA's website. Some of them have been updated several times.
  - ✓ [CTIS Training latest updates document](#) has been published.



### ONGOING:

- The team is currently working on the revision of **training modules** that will be published on EMA's website in the coming days (*see slide 16*).
- A reorganisation of CTIS training materials on the EMA corporate website is considered.

The **training catalogue** comprises **24 modules** and is **100% completed** since beginning of July.

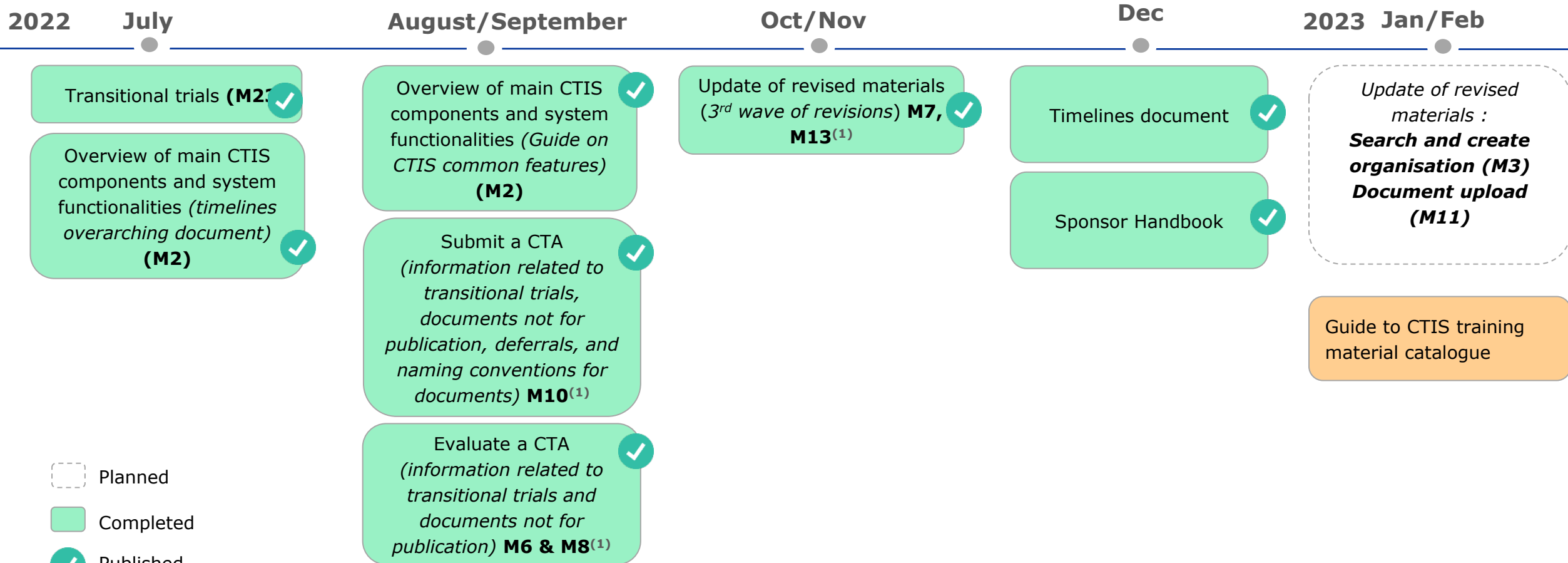
Introductory modules	Modules targeted to Member States	Modules targeted to Sponsors	Common modules for MS/EC and Sponsors	Other audience-specific modules
Introduction to new Clinical Trials Regulation	BI reporting ( <i>also the European Commission</i> )	How to manage a CT ( <i>Notifications, Ad hoc assessment, Corrective measures and Trial results</i> )	Support with workload management ( <i>tasks, notices &amp; alerts, RFI list&amp; timetable</i> )	Manage Union Controls (European Commission)
Overview of main CTIS components and system functionalities (high level)	Evaluate a CTA – Step 1 ( <i>application types, evaluation overview, RMS selection &amp; validation</i> )	How to create, submit and withdraw a CTA	User Access Management ( <i>self-registration, login &amp; user profile</i> )	Clinical Study Reports submissions (Marketing Authorisation Applicant)
	Evaluate an initial CTA – Step 2 ( <i>assessment and decision</i> )	How to search, view and download a CT and a CTA in the sponsor workspace	Management of registered users & role matrix	Supervise a CT – Inspection records (MS inspectors)
	Supervise a CT – Ad hoc assessment (including safety)	Respond to RFIs received during the evaluation of a CTA	Data protection in CTIS	Introduction to CTIS for Public Users
	How to search, view and download a CT and a CTA in the authority workspace	Submit an Annual Safety Report and respond to related RFIs		
	Supervise a CT – Corrective measures	CTIS for SMEs and academia		
	Assess an Annual Safety Report	Transition of trials from EudraCT to CTIS		

**Catalogue completion:**  
**100% completed!**

# Revision of training modules high-level plan



This plan indicates the revision of training material catalogue in Q2/3 and Q4 2022. The revision includes the creation of new materials for specific processes & materials' update to match current status of system functionalities. The plan may be adjusted, and items reprioritised based on emerging needs and team capacity.



- Planned
- Completed
- Published
- Ongoing

<sup>(1)</sup> These materials had already been revised once, but additional feedback has lead us to start subsequent revisions.

<sup>(2)</sup> On hold due to external dependencies



## URL

## QR code



[URL to CTIS training page on  
EMA website](#)



**Scan me**



# Sponsor End User Programme

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## ***CTIS Sponsor End User programme focuses on CTIS functionalities***



### **WORK DONE:**

- ✓ Identification of experts trainers
- ✓ Define agenda for the training sessions with kick off call (Dec 9<sup>th</sup>, 2021)
- ✓ Creation of training materials and updates
- ✓ Preparation of platform for the training sessions (live demo sessions)
- ✓ Training offers to be advertised on [EMA events page](#) (and DIA page)
- ✓ 8 events held in 2022



### **ONGOING:**

- Regular status update calls – with feedback on previous sessions, etc.
- Event oversight
- Organizing the sessions that will take place in 2023
- Review/Update the training materials
- Upcoming sessions
  - [7<sup>th</sup> - 10<sup>th</sup> February 2023](#)
  - [2<sup>nd</sup> -5<sup>th</sup> May 2023](#)
  - [27<sup>th</sup> – 30<sup>th</sup> June 2023](#)



# Training and Information events

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## CTIS Walk-in Clinics

- regular talks
- public events open to all (no registration required)
- live broadcast
- questions asked live and prior to the event; answered live
- recording published available post-event

Upcoming session:  
[16 February 2023](#)  
16:00 – 17:00 (CET)

## CTIS Bitesize talks

- regular themed talks
- different CTIS functionalities on each talk
- public events open to all (no registration required)
- live broadcast
- questions asked live and pre-event; answered live
- recording publicly available post-event

Upcoming session:  
End of February 2023  
More details to follow on [EMA event page](#)



# Questions and Answers

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## Closing Remarks

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Marianne Lunzer (AGES / CTCG chair)

Peter Arlett (EMA)



# CTIS – sources of information and/or updates

- [Online modular training programme](#) - training programme consisting of several modules, covering the full lifecycle of clinical trial submission, authorisation and supervision
- [Training and support page](#) - contains training and support materials aim to help users comply with their obligations under the [Clinical Trials Regulation \(Regulation \(EU\) No 536/2014\)](#)
- [EudraLex – Volume 10 – Clinical trials guidelines](#) - guidance on CTR interpretation, and national guidance for national processes and best practice
- [CTIS Release notes and list of known issues](#) - documents outlining the latest updates to the CTIS system, including the secure Sponsor and Authority workspaces, and to the Clinical Trials website.
- [Clinical Trials Highlights](#) - newsletter providing key updates on the development of CTIS, and also includes topics such as the business change programme ACT EU.
- [CTIS Newsflash](#) - contains short updates on system usage, key facts and figures, hints to help users with specific features and links to reference materials, following the launch of CTIS on 31 January 2022.



## CTIS – sources of information and/or updates

[EMA Service Desk for CTIS](#) - Questions on CTIS functionalities - for EMA account holders

[AskEMA](#) - Questions on CTIS functionalities - for non-EMA account holders

[EMA ServiceNow](#) - Assistance with information technology (IT) systems



# Thank you for attending today's event

Please provide your feedback for this event in our

**Slido survey**

Use event code: **#CTIS2023a**

Or use Slido QR code



## Further information

For the [CT Highlights Newsletter](#) sign up at [CT.NewsletterSubscriptions@ema.europa.eu](mailto:CT.NewsletterSubscriptions@ema.europa.eu).

For upcoming CTIS events, visit the [EMA events page](#).

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