



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Clinical Trials Information System (CTIS) webinar: Six months of CTIS and looking forward

Virtual Event - 1 Jul 2022





Welcome and introduction

Pieter Vankeerberghen

Head of Clinical Trials

European Medicines Agency, Netherlands



Session 1

CTIS Status and updates



Pieter Vankeerberghen

Head of Clinical Trials

European Medicines Agency, Netherlands

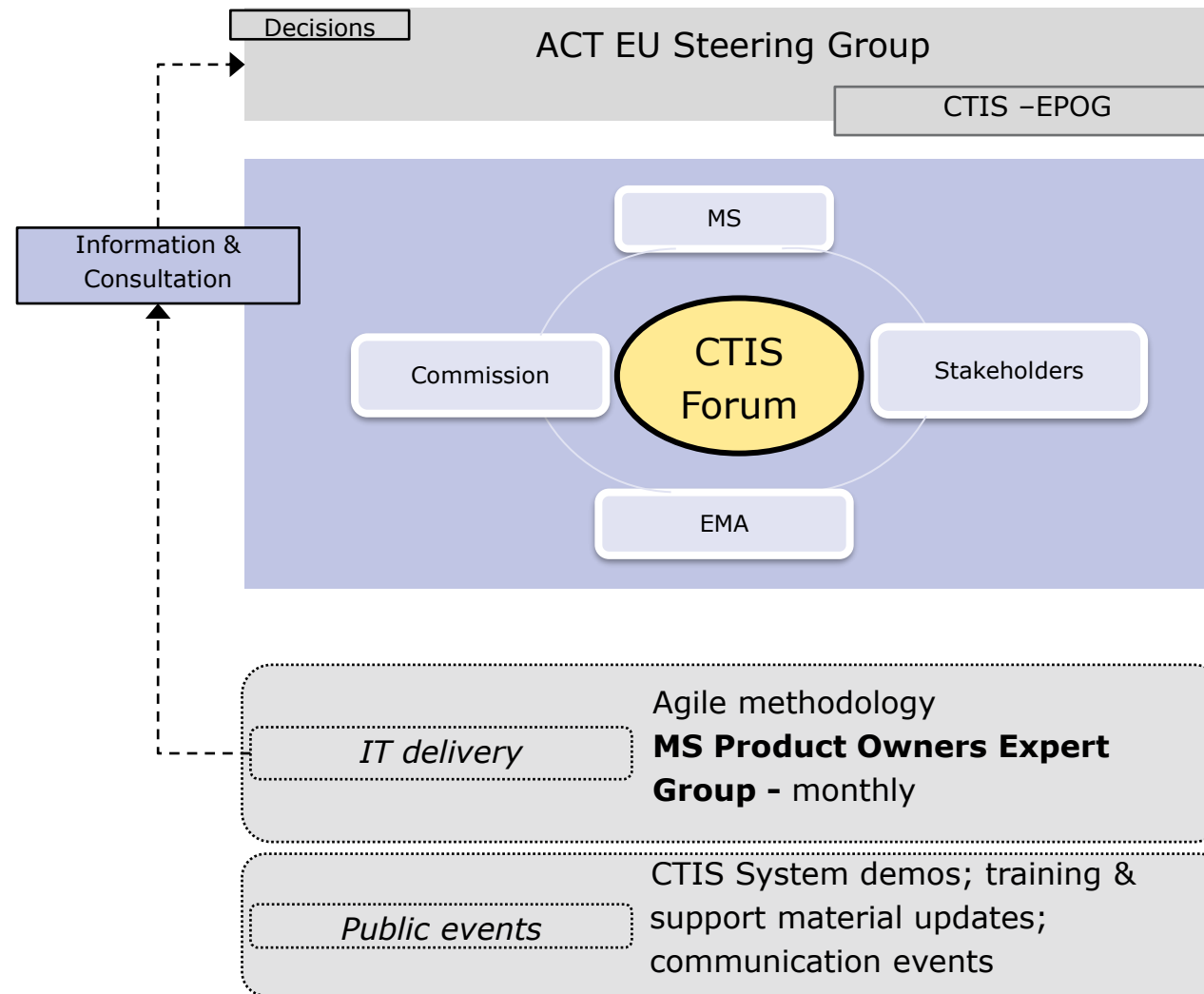
6 months of CTIS: current status

- CTIS and CTR are live since 31 Jan 2022
- Steady uptake in terms of volume of submissions
- Today +20 initial trials authorised, available on <https://euclinicaltrials.eu/>
- All planned training material was published, larger scope for the Sandbox being rolled out.
- CTIS dedicated Service Desk is in place
- System operations is monitored daily and reported through governance structures
- Two organisational structures at EMA: One operational structure (training, support) and one IT project (bug fixing, backlog, new functionality), to better serve users.
- Technical deliverables to improve system performance and resolving technical issues reported by users, supporting operational stability and good user experience.

New CTIS governance structure



EUROPEAN MEDICINES AGENCY



Looking forward: 2023 and mandatory submission of initial clinical trial applications to CTIS

2023 will be very important year as for initial trial applications, the possibility for submission under the Clinical Trials Directive stops.

Planned CTIS user training and support:

- Continuing training events, continuing updating of training materials, onboarding new users.
- Continued roll out of the CTIS info forum (4 times per year)

CTIS development plans (*pending confirmation*):

- As with 2022, ensuring operational stability and supporting users by resolving identified issues will remain a top priority. Users will be informed of plans for the development of new functionality.



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KPIs on implementation of the CTR





Laura Pioppo

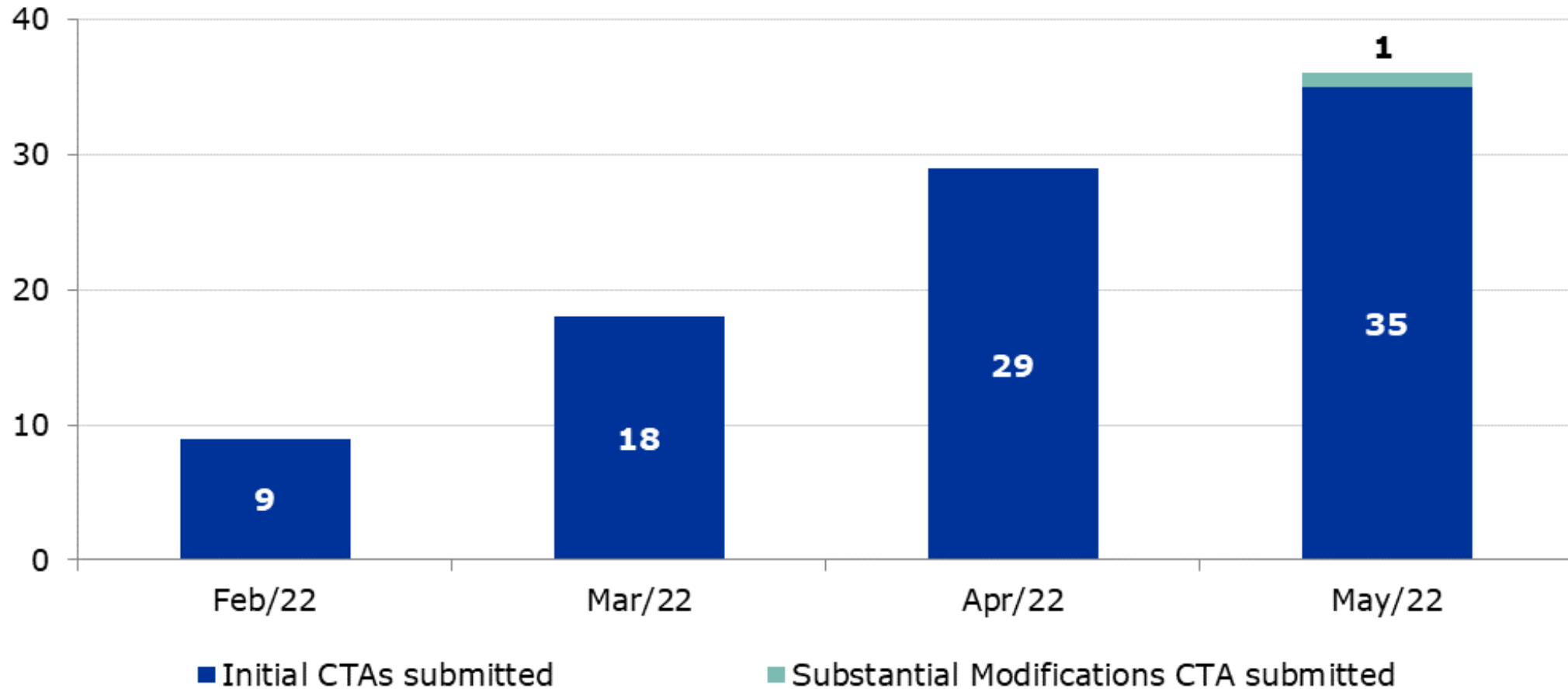
Scientific Officer, CTIS expert

European Medicines Agency, Netherlands

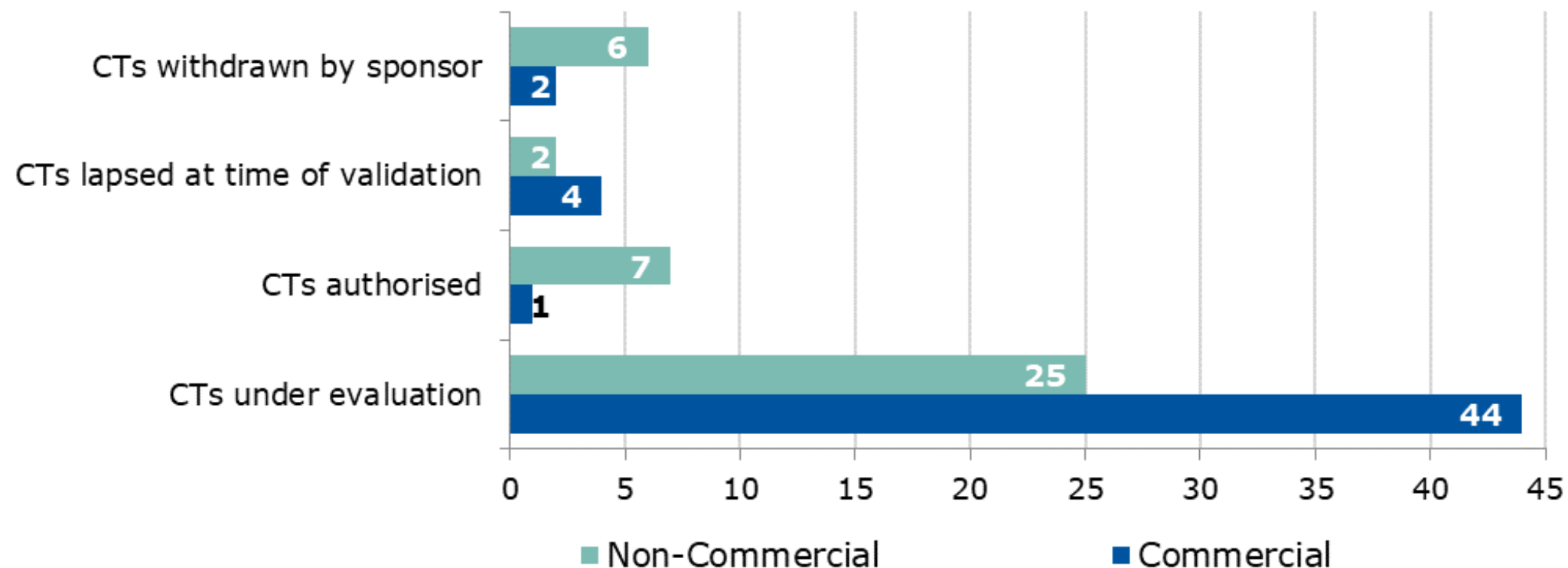
- Clinical Trials Regulation (EU) No 536/2014 (CTR) became applicable on 31 January with the launch of CTIS, a unique platform for the submission, evaluation and supervision of clinical trials in the EU/EEA
- The EMA, European Commission and EU/EEA Member States are closely monitoring the progress on 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 report has been published on Key Performance Indicators (KPIs) to measure the progress of the CTR
- The first publication occurred on 20 May, International Clinical Trials Day
- Edition 2 of the [KPI report](#) was published on 27 June

- 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
- KPIs for CTIS cover measurement of clinical trial data as well as clinical trial applications, as single CTs can have one or more applications
- A regular update of the report will be published on monthly basis

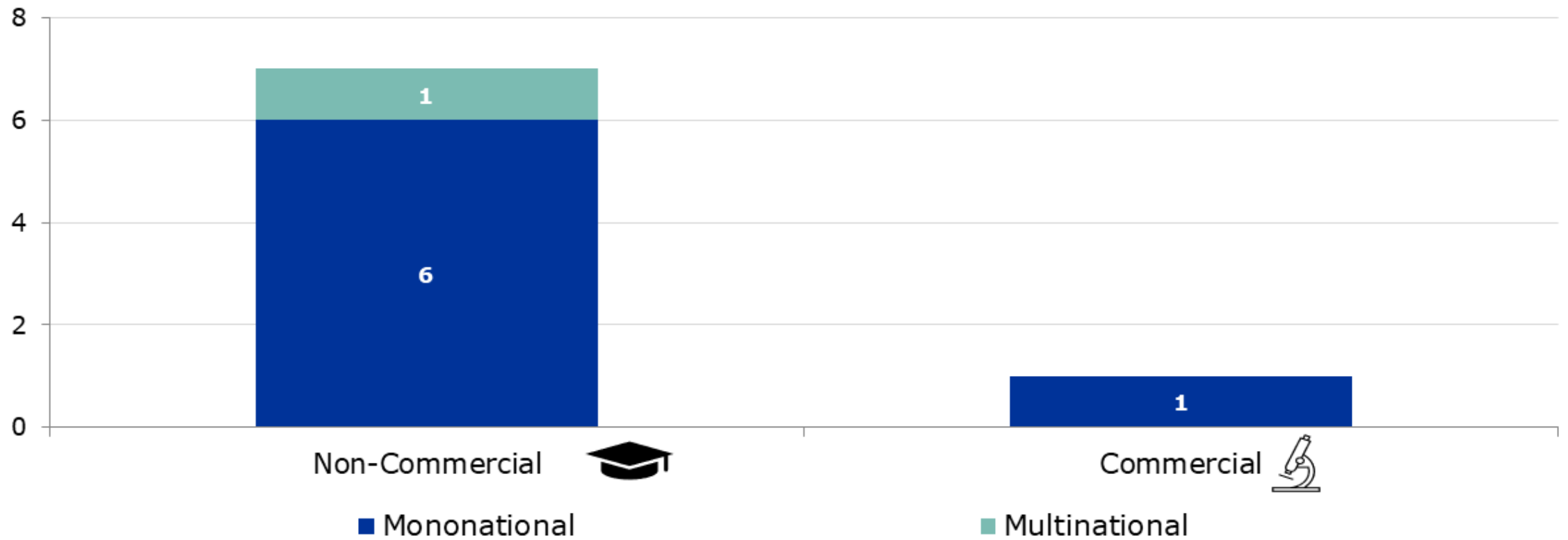
CTAs submitted in CTIS per month



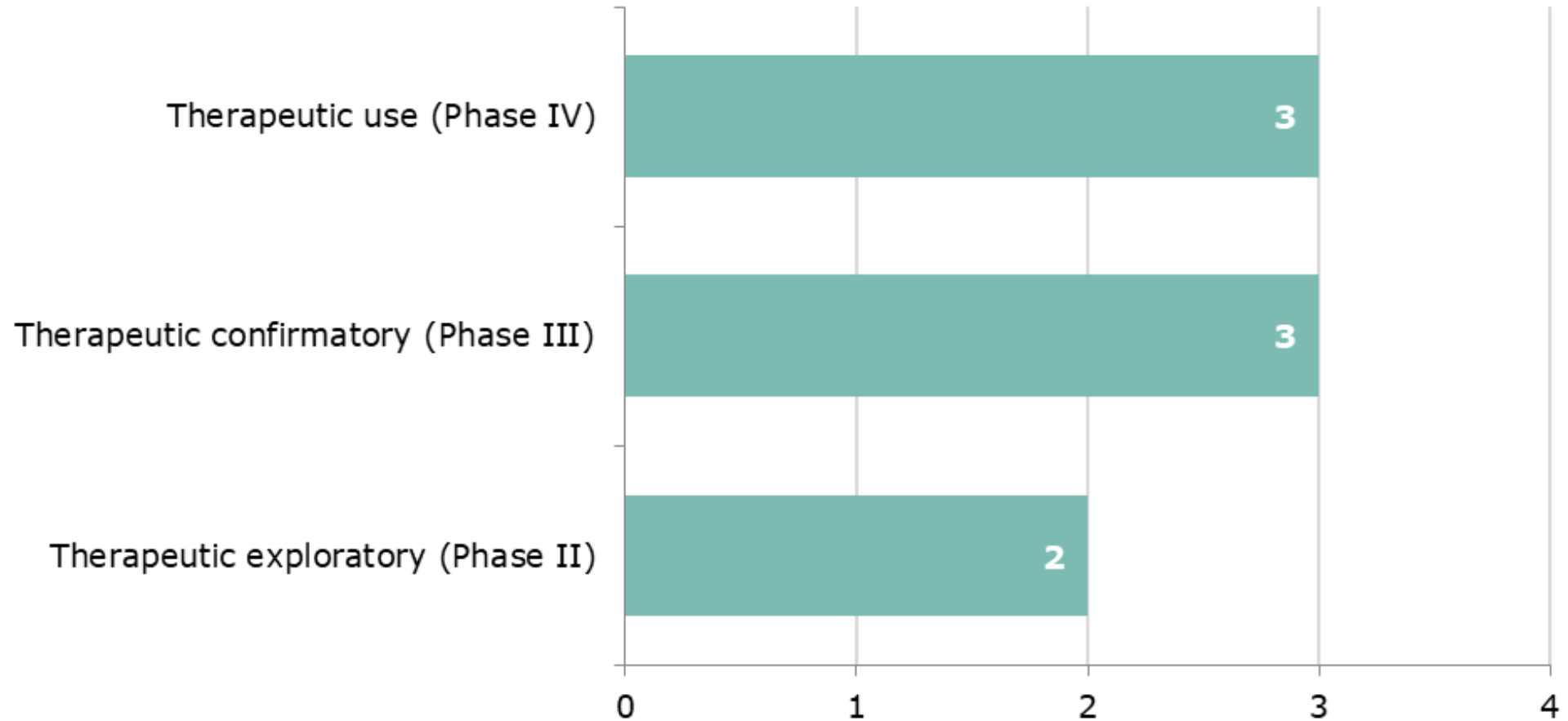
CTs per Trial status in CTIS Commercial versus Non-Commercial



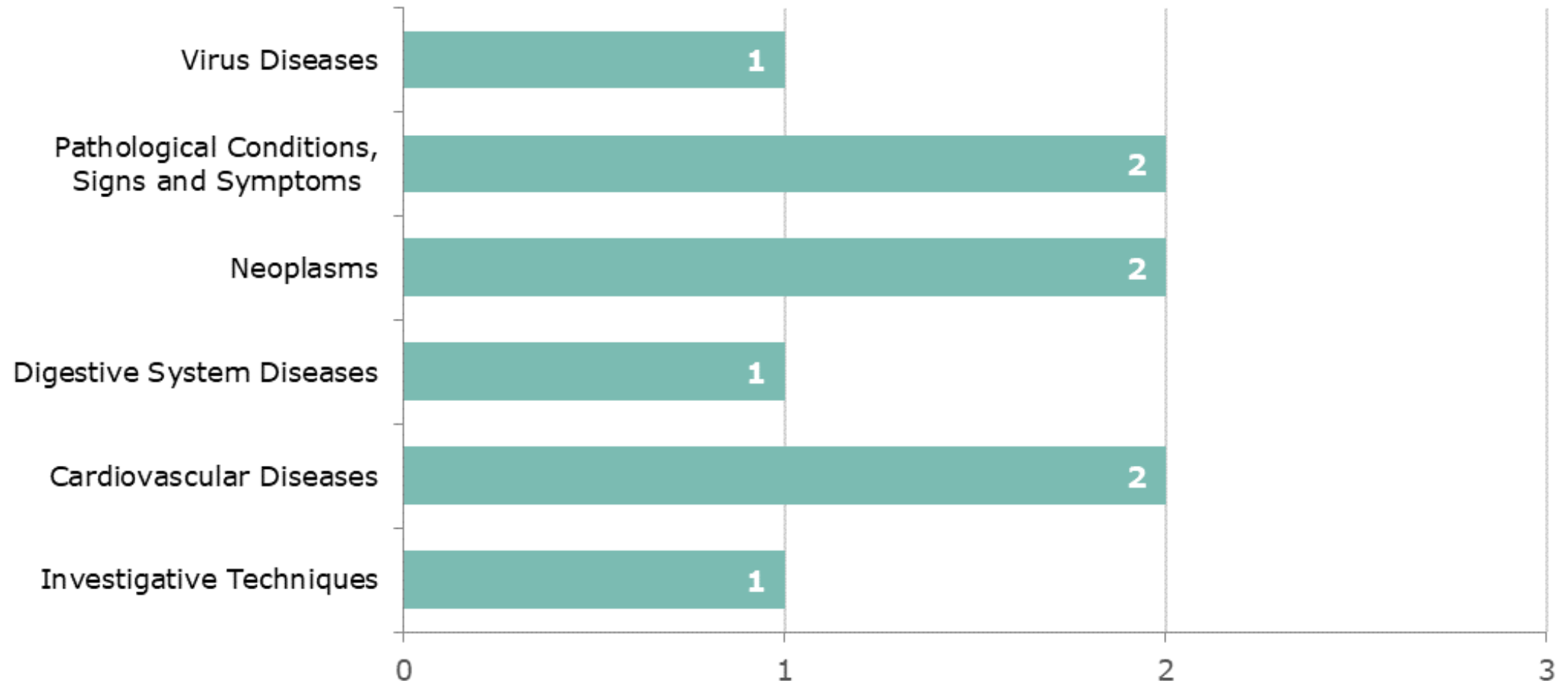
CTs with a decision in CTIS Split into Sponsor Type and Mono- vs Multinational

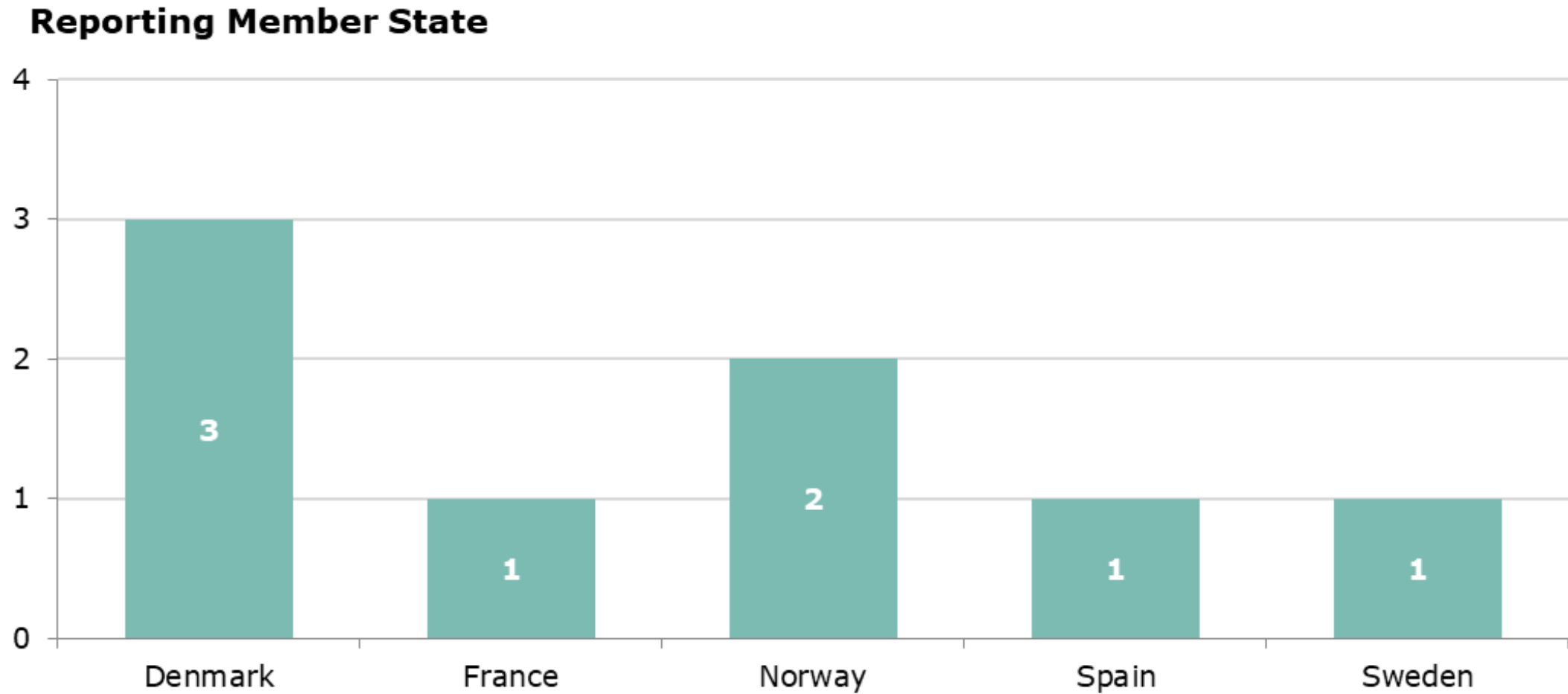


CTs with a decision in CTIS per phase



CTs with a decision in CTIS per therapeutic area







Session 2

CTR and transition period



Kristof Bonnarens

Team leader, Directorate-General for Health and Food Safety

DG SANTE, European Commission, Belgium



CTR and transition period

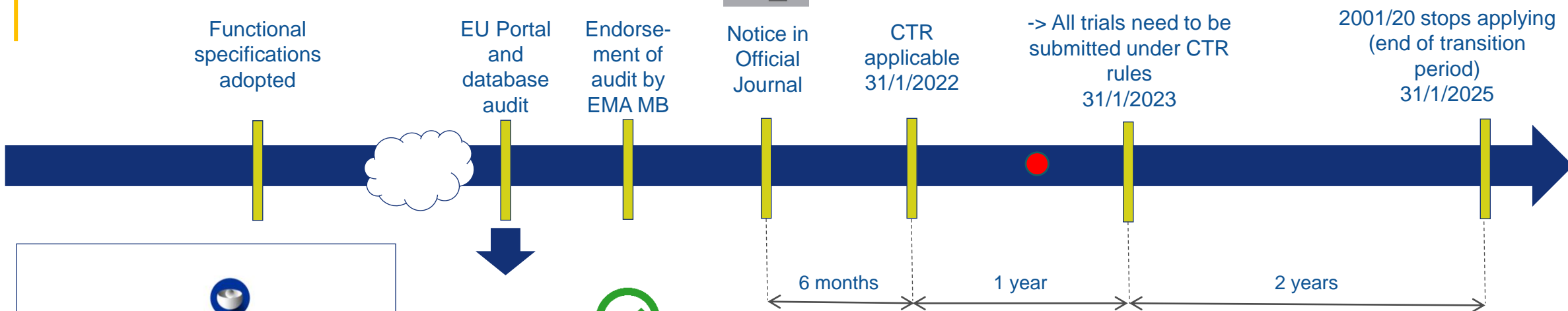
Kristof Bonnarens, DG SANTE

*Clinical Trials Information System
(CTIS) Webinar: 6 months of CTIS and
looking forward*

Clinical Trial Regulation 536/2014 (CTR)



- The CTR was **published in May 2014**. Its aim was to correct the shortcomings of the existing clinical trials directive (CTD) and to foster research in the EU while maintaining a high level of protection for participants
- It became **applicable on 31/1/2022** but is **optional** for one year
- After 31/1/2023, **every new clinical trial** will need to be submitted and authorised under the CTR
- The CTR allows that **trials authorised under the CTD continue until 31/1/2025**, after which they need to be transitioned to the CTR **if still ongoing**.



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SCIENCE MEDICINES HEALTH


25 March 2015
EMA/42176/2014 Rev. 1, Corr.*
Compliance and Inspections

Functional specifications for the EU portal and EU database to be audited



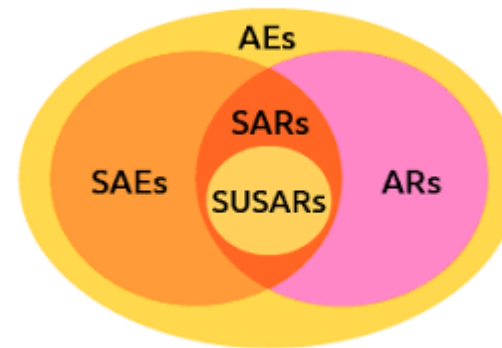
A hand is pointing to the word 'OBJECTIVES' in a word cloud. The word cloud contains various business-related terms such as 'STRATEGIC', 'PLAN', 'MISSION', 'STATEMENT', 'VALUE', 'INTEGRITY', 'ACCOUNT', 'VISION', 'EXPENSE', 'PRICE', 'FINANCE', 'GUIDING', 'RULE', 'VISION', 'GOALS', 'PREFERENCE', 'MARKET', 'COMPANY', 'PROFIT', 'DEVELOPMENT', 'BENEFITS', 'CONDUCT', 'STATEMENT', 'ACCOUNT', 'VISION', 'EXPENSE', 'PRICE', 'FINANCE', 'GUIDING', 'RULE', 'VISION', 'GOALS', 'PREFERENCE', 'MARKET'. The word 'OBJECTIVES' is the largest and most prominent in the cloud.

Streamlining of the Clinical Trial Authorisation process :

- **One submission** to all Member States concerned by a given trial of a **harmonised application** through a **single online interface** with maximum timelines
 - CT application contains
 - a “**pan-European**” **part I** (e.g. protocol, IB, IMPD), assessed by a **Reporting Member State** (RMS) in close collaboration with all Member States Concerned (MSC)
 - a “**national**” **part II** (e.g. informed consent), assessed **by every MSC**
 - Result of the assessment is a **single decision** per Member State – opt out to the part I conclusion is possible.
- 

Objective: participants rights and safety

1. Coordinated safety assessment through work-sharing and streamlined safety reporting (no more national reporting of SUSARs)
2. Strengthened rules on the protection of patients and informed consent, specific modalities on cluster trials



Objective : transparency



1. Transparency as a baseline – everything in CTIS is publicly available, provided exceptions (CCI, personal data, internal MS processes).
2. Additional information on the status of a trial in a given MS
3. Obligations for result reporting within set timelines, and specific reporting for laymen.

Implementation activities



- Extensive Q&A on the interpretation of the CTR have been prepared in collaboration with the Clinical Trial Expert Group and will be updated progressively where needed
- Additional templates and specific information on Eudralex Volume 10 https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10_en
- Implementation and delegated acts published or under preparation
- Clinical Trials Coordination and Advisory Group (CTAG) : exchange of information between the Member States and the Commission on the experience acquired with the CTR

Keep in touch



ec.europa.eu/



europa.eu/



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[@EuropeanCommission](https://www.facebook.com/EuropeanCommission)



[European Commission](https://www.linkedin.com/company/european-commission)



[europeancommission](https://www.instagram.com/europeancommission)



[@EuropeanCommission](https://www.youtube.com/@EuropeanCommission)



[EUTube](https://www.youtube.com/EUTube)



[EU Spotify](https://open.spotify.com/playlist/37i9ZQWf54XW533393333)

Thank you



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Slide xx: **element concerned**, source: **e.g. Fotolia.com**; Slide xx: **element concerned**, source: **e.g. iStock.com**





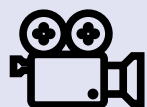
Session 1 and 2

Q&A session



Coffee break till 10:40

Next up – Member states and Sponsor experience and reflections



**Recorded
Event**

Please note that this event is being recorded. The recording, or parts thereof, may be used/published on the EMA website after the event for training and communication purposes.

For information on the processing of personal data, please refer to the [General EMA Privacy Statement](#) and the [EMA Privacy Statements on the organisation of meetings and events](#).



Session 3

Members States experience and reflections



Monique Al

Head of National Clinical Trial Office

CCMO, The Netherlands

Member States Experience and reflections – Netherlands

Monique Al

Head National Clinical Trial Office – CCMO Netherlands

CTIS webinar , 1 July 2022



Transition period – up to 31 January 2025

This transition period is as follows (see also questions 1.2 and 11.2 of the Q&A CTR, Eudralex volume 10):

1st year: initial application according to old (Directive 2001/20/EC) and new legislation (CTR) is allowed

2nd and 3rd year: all initial applications according to the CTR

4th year and later: all ongoing clinical trials should comply with the requirements of the CTR

During the three years transition period, substantial modifications of clinical trials approved under Directive 2001/20/EC can be submitted according to this old legislation.

https://health.ec.europa.eu/system/files/2022-05/regulation5362014_ga_en.pdf



Transition procedure – from CTD to CTR

Some points of attention:

- Only active clinical trials without any pending/ongoing assessment in any of the EU/EEA countries are eligible for a switch;
- Only clinical trials that comply with the Clinical Trials Regulation as regards its substantial requirements can be transitioned;
- It is the sponsor's responsibility to assess the compliance to CTR.
- The process will require a new cover letter and new application form (Part I and II) to be completed in CTIS, and in case of multinational clinical trials, a harmonised or at least a consolidated protocol;
- A submission for transition of a multinational trial should only be submitted to those MSCs where the trial is ongoing. New MSC(s) cannot be added in this submission.

- https://health.ec.europa.eu/system/files/2022-05/regulation5362014_qa_en.pdf
- [2018_05_CTFG_Best_Practice_Guide_for_sponsors_of_transition_multinational_clinical_trials.pdf \(hma.eu\)](#)



Harmonised protocol

- One identical clinical trial protocol in all MSc
- Same version and date
- If clinical trial conducted under same EudraCT number not sufficiently harmonised:
 - A sponsor needs to harmonise them via substantial amendments under Directive 2001/20/EC in order to be able to transition them as one trial under the Clinical Trials Regulation



Consolidated protocol

Core protocol information (to be identical) in any consolidated version

- EudraCT number
- CT Title
- Primary objective
- Primary end point
- End of CT definition
- Main inclusion and exclusion criteria



Consolidated protocol

Should:

- Have a specific date version
- Indicate at the beginning the version and date of the last authorised version of the document per MS used for the consolidation
- Indicate in e.g. an annex specific wording of sections where the text in the consolidated version is different from the authorised per MS

The sponsor does not require prior approval of the consolidated version in a substantial modification under CTD before transition



Transition procedure – from CTD to CTR

Part I application (latest approved versions of documents under CTD):

- new cover letter (include EudraCT number and name of the ethics committee who has given a favorable opinion on the clinical trial under CTD);
- new application form (Part I and Part II) → direct data input CTIS
- (harmonised or consolidated) protocol;
- Investigator's Brochure
- GMP relevant documents;
- IMPD;
- The latest approved version of documents related to non-investigational medicinal products (i.e. auxiliary medicinal products under the CTR, if applicable).

Redacted versions of the documents are expected when needed in compliance with transparency requirements!

Signatures on various part I and II documents (e.g. investigator CV, DoI, cover letter), are not part of the clinical trial application. The site suitability statement Annex I, section N67) shall be submitted according to the system of the Member State concerned, meaning that signature requirements for this document are subject to national law!



Transition procedure – from CTD to CTR

Part II application

- the latest approved versions of the subjects' information sheet and the informed consent form.

Important:

In case the sponsor cannot provide certain documents listed in Annex I of the Regulation, which were not required under the Directive, a sponsor should upload a blank document clarifying that this aspect was assessed by National Competent Authority (NCA) and/or Research Ethics Committee (REC) and therefore is covered by the conclusion of the assessment.

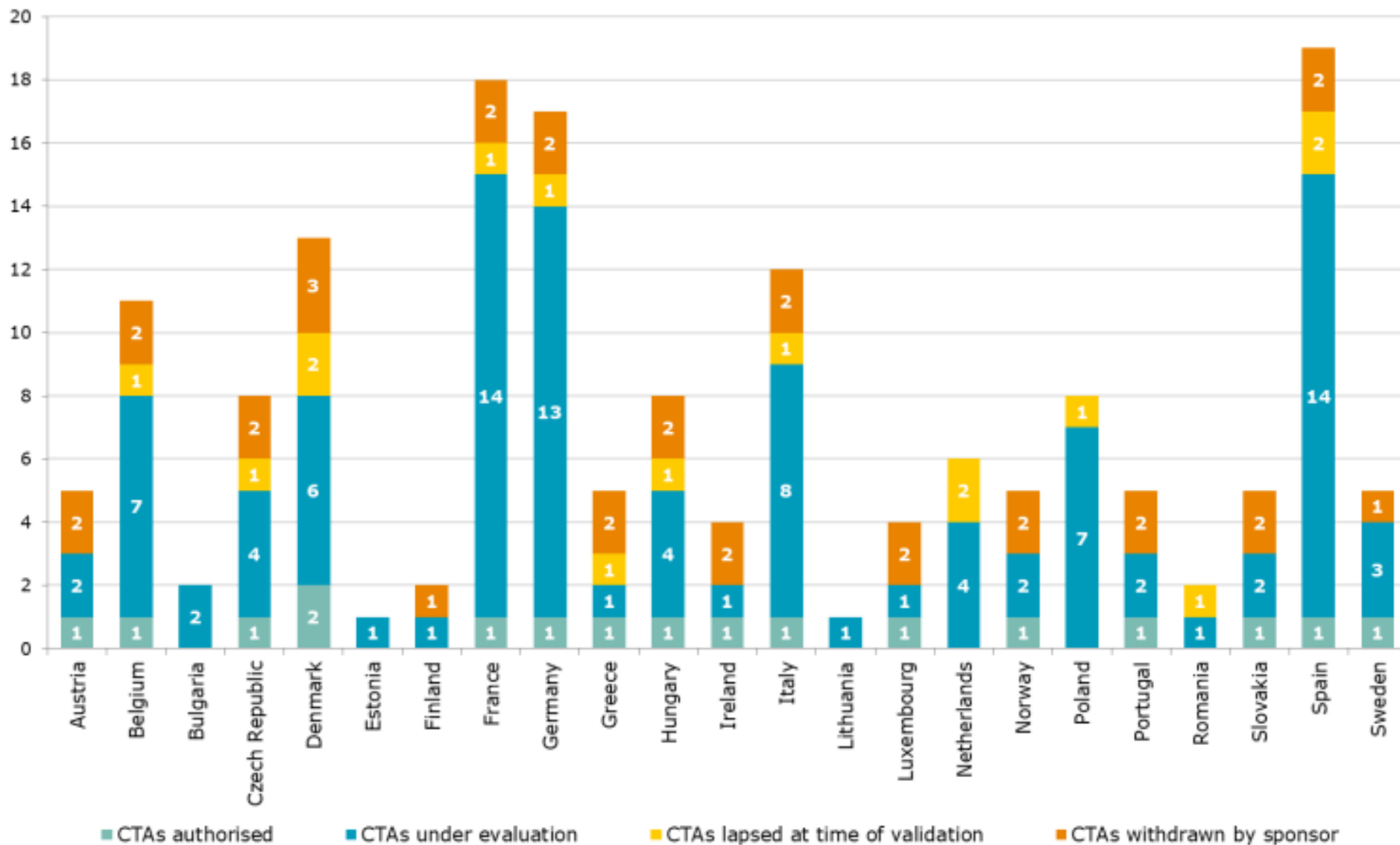
https://health.ec.europa.eu/system/files/2022-05/regulation5362014_qa_en.pdf

[2018_05_CTFG_Best_Practice_Guide_for_sponsors_of_transition_multinational_clinical_trials.pdf\(hma.eu\)](#)



Number of CTAs in CTIS per MSC, dd 20 May 2022

Member States Concerned



High number of considerations due to technical features CTIS

High number of lapsed applications

- Uploading documents: naming and structure of documents
- Update of documents due to RFI
- Resubmission of lapsed applications



See also: <https://english.ccmo.nl/investigators/clinical-trials-with-medicinal-products-ctr/preparation-ctr/compiling-research-dossier-general-information>

The documents in the clinical trial application should be in a searchable format.

Furthermore, it is strongly recommended to adhere to the structure of CTR Annex I when titling your documents in CTIS. Please use the codes and filenames as given in the [Instruction on uploading, naming and changing documents in CTIS](#). This instruction also specifies how to change your clinical trial application in CTIS if an RFI requests new documents or document changes.

Explanatory notes and templates (including national requirements) are given in the sections [Form and MSC](#), [Research dossier part I](#) and [Research dossier part II](#).



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

Document upload

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

Title*

Protocol ABC123 v4 12Feb2022

Type*

Protocol (for publication)

Language

English

Version*

1

System version

1.00

Date*

29/03/2022

Comment

(optional)

Remove

The above document(s) will be published.

Cancel

Attach

The **Title** of the document in CTIS. The filename as it was uploaded is pre-filled here, this should be changed to match the requirements for document coding and titles (see next slide). Always remove version and date from the Title, because the Title cannot be changed when uploading a newer version later.

Change the default version (1) and default date (today) to the actual date and version of the document (in this example: version 4, date 12/02/2022).

Please note: the version field is free text: e.g. a zero or N/A can be filled in for documents that do not have a version number.

The **filename** of the uploaded file. The uploaded files can have any name, except for some forbidden characters:

The filename provided is not valid. No special characters (/ , . ; |) allowed.

The CTIS System version of a document, always starting at 1.00 for the first version of a document uploaded into CTIS, and increasing when using the Update functionality. Cannot be edited. System Version therefore does not necessarily match the true version.

Document codes and titles in CTIS

Please adhere to the structure of CTR Annex I for document codes and titles when uploading files in CTIS, as shown below. Please fill in the requested information in the marked [grey fields]. Make sure that all documents have self-explanatory titles including relevant identification when applicable as mentioned below. Please note that the files uploaded into CTIS can have any filename; the coding and naming applies to the document name in CTIS (the field ‘Title’ in the upload window. The original filename is pre-filled in the field ‘Title’ but can be adapted. Version number and date should not be in the document title, instead indicate the correct version number and date in the corresponding fields in the upload window.

B. Cover letter

B1_ Cover letter [EU CT number]

D. Protocol

D1_ Protocol [EU CT number]

D1_ Protocol synopsis_ENG [EU CT number]

D1_ Protocol synopsis_NL [EU CT number]

D2_ Protocol modification nr [number] [EU CT number] *(in case of SM as separate document)*

D3_ DSMB Charter [EU CT number]

D4_ Patient facing documents [questionnaire, diary] *(if applicable)*

D5_ Master protocol [EU CT number and name] and sub-protocol [name and specific number/ID] *(applicable for complex CT)*

E. Investigator’s Brochure

E1_ IB [product name]

F. Documents GMP compliance (if applicable)

F1_ GMP declaration [abbreviated name manufacturer/importer]

F2_ QP declaration [abbreviated name manufacturer/importer]

F3_ Other statements/licences *(e.g. import license)* [abbreviated name manufacturer/importer]

G. Investigational Medicinal Product Dossier

G1_ IMPD_Q [product name]

G1_ IMPD_E-S [product name]

G2_ SmPC [product name]

H. Auxiliary Medicinal Product Dossier

H1_ AxMPD [product name]

I. Scientific advice and pediatric investigational plan (PIP)

I1_ Scientific advice [name organization]

I2_ PedCo opinion

I3_ PIP decision [name agency]

J. Labeling

J1_ Label IMP_NL [product name] *(include MS in title, example for NL)*

J1_ Label IMP_ENG [product name]

J2_ Label AxMP_NL [product name] *(include MS in title, example for NL)*

J2_ Label AxMP_ENG [product name]

K. Recruitment arrangement

K1_ Template recruitment arrangements

K2_ Recruitment material [description]

L. Subject information sheet, informed consent form, other subject information material

L1_ SIS and ICF [description] *(e.g. SIS and ICF adults, SIS and ICF 12-16 yr)*

L2_ Other subject information material [description] *(e.g. information leaflet adults)*

M. Suitability investigator

M1_ CV Investigator [name investigator and clinical trial site] *(use abbreviations)*

M2_ DoI Investigator [name investigator]

N. Suitability facilities

N1_ Site suitability form [name investigational site]

O. Proof of Insurance or idemnification

O1_ Trial participant insurance certificate

O2_ Proof of coverage sponsor or investigator [name sponsor/trial site] *(if not covered by O1)*

P. Financial and other arrangements

P1_ Template compensation trial participants, investigator, funding and other arrangements

R. Compliance GDPR

R1_ Template on the collection and use personal data

S. Biological samples

S1_ Template on the collection, use and storage of biological samples

Documents codes and titles

B. Cover letter

B1. Cover letter [EU CT number]

D. Protocol

D1. Protocol [EU CT number]

D1. Protocol synopsis_ENG [EU CT number]

D1. Protocol synopsis_NL [EU CT number]

D2. Protocol_modification nr [number] [EU CT number]

D3. DSMB Charter [EU CT number]

D4. Patient facing documents [questionnaire, diary] (if applicable)

E. Investigator's Brochure

E1. IB [product name]

J. Labeling

J1_ Label IMP_NL [product name] (include MS in title, example for NL)

J1_ Label IMP_ENG [product name]

J2_ Label AxMP_NL [product name] (include MS in title, example for NL)

J2_ Label AxMP_ENG [product name]

K. Recruitment arrangement

K1_ Template recruitment arrangements

K2_ Recruitment material [description]

L. Subject information sheet, informed consent form, other subject information material

L1_ SIS and ICF [description] (e.g. SIS and ICF adults, SIS and ICF 12-16 yr)

L2_ Other subject information material [description] (e.g. information leaflet adults)

M. Suitability investigator

M1_ CV Investigator [name investigator and clinical trial site] (use abbreviations)

M2_ DoI Investigator [name investigator]



Form details

Initial Application details

Cover letter

Cover letter *



Cover letter_notsigned [Download](#)

English · Cover letter (for publication) · **System version 1.00**
Submission date 21/04/2022
· **Version 1** · 21/04/2022



Cover letter_signed [Download](#)

English · Cover letter (not for publication) · **System version 1.00**
Submission date 21/04/2022
· **Version 1** · 21/04/2022

Proof of payment of fee

Netherlands

Proof of Payment



Invoice details [Download](#)

English · Proof of payment (for publication) · **System version 1.00**
Submission date 02/05/2022
· **Version 1** · 02/05/2022

Compliance with regulation

Compliance with Regulation (EU) 2016/679

Compliance with Regulation (EU) 2016/679 *



Declaration of compliance with data protection EU_not signed [Download](#)

English · Compliance with Regulation (EU) 2016/679 (for publication) · **System version 1.00**
Submission date 21/04/2022
· **Version 1** · 31/03/2022



Declaration of compliance with data protection EU_signed [Download](#)

English · Compliance with Regulation (EU) 2016/679 (not for publication) · **System version 1.00**
Submission date 21/04/2022
· **Version 1** · 31/03/2022

Deferral publication dates

2. Uploading documents into CTIS in response to an RFI: change application

Clinical trials

Notices & alerts 38

Annual safety reporting

RFI

User administration

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.

MSCs

Part I *

Part II

Evaluation

Timetable

Validation

RFI 1

Collapse all ^

RFI-CT-2022-501381-22-00-IN-001

Due: 07/02/2022

MSC: Netherlands

Submission date: 27/01/2022

Due date: 07/02/2022

Reason

Incomplete

Supporting documentation

MS:

Quality

No document available

Non-Quality

No document available

Sponsor:

General documentation

Quality related documentation

Please notice that in this section only supporting documentation to the response should be uploaded. If a new version of any of the documents included in the Annex I of Regulation (EU) 536/2014 needs to be provided, should be uploaded on the respective section of the application dossier and NOT here

Sort by

12

Response to consideration

Consideration number

RFI-CT-2022-501381-22-00-IN-001-01

Application section parts

Part I - Clinical

Application section and document

Protocol

Consideration

Please submit

Response

Textual response

Documents related to the response

Optional, only for documents containing the response to this specific consideration. If the consideration requests a missing or updated document, do not upload it here, but instead use 'Change application'!

Add document

Save response

For any changes to the application (documents or data) requested in the RFI. E.g. missing documents requested during validation, requests to modify document title/date/version during validation, or a new protocol version requested during assessment.

Change application

Optional, in case of a response to more than one consideration. Upload response letter here. There is a separate upload for a response on quality related considerations

Add document

Add document

Clicking 'Change application' and confirming it, leads you back to the dossier, where documents can be added similarly to the initial submission. Click the lock and navigate to the location of the dossier where the change should be made.

The screenshot displays the 'Trial specific information (Part I)' section of a CTIS dossier. At the top right, there are three buttons: 'Check', 'Save', and 'Withdraw'. Below this, the 'Trial details' section is expanded, showing a list of categories: 'Trial identifiers', 'Trial information', 'Protocol information', and 'Clinical trial protocol'. A red circle highlights a lock icon in the top right corner of the 'Trial details' section. Below the 'Clinical trial protocol' category, a document titled 'Protocol' is listed. A red circle highlights the 'Edit' icon (pencil) and another red circle highlights the 'Update' icon (document with arrow) for this document. A red arrow points from the 'Update' icon to a text box explaining its function. To the right of the document list, a red circle highlights the 'Add document' button. A red arrow points from this button to a text box explaining its function. The document details for 'Protocol' show it is in English, for publication, with system version 1.00, submission date 27/01/2022, and version 1.

Check Save Withdraw

Trial specific information (Part I)

Trial details

Trial identifiers

Trial information

Protocol information

Clinical trial protocol

Protocol *

Protocol

English · Protocol (for publication) · System version 1.00

Submission date 27/01/2022

Version 1 · 27/01/2022

Add document

Update: for uploading a new version of an existing document, e.g. protocol v2 with changes requested by the MS. You are asked to enter the version number and date, but the document title in CTIS cannot be changed!

Edit: for changing the title, version or date of an existing document. If by mistake an uploaded document contained a version or date in its title, or the indicated version and/or date do not match the documents, then you will likely be asked to correct this in the Validation RFI.

Add document: for adding fully new documents, e.g. missing documents requested by the MS during validation. The System version will be 1.00. Please use document codes and titles as explained earlier.

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

Trial identifiers

Trial information

Protocol information

Clinical trial protocol

Protocol *

Protocol

English · Protocol (for publication) · **System version 2.00**

submission date 27/01/2022

· Version 2 · 27/01/2022

Comment v2 uploaded in response to RFI

Add document

Previous versions 1

CTIS system version, does not necessarily match own version number

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

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

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

Form

MSCs

Part I

Part II

Evaluation

Timetable

Evaluation

Validation

RFI 1

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

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

Reason Incomplete

☒ Includes application changes

Changes to the application *

No document has been uploaded.

Discard changes

Add document

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

Resubmission of a trial

CT applications can lapse (e.g. when the sponsor misses a response due date), be withdrawn by the sponsor, or rejected by the authorities. CTs that are lapsed/withdrawn/rejected in all MSC, can be resubmitted.

For resubmission, go to the Summary tab of the CT page, scroll down to the Application section, and click the application you want to resubmit.

Clinical trials Notices & alerts 248 Annual safety reports

Study title

Not authorised 2022-503500-25-00 RMS: Netherlands

Summary Full Trial Information

(Scroll down)

APPLICATION AND NON-SUBSTANTIAL MODIFICATION

Type	ID	Parts
Initial	IN	Part I & Part II

Then, in the top-right corner, click Resubmit

Copy Resubmit

Form MSCs

Part I •

Part II Evaluation Timetable

Trial specific information (Part I)

Trial details

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

The documents of the original submission will be copied to the resubmission. Documents can be replaced if necessary (e.g. cover letter, or when a new version has been made). Please note: the version and date of all documents is reset to v1 and today, so click Edit (pencil icon) to enter the correct version and date for all documents. The resubmission will keep the **original CT-number, but ending with -01**.

Release notes on known issues and work arounds: <https://euclinicaltrials.eu/website-outages-and-system-releases>

On this page

[Planned interruptions CTIS](#)

[Planned interruptions related systems](#)

[About release notes](#)

[Release notes May 2022](#)

[Release notes January 2022](#)

Release notes May 2022

[Release notes v1.0.2.0 \(PDF, in English\)](#)

List of known issues and proposed workarounds:

- [for CTIS sponsor workspace users v1.0.2.0 \(PDF, in English\)](#)
- [for CTIS authority workspace users v1.0.2.0 \(PDF, in English\)](#)

Release notes January 2022

[Release notes v1.0.0.5 \(PDF, in English\)](#) [🔗](#)

List of known issues and proposed workarounds:

7. **Issue:** When responding to an RFI Part II, the user may not be able to edit part II if some of the other Member State concerned have already decided on the application. [CTCS-22231]

Workaround: The user should upload any documents that may need to be updated with the RFI consideration responses.

Thank you for your attention!

Questions?

Legal framework, guidances and standards for clinical trials with medicinal products:
<https://english.ccmo.nl/investigators/clinical-trials-with-medicinal-products-ctr>

Legal framework, guidances and standards for clinical investigations with medical devices:
<https://english.ccmo.nl/investigators/clinical-investigations-with-medical-devices>

Legal framework, guidances and standards for performance studies with IVDs:
<https://english.ccmo.nl/investigators/performance-studies-using-in-vitro-diagnostics-ivdr>





Outi Konttinen

General Secretary and Group Leader, M.Soc.Sci

The National Committee on Medical Research Ethics (Tukija), Finland



Member State experience and reflections – Finland

CTIS webinar: 6 months of CTIS and looking forward, 1.7.2022

Outi Konttinen

4.7.2022

CTR implementation in Finland

Clinical Trials Regulation (EU) No 536/2014

National legislation:

- Amendments to the Act on Medical Research (488/1999; 984/2021)
- New **Act on Clinical Trials on Medicinal Products** (983/2021)
- Amendments to related laws (Medicines Act, The Criminal Code of Finland)
 - These additions and amendments entered into force at the same time as the application of the CTR begun (31st Jan. 2022)
- Decree of the Ministry of Social Affairs and Health on Fees Charged Regarding Clinical Trials on Medicinal Products (103/2022)
- The formation of the **National Committee on Medical Research Ethics (Tukija)** and the expertise of its members are stated in the Government Decision of appointment (27 January 2022, STM/2022/21)

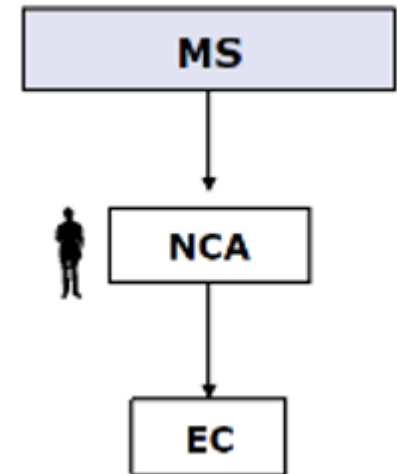
Review of clinical trials, national solution

New Act on Clinical Trials on Medicinal Products

([983/2021](#))

- Collaboration with Finnish Medicines Agency Fimea (NCA) in processing the CTAs in CTIS, but Tukija is independent and organizationally separate from the agency
- Both Fimea and Tukija evaluate CTA part I and II
- CTA part I: coordinated review of protocol and other scientific aspects; Assessment Report Part I by RMS/NCA (Fimea); no access to IMPD for Tukija
- Tukija is responsible for drafting the Assessment Report Part II (ARII): Fimea can express views in regard to evaluation of Part II and to the preparation of ARII

Organizational Model 2 (EMA)



Change management

- A project to reorganize ethical evaluation of clinical trials; years 2020-2021
 - e.g. assessment on training needs among NREC's members and secretariat; development of the IT national systems and guidelines
- National pilot on CTR
- Close collaboration with Tukija and Fimea; workflow and processes
- Communication and training both for Sponsors and Authorities

National requirements - FI

Part I, no additional national requirements

- Adherence to Annex 1
- Part I: No special national requirements, English accepted (no requirement of protocol summary in Finnish);
- No signatures required (neither wet-ink or electronic signatures, incl. protocol and GDPR statement).

Fees: Academic sponsors exempted from fees, commercial sponsors fees appx the same as under Directive. Fimea collects single fee covering both NCA + ethics assessment; the billing address (or a statement of exemption) must be provided under "Proof of Payment" -section in CTIS

Part II, national requirements

- Tukija has published a list of requirements related to part II application. [Link to the list of requirements \(Fi\)](#) (*will be translated into English soon*)

Applications in CTIS from January 31, 2022

Overall situation (28.6.2022), 7 applications concerning Finland:

- 1 authorized (Transition Trial)
- 1 withdrawn
- 1 not valid
- 4 under evaluation/pending
 - 2 x parts I & II
 - 2 x part I only
 - 3 x FI as RMS (one multinational CT)

Trial information

Conditions(s)	Aneurysmal subarachnoid hemorrhage needing ventilatory care in intensive care unit	Member states concerned	FI
Sponsor	Turku University Central Hospital	Low intervention study	No
Trial Phase	Therapeutic exploratory (Phase II)	Population type	Incapacitated population, Subjects incapable of giving consent personally, Patients
Therapeutic area	Diseases [C] - Nervous System Diseases [C10]	Transition Trial	Yes
First submitted	30/05/2022		
Last update	22/06/2022		
Medical device	No		

Evaluation time 23 days

Overall Trial status

Start of trial

Global end of trial

Trial									Recruitment		
Member state	Current status	Decision date	Last update	Start date	Temporary Halt	Restart	End (or early termination)	Reason for early termination	Start	End	Restart
Finland	Authorised	22/06/2022									

Experience, lessons learned, questions - 1

User Management

- Fimea is MS Admin and Tukija is NOA
- We experienced no major problems in registering and providing the required Roles and Permissions in CTIS
- Viewer Roles have been given to members of the committee
- Only one committee member (Vice chair) experienced difficulties in reactivating an old EMA account

Experience, lessons learned, questions - 2

Workflow/Evaluation

- The integrity of the information. Documents to be downloaded to portal as PDF-versions rather than Word; the version date of Word documents is not stable.
- Communications outside of CTIS both with Sponsors and NCA.
 - When RFI is issued, will there be an email notification to the applicant about this RFI being added to CTIS? This should not happen, since all communication is done in CTIS.
 - So far, we have not been able to avoid communication outside CTIS; *it would be very useful to have a general chat function in place*
- Responses to RFIs:
 - Important to avoid duplicate downloads
 - Sponsors seem to prefer answering in separate document rather than in structured data fields? It is important for authorities to use structured data.

Experience, lessons learned, questions - 3

- Patient cards, Questionnaires, Diaries and other so called patient facing documents are usually provided after consenting and not required per CTR. What should be done with them? Is it possible to agree on a common approach?
 - Commission will publish guideline on the issue by beginning of August.
- What happens if the Part II Assessment Report is issued first and evaluation of Part I has not finished yet but may require changes to e.g. ICF? How to update part II documents?
 - This question needs to be solved soon.

Experience, lessons learned, questions - 4

Transition trials

- Transition Trials are assessed only in the validation phase
- Sponsor may be advised to withdraw the request for transitioning the trial and submit the request for substantial amendment under the CT Directive. When to communicate this to sponsor? Via RFI during validation phase?
- What should FAR I, FAR II and National Decision on a Transition Trial include?
 - FI used blank documents with minimum reference information on CT concerned (Part I: introduction, conclusion; Part II: conclusion; Final decision)

Experience and lessons learned - 5

Publication:

- Questions and answers (structured data fields, except financial arrangement) will be published at the time of the decision unless there's a deferral
- There seems to be a need for clarity on what will be or won't be published and how?

Conclusion

- Our experience is that processing of applications in CTIS is efficient.
- The system is still under development and authorities are well committed to that work.
- The first phase of the transition phase will end in six months; we would like to receive more applications in CTIS before that.

**Thank you for your
attention!**

<https://www.tukija.fi/>
info(at)tukija.fi

@TUKIJAViestii

4.7.2022



Stefan Strasser

Head of Clinical Trials, Institute Surveillance

BASG - Austrian Federal Office for Safety in Health Care

AGES - Austrian Agency for Health and Food Safety

Austria

Clinical Trials Information System (CTIS) webinar

6 months of CTIS and looking forward

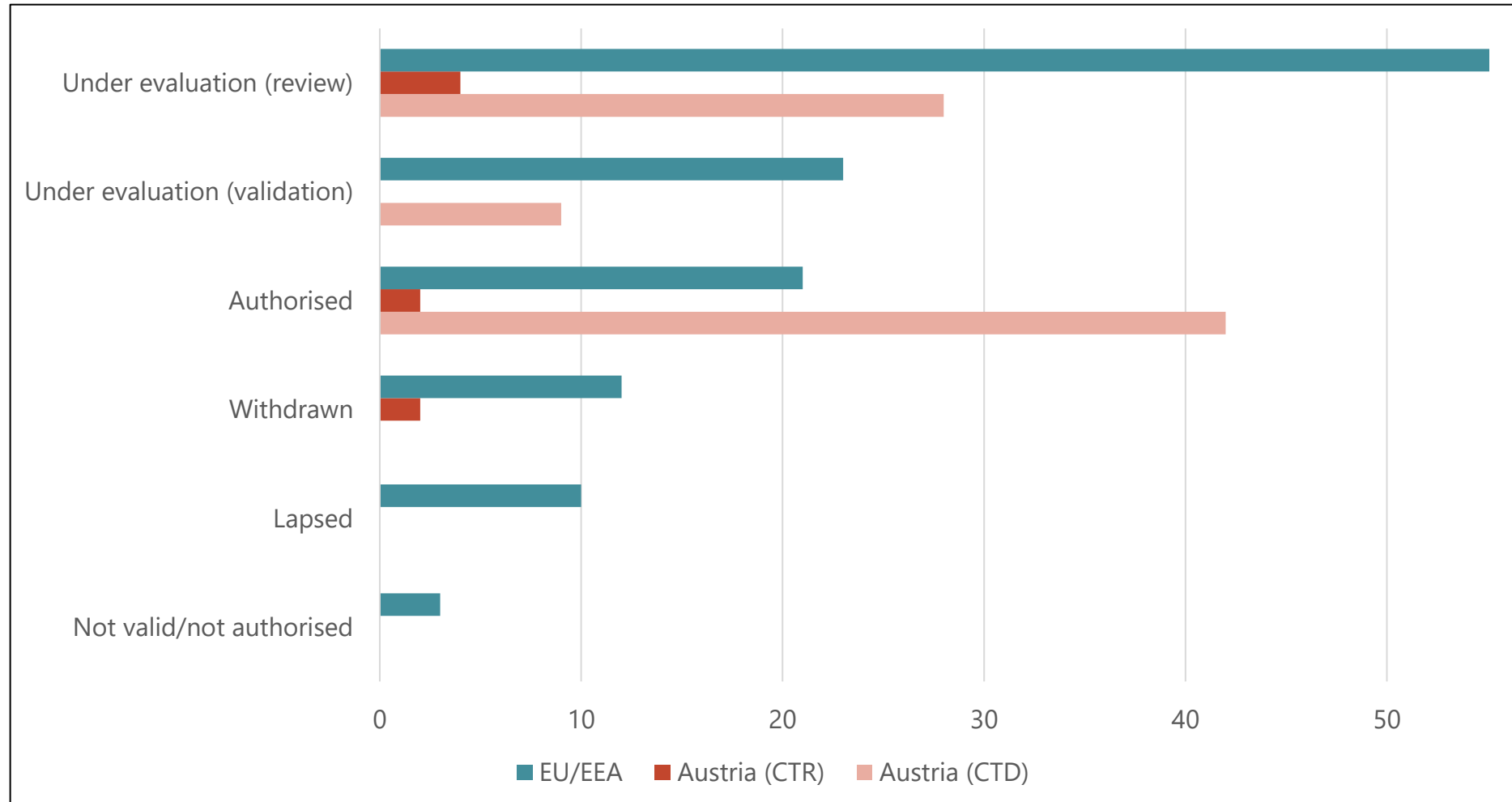
The Austrian experience

Stefan Strasser, MD, 01.07.2022

Austrian Medicines and Medical Devices Agency

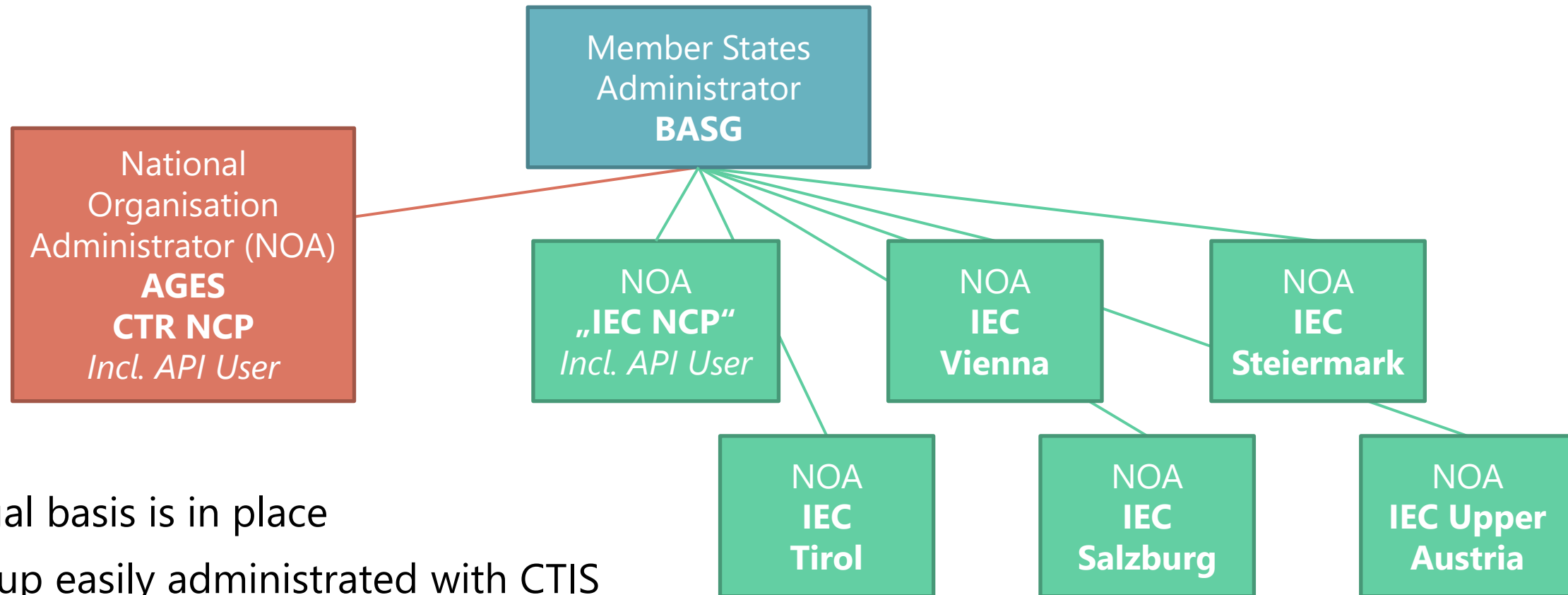
Current situation for Austria

<https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-regulation/clinical-trials-regulation-progress-implementation>



The Austrian National setup

Roles and responsibilities



- Legal basis is in place
- Setup easily administrated with CTIS
- Functionalities fully support legal structure
- So far no relevant technical issues

Notified Ethics Committees under the CTR

<https://www.sozialministerium.at/Themen/Gesundheit/Medizin-und-Gesundheitsberufe/Medizin/Arzneimittel.html>

 Bundesministerium
Soziales, Gesundheit, Pflege
und Konsumentenschutz

Coronavirus

Corona-Schutzimpfung

Services

Themen

Ministerium

  LL DE 

- Ethikkommission der Medizinischen Universität Graz
- Ethikkommission der Medizinischen Universität Innsbruck
- Ethikkommission der Medizinischen Fakultät der Johannes Kepler Universität Linz
- Ethikkommission für das Bundesland Salzburg
- Ethikkommission der Medizinischen Universität Wien

Mobilität in Europa

Mitteilungen für das öffentliche
Gesundheitswesen

Nicht übertragbare Krankheiten

- • Ethikkommission der Medizinischen Fakultät der Johannes Kepler Universität Linz
- • Ethikkommission für das Bundesland Salzburg
- • Ethikkommission der Medizinischen Universität Wien

Distribution of responsibilities

Who does what?

- **Direct access** to CTIS for all actors in the process → **ok ✓**
- **(Timely) update** in the National IT systems via API → **ok ✓**
- Ethics Committees included in
 - **Validation**
 - **Review for Part I and Part II**
- Working in the National systems → **coordination in CTIS** → **ok ✓**
- Agency coordinates „Validation“ and „Part I Assessment“ → **ok ✓**
- Responsible **Ethics Committee coordinates „Part II Assessment“** → **ok ✓**
- **Decision on the trial** („Authorise“) taken by the Agency → **ok ✓**

Assessment reports and RFI

At the end of the day it comes down to uploading a document...

BASG/AGES

Ethics Committee

Part I Section 1 - Introduction – Draft

Part I Section 2 - Quality Assessment – Draft

Part I Section 3 - Preclinical Assessment – Draft

Part I Section 4 - Clinical Assessment – Draft

Part I Section 5 - Statistical Methodological Assessment – Draft

Part I Section 6 - Regulatory Assessment – Draft

Part I Section 7 - Conclusion – Draft

Download to the National IT system

We are an „API MSC“.

- Agency IT system PHAROS is essential for
 - Workflow management
 - Legal decision making
 - Finances & Statistics
- From day 1 Austria followed the strategy of an National IT system and an API
- Similar situation for Austrian Ethics Committees (ECS)

Status quo:

- **National data model and workflow fully functional.**
- **API functional with minor bugs → dependent on EMA for fixes and updates.**
- **No manual duplication of data, minimal manual transfer (RFI list, reports).**
- **Reduction in training for „regular“ assessors.**
- **Currently most work is done by case managers.**

- Distribution of subtask to IEC → **ok** ✓
 - *description of subtask not ideal (too many mandatory fields, unclear view between designator and designee)*
- Visibility of documents → **working, but a bit messy**
 - *together with our National system it works better, especially for administrative staff*

Challenges we encountered:

- **correct naming and versioning of documents**
- **extensive use of redaction**
- **representing IMP via ATC code did not provide the required visibility**
 - *Change to representation via substance worked in this case*
 - *Best practice for future cases*

Assessment and RFI

- Distribution of subtask to IEC → **ok** ✓
- Assessment reports → **working, but formatting is inconsistent and not to handle**
 - *will have to be further improved by CTEG/CTCG and implemented by EMA*
 - *maybe MS Office is not the best tool?*

Challenges we encountered (also for validation but less critical there) :

- **RFI module is not very user-friendly**
 - **Overview in CTIS is not good → work-around via Excel Download**
 - **Formatting is lost, symbols are incorrectly translated.**
 - **Transfer to the assessment reports is burdensome.**
- **Several RFIs can be sent by „mistake“ → problem for Sponsor when responding.**
- **Second round of RFI was not possible (to be tested in Training Environment).**
- **Bug: RFI modul froze due to Part II lapse in another MSC.**

Overview and searches

Where is my trial?

- Our main search is „*Tasks* => *My group* => „*Pending*“
 - If all previous tasks are assigned, this should give only the new tasks.
 - Could be the „default setting“ of the advanced search.
- Our approach is to assign all pending tasks, before starting to work on any of them. CTIS opens a task after it has beend assigned, which is burdensome.
- The „worklist feature“ could be enhanced by opening any task in a new window. The setup of the worklist should be saved. So the „going back to my original worklist“ is faciliated.
- **We are managing the overview so far – but we have less then 10 procedures.**

Transition trials

- It was our first experience with CTIS.
- The trial was large and complicated („SolidAct“) and needed three attempts.
- Harmonisation under the Directive was not complete.
- Best-practice for transition was put to the test.

Challenges we encountered:

- **What we want is**
 - **all authorised documents uploaded at the time of transition**
 - **all documents in the right place with the right metadata**
 - **easy check between „CTIS documents“ and „national documents“ = validation**
- **Q&As for transition are under revision.**
- **„Subsequent addition of a MSC“ will be a challenge.**

Fast-track trials

In case of emergency – or anytime you really, REALLY need it...?

- *Case study: Low-intervention clinical trial for Tecovirimat for monkey pox*
 - *clearly a clinical trial (measures in addition to clinical practice)*
 - *would benefit from CTR process in harmonisation and transparency*
- Excellent management by the RMS Spain, huge (personal) effort by RMS and MSCs
- Target was „about one week“...

Challenges we encountered:

- **AT cannot do one week.**
 - **IECs are involved in Part I and they need time for their meetings.**
 - **IECs can only work on a validated dossier and translated patient-facing documents.**
 - **IECs cannot do „presubmission advice“ or „rolling submission“.**
- **Possible „minimum viable process“ is currently under discussion.**

CTR & CTIS – our way into the future!

Call me an optimist!

Source: picture-alliance/dpa



"Most people overestimate what they can do in one year and underestimate what they can do in ten years."

Embrace the change!

Choose your position...



Just keep on walking. It will get better!



Bundesamt für
Sicherheit im
Gesundheitswesen
BASG

Thank you for your attention!

Questions?



Austrian
Federal Office for
Safety in Health Care
BASG

Stefan Strasser, MD

Head of Clinical Trials

BASG -

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Sophie Accadebled

Clinical Trials Project Manager

The Authorisation Division of ANSM, France



Agence nationale de sécurité du médicament
et des produits de santé

CTIS Webinar

ANSM Experience
& Best Practices from the successful onboarding of CTIS sponsor users in France

July 1st, 2022

Review of CTA under CTR

Collaboration between French Medicines Agency - ANSM (NCA) and Ethics Committee (EC). EC is independent and separately organised from the Agency

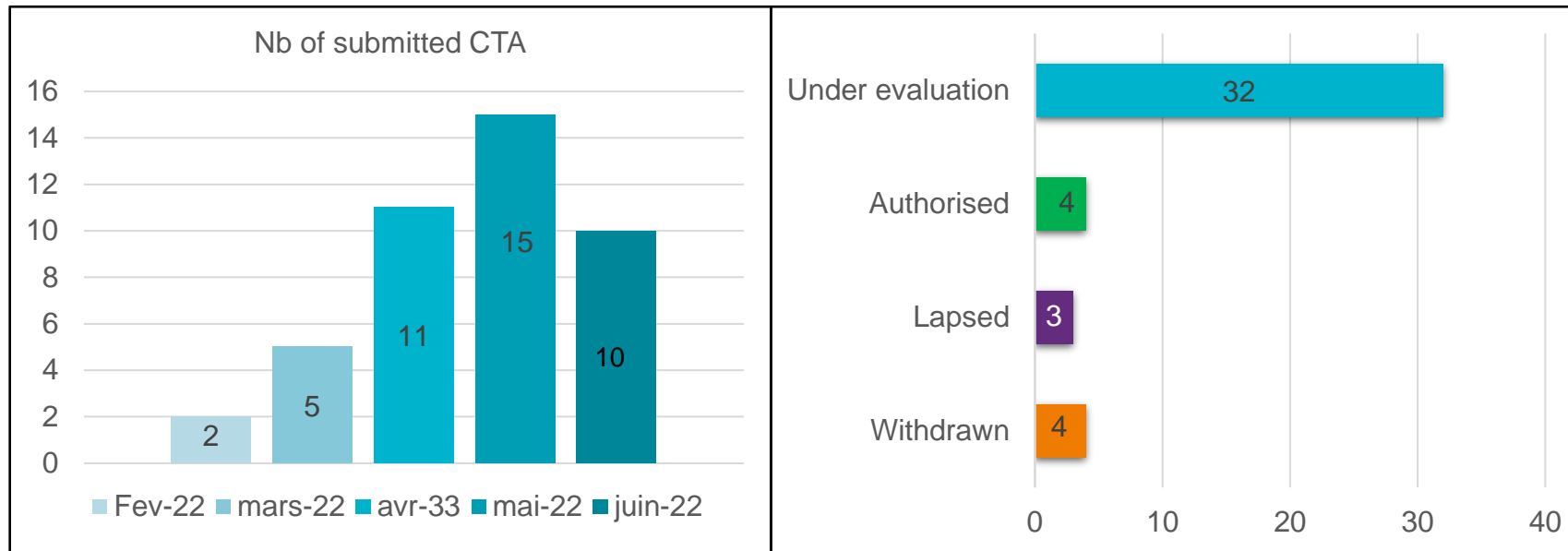
- Both ANSM and EC evaluate CTA
- **Part I** is under ANSM responsibility but protocol coordinated review with EC (no access to IMPDQ for EC)
- **Part II** is under EC responsibility

For practical information on Part II aspects:

DGS has published a list of requirements related to part II application

https://solidarites-sante.gouv.fr/IMG/pdf/documents_attendus_en_france_concernant_la_partie_ii_de_cta_2022_02_02.pdf

43 CTAs submitted in France *(Jan 31st / June 28th)*



Note : 2 CTAs under evaluation with France as RMS

CTAs under evaluation per sponsor type

commercial	Non-commercial
17	15

Initiatives to support sponsors for CTR

➤ **Open webinar on CTR including live broadcast (replay available on ANSM website) - April 2022**

- construction of the webinar on the basis of the questions received beforehand by the sponsors
- objective of this conference was to remind the key points of this regulation, the strategic points and impacts of this new regulation as well as the different vectors of exchange existing with the actors of the field

<https://ansm.sante.fr/evenements/webinaire-dedie-au-nouveau-reglement-europeen-des-essais-cliniques-de-medicaments>

➤ **Clinical Trials Working Group led by ANSM and conducted with sponsor representatives**

- objective is to discuss the implementation of the CTR

➤ **Updated ANSM notices for sponsors [Avis aux promoteurs]**

- facilitate the application of the provisions of the CTR and provide practical information in terms of procedures, format, content and modalities of submission of applications related to CTs of medicinal products

<https://ansm.sante.fr/page/essais-cliniques-procedures-pour-la-constitution-et-le-traitement-des-demandes-relevant-du-reglement-europeen-sur-les-essais-cliniques-de-medicament>

➤ **Q&A & promotion of EMA Guidances**

- regular website updates (Q&A)
- promotion of EMA guidances links to EMA and relevant events/training

<https://ansm.sante.fr/actualites/entree-en-application-du-nouveau-reglement-europeen-relatif-aux-essais-cliniques-des-medicaments>

➤ **Contact form from « Guichet usagers »**

- service to facilitate relations with sponsors

<https://ansm.sante.fr/contact>

Some Best Practices of CTIS users

➤ Cover letter

- Should mention all key information of the application to allow a clear understanding of the dossier and its constitution, in particular should be in line with the point B of the Annex I of the CTR

➤ Document naming and versioning

- The name of the document should not mention the date and the version (directly integrated in the structured data)
- The button « *update* » should be used to upload a new version of the document

➤ Publication aspects

- CTIS functionality → 2 versions of the same document : one version 'for publication' and one version 'not for publication'
- 'for publication' version should not contain commercial confidential information (CCI) and personal data
- Deferral publication functionality (all non clinical data and clinical data not considered as CCI)

➤ How to respond to RFI

- Submission of responses to considerations one by one in the appropriate box (structured data)
- New version of document uploaded directly in the appropriate section of the application (Part I or Part II)

Conclusion

General considerations will be raised to guide sponsors on CTIS functionalities

Already provided support on specific applications

- Email/call if extra RFI
- Guidances sometimes by zoom

ANSM is committed to making the best possible to gain further experience



Avertissement

- Lien d'intérêt : personnel salarié de l'ANSM (opérateur de l'État).
- La présente intervention s'inscrit dans un strict respect d'indépendance et d'impartialité de l'ANSM vis à vis des autres intervenants.
- Toute utilisation du matériel présenté, doit être soumise à l'approbation préalable de l'ANSM.

Warning

- Link of interest: employee of ANSM (State operator).
- This speech is made under strict compliance with the independence and impartiality of ANSM as regards other speakers.
- Any further use of this material must be submitted to ANSM prior approval.




Session 4

Sponsor experience and reflections



Gabriella Di Matteo

Clinical Trial Application Team Manager,
Pfizer Global Regulatory Operations, Belgium




CTIS - Sponsor experience and reflection

Clinical Trials Information System (CTIS) webinar: Six months of CTIS and looking forward

Gaby Di Matteo
Clinical Trial Application Team Manager
Pfizer Clinical Trial Regulatory Operations (CTRO)



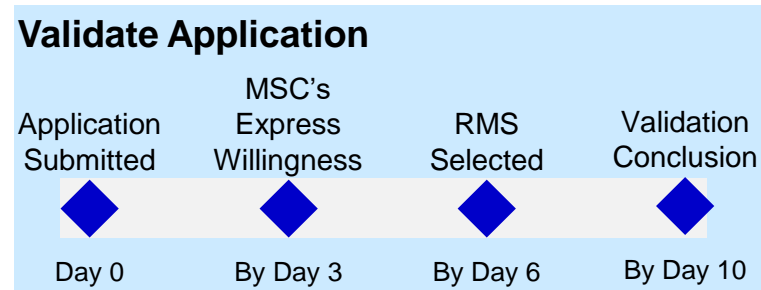


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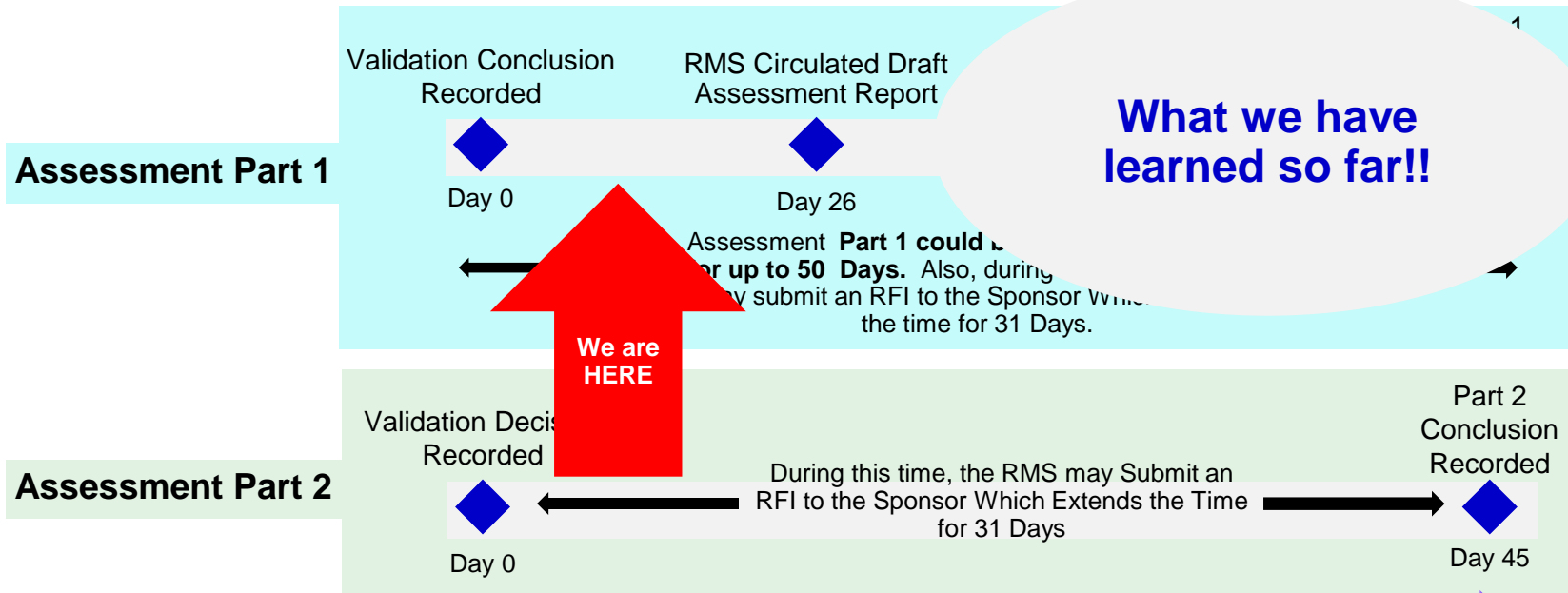
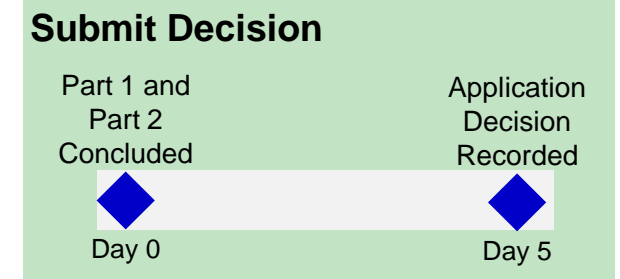
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2 EUCTR Initial Applications Submitted



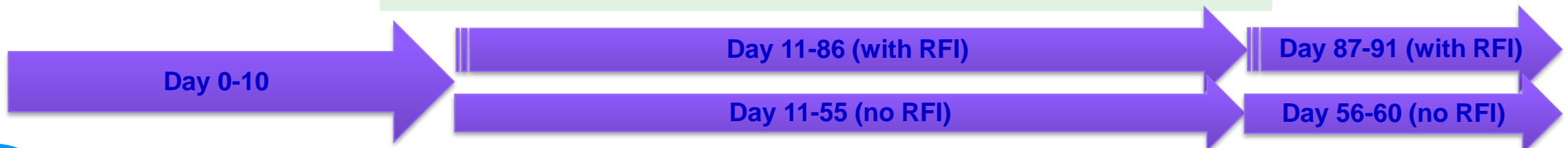
- 1 multinational
- 1 monocentric mononational



What we have learned so far!!

Acronym Buster

RMS – Reporting Member State
MSC – Concerned Member State
RFI – Request For Information
ATIMP - Advanced Therapy Investigational Medicinal Product



First 6 months goals and objectives

Balance of Adoption through transition period, learn, experience, apply - EUCTR

What went well

- Creation of trial
- Online application form
- Upload of documents
- Download of application and documents
- Application check
- Submission
- Use of both Google and Edge

Issues Encountered

- Update of some documents difficult
- File size limitation (10 MB) (known issue)
- XEVMPD New compounds registration a lengthy process
- Sites registration in CTIS not available
- File size issue

Organisational Management

Additional resources required to work in the system

Local Legislation evolving once studies already in preparation

Some EUCTR FAQs still to be provided

Improve

Capture and analyze data to understand evolving business needs and make recommendations for improvements

Feedbackk through helpdesk industry

Additional steps to be taken into account for Sponsor

Some RMS ask for pre-warning about submission & RMS request

- But ends up in rapid RMS confirmation

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

Redaction of documents

- Upload of both redacted and non redacted versions of
- Metadata to be removed from all documents
- Additional documents to be QC'd

Country-specific requirements to appear in cover letter

- Take these out as appendix to CL ?
- Create Table of Content of submitted documents (for Part I and for each Part II) until we can generate a TOC from CTIS

Risks Concerns – Discussion point

- Attention to be paid to RFIs that can target CCI information
 - Same for RFIs on Quality: important to upload RFI response under correct Q section
 - To avoid release of CCI
- Importance of training for both Sponsor and MS on this point



Some of the many questions still open

Do we know when....

Country-specific documents in Part II : is there a plan from MSCs to work with EC/EMA on alignment of requirements ?

Patient-facing material : not listed in CTR while some countries want to see them. Will EC/EMA/MS C issue aligned requirements ?

Official naming convention ?

EMA templates ?

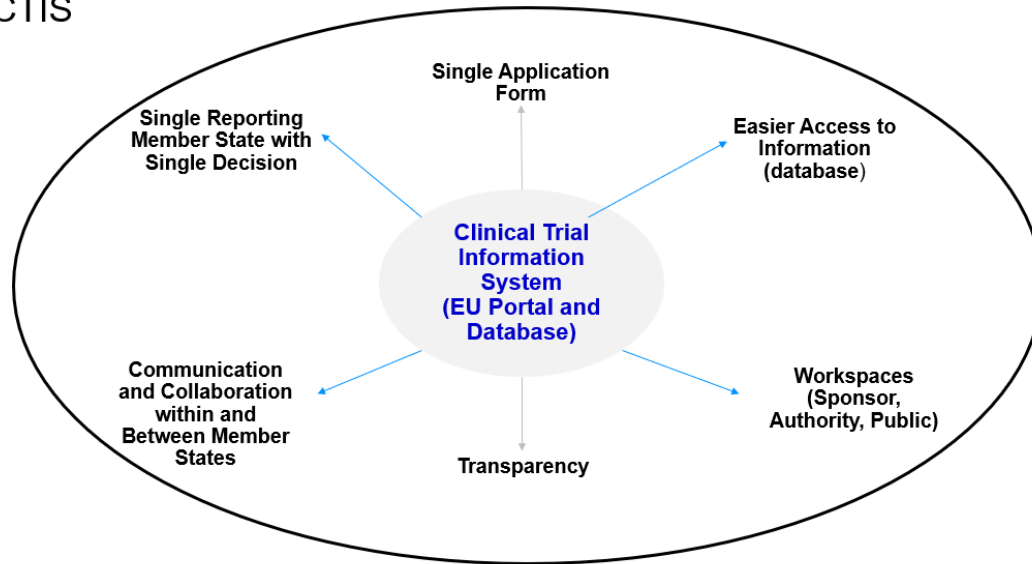
Emails generated from CTIS ?

In conclusion!

We did see some Simplification!

- **Straightforward system when you have been trained**
 - Importance of Sandbox

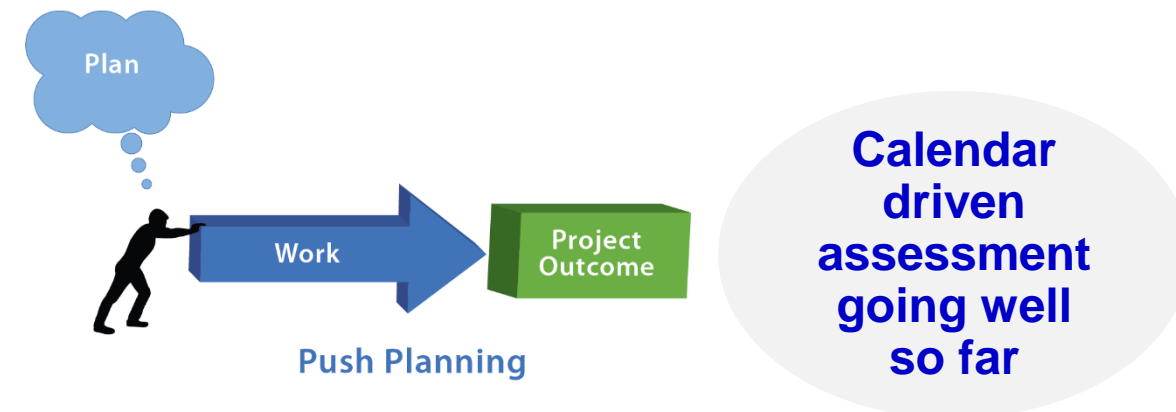
CTIS



EMA Service Desk responsiveness was good



Challenge to get all markets ready at same time

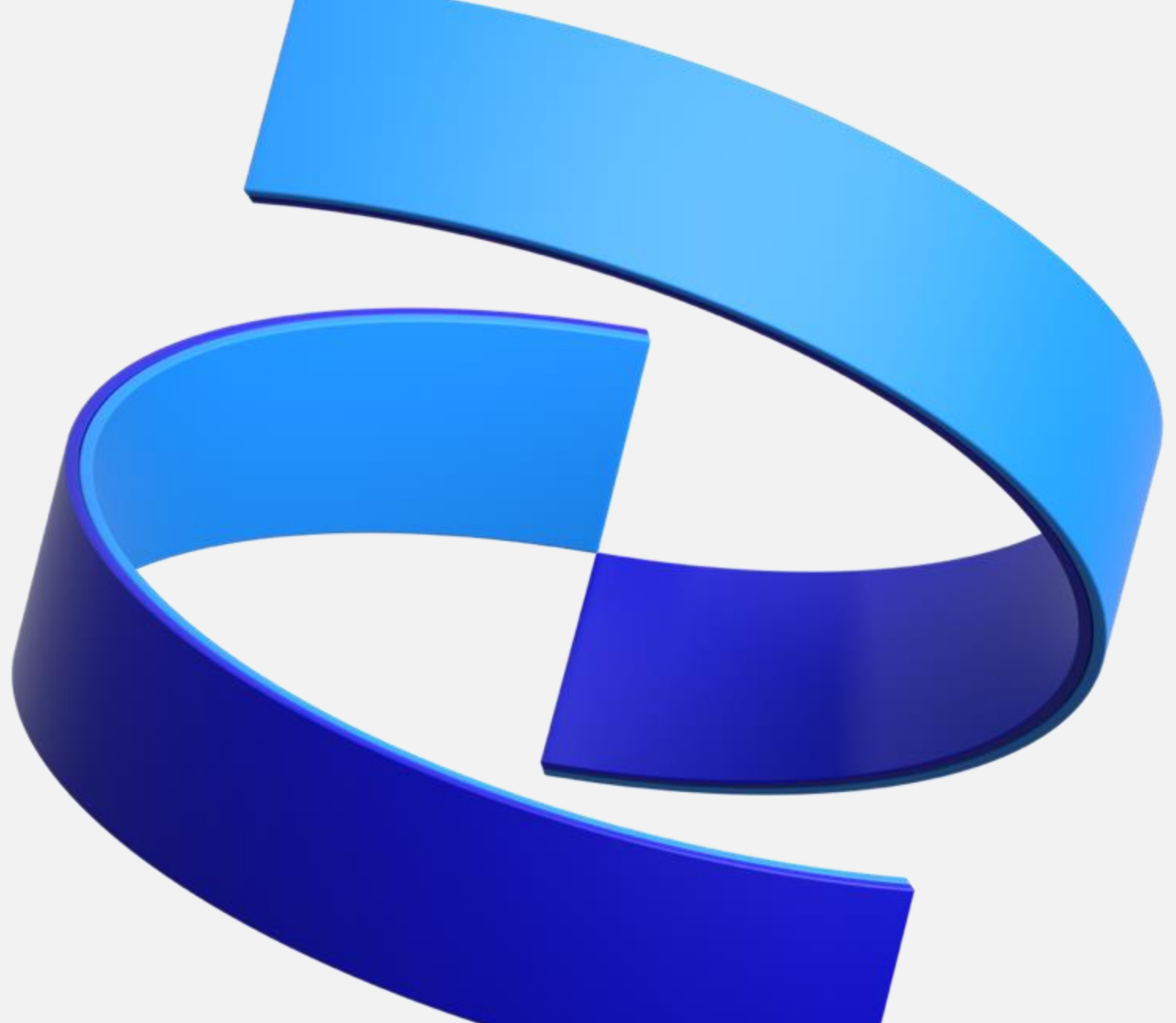


A large, abstract graphic composed of several overlapping, curved, and faceted planes in various shades of blue and purple. The shapes create a sense of depth and movement, resembling a stylized, modern architectural structure or a complex molecular model. The lighting is soft, highlighting the edges and surfaces of the planes.

To be continued...



Thank You





Session 3 and 4

Q&A session



Coffee break

Next up – Training and communication



**Recorded
Event**

Please note that this event is being recorded. The recording, or parts thereof, may be used/published on the EMA website after the event for training and communication purposes.

For information on the processing of personal data, please refer to the [General EMA Privacy Statement](#) and the [EMA Privacy Statements on the organisation of meetings and events](#).



Session 5

Training and communication



User support feedback

Thale Patrick-Brown

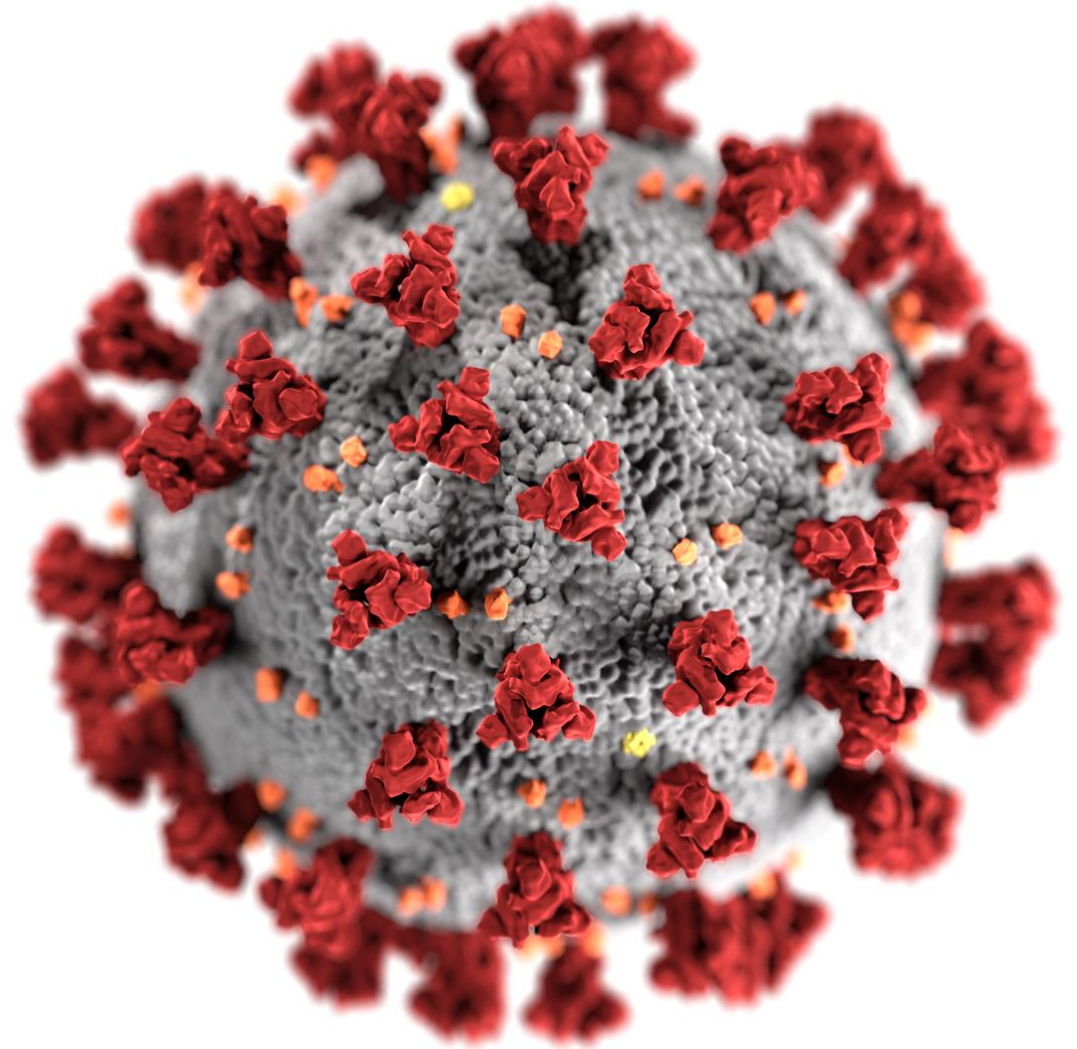
SolidAct Trial Manager

Oslo University Hospital, Norway

Experiences with the CTIS from EU-SolidAct

Thale Patrick-Brown

SolidAct Trial Manager
Oslo University Hospital, Norway



Who are we?

- Multi-centre, pan-European Clinical Trial Platform testing drugs to treat moderate and/or severe hospitalised patients with verified COVID-19
- Initial arm, Bari-SolidAct is looking at the efficacy of baricitinib for COVID patients
 - *Now only in immunocompromised patients*
- Upcoming arm, AXL-SolidAct (not authorised yet)
- Currently, 14 (+3) countries with a total of 102 centres taking part
 - **Approved:** Austria, Belgium, Czechia, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Norway, Portugal, Slovakia, Spain
 - **Coming soon:** Romania, Switzerland and Turkey to be added soon (the +3)

Positive experiences with CTIS/CTR

- Transparency
 - Most documents are made available
 - Can also be an issue – you need to be aware of GDPR and redact where appropriate
 - Full audit trail
 - No doubt to what has been approved
- One portal for everything (both regulatory and ethics)
- Fixed timelines with possibility of tacit approval

Challenges with CTIS/CTR

- The national requirements are quite high
 - Many new required documents (new for some at least)
 - A lot of signatures required (not all electronic)
 - New templates
 - Inconsistencies between countries/requirements
 - Some countries require signed site agreements before trial is approved (unusual), while most don't
 - Some require statements from Data Protection Officer, others don't
 - Some require a copy of the annotated eCRF, others don't
- Not designed for platform trials
 - Each new arm/investigation has to be entered as a brand new trial
 - This means that in many countries we must pay full fees for every arm instead of just an update fee
 - Also means that we must redo all the documents (all 600+ of them) every time we start a new arm
 - AND all documents must go through the entire inspection process – wastes a lot of time where docs are straight duplicates of already approved documents.
 - Where on Earth do you situate the Master Protocol?
- Unforgiving
 - Standardises things, but also does not allow for variations/deviations and so you have to come up with a lot of workarounds

Technical Challenges ... and some tricks...

- 27 support tickets (most highly technical issues)
 - Many support tickets closed before a resolution has been reached
- 3 false starts due to unsolvable problems
 - Lost time is a big issue. Be prepared – have all documents and info in spreadsheets, just in case you have to begin again
- Many, many outstanding issues
 - Adding sites in OMS is an onerous process
 - Make sure ALL your sites are entered into the OMS and that you know their number prior to starting
 - Difficult to work on Country-specific RFIs in parallel
 - Does not allow more than one user in ANY RFI a time – only one person can have one RFI open at a time so you have to coordinate closely to achieve goals
 - Uploaded documents not showing on the regulatory/ethics side
 - We can see them, but they cannot. If they ask – provide screen shots
 - You cannot put a date in the past, even for transitional trials that are already running
 - This can stop your application from submitting, but it doesn't always show up as an error, so be aware of this. You have to put in a fake future date, even for ongoing trials.

Suggestions

- When you submit a ticket to the Help Desk, make sure you note:
 - The time and date it happened
 - The username of the person(s) it happened to
 - The browser you are using
 - Chrome is the only one supported, but Edge “might” work too, even though most hospitals in Europe do not support Chrome or Edge
 - You may need to work from home to submit your application.
 - Take a screen shot that includes the time and date
 - Try to capture the “flag” in the top right corner
 - Grab the code if you know how
 - Explain the problem step by step
 - they’ll return the ticket for more info if you don’t
 - Be prepared to re-open the ticket multiple times
 - “We will fix this issue later” is not an appropriate reason to close a ticket
 - “We cannot re-create the problem” is not an appropriate reason either
 - “You didn’t reply fast enough” is also not an appropriate reason
 - Advocate for yourself wherever needed. If you’re not happy with a “resolution”, re-flag it!

Finally

Thanks to NoMA, EMA and the EC for a lot of help with getting our trials submitted. We represent academic sponsors without the huge resources of big pharma, but we are still able to meet the requirements thanks to a lot of constructive feedback from our regulatory counterparts.



CTIS training environment and communication

Noémie Manent

Leader of CTIS Operation Workstream

European Medicines Agency, Netherlands



CTIS Training environment

CTIS Training Environment is a copy of CTIS and a non-production environment with the aim to provide to Member States and Sponsors the possibility for a hands-on experience for training and familiarisation.

The following aspects and limitations need to be considered by CTIS Training Environment users:

- CTIS Training Environment foresees the exclusive use of fictitious data. Users must ensure that no personal data, commercially confidential or sensitive data is uploaded to the system.
- Being a training environment, the system may experience downtime periods, either planned or unplanned. EMA informs CTIS Training Environment users of planned downtimes in advance.
- CTIS Training Environment requires at certain times a data wipeout, where all data generated/clinical trials created by users will be erased. EMA informs CTIS Training Environment users about data wipeouts in advance.
- CTIS Training Environment is also used by EMA for the organisation of training events, so-called "CTIS Bitesize talks".

CTIS Training Environment has undergone **some conceptual changes** to provide **access to a larger number of Sponsors**. The approach for Member States did not undergo any changes.

November 2021 & May 2022 – access to sponsors provided under the organisation centric approach. Each sponsor organisation received 1 Sponsor Administrator and 5 generic blank accounts.

To provide access to a larger number of Sponsors, CTIS Training Environment has undergone changes:

- All previous access accounts are **revoked** and belonging data are **wiped-out**.
- Access provided through **1 generic blank account** (not a sponsor administrator account) under the **CT-centric approach**.
- Each generic account is assigned **one dedicated fictive organisation** that has to be used/indicated each time a user would create a new clinical trial in the CTIS Training Environment.
- Through CT-centric approach, the provided generic blank account is a **CT Administrator for a specific trial(s)**.

The roll out of the accounts under the new approach started 4 July 2022.

All access accounts are expected to be rolled out by 8 July 2022.



Sponsor End User Programme

CTIS Sponsor End User programme focuses on CTIS functionalities

- Virtual training programme, organised with support of DIA, to support sponsor user preparedness for the CTIS and the new way of submitting a clinical trial application and managing the life cycle of a clinical trial in the European Union (EU) and European Economic Area (EEA)
- A blended learning approach, offering on-demand components, as well as live virtual instructor-led offerings.
- 6 events held monthly in 1H 2022, starting 24 January 2022
- Upcoming sessions:
 - [20th –23rd Sep 2022](#)
 - [7th – 10th Nov 2022](#)



Training and Information events



CTIS Bitesize talks

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

Upcoming session:

[20 July 2022](#)
14:30–16:00 (CEST)

CTIS Walk-in Clinics

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

Upcoming session:

[22 August 2022](#)
16:00 – 16:45 (CET)

OMS Troubleshooting Sessions for CTIS users

- new regular sessions since June 2022
- public events open to all (no registration required)
- live broadcast
- questions asked prior to event and answered live
- recording publicly available post event

Upcoming session:

[21 July 2022](#)
14:00 – 15:00 (CEST)



Communications

International Clinical Trials Day – 20 May 2022

EMA, in collaboration with the Network, ran a communication campaign in support of International Clinical Trials Day.

- See LinkedIn posts [here](#), [here](#) and [here](#)
- See Twitter posts [here](#), [here](#) and [here](#)
- See the CTR/CTIS video, **now in all EU/EEA languages** [here](#) (has been shared with HMA Working Group of Communications Professionals for national use)
- ACT EU KPIs published, webpage created and targeted emails sent.



The social media campaign generated almost **170,000 impressions** (post views), more than **8,200 engagements** (likes, shares, comments and clicks) and almost **5,500 clicks** on the post/link.



Clinical Trials newsletter

- **Clinical Trials Highlights** issue 9 (formerly CTIS Highlights) [published](#) in May 2022
- Next issue to be published end **July 2022**
- Call for contributions/topic ideas: please send them to ct.communication@ema.europa.eu



Welcome to Clinical Trials Highlights



Andrzej Rys
Director of health systems, medical products and innovation, DG SANTE
European Commission

Welcome to the May 2022 issue of the Clinical Trials Highlights. As of 30 April 2022, 56 clinical trial applications were submitted for evaluation by Member States via CTIS. In addition, four clinical trials have been authorised and are viewable by patients, healthcare professionals and the general public through the [CTIS public search](#). The public availability of an unprecedented amount of data on individual trials through CTIS empowers patients to find recruiting trials in their country and ensures the highest levels of transparency for clinical trials in Europe.

The Heads of Medicines Agencies (HMA), the European Commission and EMA are working to deliver the ten priority actions of the [Accelerating Clinical Trials in the EU \(ACT EU\)](#) programme. On 20 May 2022, a set of Key Performance Indicators to monitor the European clinical trials environment have been published to coincide with International Clinical Trials Day, a key date to celebrate the progress achieved in the area of clinical trials and all those who make clinical research possible. Further ACT EU information and guidance which supports the transformation of clinical trials in the EU will be delivered throughout 2022 and 2023.

We look forward to collaborating with the clinical trials community in 2022 and beyond to ensure a competitive environment for clinical research in Europe and impactful clinical trials for patients' health.

INSIDE THIS ISSUE

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ACT EU methodologies guidance

The ACT EU priority action 8 focusses on developing and publishing methodologies guidance for clinical trials.

This priority action will provide guidance on innovative tools and methods for clinical trials and aims to strengthen the links between innovation and scientific advice.

As part of the methodologies priority action, ACT EU supports the implementation of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use's (ICH) addendum to the guideline on statistical principles for clinical trials on estimands and sensitivity analysis E9(R1). The estimands framework helps to link trial objectives to suitable trial design and statistical tools for estimation and hypothesis testing to ensure that trials are designed, conducted and analysed appropriately to meet their objectives.

Another key aspect of the methodology priority is the development of guidance related to complex clinical trials. The European Commission, HMA and EMA will shortly publish a Q&A on complex clinical trials, covering topics such as key

Release communications

- May 2022 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





Thank you



ACT EU

Ana Zanoletty

Programme Manager for the Accelerating Clinical Trials in the EU (ACT EU)

European Medicines Agency, Netherlands



Transforming clinical trials in Europe: the Clinical Trials Regulation, CTIS and ACT EU

Presented by Ana Zanoletty

Drivers of EU clinical trials transformation

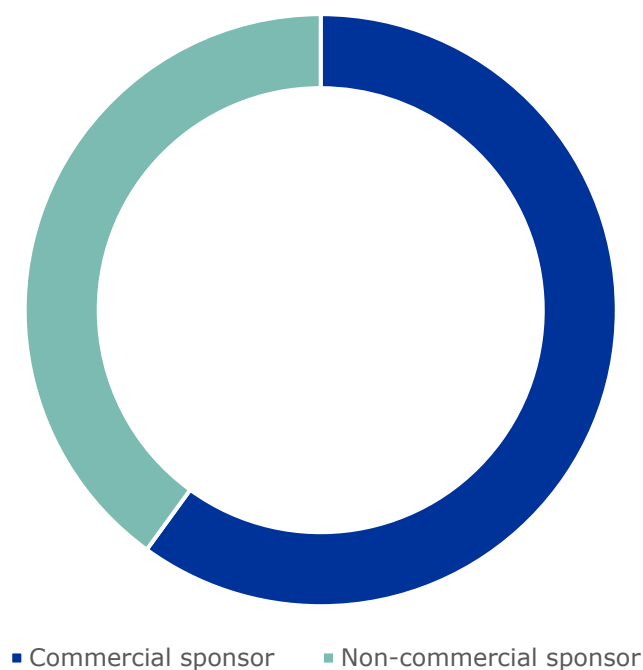
- **Clinical Trials Regulation and CTIS** - harmonisation of clinical trials regulatory processes and increased efficiency via digitisation
- **New tools and methods** e.g. decentralised and complex trials – new/updated guidance needed
- Need for **large, multinational trials** (including academic trials) to address key public health issues



The climate for clinical trials in the EU

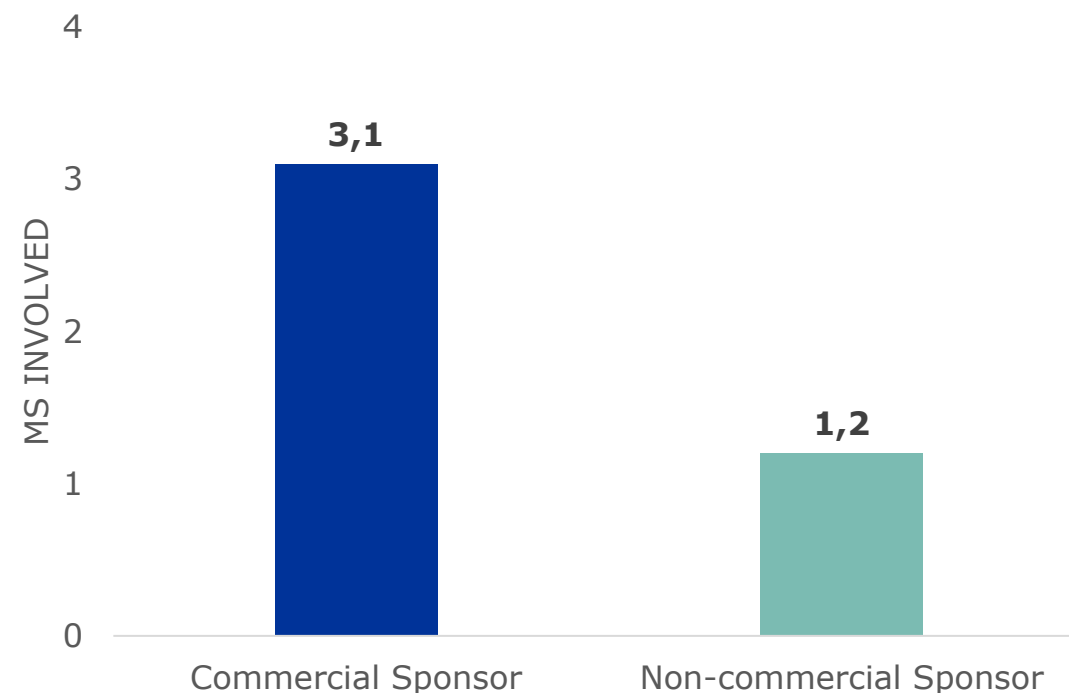
40% of clinical trials are non-commercial

Clinical trials in Europe by type of sponsor 2005-2020



Non-commercial CTs are predominantly mono-national

Average number of member states involved per trial 2005-2020



Accelerating Clinical Trials in the EU (ACT EU)

ACT EU is an initiative to **transform the EU clinical research environment** in support of medical innovation and better patient outcomes.

- **Builds on the momentum** of the Clinical Trials Regulation and CTIS
- **Supported by** the Network Strategy to 2025 and the EU Pharmaceutical Strategy
- Launched January 2022
- Read the [press release](#) and [paper](#)



ACT EU objectives



Support the conduct of **large, multinational trials** with specific support for:

- SME, academia and Health Technology Assessment bodies (HTAs); and
- Trials which address unmet needs, rare diseases & medicines for public health crises



Facilitate **coordinated scientific advice** to support trial authorisation, marketing authorisation & the medicine lifecycle



Ensure **a unified European approach** for trial processes and strategic matters at the international level



Engage all stakeholders to deliver inclusive patient-oriented medicines development and delivery across populations

1. Develop a **governance rationalisation strategy** (aligning different expert groups and working parties)
2. The successful and timely **implementation of the CTR** and its implementing acts.
 - **KPIs** to track performance of the European CT environment.
 - **Promote larger, multinational trials** specifically in academia
3. Establish a **multi-stakeholder platform**, including patients, after stakeholder analysis.
4. Implementing the **GCP modernisation** informed by the development of guidance at ICH.
5. Analyse **data about clinical trials** leveraging academic, non-profit, European, and international initiatives, improving the impact of policymaking and funding to support evidence-based decision making.
6. Plan and launch a targeted **communication campaign** to engage all enablers.
7. Reinforce the **coordination between scientific advice on CT approval and CT design** and link to the methodologies working party domain.
8. Develop and publish key **methodologies guidance** e.g. on AI/ML impacted CTs, complex trials, decentralised CTs and IVDR/CTR interface (to strengthen links between innovation and scientific advice fora).
9. Successfully establish **CT safety monitoring** and bridge to the EU4Health Joint Action and start its integration into a pre- and post-marketing safety monitoring framework.
10. Deliver a clinical trials **training curriculum** on drug development and regulatory science with links to SMEs & academia

Governance & Integration



1. Develop a **governance rationalisation strategy** (aligning different expert groups and working parties)
7. Reinforce the **coordination** between **scientific advice on CT approval and CT design** and link to the methodologies working party domain.
9. Successfully establish **CT safety monitoring** and bridge to the EU4Health Joint Action and start its integration into a pre- and post-marketing safety monitoring framework.

Methods & Practice



4. Implementing the **GCP modernisation** informed by the development of guidance at ICH.
8. Develop and publish key **methodologies guidance** e.g. on AI/ML impacted CTs, complex trials, decentralised CTs and IVDR/CTR interface (to strengthen links between innovation and scientific advice fora).

Engagement



3. Establish a **multi-stakeholder platform**, including patients, after stakeholder analysis.
6. Plan and launch a targeted **communication campaign** to engage all enablers.
10. Deliver a clinical trials **training curriculum** on drug development and regulatory science with links to SMEs & academia.

Impact



2. The successful and timely **implementation of the CTR** and its implementing acts.
 - **KPIs** to track performance of the European CT environment.
 - **Promote larger, multinational trials** specifically in academia
5. **Analyse data about clinical trials** leveraging academic, non-profit, European, and international initiatives, improving the impact of policymaking and funding to support evidence-based decision making.

Spotlight on Priority action 8: Methodologies guidance

Complex trials

- Guidance to trial sponsors on the planning and conduct of complex clinical trials and for the design of master protocols
- Read the [complex trial Q&A](#)

Decentralised trials

- ACT EU works in collaboration with the EU DCT project group (CTCG, CTEG, GCP IWG)
- Upcoming multi-stakeholder event – read the [Clinical Trials Highlights](#) newsletter for updates



Other important initiatives to strengthen clinical trials

- Clinical Trials Coordination Group (**CTCG**)
- Safety implementing regulation and Joint Action on **safety monitoring**
- Joint Action on expedited **COVID-19 assessment**
- EMA Emergency Task Force (**ETF**) mandate strengthened for clinical trial support



How to get involved

The **ACT EU Multi-Stakeholder Platform** will:

- Bring the clinical trials community together, including patients, sponsors, assessors and inspectors to discuss key topics
- Help EU clinical trial environment identify and respond to new developments in tools and methods



Workshops and events to be announced [on the EMA website](#) and via the [Clinical Trials newsletter](#) later in 2022 and 2023.

Any questions?

Further information

ACTEU@ema.europa.eu



Session 5

Q&A session



Wrap up and closing remarks

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Oslo University Hospital, Norway



Thank you for attending today's event

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Further information

For CTIS communication, training & change management queries, e-mail CT.Communication@ema.europa.eu

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

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