EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update on CTIS and ACT EU

Industry Standing Group (ISG) meeting, 22 November 2022

Presented by Peter Arlett
Head, Data Analytics and Methods Task Force

CTIS supports the goals of the Clinical Trials Regulation

The Clinical Trials Information System (CTIS) is the single submission portal which **harmonises the submission, assessment and supervision of clinical trials** in the EU/EEA.

Public health

Facilitates multinational trials to address key health issues, increase transparency & enables patient enrolment

Research and innovation

Enables collaboration and access to clinical research data.

Global hub for clinical trials

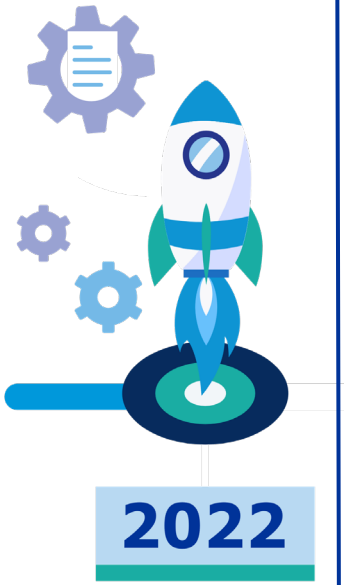
Ensures the EU/EEA remains an attractive clinical research hub globally.

CTIS for sponsors

With CTIS sponsors can:

- Apply for a clinical trial in up to 30 EU/EEA countries with a **single application**
- Facilitate involvement of trial participants by allowing **easy expansion of trials to other EU/EEA countries**
- **Collaborate across borders** for better results and knowledge sharing
- Ensure the EU/EEA remains an attractive location for **clinical research investment**
- Fulfil all **clinical trial publication requirements** with no additional effort

CTIS in 2022: 1st year of transition of Clinical Trials Regulation

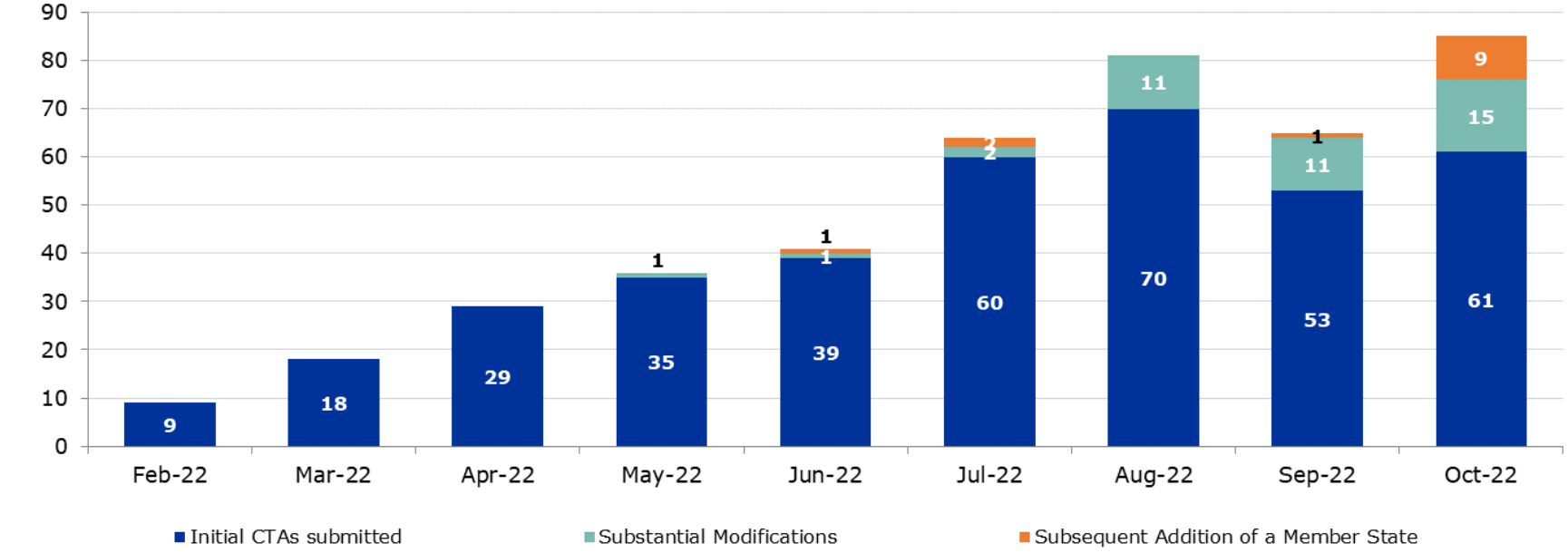


- **121 initial clinical trial applications authorised** and 8 not authorised in CTIS as of end Oct 2022
- **163 CTs under evaluation** as of end Oct 2022
- CTIS Forum launched on 12 Oct to facilitate exchange of experience between stakeholders; next planned 1 Feb 2023
- Reporting of incidents by users enables their successful resolution via workarounds or definitive solutions

CTIS Status

Key monitoring metrics graphs - data until end October 2022

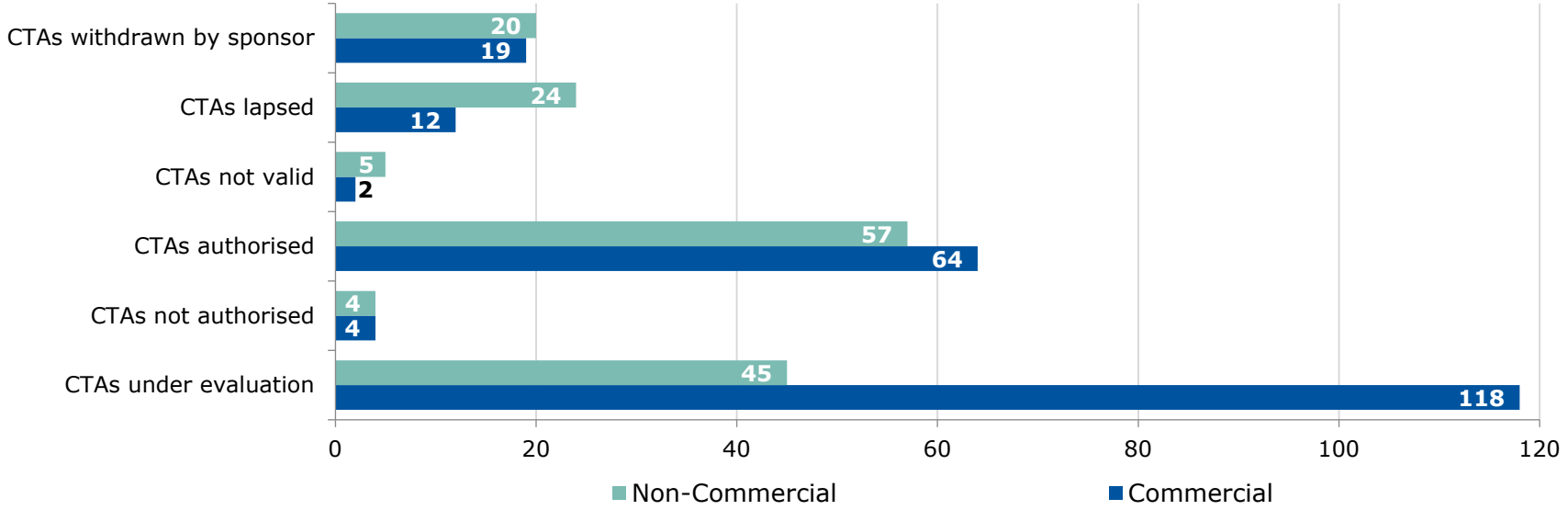
CTAs submitted in CTIS per month



CTIS Status

Key monitoring metrics graphs - data until end October 2022

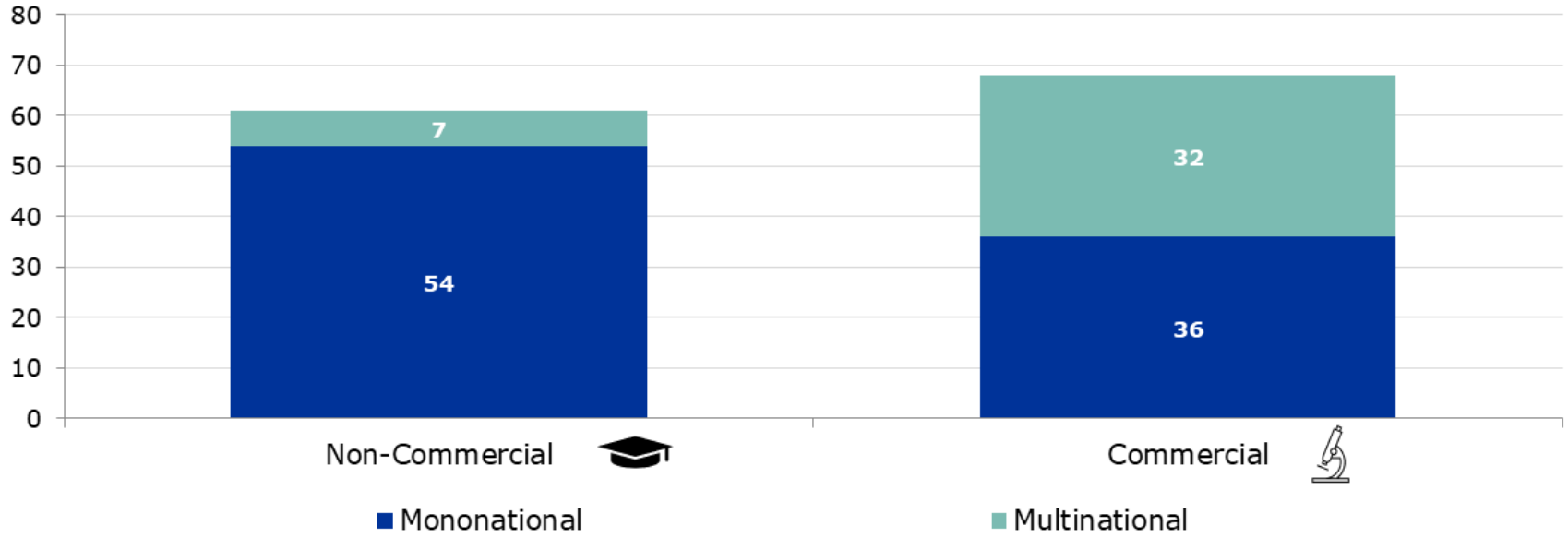
CTAs per Trial status in CTIS
Commercial versus Non-Commercial



CTIS Status

Key monitoring metrics graphs - data until end October 2022

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



Recent improvements in CTIS

For more information, see Release Notes and Known Issues:
Website outages and system releases - EMA (euclinicaltrials.eu)

Fixes, improving the system, have been deployed in the areas of

- ***User registration and authentication***
  Enhanced security:
  - by requiring user email address when assigning roles to users and
  - by preventing specific sponsor roles having viewer access to RFIs/notices & alerts outside their role scope
- ***Application creation/preparation of documents and data***
  Issues related to RFI responses, preventing trials from lapsing
- ***Authorisation and supervision of clinical trials***
  Issue related to allowing the submission of the restart of trial notification after a Temporary Halt due to risk/benefit reasons once a Substantial Modification has been authorised or authorised with conditions
- ***Communication between sponsors and Member States***
  Ensuring CT access to non-MSC and facilitating the Annual Safety Report workflow

Registration in OMS – *new processes since 3 November*

Registration as **Sponsors** – *new process*

- Sponsors not registered in a National Business registry can request to be registered in **Organisation Management Service (OMS)** by attaching a **CT registration Headed letter -** template in SPOR Portal OMS Web UI (europa.eu)

Registration as **Clinical Trial Site** – *temporary process*

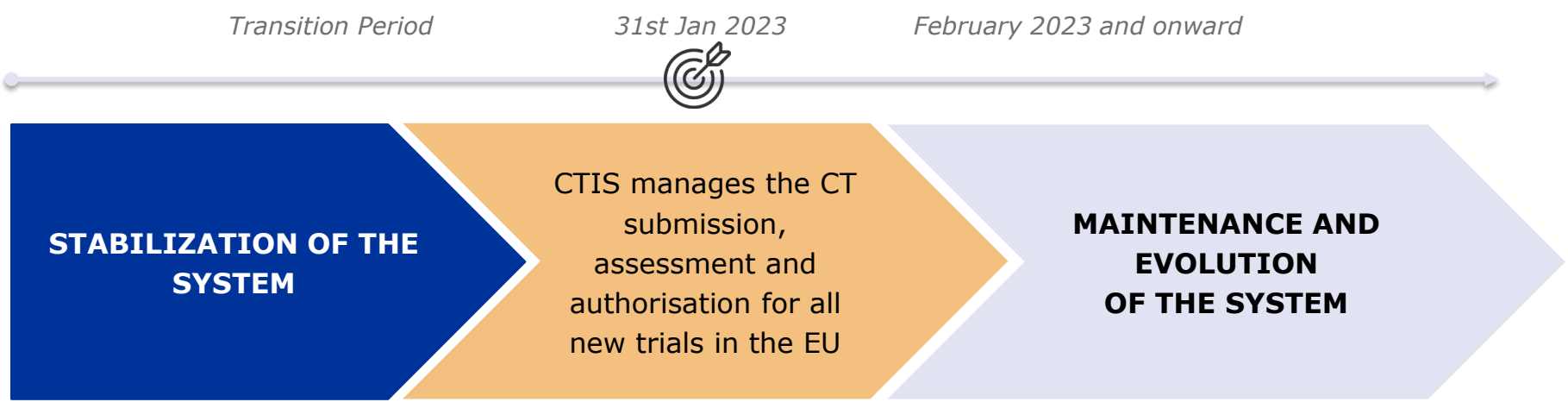
- Clinical Trial Sites not registered in a National Business registry can also register in OMS by submitting a change request to register the CT site directly to OMS, including a **CT registration Headed letter** – template in SPOR Portal OMS Web UI (europa.eu)
- **Change to be implemented in CTIS** (planned for 6 December 2022) to allow recording of sites, not registered in OMS, directly into the clinical trial application; afterwards, all CT sites registered based only on the headed letter (temporary process) will be deactivated

Two factor authentication (2FA) for CTIS

- **Two-factor authentication (2FA) strategy for user logins to EMA-managed systems** to be rolled out, reinforcing security of user accounts
- Users will be asked to choose their preferred second factor method to verify their identity during log-in, via:
  - a token received in Microsoft Authenticator mobile app, or
  - an automated phone call or
  - a text to mobile phone, or a call to office phone
- To prepare, it is recommended that each user is equipped with a mobile phone, or an office phone that can be used for one of the three methods of 2FA
- The date of deployment, and later activation of 2FA in CTIS is tentatively set for **December 2022**
- 2FA will be deployed inactive, and activated at a later stage to ensure large notice to users
- **Notices about 2FA were already published in the EMA Clinical Trials Newsletter in July 2022, and communicated via email to CTIS Administrators also in July**

Objective: CTIS is ready for mandatory use on 31/1/2023

Ensure the stability of CTIS by resolving any new issues reported by end users and addressing known issues.



Aim: **no blocking bugs in CTIS core processes by 31 January 2023.**

CTIS planning 2023 - 2024

Planning assumptions

- Continued support for production incidents as the volume of use will increase substantially
- New functionality will be developed based on the priorities set by the Product Owners
- Implementation of refactoring assessment outcomes to enhance maintainability and sustainability
- Prepare and plan for the unexpected, leave room for adapting plans in an agile manner

Options have been elaborated and will be presented to the ACT EU SG and to EMA MB for agreement

Governance meetings	Late November	Mid December
	ACT EU Steering Group	The EMA Management Board

CTIS Training material production & revision: 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:

- Updates to **modules 3 (user management) and 11 (respond to RFI)** are ongoing
- A Reorganisation of CTIS training materials on the EMA corporate website under consideration

CTIS Sponsor End User programme 2022: focus on CTIS functionalities

WORK DONE:

- ✓ Identification of experts trainers
- ✓ Define agenda for the training sessions
- ✓ Creation of training materials to be used in sessions
- ✓ Kick off call (Dec 9th, 2021)
- ✓ Review/Update training materials to be used in the following training sessions
- ✓ Preparation of platform for the training sessions (live demo sessions)
- ✓ Training offers to be advertised on EMA events page (and DIA page) (search e.g. "CTIS", "Sponsor end user")
- ✓ 7 events held in 2022 till now

ONGOING:

- Event oversight (participation, assistance, focal point for change requests)
- Participants receive temporary CT centric accounts to Sandbox
- Review/Update the training materials to be used in the following training sessions
- Upcoming sessions
  - 7th – 10th Nov 2022
  - 7th - 10th February 2023 (link will be available on EMA website shortly)
  - 2nd -5th May 2023(link will be available on EMA website shortly)
  - 27th – 30th June 2023(link will be available on EMA website shortly)

CTIS information – training sessions

EMA is offering **training sessions** in classroom format, to provide additional learning opportunities.

In 2022, EMA offered:

- 10 CTIS walk-in clinics - Upcoming session: 12 December 2022 15:00–15:45 (CEST)
- 7 CTIS Bitesize talks - Upcoming session: 23 November 2022 14:30–16:00 (CEST)
- 3 OMS Troubleshooting sessions for CTIS users - Upcoming session: 24 November 2022 14:00–15:00 (CEST)

For more information on each training session, including supporting materials, see: Clinical Trials Information System: training and support | European Medicines Agency (europa.eu)

Additional support to CTIS users

- New wave of access to CTIS Training Environment (Sandbox)
- **Daily proactive support to all Sponsor users** prior to RFI due date(s), ensuring timely submission of RFI responses to avoid lapsed CTAs
- **Latest updates** to the CTIS system & the **list of known issues** for both the authority and sponsor workspaces and their workarounds, published on: https://euclinicaltrials.eu/website-outages-and-system-releases
- **Webinar** on 9 months of CTIS and looking forward held on 16 November 2022: recording, presentations, and agenda will be available shortly on the EMA events page

Accelerating Clinical Trials in the EU (ACT EU)

ACT EU is business change 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
- **Driven by** the Network Strategy to 2025 and the EU Pharmaceutical Strategy
- Launched 13 January 2022
- Read the press release and paper
- Workplan for 2022-2026 has been published on 30 August 2022

ACT EU objectives

Support the conduct of **large, multinational trials**:

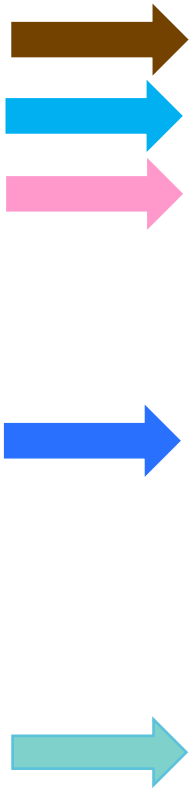
- Facilitate the conduct of trials to address unmet needs, rare diseases & medicines for public health crises
- Provide methodological guidance and drive innovation on clinical trials methods
- Facilitate high-quality clinical trials which ultimately deliver high-quality, safe and effective medicines

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

ACT EU priority actions



PA 1	Map existing initiatives and develop a governance rationalisation strategy (aligning different expert groups and working parties in the EMRN and ethics infrastructure).
PA 2	Successful and timely implementation of the CTR and its implementing acts: • develop KPIs and dashboard to track performance of the European clinical trials environment; • including the promotion of larger, multinational trials specifically in the academic setting.
PA 3	Establish a multi-stakeholder platform, including patients, after stakeholder analysis
PA 4	Implementing the GCP modernisation informed by the development of guidance at ICH
PA 5	Analyse data about clinical trials leveraging academic, non-profit, European, and international initiatives, improving the impact of policymaking and funding on research outputs to support evidence-based decision making
PA 6	Plan and launch a targeted communication campaign to engage all enablers (including data protection experts, academia, SMEs, funders, HTA bodies, healthcare professionals)
PA 7	Reinforce the coordination between scientific advice on CT approval and CT design and link to the methodologies working party domain
PA 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)
PA 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
PA 10	Deliver a clinical trials training curriculum including modules on drug development and regulatory science with links to universities and SMEs (serving as an educational 'ecosystem')

CTIS

Conclusions

- Continue stabilising the system in production, proactively solving known issues
- **No blocking issues in core CTIS processes by 31 January 2023**
- Providing further support to CTIS user community: MS, Sponsors, Academia
- Engaging stakeholders in ACT EU and CTIS:
  - CTR communication campaign launched in Nov 2022
  - Workshops, events, and open consultations announced on the EMA website and via the Clinical Trials newsletter

Thank you for your continued engagement and support
as we prepare for compulsory CTR/CTIS use from 31 January 2023

Any questions?

Further information

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Send us a question Go to www.ema.europa.eu/contact

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The Clinical Trials Regulation foresees a **3-year transition period** to CTIS: