Clinical trials in the EU

18 October 2024
SME info day

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An agency of the European Union

Disclaimer

The presenters do not have any conflict of interests.

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Accelerating Clinical Trials in the EU (ACT EU)

Challenges

Need for more impactful multi-state trials to drive decision-making

Need for an overarching strategy to bring stakeholders together

Multiple actors requiring clear roles and responsibilities

Need to leverage the EU's strong healthcare and research infrastructure

A multi-stakeholder approach for progress in clinical trials

ACT EU vision

EU as an attractive region for clinical research

Larger and more impactful CTs, with seamless coordination among regulators and stakeholders

Smart CTs through **regulatory, technological and process innovation**

Empowering, engaging and supporting **stakeholders**

ACT EU Priority actions 2023-2026

ACT EU is delivering benefits to clinical trial stakeholders across key areas. It is a joint initiative of EMA, European Commission and Member States, through HMA:

Mapping & governance

Implementation of the Clinical Trials Regulation

Multinational clinical trials by non-commercial sponsors

Multi-stakeholder platform

Good clinical practice modernisation

Clinical trials analytics

Consolidated advice on clinical trials

Clinical Trials methodologies

Clinical trials safety

Clinical trials training curriculum

Clinical trials in public health emergencies

Mapping & governance

Map existing expert groups dealing with clinical trials considering a governance rationalisation strategy

Aligning different expert groups and working parties in the EMRN and ethics infrastructure

- Mapping of existing clinical trials governance groups published
- **CTR Collaborate** established, anchored to PA1
- CTR collaborate, led by CTCG, aims at achievieving harmonisation within and between MSs, taking into account involvement of Ethics Committees

Implementation of the CTR

Supporting the successful and timely implementation of the Clinical Trials Regulation and its implementing acts

1. Key performance indicators (KPI) tracking implementation of the CTR via monthly reports since May 2022

2. Launch of regular surveys submitted to CTIS users to capture feedback on their user experience on CTIS/CTR implementation

3. Transitioning clinical trials

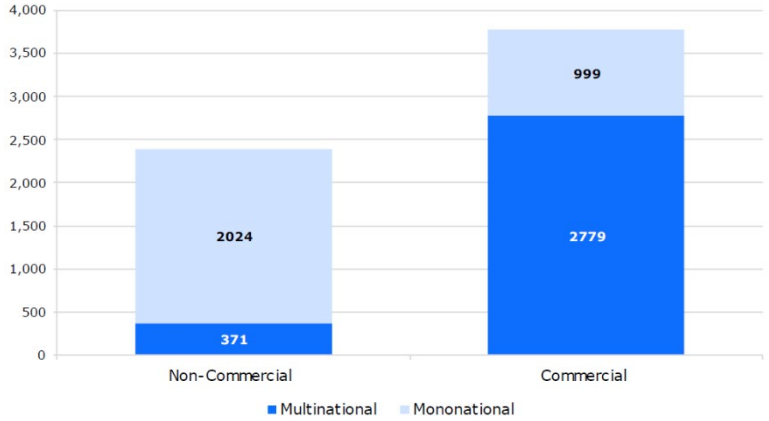
   - Workshops (Q1 2024), publication of key documents defining requirements to transition clinical trials on Eudralex V 10 and CTCG websites
   - Communication campaign

4. Revised CTIS transparency rules: launch of new CTIS public portal in June with additional features on search functionality implemented in September

Support to non-commercial sponsors

Create an action plan to help non-commercial sponsors to plan and initiate multinational clinical trials

Authorised clinical trials since 31 January 2022



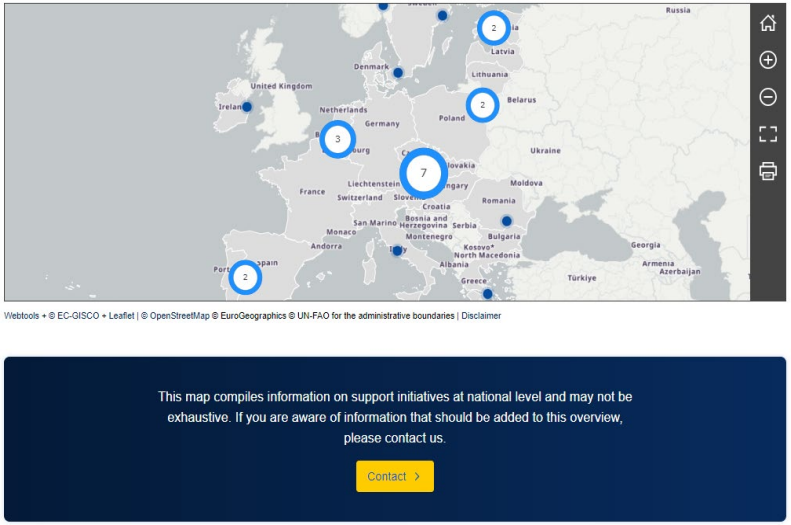
Tailored initiatives, resulting in:

- **higher number** of non-commercial CTs conducted in more than one EU/EEA MS
- **high quality** scientific evidence generated by non-commercial clinical trials
- benefit for **EU citizen's** health through optimised therapies and access to innovative medicines

Source: Monitoring the European clinical trials environment September 2024

Support to non-commercial sponsors

1) Interactive map showing existing initiatives at national level (via CTCG) and other stakeholders initiatives published in June 2024:
   - page updated on regular basis with feedback from member states; as soon as new information becomes available;
   - page populated with other initiatives (Enpr-EMA)
2) Launch of the helpdesk for non-commercial sponsors:
   - dedicated support on CTR and on CTIS use with involvement of NCAs
3) Next steps:
   - closer collaboration with the MSP Advisory Group (MSP AG) to gather feedback on needs;
   - organization of training material and guidance for non-commercial sponsors



Good Clinical Practice modernisation

Support the modernisation of good clinical practice in order to align with the increasingly diverse range of clinical trial types and data sources

- CHMP adoption of final text for principles and Annex I expected in Q4 followed by implementation in the region
- Annex II public consultation expected Q4 2024
- Broadcasted workshop planned for 19 and 20 February 2025, to discuss final adopted text
- Impact analysis and change management in relation to the implementation of ICH E6(R3) and interplay with EU guidance
- Coordinate with relevant stakeholders (e.g. GCP IWG, ICH E6(R3)) Expert Working group on relevant training/communication and change management

Consolidated advice pilots

1. SAWP/CTCG scientific advice pilot
2. Pre-CTA regulatory/ administrative pilot

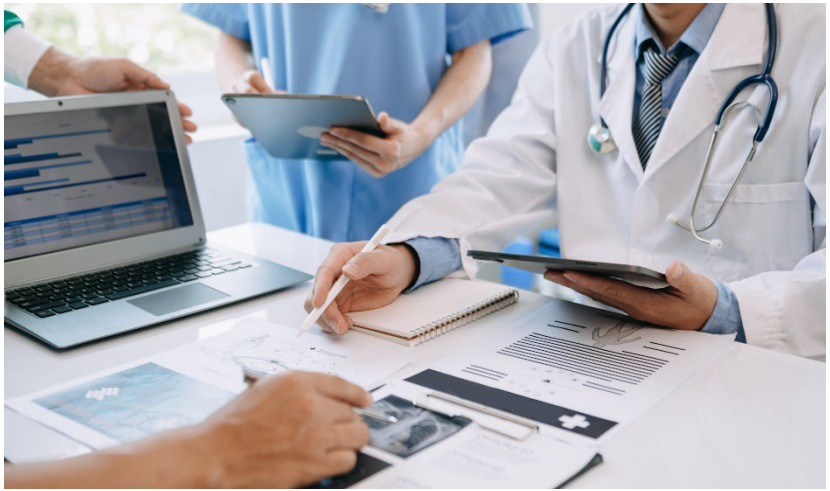
Improved quality of applications; improved EU environment for clinical trials

Consolidated advice for sponsors clarifying the landscape

Increased network coordination & efficiency

Launched in June 2024

9 applications already received



In line with ACT EU's vision, aiming to benefit patients and healthcare in the region.

Learn how to apply:
Consolidated advice on clinical trials

Additional ACT EU Priority Actions

Data Analytics:

- Development of a research priorities paper based on the outcome of the January 2024 Multi-stakeholder workshop (Report) on clinical trials data analytics with possibility to link the EU-level funding to deliver the research priorities

Methodologies:

- November 2023 Multi-stakeholder methodology workshop (Report) setting the scene for activities occurred in 2024
- Established process in place for regular exchange between MWP, CTCG and HTA coordination group
- Ongoing development of a best practice document on guidance development in the European Medicines Regulatory Network

Additional ACT EU Priority Actions

Training curriculum:

- Summary of gap analysis report for regulators published in March 2024
- Training needs for **academia and SME** being defined, starting from STARS curriculum, consulting first regulators moving then to the interested parties (academia and non-commercial sponsors)
- Stakeholders' engagement exercise planned

Public health emergencies:

- Establishment of a PHE Ethics Advisory Group, through MedEthics (July 2024), with 14 members
- Proposal of simplifications in the CTR annexes and listing language requirements per MS
- Analysis of the COVID-19 guidance and existing guidance documents, adjusting to extend to PHEs

How stakeholders are involved

Multi-stakeholder platform

Multi-stakeholder workshops

Engagement tools

(consultations, surveys…)

+

MSP Advisory Group
Stakeholder representatives

MSP Advisory Group members - European Union

MSP AG

- 1 **Regulator Co-chair** (Maria Jesus Lamas AEMPS)
- 1 **Stakeholder Co-chair** (Denis Lacombe EORTC)

Stakeholder permanent representatives
appointed via **public call for expression of interest**:

- 5 patients/consumers
- 4 industry EU trade organisations
- 4 healthcare professionals organisations
- 4 academia
- 2 funders

→ Ad hoc participation of other stakeholders based on agenda.

ACT EU

- ACT EU regulatory partners.
- 2 Ethics Committee representatives.
- Ad hoc participation of other experts (HTA, ACT EU Priority Actions, payers, international authorities).

Which stakeholders are involved

MSP Advisory Group
Permanent stakeholder organisations

Patients/consumers

CANCER PATIENTS EUROPE
EATG European AIDS Treatment Group
eYPAGnet
EPF European Patients Forum
EURORDIS RARE DISEASES EUROPE

Healthcare professionals

ean european academy of neurology
EHA EUROPEAN HEMATOLOGY ASSOCIATION
ESOP European Society of Oncology Pharmacy
ESC European Society of Cardiology

Academics

ecrin eatris
TEDDY NETWORK
EORTC European Organisation for Research and Treatment of Cancer

Industry

ACRO ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS
EuropaBio The European Association for Bioindustries
EUCOPE European Confederation of Pharmaceutical Entrepreneurs AISBL
efpia

Funders

innovative health initiative
KWF Dutch Cancer Society

Ethics committees

ccmo Centrale Commissie Mensgebonden Onderzoek
Arbeitskreis Medizinischer Ethik-Kommissionen in der Bundesrepublik Deutschland e.V.

ACT EU partners

EMA EUROPEAN MEDICINES AGENCY
HMA Heads of Medicines Agencies

Looking ahead

Q3-Q4 2024

- ACT EU multi-stakeholder platform annual meeting (22 October), more details on ACT EU multi-stakeholder platform annual meeting.
- Revision of the ACT EU multi-annual workplan by the end of the year

Q1 2025

- ACT EU multi-stakeholder workshop on ICH E6 R3 principles and Annex I
- ACT EU multi-stakeholder workshop on methodology guidance in CTs

Please consult our website for latest information: Accelerating clinical trials in the EU (europa.eu)

The European Clinical Trials Regulation

Before the Clinical Trials Regulation

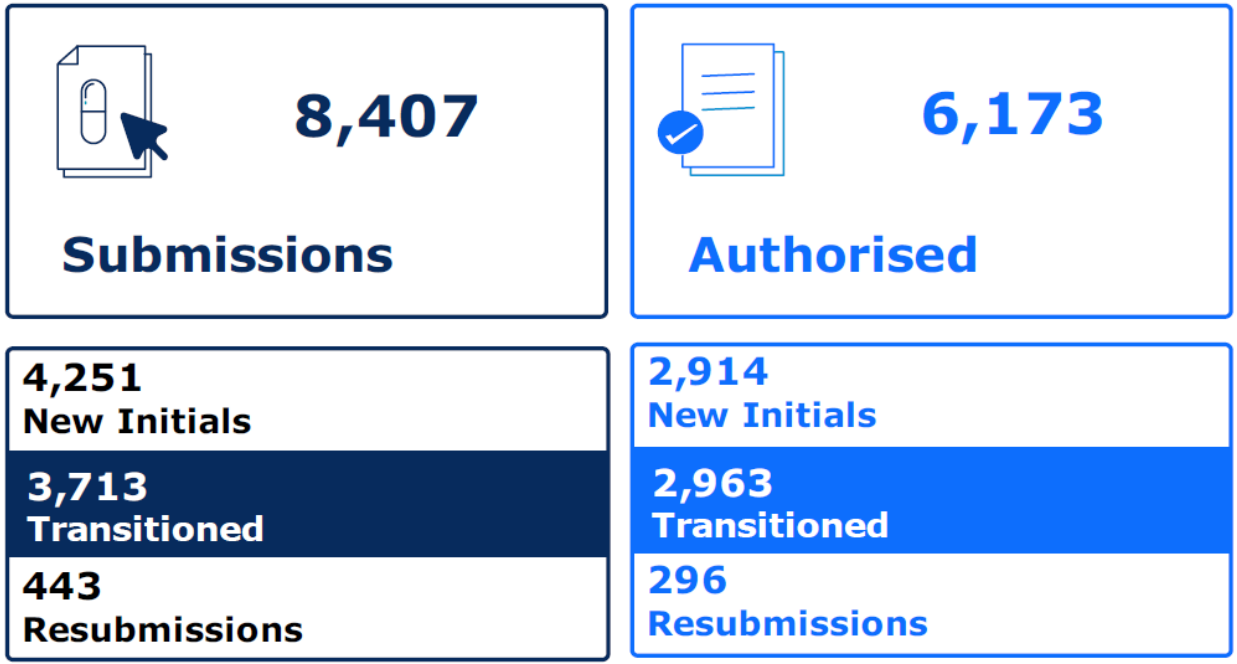
Clinical trial applications were submitted separately to regulators and ethics committees in each EU Member State

After the Clinical Trials Regulation

Single clinical trial application covering regulatory and ethics submission in up to 27 Member States

Applies as of **31 January 2022**

Clinical trials in the EU*

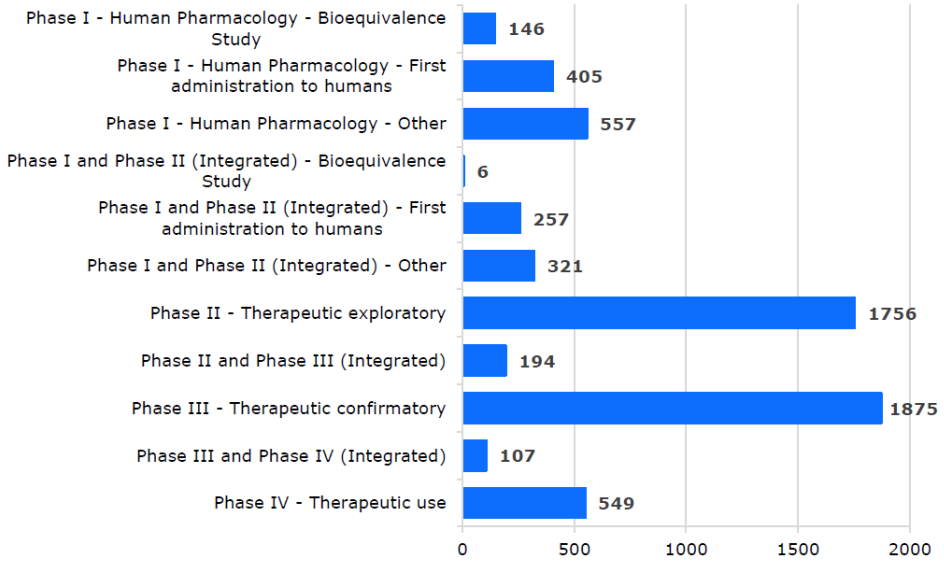


Monthly KPI reports published to monitor the EU clinical trials environment

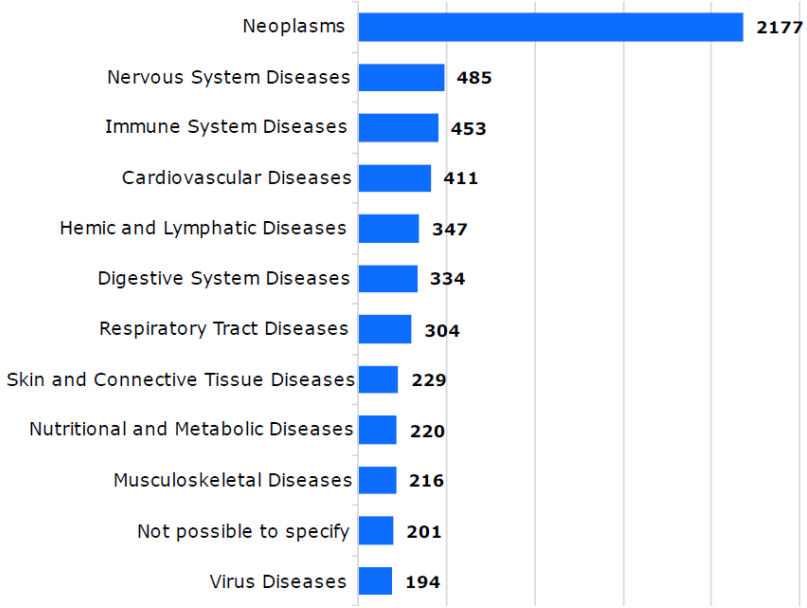
*data January 2022 – September 2024

Clinical trials in the EU*

Authorised CTs per phase



Authorised CTs per therapeutic area



* data January 2022 – September 2024

Transition trials to the CTR/CTIS

- **By 30 January 2025**, any ongoing trials under the Clinical Trials Directive will need to be transitioned to CTIS to follow the CTR
- Sponsors have submitted around 3,713 transitional trials in CTIS (as of end of September 2024)
- Guidance to sponsors transitioning trials available from the European Commission, EMA and Clinical Trials Coordination Group (CTCG)
- Ongoing support to sponsors as the end of the transition period approaches

CTIS Delivery: 2024 Roadmap- key milestones status

System Stability:
Enhance user experience
Over 15.000 applications (IN, SM, AMSC) submitted.
Noted an increase in the number of transitional trials

Performance:
Continuous monitoring
Improved performance for creation of SM and in the context of RFIs in multinational trials.

Security:
Continues monitoring
Monitoring of threat concerns, including cyberattacks and quality coding.

System improvements: To improve UI and reduce workload.

Submission of SM: Analysis to started in Q4 under the Simplification Task Force to modify the rules for SM submission.

Public Portal:
Simplified transparency rules.
New public portal launched on 18th June.

CTIS Simplification:
Revision and Simplification of Business Rules towards modernization. *There are 3 topics ongoing (Role Matrix, Safety and Timetable).*

SAFe Agile: complete transition to SAFe Agile from Q2 2024.

WHO: CTIS already data provider, request submitted to become WHO primary registry.

Paediatric Legislation:
Third country paediatric module. Analysis to start in Q4.

Training & Communications:
Continued engagement with stakeholders through dedicated clinics and bite-size events, material updated regularly.

The Clinical Trial Information System publication rules

Article 81(4) of Regulation (EU) No. 536/2014: legal basis for the establishment a publicly accessible EU clinical trials database, while protecting commercially confidential information (CCI), personal data (PD) and confidential information on the assessment conducted by MSs

The CTIS publication rules recently underwent a simplification process, as a result of a public consultation conducted in 2023

The Revised transparency rules now foresee an **earlier** publication of **key** documents of interest, which brings the following benefits:

- increases the public engagement and trust
- allows a faster preparation of application dossier by sponsors (including SMEs and Academia)

- ✓ Patients and HCPs can access key data and documents as early as possible in the clinical trial lifecycle
- ✓ Increased awareness on possible treatment options
- ✓ Clinical trial information is easier to find and to consult
- ✓ Simplified publication rules reduced the burden to CTIS users and help to promote conduct of clinical research in the EU

Principles of the revised CTIS transparency rules

- Clinical trials are made publicly available as per timelines based on their development phase (trial category) and population age
- For most of the trials publication of data and documents occurs at the time of Member State decision on the application
- Specificities are in place for early development phase trials ('Category 1' trials and integrated phase I and II trials)
- Summary of results and of Clinical Study Reports are published upon submission to CTIS

Reference training:
Quick user guide + CTIS Bitesize Talk on revised transparency rules

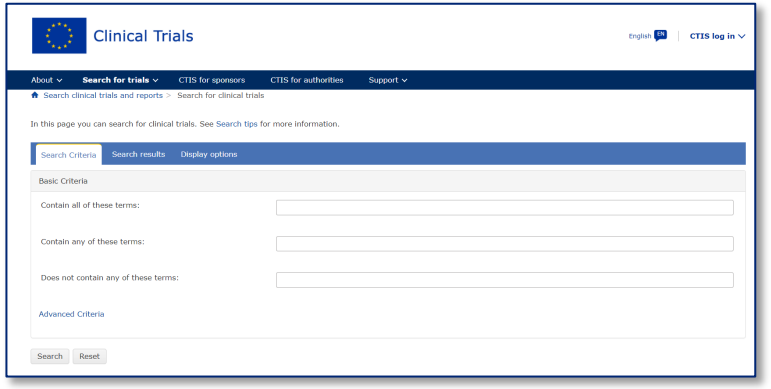
Intermediate summary of results is NOT published

Category	Trial type	Publication rules
Category 1 Pharmaceutical development clinical trials	Phase I, Phase 0, Bioequivalence, similarity trials for biosimilars, equivalence trials	On adults: most info (structured data/docs) is published 30 months after EU/EEA End of Trial On paediatrics: structured data published at decision date, documents published at submission of results
Category 2 Therapeutic exploratory & confirmatory clinical trials	Phase I and phase II integrated, Phase II, Phase II and phase III integrated, Phase III clinical trials	All info published upon decision date, except for details on product dosage of integrated phase I and II (published 30 months after EoT)
Category 3 Therapeutic use clinical trials	Phase III and phase IV integrated, phase IV trials	All info published upon decision date

SmPC, Subject information and informed consent form, Recruitment arrangements are never published for all Category 1 trials

Launch of new CTIS Public Portal on 18 June 2024

- The Revised CTIS transparency rules became applicable on 18 June 2024 with the launch of a new version of CTIS public portal
- Applications submitted as of 18 June follow the revised rules. For those submitted before, only structured data were published ('historical' trials)
- **Over 6,500 trials are public**, of which over **2,600 with documents.** Overall, more than 64,300 documents are now publicly available



CTIS publication rules are summarised in the Annex 1 to the Guidance document on how to approach the protection of personal data and CCI while using the CTIS

More info is in the Q&A on the protection of CCI and Personal Data, and detailed list of fields subject to publication is the List of CTIS application fields and documents + notifications fields

What you can search for…

Information you can view on each clinical trial includes:

- Trial identifiers (EU CT number, protocol code, title etc)
- Therapeutic intent, objectives, endpoints and trial design
- Participants inclusion and exclusion criteria
- Trial locations and contact details of principal investigator
- Sponsor(s) contact information
- Start and end dates and recruitment timelines
- Safety notifications and corrective measures

You can also view the following trial **documents**:

- Protocol and protocol synopsis
- Summary of the products characteristics, when applicable
- Recruitment arrangements, Subject information and informed consent form
- Summary of results, layperson summary and Clinical Study Report, when posted

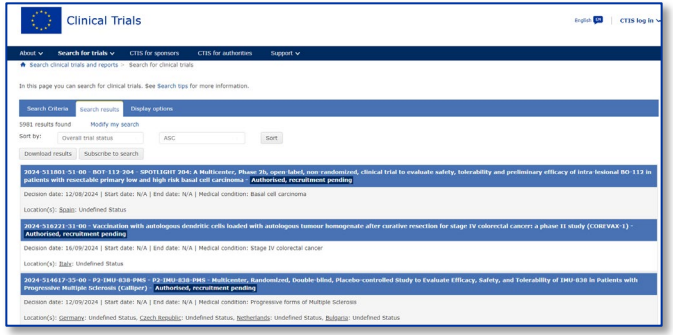
See: what you can search for

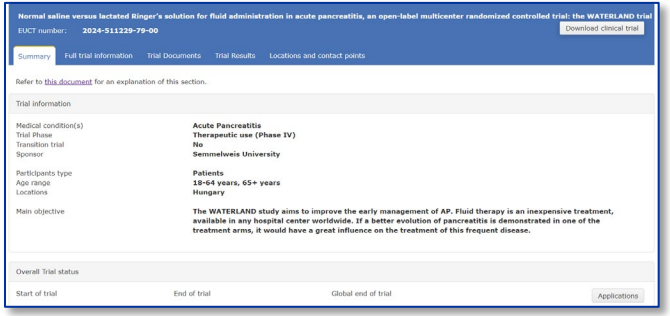
… and how:

Several stakeholders were consulted for proposals of further improvements of our CTIS public portal, including patients, researchers and HCPs

New features deployed in September 2024:

- Advanced Search, users can perform more detailed searches (e.g. CT status per Member state)
- Download specific CT information
- Download results of a performed search (granular information on participants' age is now also included in the 'Display options' and in the 'Download clinical trials' file)
- RSS-feed, users can subscribe to alerts on updates
- Major user interface improvements (clearer list of search results, recruitment status displayed, ad hoc sections on docs & on locations and contact points, lay language explanations of fields)





Better, faster, optimised CTs

We must seize the opportunity to get better medicines to patients faster

- A single clinical trial application covering up to 27 countries
- Streamlined process for the authorisation and supervision of clinical trials
- Public, searchable database for healthcare professionals, patients, and other interested parties with highest level of transparency
- Outstanding academic settings for patients' care

How to stay informed

Subscribe
to the CT Highlights newsletter and CTIS Newsflash

Previous issues here

Follow
the ACT EU website for updates

Contact
the ACT EU mailbox

Training and Support to CTIS Users

Regular Communications

- Clinical trials KPI reports are published as part of the ACT EU programme (link)
- Bi-weekly Newsflash to all users - link
- Clinical Trials Highlights Newsletter – link

Regular Events

- CTIS Walk-in Clinics - link– *next on 20 November 2024*
- Bitesize talks – link *next on 16 October 2024*

Trainings & related materials

- Sponsor end user trainings – link *next on 28-31 October 2024*
- Revised Transparency rules - link
- CTIS Training environment – survey link to request access
- Query Management Working Group Q&A on CTR and CTIS – link
- Step by step guide on registering organisations locally in CTIS - link
- 23 online training modules published
- Sponsor handbook - link

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 Help desk and tips for users

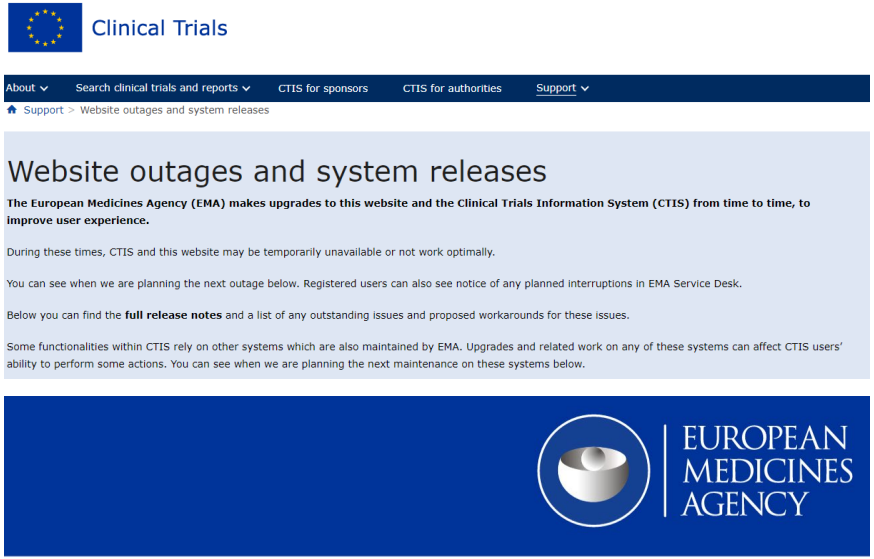
CTIS Help desk and tips for users

The Website outages and system releases section of the CTIS website includes all relevant resources on system updates:

- Release notes
- List of known issues and proposed workarounds (for sponsor workspace)
- Planned system interruptions (information also available in EMA service desk)

Tips for end-users

Newsflash



Tips for users: reporting issues to CTIS User Support Service

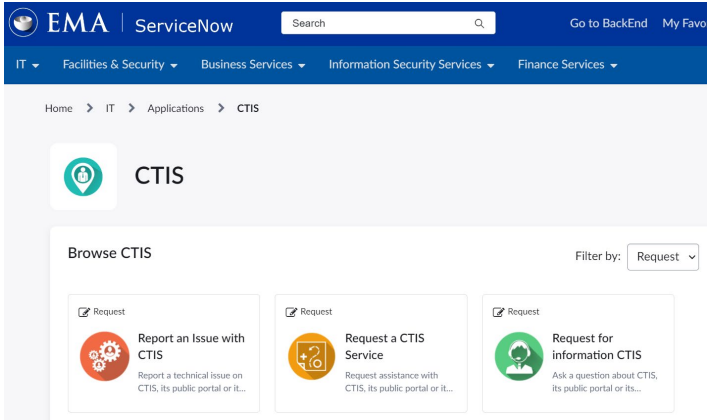
CTIS: submitting a ServiceNow ticket

Detailed incident description

Provide as much information as possible

- Username and role(s)
- **CTA number**/ RFI number
- Application ID

- Describe steps taken
- **Indicate due date** (if any)
- Attach screenshots of the issue



Incident management

- Service desk set up and operating according to industry standards
- Daily monitoring of incoming CTIS tickets
- Prioritisation according to urgency and impact
- Daily briefings between colleagues operating service desk, IT and business

Transition trials: useful material

Reference documents to Transition trials have been published in the EC website, EMA website and CTCG website:

- EC: Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation
- CTCG: CTCG Best Practice Guide for sponsors of multinational clinical trials (at the HMA webpage https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html), under key documents.
- EMA: BiteSize event June 2022 dedicated to Transitional trials (demo of functionality included).
- EMA: BiteSize event June 2023 dedicated to Transition trials (CTCG participation)
- CTIS webinar July 2023, Second year of transition
- EMA: Bitesize event February 2024 dedicated to Transition Trials (CTCG participation)
- EMA: Training for non-commercial sponsors event February 2024
- CTIS webinar March 2024, Last Year of Transition
- EMA: Sponsor Handbook / Chapter 05
- EMA: Training Module M23

Transparency rules: useful material

Reference documentation

- Revised transparency rules
- Quick guide for users
- Guidance document on how to approach the protection of personal data and commercially confidential information (CCI) while using CTIS and its Annex I
- Q&A on the protection of CCI and Personal Data while using CTIS
- List of CTIS application fields and documents (with publication details)
- List of CTIS notifications fields and documents (with publication details)
- CTIS Bitesize talk on the transparency rules