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SCIENCE MEDICINES HEALTH

Clinical Trials Regulation (EC) No. 536/2014 Update on the EU Portal and Database

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The Clinical Trial Regulation: what is new?

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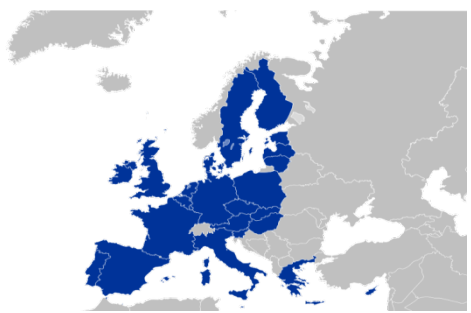
Before May 2004

Different processes and requirements for clinical trial authorisations in each Member States…

… resulted in delays and complications effecting conduct of clinical trials in the EU.

Directive 2001/20/EC

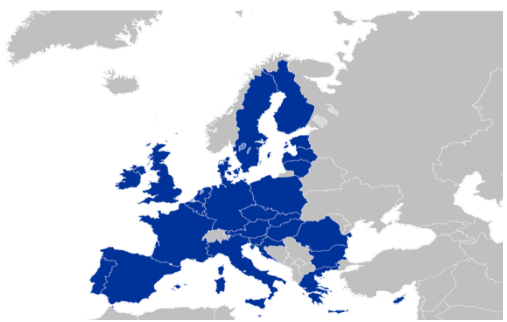


First step to harmonise processes and requirements for clinical trial authorisations.

Implementation 1 May 2004.

Concerns expressed soon after its implementation.

Regulation (EU) 536/2014



Published on 27 May 2014.

Application 6 months after confirmation published in the OJ of full functionality of EU portal and EU database, in any event not earlier than 28 May 2016.

Transitional arrangements.

The Clinical Trial Regulation: Objectives

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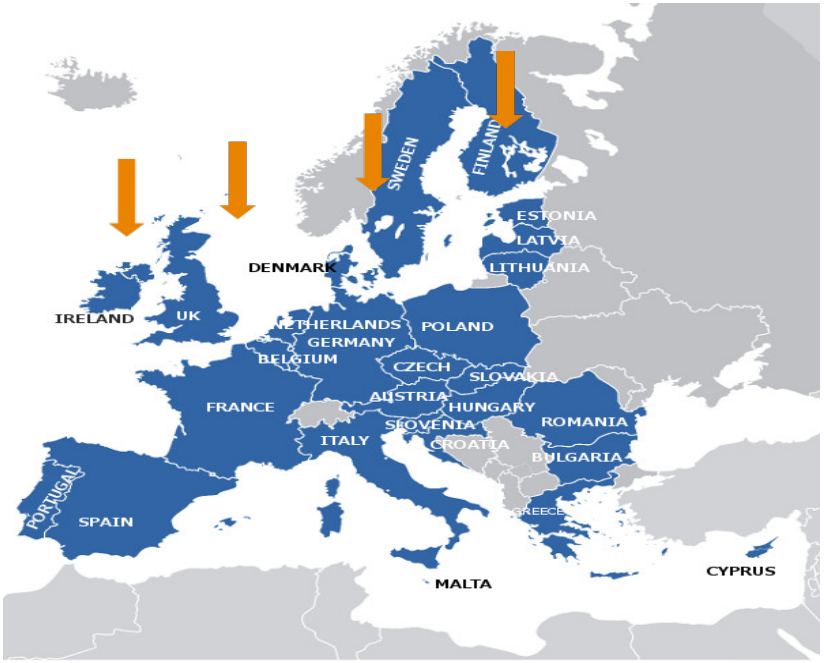
Directive versus Regulation

Implemented in national laws



Directly applicable

Objectives of new CTR

- To protect the rights, safety, dignity and well-being of subjects and the reliability and robustness of the data generated in the CT,
- To foster innovation and simplify the clinical trial application process, in particular for multi-national trials,
- To increase transparency, keeping the balance between protecting public health and fostering the innovation capacity of European medical research while recognising the legitimate economic interests of the sponsors.
- Overall objective: Make EU attractive for R&D.

Scope of Regulation (EU) 536/2014

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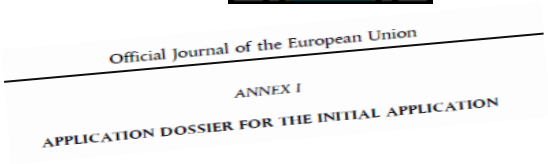
- **Unchanged scope:**
  - **Interventional clinical trials with human medicinal products.**
  - **NEW:** new category of low intervention clinical trials with adapted requirements.
    - The investigational medicinal products (IMP) are authorised,
    - If the IMP is not used in accordance with the terms of the MA, that use is supported by published scientific evidence on S&E,
    - Minimal additional risk or burden to the safety of the subjects compared to normal clinical practice.

- **Not covered:**
  - Non-interventional trials,
  - Trials without medicinal products (e.g. devices, surgery, etc).

Key changes from the CT Regulation

- **Single e-submission to all MSs** via an EU portal (accessible to MS NCAs and Ethics Committees). The EU CT system is to be developed and managed by EMA.
- **Harmonised dossier** (Annex I to the Regulation / language of the documents decided by each MS).
- **Coordinated assessment** between Reporting MS and Concerned MSs.
- One **single** Member State **decision.**


Official Journal of the European Union

ANNEX I

APPLICATION DOSSIER FOR THE INITIAL APPLICATION

Authorisation procedure: important changes

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- **Reporting MS**: proposed by sponsor but proposal discussed between MS.
- **Part I (coordinated assessment) and Part II:** parallel assessment of common documents and MS-specific aspects
- **Possibility to opt-out from Part I conclusions** allowed if:
  - ❖ CT will lead to patients receiving inferior treatment than normal practice in that MS,
  - ❖ Infringement of national law (e.g. CT of medicinal product forbidden in that MS),
  - ❖ Concerns as regards subject safety, data reliability and robustness.
- **MS decides** who **is involved in Part I and Part II** of the assessment (i.e. NCA/EC) to reach single decision.
- **Ethics Committee (EC) role and composition remains national decision** but need to comply with procedure and timelines. Take account view of **a layperson**.

Key changes – supervision and publication

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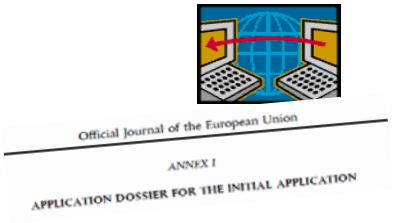
- Introducing a **risk adapted approach** by applying less stringent rules to low-intervention trials
- **Simplifying safety reporting requirements.**
- **Reinforcing supervision of clinical trials** by introducing Union Controls in Member States and third countries to ensure that the Regulation is properly supervised and enforced.
- Provisions concerning **clinical trials conducted outside the EU** but referred to in a clinical trial application within the EU, which will have to comply with regulatory **requirements** that are at least **equivalent to those applicable in the EU.**
- **Increasing transparency** as regards clinical trials and their outcomes.
  Appendix, on disclosure rules to the "functional specifications for the EU Portal and EU Database to be audited – EMA/42176/2014"



Transition period

Directive 2001/20/EC

Regulation (EU) 536/2014

3 year transition period

- Starts when Regulation becomes applicable
- First year: CT can be submitted under old (Dir.) or new (Reg.) systems,
- Years 2 & 3: trials authorised under old system remain under that system.

End of legacy

- 3 years after entry into force. All CTs to switch to new Regulation.

The EU portal and database project

What should the Agency deliver?

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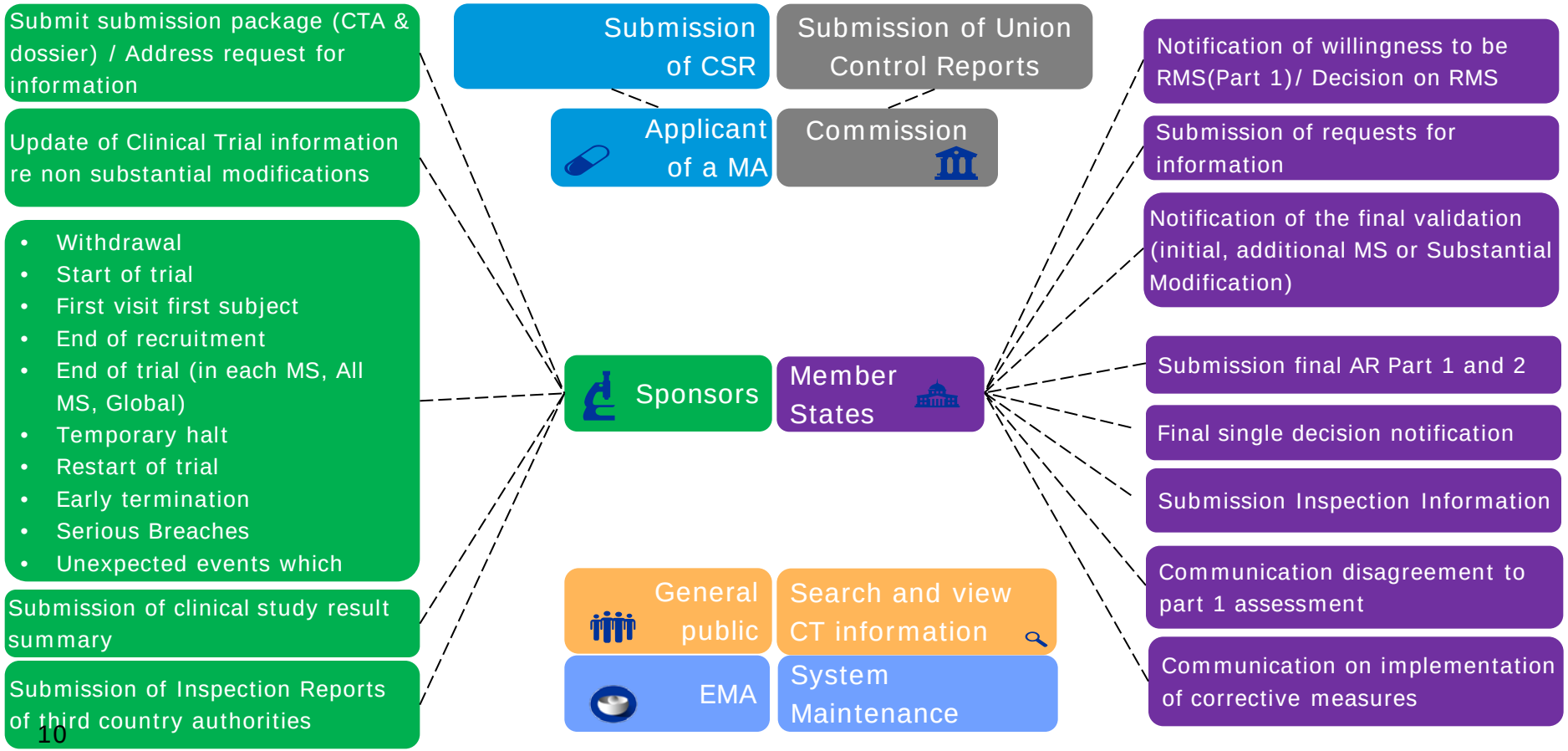
The Agency has to deliver, and maintain the IT platforms needed for the implementation as required by Regulation:

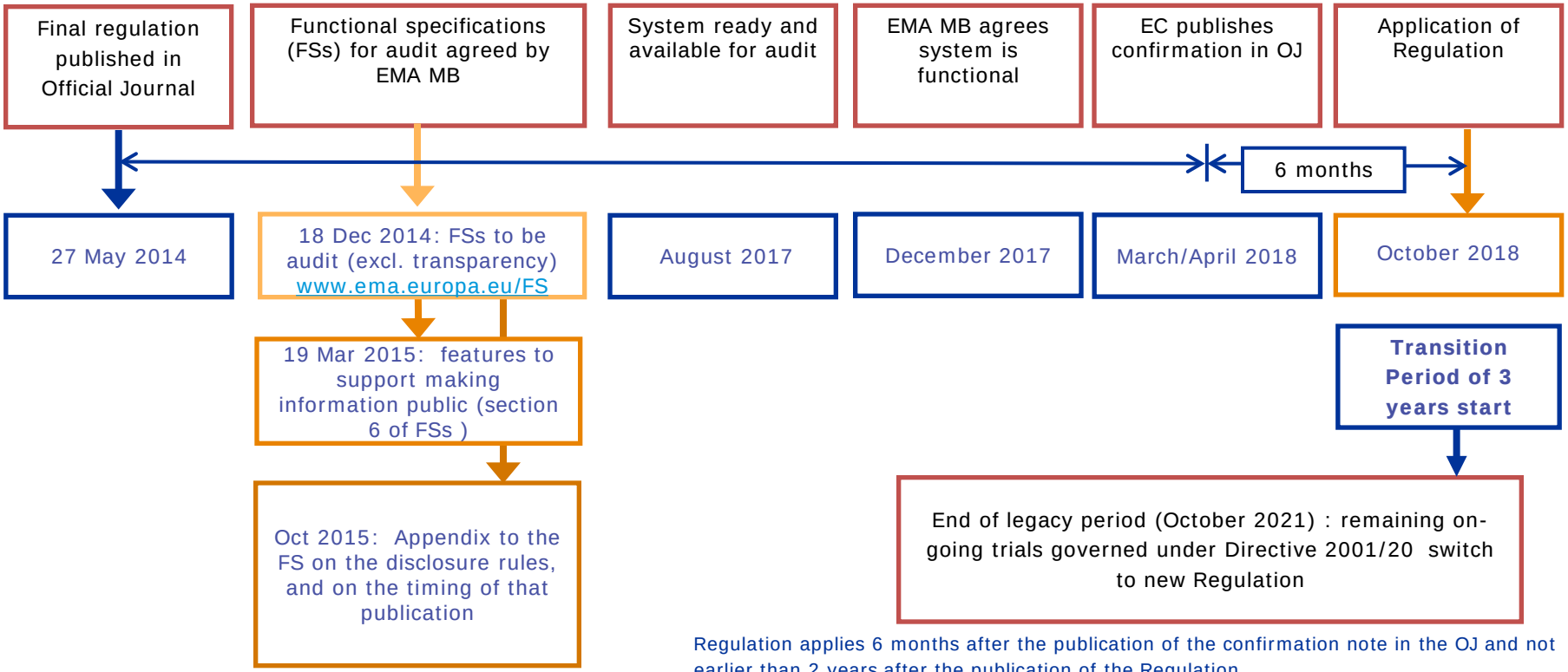
> Article 81(1) “The Agency shall, in collaboration with the Member States and the Commission, set up and maintain a EU database at Union level. The Agency shall be considered to be the controller of the EU database and shall be responsible for avoiding unnecessary duplication between the EU database and the EudraCT and Eudravigilance databases.”

- **EU Portal and database project** (Art. 80, 81, 82 and 84)
- **Safety Reporting project** (Art. 40 to 44)
- EudraCT and EU Clinical Trial Register Legacy project (Art. 98)
- A data warehouse is part of these developments to facilitate the reporting tools between the different systems

Activities in the system



CT regulation timelines/key milestones



Regulation applies 6 months after the publication of the confirmation note in the OJ and not earlier than 2 years after the publication of the Regulation

EU portal and database - Maximum project timeline

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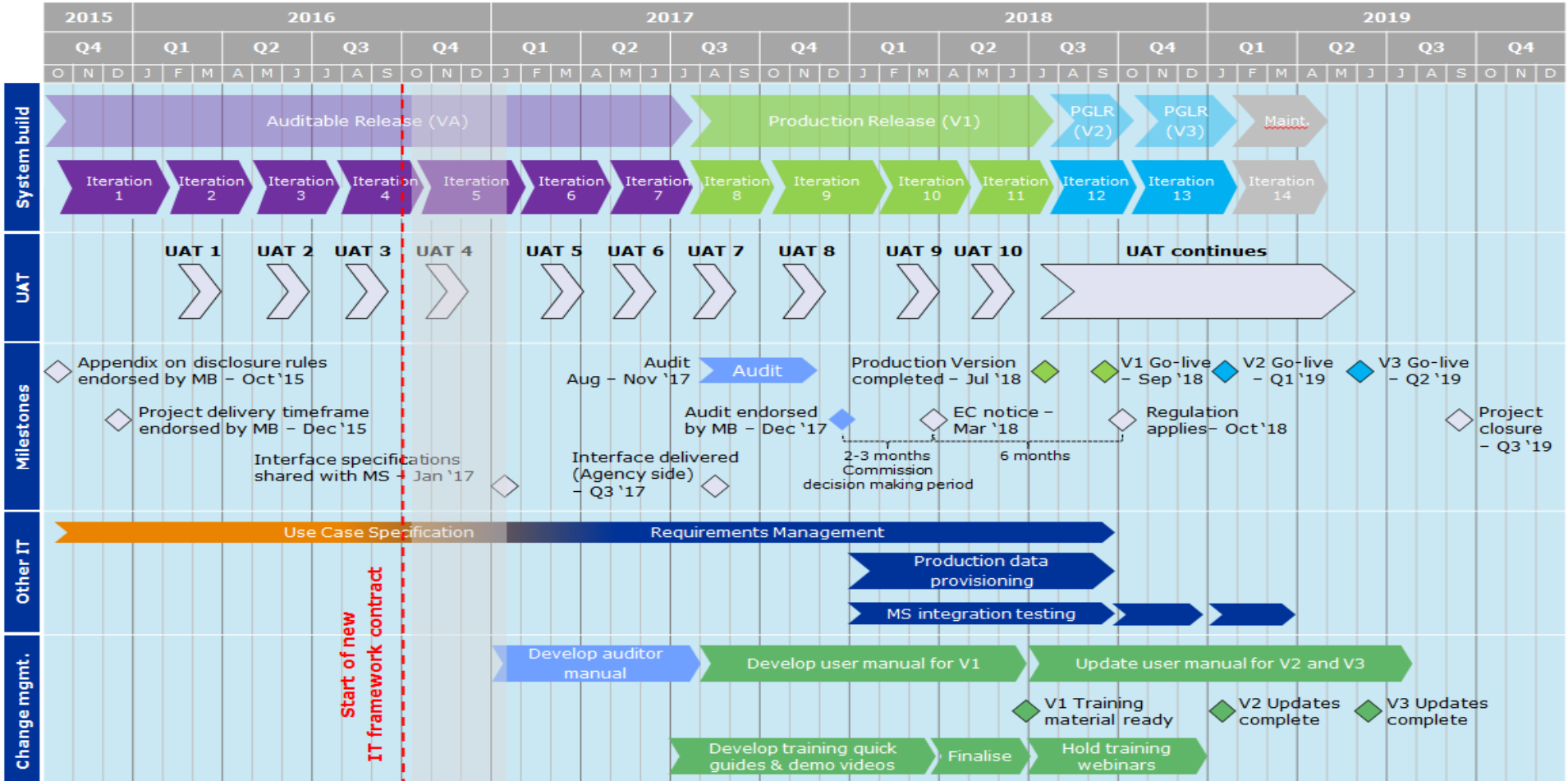

UAT (User Acceptance Testing)

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- UAT verifies the system has the **right features** (business functions and the system flow against business requirements)
- Other IT test types verify the system has **no significant bugs** and are carried out prior to UAT
- All Member States and wide range of stakeholders can participate using remote access
- UAT is planned every **three months** (once per iteration)
- Each UAT is carried out **remotely** during a fixed period, although some on-site testing is planned.

EU Portal and Database UAT 5 Overview

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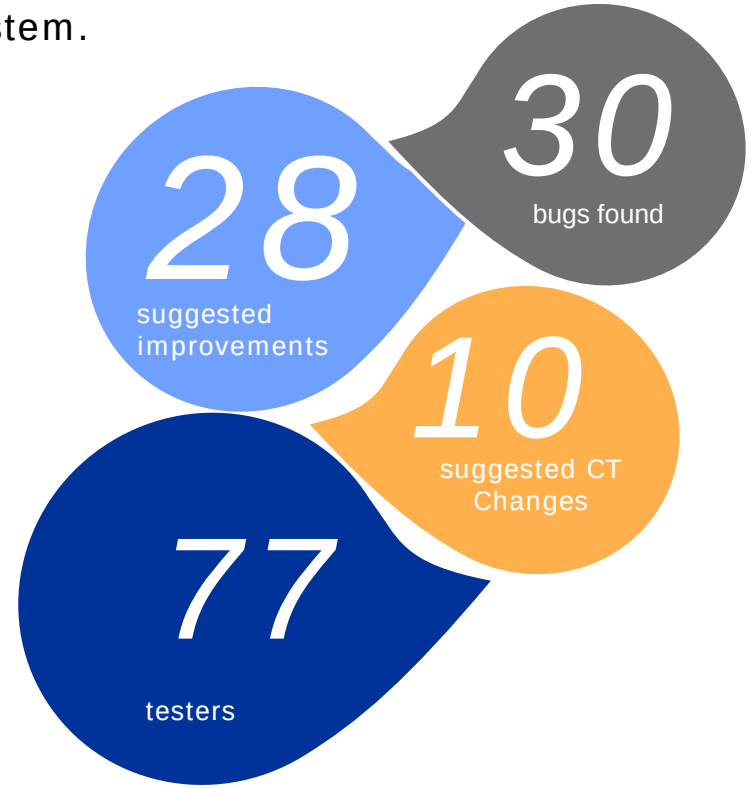
UAT 5 for the EU Portal and Database was successful testers (representing a total of **39** sponsor organisations, EU member states and the EC) participating and providing feedback on the latest version of the system.

These organisations included:

- The European Commission
- 24 Member States
  - Comprising of *NCA* representatives and *ethics committee* representatives
- 14 Sponsor organisations
  - Including both *commercial* organisations and *non-commercial* organisations



- All scenarios and freeform testing received an average rating between **5.9 and 7.3** out of 10
- The average ratings given by each tester about functionalities of the system:
  - Satisfaction – **6.84**
  - Usability – **6.63**
  - Design – **6.66**

Summary:

- **IT maintenance** : EMA will build, maintain and update the IT platforms that support the CT Regulation
- **Harmonisation**: One single submission for authorisation of a clinical trial to National Competent Authority & Ethics Committee and for public registration (primary register of clinical trials)
- **Member state collaboration**: Facilitate cooperation among MSCs in assessing an application for authorisation of a clinical trial
- **One single decision** per Member States
- **Public data** and information about medicines, their development
  - To generate trust – information is available
  - To build confidence – I understand what is happening
  - To empower – knowledge enables decision-making

Thank you for your attention

Further information

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