



# Clinical Trial Regulation: Implementation tasks for the European Commission

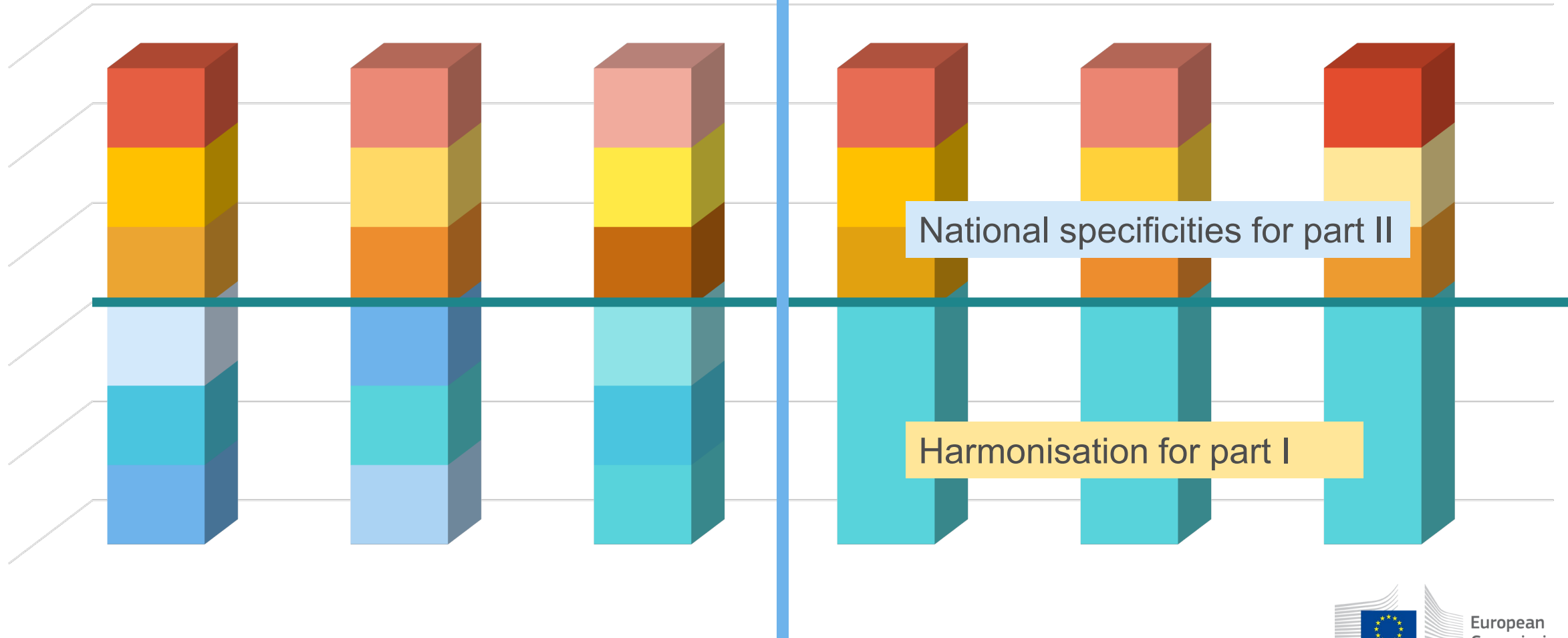
*ACT EU Multistakeholder platform*

*EMA workshop 22 – 23 June 2023*

# CTR: a new legal framework

CTD

CTR



# Delegated and implementing acts

- [Implementing Regulation \(EU\) 2017/556 of 24 March 2017](#) on detailed arrangements for the good clinical practice inspection procedure
- [Commission Delegated Regulation \(EU\) 2017/1569](#) specifies principles and guidelines for good manufacturing practice for investigational medicinal products and arrangements for inspection
- [Commission Implementing Regulation \(EU\) 2022/20](#) setting up the rules and procedures for the cooperation of the Member States in safety assessment of clinical trials, became applicable on 31/1/2022.
- [Commission Delegated Regulation \(EU\) 2022/2239](#) as regards labelling requirements for unauthorised investigational medicinal products

# Guidance on the CTR application: the Q&A document

- Under EUDRALEX Volume 10 - The rules governing medicinal products in the European Union
- Version 6.4, CTEG consulted, CTAG endorsed.
  - Annex II: Language requirements for part I documents
  - Annex III: Part II documentation - where sponsors can find national requirements
- Size:
  - 127 pages, 162 with annexes
  - 527 paragraphs
  - 12 chapters

National competent authorities, ethics committee  
EMA (CTIS helpdesk, Product Owner Expert Group, ACT EU)

Escalate if horizontal issue



CTCG  
Best practices  
Roundtable of assessors

Escalate if not solved by best practices



CTAG / CTEG

Amend Q&A

# From the CTR provision to CTIS functionality

REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 16 April 2014

on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC

(Text with EEA relevance)

CHAPTER I

GENERAL PROVISIONS

Article 1

Scope

This Regulation applies to all clinical trials conducted in the Union.

It does not apply to non-interventional studies.

Article 2

Definitions

Example:

CTR – Article 2

Definition of substantial modification

13) 'Substantial modification' means any change to any aspect of the clinical trial which is made after notification of a decision referred to in Articles 8, 14, 19, 20 or 23 and which is likely to have a substantial impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the clinical trial;





# Q&A – procedures and conditions

February 2023

The rules governing medicinal products in the European Union  
VOLUME 10 - Guidance documents applying to clinical trials

CLINICAL TRIALS REGULATION (EU) No 536/2012

QUESTIONS & ANSWERS

VERSION 6.1

Regularly updated

Submitted for discussion to the Expert Group on Clinical Trials and through written procedure to the Clinical Trials Commission and Advisory Group

3. SUBSTANTIAL MODIFICATIONS	37
3.1 Question: How is "substantial modification" defined?	37
3.2 Question: How are the different changes to ongoing clinical trials classified in the Clinical Trials Regulation?	37
3.3 Question: What are the sponsor's responsibilities regarding changes to a clinical trial, which are not substantial modifications (SM), but are relevant for the supervision of the trial (Art. 81.9)?	38
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3.5 Question: When can a sponsor submit a substantial modification concerning Part I and II?	40
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3.7. Question: How should a sponsor proceed in case a substantial modification is required while the assessment of another application for the same clinical trial is ongoing (under evaluation)?	42
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3.9. How are MSC that have received a partial submission involved in the assessment of part I substantial modifications ?	48
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3.15 Question: can there be different decision of a part I SM in different MSc ? ..	51
3.16 How should the change of the source country of an IMP or AxMP be implemented?	51

# CTIS

EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

## Step-by-step guide

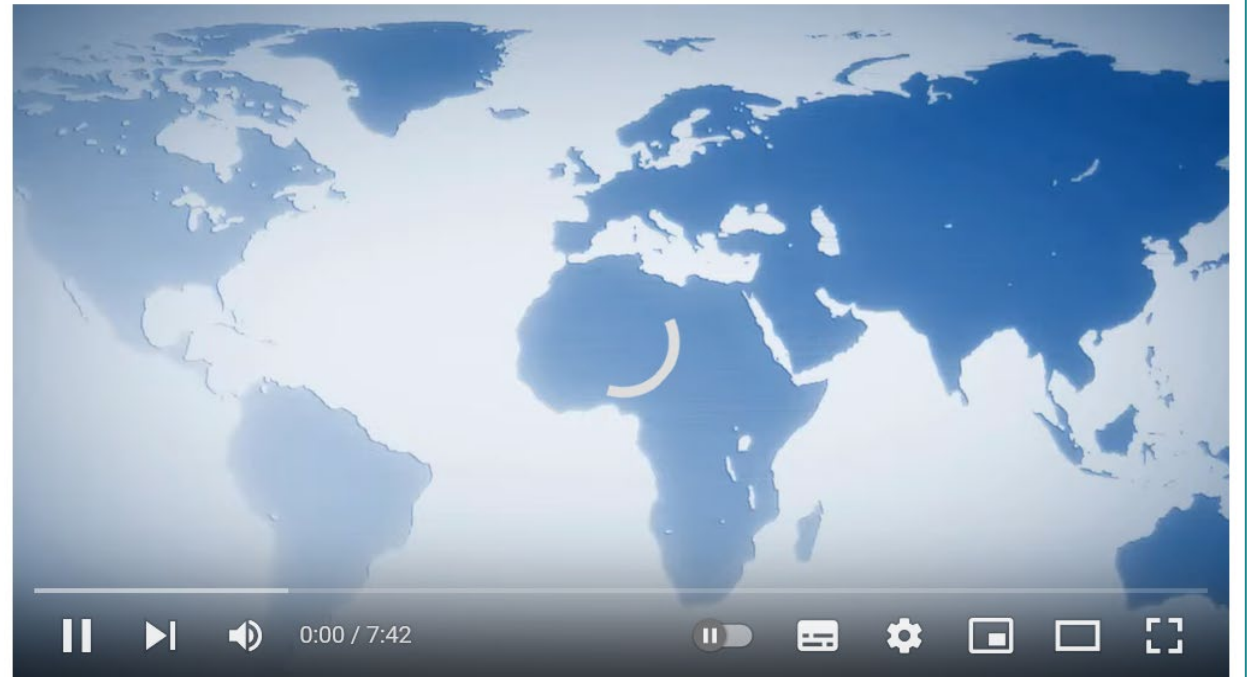
How to evaluate a Substantial  
Modification clinical trial application

CTIS Training Programme – Module 08

Version 1.1 – March 2022

YouTube<sup>LU</sup>

Rechercher



CTIS – M10 How to submit a single trial substantial modification in the CTIS  
Sponsor workspace



European Medicines ...  
18,5 k abonnés

S'abonner

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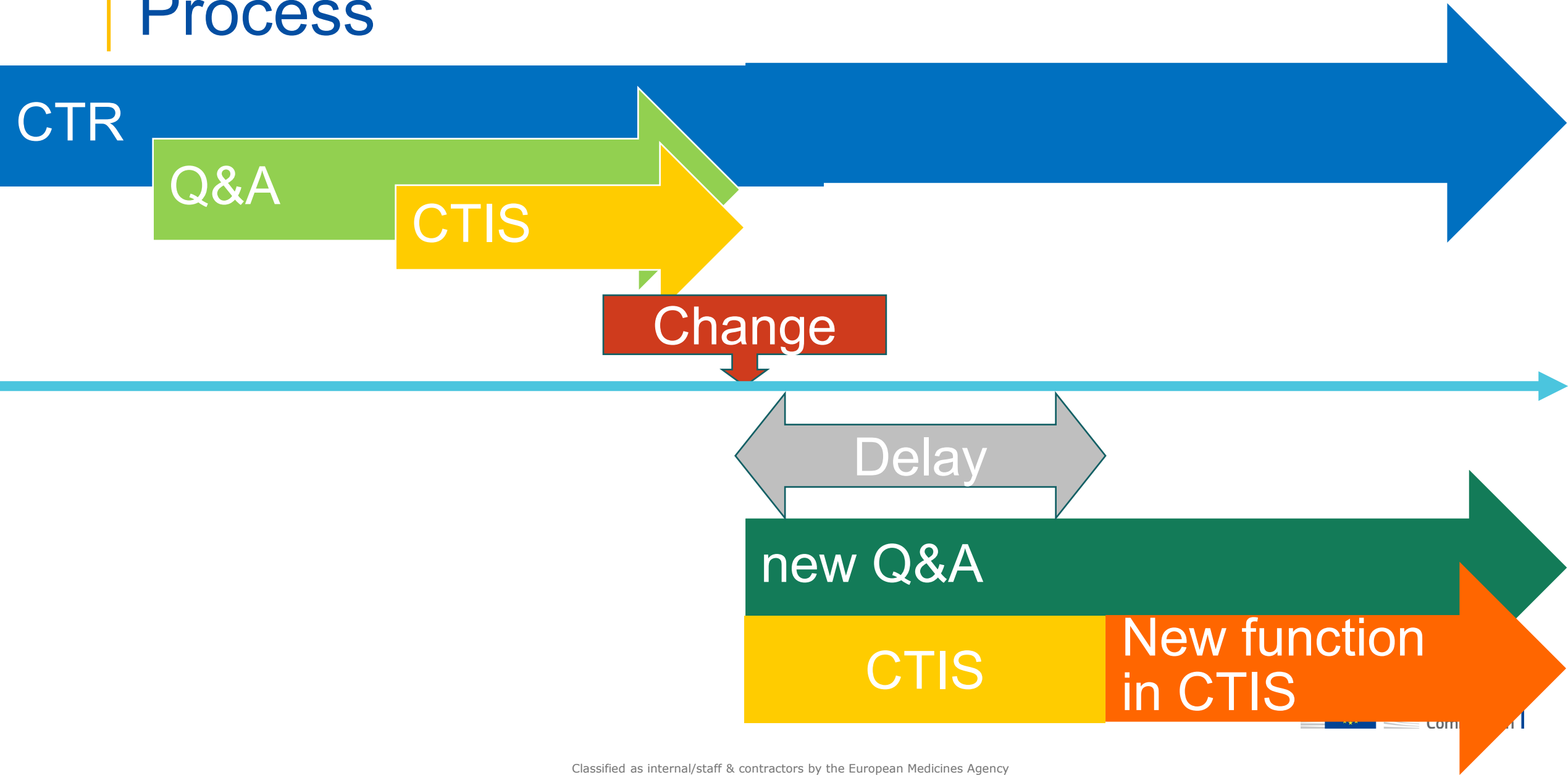


Partager





# Process





# EU Survey on the implementation of the Clinical Trials Regulation



# Survey on the implementation of the Clinical Trials Regulation – round 1

Survey run between 18 July and 9 September 2022 from commercial and non-commercial sponsors

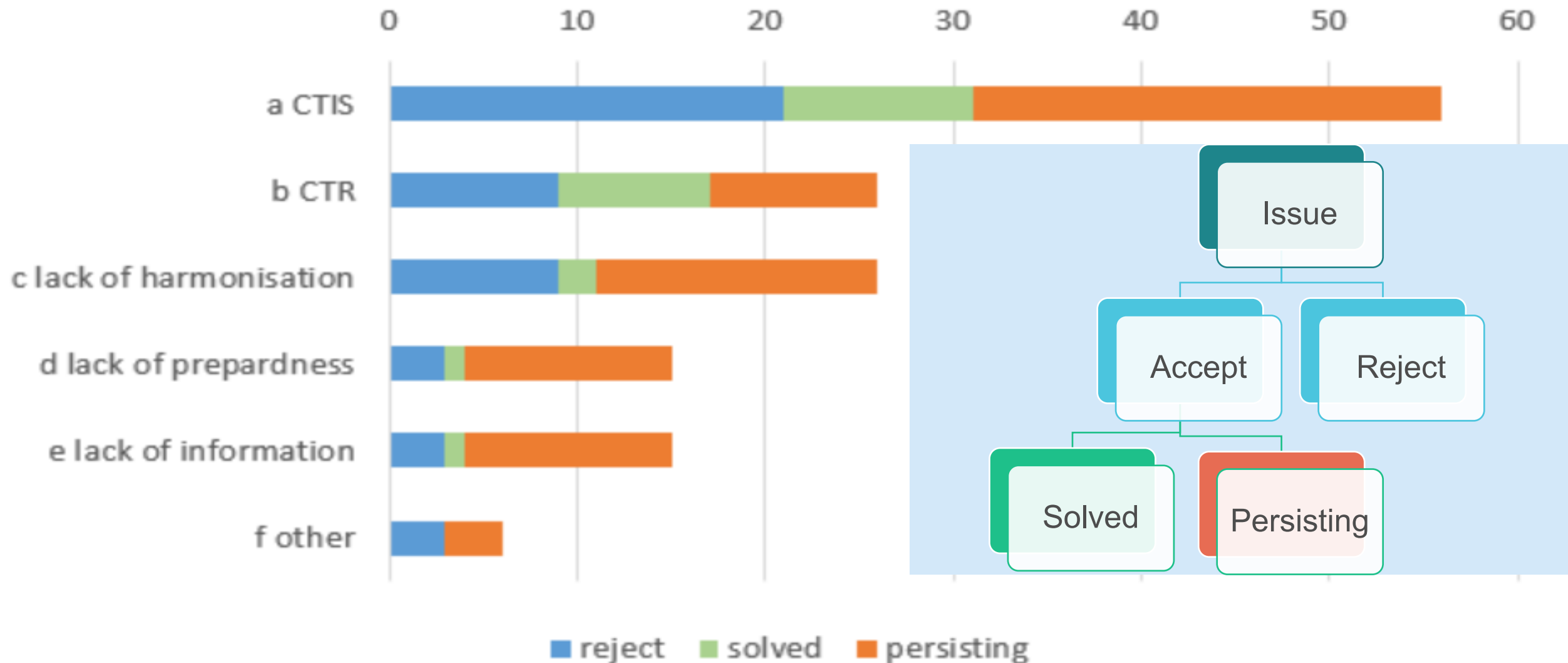
**CTIS:** difficult to use, bugs, lack of functionalities

**CTR:** difficult to cope with the deadlines for RFIs, with new provisions on transparency

**Lack of preparedness of certain MS:** (use of CTIS, national legislation not yet aligned)

**Lack of harmonization:** additional requirements out of the scope of the CTR, guidelines not followed

# Survey on the implementation of the CTR - Identification and screening of comments



# Solutions provided by:

## EMA - CTIS

- CTIS releases
- Guidance revision and production (Q&A on transparency)
- Revision of the rules on transparency

## CTAG and CTEG

- Guidance revision and production (Q&A)
- List of web link to national contact for specific requirements
- Clarification of language requirements

## CTCG

- Enhanced Member States coordination and cooperation
- Assessor roundtable, Ethics Committee forum
- Guidance revision and production (Best practices documents)

## Commission / Member States

- Commission structured dialogue with Member States to ensure full alignment of national rules with the CTR



# Survey on the implementation of the Clinical Trials Regulation - second round

## Objectives

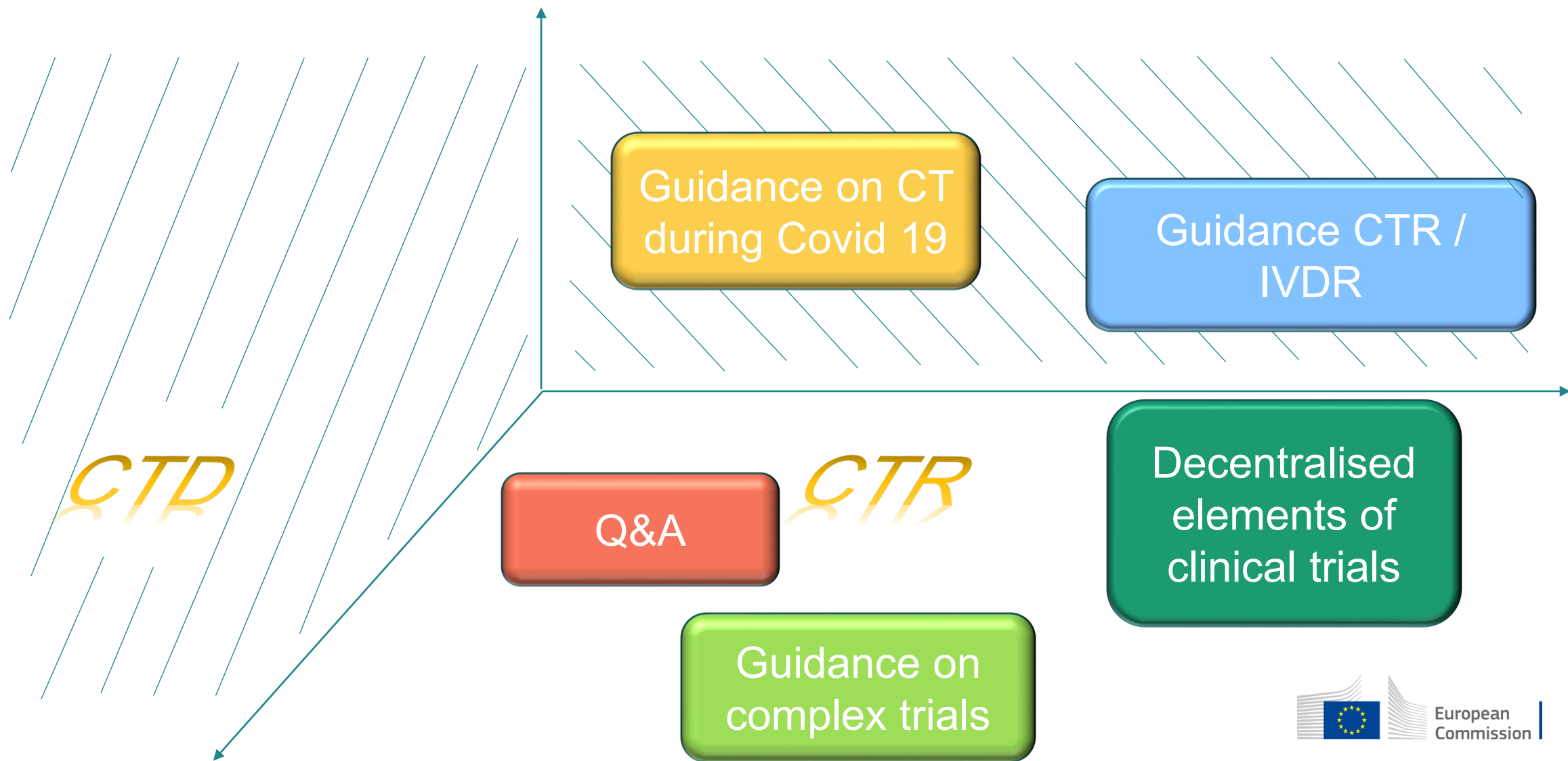
- To understand the remaining hurdles that hamper:
  - a smooth **implementation** of the CTR
  - a smooth **transition** of the clinical trials from EudraCT to CTIS
  - **CTIS** user friendliness
- To measure the **progress** achieved since the last survey

**Deadline for responses:** 30 September 2023

**Duration:** 3 weeks




# CTR framework



# THE LANCET

CORRESPONDENCE | VOLUME 401, ISSUE 10385, P1339, APRIL 22, 2023

## Decentralised elements in clinical trials: recommendations from the European Medicines Regulatory Network

Monique Al • Solange Levison • Wolfgang E Berdel  • Ditte Zerlang Andersen •  
for the Decentralised Clinical Trials Task Force

Published: April 22, 2023 • DOI: [https://doi.org/10.1016/S0140-6736\(23\)00463-4](https://doi.org/10.1016/S0140-6736(23)00463-4)





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