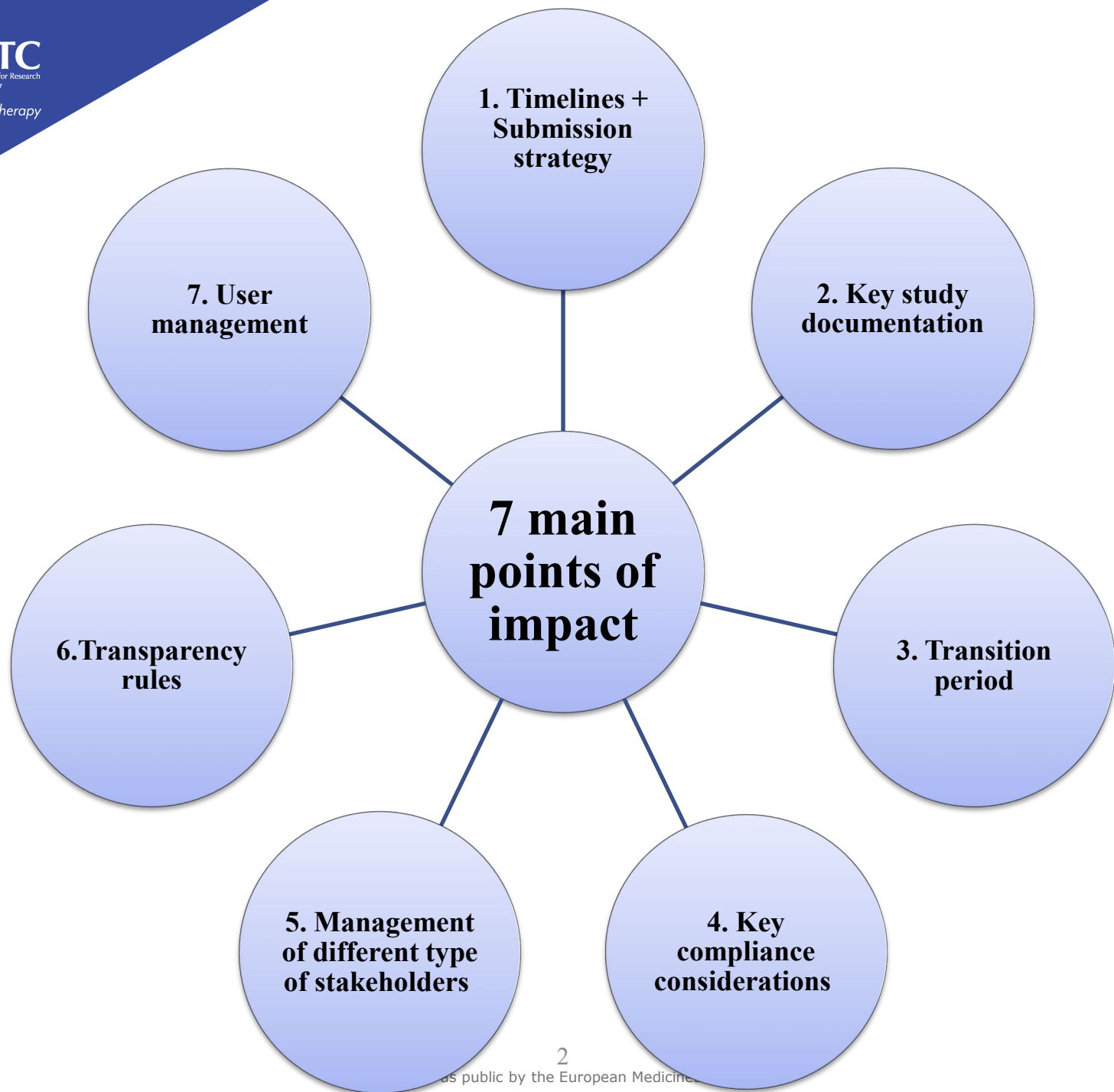


Clinical Trials Regulation No. 536/2014: 7 main points of impact from EORTC perspective



Stéphanie Kromar
EORTC, Sr. Regulatory Affairs Manager
CTIS, Sponsor Product Owner



Initial submission

1. Timelines + Submission strategy

Part

Validation

Assessment

Time for decision

Part I&II
10 days
(Max 25 days)

Part I&II
45 days
(Max 76 days)

Type of RFIs

Completion
10 days

Content
12 days

Substantial modification

1. Timelines + Submission strategy

Part

Validation

Assessment

Time for decision

Part I&II
6 days
(Max 21 days)

Part I&II
Max 69 days

Type of RFIs

Completion
10 days

Content
12 days

Notifications

1. Timelines + Submission strategy

Trial progress

- Start of the trial
- Temporary halt
- Re-start of trial (SM)
- Early termination
- EoT

15 days



Recruitment

- First visit of the first subject
- End of recruitment (temporary or permanent)
- Re-start of recruitment

15 days

Incidents

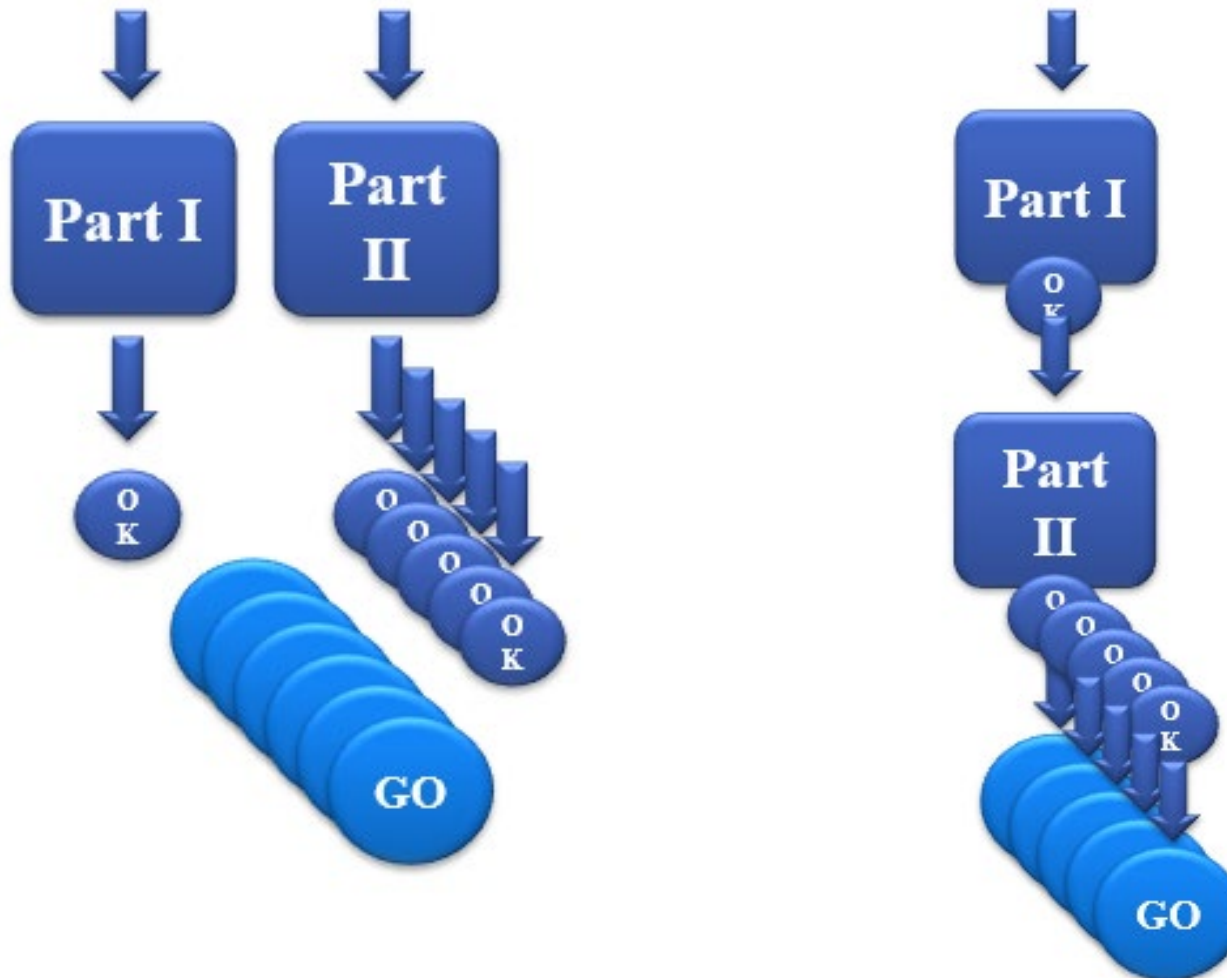
- Serious GCP breach (one or more trials, to concerned MS) **7 days**
- Urgent safety measure **7 days**
- Unexpected event affecting a clinical trial **15 days**
- Inspection reports of third country CA (if requested translated) **? days**

Summary of the CT results + Summary of the CT results for lay persons:

within 1 year after EoT and disregarding the outcome

Submission strategy:

1. Timelines + Submission strategy



Annex I: initial submission

2. Key study documentation

- A. INTRODUCTION AND GENERAL PRINCIPLES**
- B. COVER LETTER**
- C. EU APPLICATION FORM**
- D. PROTOCOL**
- E. INVESTIGATOR'S BROCHURE (IB)**
- F. DOCUMENTATION RELATING TO COMPLIANCE WITH GOOD MANUFACTURING PRACTICE (GMP) FOR THE INVESTIGATIONAL MEDICINAL PRODUCT**
- G. INVESTIGATIONAL MEDICINAL PRODUCT DOSSIER (IMPD)**
- H. AUXILIARY MEDICINAL PRODUCT DOSSIER**
- I. SCIENTIFIC ADVICE AND PAEDIATRIC INVESTIGATION PLAN (PIP)**
- J. CONTENT OF THE LABELLING OF THE INVESTIGATIONAL MEDICINAL PRODUCTS**

- K. RECRUITMENT ARRANGEMENTS** *(information per member state concerned)*
- L. SUBJECT INFORMATION, INFORMED CONSENT FORM AND INFORMED CONSENT PROCEDURE** *(information per member state concerned)*
- M. SUITABILITY OF THE INVESTIGATOR** *(information per member state concerned)*
- N. SUITABILITY OF THE FACILITIES** *(information per member state concerned)*
- O. PROOF OF INSURANCE COVER OR INDEMNIFICATION** *(information per member state concerned)*
- P. FINANCIAL AND OTHER ARRANGEMENTS** *(information per member state concerned)*
- Q. PROOF OF PAYMENT OF FEE** *(information per member state concerned)*
- R. PROOF THAT DATA WILL BE PROCESSED IN COMPLIANCE WITH UNION LAW ON DATA PROTECTION**



Some updates...

2. Key study documentation

New harmonised CV template
Protocol
ICF

Lay language protocol synopsis

1. EU trial number and full trial title
2. Rationale
3. Objective
4. Main trial endpoints
5. Secondary trial endpoints
6. Trial design
7. Trial population
8. Interventions
9. Ethical considerations relating to the clinical trial including the expected benefit to the individual subject or group of patients represented by the trial subjects as well as the nature and extent of burden and risks

Lay language summary of results

1. Clinical trial identification (including title of the trial, protocol number, EU trial number and other identifiers);
2. Name and contact details of the sponsor;
3. General information about the clinical trial (including where and when the trial was conducted, the main objectives of the trial and an explanation of the reasons for conducting it);
4. Population of subjects (including information on the number of subjects included in the trial in the Member State concerned, in the Union and in third countries; age group breakdown and gender breakdown; inclusion and exclusion criteria);
5. Investigational medicinal products used;
6. Description of adverse reactions and their frequency;
7. Overall results of the clinical trial;
8. Comments on the outcome of the clinical trial;
9. Indication if follow up clinical trials are foreseen;
10. Indication where additional information could be found.

Transition period

3. Transition period

Before Go-live

Any CTA submitted at this time, is still governed by the old Directive until 3 years after Go-live

Initial 12 months

A CTA *may* still be submitted in EudraCT and governed by the **old Directive**.

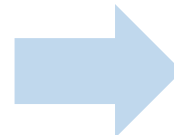
A CTA *may* be submitted in the new EU portal and be governed by the **new Regulation**.

Next 24 months

All initial CTAs *must* be submitted in the new EU portal and be **governed by the new Regulation**.

From 3 years after Go-live

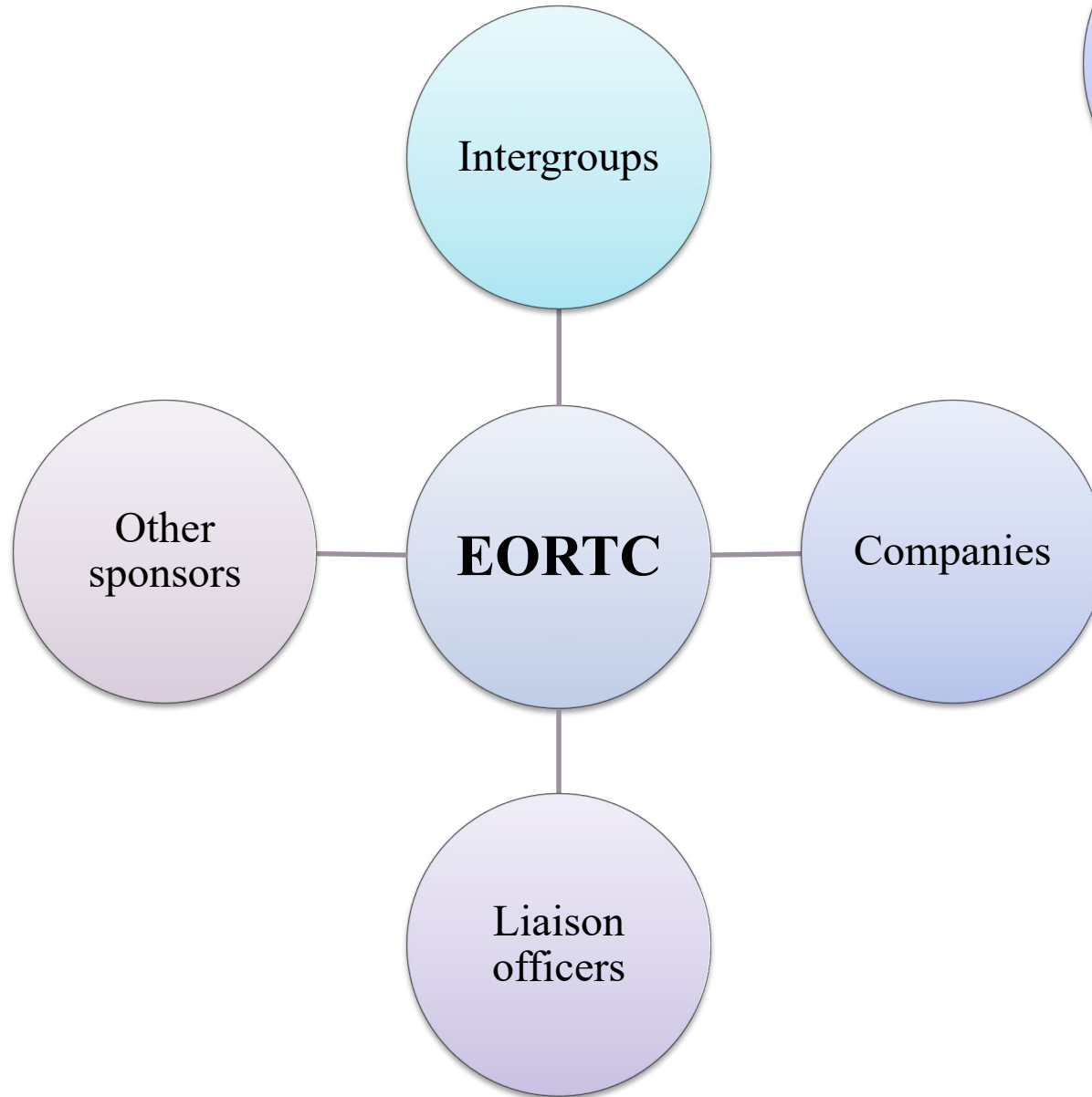
All CTAs are **governed by the new Regulation**, regardless of their date of submission.



Assess your strategy for migration !

The CTR will be there but...

- WMA' s Declaration of Helsinki
- ICH-GCP guidelines
- The General Data Protection Regulation
- ...



**5. Management
of different type
of stakeholders**

(Co-)Sponsorship

5. Management of different type of stakeholders

EU Sponsors

Sponsor: the concept + responsibilities remain = Dir. 2001/20/EC

Co-Sponsorship: Joint responsibility, new term clarified under the CTR

- All of the Sponsors are subjected to the obligations as a sponsor under CTR; unless: splitting the responsibilities
- The sponsors should clearly map the roles and responsibilities in terms of:
 - i) compliance with the authorization of initial and SM of CTs;
 - ii) contact point for all Q from subjects, PIs or regulatory bodies of MSs+ providing the replies;
 - iii) who is responsible for implementing the measures issued during audits and inspections

non-EU Sponsors

Legal representation for non-EU Sponsors:

- Ensures compliance with CTR
- to ensure that enforcement action may be taken by MSs
- to ensure that legal proceedings may be brought in appropriate cases
- choice of MSs (provided there is at least one contact person in EU)

Transparency rules

6. Transparency rules



EU Database will be publically accessible by default, with exceptions justified on any of the following grounds:

Transparency

- Protection of personal data
- Protection of commercially confidential information in particular, taking into account the MA status of the medicinal product, unless there is an overriding public interest in disclosure
- Protecting confidential communication between Member State in relation to the preparation of the assessment report
- Ensuing effective supervision of the conduct trial Member States

User management: approaches

7. User management



Organisation centric

- Available to all groups of users (sponsor, MSs, EC, MAH)
- A high level administrator is required i.e. needs to be assigned in EMA Identity and Access Management system (IAM) (sponsor admin, MS admin, EC admin) or in CTIS by the EMA Admin (MAA admin)
- Management of the users by this Administrator is at organizational level
- Users become affiliated to the organization of the high level administrator

Trial centric

- Available only to sponsor
- Only feasible if no Sponsor Administrator is registered in IAM
- The user will be able to create a CTA through this approach becoming CT Administrator for that specific CTA
- Management of the users by the CT Administrator is at trial level
- Users are not affiliated to any sponsor organization

Thank you