EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

Clinical Trials Regulation No. 536/2014 and its impact on oncology: The clinical research perspective

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EORTC in few words

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Who we are?

Independent	• **Not for Profit organization** where research is done with **unwavering independence** and accountability for making all results public
Multidisciplinary	• Our research spans **all aspects of cancer management**: medical, radiation, surgical, imaging, and translational research
Multi-tumour	• Network of **over 5.300 oncology experts**. Our research is solution-driven, for all types of cancers, leaving no-one behind
International	• A network of **over 920 institutions** in **36 countries;** coordinated and managed from headquarters in Brussels with over **230 core staff**
Regulatory compliance	• Our experts ensure our clinical research activities meet the **strictest regulatory standards and quality assurance requirements**

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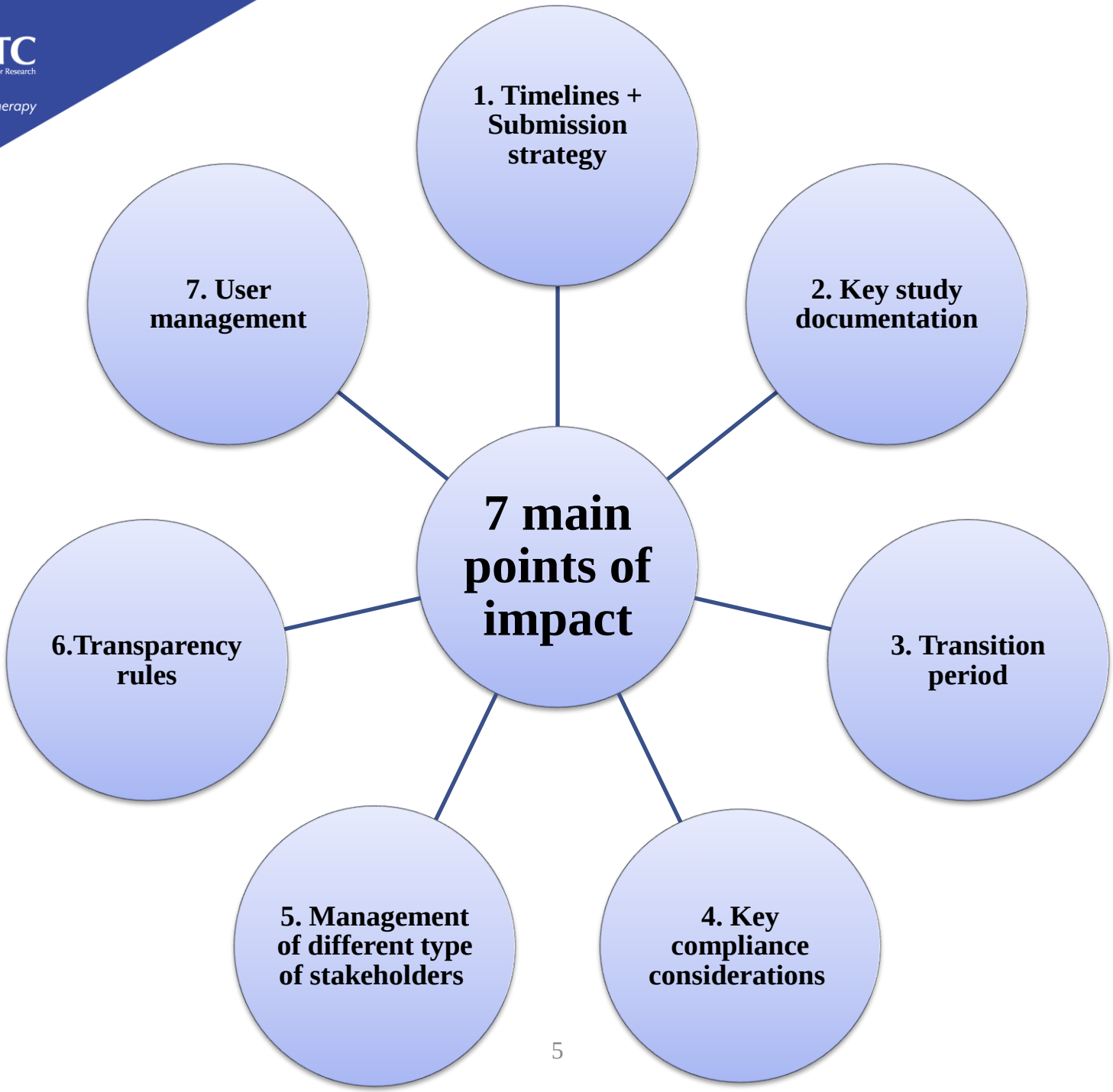
EORTC's CTR impact assessment


1. Timelines + Submission strategy
2. Key study documentation
3. Transition period
4. Key compliance considerations
5. Management of different type of stakeholders
6.Transparency rules
7. User management
7 main points of impact

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1. Timelines + Submission strategy

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Initial submission

Part	Time for decision	Type of RFIs
Validation	**Part I&II** **10 days** (Max 25 days)	**Completion** **10 days**
Assessment	**Part I&II** **45 days** (Max 76 days)	**Content** **12 days**

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Substantial modification

Part	Time for decision	Type of RFIs
Validation	**Part I&II** **6 days** (Max 21 days)	**Completion** **10 days**
Assessment	**Part I&II** **Max 69 days**	**Content** **12 days**

Notifications

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

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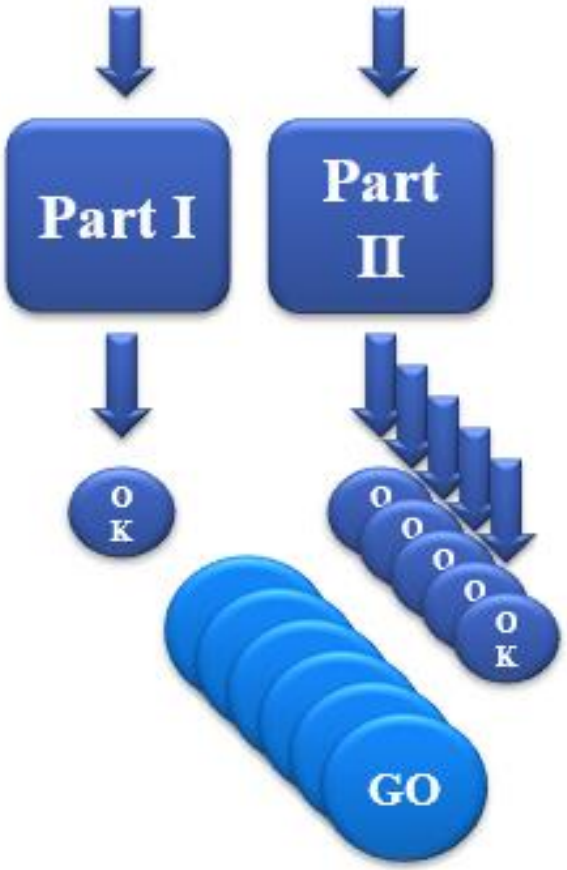
Submission strategy:



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2. Key study documentation

Annex I: initial submission

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 documents updates…

- New harmonised CV template
- Protocol
- ICF

New required documents…

- 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.

3. Transition period

Transition period

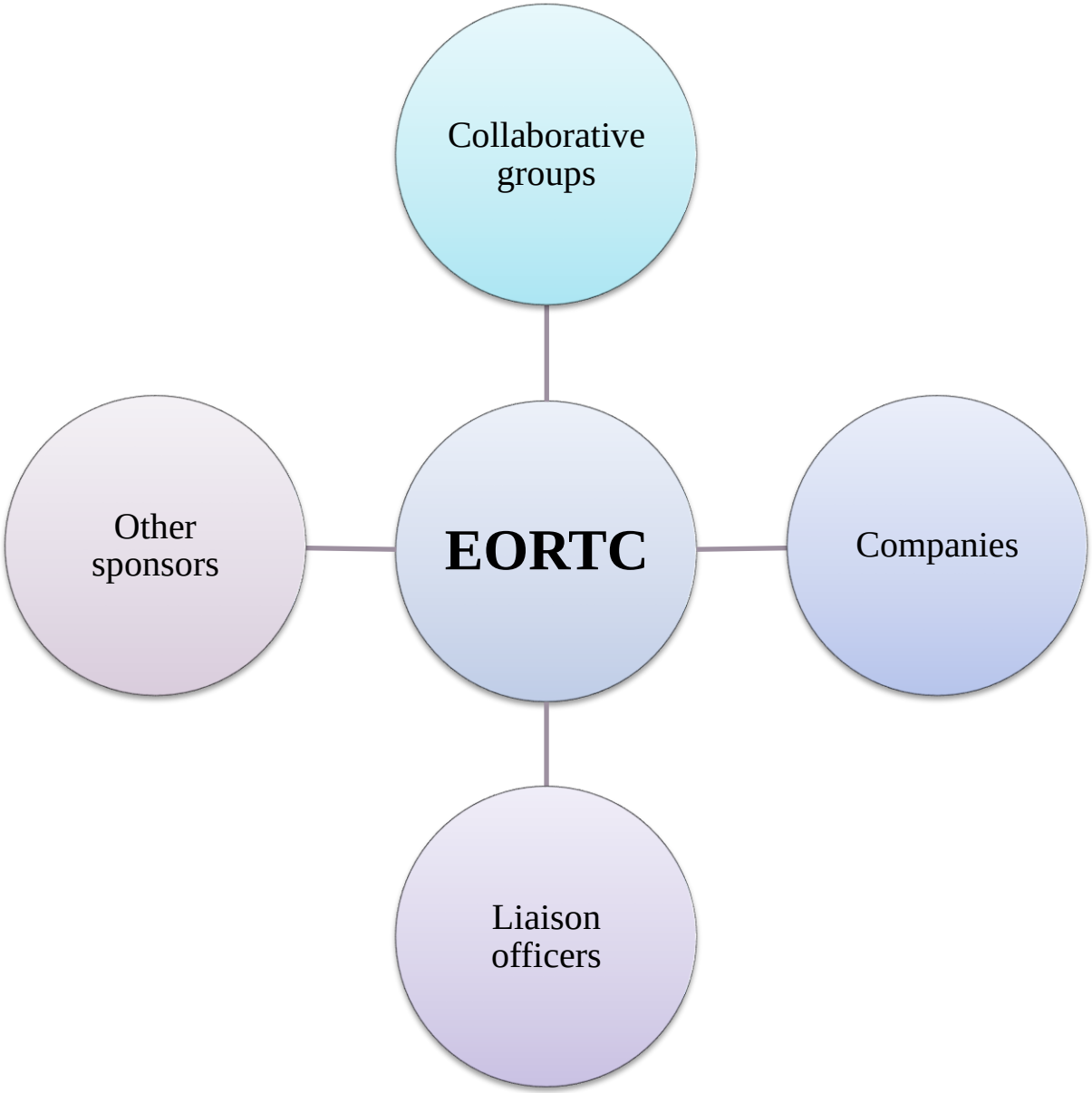
The CT Regulation will repeal the CT Directive from its application date. A 3-year transition period is foreseen in which the CT Directive will still apply. Initial clinical trial applications from the second year of application of the CT Regulation must be submitted under the new regime.

Before Go-live	**Initial 12 months**	**Next 24 months**	**From 3 years after Go-live**
Any CTA submitted at this time, is still governed by the old Directive until 3 years after Go-live	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.**	All initial CTAs ***must*** be submitted in the new EU portal and be **governed by the new Regulation**.	**All CTAs are governed by the new Regulation**, regardless of their date of submission.

4. Key compliance considerations

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

5. Management of different type of stakeholders


Collaborative groups
Other sponsors
EORTC
Companies
Liaison officers

(Co-)Sponsorship

EU Sponsors

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

(*individual, company, institution or organisation which takes responsibility for the initiation, for the management and for setting up the financing of the clinical trial*)

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 SA 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 on contact person in EU)

! MSs provides conditions for the criminal and civil liability and the compensation system for damages suffered by subject, including the responsibilities and liabilities for the Legal rep in EU.

6. Transparency rules

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

7. User management and coordination of communication flow

User management: approaches

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 to are not affiliated to any sponsor organization

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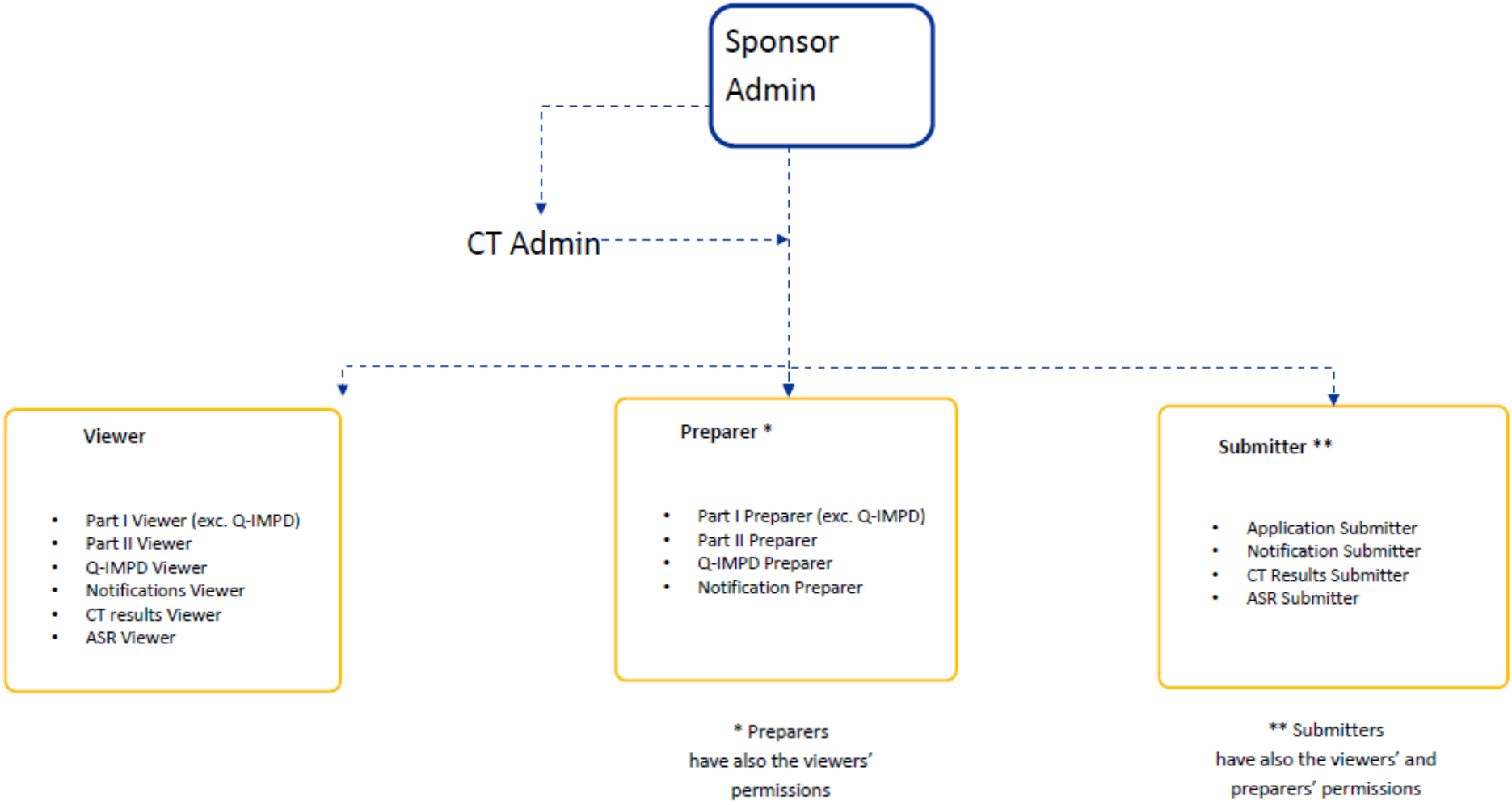
User management: Sponsor workspace roles



* Preparers have also the viewers' permissions

** Submitters have also the viewers' and preparers' permissions

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Thank you

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