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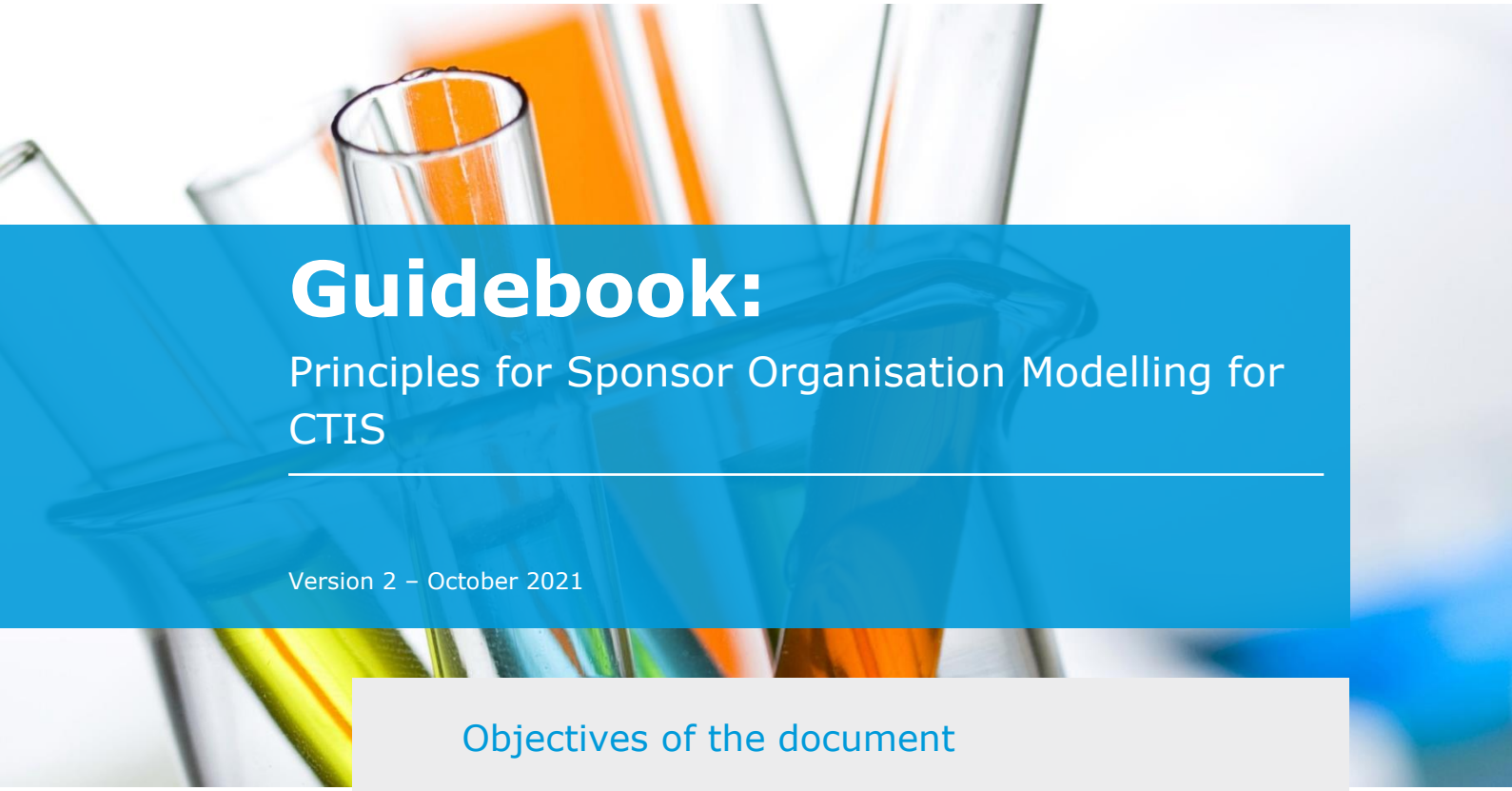

Guidebook:

Principles for Sponsor Organisation Modelling for CTIS

Version 2 – October 2021

Objectives of the document

- Outlines the key concepts for sponsor organisation modelling for CTIS.
- Provides principles & considerations for sponsors when implementing CTIS in their organisation.
- Describes examples of organisation models.

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01

Introduction

Introduction

This document is aimed at individuals that will be involved in implementing CTIS in clinical trial sponsor organisations. It outlines **key principles & considerations** that may be relevant when deciding **how to organise user access, responsibilities, and user roles in CTIS**.

It is understood, based on sponsor feedback, that **clinical trial organisational aspects can vary significantly for different sponsors and types of trial**. This document therefore describes key considerations that may be relevant when deciding how to organise user access, responsibilities and roles in CTIS for different kinds of sponsors and clinical trials. It also contains a set of illustrative examples of how sponsors can organise in CTIS for certain kinds of clinical trial.

Parts 1 to 4 of the document consist of the presentation of the key concepts and elaboration of key principles and considerations that may help sponsors deciding how to organise for CTIS.

Examples of organisation models are described in **Part 5** of the document.

This document acts as a starting point for sponsors when defining organisational processes for CTIS. Sponsors may choose to organise in CTIS as they wish.

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Key concepts

Key concepts for sponsor organisation models

User Personas for CTIS

User Personas are visual models that describe different types of individuals who will use CTIS. The User Personas are used as an input to the sponsor organisation modelling.

The User Personas describe **who typically will do what in CTIS** in the different kinds of organisations involved in clinical trials, including large pharmaceutical companies, Contract Research Organisations (CROs), micro, Small and Medium Enterprises (SMEs) and academic organisations.

The User Personas **show the possible CTIS user roles** each individual may be given to perform their tasks.

The CTIS User Personas are archetypes. They encompass a whole group of people who may vary in the details of their job roles or responsibilities. Therefore, CTIS User Personas constitute a 'best fit' and a guide in mapping user roles.

➔ The CTIS User Personas can be found here.

User Role Matrix for CTIS

CTIS enables users to perform actions depending on the permissions attached to their user role(s).

Permissions allows users to perform actions in CTIS. There are business permissions (e.g. create considerations, create AR, create responses to FRI) and access permissions (view, prepare and submit).

There are multiple roles in CTIS, which allow users to execute different actions in the system. The role matrix provides a summary of all CTIS roles mapped to their permissions.

➔ The User Role Matrix can be found here.

Sponsor organisation models

Sponsor organisation models describe clinical trials processes at a high level and **how sponsors and their partner organisations may organise** for CTIS.

A set of **4 illustrative organisation models are outlined in this guidebook.** The models were selected based on sponsor feedback, which represent the different organisational possibilities for clinical trials.

The models selected and developed in Part 5 of this document demonstrate, for different types of clinical trial:

- ***Which organisations are involved in the trials and have access to CTIS:***

  For example, commercial sponsor(s), CROs, academic sponsors.

- ***What tasks the organisation is responsible for:***

  For example, for a given clinical trial it is possible that the commercial sponsor is responsible for completing part I including the IMPD-Q, while CROs are responsible for Part II for different Member States Concerned (MSCs).

- ***The User Persona which will access CTIS:***

- ***The CTIS user roles the User Persona will have to complete their task in the clinical trial.***

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Key principles

Key principles for sponsor organisation models

The following key principles for sponsor organisation models in CTIS have been developed with sponsor feedback. They aim at highlighting **important topics to consider when implementing CTIS processes** within an organisation, with a particular focus on the areas of user access, user roles and responsibilities in CTIS.

CTIS is a regulatory submission system

CTIS is designed to function as a **regulatory submission system**, replacing national processes for submitting clinical trial applications to national health bodies for approval. It is not intended to replace clinical trial management systems, which sponsors and other organisations use to manage their work on the clinical trial.

It is possible that some organisations that work on a clinical trial (e.g. CROs or co-sponsors in co-sponsored trials) **do not access CTIS directly**. Instead, these organisations may prepare their parts of the clinical trial submission outside of CTIS. Their contributions would then be collected by an organisation working on the clinical trial that has access to CTIS (e.g. the sponsor or one appointed CRO), who will input the clinical trial submission data in CTIS. Similarly, within the same organisation, some individuals contributing to the submission may work outside of CTIS and provide input to individuals that have access to CTIS (such as CTIS submission managers). Alternatively, all organisations or individuals within an organisation contributing to the submission can have access to CTIS.

Ultimately, it is up to the sponsor to decide whether some or all organisations and individuals working on the clinical trial need access to CTIS. It should be noted that there may be a benefit to limiting user access to CTIS in the form of data control and security: the less individuals that have access to CTIS, the easier it may be to manage data access and prevent incidents (e.g. security breaches).

Centralisation vs decentralisation of access to CTIS

There are two broad approaches for granting access to CTIS in different organisation models:

- **Centralised approach**:

  One or a small number of organisations/individuals working on the clinical trial application access CTIS, gathering the inputs of others outside of CTIS.

- **Decentralised approach**:

  Most or all organisations/individuals working on the clinical trial application access CTIS, each inputting their own work on the submission directly into CTIS.

Each approach has benefits and points for consideration.

The **pros and cons of each approach** have been gathered below.

Table 1 Overview of the pros and cons of the centralised and de-centralised approaches to CTIS access

	PROS	CONS
CENTRALISED APPROACH	**Simplifies user access management processes** with less users accessing the system.	**Centralises CTIS-related work** with a few colleagues.
	Provides **easier oversight** of what is submitted in the system by each user.	May require **dedicated team/individuals** to manage CTIS submissions.
	Reduces work related to **user role management** with a small number of users having access to CTIS.	Requires **gathering information from contributors** outside CTIS. **Potential lag** in providing documents to be uploaded in CTIS, due to need for communications outside of CTIS.
	Ensures a **single point of awareness** on CTIS alerts and RFIs.	Raises potential **need of offline follow-up** to inform other colleagues of alerts and RFIs.
	Reduces training needs to one team of experts.	**Less diffusion of CTIS knowledge** in the organisation, e.g. for holiday backups.
DE-CENTRALISED APPROACH	Gives users **immediate access** to important information in CTIS.	Need **for training, user access and role management** for wider group of users.
		Allows users to **potentially see/edit data they are not responsible for** (e.g. Part II Preparers can see/edit data for all countries on a trial). Increases the work of **internal coordination** to manage dependencies in the submission process within CTIS.

User access and data sharing

When **assigning roles to users in CTIS**, the extent of data that users will be able to view must be carefully considered.

For example, users with Part II Preparer rights will be able to see all data related to Part II for the clinical trials they have access to, not just the data they input themselves. This means that they will be able to see Part II data related to Member States Concerned that they are not working on, but that other Part II Preparers are working on.

From sponsor feedback, a key consideration for **user access to data is that the CTIS user role of CT Admin can view and edit the IMPD-Q.**

Due to the commercially sensitive nature of the IMPD-Q, sponsors may **decide to assign CT Admin roles to people within their company**, or to ensure **confidentiality arrangements** are in place if they delegate the CT Admin role to a CRO. Sponsors may also **limit access to IMPD-Qs by cross-referencing to an IMPD-Q in an existing trial** where appropriate.

The pros and cons of delegating CT Admin role to CROs and of cross-referencing to an IMPD-Q in an existing trial have been gathered below.

Table 2 Overview of the pros and cons of delegating CT Admin to CRO

	PROS	CONS
DELEGATING CT ADMIN ROLE TO CRO	Allows CROs to **fully manage the application** process.	Allows the **CROs to view/edit the IMPD-Q** which is commercially sensitive.

Table 3 Overview of the pros and cons of using cross-referencing for IMPD-Q

	PROS	CONS
CROSS REFERENCING (where appropriate)	**Limits sharing of** IMPD-Q.	Need for **RFI management process**, if RFIs are raised related to the IMPD-Q.

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Quick guide per model

Quick guide of each organisation model

Below, each example organisation model describes which organisations may access CTIS, what tasks they will perform related to an initial clinical trial application, what User Personas will perform the tasks, and what user roles the User Personas may have.

The initial clinical trial application processes for the models listed below shows examples of possible ways to organise; sponsors may choose to organise as they wish in CTIS.

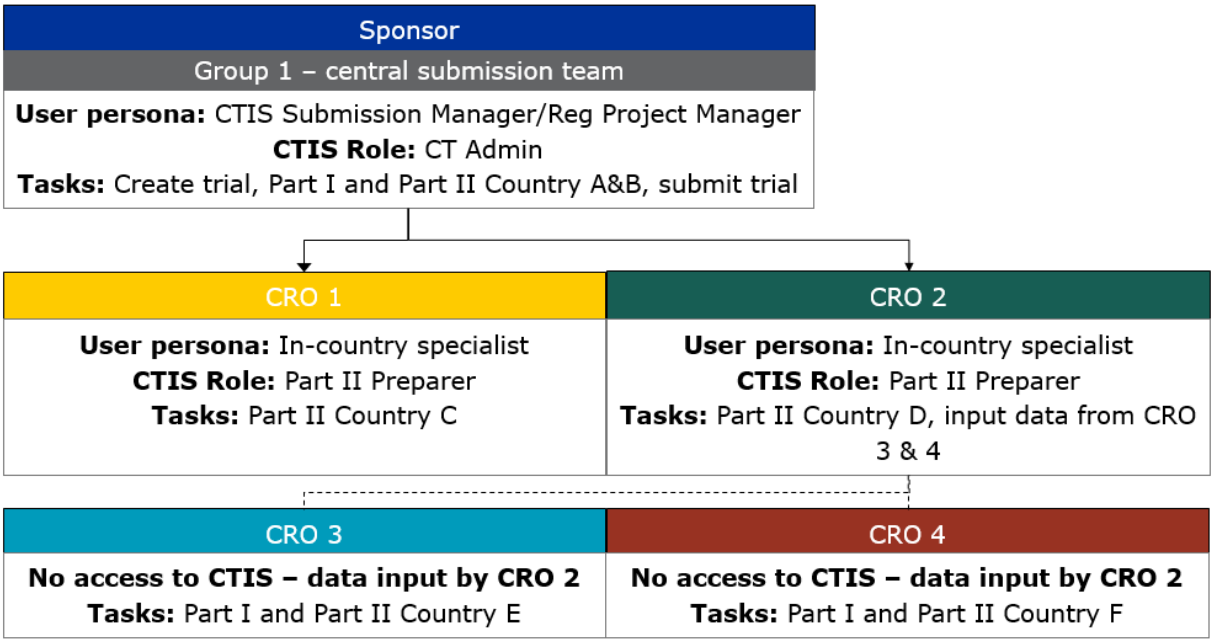
Simple Model

In the simple model, the sponsor retains responsibility for Part I of the clinical trial application and delegates responsibility for some countries in Part II to a group of CROs.

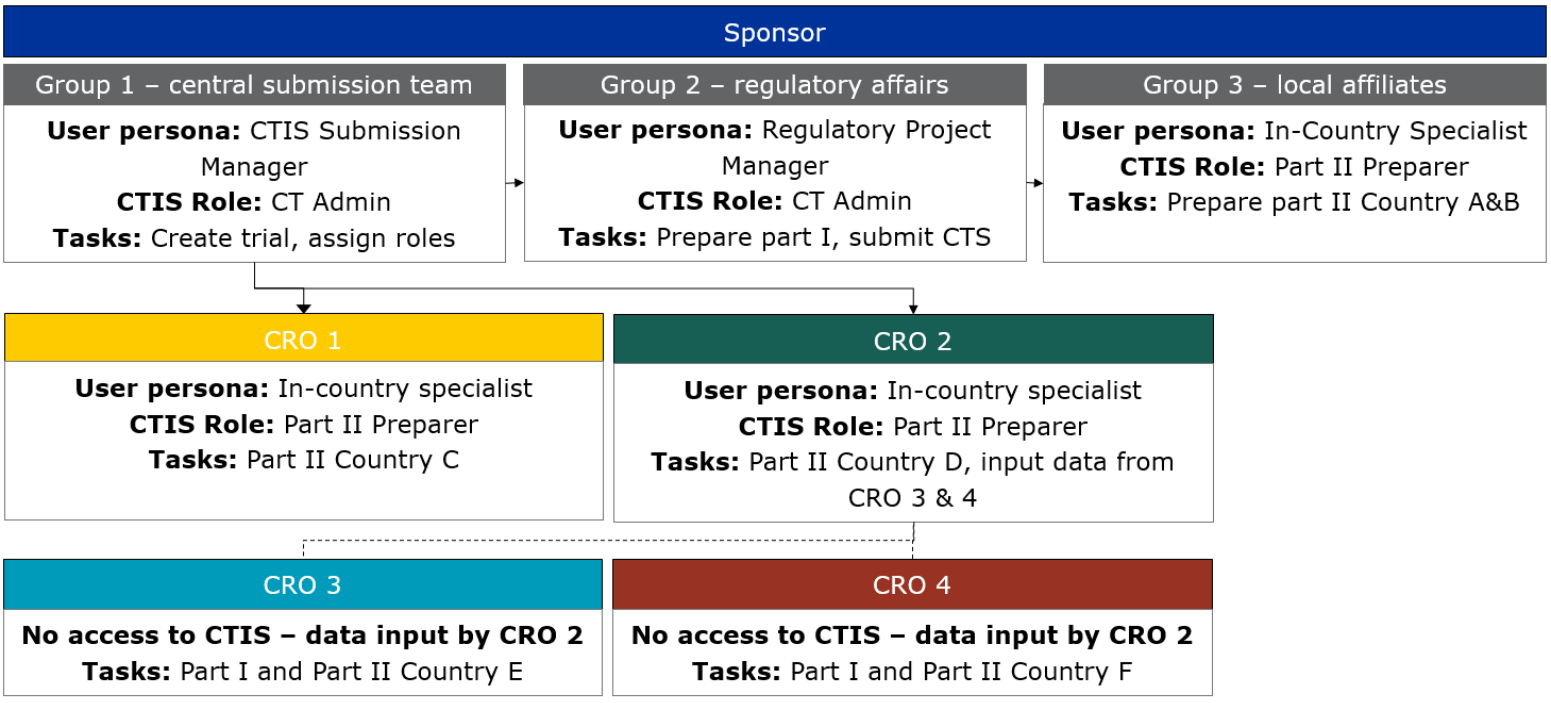
A further split of responsibility for Part II is also possible, for example where a CRO covers a region (e.g. the Baltics) and subcontracts work to smaller CROs in the different countries within that region.

Figure 1 Simple Model

Option 1 – Sponsor centralised approach



Option 2 – Sponsor decentralised approach



Originally presented by CTIS Stakeholder associations (ACRO, EFPIA, EORTC, EUCROF, EuropaBio Vaccines Europe) at the CTIS Stakeholders Group meeting, 23 April 2021

Table 4 Simple Model organisations, user access, roles and responsibilities in CTIS

	Sponsor	CRO1	CRO2	CRO3	CRO4
Access to CTIS?	Yes	Yes	Yes	No	No
Responsibilities in CTIS	Create CTA Prepare part I Submit CTA	Prepare Part II	Prepare Part II	N/A CRO2 manages CRO3's inputs	N/A CRO2 manages CRO4's inputs
User Persona	CTIS Submission Manager/Regulatory Project Manager/In-country specialist	In-Country Specialist	In-Country Specialist	N/A	N/A
User role	CT Admin	Part II Preparer	Part II Preparer	N/A	N/A

For all models, the sponsor may decide to retain the CT Admin role within their own organisation and provide CROs working on the trial with more limited roles, such as Part I and Part II Preparer. This would mean that the sponsor must create the clinical trial application and submit once all sections are ready. This approach means that only the sponsor can view and edit the IMPD-Q, allowing for control of the sensitive IMPD-Q information. As the CROs have Part I (excluding IMPD-Q) and Part II rights only, this approach also means the Sponsor retains responsibility to submit the CTA, they maintain oversight of the entire application prior to submission.

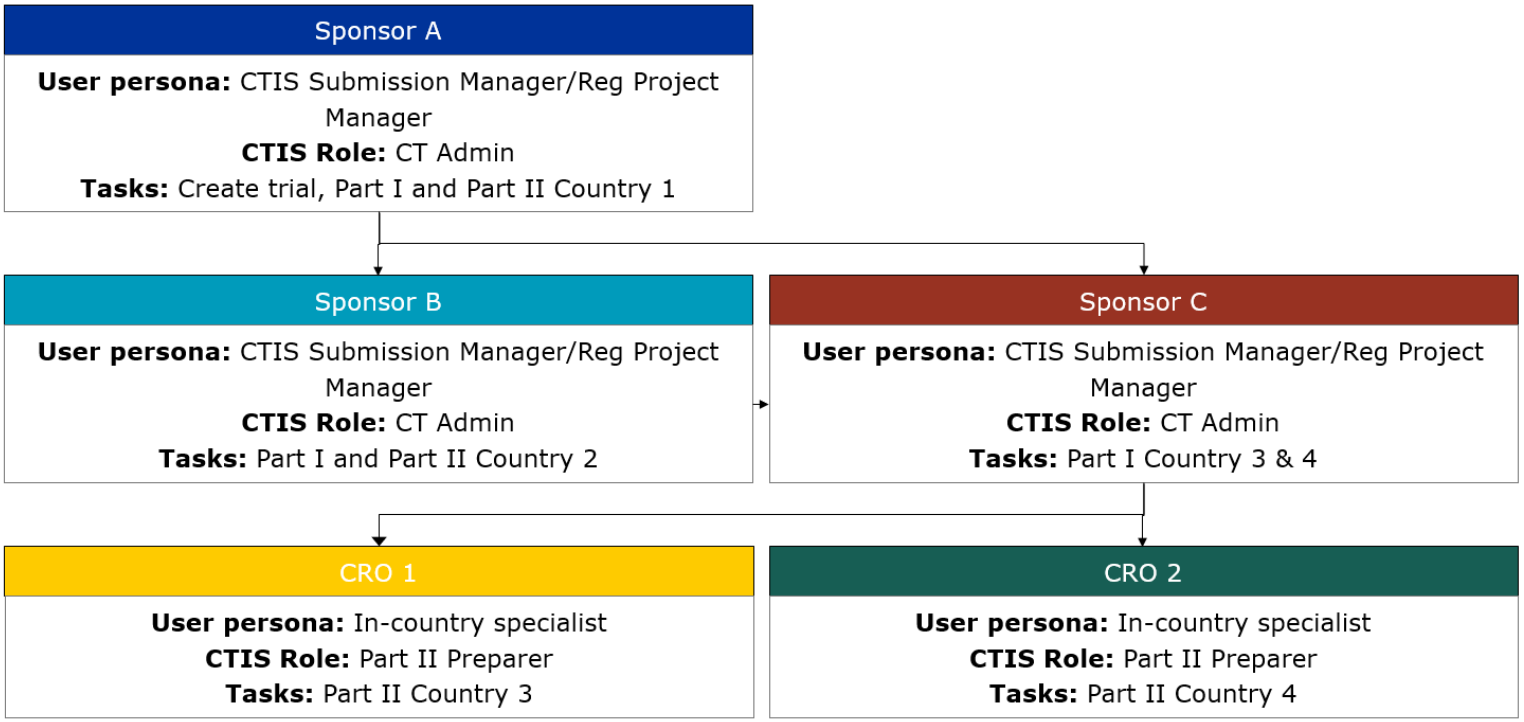
Sponsors can also delegate any of their activities to CROs, e.g. by giving users within their CROs the IMPD-Q Preparer role, or by appointing users from CROs as CT Admins or Application Submitters.

Complex Model 1

Complex Model 1 is an example of co-sponsorship, where sponsors responsible for different countries are co-developing a medicinal product within the same clinical trial. Under this model, one sponsor must initiate the clinical trial in CTIS.

Each sponsor may contribute to part I and part II of the CTA within their own company, or alternatively sponsors may work with CROs to complete their parts of the CTA.

Figure 2 Complex Model 1



Originally presented by CTIS Stakeholder associations (ACRO, EFPIA, EORTC, EUCROF, EuropaBio Vaccines Europe) at the CTIS Stakeholders Group meeting, 23 April 2021

Table 5 Complex Model 1 organisations, user access, roles and responsibilities in CTIS

	Sponsor A	Sponsor B	Sponsor C	CRO1	CRO2
Access to CTIS?	Yes	Yes	Yes	Yes	Yes
Responsibilities in CTIS	Create CTA Prepare part I Prepare part II May submit CTA	Prepare Part I Prepare Part II May submit CTA	Prepare Part I Oversight of Part II work by CROs May submit CTA	Prepare Part II	Prepare Part II

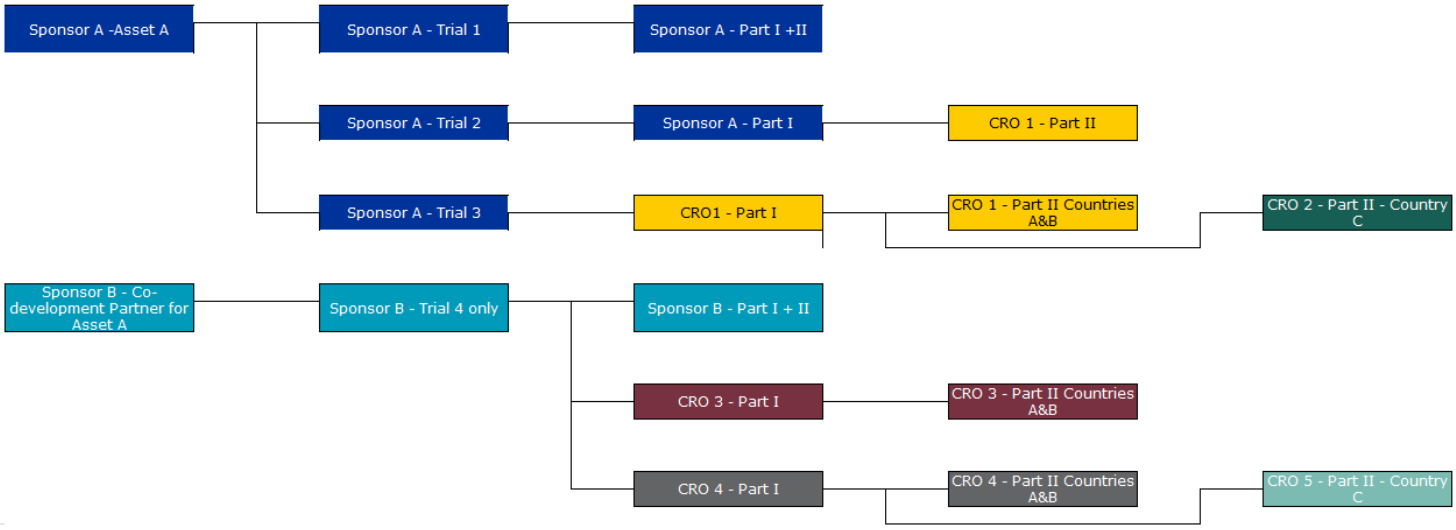
User Persona	CTIS Submission Manager/Regulatory Project Manager	CTIS Submission Manager/Regulatory Project Manager	CTIS Submission Manager/Regulatory Project Manager	In-Country Specialist	In-Country Specialist
User role	CT Admin	CT Admin	CT Admin	Part II Preparer	Part II Preparer

In the organisation model shown above, Sponsor A initiates the clinical trial application in CTIS. Sponsor A, B and C all contribute to part I of the CTA, and one or all sponsors may contribute to the IMPD-Q. If multiple sponsors contribute to the IMPD-Q section, they will be able to see each other's IMPD-Q inputs. As this type of clinical trial deals with the co-development of an asset, the sensitivity of sharing IMPD-Q data among the sponsor companies is reduced, and confidentiality agreements among the sponsors are likely already in place. For part II, the sponsors may contribute themselves, or delegate contributions to CROs (as in the case of sponsor C). As mentioned above, each user with access to Part II will be able to see the Part II data submitted by other sponsors or CROs. Sponsor A, B or C may submit the application – if done by Sponsor B or C, they will need to be granted Application Submitter or CT Admin roles.

Complex Model 2

In Complex Model 2, multiple sponsors are responsible for different clinical trials in the development of the same asset. Each sponsor has responsibility to run one or more clinical trials, and may work with CROs. In addition, these CROs may subcontract to smaller CROs working in particular countries.

Figure 3 Complex Model 2



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Complex Model 2 is expected to managed in a similar way as the Simple Model, with each sponsor creating an running their clinical trial(s) separately and potentially engaging CROs

for some tasks (e.g. Part I excluding IMPD-Q preparation). Sponsors can then use the Associated clinical trials functionality in CTIS to create a link between their clinical trials. Please refer to section Simple Model for the simple model.

The Academia Simple Model

The Academic Simple Model describes a scenario in which an academic sponsor relies on a CRO to help them complete Part I of the clinical trial application. The CRO may be a commercial entity, or could also be part of an academic institution.

The academic sponsor in this model relies on a commercial sponsor to provide an IMPD-Q. Where possible and considered acceptable, the commercial sponsor may provide a cross-reference to another approved trial that contains the relevant IMPD-Q information, once that trial has a CTIS or EudraCT trial number. This avoids the need to send sensitive IMPD-Q information to the academic sponsor or their CRO for Part I, or the need for the commercial sponsor to gain access to CTIS for the trial and input the IMPD-Q using the IMPD-Q Preparer role. If the academic sponsor's CRO is part of the same academic institution and therefore the same legal entity, sensitivity with regard to data sharing by the commercial sponsor may be reduced due to the legal arrangements already in place with the academic sponsor.

Figure 4 Academia Simple Model

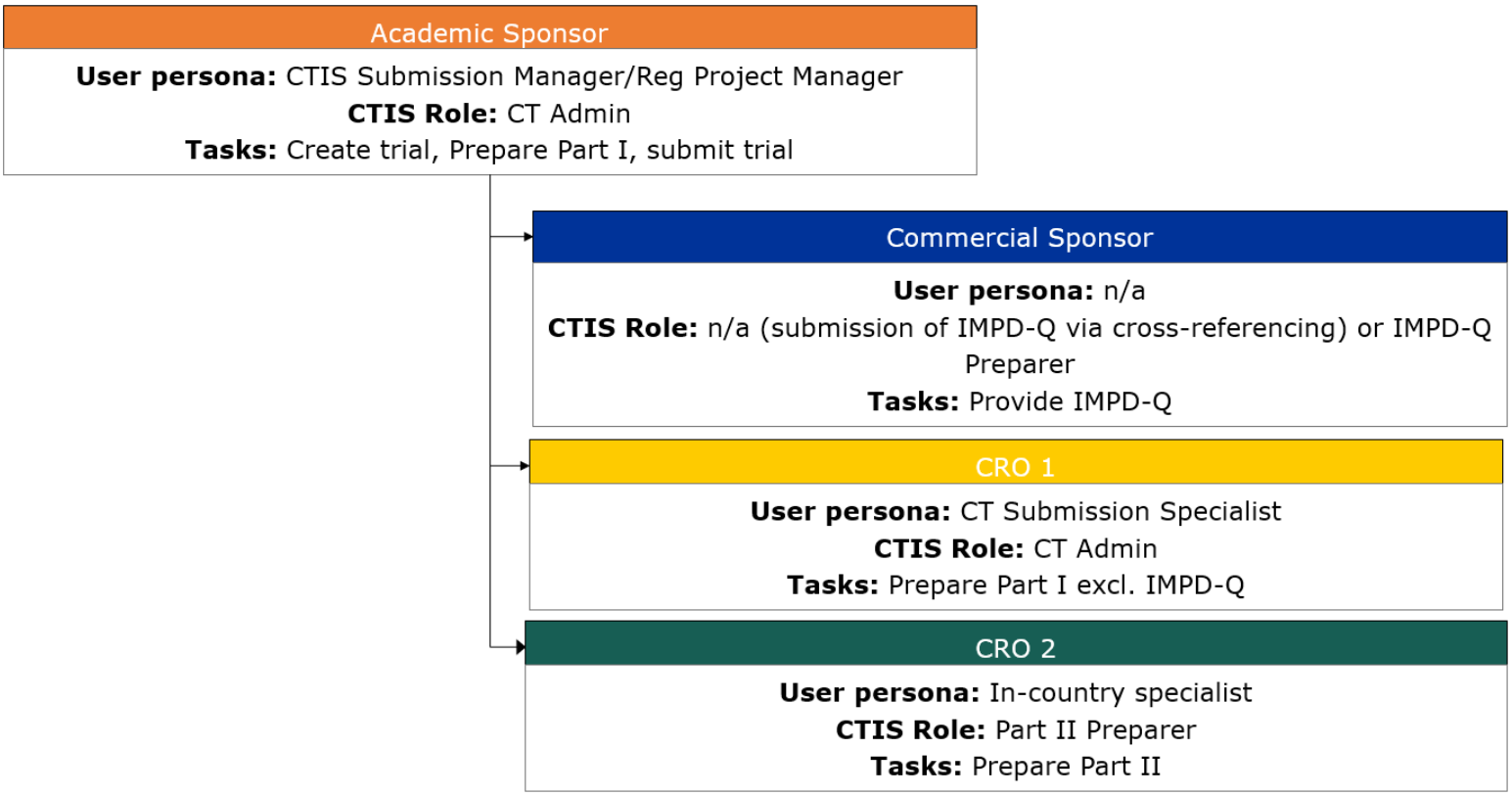

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Table 6 Commercial Complex Model A organisations, user access, roles and responsibilities in CTIS

	Academic Sponsor	Commercial Sponsor	CRO1	CRO2
Access to CTIS?	Yes	No – will likely ask academic sponsor to use cross-referencing for IMPD-Q	Yes	Yes
Responsibilities in CTIS	Create CTA Prepare part I excl IMPD-Q Cross-reference to or input commercial sponsor's IMPD-Q Submit CTA (or delegate to CRO)	N/A	May Create CTA Prepare Part I excl. IMPD-Q May submit CTA on behalf of academic sponsor	Prepare Part II
User Persona	Study Coordinator/Study Nurse	N/A	CT Submission Specialist	In-Country Specialist
User role	CT Admin	N/A	CT Admin	Part II Preparer

In the Academia simple model, a Study Coordinator or Study Nurse working on the academic trial may create the application and prepare part I excluding the IMPD-Q. They may also delegate some or all of these tasks to CRO 1. Where possible, the IMPD-Q may be added via cross reference, or the commercial sponsor may provide the IMPD-Q to the academic sponsor or CRO1 outside of CTIS. This reduces the need for user role administration and coordination in CTIS, however confidentiality arrangements surrounding the IMPD-Q must be considered. An in-country specialist within CRO2 would then prepare Part II. Then, the academic sponsor may review the application and submit, or alternatively they may delegate this task to CRO1.

05

Preliminary considerations

Preliminary considerations before implementing CTIS

The following organisational topics can be considered as starting points before using CTIS.

1. **Map your organisation's clinical trial submission processes**:

   Models are illustrative examples and are not meant to fit one specific organisation. The first step should be to consider your organisation's own processes when it comes to clinical trial submission, and how they will need to adapt when using CTIS. It is recommended to complete a mapping of business processes pointing out CTIS submission needs as a first step.

2. **Define CTIS responsibilities:**

   Following the process mapping, CTIS responsibilities can be thought of more precisely. The organisation's own way of working and culture can be considered. Is there a centralised way of working already (e.g. a centralised clinical trials submissions team)? How do CROs and co-sponsors usually contribute for clinical trials submissions? The possibility of limiting access to a specific group of people can be considered at this point.

3. **Consider user personas and roles:**

   Once CTIS responsibilities have been decided at a high level, it is time to consider what tasks each individual will do in CTIS, and what user roles they need to complete these tasks. The CTIS user personas provide a template and guide for this step.

4. **Consider training needs for users before granting them access to CTIS**

   Appropriate training on CTIS is key to successful adoption. After defining CTIS responsibilities and user personas, identifying what kind of training different users need to support their use of CTIS will ensure users are well-prepared for clinical trial submission.

European Medicines Agency

Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands

Telephone +31 (0)88 781 6000
Send a question

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