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SCIENCE MEDICINES HEALTH

Introduction to the Clinical Trials Information System (CTIS)

Enpr-EMA- 28th September

Presented by:
Ana Rodriguez, CTIS Deputy Programme Manager

Disclaimer

The presenter does not have any conflict of interests.

The views expressed are those of the presenter.

Content

- **CTR and CTIS Benefits for sponsors**
- CTIS high-level system overview and actors
- CTIS User Management
- Sponsor Workspace functionalities
- Transparency rules
- Public module
- CTIS Sponsor support
- CTR Application and transition period
- Next steps

CT Regulation (EU) No. 536/2014: what is new?

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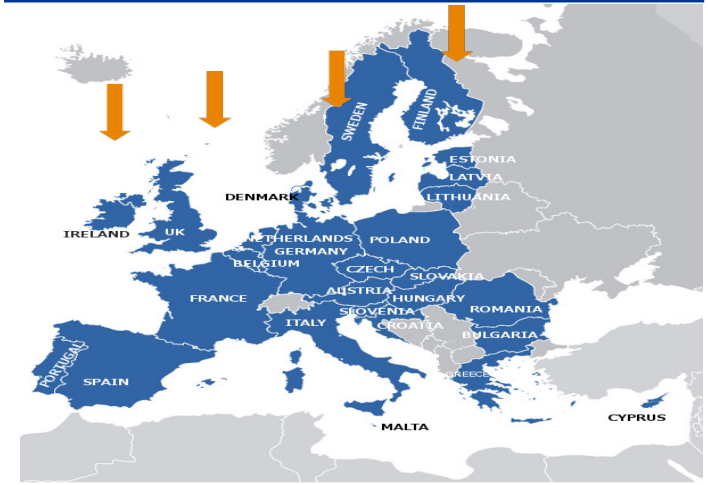
Directive (since 01/05/04) versus Regulation (from 31/01/22)

Implemented in national laws



First attempt to harmonise processes and requirements for CT authorizations;

Introduction of the e- application Form

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 multistate 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.

Why CTIS?

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CTIS is the business tool of the **Clinical Trials Regulation**.
CTIS **harmonises the submission, assessment and supervision of clinical trials**.

Public health

Facilitates large-scale trials to address key health issues (COVID, EU Beating Cancer plan…)

Research and innovation

Enables knowledge sharing and expert collaboration.

Investment in research

Ensures the EU/EEA remains an attractive clinical research hub globally.

CTIS Benefits

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With CTIS sponsors can:

- Apply for a clinical trial in up to 30 EU/EEA countries with a **single application**
- Facilitate involvement of trial participants by allowing **easy expansion of trials to other EU/EEA countries**
- **Collaborate across borders** for better results and knowledge sharing
- Ensure the EU/EEA remains an attractive location for **clinical research investment**
- Fulfil all **clinical trial publication requirements** with no additional effort

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CTIS high level overview and interactions with other systems

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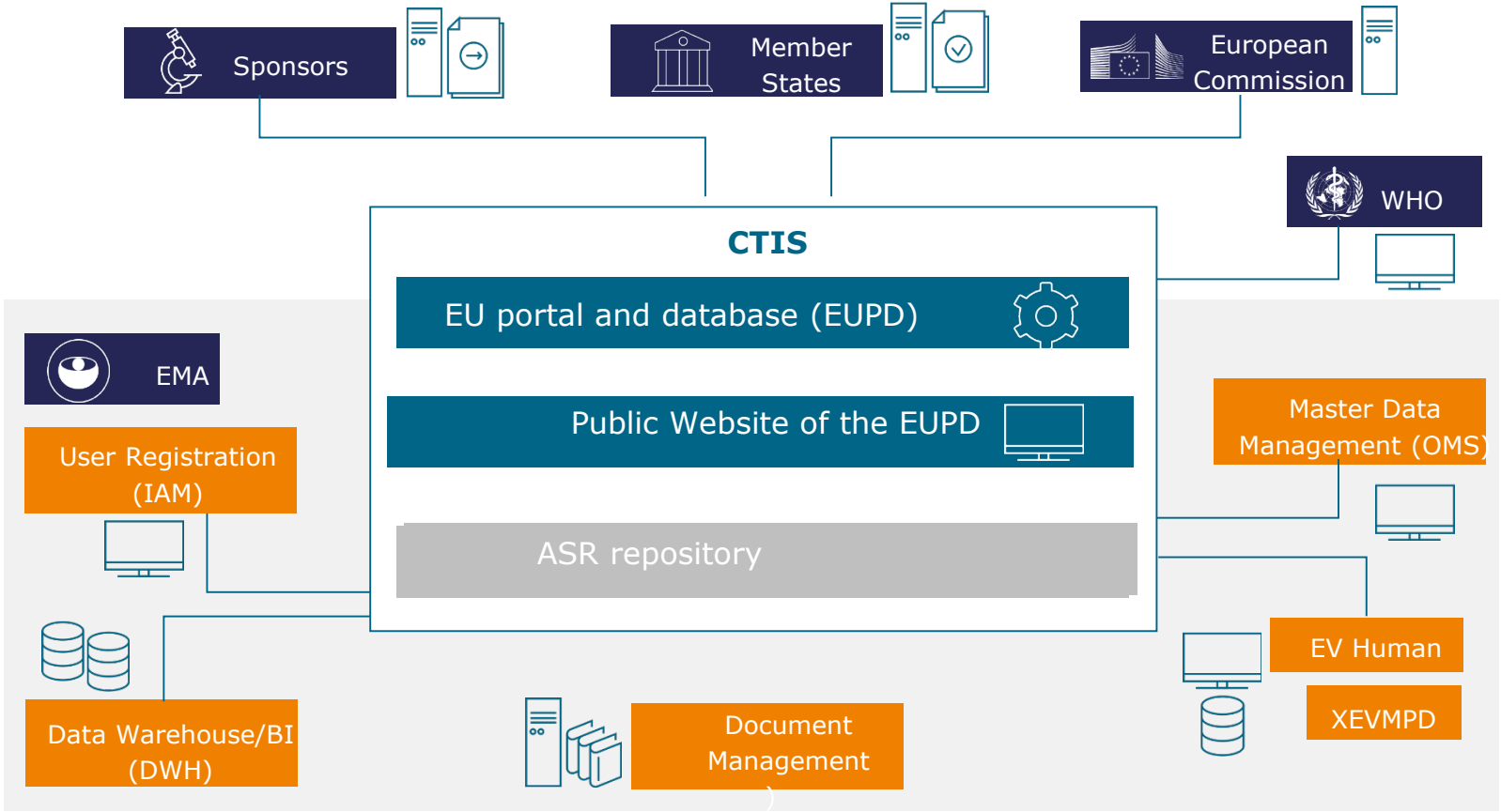

Two dedicated and secure workspaces and a public portal

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Sponsors: industry and academia

Marketing authorisation applicants

Member States *NCAs and ethics committees

European Commission

European Medicines Agency

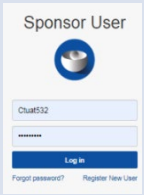
General public

*National competent authorities

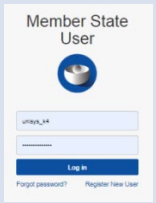
secure access

open access

sponsor workspace



authority workspace



EU Portal

EU CT Database

public website

Data accessible to the public

CTIS future users

Sponsors/MAH

Commercial: large pharmaceutical companies & CROs, SMEs

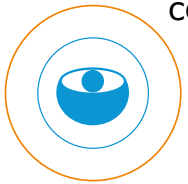
Academia

MAH

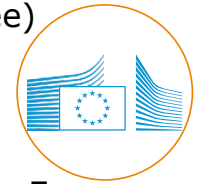
Will **input clinical trial data** (CTA, notifications, summary of results, CSR etc) in CTIS

Authorities

Member States (NCA & ethics committee)



EMA



European Commission

Will **review clinical trial data** (MS/EMA) (Assessment Reports, corrective measures etc.) and create **Union Control Reports** (COM)

Public

Public users (Healthcare professionals, patients, other)

Will **search for publicly available clinical trial data** in CTIS

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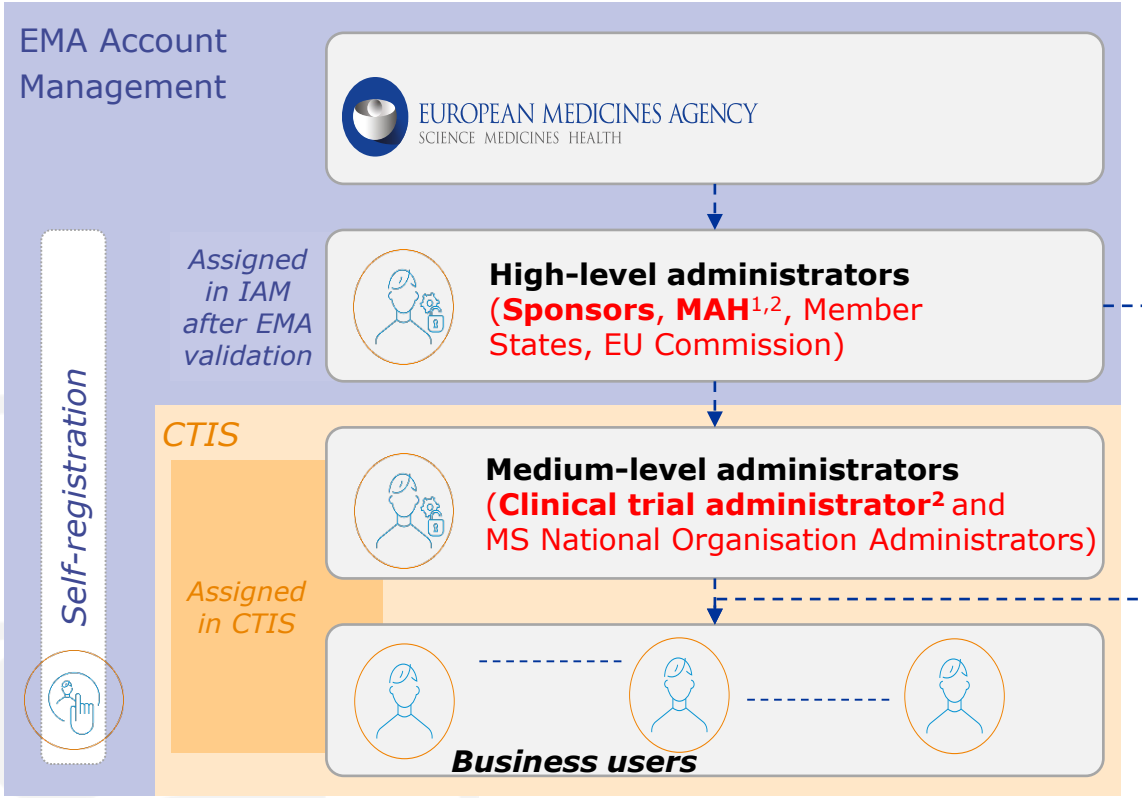
CTIS Key Principles

- **User management** is a set of features and capabilities that enable CTIS administrators to **manage user access** to CTs through role assignment as well as for each user to manage their **own roles/profiles**
- **Only users previously self-registered** in the EMA Account Management system can be assigned with CTIS roles
- The CTIS User Management follows a **hierarchical approach**
- The CTIS **administrator roles** (Sponsor, MSs, EC, MAH, EMA) are the ones responsible to manage users though the CTIS user management functionality
- **More than one user administrator** per organization or per CT is possible in CTIS
- **The CTIS users** will have **access** to the CT system functions **according to their business role**, so the system will display the appropriate data and also the appropriate activities for them
- The **profile of a user** can be built by combining roles

User management hierarchy



A structured top-down approach is used to maintain the integrity of the system:

Administrator Roles

- *Assign new role/CT access*
- *Amend role/CT access*
- *Revoke role/CT access*
- *Approve/reject user requests for a role (only applicable to sponsor users)*

Business roles

- *Role allocated to perform CT related activities in the system*

1 The MAH role is the only high level administrator role that will be assigned in CTIS by the EMA Administrator
2 These roles have also mapped the permissions of business roles: able to perform CT actions in CTIS on top of user administration

Organisation centric vs trial-centric approach

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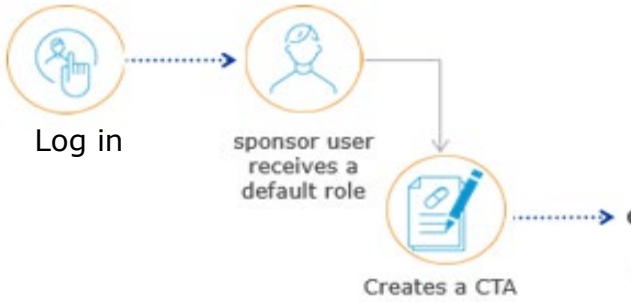
***Two user management approaches** in CTIS for the sponsor group of users. They **are automatically applied by the system** based on whether there is an Sponsor Administrator registered in the EMA account management system*



Select Sponsor Organisation

System automatically checks if the sponsor organisation selected for the CTA has registered a sponsor administrator

Yes- Organisation Centric
The **user** cannot proceed to create the CTA unless has been **assigned with the CT Admin** role by the sponsor administrator of the organization selected

No- CT Centric
The user can proceed and create the CTA

User becomes CT Administrator

Organization centric

- **Centralised management of access and roles** across trials within one organization (Sponsor Oversight)
- Improves **security**
- **Prevents duplication** of sponsor organization details

CT centric

- **Faster CTA process** in case of a first initial application
- Has **less admin burden:** not required MS Admin registration
- Recommended **only for academic sponsor** that conduct 1-2 CTs in their live

Sponsor workspace roles

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The Sponsors workspace comprises **15 roles business roles and 3 administrator roles** (including Sponsor Admin, CT Admin and MAH Admin):

Administrator roles

Sponsors Admin

CT Admin

MAH Admin*

Business roles

Viewer

- Part I Viewer (exc Q-IMPD)
- Part II Viewer
- Q-IMPD Viewer
- Notifications Viewer
- CT results Viewer

View structured data, documents, and includes download of documents

Preparer

- Part I Preparer (exc Q-IMPD)
- Part II Preparer
- Q-IMPD Preparer
- Notifications Preparer

Edit, upload documents, save, cancel saved drafts, update saved drafts

Submitter

- Application submitter
- Notification submitter
- CT results Submitter
- ASR Submitter

Submit/ update and withdraw data/ documents from the workspace to the EU database

Submitter

Viewer

- CSR Viewer
- CSR Submitter

***Marketing Authorisation applicants/holders (MAH):** user group within the sponsor workspace that is responsible for managing CSRs.

NOTE: A role can be assigned with the scope "all trials" or "specific trials" . In the las case the administrator has to indicate the trial for which the user will have access

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Introduction to the common sponsor functionalities

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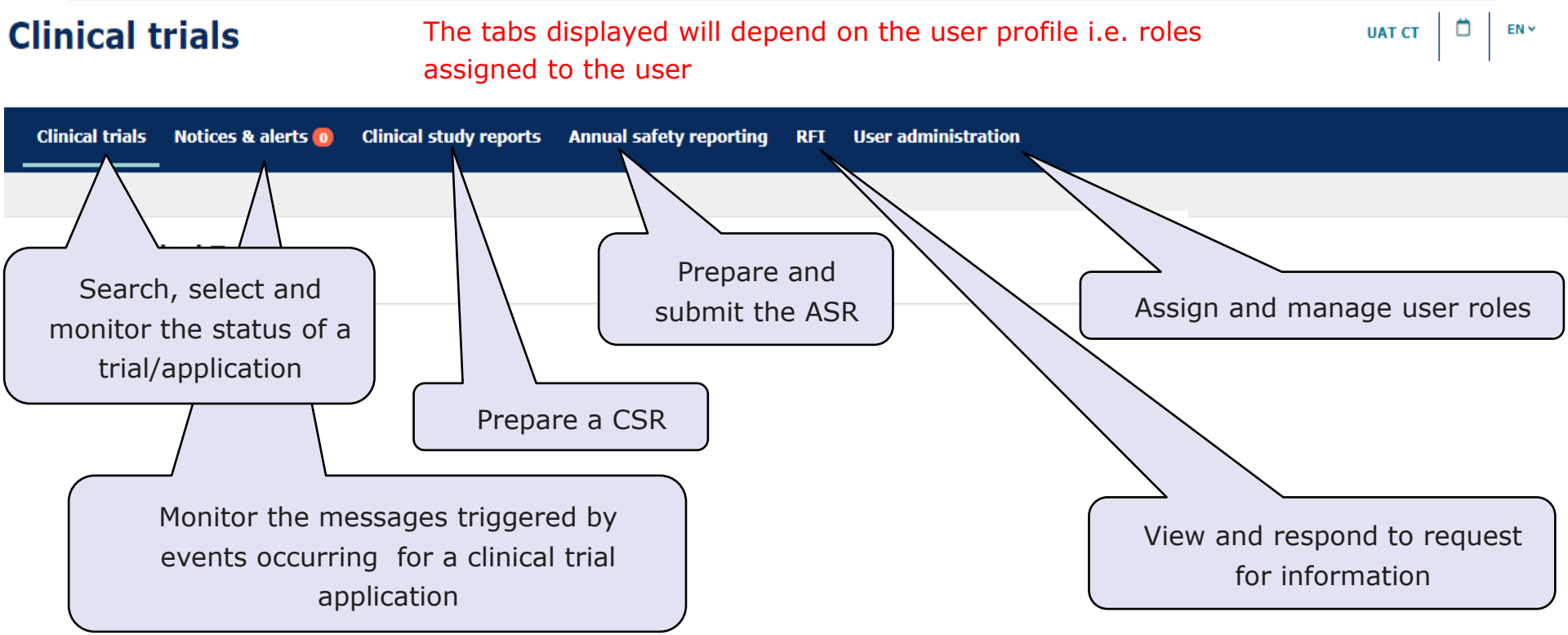
CTIS offers these high-level functionalities to sponsors users. These are: Overview of Clinical Trials (search functionality), Notices & alerts, Annual Safety Reporting, Requests for Information and User administration.



Clinical Trials Search

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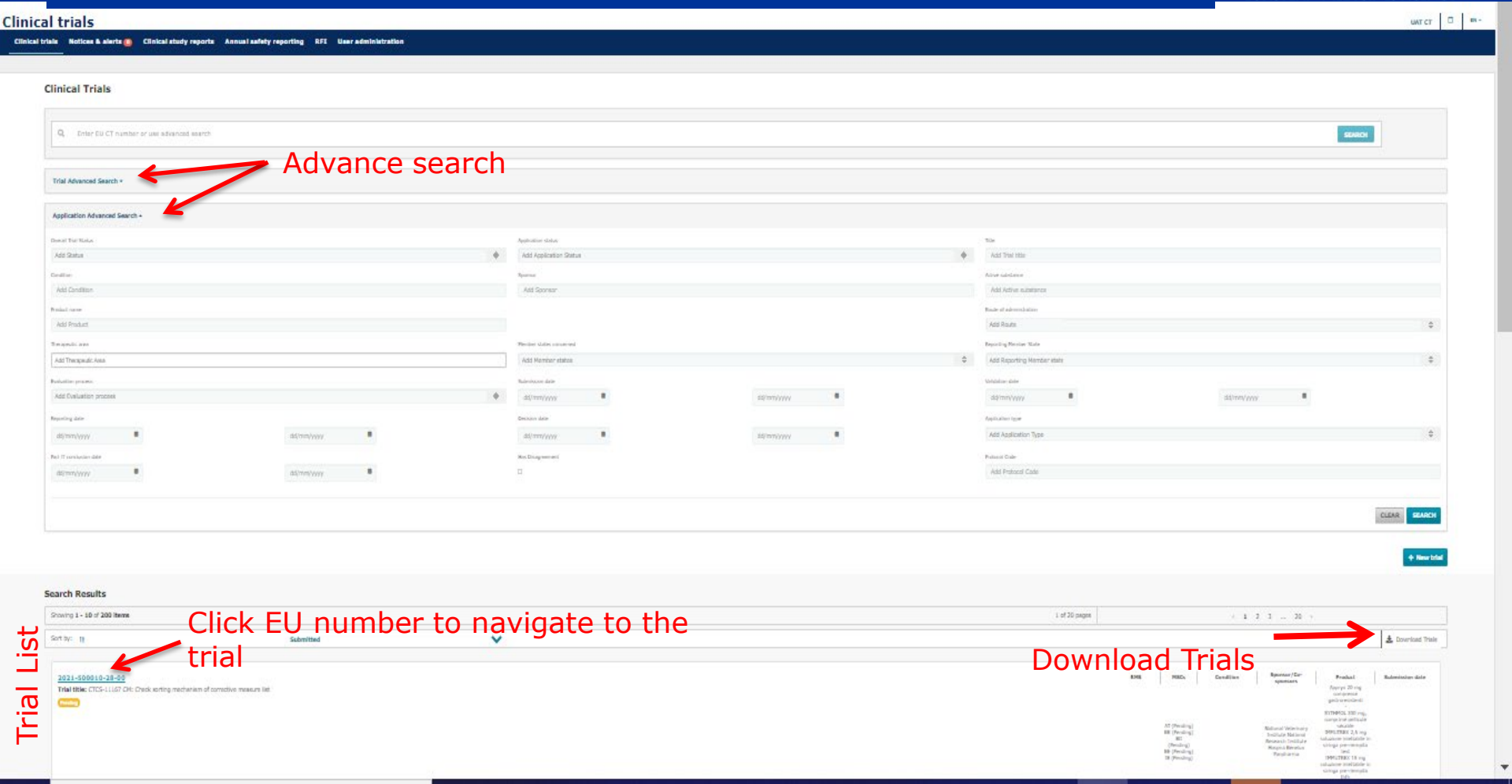
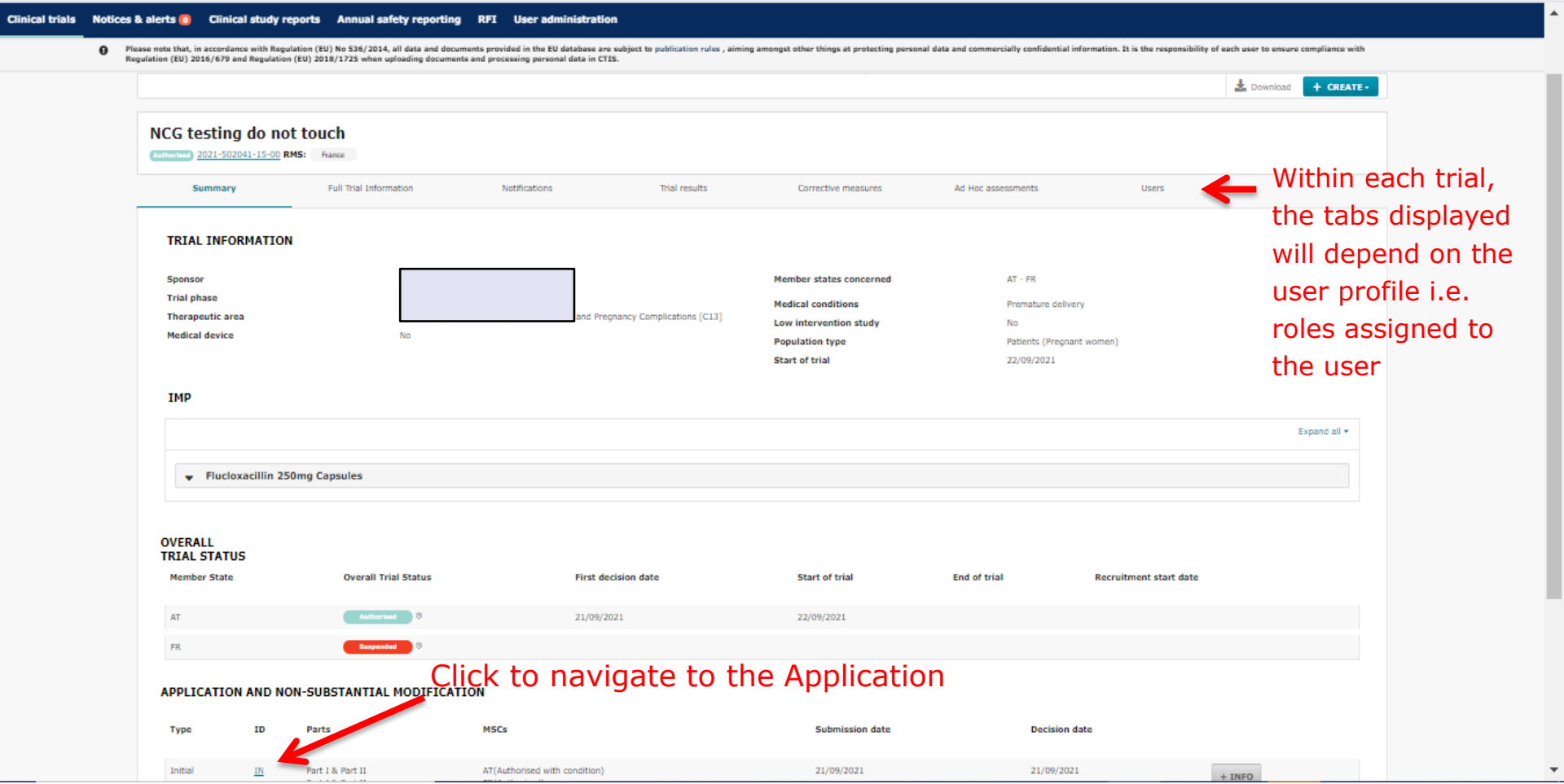


CT Overview



Within each trial, the tabs displayed will depend on the user profile i.e. roles assigned to the user

Click to navigate to the Application

CT Application Dossier structure

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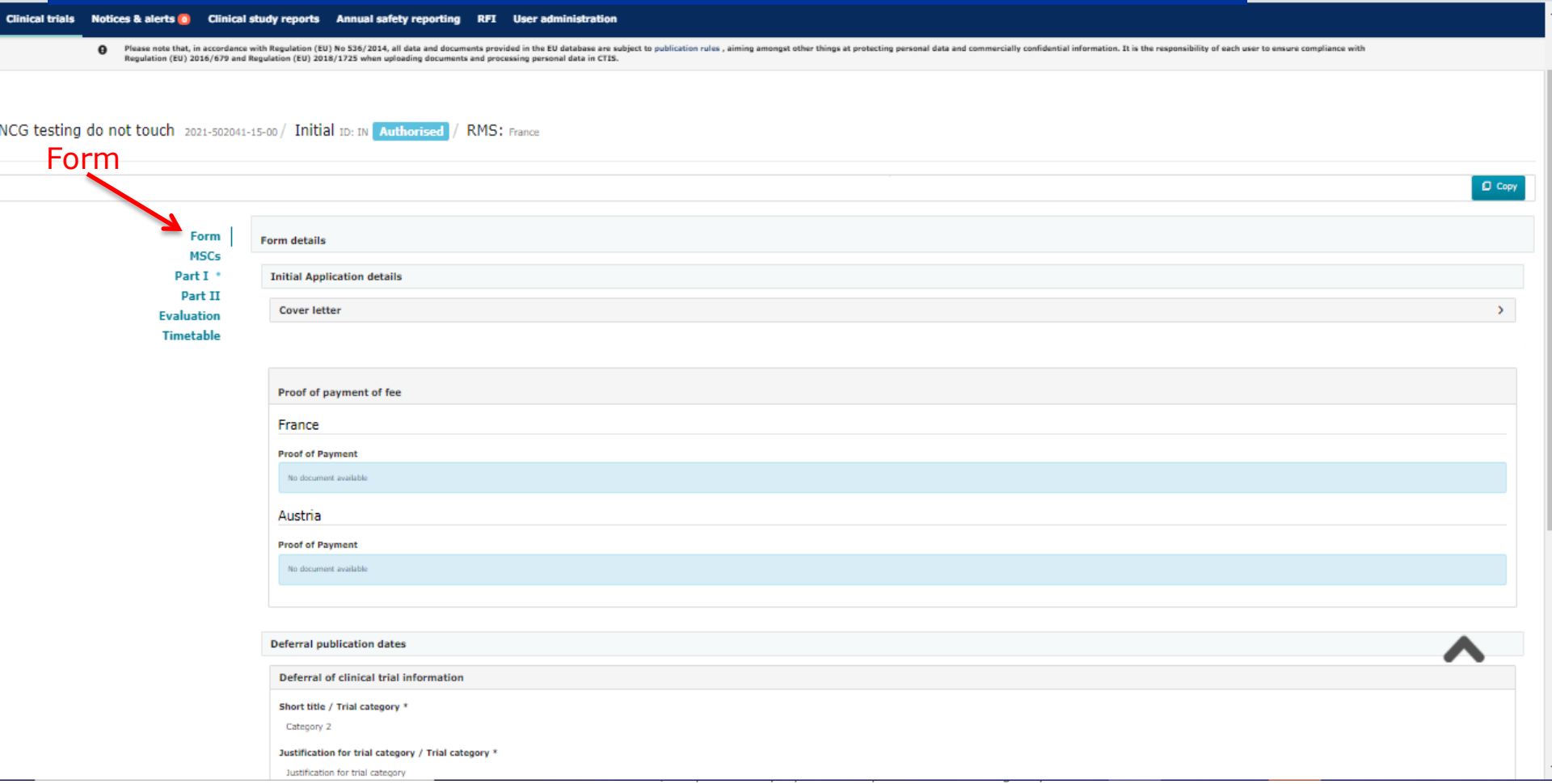

CT Application Dossier structure

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Clinical trials | Notices & alerts | Annual safety reporting | RFI | User administration

Please note that data and documents provided in the EU Database are subject to **publication rules**, which take into account the need to protect personal data and commercially confidential information. Once available, a redacted version of the documents will be made publicly available in accordance with these rules.

Group B–Mono 01– CMS AT– 14-Oct- An Open Phase III Trial of MK-3475 (Pemb... 2019-500291-28-00 / Initial ID: IN Draft

MSCs

Check | Save | Cancel | Submit

Form
MSCs
Part I
Part II
Evaluation
Timetable

Member states concerned

+ Add member states

Member states concerned	Reporting Member State	First submissions date	Subjects	Actions
Austria	◉		10	🗑
Belgium	○		13	🗑

Countries outside the European Economic Area

- Argentina
- Australia
- China
- Colombia
- Japan
- Mexico
- New Zealand

Rest of the world subjects*

10

Estimated total population for the trial

EEA subjects
23
Rest of the world subjects*
10
Total subjects
33

CT Application Dossier structure

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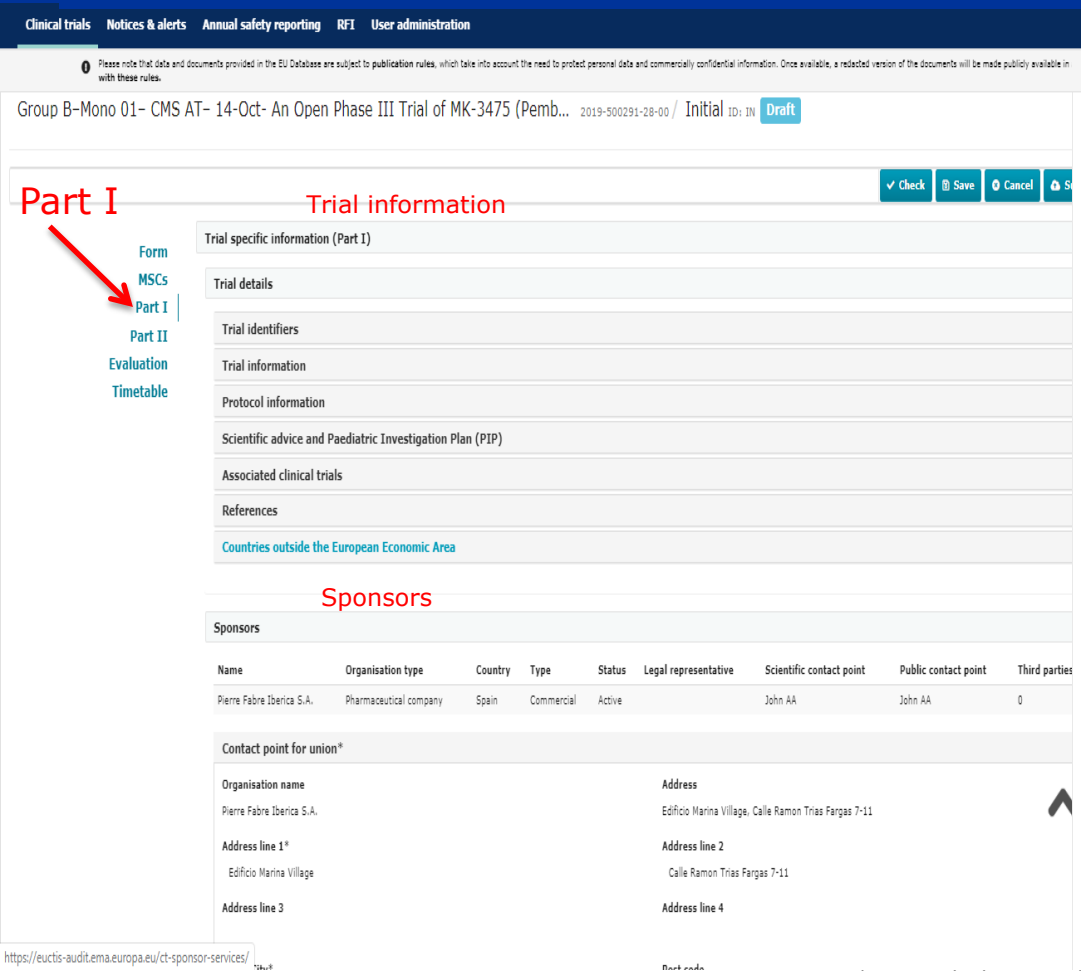
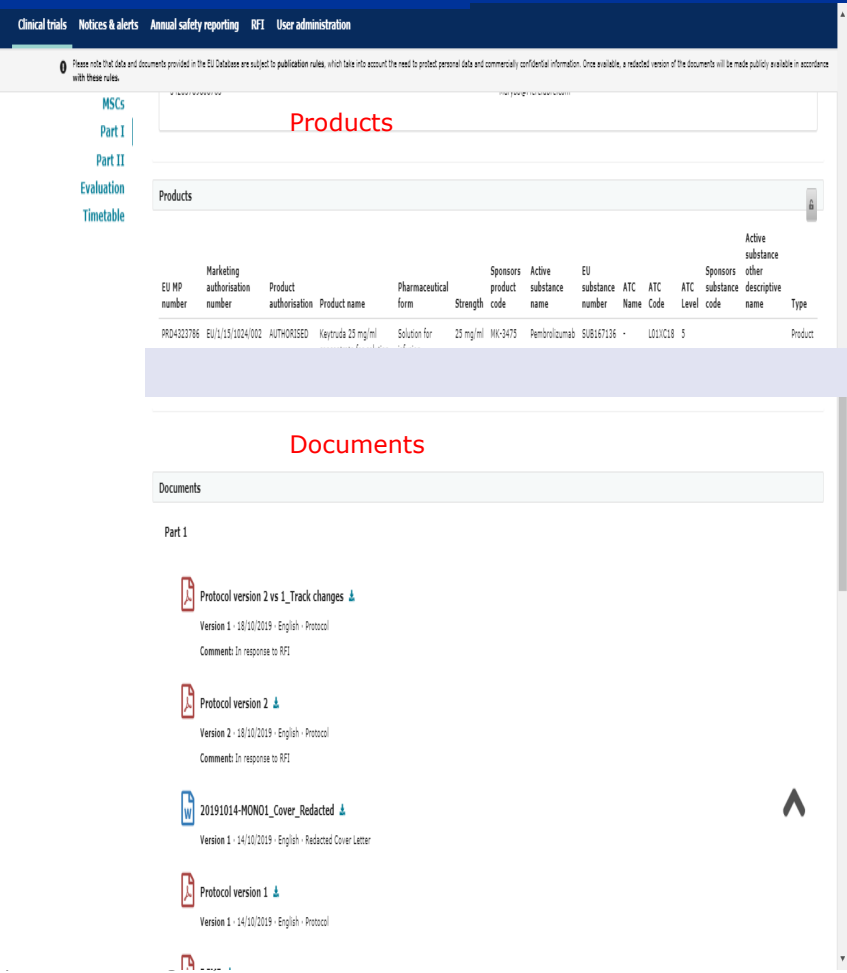
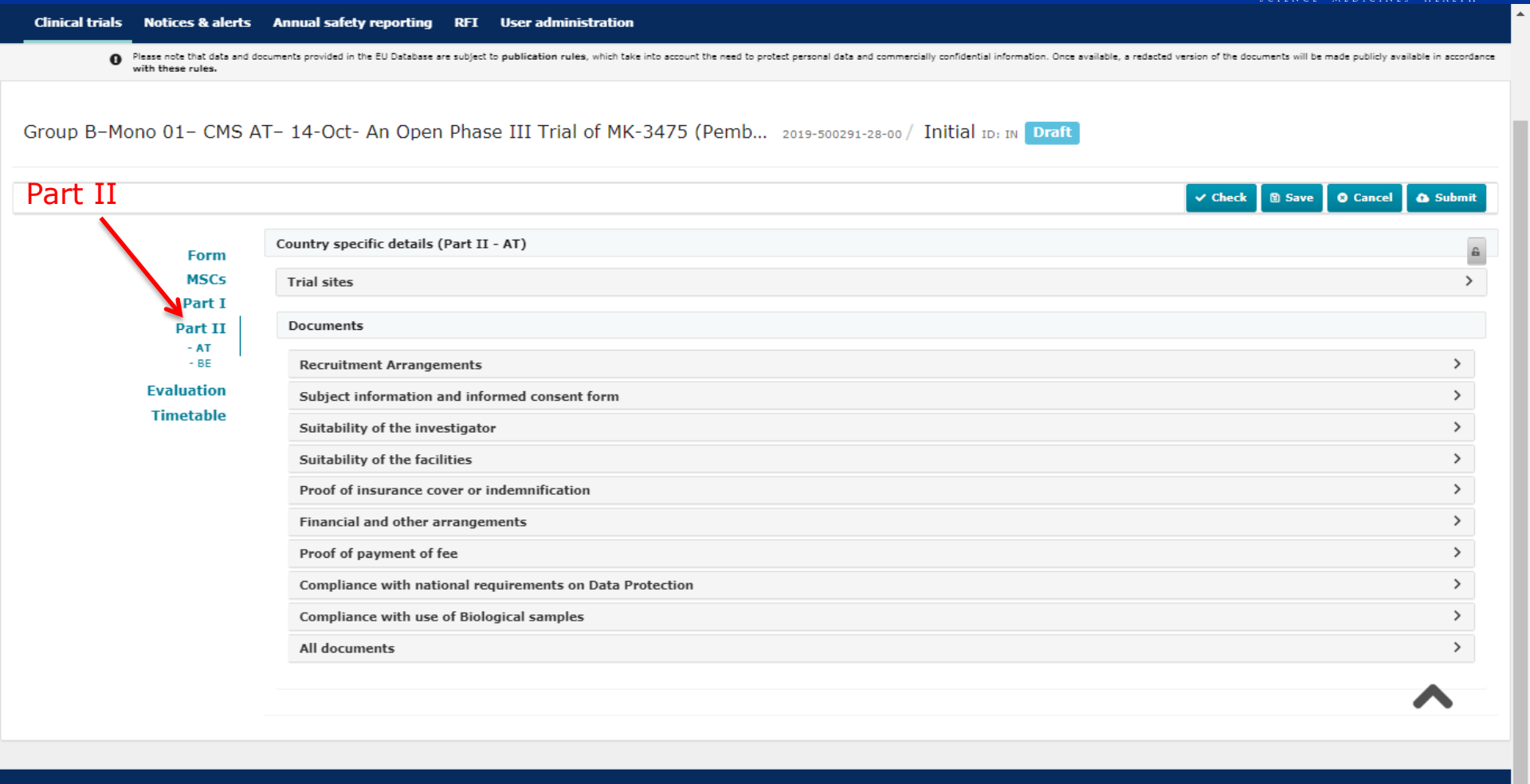
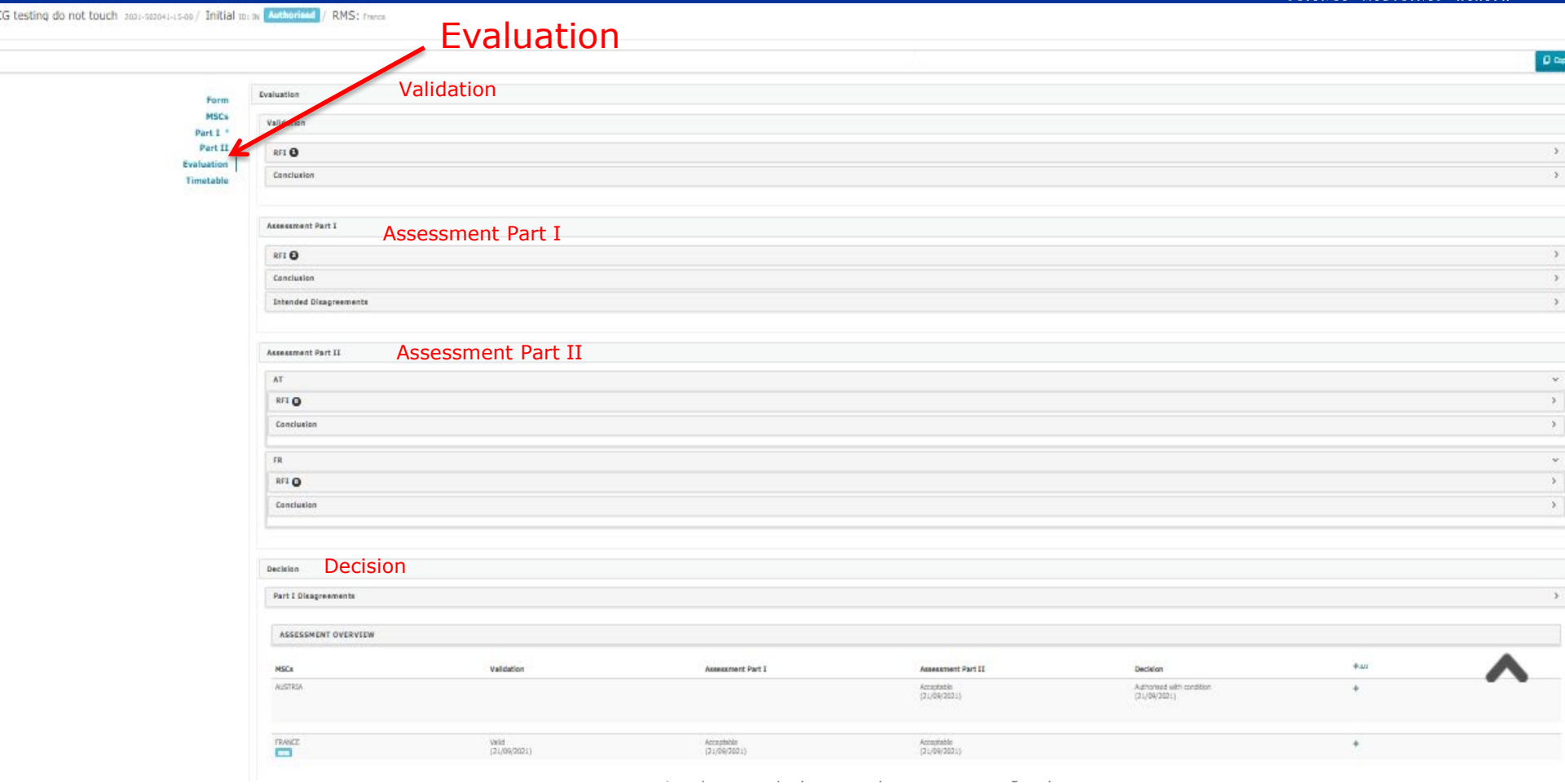




CT Application Dossier structure



Evaluation section



Timetable

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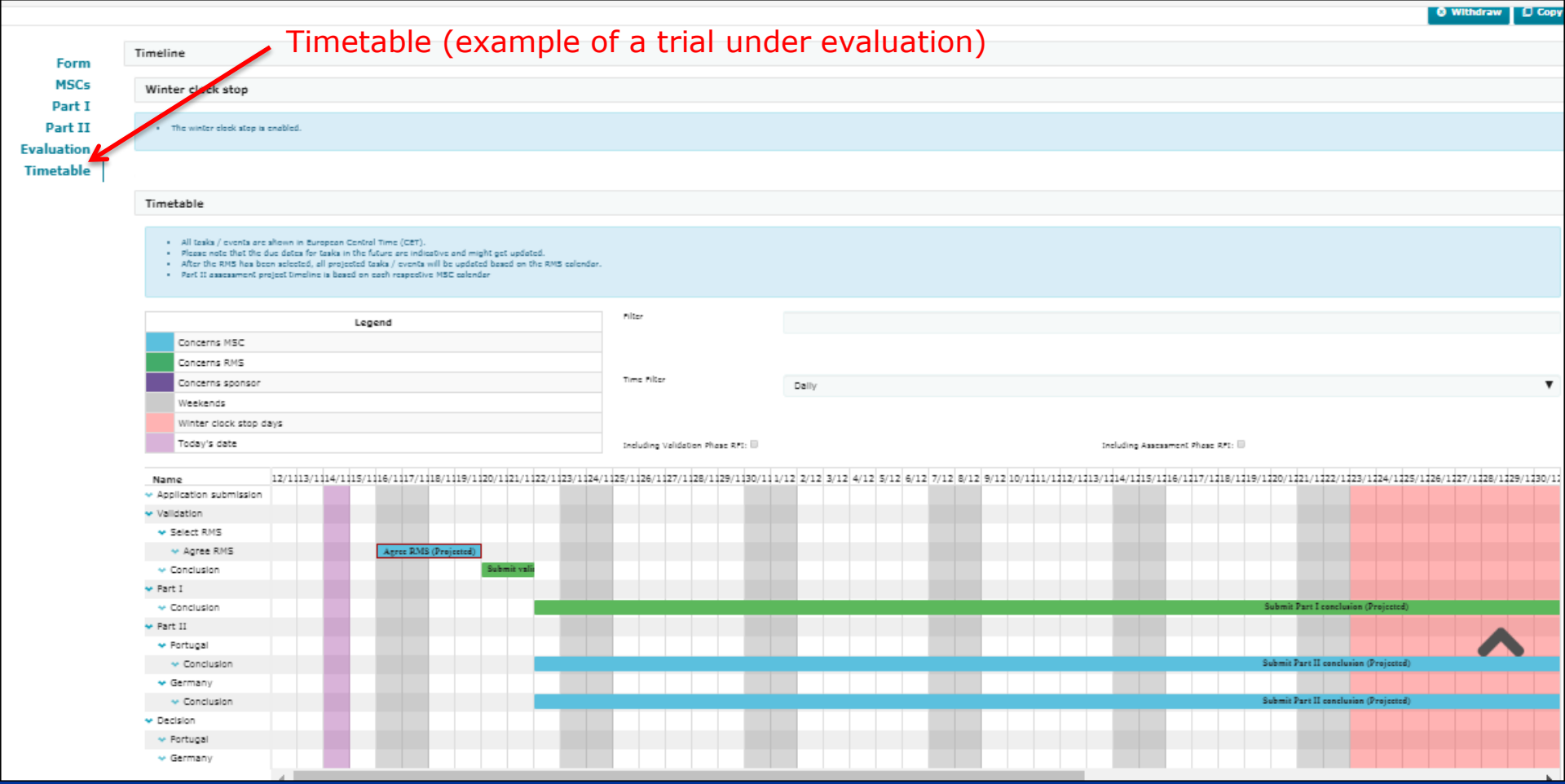
Timetable (example of a trial under evaluation)



Notices & Alerts

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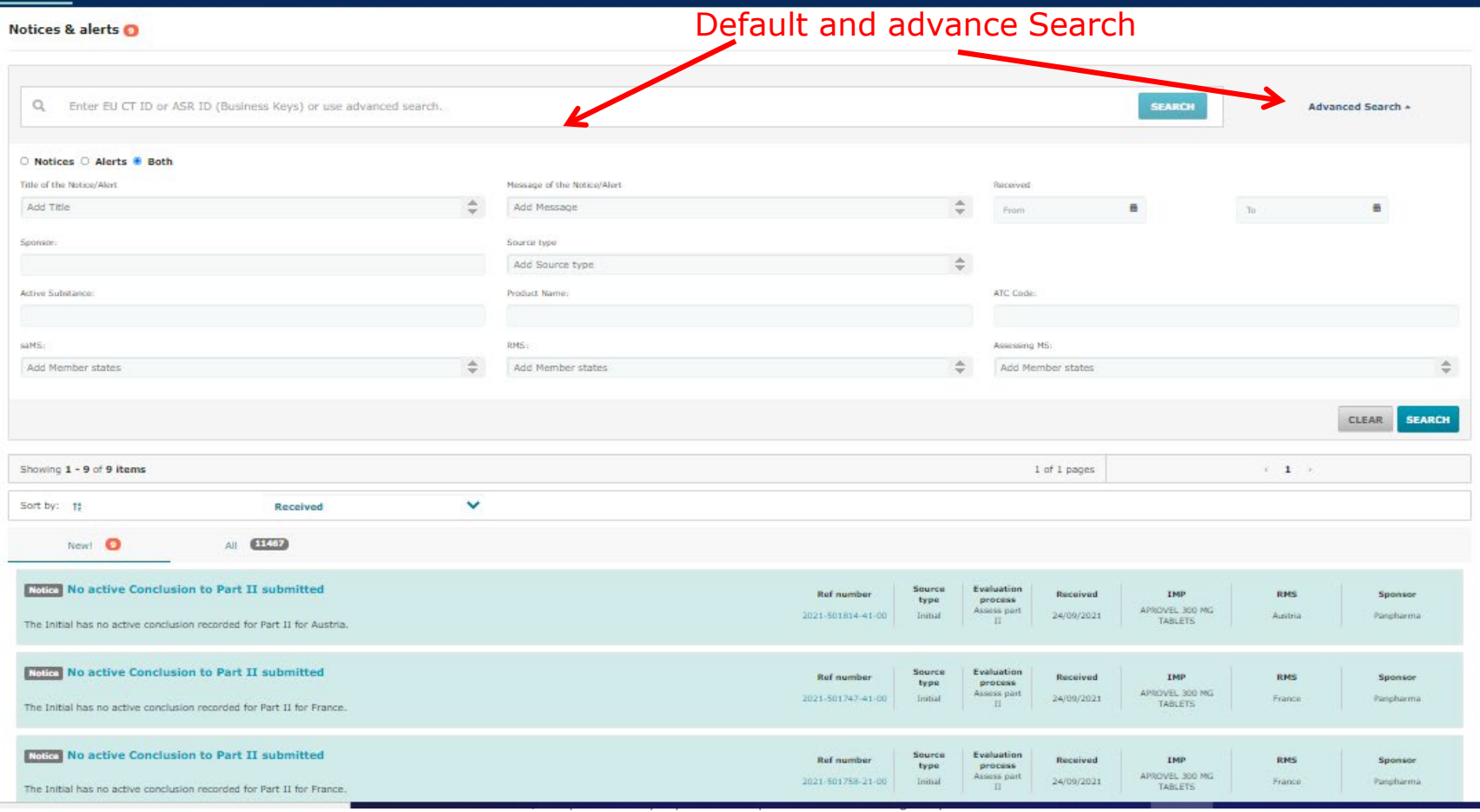
Clinical trials | Notices & alerts 9 | Clinical study reports | Annual safety reporting | RFI | User administration

N&A List



Request for Information (RFI)

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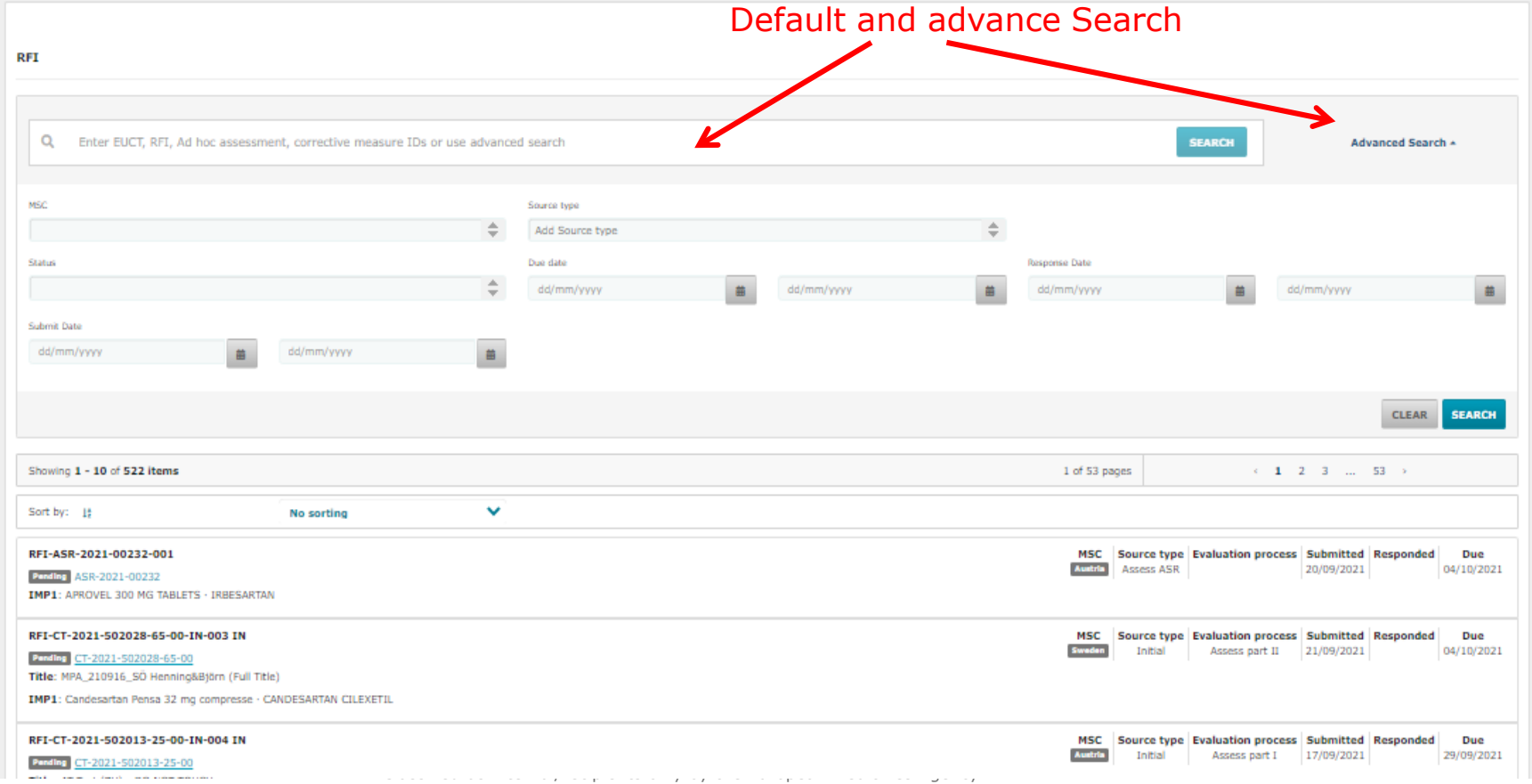
Clinical trials | Notices & alerts 9 | Clinical study reports | Annual safety reporting | RFI | User administration

Default and advance Search

RFI List



User Management

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Clinical trials | Notices & alerts | Annual safety reporting | RFI | User administration

Administration of users

Default and advance Search

Enter EU CT ID or ASR ID or use advanced search

SEARCH

Advanced search

Search Results

Showing 1 - 10 of 17 items

1 of 2 pages

‹ 1 2 ›

Sort by: User Id

Approve | Reject | Revoke | ASSIGN NEW ROLE

User List

unisys_i1 | uat.ct17@ext.ema.europa.eu

approved

EU CT Number:

Scope: All trials

Employer:

Organisation name: Pierre Fabre Iberica S.A.

Organisation Id: ORG-100003995

Role: Sponsor Admin | **Creation date:** 04/10/2019 | **Assesment date:** 04/10/2019 | **Authorised from:** 04/10/2019 | **Authorised to:**

ctuat386 | uat.ct574@ext.ema.europa.eu

approved

EU CT Number:

Scope: All trials

Employer:

Organisation name:

Organisation Id: ORG-100003995

Role: CT Admin | **Creation date:** 11/10/2019 | **Assesment date:** 11/10/2019 | **Authorised from:** 11/10/2019 | **Authorised to:**

AMEND

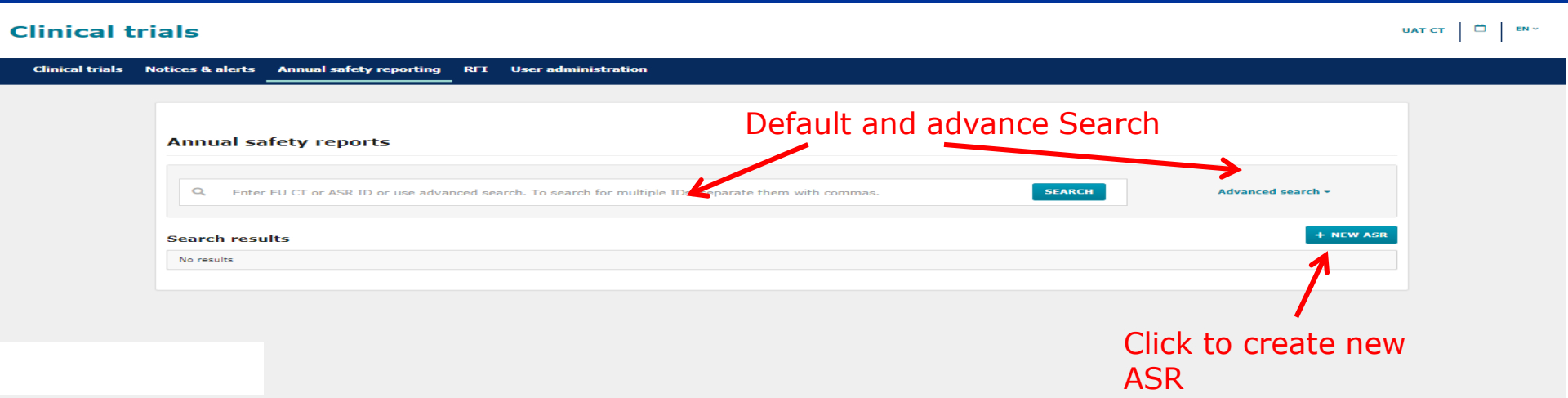
ctuat389 | uat.ct577@ext.ema.europa.eu

approved

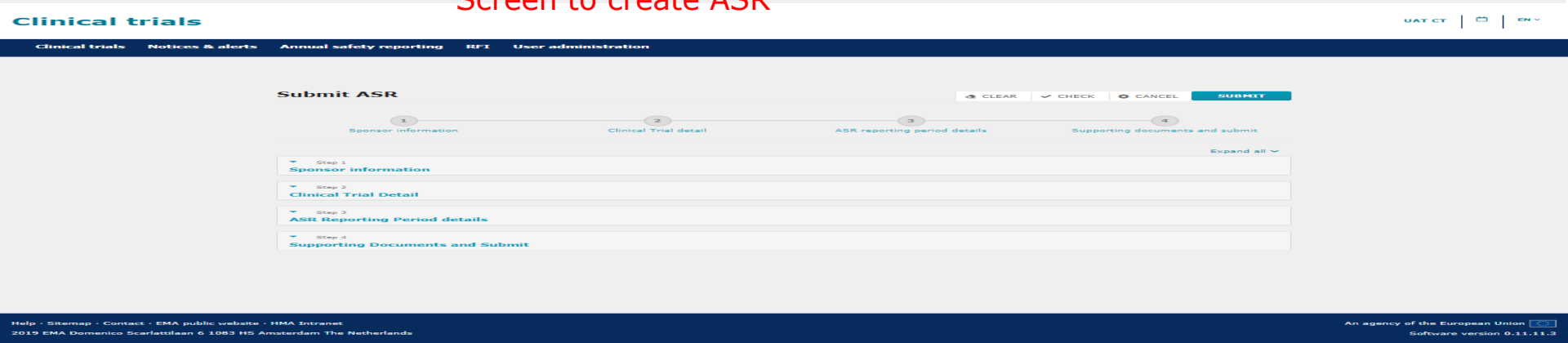
EU CT Number:

Role: Application Submitter | **Creation date:** 11/10/2019 | **Assesment date:** 11/10/2019 | **Authorised from:** 11/10/2019 | **Authorised to:**

Annual Safety Report



Screen to create ASR



Clinical Study Reports

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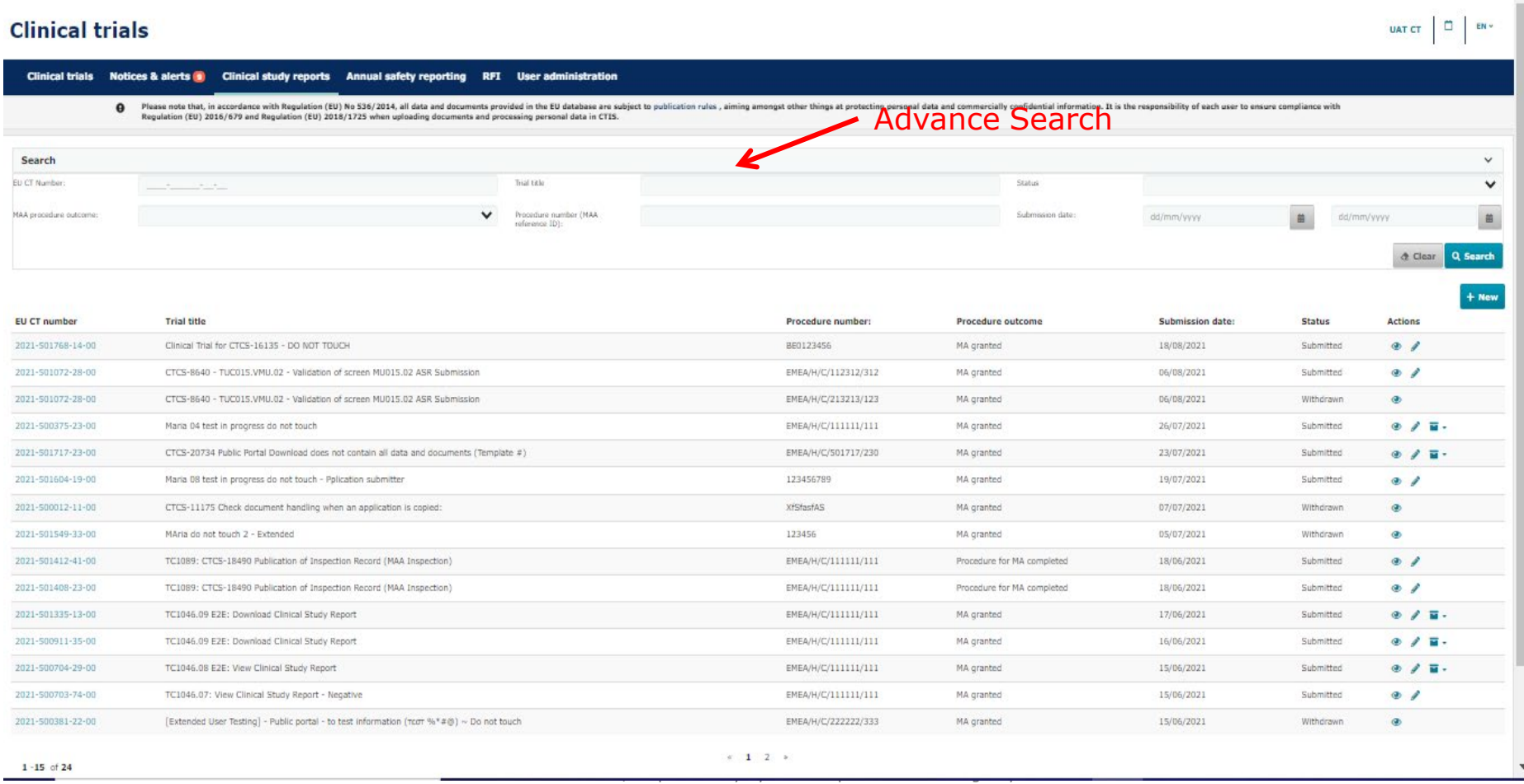

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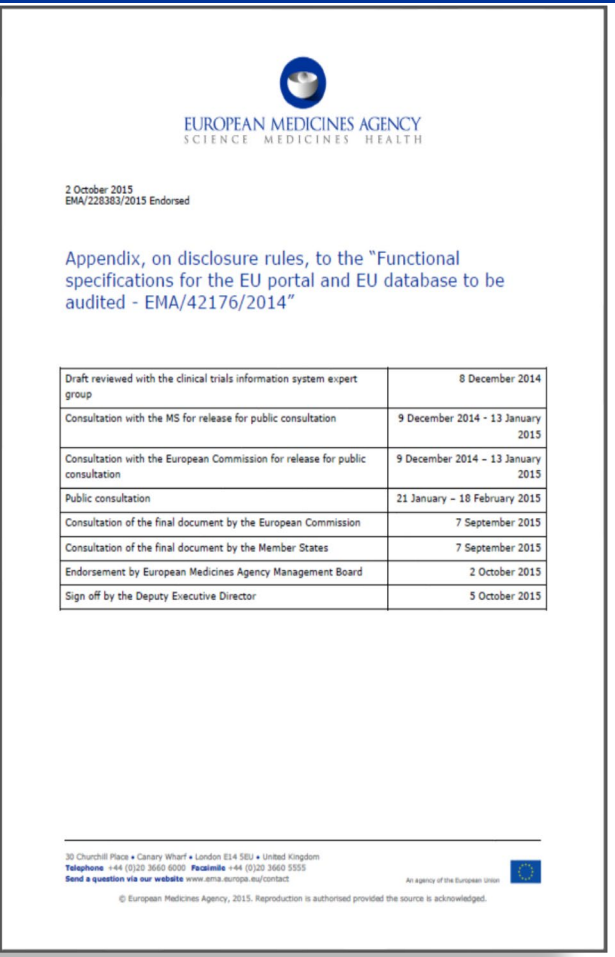
Transparency rules: legal requirements



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2 October 2015
EMA/228383/2015 Endorsed

Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"

Draft reviewed with the clinical trials information system expert group	8 December 2014
Consultation with the MS for release for public consultation	9 December 2014 - 13 January 2015
Consultation with the European Commission for release for public consultation	9 December 2014 – 13 January 2015
Public consultation	21 January – 18 February 2015
Consultation of the final document by the European Commission	7 September 2015
Consultation of the final document by the Member States	7 September 2015
Endorsement by European Medicines Agency Management Board	2 October 2015
Sign off by the Deputy Executive Director	5 October 2015

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- Article 81(4) of Regulation (EU) No. 536/2014: EU database publically accessible by default, with exceptions justified on any of the following grounds:
  (a) protecting personal data in accordance with Regulation (EC) No 45/2001;
  (b) protecting commercially confidential information, in particular through taking into account the status of the marketing authorisation for the medicinal product, unless there is an overriding public interest in disclosure;
  (c) protecting confidential communication between Member States in relation to the preparation of the assessment report;
  (d) ensuring effective supervision of the conduct of a clinical trial by Member States

- Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"- General pronciples
  http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/10/WC500195084.pdf

Transparency rules: general principles

- The same rules apply whether the sponsor is a pharmaceutical company, academic research group or other type of organisation;
- Only applications on which a decision has been reached will be made public;
- Public registration of trials at their start including all information needed for patients who may wish to participate in therapeutic or preventive trials;
- All data and documents in the system will be made public except for manufacturing/quality information, details of financial agreements between sponsors and investigators, and specified personal data;
- The default is always to make public at the first opportunity;
- The rules depend on the IMPs used in a trial and how they are used;
- Depending on the category of trial Sponsors have options to defer the timing of publication of specific data/documents up to a maximum time limit (see background slides as reference);
- The use of deferrals will be monitored and should not exceed what is really needed.

What will not be made public

- Quality related information that include:
  - ❑ The IMPD quality
  - ❑ Scientific advice on quality
  - ❑ Quality related request of information (RFI) raised during the assessment
  - ❑ Quality Assessment reports (draft and final)
- Drafts of assessment reports;
- Versions of documents that are 'not for publication', which may include personal information identifying Member States experts, sponsor staff, MAH/applicant staff, as needed;
- Financial agreements between the sponsor and the investigator site;
- Any requests for information from MS to the sponsor and responses recorded outside of an assessment of an application

CTIS: functionalities and support for clinical trial sponsors, availability of clinical trial data to the public

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Public Module –public search for data

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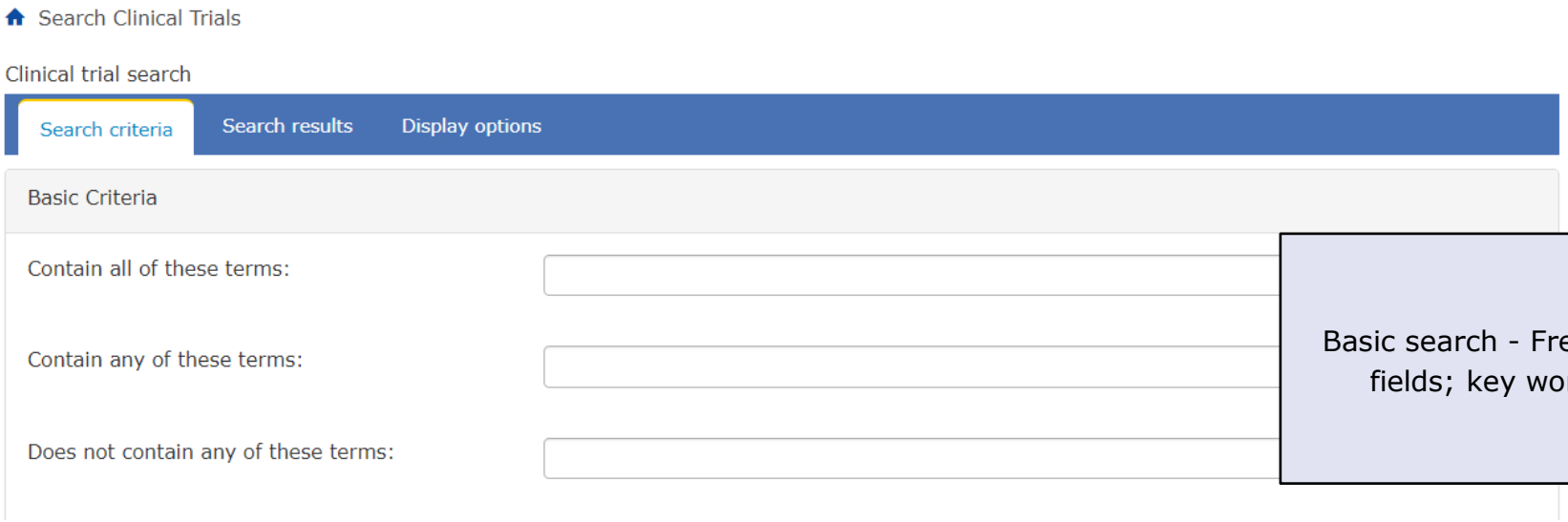
The data in CTIS will accumulate over time as sponsors submit their applications and results.
There is a basic search on free text and an advanced search with more options



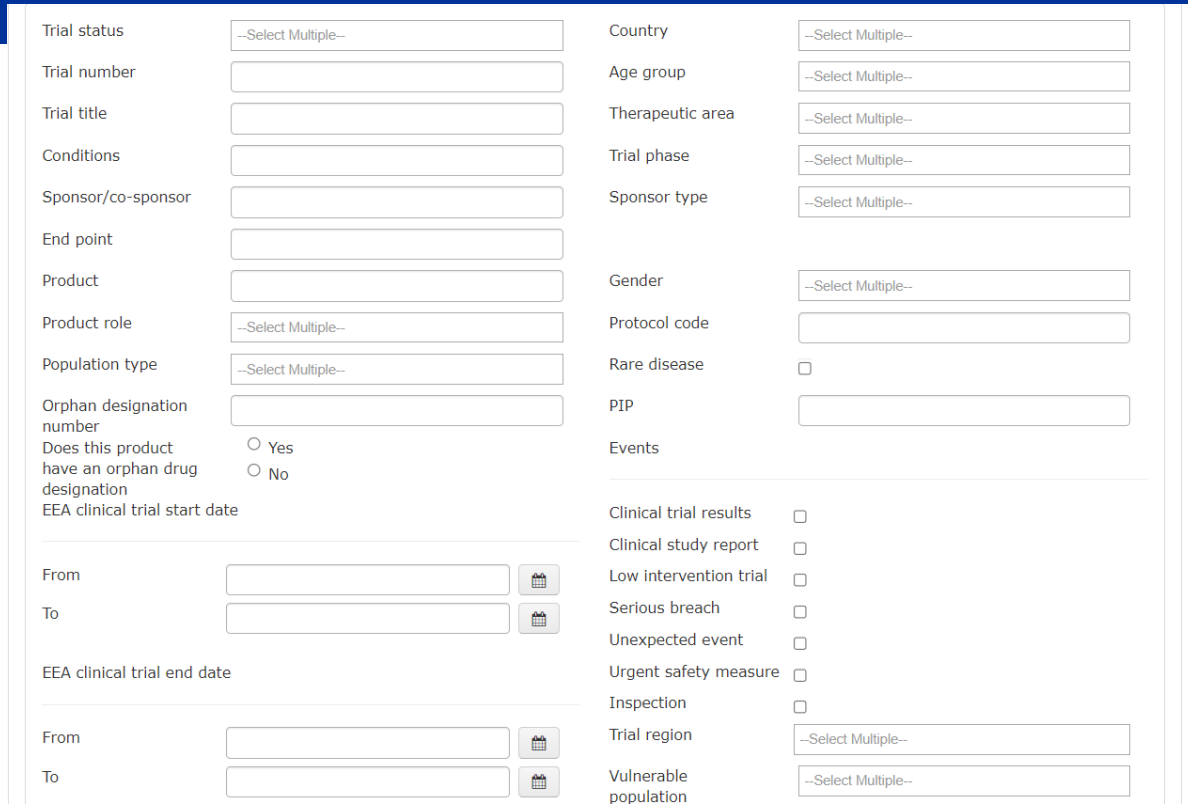
Basic search - Free text fields; key words

Public Module – what the public will be able to search for - advanced

Options for search include elements of, e.g.:

- Trial information
- Sponsor
- End point
- Therapeutic area
- Orphan status and number
- Rare disease status
- Paediatric trial (PIP)
- Trial phase
- Product
- Time ranges
- Trial events
- Country
- Age group
- Gender
- Vulnerable population

… etc



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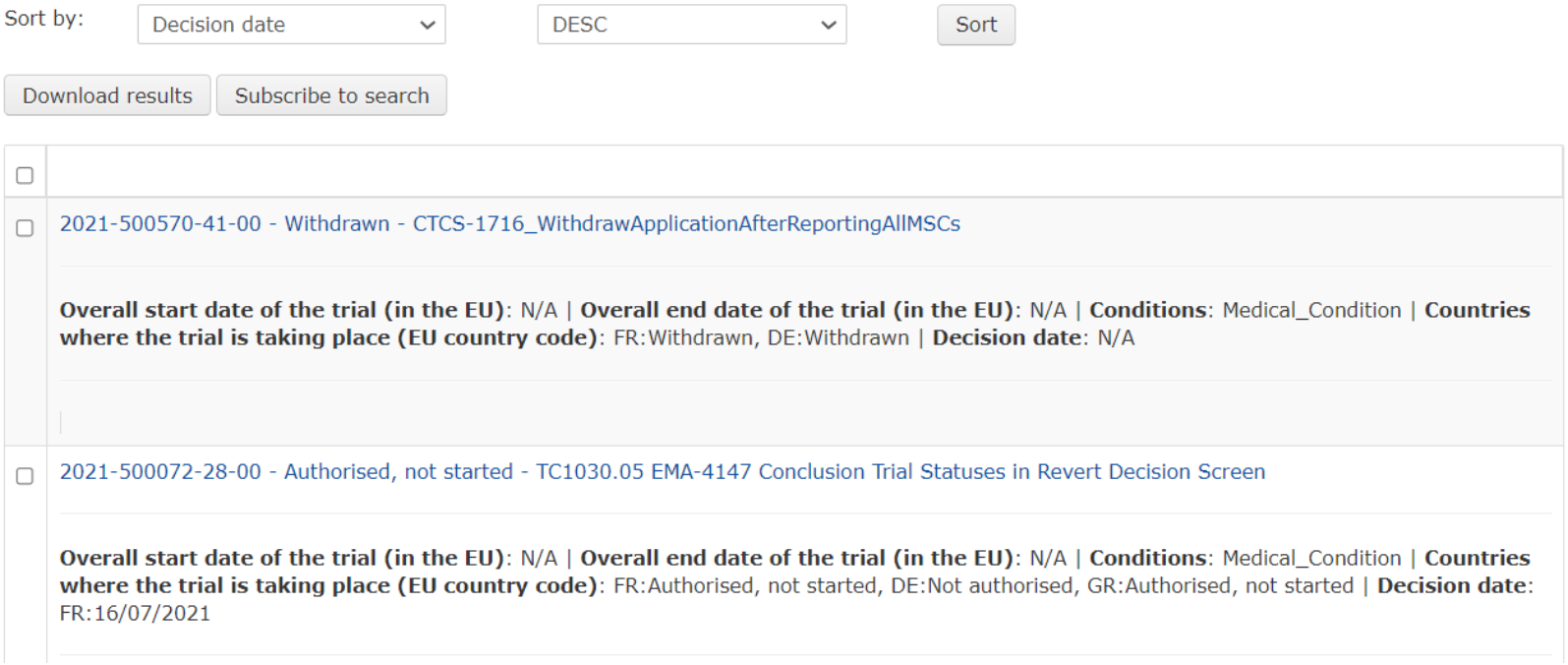
The results can be sorted, downloaded and a subscription to the search can be made.



Public Module –display options of searches

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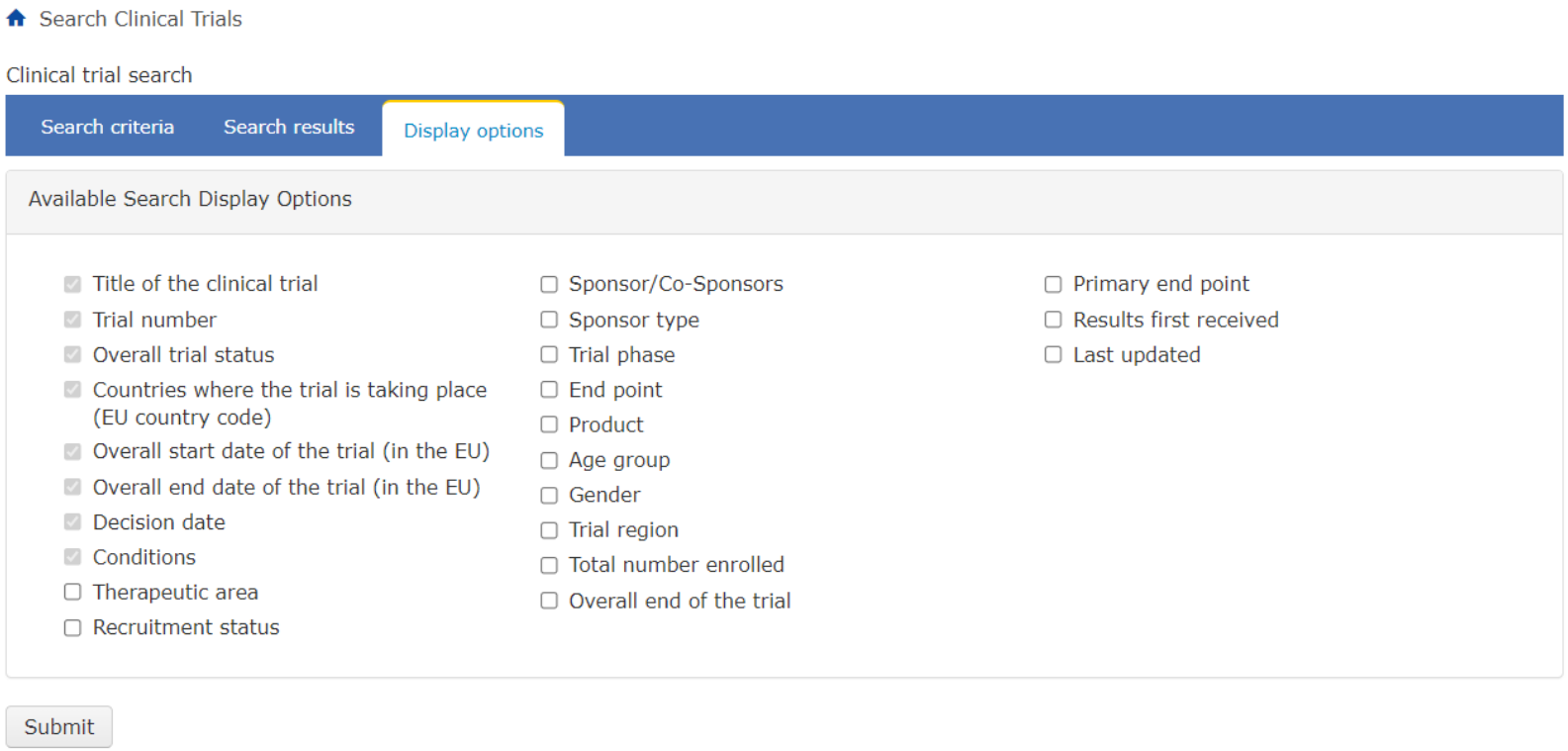
It will also be possible to choose the type of data that will be displayed.



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CTIS Sponsor Support

Engagement	Info events (recorded & published) Collaborative approach
Online Training	Extensive online programme available Sponsor Master Trainer programme
Online Support	EMA CTIS Sponsor Handbook Supportive materials and references
Research community/SME	Targeted SME/academia trainings
EMA CTIS info	EMA CTIS Highlights Newsletters (subscribe by writing to CT.Communication@ema.europa.eu)
All above are available on www.ema.europa.eu	

Next open CTIS Information/Training Events for sponsors

EUROPEAN MEDICINES AGENCY

Events are planned to help future CTIS users prepare for CTIS Go-Live.
Find on EMA events page (search e.g. "CTIS")

26 October info event

Target audience
MS and sponsor end users

Objectives

- Ensure **awareness of CTIS** across the end-user base
- **Prepare users for the new way of working** with CTIS

Supported by DIA; fee applies

29 November training event

Target audience
SME/academia sponsors & end users

Objectives

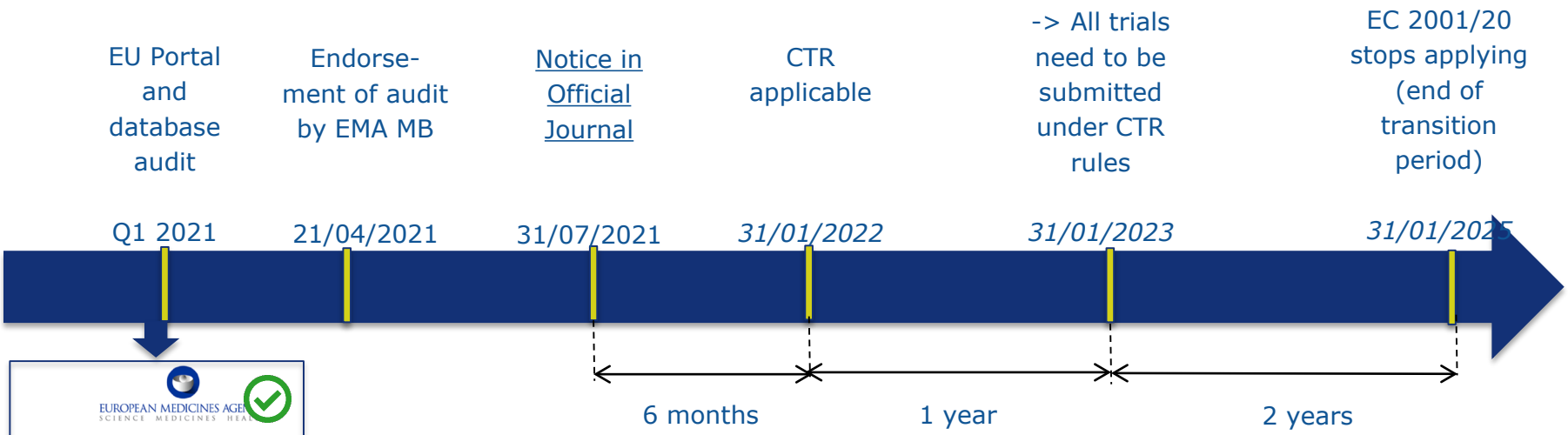
- Ensure **awareness of CTIS** across the end-user base
- **Prepare SME/academia users** for the new way of working with CTIS

Open event, no fee

Content

- CTR and CTIS Benefits
- CTIS high-level system overview and actors
- User Management
- Sponsor Workspace functionalities
- Transparency rules
- Public module
- CTIS Sponsor support
- **CTR Application and transition period**
- Next steps

CTR Application and Transition Period



- EMA MB endorsement of full functionality is a condition for the publication of the notice in the official journal and was confirmed on 21/04/2021. 6 months later, the CTR starts to apply
- The date of application is January 31, 2022

Content

EUROPEAN MEDICINES AGENCY

- CTR and CTIS Benefits
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- CTR Application and transition period
- **Next steps**

EUROPEAN MEDICINES AGENCY

Clinical Trials Information System - CTIS

- *Focus:*
  - *Ensure quality and stability of CTIS*
  - *Deliver CTIS for go-live*
  - *Put effort now into preparing for CTIS Go Live*
- *Get ready:*
  - *Define functions and processes embedding CTIS*
  - *Nominate the Administrator (if applicable)*
  - *Define the form of your organisations*
  - *Choose the people to work with CTIS, train the people implement the processes*
- *Countdown has started:*
  - ***Go Live 31 January 2022***

Thank you for your attention

Further information

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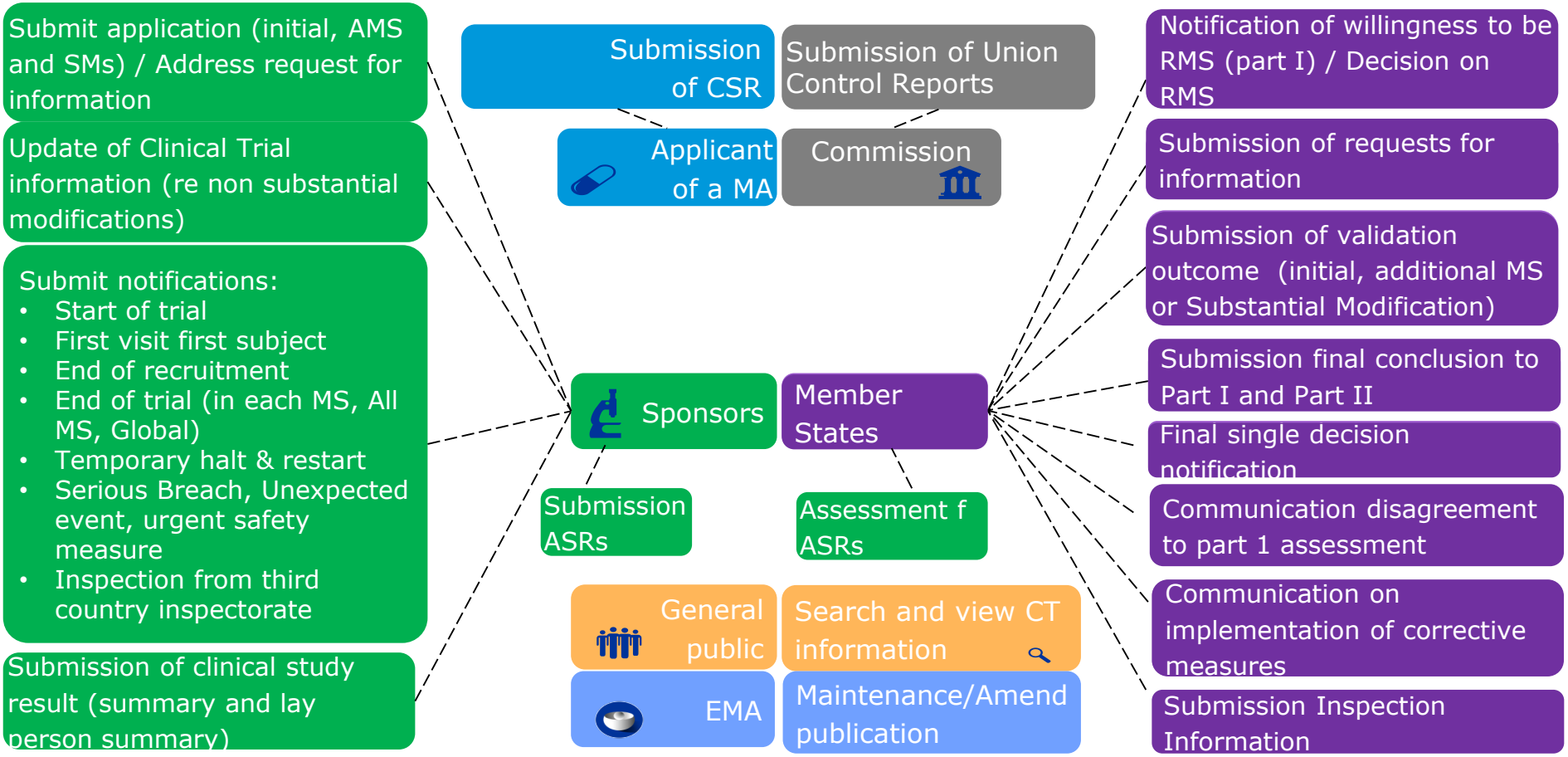
CTIS- Actors and activities in the CTIS system



OPTIONS FOR DEFERRALS

		CATEGORY 1	CATEGORY 2	CATEGORY 3
Main Characteristics of the trial		For a subset of information and up to the time the CT Results Summary is posted (Justification)	No deferral	No deferral
Trial related documents	Subject Information sheet	Up to the time of MA using this trial or up to 7 years after the end of the trial, whichever is earlier	Up to the time of MA using this trial or up to 5 years after the end of the trial, whichever is earlier	No deferral
	Protocol	As above	As above	Up to the time the CT Results Summary is posted (usually 12 months after the end of the trial in the EU)
Product related Documents	IB	As above	As above	As above
	IMPD, S&E	As above	As above	As above
Assessors documents /data	Request for information	MS decides but takes into account the exceptions of the legislation and the deferral time proposed by the sponsor		No deferral
	AR (I & II)			
	Conditions			

OPTIONS FOR DEFERRALS

		CATEGORY 1	CATEGORY 2	CATEGORY 3
Substantial modifications		Deferral possible only for changes or additions to data/documents not yet made public because of the legal deadline is not reached or a deferral was requested. Publication will take place when the legal deadline is reached or deferral deadline expires.		
Notifications	Unexpected events, urgent safety measures	Up to the time when summary results are posted - except for early terminations for reasons involving subject safety or if Corrective measures (Justification)	No deferral	No deferral
Clinical Trials Summary Results	Scientific Summary	Up to 18 months after the due date for the publication of the summary of results (usually 12 months after the end of the trial unless article 37(4) applies/or 6 months for paediatric CTs according to the Paediatric Regulation) (Justification)	No deferral	No deferral
	Lay person	As above	No deferral	No deferral
Clinical Study Report		No deferral	No deferral	No deferral

OPTIONS FOR DEFERRALS

		CATEGORY 1	CATEGORY 2	CATEGORY 3
Supervisory measures	Serious Breaches	If the sponsor requested a deferral up to the time of publication of summary results the same will apply here.	No deferral	No deferral
	Inspections Reports (EU)	As above		
	Inspections Reports (by third country CA)	As above		
	Union Controls	As above		
	Corrective Measures	No deferral		