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European Medicines Agency

European Union Clinical Trials Information System CTIS: Go-live Planning

Summary of key areas in preparation of the operation of CTIS

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1. Executive summary

The Clinical Trials Regulation (CTR)[1] was adopted and entered into force in 2014 with the timing of its application being subject to confirmation of full functionality of the Clinical Trials Information System (CTIS) through an independent audit.

On 21 April 2021, following an independent successful audit of CTIS, the EMA's Management Board confirmed that CTIS is fully functional and meets the agreed functional specifications. The European Commission subsequently issued a Commission Decision[2] which specifies that the entry into application of the CTR and hence the go-live date for the CTIS will be on 31 January 2022.

This CTIS Go-Live Plan provides an overview of the final remaining activities with the aim to:

- Address the functional and non-functional areas as set out in the CTIS Project Release Plan for go-live, which includes working towards fixing the observations of the audit and of user-testing, and delivering priority areas as agreed by the EMA Management Board;
- Prioritise the development of the sponsor workspace, followed by the authorities workspace and the public portal;
- Set up of a dedicated EMA Service Desk;
- Address operational and procedural aspects in relation to CTIS and supporting systems;
- Prepare extended stakeholder training;
- Support change management;
- Prepare for the initial scope of safety reporting and monitoring in clinical trials.

Priorities are stability, performance, security of CTIS.

The CTIS programme is organised into four topics, which are the core of this go-live plan:

Topic 1: CTIS Functional and Non-Functional Requirements and other IT related matter

Topic 2: Business Processes and Operational Activities, including interfaces with other systems

Topic 3: Clinical trials Safety Reporting and Monitoring

Topic 4: CTIS Change Management Activities

The planning focusing on the activities post 31 January 2022 (post go-live releases, CTIS operation and maintenance, continued training offerings and stakeholder support and interaction) will be published in Q1 2022.

[1] 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. OJ L 158, 27.5.2014, p. 1–76

[2] Commission Decision (EU) 2021/1240 of 13 July 2021 on the compliance of the EU portal and the EU database for clinical trials of medicinal products for human use with the requirements referred to in Article 82(2) of Regulation (EU) No 536/2014 of the European Parliament and of the Council (Text with EEA relevance) C/2021/5063; OJ L 275, 31.7.2021, p. 1–2

2. Introduction

The CTR establishes a harmonised approach to submission, assessment and authorisation of clinical trial applications as well as reporting and supervision of clinical trials with the implementation of consistent rules throughout the Member States. These processes are to be supported by an EU portal and EU database which will ensure a single-entry point with a workflow with monitoring and decision-making by the relevant parties.

Articles 80 to 82 of the CTR set out the following obligations for the European Medicines Agency (hereinafter "the Agency"):

- In accordance with Article 80 of the CTR, the Agency shall, in collaboration with the Member States and the Commission, set up and maintain a portal at Union level as a single entry point for the submission of data and information relating to clinical trials in accordance with this Regulation. The EU portal shall be technically advanced and user-friendly to avoid unnecessary work. Data and information submitted through the EU portal shall be stored in the EU database referred to in Article 81 of CTR.
- In accordance with Article 81 of the CTR, the Agency shall, in collaboration with the Member States and the Commission, set up and maintain an EU portal and EU database at Union level. The Agency shall be considered to be the controller of the EU database and shall be responsible for avoiding unnecessary duplication between the EU database and the *EudraCT*[3] and *EudraVigilance*[4] databases. The EU database shall contain the data and information submitted in accordance with the CTR.
- In accordance with Article 82, paragraph 1 of the CTR, the Agency shall, in collaboration with the Member States and the Commission, draw up the functional specifications for the EU portal and the EU database, together with the timeframe for their implementation. As set out in Article 82, paragraph 2 of the CTR, the Management Board of the Agency shall, on the basis of an independent audit report, inform the Commission when it has verified that the EU portal and portal and the EU database have achieved full functionality and the systems meet the functional specifications (referred to above).
- Furthermore, as set out in Article 82, paragraph 3 of the CTR, the Commission shall, when it is satisfied that the EU portal and the EU database have achieved full functionality, publish a notice to that effect in the Official Journal of the European Union. Pursuant to Article 99 of CTR, six months after the publication of this notice the Regulation shall apply.

2.1. CTIS overview

This system includes **three main components** that fulfil the needs of its different users:

1. **Submission workspace** – for clinical trial sponsors to prepare and compile data and information to submit via the clinical trials EUPD.
2. **Authority workspace** – for the EU Member States and European Commission to support evaluation of documents and structured data submitted by sponsors as well as submission of assessment reports and handling of requests for information to sponsors and their replies to these as well as supervision, allowing collaboration between Member States concerned in multinational clinical trials via the EU portal.

[3] EudraCT active time ends after transition period i.e. the transitional period, will last for a period of 3 years starting from when the Regulation becomes applicable. At the end of the transitional period all clinical trials shall be conducted under Regulation No 536/2014 (Article 96).
[4] https://www.ema.europa.e u/en/human-regulatory/research-development/pharmacovigilance/eudravigilance

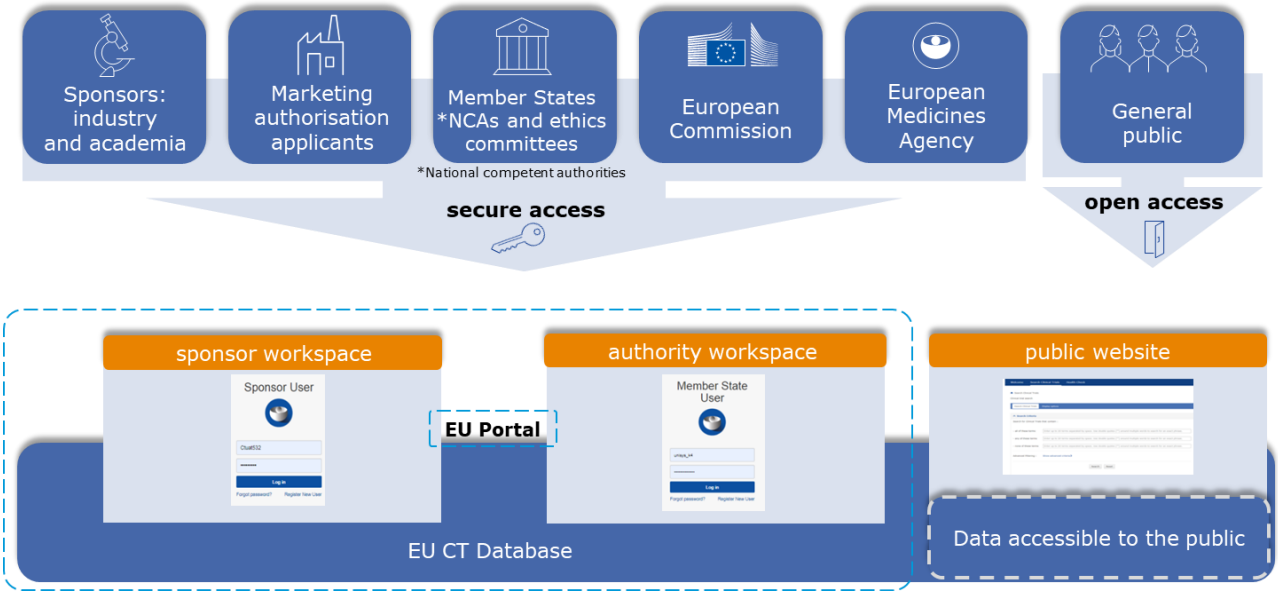
3. **Public website** – for the public to search and view publicly available data and information relating to clinical trials in the EU.

In accordance with the CTR, the EUPD provides a single entry point for the submission of data and information relating to interventional clinical trials of medicines in human subjects throughout the life cycle of a trial including planning and outcome of inspections as well as a workflow with communication features to address the collaboration of Member States concerned.

The system also includes an Application Programming Interface (API) for the clinical trials EUPD (CT-API) for Member States.

Data and information submitted through the EU portal will be stored in the EU database. As outlined in Article 81, paragraph 4 of the CTR, the EU database shall be publicly accessible unless, for all or part of the data and information contained therein, confidentiality is justified on any of the grounds for confidentiality established by Article 81 paragraph 4(a) to 4(d) of the CTR.

3.1



3. CTIS Go-Live Planning

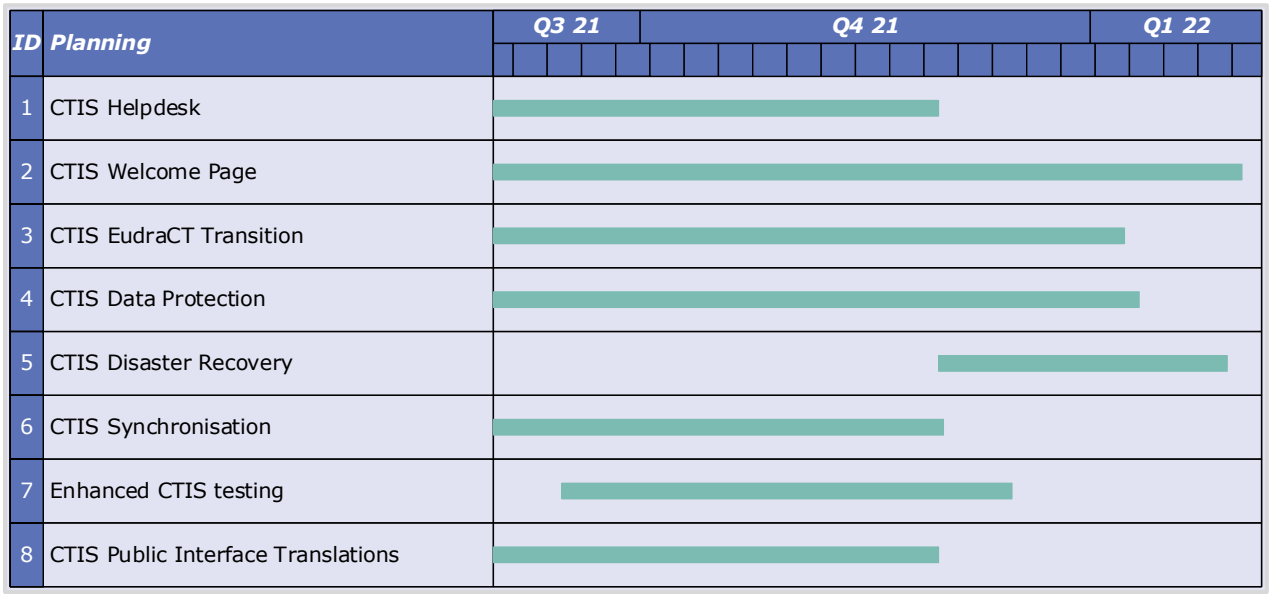
3.1. CTIS Functional and Non-Functional Requirements and other IT related matters

3.1.1. Project Release Plan for go-live

A Project Release Plan for go-live is in place that addresses functional and non-functional areas, which include working towards fixing the observations of the audit and of user-testing and delivering the priority areas as agreed by the EMA Management Board by 31 January 2022.

3.1.2. Additional activities beyond the Project Release Plan for go-live

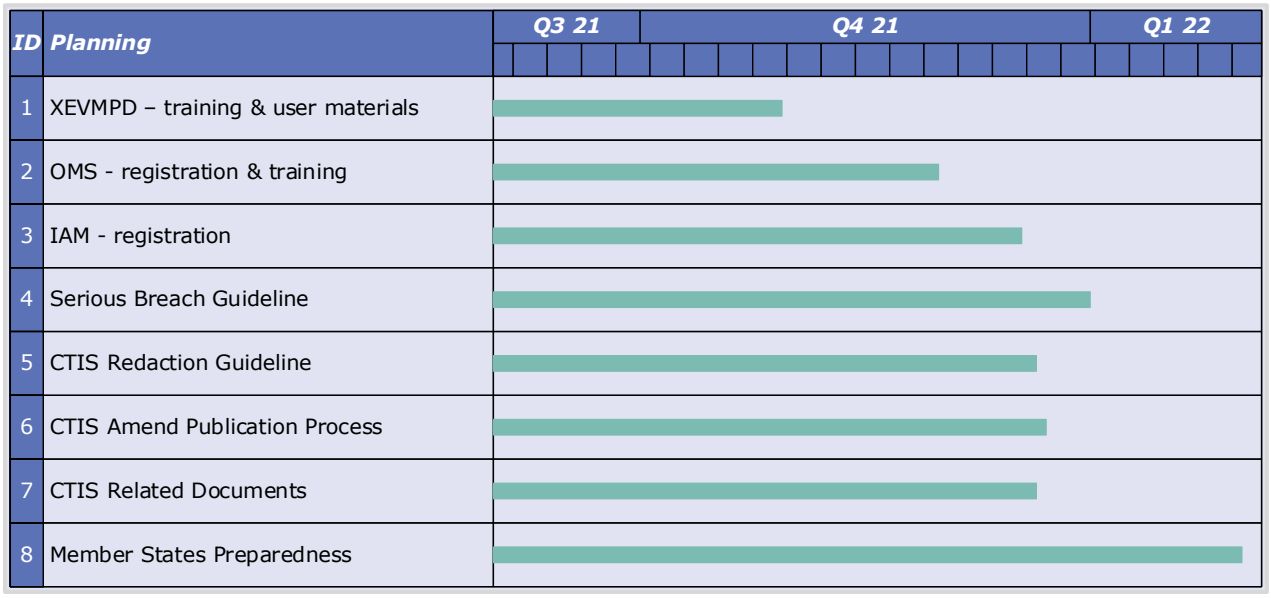
Besides the Project Release Plan, additional IT/technical/infrastructure related activities in preparation of the launch of CTIS are also addressed. These are outlined as follows:



1. The **CTIS Helpdesk** area is designed to deliver an operational helpdesk in support of CTIS users taking into account the service desk model covering business and IT support address staffing needs, use of service desk tools and staff training.
2. The **CTIS Welcome Page** area focuses on the design, creation of content of the CTIS public website.
3. The **CTIS EudraCT Transition** area provides the mechanism for sponsors to changeover trials from EudraCT to CTIS during the transition period defined in Article 98 of the CTR. This is to indicate in CTIS that this concerns a clinical trial authorised in the context of Directive 2001/20/EC and to indicate that the trial is transitioning.
4. The **CTIS Data Protection** area focuses on key activities and timelines in relation to the technical adaptations required to comply with Union data protection rules including the electronic acceptance of the CTIS Joint Controllership Arrangement (JCA) at the time of first log-in by CTIS users and future updates.
5. The **CTIS Disaster Recovery** area addresses the necessary business continuity and disaster recovery processes with the applicable functionalities in place.
6. The **CTIS Synchronisation** area ensures synchronisation of CTIS with supporting systems such as EudraVigilance, the Extended EudraVigilance Medicinal Product Dictionary (XEVMPD), EudraCT, the Organisation Management Service (OMS), the Identity and Access Management (IAM) and others.
7. The **Enhanced CTIS Testing** area provides for heightened testing in preparation of CTIS go-live.
8. The **CTIS Public Interface** area addresses the technical implementation of the public interface in all official EU languages.

3.2. Business Processes and Operational Activities

The focus is on business processes and operational areas required in support of the go-live and operation of CTIS. The following topics are addressed:



1. The **CTIS Extended EudraVigilance Medicinal Product Dictionary (XEVMPD)** area focuses on the delivery of dedicated training materials (e.g. step by step guide), an update of XEVMPD user manuals and guidance documents for CT sponsors on the submission/management of Investigational Medicinal Product (IMP) information in the XEVMPD in the context of the submission of clinical trial applications through CTIS.

2. The **Agency's Organisation Management Service (OMS)** area facilitates the registration of Member States organisations (National Competent Authorities, Ethics Committees) by EMA and the provision of online training material to guide stakeholders, in particular sponsors, on the registration process specific to CTIS.

3. The **Identity Access Management (IAM)** area is designed to ensure the initial registration of the administrators from Member States and the European Commission by EMA. These administrators can subsequently register additional users within their organisation. In addition, EMA opens the sponsors and marketing authorisation holders registration, based on a phased approach. This area also includes the delivery of dedicated training material that describes step by step the registration process and the update of the IAM webpage.

4. The **Serious Breach Guideline** area delivers the Guideline for the notification of serious breaches of Regulation (EU) No 536/2014 or the clinical trial protocol taking into account the consultation comments as well as the procedure for managing serious breaches by EU/EEA Member States including their assessment and the appointment of a lead Member State.

5. The **CTIS - Redaction Guideline** area delivers an overarching guideline for the redaction of documents such as inspection reports and clinical study reports, which is being prepared taking into account alignment with the Agency's Policy 0070.

6. The **CTIS Amend Publication Process** area delivers an SOP defining the process to remove data from the public domain and push forward for publication in case of overriding public interest.

7. The **CTIS Related Documents** area focuses on the delivery of the Clinical Trial Application (CTA), (adding Member State Concerned application and Substantial Modification) and notification forms, which provide information on the data fields and documents that sponsors need to complete, as applicable, in the context of clinical trials applications and notifications to be submitted to CTIS. It also includes other relevant documents which better clarify the CTIS role permissions in line with the business processes and the notices and alerts per role.

8. The **Member States Preparedness** area intends to provide support to Member States in the designs of their Member State organisation model with the identification of the organisations that are going to use CTIS. This includes the identification of the business processes in which each organisation will be involved and the groups of users per organisation that will be assigned with CTIS roles. It also addresses the interaction among organisations for the workload distribution and the testing of their model in the training environment for further refinements in preparation for go-live.

3.3. Cooperation in safety assessment

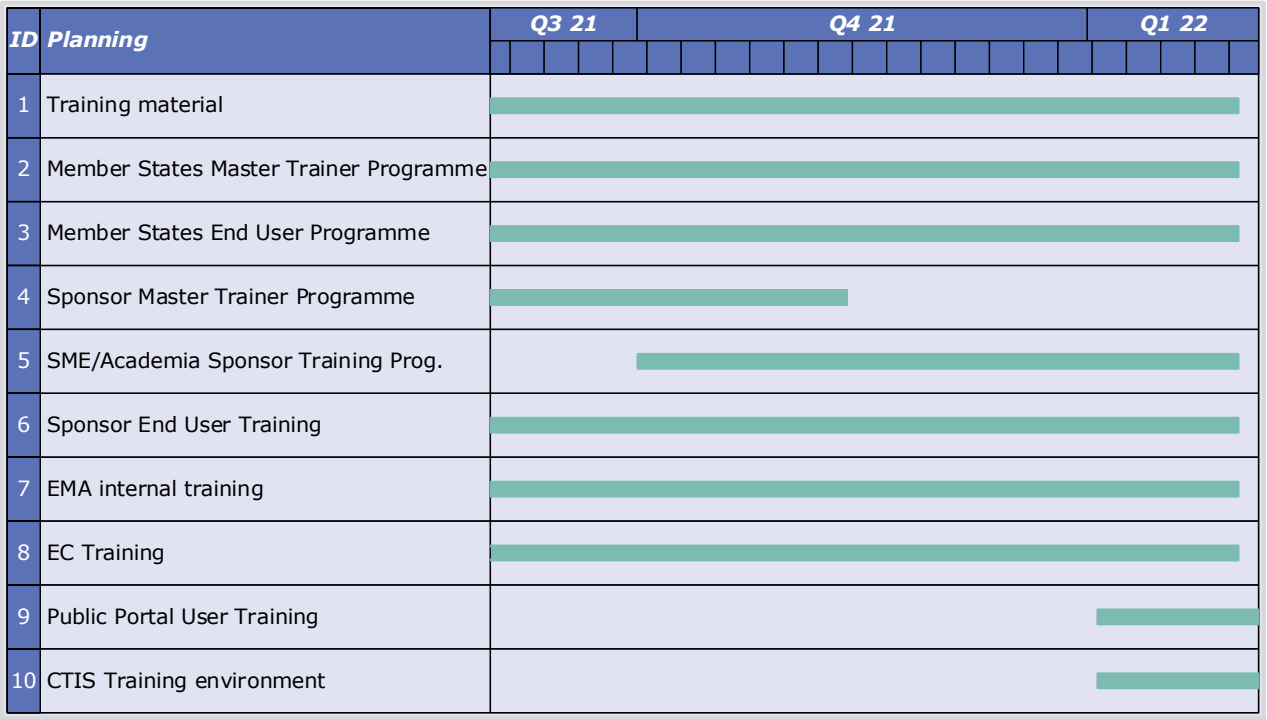
The objective is defining business requirements in relation to the Commission Implementing Regulation on setting out the rules and procedures for Member States cooperation on safety assessment in clinical trials by developing the business process and workflow of safety data, the prioritisation of requirements for go-live and the development of proposals for simple, pragmatic solutions to meet Member States' needs to fulfil their legal obligations.

3.4. CTIS Change Management Activities

This area focuses on training, communication and engagement areas in support of future CTIS users and stakeholders in preparation for go-live and operation of CTIS.

3.4.1. Delivery of Training

This area focuses on training planning and delivery based on an agile methodology, the activity type and target group. The underlying principles of training are strong online presence of a wide variety of training materials and a train-the-trainers approach, complemented with training events for end users. A phased approach to the training of audiences is applied, starting with sponsor and MS users to facilitate organisational preparedness in these large communities.



1. The **Training Material** area focuses on the delivery of materials on how to use the CTIS. Further information is available at the dedicated Clinical trials information system: training and support.

2. The **Member States Master Trainer Programme** area is based on strong presence of a variety of online materials for self-study coupled with a train-the-trainers approach and end user training events organised by Master Trainers at national level within their organisations. MS Master Trainers have been nominated for all Member States and EEA countries and are participating actively in the programme. The process includes selection of training modules, preparation of sessions, presentations, surveys, demos and answers to predefined questions, analysis and reporting of Master Trainer feedback on satisfaction, confidence and learning.

3. The **Member States End User Programme** area is focusing on supporting Member States and Master Trainers within their organisations to deliver CTIS training. In addition to the Master Trainers programme, specialised experts from Member States are trained prior to go-live to support their Master Trainers in modules on CTIS functionalities for inspection records in the supervision of a clinical trial and assessment of an annual safety report. A training on the CTIS sponsor workspace to enable support to clinical trial sponsors at national level will also be provided to Member States staff. CTIS authority workspace training will be offered more widely by EMA after go-live to complement the trainings organised by Member States Master Trainers by use of agreed user personas linked to organisation models and organisation types (national Competent Authorities/Ethics Committee).

4. The **Sponsor Master Trainer Programme** area is targeted at the sponsor community with a strong presence of a variety of online materials for self-study coupled with a train-the-trainers approach for larger organisations. The sponsor Master Trainer programme is well suited for large companies/organisations and their users that are likely to use CTIS on a daily basis and frequently for multiple trials. The sponsor Master Trainers will organise training for their end users within their organisations.

5. The **Small and Medium-Sized Enterprises (SMEs)/Academia Sponsor Training Programme** area addresses specific needs of sponsors representing SME/academia that are likely to represent small organisations/networks with single/a few CTIS users who operate CTIS on a less frequent basis. Therefore, materials and events will be tailored to their needs. Trainings are organised in liaison with their networks and EU level associations to ensure efficient scoping based on their needs. Training organised for sponsors in other streams may also be suitable for SME/academia.

6. The **Sponsor End User Training** area is focusing on supporting sponsor end user training, which is initially the responsibility of CTIS sponsor Master Trainers within those organisations having a CTIS Master Trainer. The strong presence of a variety of online materials for self-study serves end user training, however where additional sponsor end user training is organised by EMA it is based on agreed CTIS user personas, linked to organisation models (organisation-/trial-centric) and organisation types (SME/academia; large organisations).

7. The **EMA Internal Training** area is designed to provide dedicated training to EMA staff responsible to support the operation and administration of CTIS.

8. The **European Commission Training** area is delivering dedicated training with focus on Union control functionalities pertinent to the European Commission, making use of the training module material.

9. **Public Portal User Training** aims to provide dedicated and reusable training to key sub-groups such as researchers, health care professionals, patient organisations, once CTIS starts to become populated with data. This training is largely based on online materials and some events may be organised after go-live once CTIS starts to become populated with data.

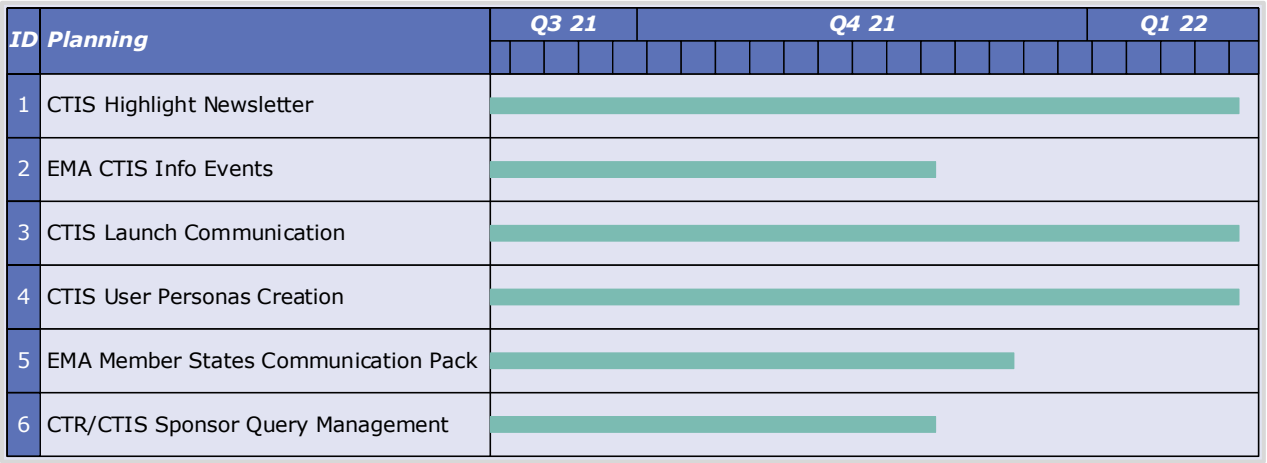
10. **CTIS Training Environment**: a dedicated training environment will be made available for use by Member States and sponsors. A phased rollout schedule and controlled access based on needs and

the condition of prior training will be applied. Access will first be provided to Master Trainers enabling them to train users within their organisations. The roll out is foreseen first for Member State Master Trainers mid October 2021, followed by providing access to Sponsor Master Trainers from mid November 2021 and thereafter additional Member States and sponsor users in subsequent batches.

3.4.2. Communication Planning

This area focuses on communication activities in support of user and organisation readiness and is based on stages of readiness: awareness, understanding, preparedness, adoption and refresh. There are several communication channels. At the centre is the CTIS Highlights Newsletter that will be disseminated and capitalised upon through other channels including e.g. social media, meetings, email distributions, events/meetings, conferences, and EMA intranet.

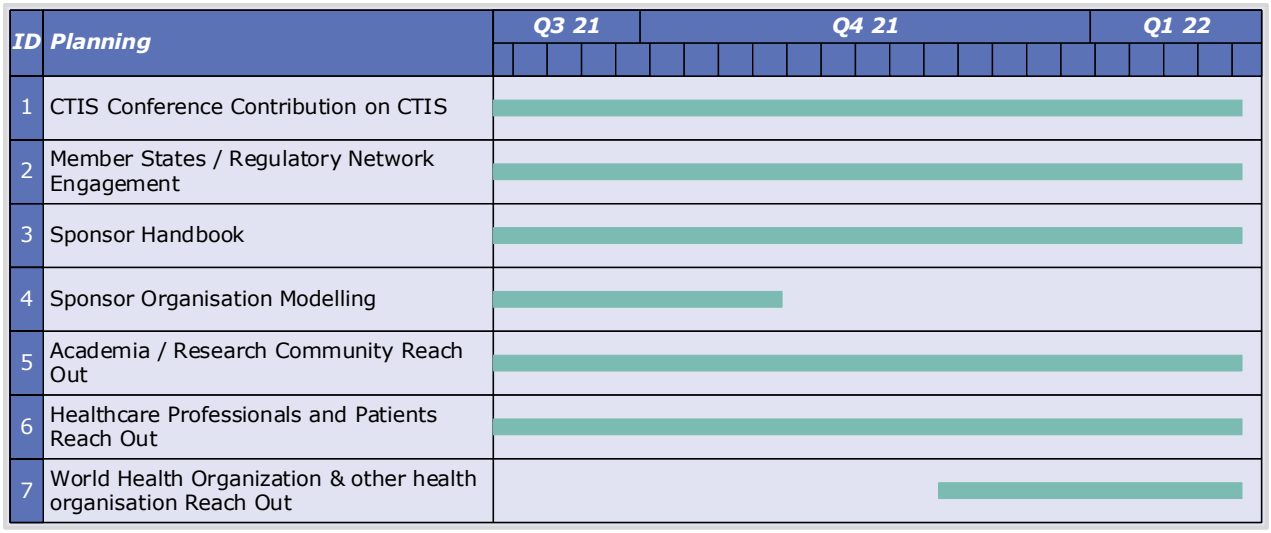
General messages on benefits of CTIS as well as key messages for each readiness phase will be generated and tailored to the different stakeholder groups: management bodies, MS (NCA, ethics committees), sponsors (industry, SME, academia), the European Commission, EMA, the public and key subgroups e.g. healthcare professionals, researchers, patients and the general public.



1. The **CTIS Highlight Newsletter** area focuses on regularly providing CTIS stakeholders with news, views and interviews for the CTIS.
2. The **EMA CTIS Info Events** area is dedicated to the organisation of Information events to facilitate sponsor organisation preparedness.
3. The **CTIS Launch Communication** area is designed to develop a communication strategy and deliver key messages to stakeholders in the context of the go-live of CTIS.
4. The **CTIS User Personas Creation** area is developing a visual model to represent different stakeholder groups, which provides insights into the different user groups and explain more about their preferences of learning, communications, needs and frustrations. The user personas will be used to tailor further training and communication activities to the needs of each user group, help in mapping user roles in CTIS to the end-user groups working within Member State and Sponsor organisations and enhance storytelling techniques by bringing users to life in training and communication materials.
5. The **EMA MS Communication Pack** area is developing communication material in support of MSs for national use in communication about CTIS to the public.

6. **CTR/CTIS Sponsor Query Management** area is focusing on developing an harmonised and efficient query management process to ensure consistent answers across the European Medicines Regulatory Network to any queries in relation to the Clinical Trials Regulation ((EU) No 536/2014) and CTIS.

3.4.3. CTIS Engagement



1. The **Conference contributions on CTIS** area is dedicated to providing updates on the CTIS go-live planning including speaker and content coordination for external events.

2. The **Member States/regulatory network engagement** area focuses on the Member States outreach, collaboration and support, taking into account engagement of Member States experts in training production as validating experts and establishing a Member States Master Trainers network (see above), Member States Mentors network that is intended to provide Member State-to-Member State support for Master Trainers and a Member States training expert panel to support the revision of the training materials and to provide a networking ground for those Member States experts engaged in providing or supporting CTIS training.

3. The **Sponsor Handbook** area delivers the EMA CTIS Sponsor Handbook ("Handbook") for clinical trial sponsors representing pharmaceutical industry, SME, academia, research organisations and other clinical trial sponsor organisations providing information needed for the use of CTIS. The handbook has been developed by EMA in collaboration with representatives of sponsor stakeholders and will be revised as more information becomes available or CTIS functionalities are updated.

4. The **Sponsor Organisation Modelling** area is dedicated to facilitating the engagement, collaboration with and outreach to sponsors and address their specific information needs concerning CTIS. The models are developed in collaboration with representatives of sponsor stakeholders and will be used also for training purposes.

5. The **Academia/Research Community** area focuses on facilitating the engagement, collaboration with and outreach to academia and the research community to address their specific information needs concerning CTIS.

6. **Healthcare Professionals and Patients** area focuses on facilitating the engagement, collaboration and outreach with the healthcare professionals and patients community and address their specific information needs concerning CTIS.

7. **WHO and Other Health Organisations** area focuses on facilitating the engagement, collaboration with and outreach to World Health Organization (WHO) and other Healthcare Organisations and address their specific information needs concerning CTIS.