Linking TMF and RIM for Submissions under EU-CTR

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Meet the Speaker

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Title: Systems Excellence Project Leader

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25+ years in the industry with various roles in

- Clinical quality assurance
- Clinical project management
- Process Excellence

I have led implementation of Bayer's first eTMF solution and implementation of EU-CTR at Bayer. Currently I'm co-leading the EU-CTR Focus team ensuring process optimization and smooth adaptation to changes in CTIS and requirements, managing introduction of ICH E6 R3, and leading an initiative for a holistic cross-functional TMF approach.

I'm actively supporting CDISC TMF RM and currently co-leading Workstream 3 of the Risk Initiative and being member of the V4 Triage Committee

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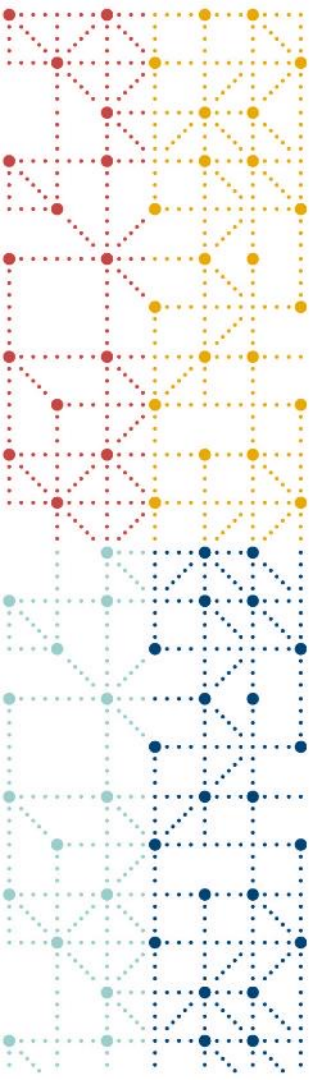
Agenda

1. Introduction
2. Challenges with EU-CTR submissions
3. Compilation of packages in the TMF
4. Management of the submission packages in RIM
5. Linking RIM and TMF to promote efficiency



Introduction

Introduction

Key aspects of EU-CTR

1. Harmonization and Simplification
   Single set of rules across all EU member states
   Single EU submission of clinical trial applications and approval via single Clinical Trial Information System (CTIS) covering health authority and ethics approval

2. Transparency and Public access
   Publication of detailed information about clinical trials, including trial protocols and summaries of results through CTIS

Introduction

Good To know

- Use of CTIS is compulsory for all submissions
- CTIS provides pertinent information to regulatory bodies, ethics committees, and the public.
- CTA packages for studies involving multiple countries or sites are extensive and require considerable coordination efforts.
- There are strict maximum timelines for the EU CTR CTA assessment process.
- The approval process consists of two steps: a decision on Part I is coordinated and communicated by the Reporting Member State, and a unified decision and communication for Part II assessment for each Member State concerned.
- CTIS does not allow parallel submission of substantial modifications for a trial which can be a significant limitation for the operational conduct of a global study

Introduction

Content of a CTA (High level)

- Part I (combined scientific assessment)
  - Protocol
  - Product related information
  - Regulatory information
- Part II (individual MSC assessment/ ethical review)
  - Country specific information
  - ICF and recruitment material
  - Site and investigator information

Submission Process

- Submission planning
- Package preparation
- Package finalization
- Submission
- RFI and response to RFI
- Approval and tracking

Modifications throughout the study follow the same process

Challenges with EU-CTR submissions

Challenges with EU-CTR submissions

Complexity of the CTA submission packages

Dimensions of the packages	Origin of the records	Structured data
• For an initial Clinical Trial Application (CTA) under the EU Clinical Trials Regulation (EU-CTR) for a study with multiple countries and sites the number of documents required can be substantial	• Records are created/ collected by various functions, can be internal or external, and hosted in a number of systems	• Coordination of collection from different functions, alignment with information in the records, must be readily available

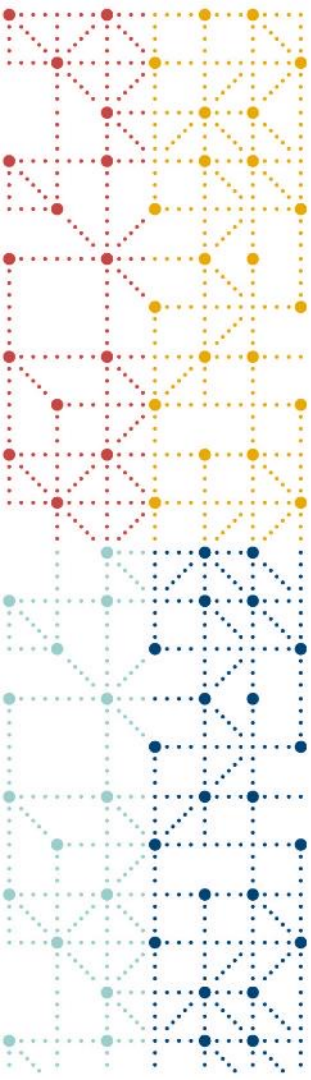
Control of the packages is key for successful CTA application

Challenges with EU-CTR submissions/ CTIS

Follow up on submissions

Need for regular monitoring of the portal in order not to miss messages as CTIS does not send eMail notifications

Regular notifications on study events



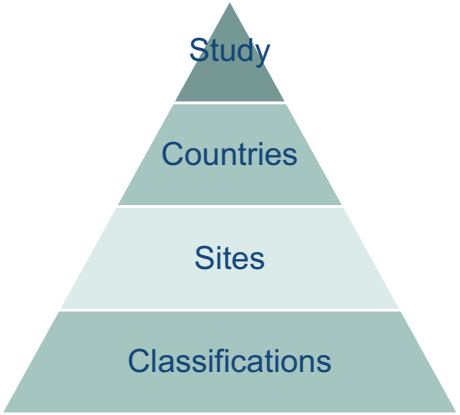
First approach

Compilation of packages in the TMF

Compilation of submission content in the TMF system

System set up

Data structure of records by



Package compilation

Definition of Milestone expected documents lists (EDL) for each planned submission on study level and per country

Download of completed milestone packages for upload to CTIS

Tracking of the completed packages and control of CTIS uploading via working table of content (wToC) reflecting the CTIS structure and nomenclature

Compilation of submission content in the TMF system

Challenges

- Data structure of the packages not the same as the CTIS structure
- Naming conventions not matching CTIS requirements
- Maintenance of the wToC for control of the submission
- Need to upload records to the TMF which are usually not filed in TMF
- Uploading of packages from CROs or external partners

Changed approach

Management of EU-CTR submissions in RIM

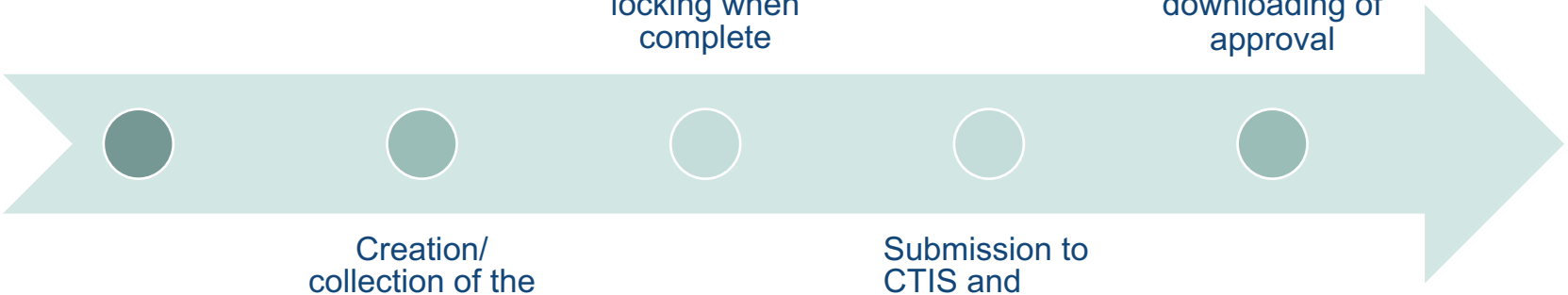
Introduction of the Regulatory Information Management System (RIM) to control CTIS submissions

System set up

- Data structure:
  - Product family -> study -> EU CTR (all countries) -> submission type
- Content Plan (CP) template per submission type
  - Covering Part I and Part II records for all countries
  - Reflecting CTIS structure
  - Records from associated system libraries can be matched with the CP
  - CTIS nomenclature can be applied to the records
- CP structure needs to be refined to the match the planned submission

Introduction of the Regulatory Information Management System (RIM) to control CTIS submissions

Processs



Three pilot studies demonstrated the feasibility of the process before broader roll-out

Advantages of the process utilizing the RIM Content Plan

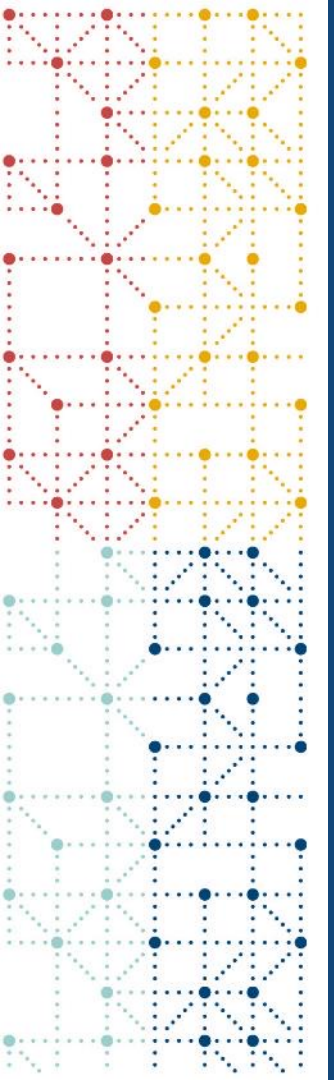
Reduced effort for uploading of records

- Records in the RIM library can be directly matched with the content plan (CP)
- Automated crosslinking of TMF records for EU-CTR submissions for matching with the CP
- Records in TMF (mainly Part II documents)can stay in the TMF

Better overview of package preparation in the content plan than in the wToC

Simplified tracking of submission and communication through CTIS

Meanwhile rolled out to all studies



Linking RIM and TMF to promote efficiency

Linking of TMF records to RIM

Options for Linking

- Linking for transfer from TMF into a RIM library
  - Pro: packages in the RIM system reflecting what was submitted
  - Con: duplication of records, separate tracking of changes, need for alignment
- Cross-linking connecting the record in the TMF to RIM
  - Pro: changes to the record in TMF will also apply in the RIM system
  - Con: recording of the package that has been submitted is a separte step

=> We decided for cross-linking and keeping the connection to the record in the source system
To enhance efficacy automation was built to cross-link documents that are used for submission as a standard in addition to the manual creation of cross-links between 2 vaults

Cross-linking of records from RIM to TMF

Work in progress

Cross-linking of records from RIM to TMF

- Product related records, records created for the submission in the RIM …
- Records downloaded from CTIS (e.g. approvals)

These records are being cross-linked to the respective classifications in the TMF if they are needed for downstream workflows in the TMF

Depending on need, only the latest version of a record will be visible in the TMF or all versions which are created in the course of the study

Thank You!