EU CTR - Regulatory or EC/IRB submissions – how to file?

Presented by Martina Duevel, Systems Excellence Project Leader, Bayer

Meet the Speaker

Martina Duevel

Title: Systems Excellence Project Leader

Organization: Bayer Pharma R&D

Almost 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 most recently implementation of EU-CTR at Bayer.

I'm actively supporting CDISC TMF RM and currently co-leading Workstream 3 of the Risk Initiative.

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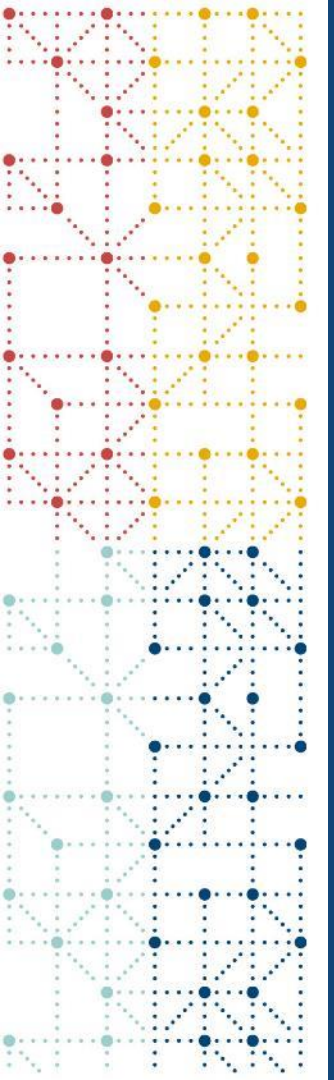
- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

- *The author(s) have no real or apparent conflicts of interest to report.*

Agenda

1. Introduction
2. EU CTR Specifics
3. Impact of EU CTR on TMF Filing
4. Ethical Review under EU CTR and Filing of CTIS Records



Introduction

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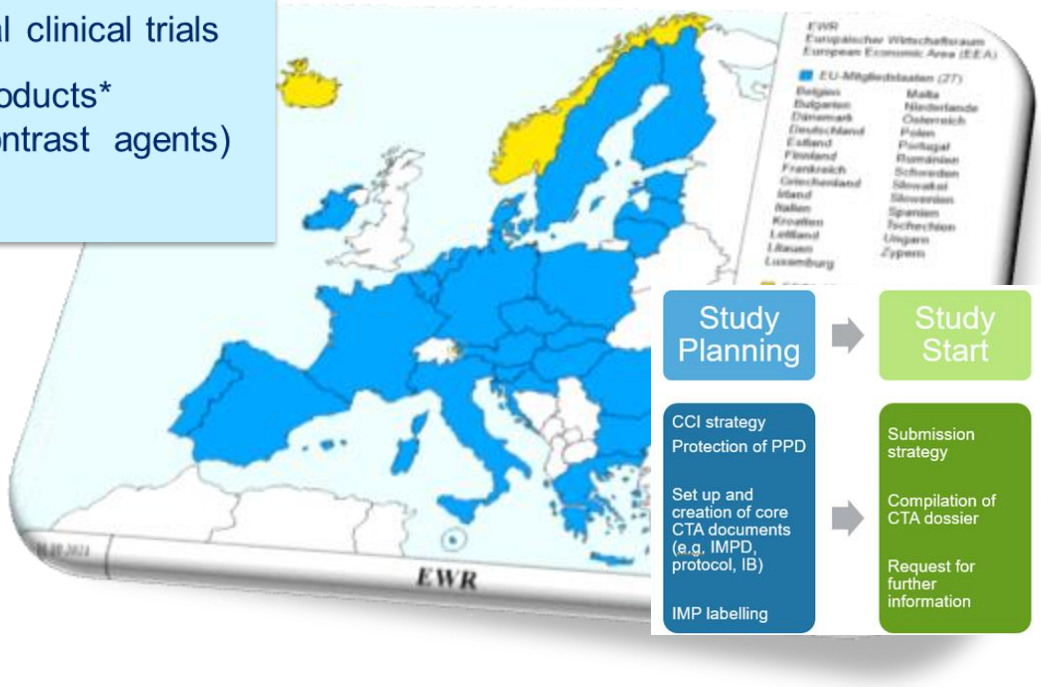
European Clinical Trials Regulation (EU CTR)

Applies to

- Interventional clinical trials
- Medicinal products* (including contrast agents)



Study Planning	Study Start	Ongoing Study	End of Study
CCI strategy Protection of PPD Set up and creation of core CTA documents (e.g. IMPD, protocol, IB) IMP labelling	Submission strategy Compilation of CTA dossier Request for further information	Submission of changes Event notifications Safety notifications Serious Breach notifications	End of trial notification(s) CSR Lay Summary CSR (after marketing authorization

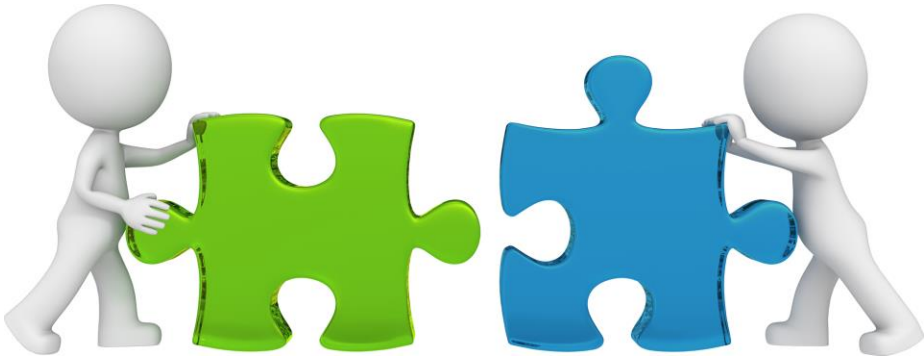
Introduction

EU Vision for the Future

Introduction

EU regulation 536/2014 was adopted in 2014

Implementation was bound to roll-out of Clinical Trials Information System (CTIS) on 31 Jan 2022



CTIS is the single tool for interaction between sponsors and member states

EU CTR Specifics

CTA Documentation

Part I (combined scientific assessment)		Part II (individual MSC assessment)
non-core Part I*	core Part I*	Part II*
cover letter	protocol	ICF country version and ICF procedure
proof of payment	IB	insurance
scientific advice summary	IMPD-Q	investigator CV
PIP opinion	IMPD-S and E	financial arrangements
IMP supportive docs (e.g. MIA, QP declaration)	SmPC	suitability of sites and investigators
IMP label	sIMPD-Q	recruitment material
DMC charter	AxMP-Q	patient material

* Not an exhaustive document list

Event Reporting

Regular study events (CTIS)

- Start of recruitment notification – First site ready to enroll (per MSC)
- Start of trial notification - FPFV (per MSC)
- End of recruitment notification - LPFV (per MSC)
- End of trial notification – e.g. LPLV (per MSC, per EU, per study)
- Anticipated date of summary results – e.g. planned CSR approved (per study)

CTMS data points

Ad-hoc study events (CTIS)

- Temporary halt notification recruitment and/or treatment (per MSC, per study)
- Restart of recruitment notification (per MSC)
- Restart of trial notification (per MSC)
- Early termination (per MSC, per study)
- Unexpected event notification (per MSC, per study)

Data points manually provided

Change in EMA Disclosure Rules for CTIS

Original transparency rules implemented with CTIS

- Almost all documents submitted through CTIS will be published
- Deferral of publishing is possible
  - Commercial confidential information (CCI) and Protected personal data (PPD) need to be protected by
    - Deferral and or
    - Redaction of PPD and CCI

  =>Two versions – "for publication" and "not for-publication" needed for many documents

New transparency rules communicated by EMA

- Only limited key data and documents will be published
- Deferral of publishing not possible
  - Redact all CCI and PPD from documents which will be published per revised rules. Documents which will be published are
    - Part 1: protocol, protocol synopsis, patient facing materials , SmPC
    - Part 2: PIIC, recruitment arrangements including procedures for inclusion and copy of advertising materials

Appendix on disclosure rules

Impact of EU CTR on TMF Filing

Impact of EU CTR on TMF Filing

Trial Master File Reference Model (TMF RM) group workshop in April 2022

- Document types in trials under EU CTR are similar
- The ‘new’ document types could be mapped to the TMF Reference Artifacts, with some new sub-artifacts
- Details can be found in the TMF Reference Model White Paper on the Impact of the EU CTR on TMF Content

Ethical Review under EU CTR and Filing of CTIS Documents

Ethical Review under EU CTR

Article 4

Prior authorisation

A clinical trial shall be subject to scientific and ethical review and shall be authorised in accordance with this Regulation.

The ethical review shall be performed by an ethics committee in accordance with the law of the Member State concerned. The review by the ethics committee may encompass aspects addressed in Part I of the assessment report for the authorisation of a clinical trial as referred to in Article 6 and in Part II of that assessment report as referred to in Article 7 as appropriate for each Member State concerned.

Member States shall ensure that the timelines and procedures for the review by the ethics committees are compatible with the timelines and procedures set out in this Regulation for the assessment of the application for authorisation of a clinical trial.

- Ethical review is required for trial authorisation
- Ethical review is done in accordance with law of the member states
- Member states organise involvement of the ethics committee and compliant set up

Ethical Review under EU CTR

- ECs Use Part I and Part II documents uploaded to CTIS for their review
- There is no direct communication with the ECs
- Decisions are communicated by the Member states
- Usually, we do not even have background information regarding the ECs involved

>> We do not have specific content that needs to be filed in Zone 04

TMF filing of CTIS Records Related to Ethical Review

TMF reference model is set up for Separate filing of Regulatory and EC/ IRB records in Zones 3 and 4

CTIS does not distinguish between content for regulatory and ethical review

Separate content that needs to be filed in Zone 4 is not available

TMF filing of CTIS documents
Possible strategy

Records that are collected for EU CTR applications (e.g. principal investigator curriculum vitae) can be filed according to the TMF Reference Artifacts

Records that are created specifically for an EU CTR application (e.g. cover letter) and are submitted via CTIS are filed as „Regulatory submission" documents

Records that are received through CTIS are filed either in 3.1.1 „Regulatory submission", in 3.1.2 „Regulatory authority decision" or in "Relevant Communications"

Explanation of the EU CTR process in the TMF plan or a standard file note may help to avoid questions in inspections ad interim

Thank You!

Qustions?