DIA Document & Records Management SIAC

EDM Reference Model Clinical Domain

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Points to Cover

- Clinical Domain
  - In scope: CTD clinical documents
  - Out of scope: Clinical TMF
- Progress to date – the Clinical Domain model
- Rationale for decisions
- Q&A

Reference Model Project – Domain Descriptions

Domain	Description
Administrative Information	
Prescribing Information	
Pharmacovigilance	
Nonclinical	
Clinical	CTD module 5 clinical study reports and supporting documents, plus the clinical overview and summaries from modules 2 and 5
Quality	

Clinical Domain

- Status (Release 1.0)
  - Documents and attributes for the clinical domain
- Next Steps:
  - Clinical Trial Master File

Clinical Domain

- Includes clinical documents and other file types listed in
  - ICH CTD guidance
  - ICH E3 CSR guidance
  - FDA STF specification
- Excludes documents with clinical content in the Administrative Information domain, e.g.
  - Investigator's brochure
  - General investigational plan
  - Annual report
  - CTA

Clinical Domain

- Document types
  - Documents submitted to agencies that are produced during the course of a clinical study
  - Documents and other files collected or created specifically for a clinical study report
    - Includes documents included in CSRs that are also part of the clinical TMF
  - Documents and other files collected or created for specific regulatory submissions

Document Granularity

- Reasonably straightforward guidance for clinical documents
  - Granularity Document – Annex to M4: Organization of the CTD
  - ICH E3 CSR guidance
  - FDA STF specification

Clinical Domain Documents

- Three main categories
  - Clinical overview and summary documents – m2
    - Created for a specific CTD submission
  - ISS and ISE – m5
    - Created for a specific NDA or BLA
  - Clinical study reports and related information – m5
    - Generated at different times during a clinical study
    - Multiple versions of some documents may be used in a study before the study report is final, e.g. protocol

Progress to Date – Current Model

- Spreadsheet includes clinical documents and other files and domain-specific metadata

Group	CTD Section	Artefact Name	Indication	Clinical Study Number	Clinical Study Title	Route of Administration	Study Phase	Clinical Trial Identifier	Type of Control	Site Identifier	Subject Identifier	eCTD STF File Tag Element Valid Value
Clinical summary	2.5	Clinical Overview	M									
Clinical summary	2.7.1	Summary of Biopharmaceutic Studies and Analytical Methods	M									
Clinical summary	2.7.2	Summary of Clinical Pharmacology Studies	M									
Clinical summary	2.7.3	Summary of Clinical Efficacy	M									
Clinical summary	2.7.4	Summary of Clinical Safety	M									
Clinical summary	2.7.5	References	M									
Clinical summary	2.7.6	Synopses of Individual studies	M									
Clinical summary	5.3.5.3	Integrated Summary of Safety	M									M
Clinical summary	5.3.5.3	Integrated Summary of Efficacy	M									M
Clinical study	5.3.x.x	Legacy clinical study report	M	M	M	M	M	M	M			M
Clinical study	2.7.6 / 5.3.x.x	Synopsis	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Report body	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Statistical output	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Full protocol	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Protocol amendment	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Sample CRF	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	List of IECs and IRBs	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Informed consent	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	List and description of investigators and sites	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Signature page	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	List of patients receiving test drug	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Data Monitoring Committee	M	M	M	M	M	M	M			?
Clinical study	5.3.x.x	Data management plan	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Randomization scheme	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Audit certificates report	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Statistical analysis plan	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Interlaboratory standardization methods	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Publications based on study	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Investigator CVs	M	M	M	M	M	M	M	M		M
Clinical study	5.3.x.x	Publication	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Patient data listing	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Discontinued Patients Listing	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Protocol Deviation Listing	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Patients Excluded from Efficacy Analysis Listing	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Demographic Data Listing	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Compliance and/or Drug Concentration Data Listing	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Individual Efficacy Response Data Listing	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Adverse Event Listings	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Individual Laboratory Measurements Listing	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	CRF	M	M	M	M	M	M	M	M	M	M
Clinical study	5.3.x.x	Data tabulation dataset	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Data definitions for data tabulation	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Datasets	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Data listing dataset	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Data definitions for data listing datasets	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Analysis datasets	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Program file for analysis dataset	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Data definition for analysis datasets	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Annotated CRF	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Annotated ECG waveform dataset	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Image files	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Subject profiles	M	M	M	M	M	M	M	M	M	M
Clinical study	5.3.x.x	IND safety report	M	M	M	M	M	M	M			M
Clinical study	5.3.x.x	Individual subject data listing	M	M	M	M	M	M	M			M

Clinical Metadata

- Indication
- Clinical study number
- Route of administration
- Study phase
- Clinical trial identifier
- Type of control
- Site identifier
- Subject identifier
- eCTD file tag element valid value

Clinical Metadata – Indication

- Applies to all clinical documents/files
- A document/file may have more than one indication
- Use pick-list of standard terms for clinical indication
- Healthy subjects as well as disease indications
- Can be more than one value

Clinical Metadata – Clinical Study Number

- Applies only to module 5 clinical study components
- No standard convention – each sponsor has own format
- Can be more than one value

Clinical Metadata – Clinical Study Title

- The actual title of the study
  - A double-blind, placebo-controlled study of the effect of LSD-25 on patients with mild to moderate lack of imagination
- Applies to all documents/components in the study
- Not the file name – 12345clinicalprotocol.doc
- Not the document type – clinical protocol

Clinical Metadata – Route of Administration

- Need to determine if this should be a free text field or a pick-list of standard terms for route of administration
- eCTD STF metadata options (from nonclinical study report)
  - Oral
  - Intravenous
  - Intramuscular
  - Intraperitoneal
  - Subcutaneous
  - Inhalation
  - Topical
  - Other

Clinical Metadata – Study Phase

- Phases I – IV (with a and b if needed)

Clinical Metadata – Clinical Trial Identifier

- EudraCT number
- ClinicalTrials.gov identifier

Clinical Metadata – Type of Control

- Applies only to module 5 clinical study components
- Values
  - Placebo
  - No-treatment-control
  - Dose-response-without-placebo
  - Active-control-without-placebo
  - External-control
  - Other (not eCTD)

Clinical Metadata – Site Identifier

- Sponsor or CRO code for specific clinical trial site
- Applies to CRFs, subject profiles and investigator CVs in m5

Clinical Metadata – Subject identifier

- Sponsor or CRO code for specific subject
- Applies only to CRFs and subject profiles in m5

Next Steps for the Clinical Domain

- Some clinical study components not covered by the ICH E3 guidance or the STF specification
- Excluded the TMF so far except for submission documents – dual context of use for some documents
- TMF may be separate from EDMS
  - Multiple copies?