2026 Europe Interchange

THE FUTURE IS CONNECTED: STANDARDS AND AI POWERING DIGITAL TRANSFORMATION

MILAN, ITALY | MAIN CONFERENCE: 20-21 MAY | TRAININGS & WORKSHOPS: 18, 19, & 22 MAY

TMF Interoperability: The critical importance of standard integrations of Clinical Trial Management Data to promote eTMF Health and completeness

Presented by Jay Smith, Vice President Product, TransPerfect Life Sciences

Speaker

Jay Smith

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- Jay currently leads product and tech at Transperfect, responsible for the Trial Interactive platform. Prior to Transperfect, Jay has led product teams at Medidata, Sparta Systems, and Thomson Reuters. Jay has supervised the creation and management of eTMF, CTMS, EDMS, QMS, RTSM, EDC, LMS, and Site Portal solutions. Further back, Jay has also created and managed products for RIMS and eCTD submission publishing and review.

Agenda

1. The Basic Conundrum
2. Regulatory Drivers
3. Anatomy of the Problem
4. The TMF Ecosystem
5. Pragmatic Solutions
6. TMF Digitalization Roadmap
7. The Case for an Open Standard
8. Best Practice
9. Proof of Concepts
10. Next Steps

“We do not rise to the level of our goals. We fall to the level of our systems.”

or

“Nothing is more permanent than a temporary solution.”

Integration Problems ~= eTMF Problems

WHAT GETS BLAMED

- Quality control processes
- TMF management plans
- Site-level filing discipline
- CRO oversight gaps
- Lack of Inspector-readiness culture

WHAT'S ACTUALLY BROKEN

- Events don't flow from EDC to CTMS to eTMF
- Metadata schemas don't align across systems
- Integrations break when vendors update
- Documents from must be indexed again and again
- Standards exist in pockets, not across the ecosystem

Four regulations sponsors must operate under

ICH E6(R3)

Good Clinical Practice

Adopted 6 Jan 2025

EEA effective 23 July 2025

Risk-based quality, real-time investigator oversight, essential records concept

EMA Computerised Systems

EMA/226170/2021

Effective 10 Sept 2023

ALCOA++ formalised

Every system in scope, including integrations between them, must be validated

EU CTR 536/2014

via CTIS

Full force 31 Jan 2025

Single EU/EEA entry point

Sponsors must operate from coherent, machine-readable trial data

EMA 2024 GCP Report

Inspectors' Working Group

335 major/critical findings

Essential documents = #1 category

Current TMF practice is not meeting current expectations

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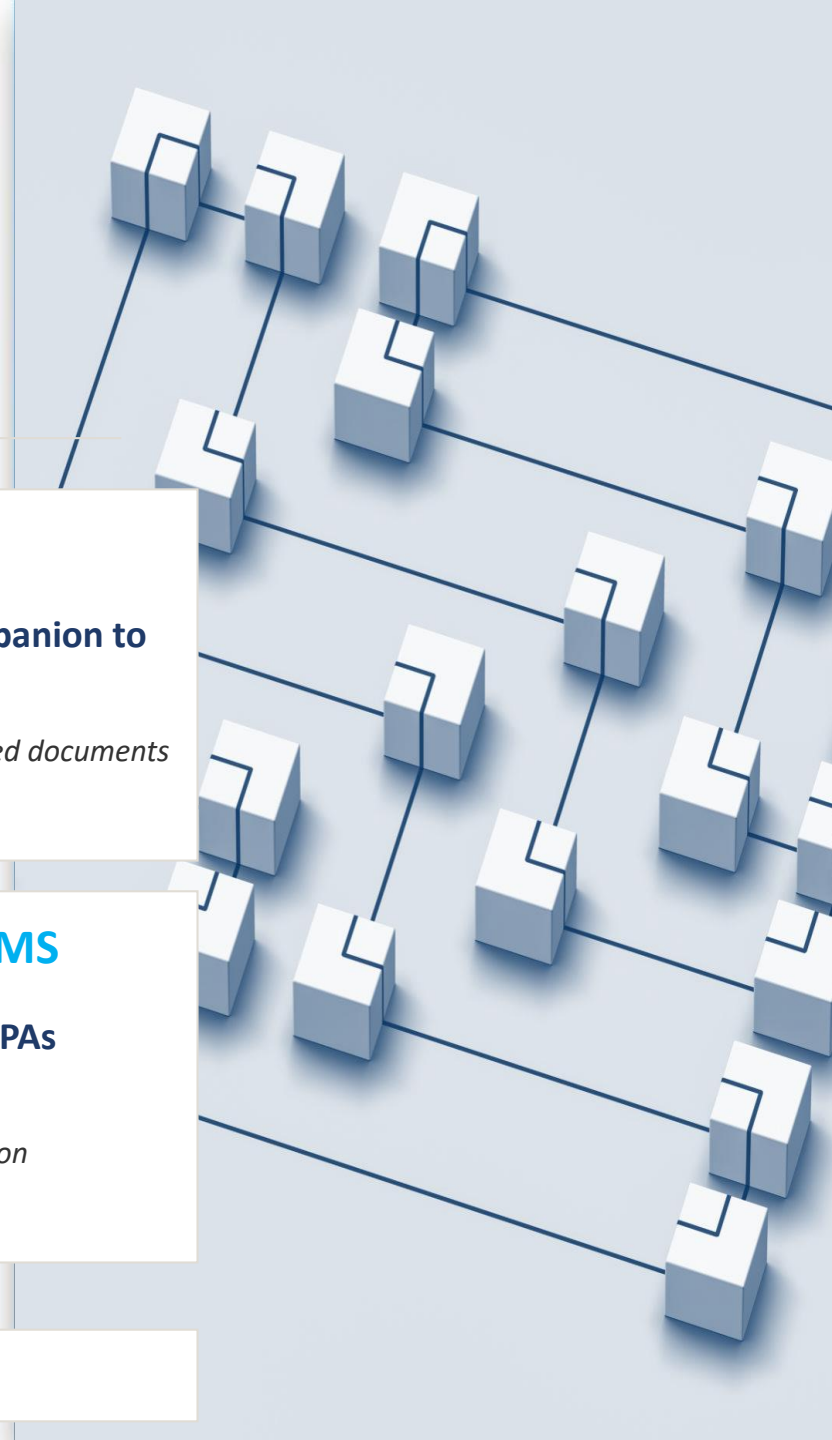
The Digital Clinical Ecosystem



CTMS

Master of trial structure

Studies, sites, milestones, visits

EDC

System of record for subject data

Source for monitoring outputs and queries

IXRS / RTSM

Randomisation & supply

Driving site-level documentation events

eISF

Site-level companion to eTMF

Where many signed documents originate

RIM / Med Writing

Submission and protocol sources

Versions to be archived

Safety / PV

Reportable events

SUSAR notifications and safety letters

LMS / Training

Competency evidence

Certificates, training logs

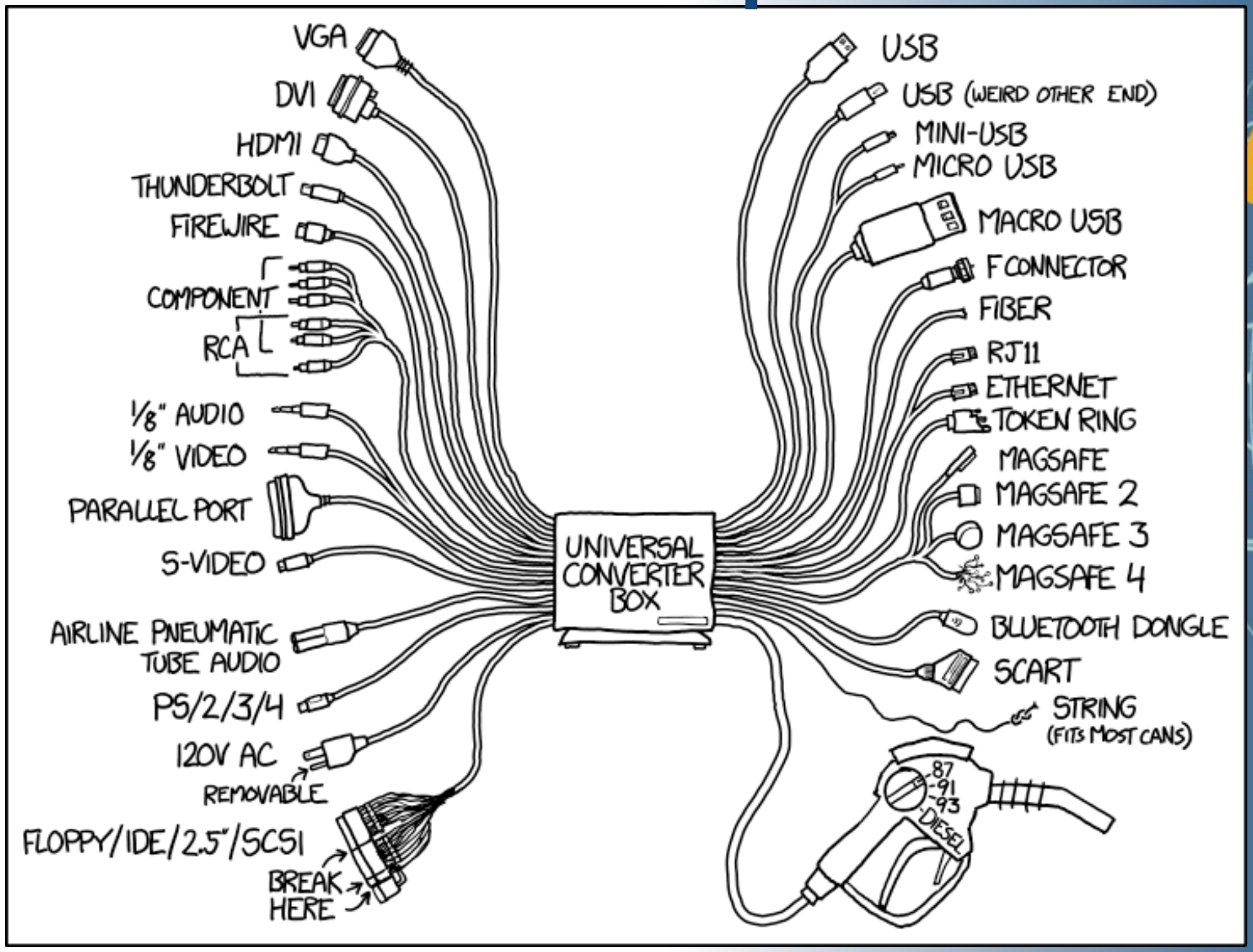
Quality / QMS

Deviations, CAPAs

Audit and inspection documentation

Trial Master File

Current Situation: Hub and Spoke

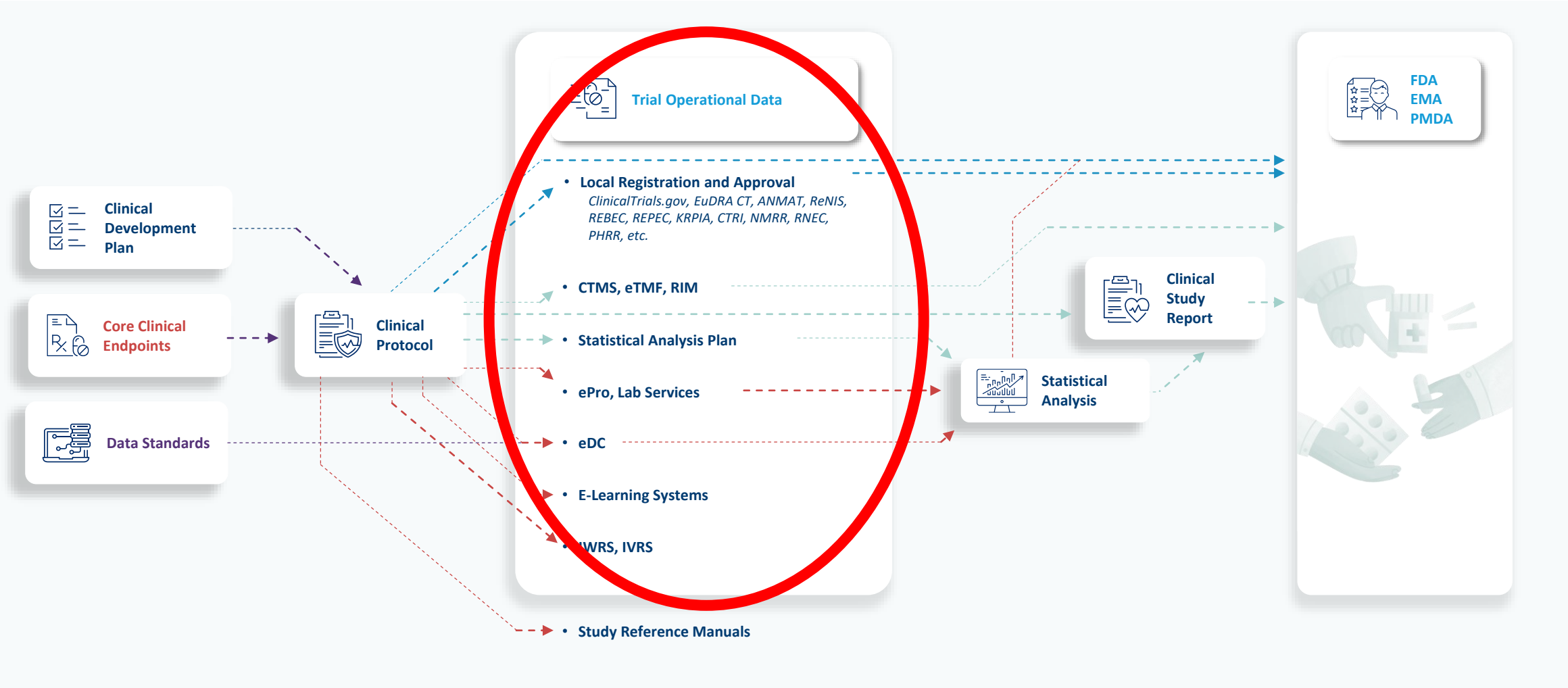


Why current integrations keep failing

- Vendor-mediated point-to-point
- Legacy interface paradigms
- Implementation timeframes
- Constant software updates, no contract testing
- Data ownership <> data access
- No legitimate standard
- Uncooperative Platforms

"Essential documents represent the single largest category of major and critical findings." - EMA GCP Inspectors' Working Group, 2024 Annual Report

Clinical Trial Information Flow



1572 Form	Electronic form filled out that provides investigator, site, contact, and organization data to CTMS and eTMF
Delegation Log	Written form that tracks site personnel changes with their delegations, used for access, training, and documentation requirements.
SUSAR	AE/SAE forms with fielded data is extracted into document metadata, notification workflow is initiated to capture acknowledgements from investigators and agencies are notified
Informed Consent	eConsent process is initiated that activates a patient account, provides remote telephony or virtual meeting to ensure comprehension and compliance, and captures an eSignature (eIC)
Training Certificate & Evidence	Training Certificates and Logs are outputs of the Site Training program, Investigator Meetings, eLearning, coursework, and compliance activities. These must be stored in the eTMF, recorded in the CTMS, and carefully tracked.
Clinical Trial Agreement	Can be generated from the budgeting system and reviewed online in a collaboration space, or directly from a contracting solution
Feasibility Questionnaire	Fully-electronic feasibility questionnaires can provide consistent data from sites that may be captured and re-used to assist in planning and future decision-making
eCRF	EDC, ePRO, eCOA
Protocol Deviation	Electronic form that can be captured immediately into a workflow in the CTMS
Note to File	A Quality Management workflow, with QA signatories and approvers
Subject Enrollment Log (Redact)	Can be generated from the EDC and generated (if necessary) to an electronic document as evidence
Site Monitoring Log	Can be generated from the EDC and generated (if necessary) to an electronic document as evidence

Digitization of Trial Documents into Fully Digital Business Workflows

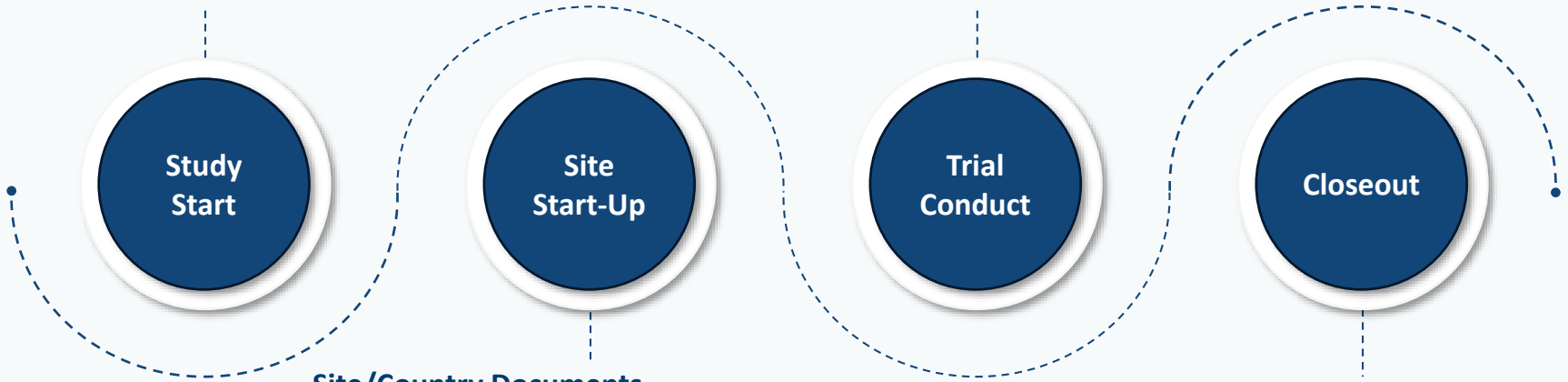
EDC/CTMS → eTMF Integration Points

Protocol Creation

- Prepare eTMF with basic information needed to provision the study (IP, protocol #, etc.)
- Trial information - product, protocol number, protocol title, phase, type
- Labs and third-party vendors

Mid-Trial Updates

- New sites indicates new sets of docs against site milestones
- New investigator requires new 1572, CV, etc.
- Monitoring approved visit reports and letters
- Study, country, and site milestones that indicate a new document must be provided (e.g., protocol amendment)



Site/Country Documents

- Country/study status based on TMF milestone completion
- Countries - where the study will be conducted
- Automatic update of clinical sites that will participate and the principal investigators, sub-investigators, and site staff who will participate

Study Milestone Updates

- DB lock and archival milestones and study status that close out and archive the trial in the TMF
- Final regulatory documents archived in the TMF

eTMF Integration Points

- Studies
- Countries
- Sites
- Investigators
- Contacts
- Participants
- Visits
- Milestones
- Safety/PV
- Issues
- Activities
- Organizations
- Events and Milestones
- Documents

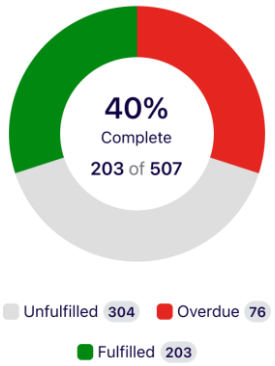
External eTMF Inter-Connects

Business Goals for eTMF:

- eTMF health is timely and contemporaneous
- Completeness and accuracy
- Quality and inspection-ready

Ecosystem Connects:

- Sites, organizations, and contacts
- Regulators, External parties, third parties, and affiliates
- Business arrangements constantly shifting



Clinical Trial Awareness:

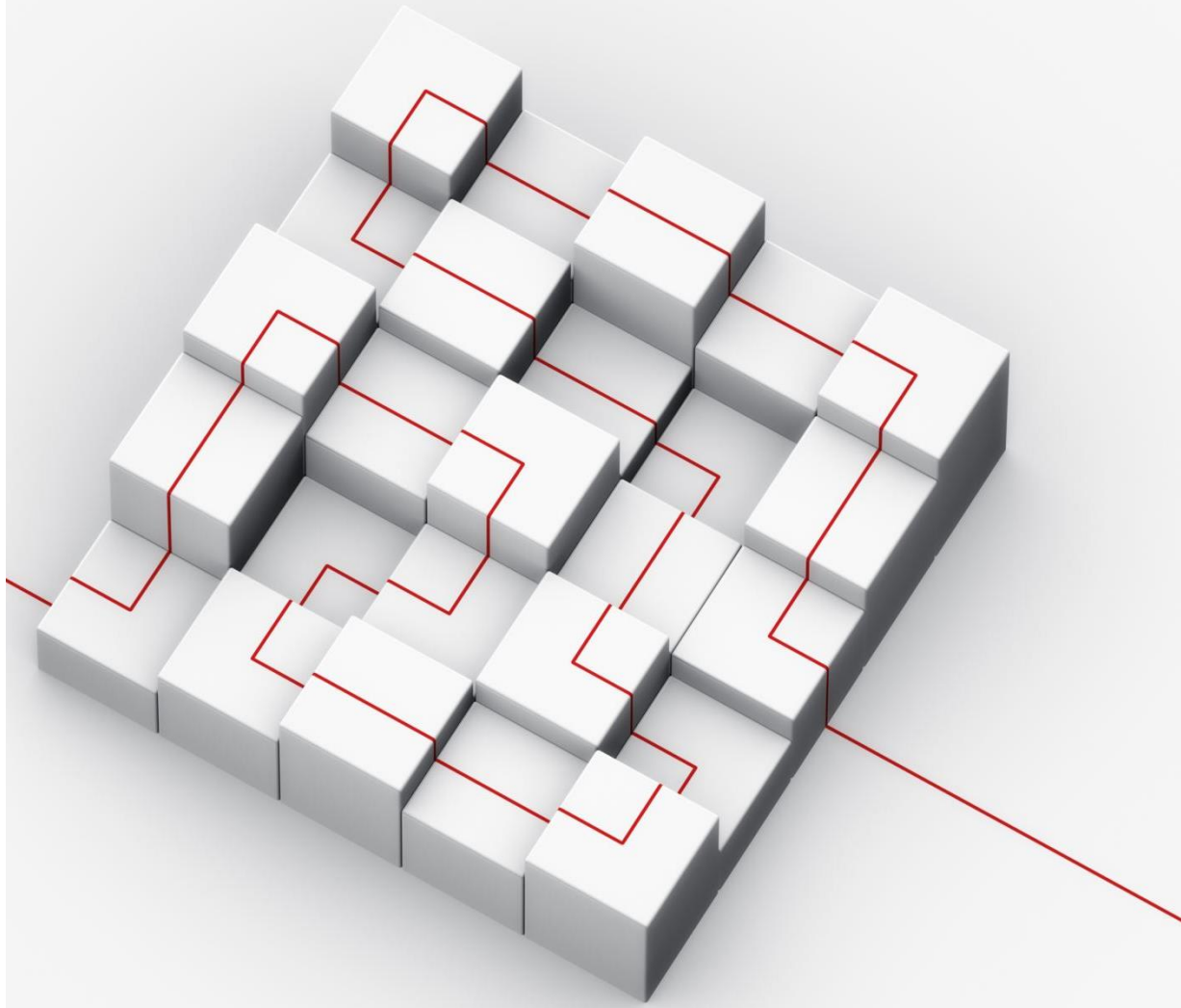
- Data flows exist between EDC, IXRS, RBQM, and CTMS
- eTMF must be “trial aware” of study milestones, visits, events, and status

Document Data Flows:

- Clinical, quality, and RIM document workflows can impact the eTMF
- eTMF should be aware of the data classifications

Pragmatic, Imperfect Solutions

- Vendor-Maintained
- Standards-Based Connections
- Configurable Data Mappings
- Re-usable and Serverless
- Flexible and Adaptable
- Migration-Capable

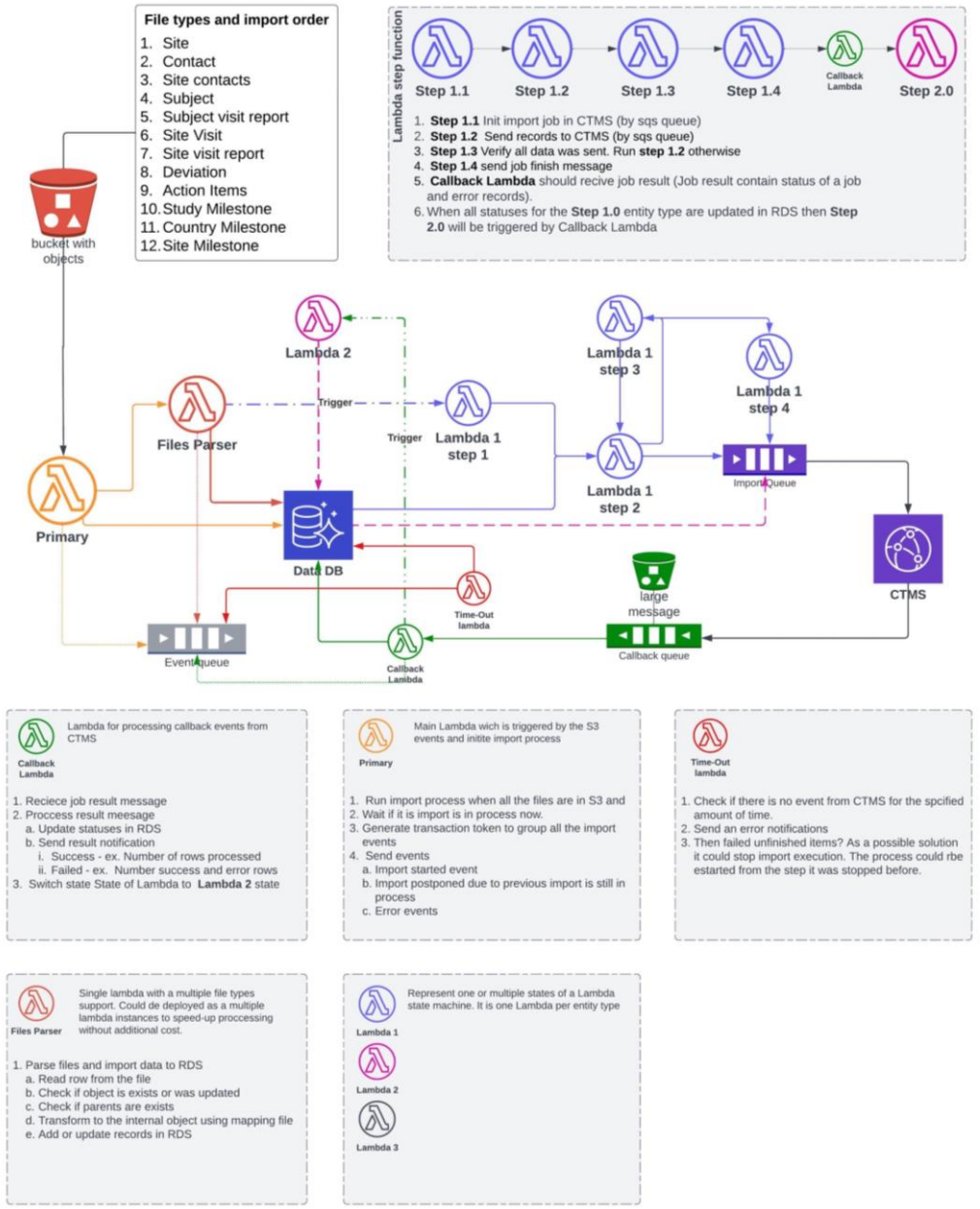


Connector Architecture

Hub and Spoke

MACH (Microservices, API-first, Cloud-native, and Headless) as a standard

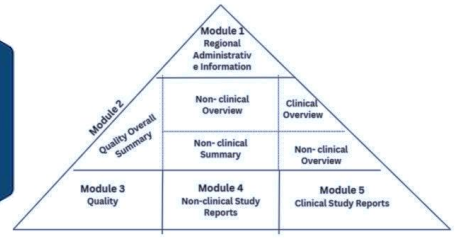
- Each connector has its own mapping and set of instructions for interfacing with the 3rd party vendor
- Connectors can work with an Excel/CSV dropbox import file as well as API interface.
- Connectors are server-less processes that can operate within a secure subnet or VPC between two cloud or on-premise hosting environments.
- Each connector may be configured through a dashboard to ‘come alive’ on some hourly, daily, or weekly interval to synchronize data
- Connectors are verified and validated separately from the core products, allowing simpler maintenance and handling product releases seamlessly without requiring larger validation efforts.
- Connectors also include a status dashboard, logging, audit trails, configurable alerts upon failure states with a support model for consistent maintenance.



Integration Best Practice – A Composable Data Standard

- **Modularity**: Building with Lego blocks
- **Orchestration**: Aligning these blocks for a common goal
- **Discoverability**: Ability to find and utilize these Lego blocks
- **Autonomy**: Independent functionality of each Lego block
- **Composable**: Dynamic adjustment of calls and expected datapoints based on interface discovery, in sync with other components

Lessons Learned from Past Initiatives



ODM (Operational Data Model)

- Highly prescriptive technology approach (XML)
- Completely flexible structure
- Designed for data, not documents
- Focused on metadata and data model
- Focused use cases on subject data (not comprehensive)
- High machine readability (can be parsed easily by any software)
- Allows expansion and extensions
- Poor human readability
- Vendor supported
- Industry adoption is optional and strong

ICH eCTD (Electronic Common Technical Document)

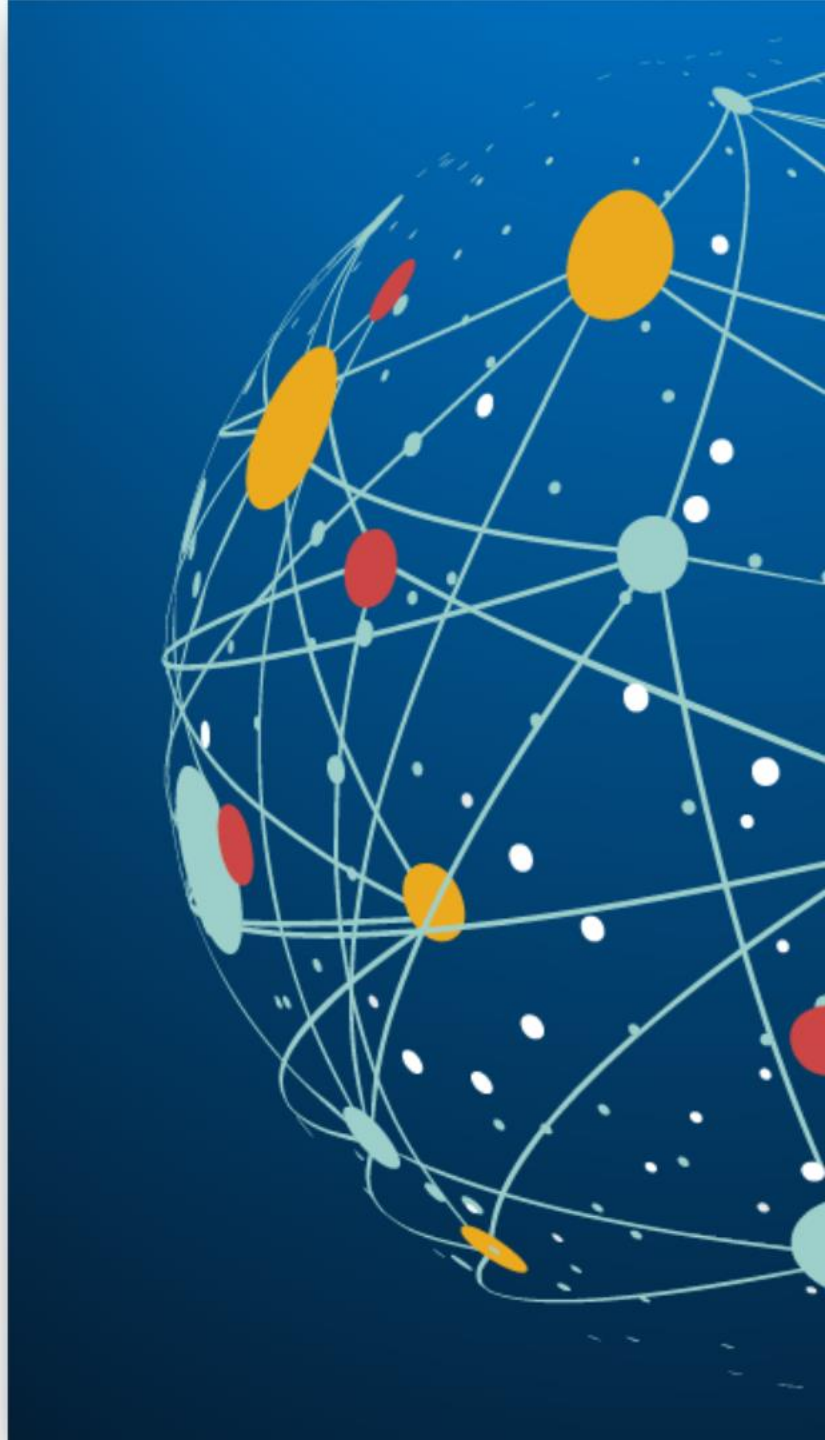
- Highly prescriptive technology approach (XML)
- Highly prescriptive index structure
- Designed for submissions and documents, not data
- Comprehensive use cases to capture all submission types (except med device)
- Poor machine readability (requires specialized software)
- Limited flexibility, not expandable
- Poor human readability
- Agency supported
- Industry adoption is weak but enforced
- **NOTE: eCTD 4.0 is a Composable Standard!**

Clinical Research Interoperability Standards Initiative (CRISI)

- Focus is on operational and management data exchange between core systems (EDC, CTMS, eTMF, IRB/EC, IXRS, Site Portals, and Investigative Sites).
- Focus is on a standard that pragmatically resolves study start timeframe requirements and defines the core data elements required for sharing.
- Focus is on utilizing existing data standards in a way that addresses the business challenge.
- Focus is on an open standard to avoid a hub-and-spoke model or vendor-centric model.
- Focus is on operational data and documents. (Like SMPP or IRC Protocol for SMS Messaging, not iMessage or Signal)

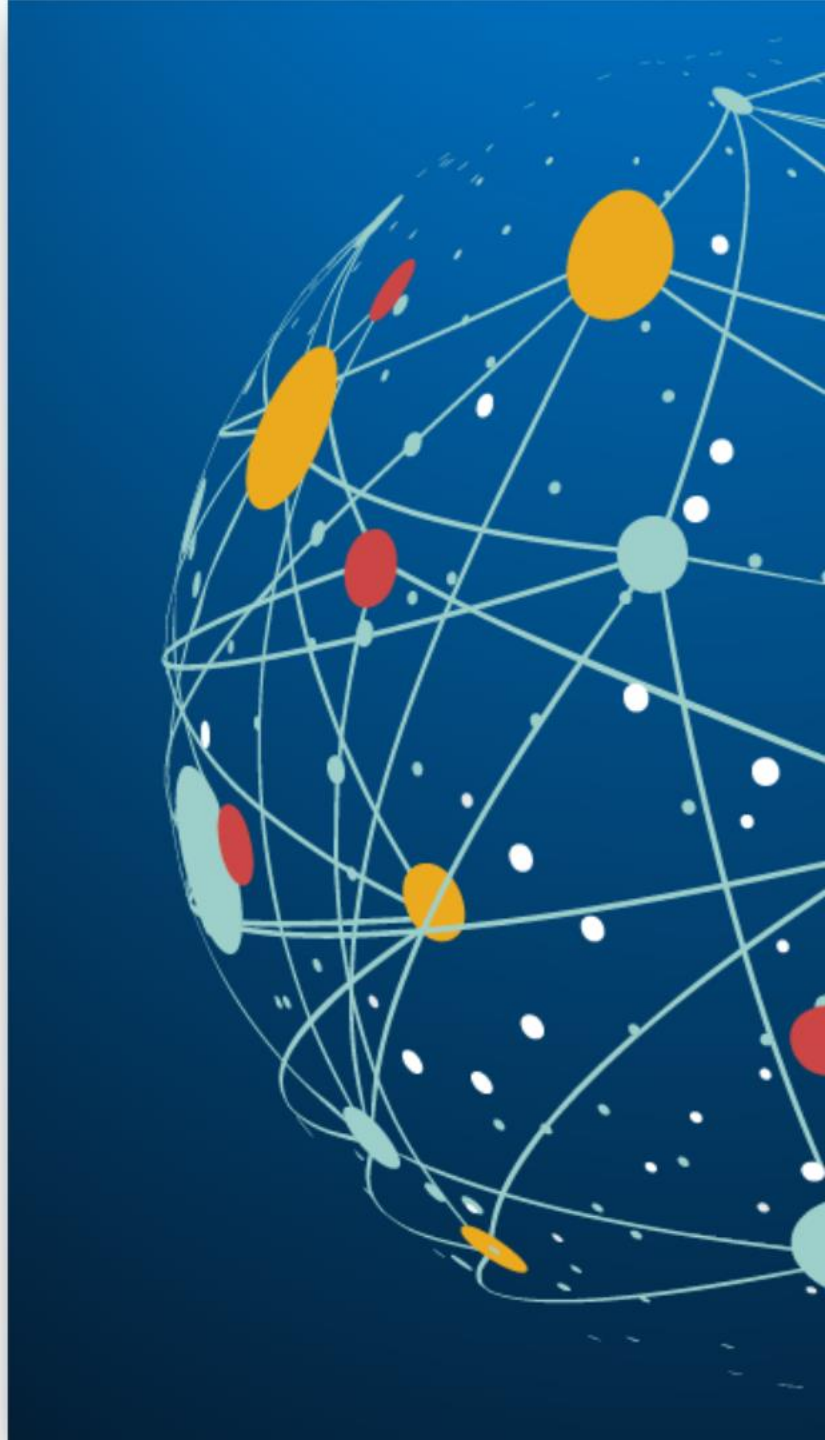
2026 Status:

- API and data model proof of concepts
- Buy-in from Sponsors, CROs, and Sites



CRISI Proof of Concept

- Basis is FHIR
  - Fast Healthcare Interoperability Resources
  - Developed by Health Level Seven (HL7)
- POC Can support
  - Study → ResearchStudy
  - Site → Location
  - Contact → Practitioner
  - Participant → ResearchSubject
  - Clinical Document → DocumentReference
  - Document Metadata → TMF Extension w/ StructureDefinition
  - Audit Trail → AuditEvent



A Fully Interoperable Standard for Migrations and Integrations

4.1.1.1 Study Object (ResearchStudy) JSON Example

```
{
  "resourceType": "ResearchStudy",
  "id": "study-001",
  "identifier": [
    {
      "use": "official",
      "system": "https://clinicaltrials.gov",
      "value": "NCT01234567",
      "type": {
        "coding": [
          {
            "system": "http://terminology.hl7.org
            "code": "CT",
            "display": "Clinical Trial Number"
          }
        ]
      },
      "assigner": {
        "display": "ClinicalTrials.gov"
      }
    }
  ],
  "title": "A Phase III Randomized Study of Drug
  "status": "active",
  "description": "This study aims to evaluate the
hypertension.",
  "primaryPurposeType": {
    "coding": [
      {
        "system": "http://terminology.hl7.org/Cod
        "code": "treatment",
```

4.2.1.1 Trial Document Object (DocumentReference) JSON Example

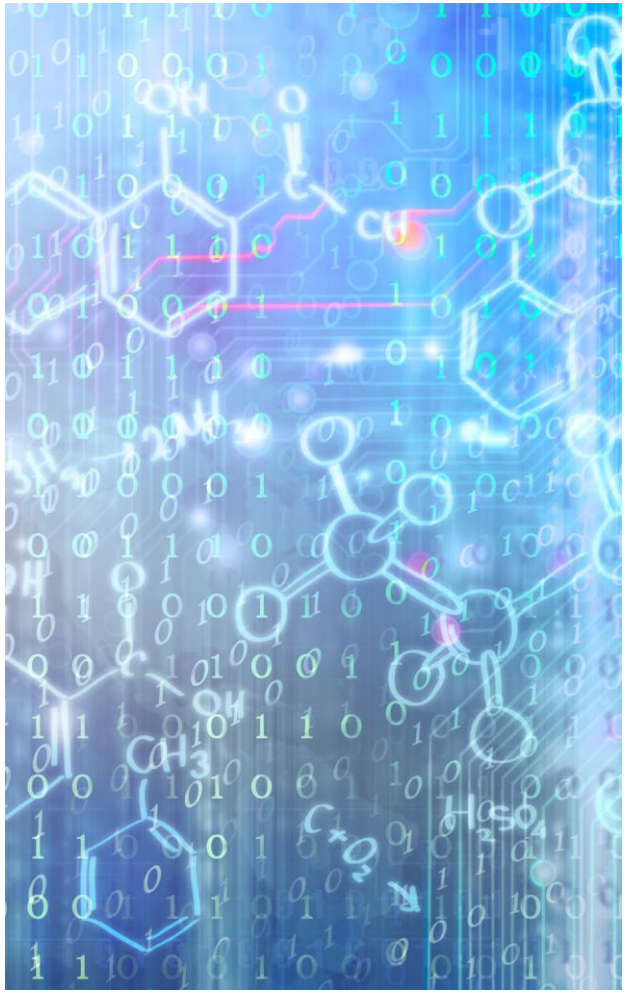
```
{
  "resourceType": "DocumentReference",
  "id": "doc-001",
  "identifier": [
    {
      "use": "official",
      "system": "http://example.org/documents",
      "value": "ICF-123456"
    }
  ],
  "status": "current",
  "type": {
    "coding": [
      {
        "system": "http://loinc.org",
        "code": "34108-1",
        "display": "Informed Consent Form"
      }
    ]
  },
  "description": "Informed Consent Form for Clinical Trial",
  "extension": [
    {
      "url": "http://example.org/fhir/StructureDefinition/tmf-level",
      "valueString": "Site"
    },
    {
      "url": "http://example.org/fhir/StructureDefinition/tmf-zone",
      "valueString": "Central Trial Documents"
    },
```

cdisc

Benefits of a Pure Metadata Approach

Reduced data entry	Across all integrated systems. Improved inspection, searching.
De-risk integrations	As above, data is fungible across ecosystem. Integrations become low risk or unnecessary.
More, higher quality metadata	Quality improves with automation. Extraction often limited by human effort.
AI foundations	Deterministic automation (completeness checks). Probabilistic AI (insights, risk detection).
Digital → intelligence	Document extraction still requires HITL support automation. AI/LLM requires data for intelligence.

TMF Digitalization Roadmap



2024–2025

- Public roadmap published
- Vendor panel started
- Interoperability discussions

2026

- Public review/comment period
- Controlled terminology finalized

2027

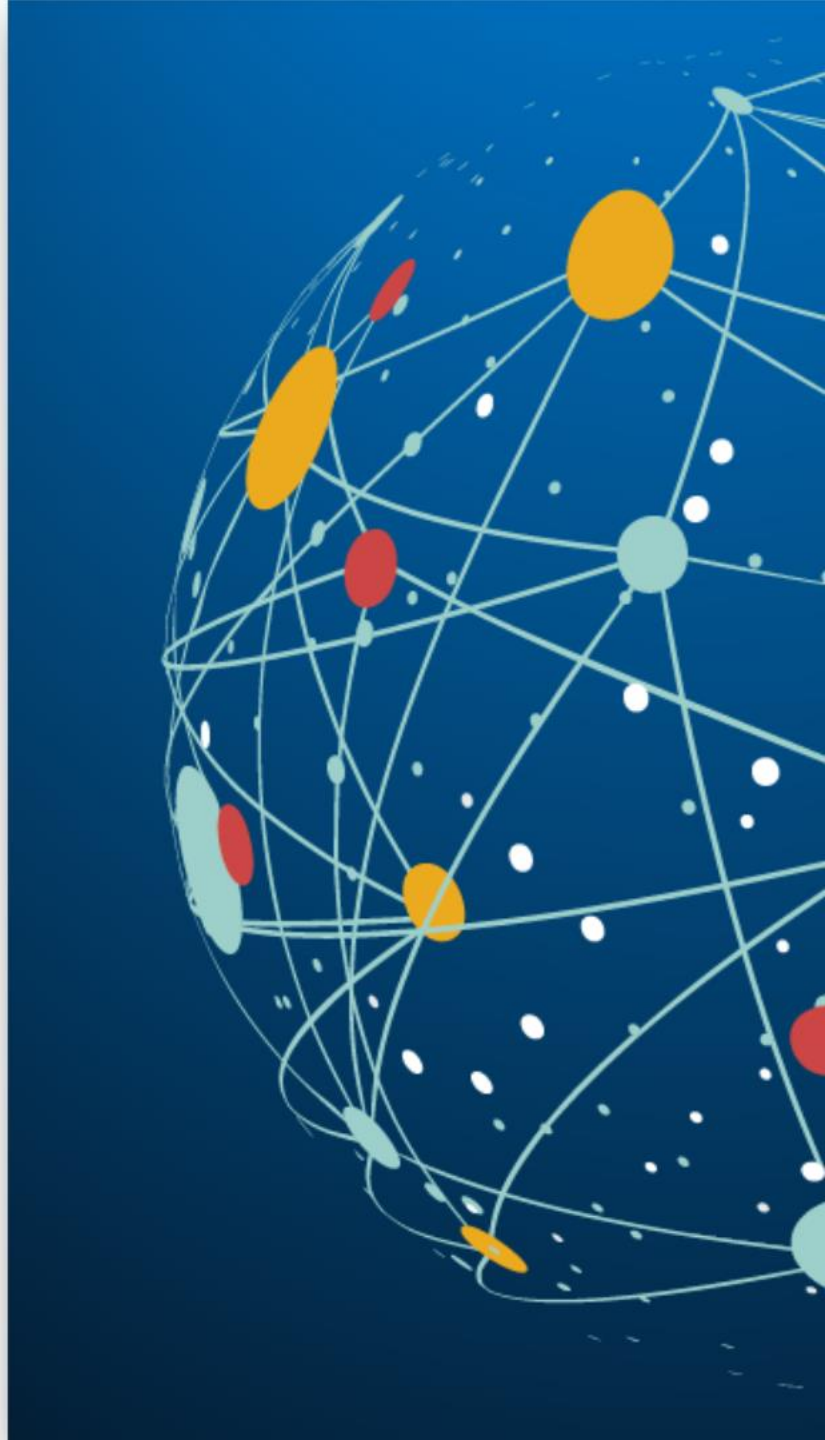
- CDISC TMF Version 1 release
- 360i and USDN 1.0

(Possible) Future

- Merge with DDF/USDN
- Data-first, metadata-centric TMF

Actions and Next Steps

- Industry should align on a new standard by focusing on the most pragmatic approaches that solve real operational business challenges.
- Sponsors and CROs should consider their entire clinical ecosystem, going beyond their four walls and their own platforms and focusing on solving the problems their customers face.
- Sponsors and CROs should carefully consider how they want to integrate systems, as it's often more challenging than it appears on paper. Moving beyond a hub and spoke model to a more composable approach can enable consistent, flexible digital interconnectivity



Thank You!