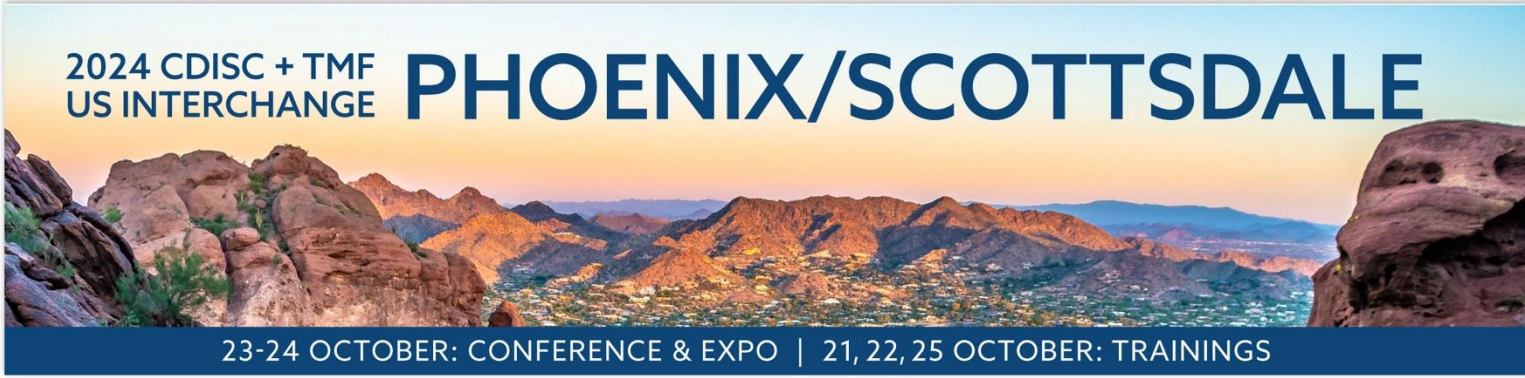

TMF Interoperability: The Critical Importance of Standard Integrations of Clinical Trial Management Data to Promote eTMF Health and Completeness

Presented by Jay Smith, Head of Product, Trial Interactive, Transperfect

Meet the Speaker

Jay Smith

Title: Head of Product, Trial Interactive

Organization: TransPerfect, Inc.

Jay currently leads product and tech at Transperfect, responsible for the Trial Interactive platform. Prior to Transperfect, Jay has led product teams at Medidata Solutions, Sparta Systems, VenueNext, and Cureatr. 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.

Disclaimer and Disclosures

- *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.*

Agenda

1. Introduction
2. Industry Drivers
3. Integration Challenges
4. Interface Best Practices
5. Information Flow Framework
6. Critical Operational Data Interconnects
7. Connectors
8. Standards
9. Next Steps

Why Integrate?

- Data Integrity / MDM
- Efficiencies in Automation
- Duplication of Effort
- Human Error
- Trial Oversight / Silos
- Flexibility

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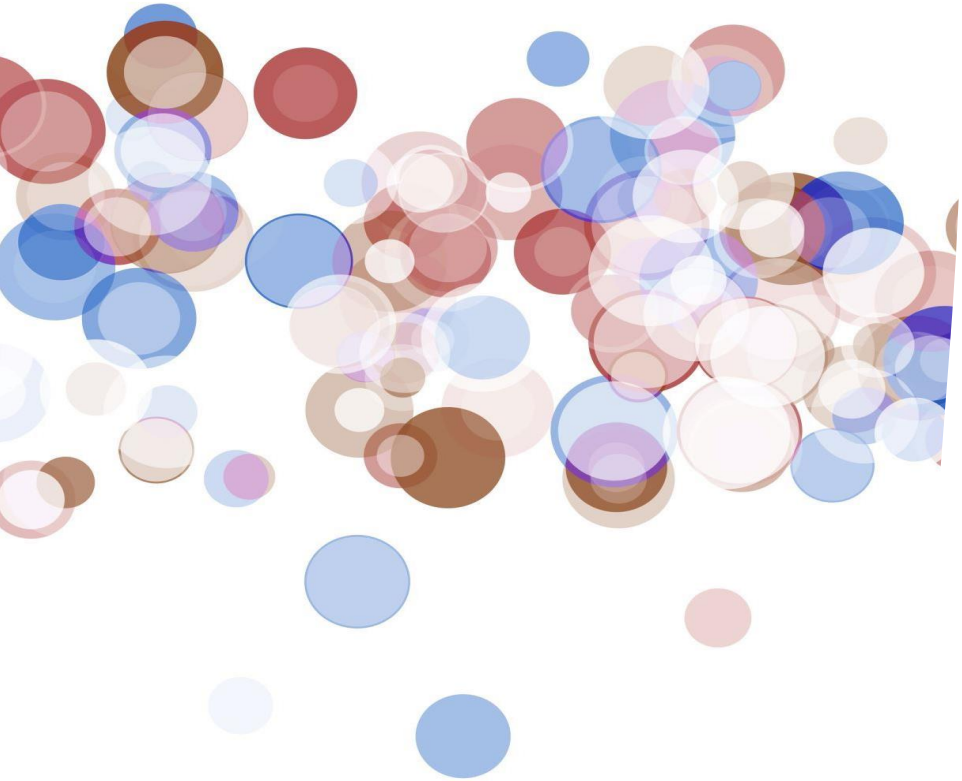
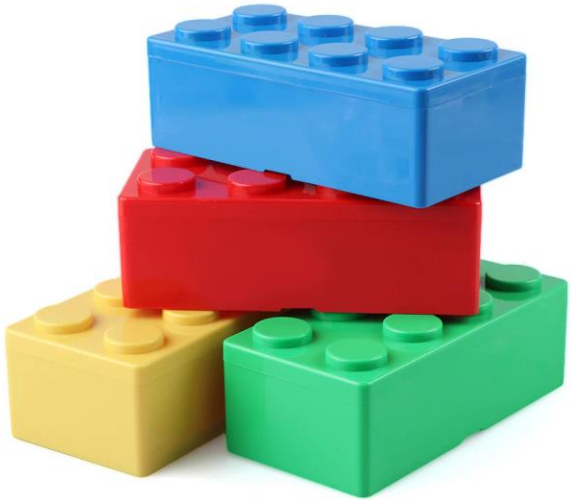


Current Integration Problems

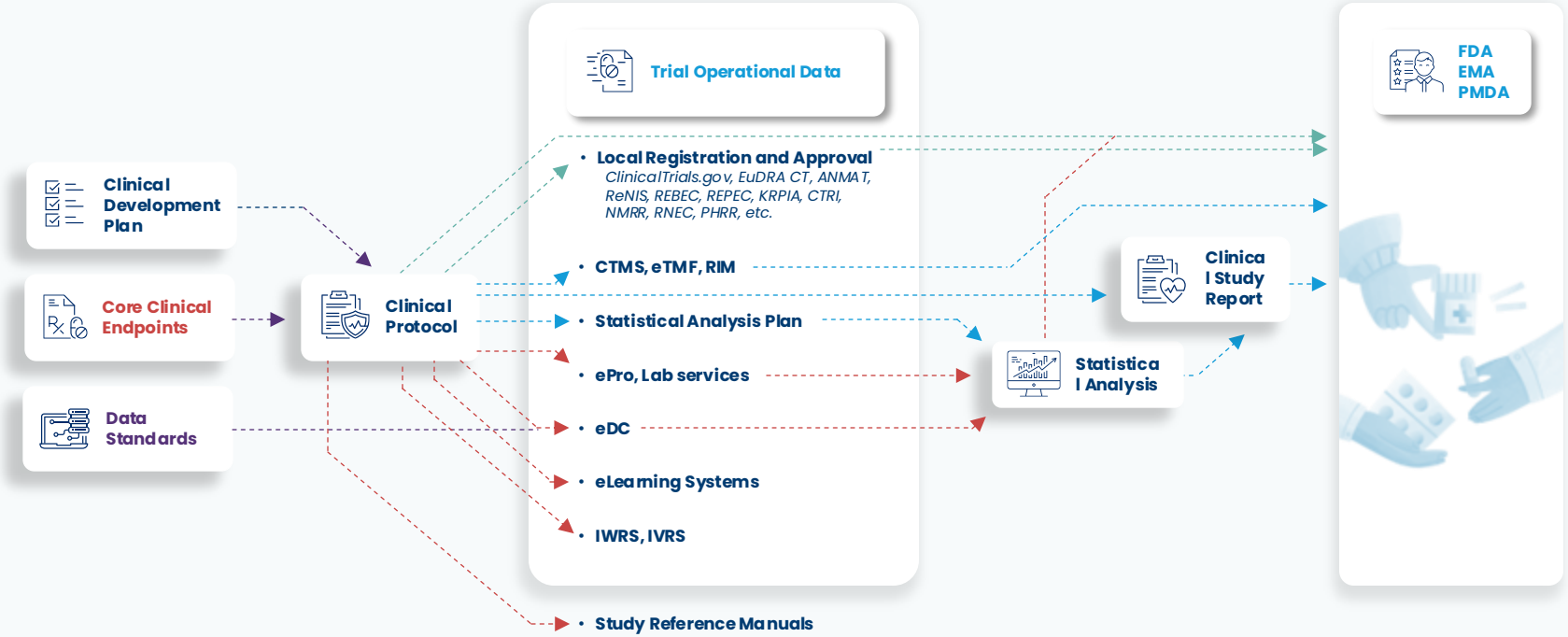
- Uncooperative Platforms
- Legacy Interfaces
- API Maintenance
- Developer Experience
- Implementation Timeframes
- Constant Updates
- Shifting Standards

Interface Best Practice

- **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



The Clinical Trial Information Flow



System Interconnects

Electronic Data Capture (EDC)

Clinical Trial Management System (CTMS)

Sites and Electronic Investigator Site File (eISF)

Learning Management System (LMS)

Institutional Review Board (IRB)

Electronic Trial Master File (eTMF)

Randomization and Trial Supply Management (RTSM)

Clinical Data Repository and Analytics

What about the TMF?

Business Goals for eTMF:

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

Ecosystem Connects:

- Sites, Organizations and Contacts
- External parties, 3rd parties, affiliates
- Business arrangements constantly shifting

Clinical Trial Awareness:

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

Document Data Flows:

- Clinical, Quality, RIM Document workflows can impact the eTMF
- eTMF should be aware of the data classifications

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

Data Systems

ELECTRONIC DATA CAPTURE

Baseline entities and record types are sent through a standard API, ESB Event-based or sFTP integration between systems.

Often Includes:

- Studies
- Countries
- Sites
- Contacts
- Participants
- Visits
- Milestones
- Safety / PV
- Issues
- Activities

CLINICAL TRIAL MANAGEMENT SYSTEM

CTMS

Overall management of the clinical trial from investigator selection to close-out, with close management of site involvement, collected content, and archive

Investigator Database

Basic Investigator data including core documentation

Institution Profile

Site profile data including contact data, organizational information, delegations

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Content Systems

- Studies
- Countries
- Sites
- Investigators
- Contacts
- Milestones
- Activities
- Documents
- Organizations

Start-Up

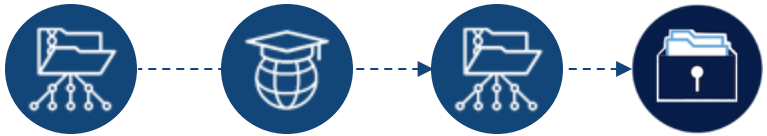
Collection of critical Site Start Up Documents with standard Country workflows

Mobile

Mobile Document Collection, Mobile Site Visit Data and Reports

Safety

Distribution of Safety Forms, Letters, and Notifications between Site, Sponsor, IRB, Country



eISF

Site Portal and Remote Monitoring for Investigator Sites

Training

Virtual Site and Study Team Training, Patient Training

EDMS

Medical Writing, Sponsor/CRO Collaboration, Trial Content

eTMF

Final Archived and indexed Clinical Trial

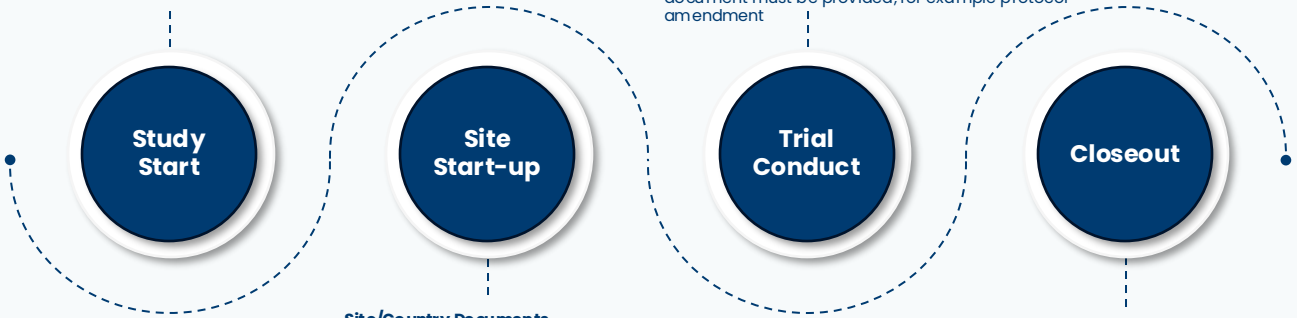
EDC → CTMS → eTMF Integration Points

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 3rd 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, for example 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

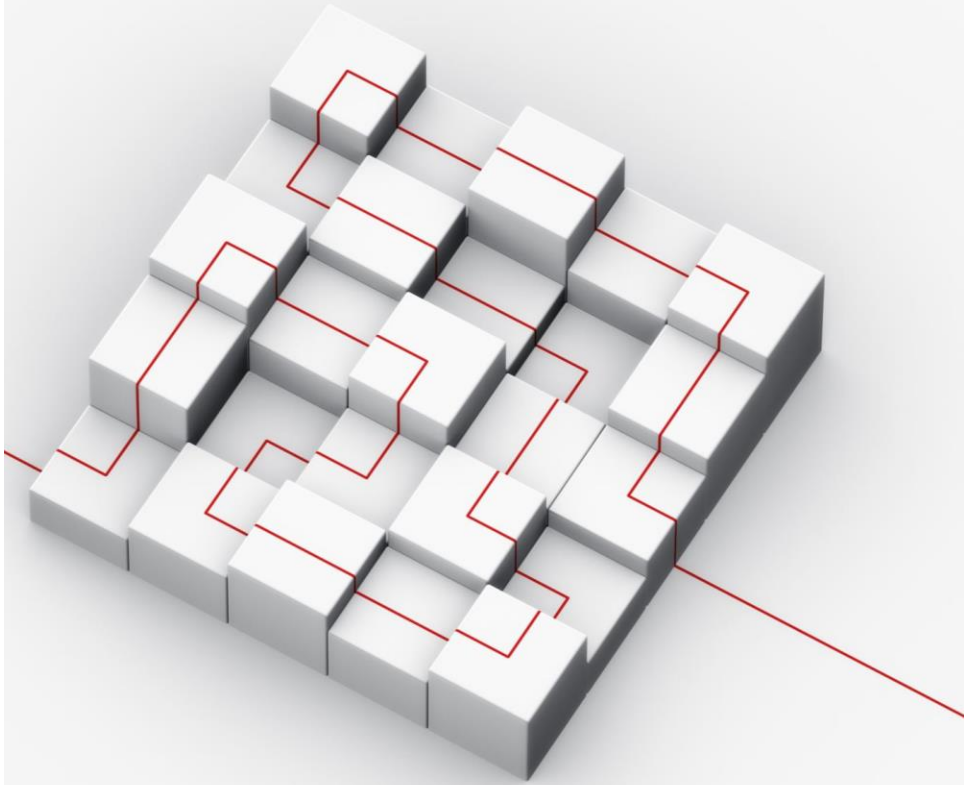
- DB Lock and Archival Milestones and Study Status that close out and archive the trial in the TMF
- Final regulatory documents archived in the TMF

eTMF Integration Points

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

Pragmatic Solutions

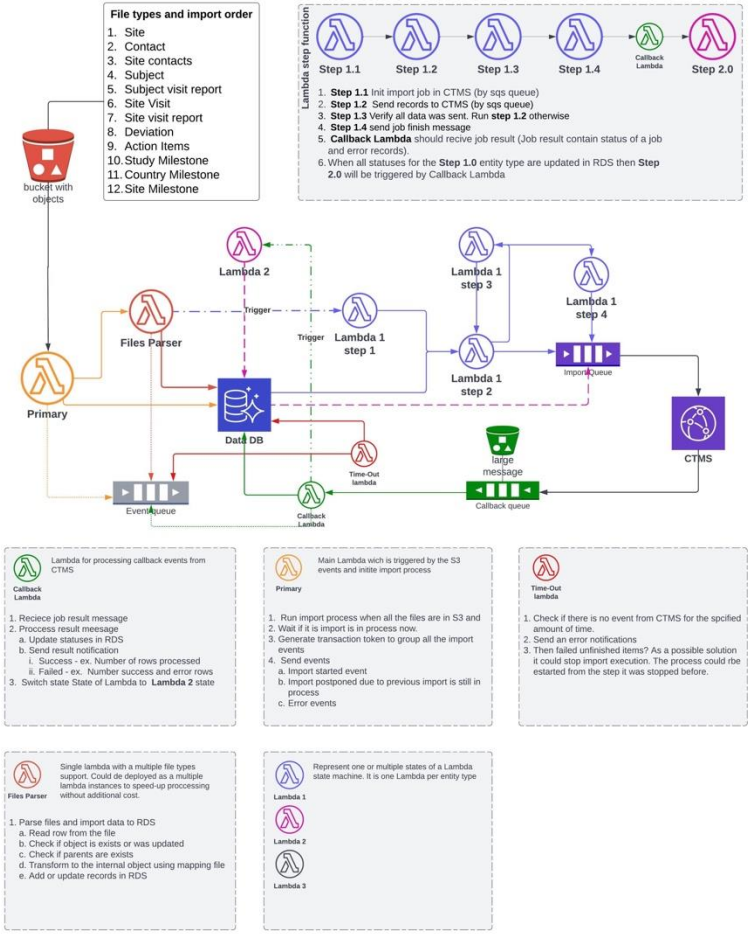
- Standard Framework
- Vendor-Maintained
- Standards-Based Connections
- Configurable Data Mappings
- Re-usable and Serverless
- Flexible and Adaptable



Example Architecture

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.



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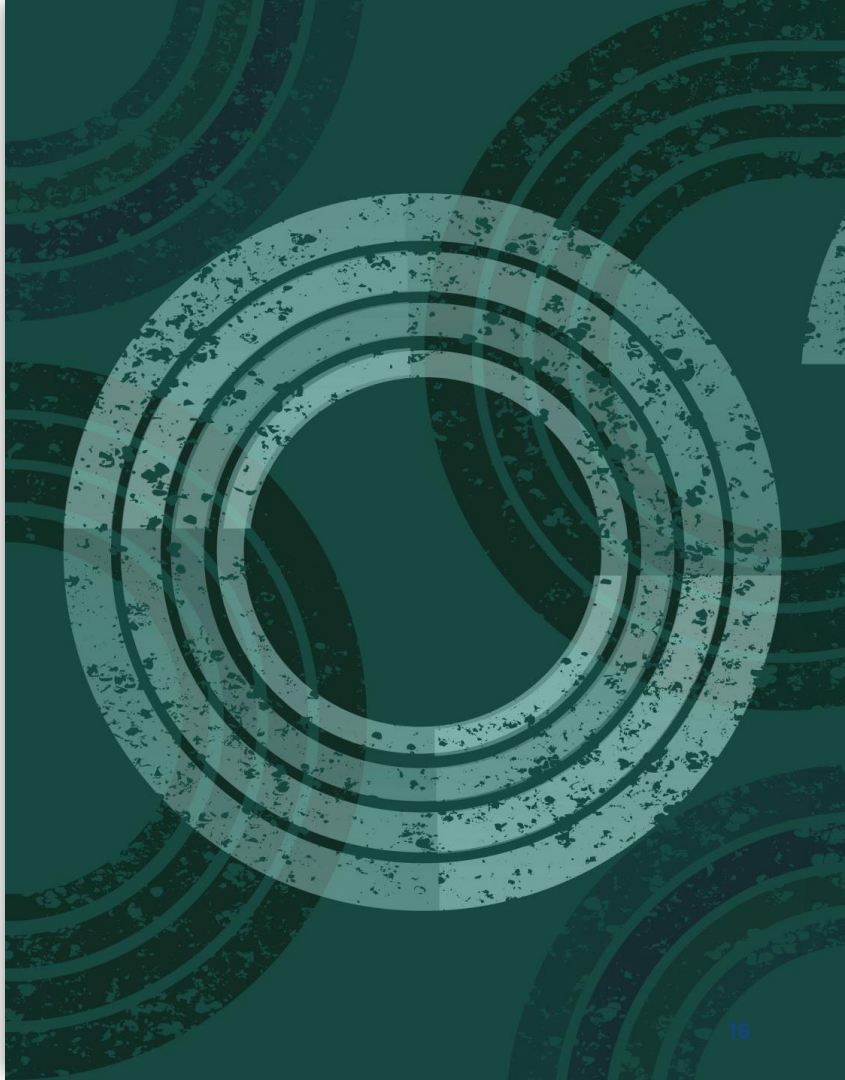
Existing & Future Standards

- eTMF EMS
- CDISC ODM 2.0 / 3.0
- ICH M11
- HL7 FHIR



CRISI Initiative

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)

2024 Status:

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

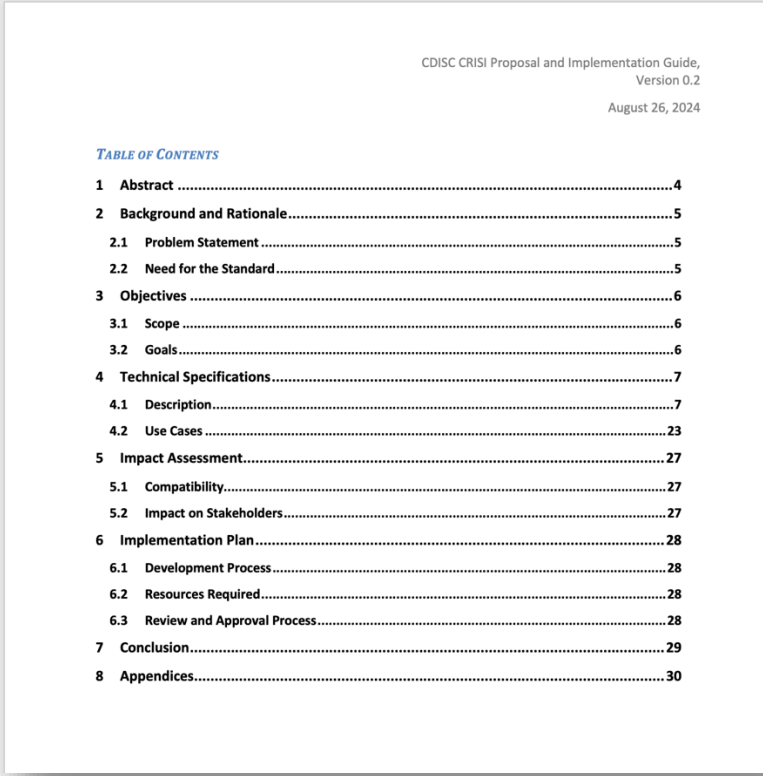
CRISI Initiative

- Basis is FHIR
  - Fast Healthcare Interoperability Resources
  - Developed by Health Level Seven (HL7)
  - Can support:
    - Study → Research Study
    - Site → Location
    - Contact → Practitioner
    - Participant → Research Subject
    - Clinical Document → Document Reference

CRISI Initiative

Development Process

- Phase 1 (Q4 2024): Finalize the CRISI standard draft and submit for CDISC review.
- Phase 2 (Q2 2025): Conduct pilot implementations with selected sponsors, CROs, and sites.
- Phase 3 (Q4 2025): Collect feedback, refine the standard, and prepare for broader adoption.



CDISC CRISI Proposal and Implementation Guide, Version 0.2

August 26, 2024

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Actions and Next Steps

- Industry should align with these new standards by focusing on the most pragmatic approaches that solve real operational business challenges.
- Vendors should consider integration as a baseline requirement for their systems, thinking beyond the boundaries of their own platforms and focusing on 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. A more composable approach can enable consistent, flexible digital interconnectivity and pragmatic integration.

Thank You!