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

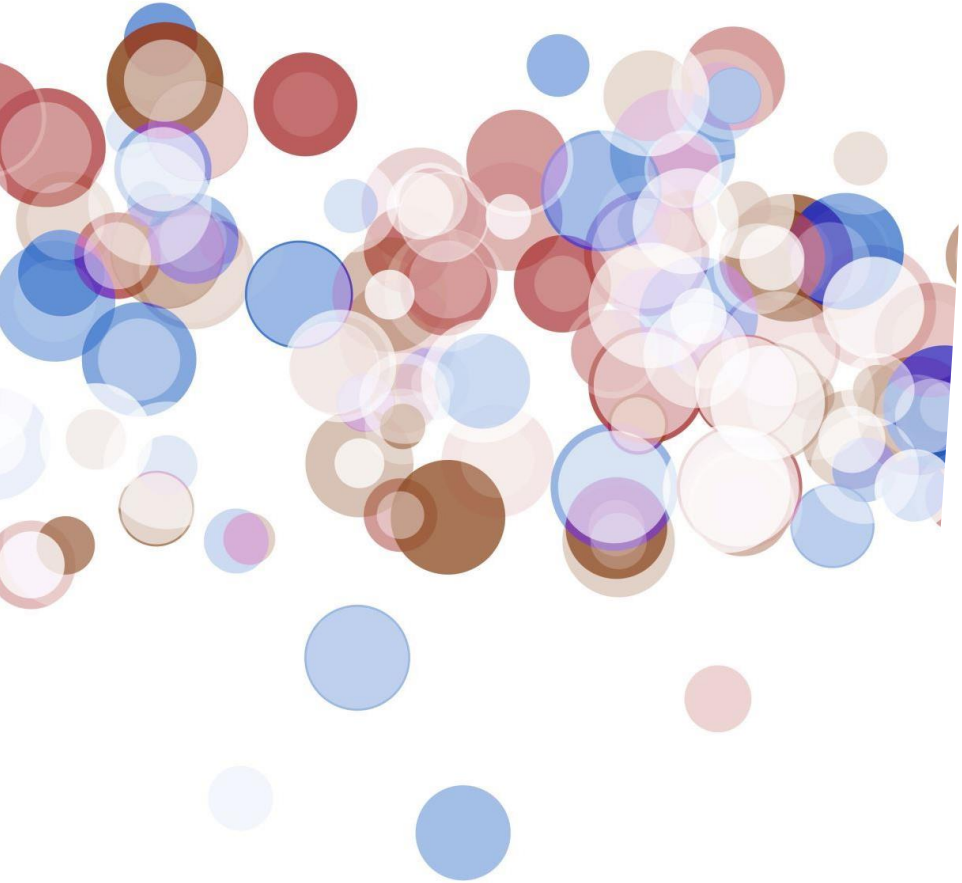
- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

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

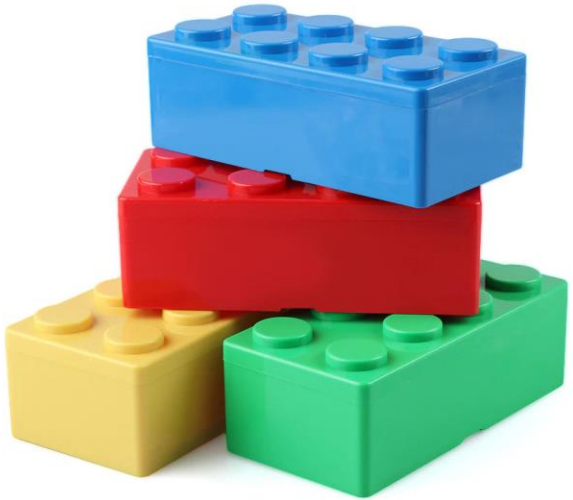


Current Integration Problems

- 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



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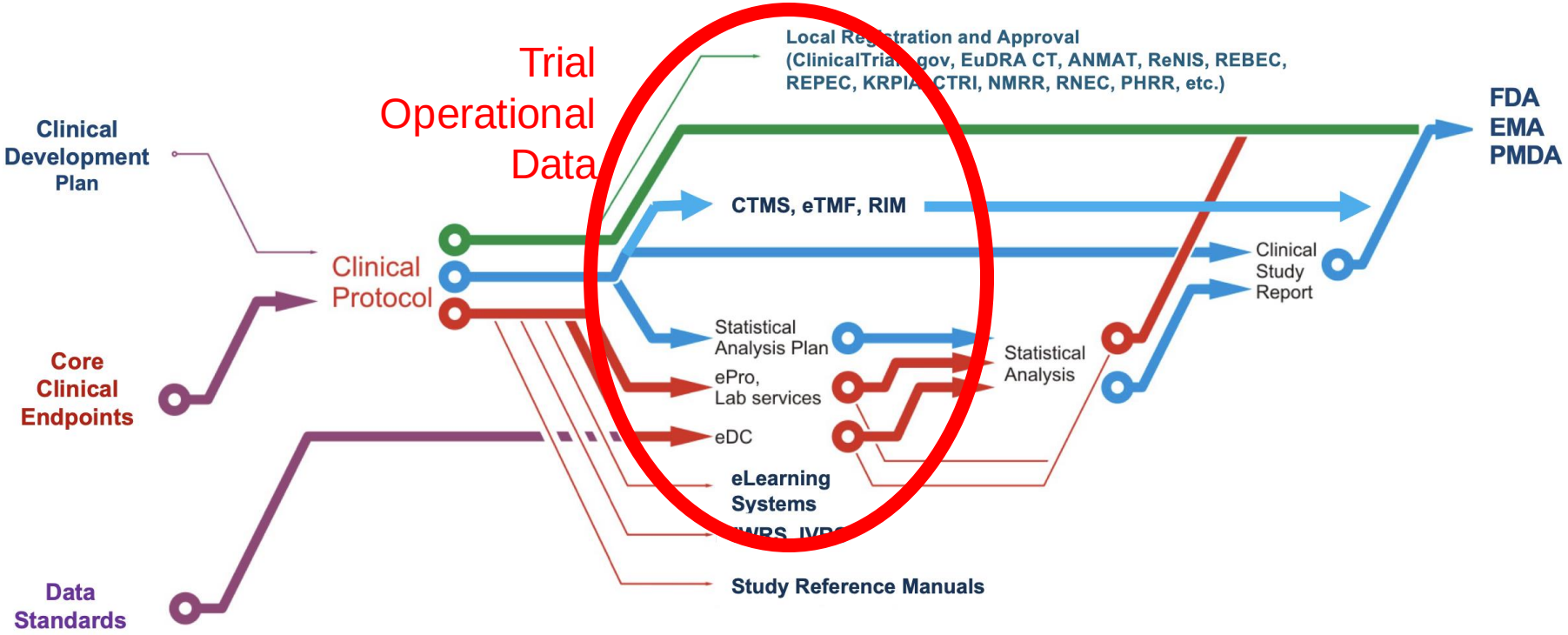
The Clinical Trial Information Flow



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System Interconnects

ELECTRONIC DATA CAPTURE (EDC)

CLINICAL TRIAL MANAGEMENT SYSTEM (CTMS)

SITES AND ELECTRONIC INVESTIGATOR SITE FILE (EISF)

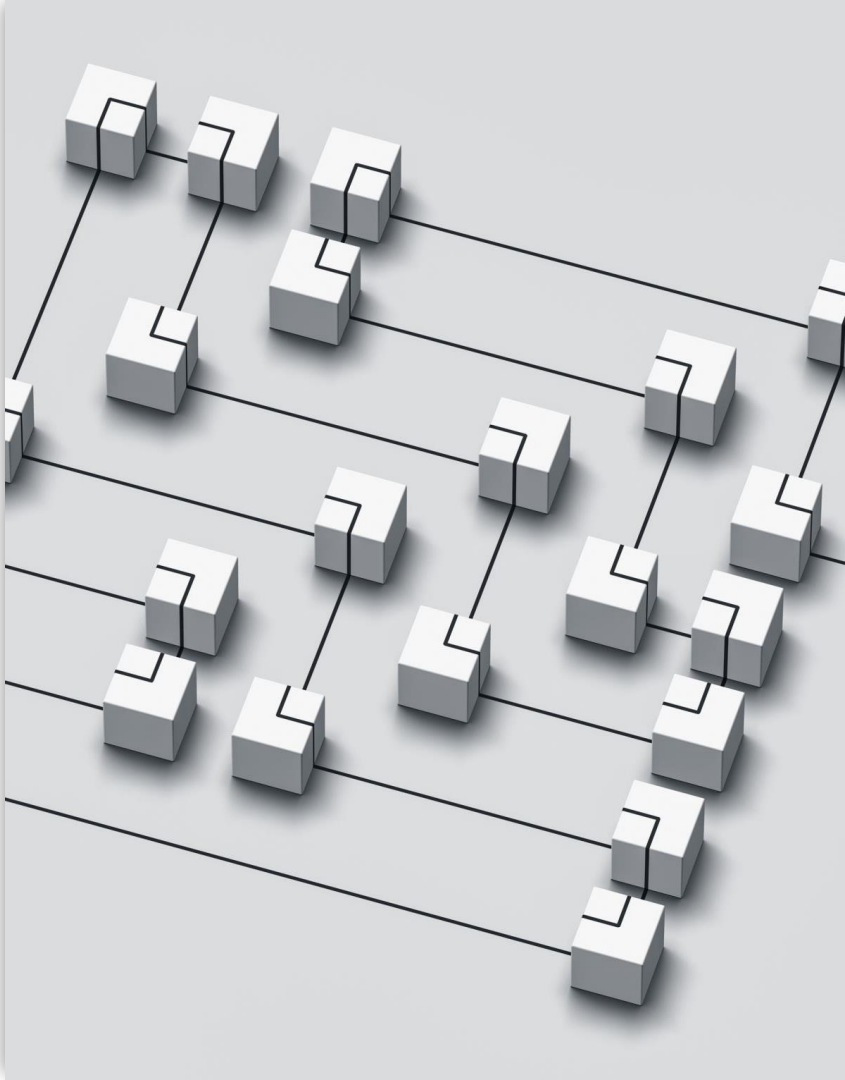
LEARNING MANAGEMENT SYSTEM (LMS)

INSTITUTIONAL REVIEW BOARD (IRB)

ELECTRONIC TRIAL MASTER FILE (ETMF)

RANDOMIZATION AND TRIAL SUPPLY MANAGEMENT (RTSM)

CLINICAL DATA REPOSITORY AND ANALYTICS



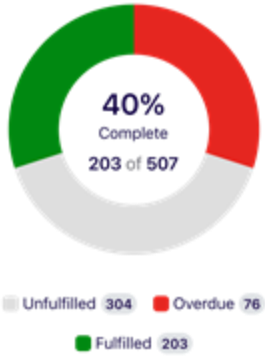
What about the TMF?

Business Goals for eTMF:

- eTMF Health is timely and Contemporaneous
- Completeness and Accuracy
- Quality and Inspection Ready

Ecosystem Connects:

- Sites and 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

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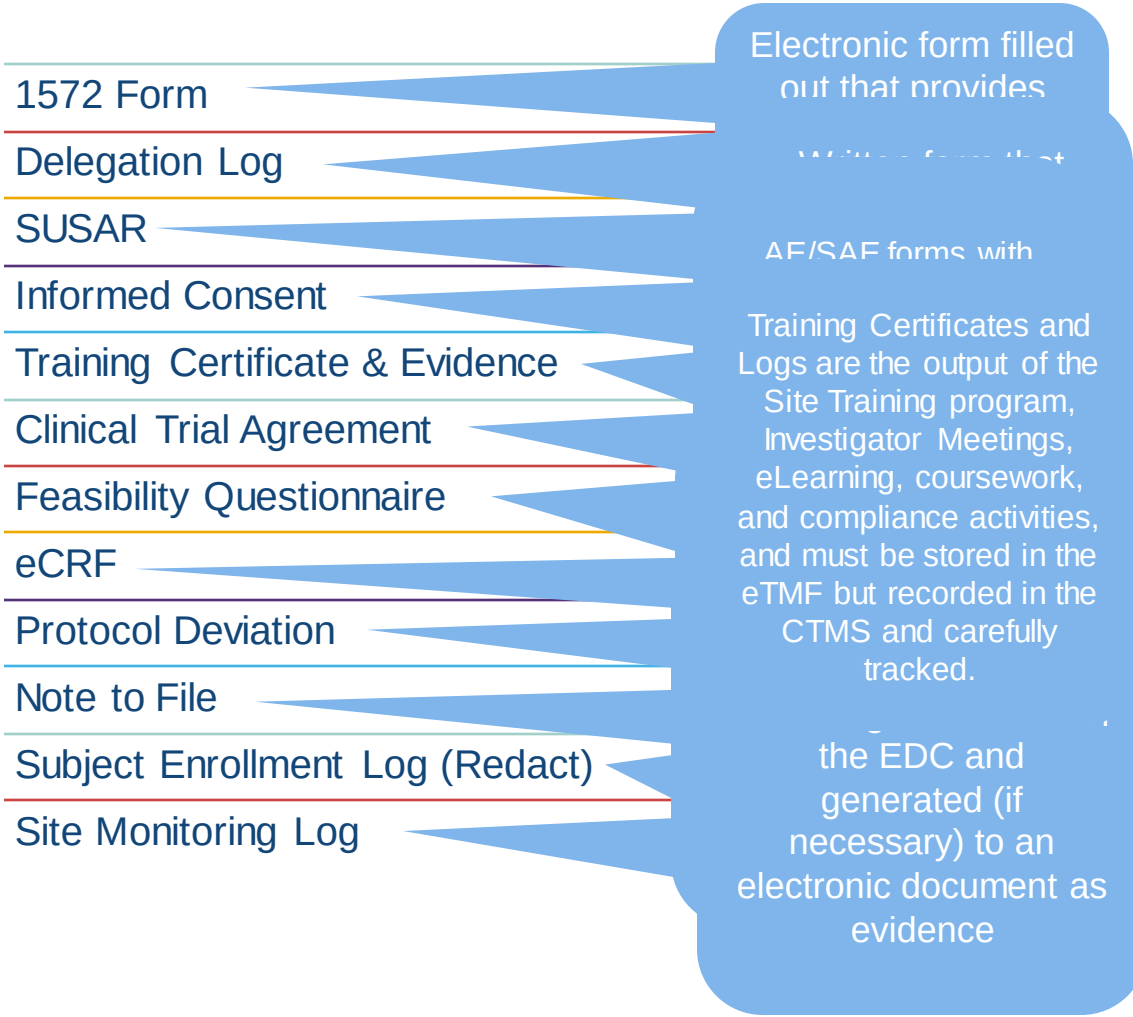
Digitization of Trial Documents into Fully Digital Business Workflows



Data Platform

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 Platform

- 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 Visits, Mobile Trip Monitoring Reports

Safety

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

Site Portal

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

STUDY START

SITE START-UP

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

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

TRIAL CONDUCT

CLOSEOUT

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

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

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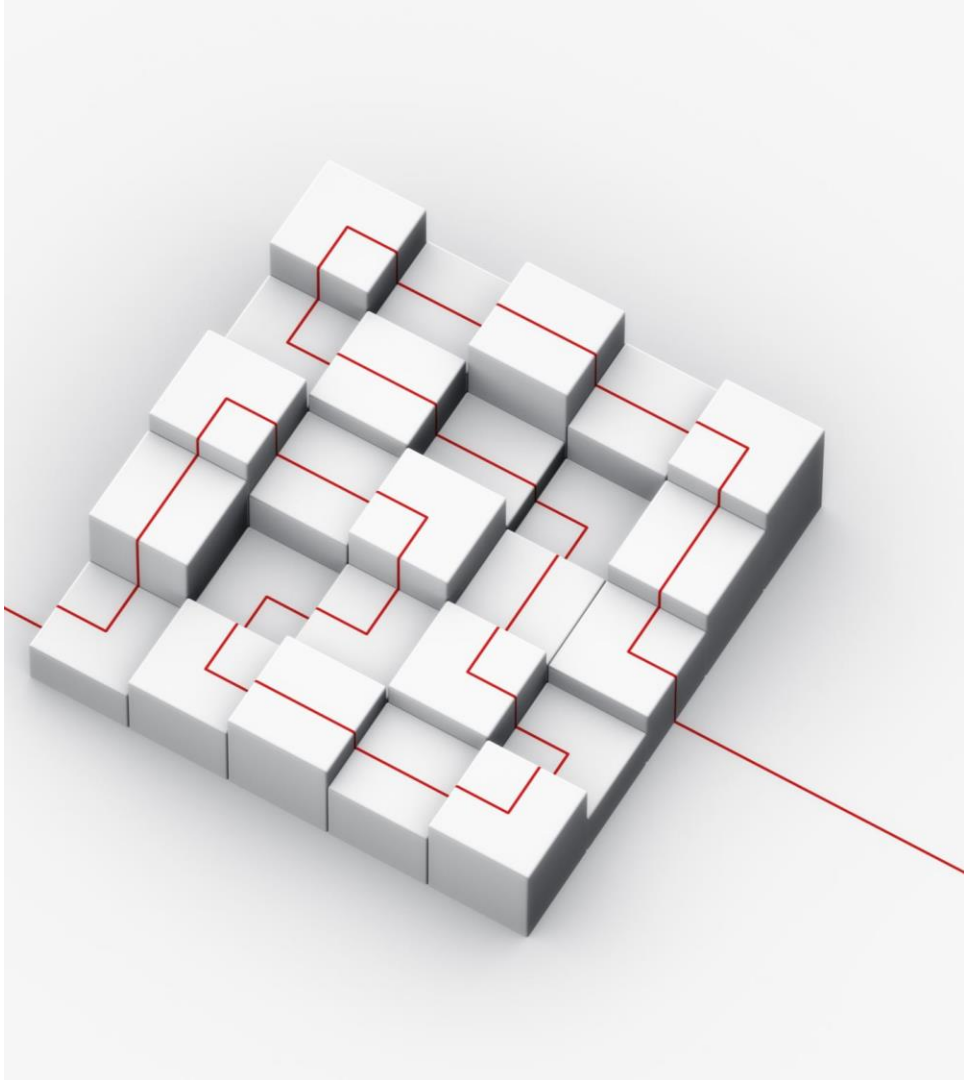
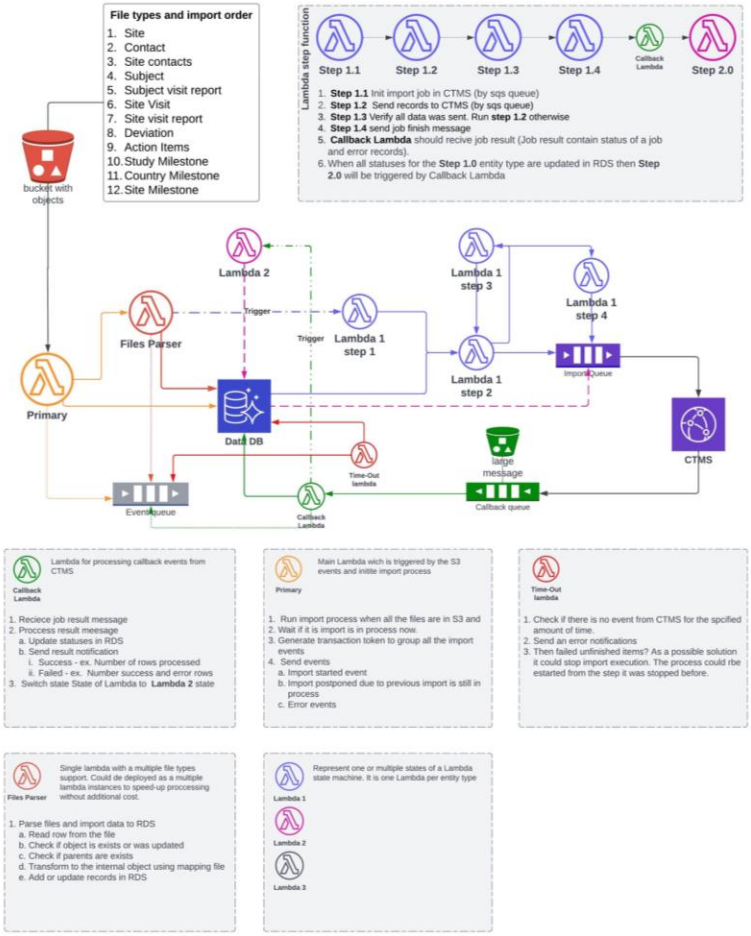
A Pragmatic Approach

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



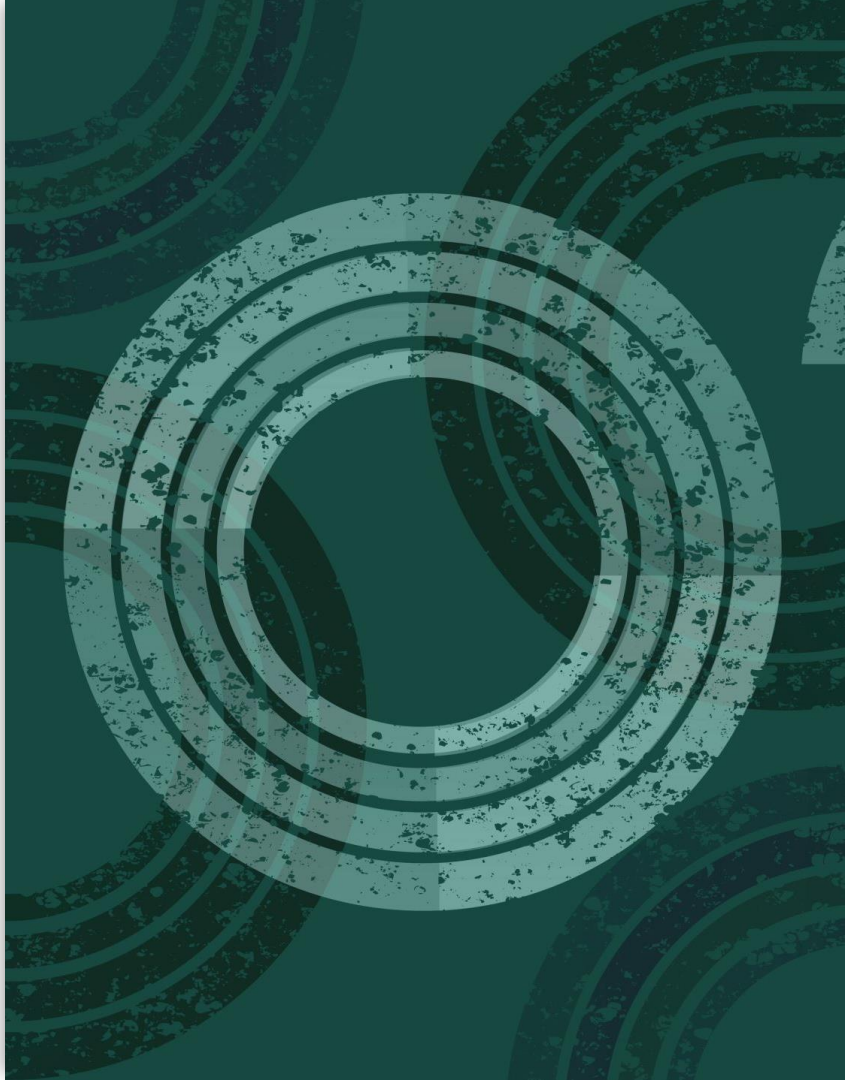
Example Architecture

- **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.



Existing and Future Standards

- TMF
- CDISC ODM 2.0
- ICH M11
- HL7 FHIR



CDISC CRISI Initiative

- Clinical Research Interoperability Standards Initiative (CRISI)
  - Focus is on operational data between core systems (EDC, CTMS, eTMF, IRB/EC, IXRS, Site Portals and Investigative Sites)
  - Focus is on a standard that will pragmatically resolve the study start timeframe requirements and the core data elements required to share.
  - Focus is to use existing data standards in a way that is focused on the business challenge
  - Focus is on an open standard to avoid a hub and spoke model, or a vendor-focused 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, Sites
  - API and data model proof of concepts (FHIR)

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Next Steps

- Industry should align on these new standards. Focus on the most pragmatic approaches first, that solve real operational business challenges.
- Vendors should consider integration as a baseline requirement of their systems and think beyond the borders of their own platforms, and about the problems their customers have
- Sponsors and CROs should think carefully about how they want to integrate system … it's always harder than it seems on paper. A more composable approach can provide a consistent, flexible digital interconnect and pragmatic integration.

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Thank You!