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2023
EUROPE
INTERCHANGE
COPENHAGEN | 26-27 APRIL

CDISC Conformance Rules and the CORE Engine: Progress and Roadmap

Presented by Peter Van Reusel, Chief Standards Officer, CDISC

Meet the Speaker

Peter Van Reusel

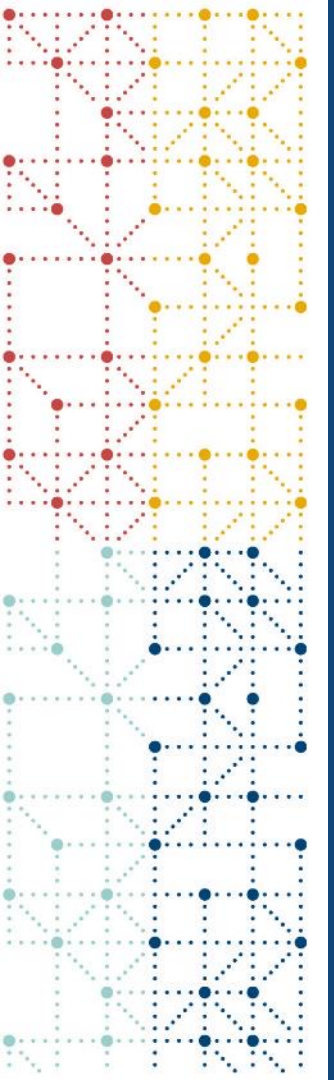
Title: Chief Standards Officer
Organization: CDISC

Peter Van Reusel provides executive leadership to the development and implementation of clinical standards in line with CDISC's strategy and operational plans, working closely with the President and CEO, as well as CDISC staff and stakeholders. He has over 20 years' experience in senior roles in pharma and at CROs, providing standards expertise and carrying out other standards work in various organizational settings. A long-time, CDISC-authorized instructor, Peter has helped significantly in developing CDISC training courses.

He previously served as CDISC's European Liaison, shepherding relationships with key European regulatory, academic, and biopharma stakeholders. Peter is also an active PHUSE collaborator.

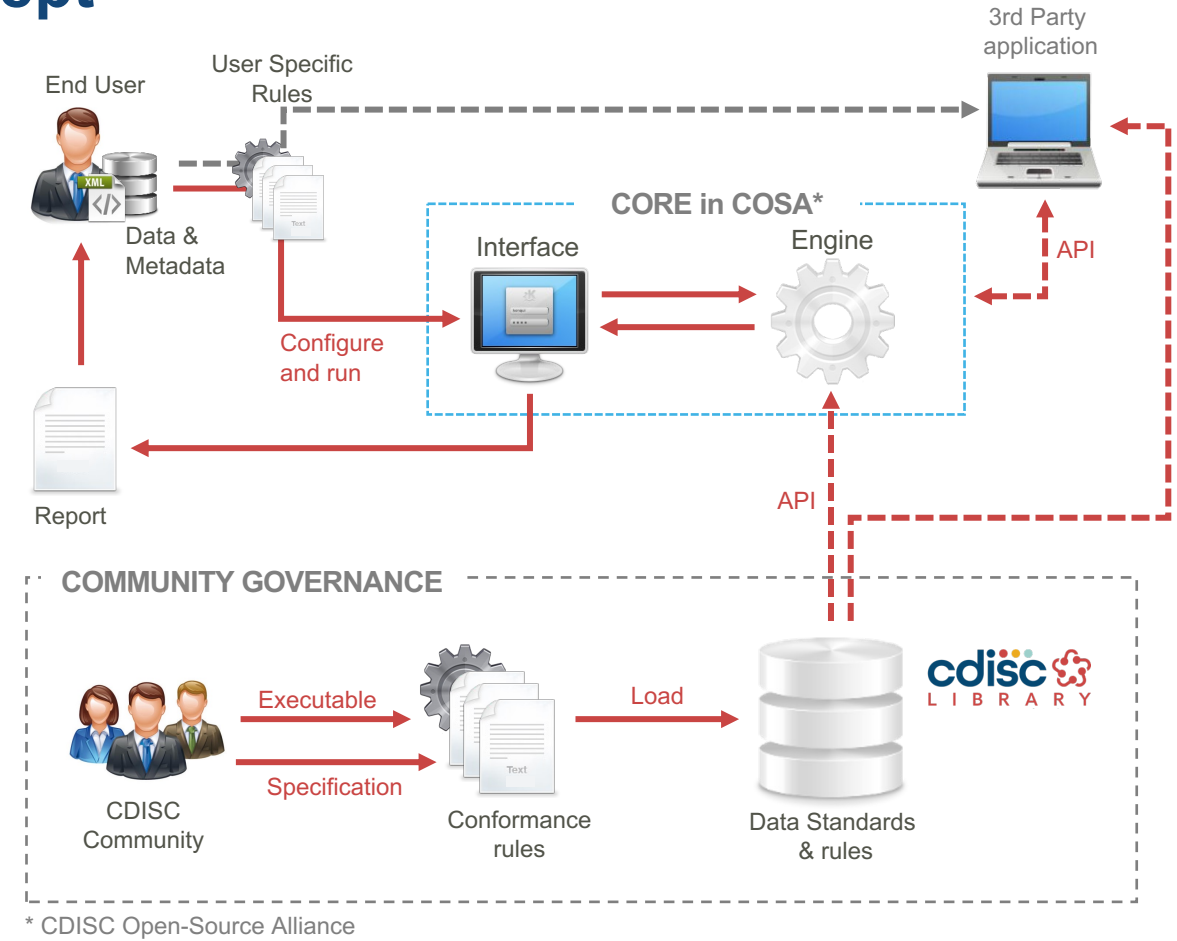
Agenda

1. Concept of CORE
2. High-level Status and Roadmap
3. CORE Rules
4. CORE Engine and Deployments
5. Rules Governance Model
6. CORE Roadmap Board
7. Next Steps



Concept of CORE

CORE Concept



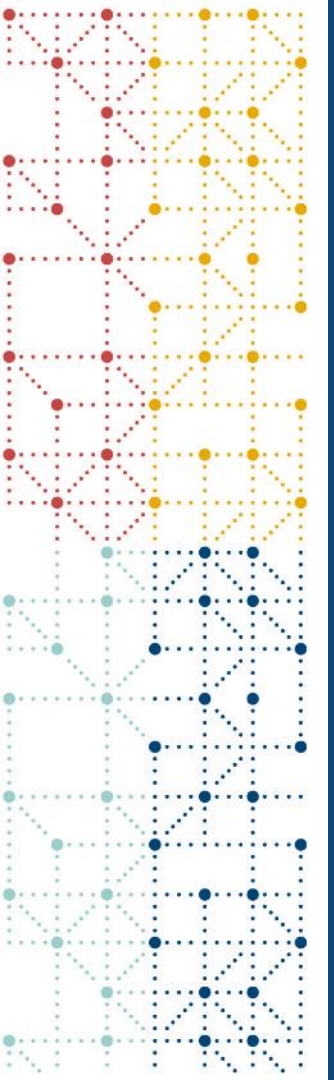
* CDISC Open-Source Alliance

Why is CDISC doing CORE?

- Ensure each standard has a set of unambiguous, executable Conformance Rules
- Ensure consistency across Conformance Rule implementations
- Expedite the availability of executable Conformance Rules for new Foundational Standards
- Create executable Conformance Rules vetted by the CDISC standards development teams
- Develop an open-source engine that serves as a Reference Implementation
- Publish the Rules in the CDISC Library and the engine under the CDISC Open Source Alliance (COSA)

➡ *CORE Initiative = Rules + Engine*

https://www.cdisc.org/core



High-level Status and Roadmap

CORE Program Roadmap

Future Releases: Enhanced Engine and Rules

- **Engine**: Open-Source under COSA; evolved; maintained by CDISC
- **Conformance Rules**: New CDISC Standards released with Conformance Rules
- **Functionality**: Advanced functionality
- **Deployments**: Vendor- or user-provided cloud & local production environments

Q3 2022 – …

Stable Release: Submission-ready Engine and Rules

- **Engine**: Open-Source under COSA; evolved; maintained by CDISC
- **Conformance Rules**: Remainder of CDISC Foundational Standards
- **Functionality**: Complete conformance checking functionality
- **Deployments**: Vendor- or user-provided cloud & local production environments
  - Desktop evaluation

Establish CORE Roadmap Board

Q3 2021- Q2 2022

Evaluation Release

- **Engine**: Open-Source, developed by CDISC, published under COSA
- **Conformance Rules**: SDTM 2.0 and SDTMIG 3.4
- **Functionality**: Basic conformance checking functionality
- **Deployments**:
  - CDISC cloud evaluation
  - Azure Marketplace evaluation
  - Desktop evaluation

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Vendor/User

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Assessment to Date

- **Major accomplishments**
  - Quick establishment of YAML schema
  - Rule Editor (authoring tool)
  - Engine and Rule Editor released as open-source in GitHub
  - Vendor engagement and adoption
    - attend Session 6B: “Implementing CORE”
- **Challenges**
  - Community engagement
  - Volume of Rules development work
  - The road to adoption

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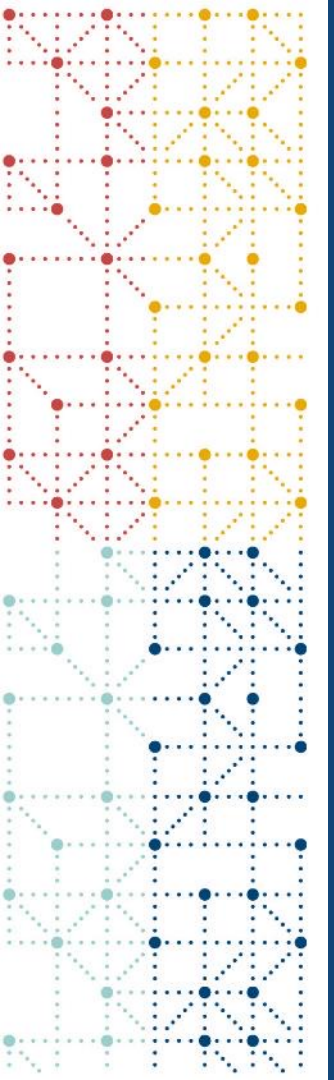


CORE Rules

Rules Specifications and Executable Rules: Overview

Conformance Rule Specification Development

Human-readable Specification

Rule ID	SDTMIG Version	Rule Version	Class	Domain	Variable	Condition	Rule
CG0225	3.4	1	ALL	ALL	VISITDY	VISITNUM is NOT in TV.VISITNUM	VISITDY = null
Document	**Section**	**Item**	**Cited Guidance**				
IG v3.4	4.4.5		VISITDY must not be populated for unplanned visits, since VISITDY is, by definition, the planned study day of visit, and since the actual study day of an unplanned visit belongs in a --DY variable.				

Authoring Sources:

- CDISC Standards
- Regulatory Authority Validation Rules
- Community proposals - curated per CDISC Operating Procedure (COP)

Centralized

Specifications Catalog

CORE Rule Development

Executable Rule (YAML) in CORE Rule Editor

```yaml
Core:
  Id: CDISC.SDTMIG.CG0225
  Version: '1'
Authority:
  Organization: CDISC
Description: Trigger error if VISITYDY is populated when VISITNUM is not in TV.
References:
    Origin: SDTM and SDTMIG Conformance Rules
    Rule Identifier:
      Id: CG0225
      Version: '1'
    Version: '2.0'
Sensitivity: Record
Severity: Warning
Rule Type: Value Presence
Scopes:
  Classes:
    Include:
      All
  Domains:
    Include:
      All
  Standards:
    - Name: SDTMIG
      Version: '3.4'
Operations:
  - domain: TV
    id: $tv_visitnum
    name: VISITNUM
    operator: distinct
```

Rule developed and tested in CORE Rule Editor and CORE Engine, per CDISC COP

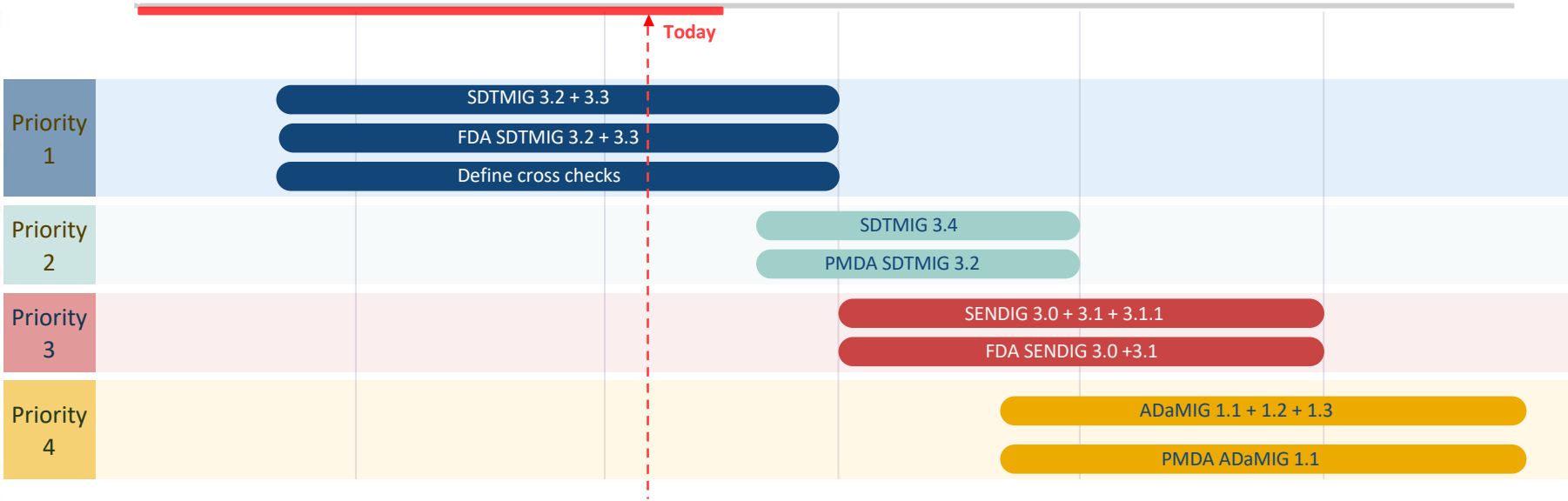
Publish

CDISC Library

Rules Development Progress

Components	Status										
	OPEN	DONE	BLOCKED	UNIT TESTING	QC IN PROGRESS	READY TO PUBLISH	PUBLISHED	AWAITING QC	AUTHOR IN PROGRESS	BACK TO AUTHOR	T:
ADaMIG v1.0	314	0	0	0	0	0	7	0	0	0	**321**
ADaMIG v1.1	419	0	0	0	0	0	7	0	0	0	**426**
ADaMIG v1.2	591	0	0	0	0	0	7	0	0	0	**598**
ADaMIG v1.3	568	0	5	4	2	0	7	9	1	0	**596**
FDA SDTMIG v3.2	493	0	0	0	0	0	0	0	0	0	**493**
FDA SDTMIG v3.3	501	0	0	0	0	0	0	0	0	0	**501**
FDA SENDIG DART v1.1	350	0	0	0	0	0	0	0	0	0	**350**
FDA SENDIG v3.0	316	0	0	0	0	0	0	0	0	0	**316**
FDA SENDIG v3.1	330	0	0	0	0	0	0	0	0	0	**330**
FDA SENDIG v3.1.1	335	0	0	0	0	0	0	0	0	0	**335**
FDA SENDIG-AR v1.0	466	0	0	0	0	0	0	0	0	0	**466**
SDTMIG v3.2	279	37	14	0	3	0	74	0	5	4	**416**
SDTMIG v3.3	295	48	14	1	4	0	78	0	5	4	**449**
SDTMIG v3.4	7	60	51	10	4	0	272	2	35	3	**444**
SENDIG v3.0	259	0	0	0	4	0	1	0	0	0	**264**
SENDIG v3.1	174	2	2	3	4	9	1	96	11	1	**303**
SENDIG v3.1.1	307	0	0	0	4	0	1	0	0	0	**312**
SENDIG-DART v1.1	353	0	0	0	4	0	1	0	0	0	**358**
Total Unique Issues:	**6357**	**147**	**86**	**18**	**29**	**9**	**456**	**107**	**56**	**12**	**7277**

Rules Development Priority



➡ *Timelines depend on community engagement*

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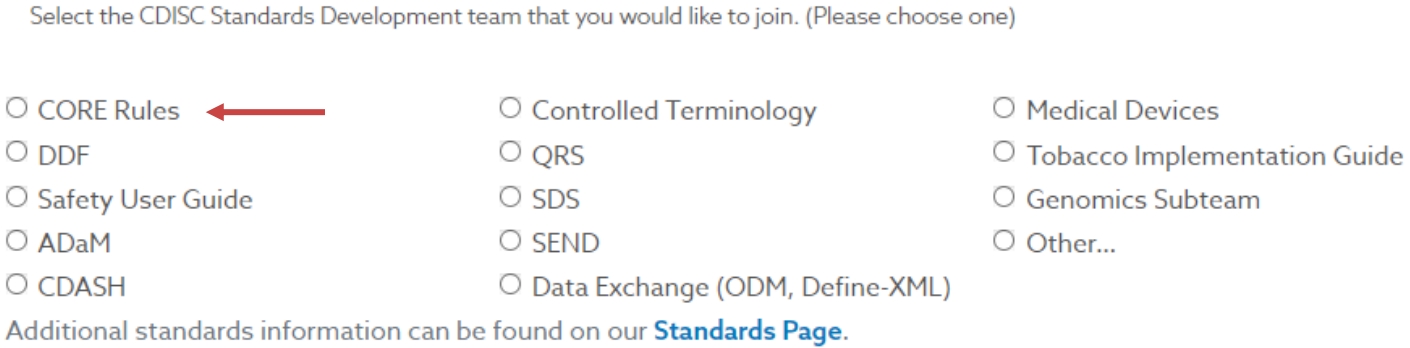
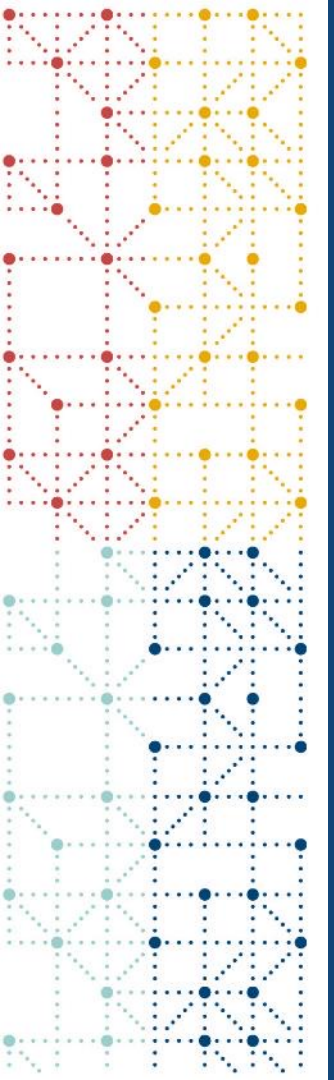
How to sign up as a volunteer

- https://www.cdisc.org/volunteer/form
  - Select CORE Rules Team





CORE Engine and Deployments

What does the CORE Engine do?

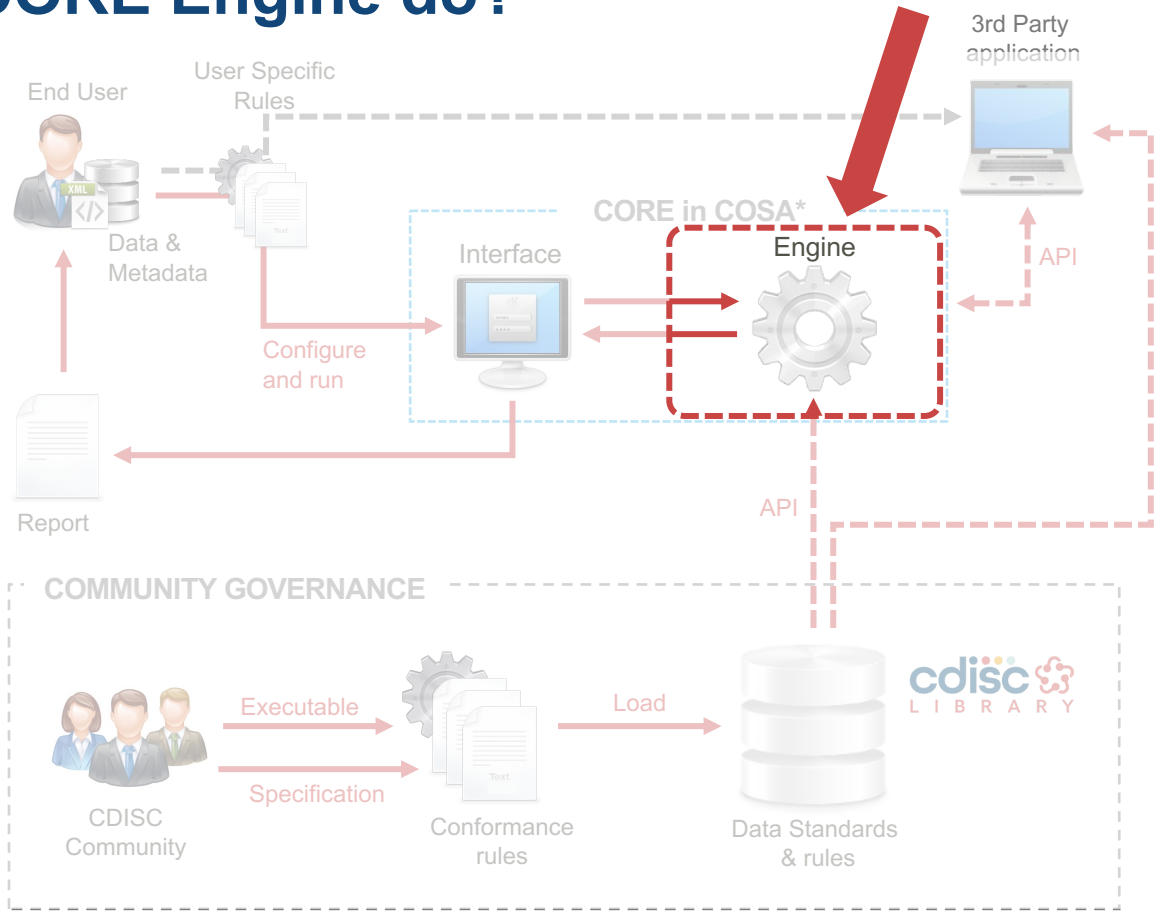
CORE Engine

Functionality:

- Executes CORE Rules (YAML) against clinical data and returns results
- Deployment agnostic
- Open-source, available in GitHub

Current focus:

- Process new YAML operators added to express new rules
- Process new clinical data formats
- Support Define xml cross-checking



* CDISC Open-Source Alliance

CORE Engine is Open-Source

- Open-source framework
  - Listed in the COSA (CDISC Open-Source Alliance) directory
  - Permissive MIT open-source license
  - Provided via GitHub
- Free to all in CDISC community
- Very flexible implementation options
  - attend Session 6B: “Implementing CORE”

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CORE Engine Deployment

- CORE Engine deployments are the domain of the greater CDISC community, including commercial software vendors
  - End-user implementations
  - Commercial vendors offerings for end-users
- CORE deployments may include
  - Enhanced UI / Enhanced reporting and issue tracking
  - Additional clinical data formats
  - Ongoing support (e.g., service level agreement)
- CORE deployments must be validated by the deployer
  - Separate from CORE Engine base testing done by the open-source community

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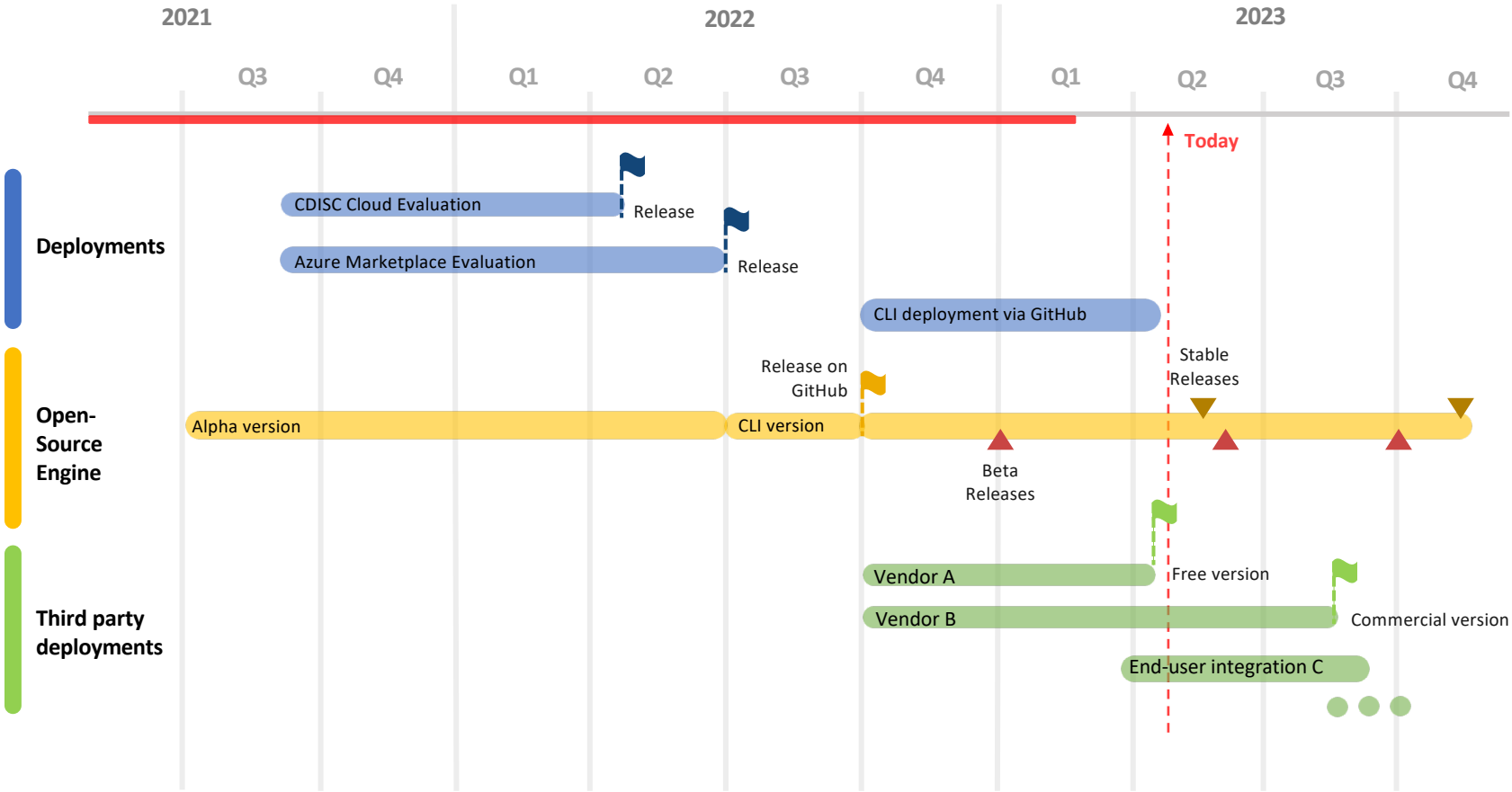
Engine and Deployments Overview



Third-party Desktop Deployments

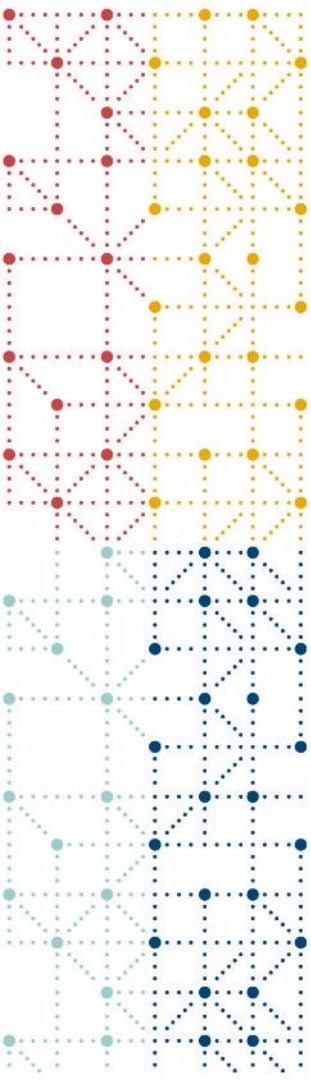
- Early discussions with vendor community re early provision of standalone CORE Engine desktop version
  - Simple to install and use
  - Provide a UI
  - Will make it easier for the CDISC community to evaluate CORE without IT support
- Multiple vendors are currently preparing an early-release desktop version
- First free, publicly available, vendor-provided CORE desktop version announced at this Interchange

➡ *Drive adoption*

CORE Registered Solution Provider

- Program purpose
  - For CORE vendors (solution providers)
    - A means to officially certify with CDISC that their CORE solutions correctly use the CORE Rules
  - For CDISC
    - A means to treat all CORE vendors equally regarding
      - Certifying vendor solutions – by testing all solutions with the same “certification test package” – Rules, test data, and test run set
      - Informing the CDISC community of available vendor CORE solutions – by announcing every and only certified solutions
    - A means to achieve a level playing field re use of any Engine with the CORE Rules

- Testing for certification will include
  - Generating results with CORE Rules and test study data reflecting an “average study”
  - No system functionality testing



Rules Governance Model

CORE Rules Governance

Rules Governance Team

(CDISC; Regulatory Agencies; Community)

Rule Specifications

CORE Rules (executable)

cdisc Standards

Provide rule specs

Regulatory Agencies

Provide validation rules

Community

Propose new / updated rule specs

Rules Gov Team Activities

- Receive specifications
- Load to central catalog

Rules Gov Team Activities

- Govern specs content
- Curate content
- Mark rules for dev.
- Prioritize rules for dev.

Central Specifications Catalog

Freely Available

Rules Gov Team Activities

- Govern CORE Rules dev. process
- Assign Rules for development
- Review/approve Rules for release

Rules Development

Community

Publish

CDISC Library

API

CORE Engine

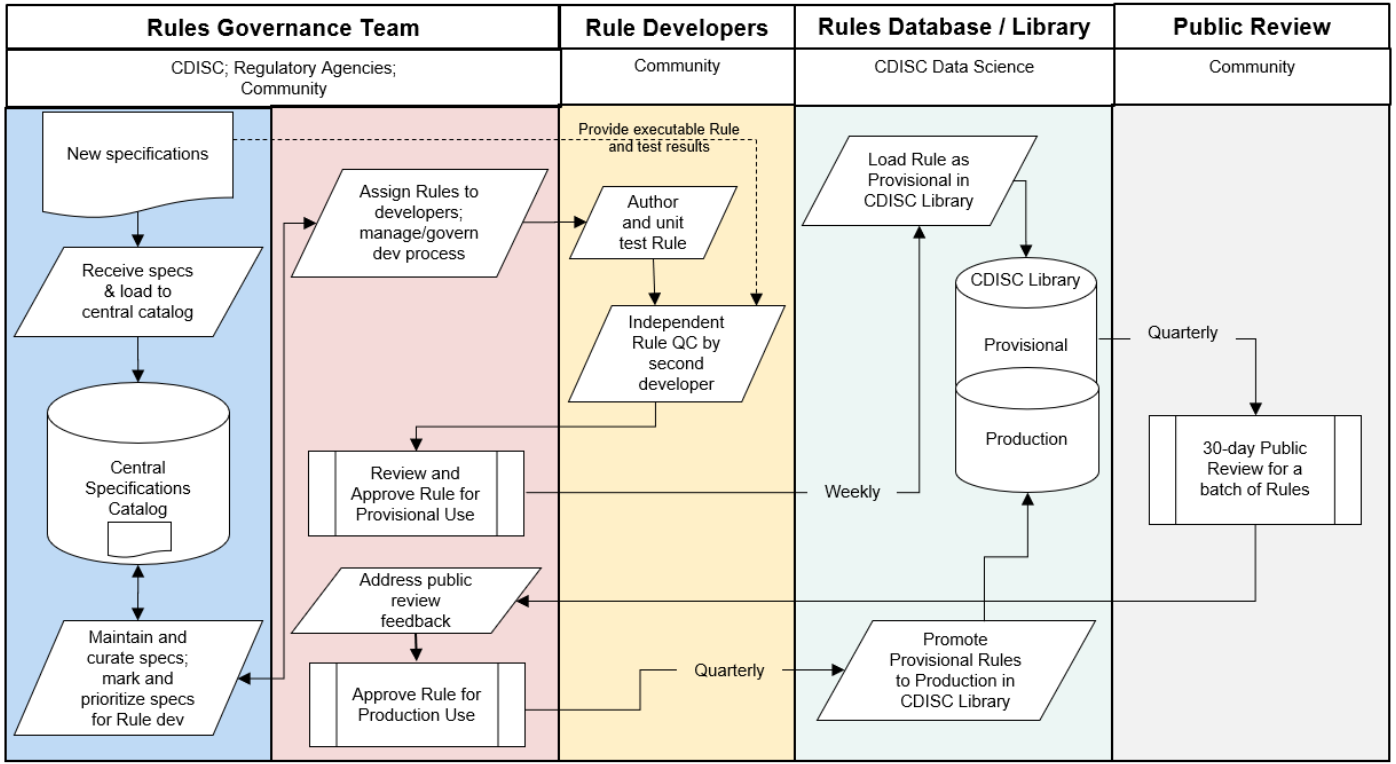
3rd Party Applications

Adoption by Regulatory Agencies

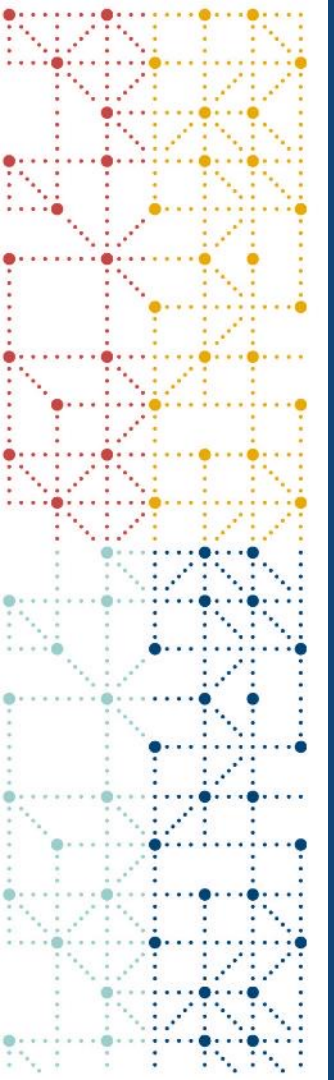
- One version of the truth will benefit the regulatory submission ecosystem
- CDISC and FDA are discussing joint governance and publication of rule specifications
- Single version of rule specifications followed by single version of executable rules implementation

A future where regulatory agencies use CORE Rules

Conformance Rules: Governed Development Process

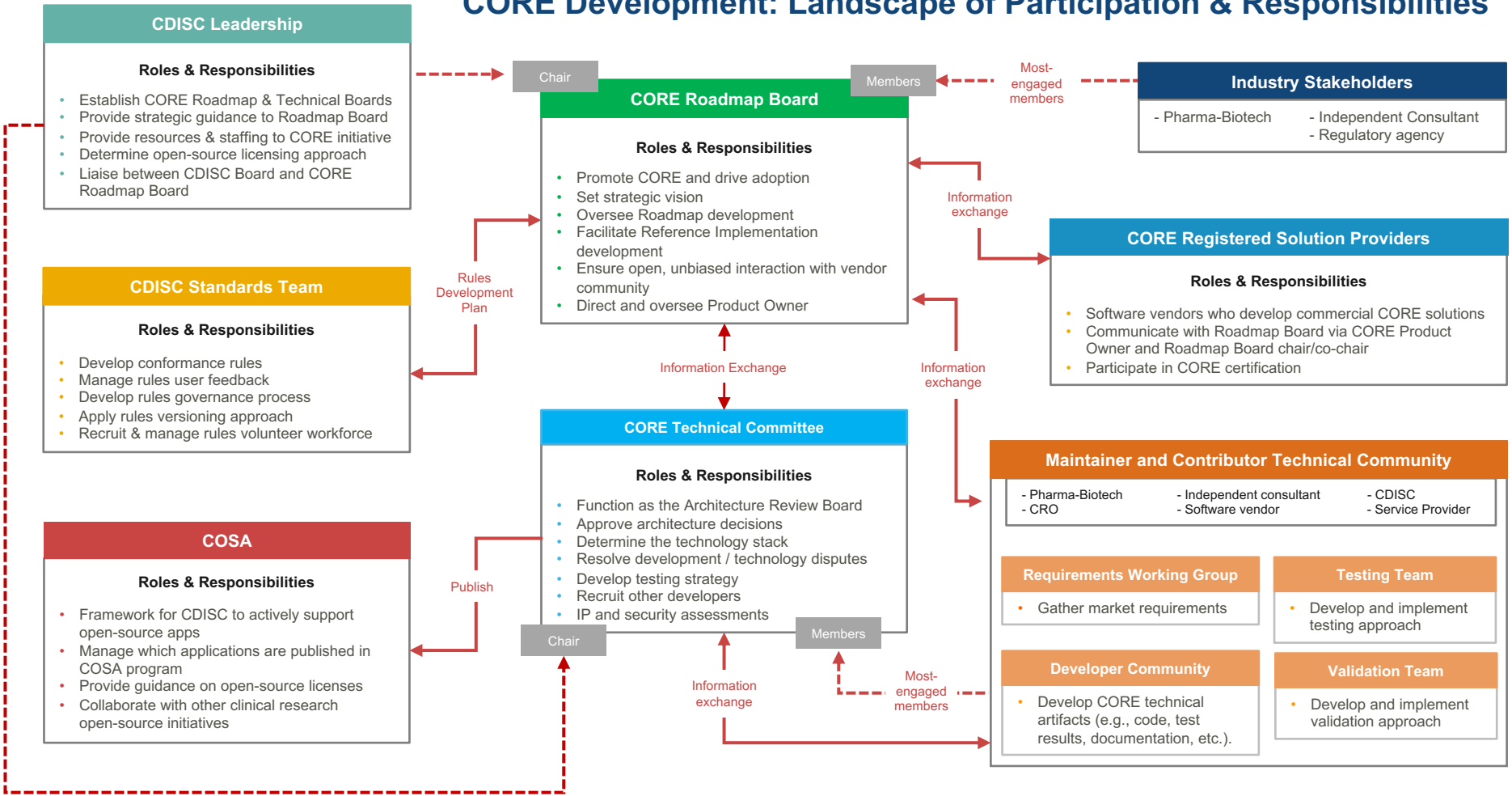


Governance model is complete; implementation is in progress



CORE Roadmap Board

CORE Development: Landscape of Participation & Responsibilities



CORE Roadmap Board Overview

Highlights of Responsibilities

- Promote CORE and drive adoption
- Set strategic vision
- Oversee Roadmap development
- Ensure open, unbiased interaction with vendor community

Membership from

- Most-engaged Pharma-Biotech; CDISC; Independent consultants; Service providers
- Software vendors opportunity to participate on CORE Technical Committee and as CORE Registered Solution Providers

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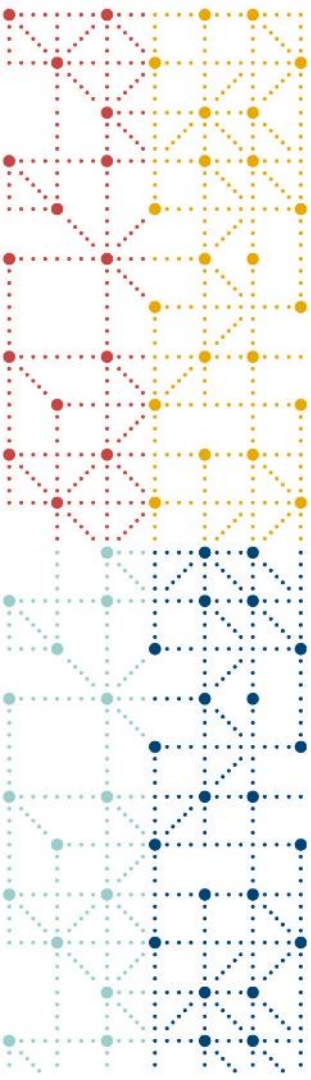

Next Steps

Next Milestone

- The complete ruleset for
  - SDTM 3.2 and SDTM 3.3
  - Define.xml crosscheck rules
  - FDA validator rules v1.6 (that apply to SDTM 3.2 and SDTM 3.3)
  - FDA rejection rules
- CORE Engine Stable Release
  - Engine can run all the rulesets above
  - Thorough testing and validation documentation
- Purpose
  - Test with real study data and roll out rules governance process

Implementers can integrate this stable version
Drive adoption and test with real study data

CORE Future State

- Rules
  - Full set of executable rules for submission standards (SDTM, SEND, ADaM)
  - Including Regulatory-specific rules
  - Including Define.xml cross-check rules

  ➔*Continuing volunteer engagement is critical!*

- CORE is the Reference Engine
  - Engine with all basic functionality for full set of machine-executable rules
  - Includes a validation package

- CDISC will establish a CORE certification program
  - To verify output of different applications versus the CORE Reference Engine
  - CDISC conformance rules are the single version of the truth

Rules are part of the Standards!
Expect Regulatory Agencies to mandate use of CDISC Conformance Rules

Thank You!