WITH STANDARDS – UNLOCK THE POWER OF DATA

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2022
US
INTERCHANGE
26-27 OCTOBER | AUSTIN

CDISC Conformance rules and the CORE engine

Progress and roadmap

Peter Van Reusel
26 October 2022

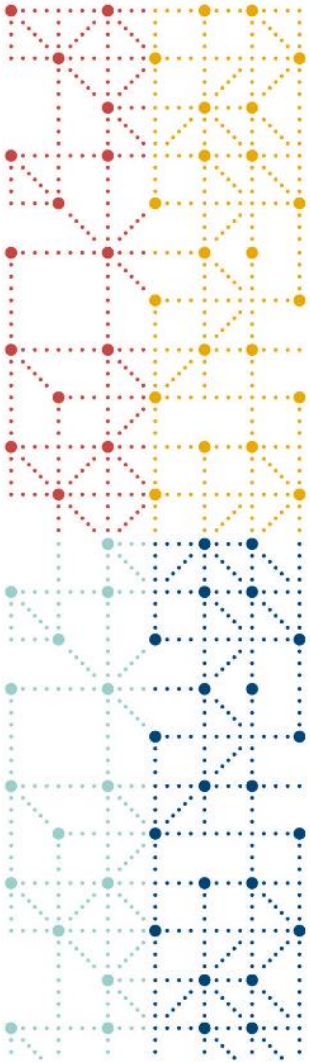
Meet the Speaker

Peter Van Reusel

Title: Chief Standards Officer
Organization: CDISC

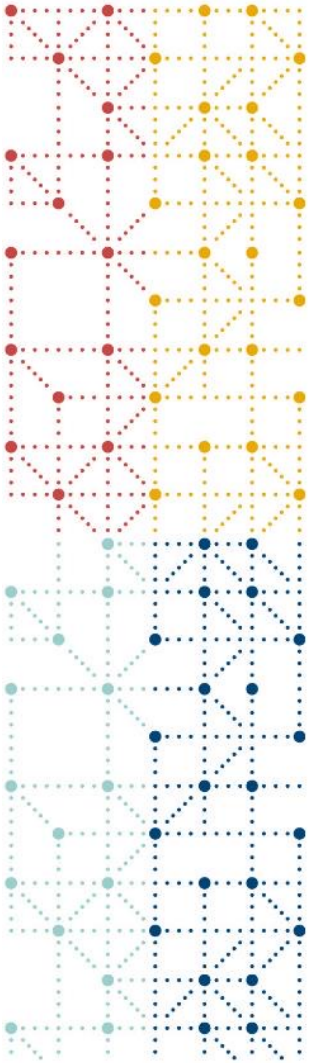
Peter Van Reusel provides executive leadership to the development and implementation of clinical standards in line with CDISC's strategy and operational plans, working closely with the President and CEO, as well as CDISC staff and stakeholders. He has over 20 years' experience in senior roles in pharma 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.



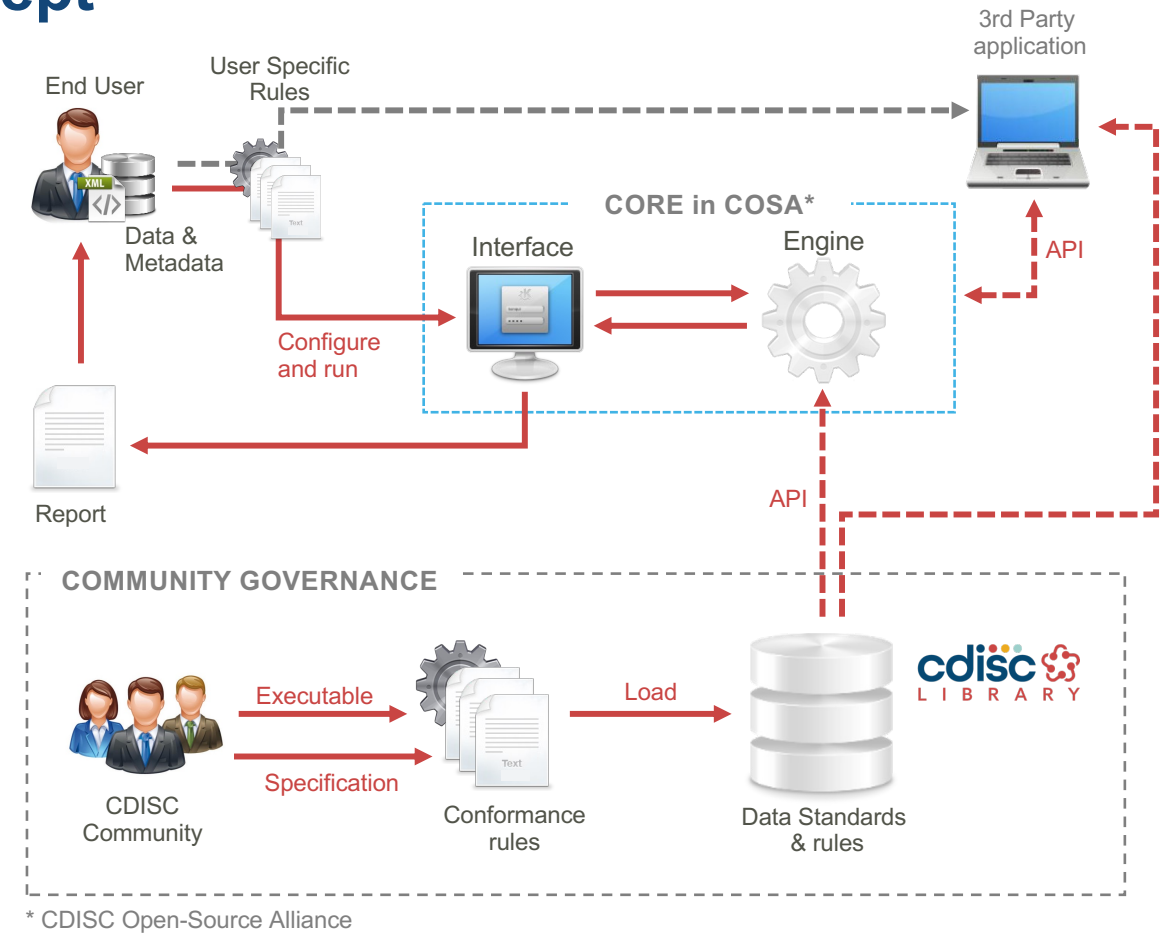
Agenda

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



Concept of CORE

CORE Concept



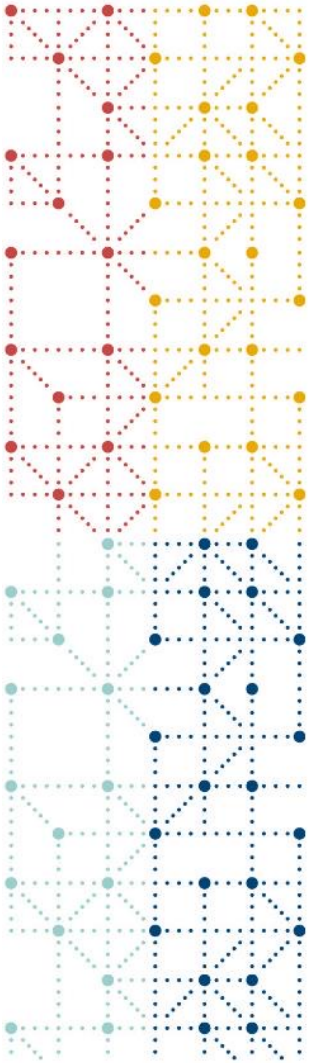
* CDISC Open-Source Alliance

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)

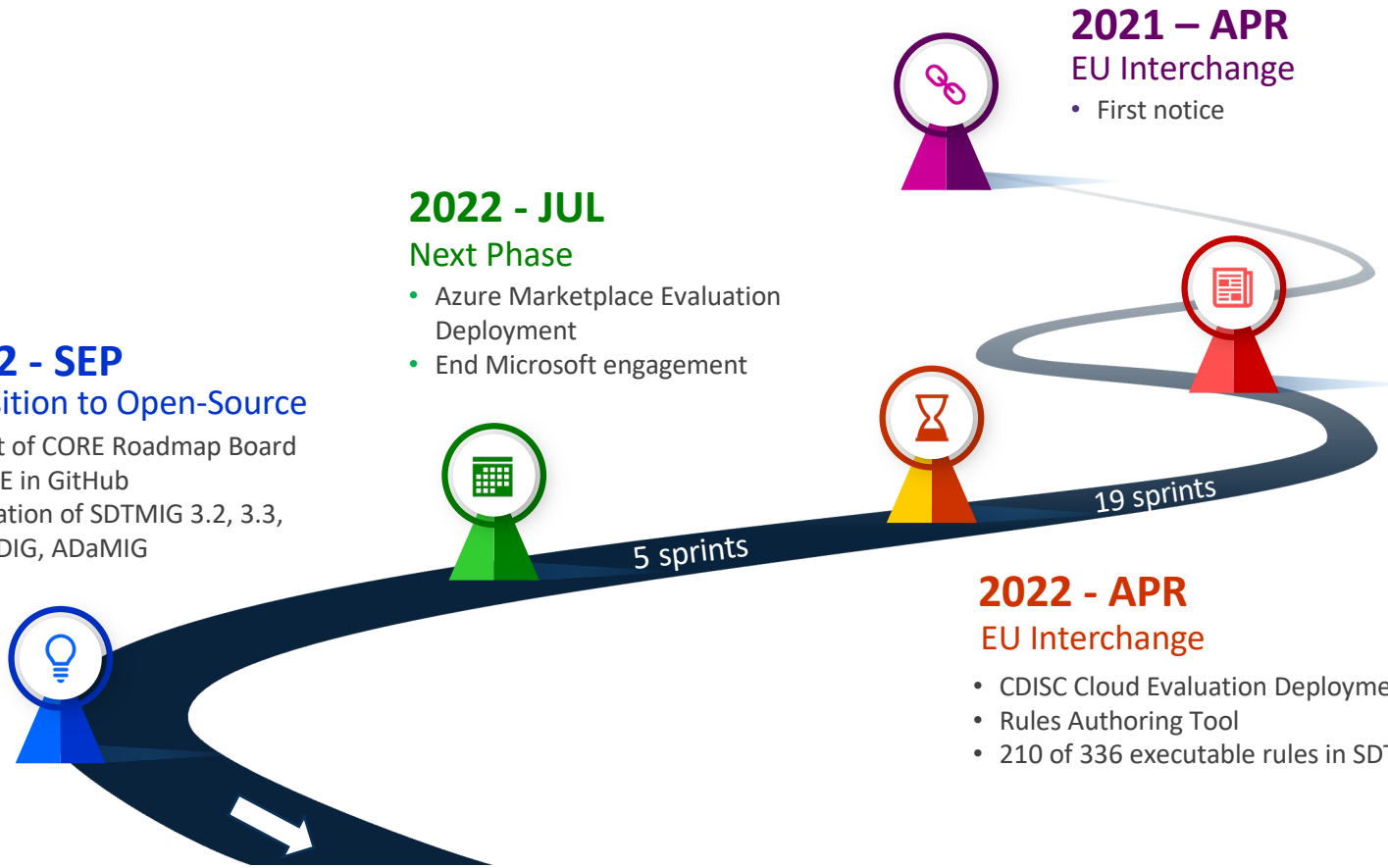
➡ *CORE Initiative = Rules + Engine*

https://www.cdisc.org/core



High-level Status and Roadmap

CORE To Date



2022 - SEP
Transition to Open-Source

- Start of CORE Roadmap Board
- CORE in GitHub
- Initiation of SDTMIG 3.2, 3.3, SENDIG, ADaMIG

2022 - JUL
Next Phase

- Azure Marketplace Evaluation Deployment
- End Microsoft engagement

2021 – APR
EU Interchange

- First notice

2021 - JUL
Kick-off

- Kick-off meeting
- Start Microsoft engagement
- Sprint 0

2022 - APR
EU Interchange

- CDISC Cloud Evaluation Deployment
- Rules Authoring Tool
- 210 of 336 executable rules in SDTMIG 3.4

CORE Program Roadmap

Q3 2023 – Q2 2024

Production Release 2: 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 – Q2 2023

Production Release 1: 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

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 – not achieved yet

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Vendor/User

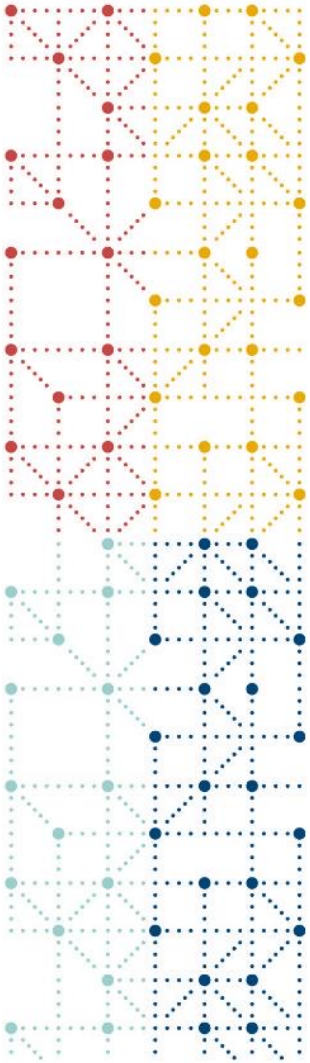
Assessment to Date

Major accomplishments

- Quick establishment of YAML schema
- Rule authoring tool
- Signs of life (deployment of evaluation versions)
- Release as open-source in GitHub

Next focus

- Standalone desktop deployment to drive adoption
- Complex rules and volunteer engagement
- Acceptance by Regulatory Agencies



CORE Rules

Rule Development Process

- Express human-readable rule specification in machine-readable form
- Enter it in CORE Rule Editor using a structured language (YAML)
- Start with a template or copy from an existing similar rule
- Rule Editor provides hints & completion suggestions, & structures the syntax for visual review

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.				

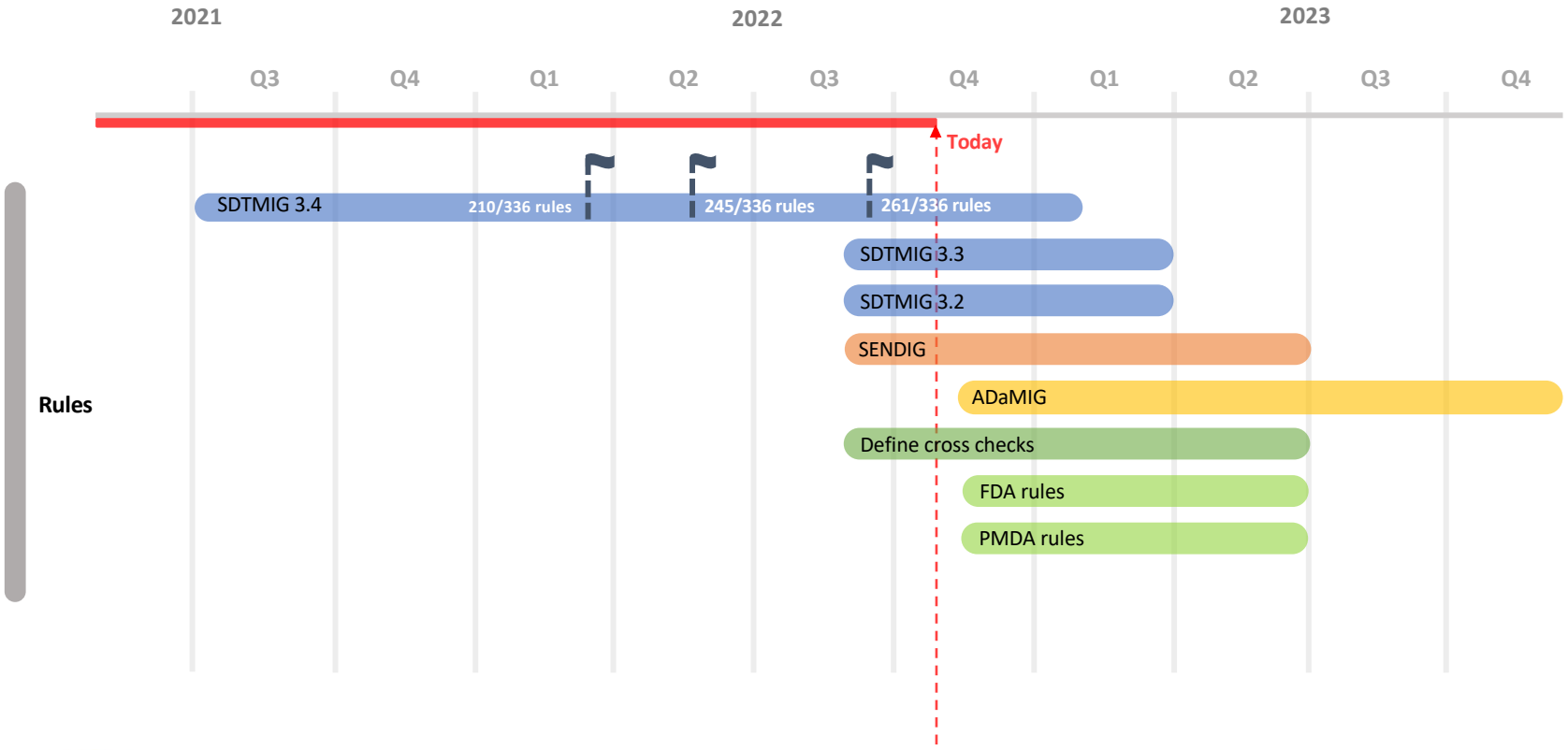
Executable Rule (YAML) in Rule Editor

```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 Count by Standard/Version

Foundational Standard	Rule Count
SDTMIG v3.4	336 fully executable 445 total rules
SDTMIG v3.2	416 total rules
SDTMIG v3.3	450 total rules
SENDIG v3.1	303 total rules
ADaMIG v1.3	595 total rules
Other Rules	
Regulatory Rules FDA	SDTMIG (3.3/3.2) 186 SENDIG (3.0/3.1) 175
Regulatory Rules PMDA	To be analyzed
Define-XML Cross-Check	Definitions are being generated (±172)

Rules Development Timeline



Rule Developer Skill Set

Core Skills

- Data savvy with science background; e.g., statistics, biometrics, data science
- A CDISC standards practitioner. Solid implementation experience with SEND, SDTM, and/or ADaM
- Experience in data specifications & associated verification & validation tasks

"Plus" Skills

- Some familiarity with the associated conformance rules
- Knowledgeable in structured data, such as XML, JSON, YAML
- A member of an organizational standards council or governance body

Rule Developer Onboarding Process and Support

Training tools on the wiki, will further refine

Training webinars

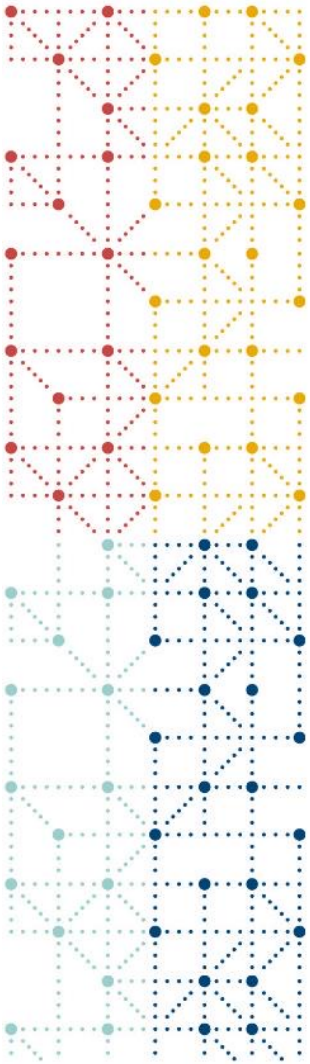
Rule Workshops at F2F meetings

Weekly 1-hour CORE Rules Developer Meeting

Weekly 2-hour CORE Rules Developer "Office Hours"

Volunteers needed!

Currently limited number of active volunteers from industry



CORE Engine & Deployments

What does the CORE Engine do?

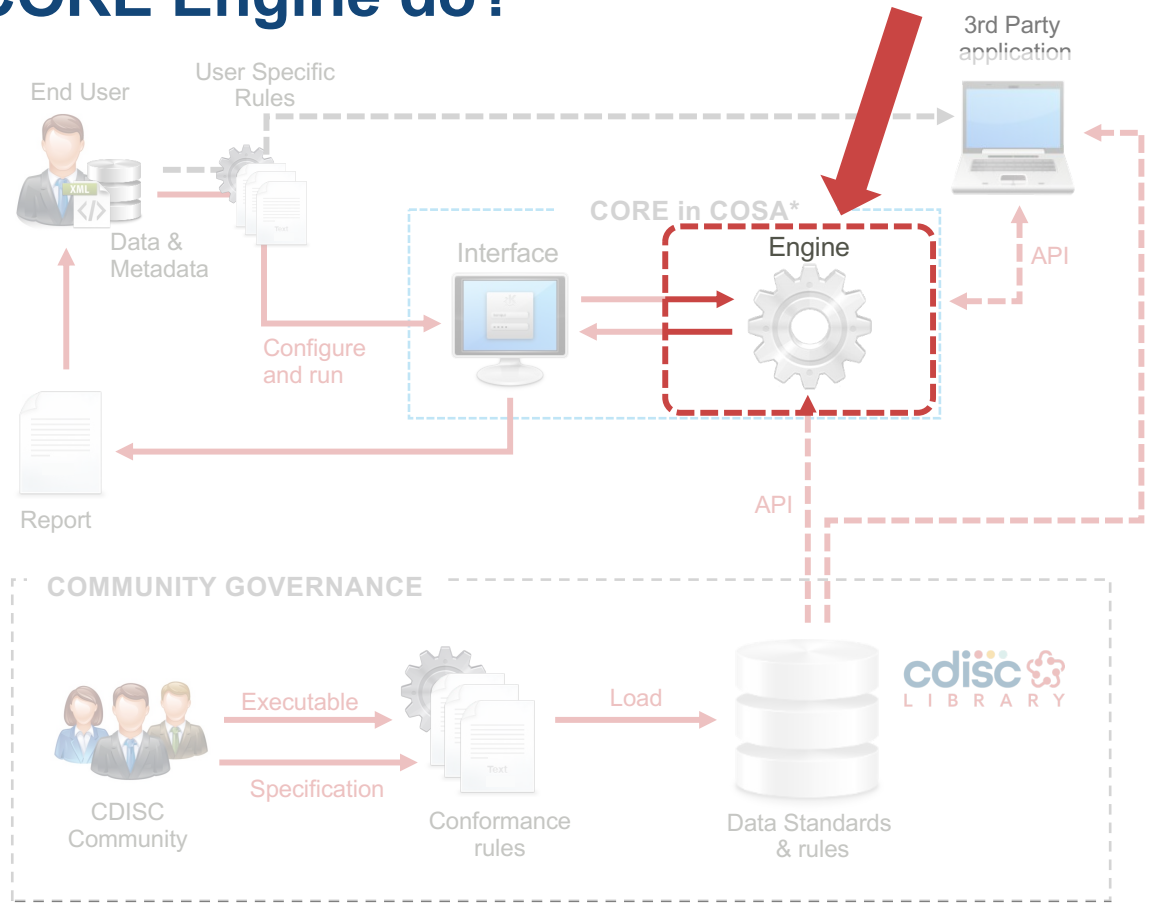
CORE Engine

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 enhanced reporting



* CDISC Open-Source Alliance

CORE Engine is Open-Source

- Development transitioned to open-source framework during summer of 2022
  - Guided by the CORE Roadmap Board and CORE Technical Committee
  - Listed in the COSA (CDISC Open-Source Alliance) directory
  - Permissive MIT open-source license

- Development and validation is the domain of the open-source community
- Free to all in greater CDISC community, who can deploy it in their preferred environment (e.g., cloud, on-premises standalone/desktop, on-premises server)
- Provided to greater CDISC community via GitHub
- CORE Engine in GitHub has a command line interface (CLI) for execution

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CORE Engine Deployment

- CORE Engine deployments are the domain of the greater CDISC community, including commercial software vendors
  - Prepared by and for the user community
  - Commercial vendors offerings for the user community
- 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
  - Is separate from CORE Engine validation which is done by the open-source community

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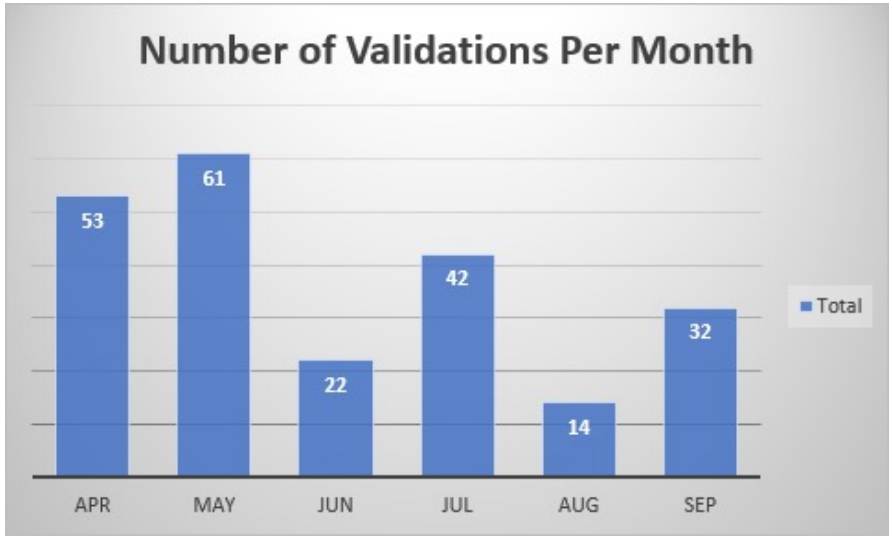
CORE Engine Deployments

Available → | Planned →

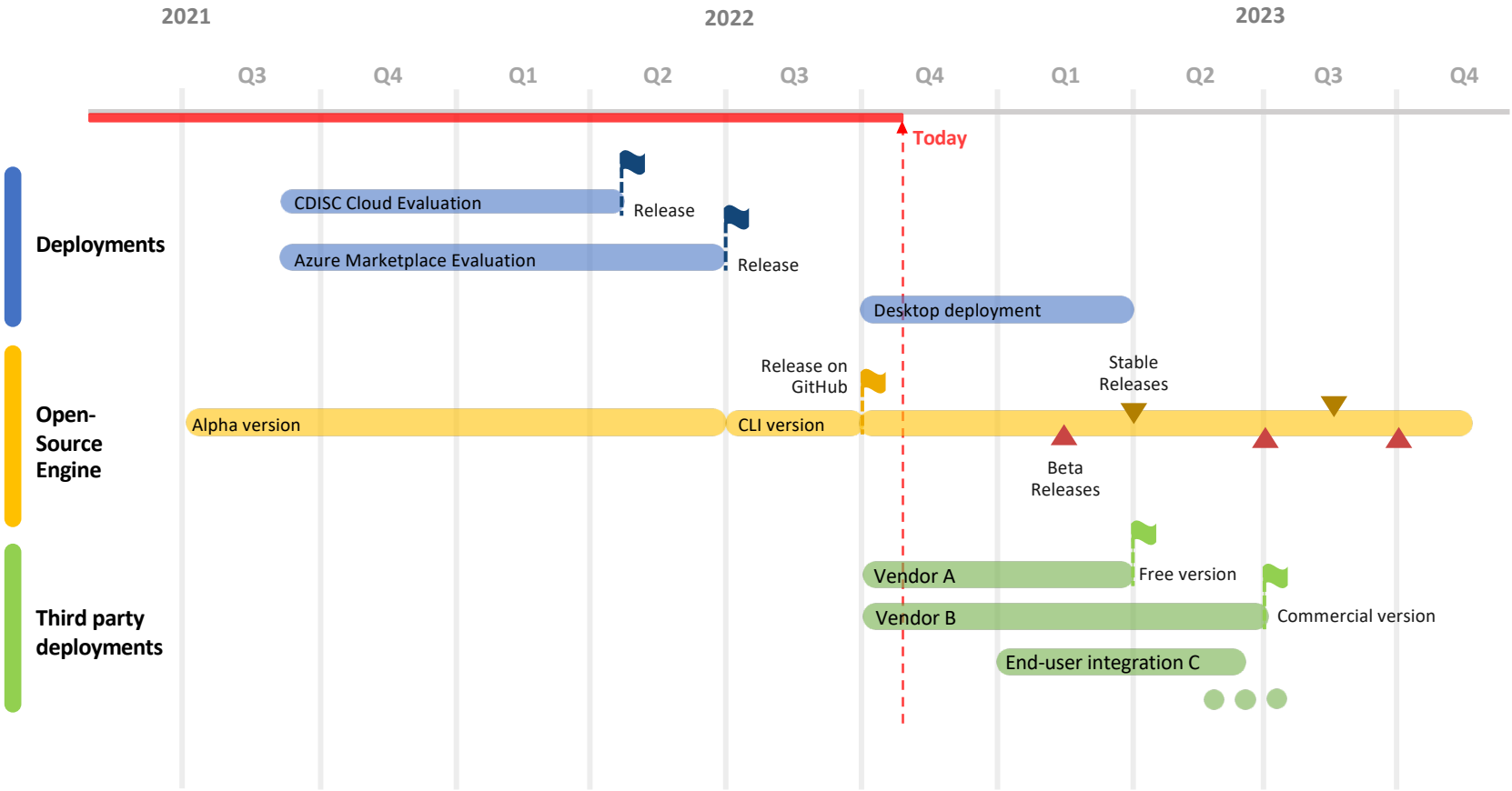
	CDISC Cloud Evaluation	Azure Marketplace Evaluation	Desktop
Feature			
Engine evaluation version	✓	✓	Current Engine version
Cloud Deployment	✓	✓	X
Standards Rules from CDISC	✓	✓	✓
User Rules can be added	X	✓	✓
Test data from CDISC	✓	X	X
User data can be added	X	✓	✓
Validate multiple studies concurrently	X	✓	✓
Secure Data Handling	N/A	✓	Depends upon infrastructure
Free to use	✓	X	✓

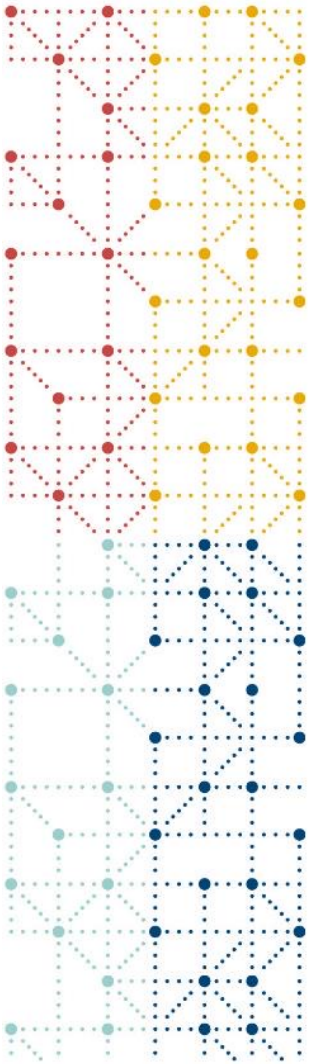
CDISC Cloud Evaluation Deployment: Validation runs

- APR: CORE launch
- MAY: workshop PHUSE US connect
- 1400 new CDISC Library accounts
- 224 validation runs
- 90 individuals



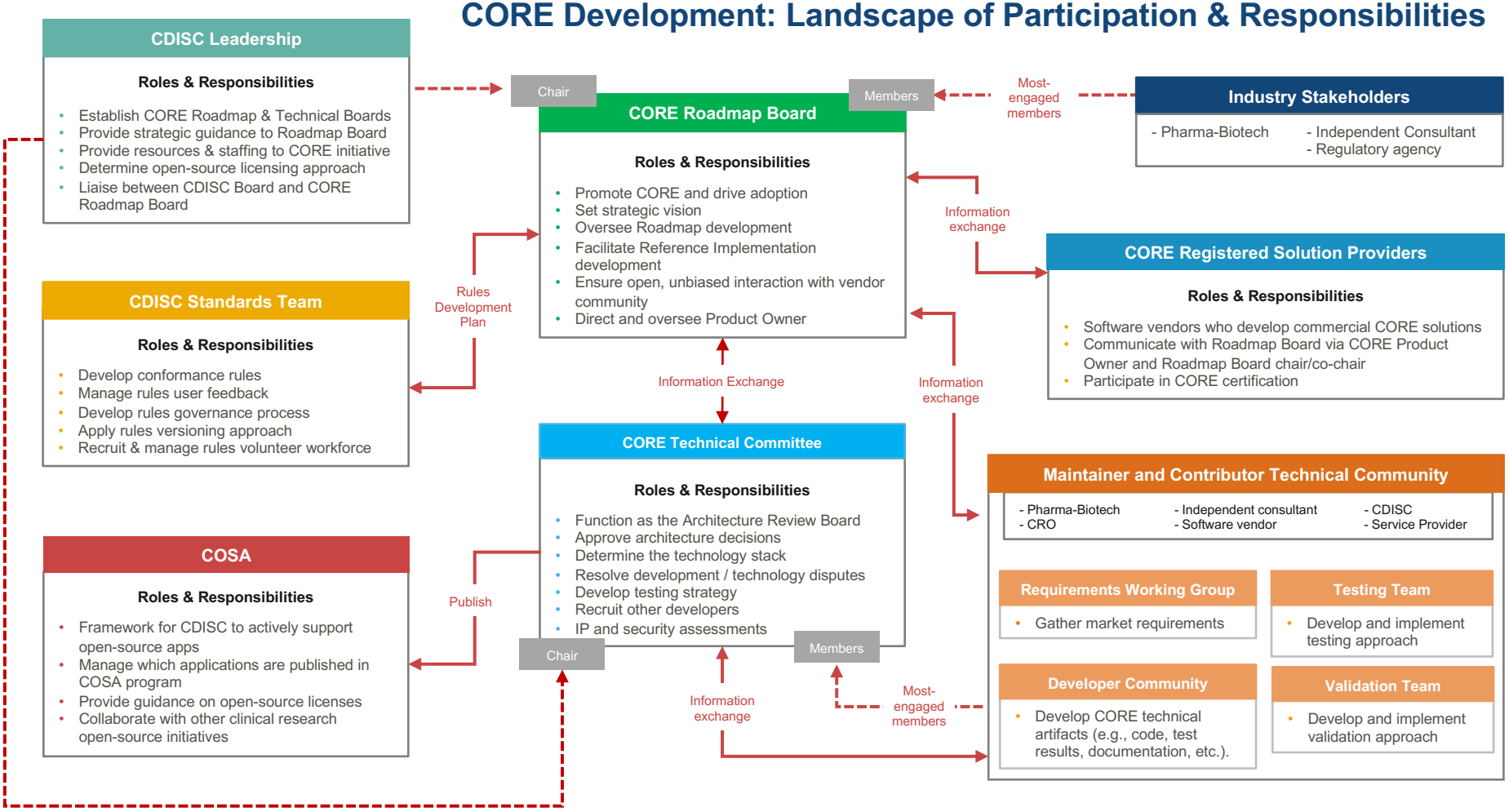
Engine and Deployments Timeline





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
- Facilitate Reference Implementation 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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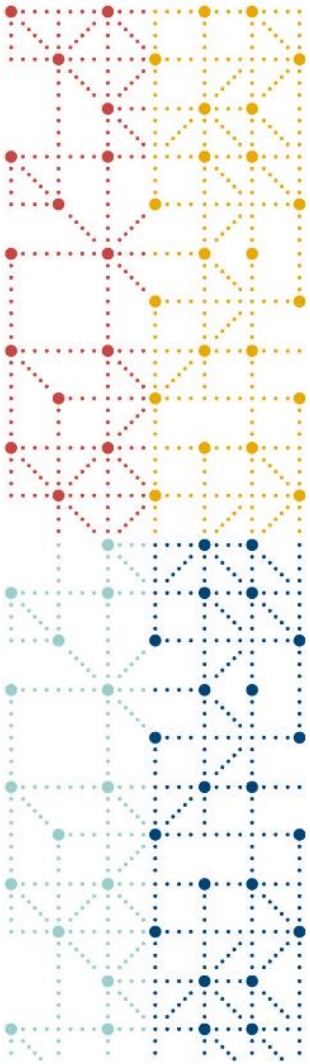
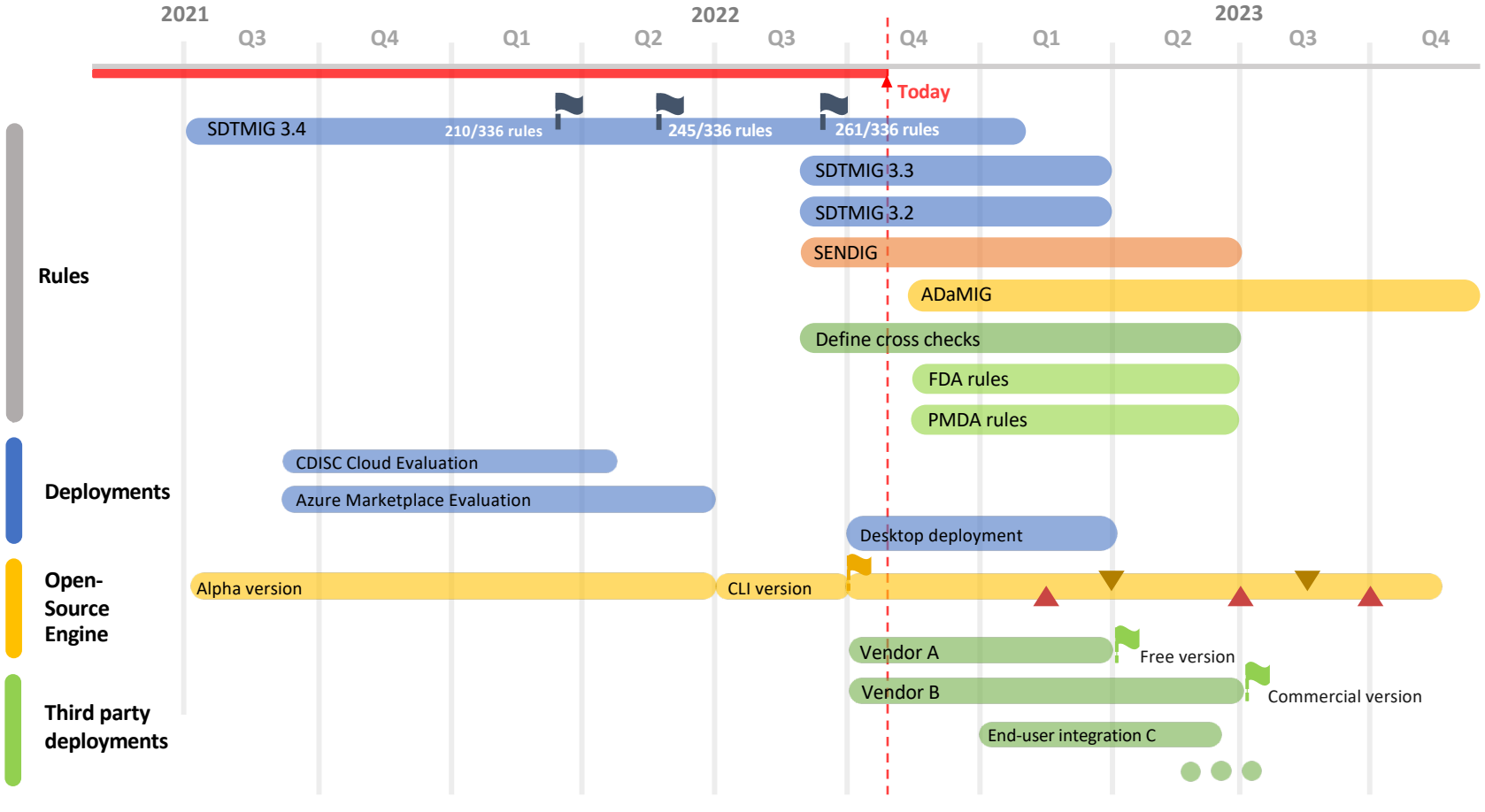


Next Steps

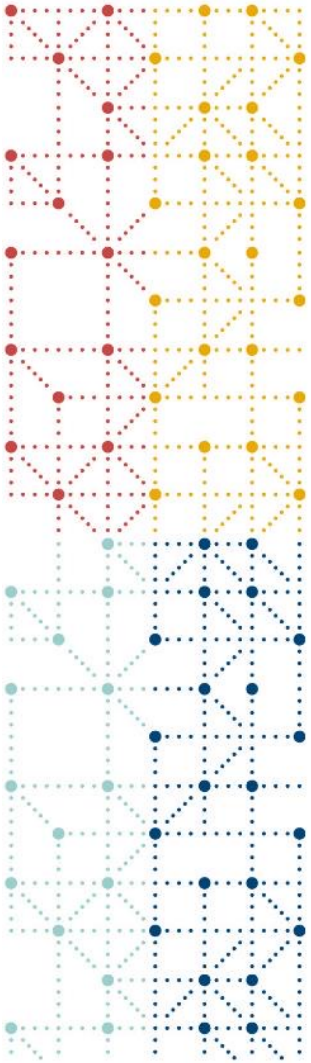
CORE Timeline



What is submission-ready CORE?

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

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