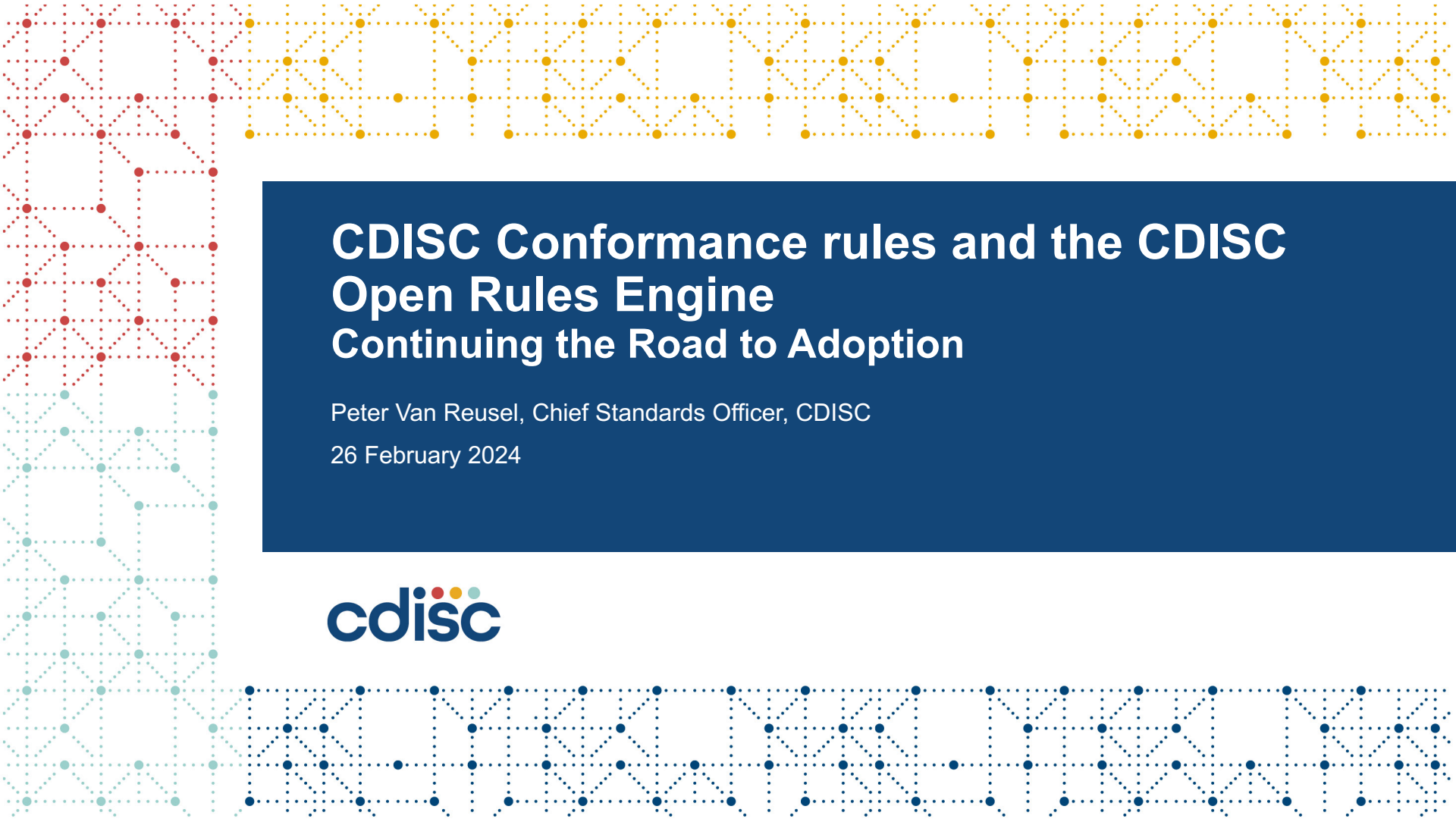




CDISC Conformance rules and the CDISC Open Rules Engine

Continuing the Road to Adoption

Peter Van Reusel, Chief Standards Officer, CDISC

26 February 2024





Agenda

- CORE Concept
- Conformance Rules
- Rules Governance Model
- CORE Engine and Deployments
- What's Next



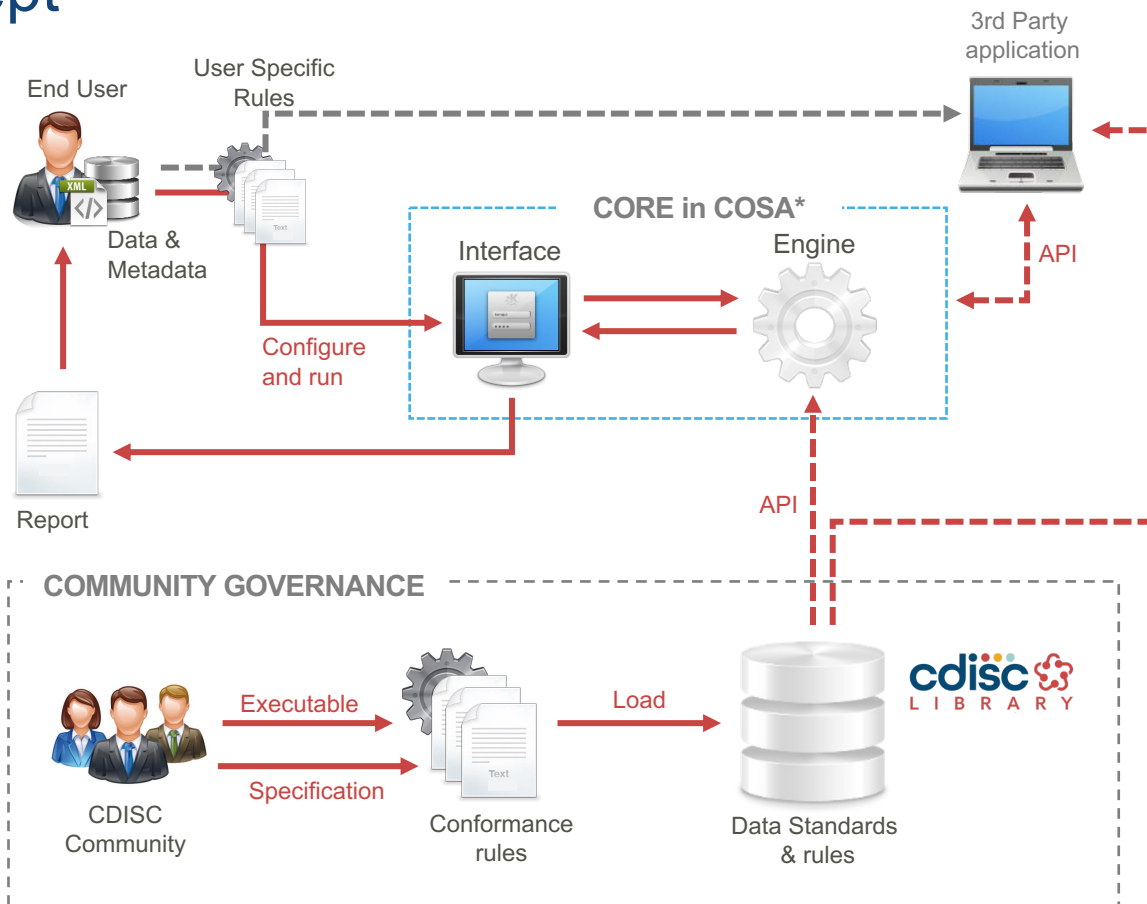
CORE Concept

The Challenge

A single source of truth for all conformance rules

Consistency across conformance rule implementations

CORE Concept





Conformance Rules

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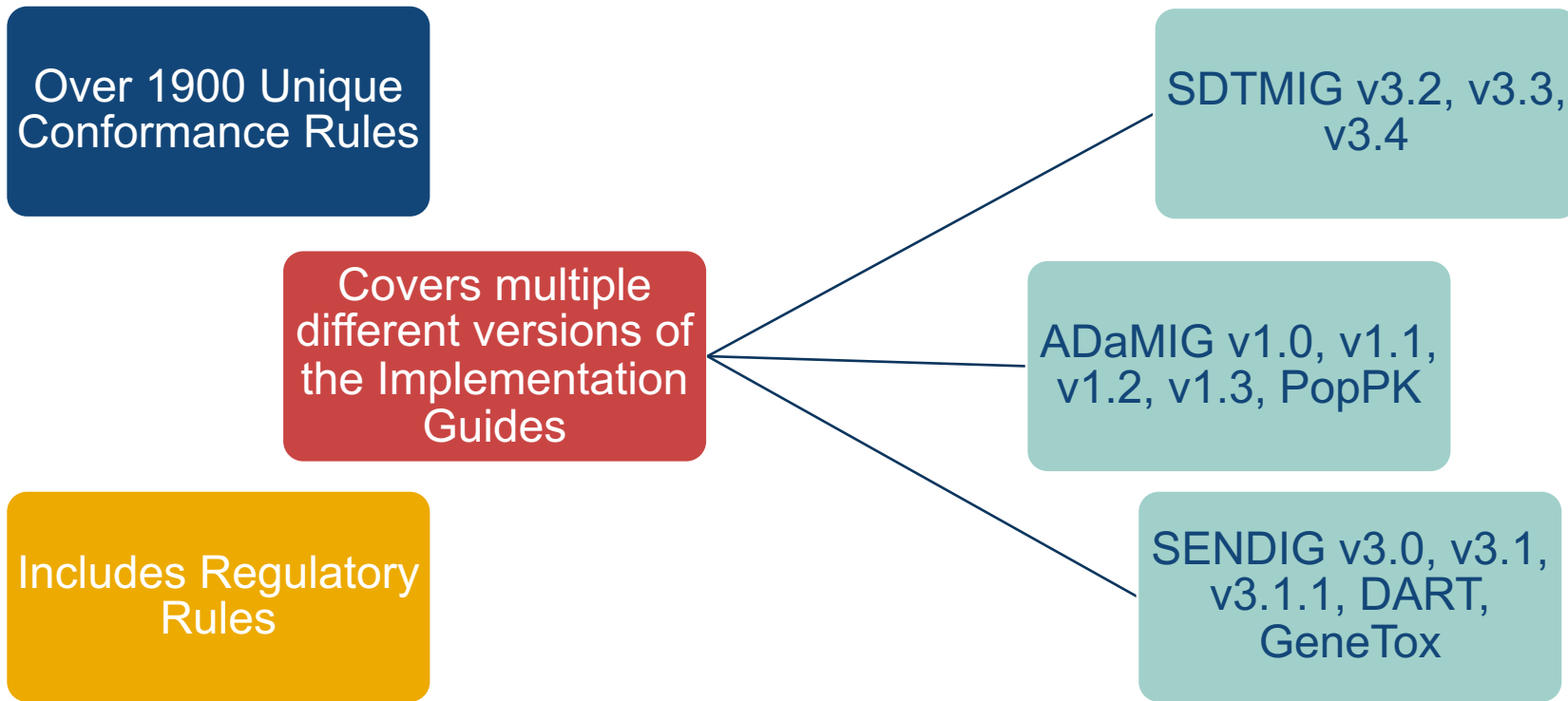
1  # Variable: EXMETHOD
2  # Condition:
3  # Rule: EXMETHOD not present in dataset
4  Authorities:
5    - Organization: CDISC
6      Standards:
7        - Name: SDTMIG
8          References:
9            - Citations:
10              - Cited Guidance: Method of administration of the treatment. Not to be used with
11                human clinical trials.
12                Document: Model v1.7
13                Item: EXMETHOD
14                Section: Table 2.2.12.1
15                Origin: SDTM and SDTMIG Conformance Rules
16                Rule Identifier:
17                  Id: CG0568
18                  Version: '1'
19                  Version: '2.0'
20                  Version: '3.3'
21  Check:
22    all:
23      - name: EXMETHOD
24        operator: exists
25  Core:
26    Id: CORE-000326
27    Status: Published
28    Version: '1'
29    Description: Trigger error when EXMETHOD exists in the EX dataset for human clinical trials
30    Executability: Fully Executable
31    Outcome:
32      Message: EXMETHOD is not to be used with human clinical trials
33    Rule Type: Record Data
34    Scope:
35      Classes:
36        Include:
37          - INTERVENTIONS
38      Domains:
39        Include:
40          - EX
41    Sensitivity: Record
42

```

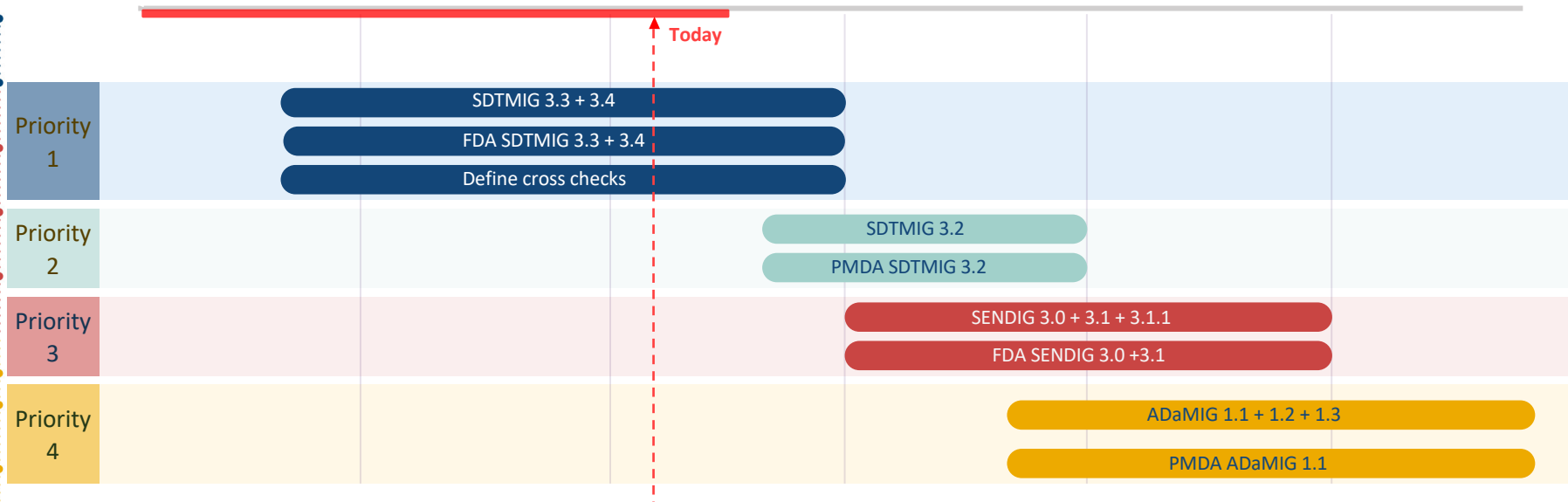
CORE Rule Editor

- Web-based application, no software to install
- Structured document, 1 CORE rule per file containing rule's metadata & check logic
- Real-time syntax checking

Volume and Breadth of Conformance Rules



Rules Development Priority



➡ *Timelines depend on community engagement*

Developing CORE Rules in the Future



Plan to draft the rule logic within the CORE Rules Editor



Use the Rule Description and Outcome Message to review rule during Internal and Public Review



Cited Guidance is part of the Rule



Rule Logic is transparent



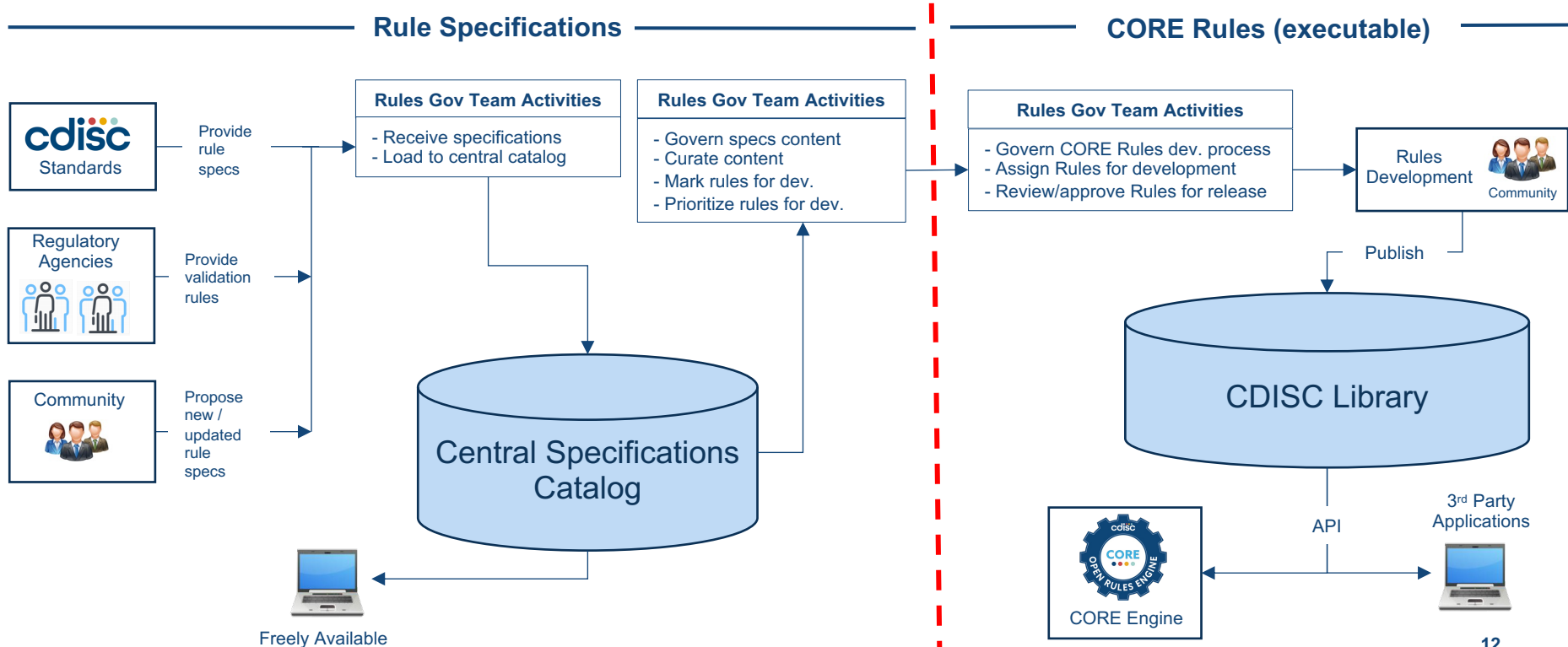
Rules Governance Model

CORE Rules Governance

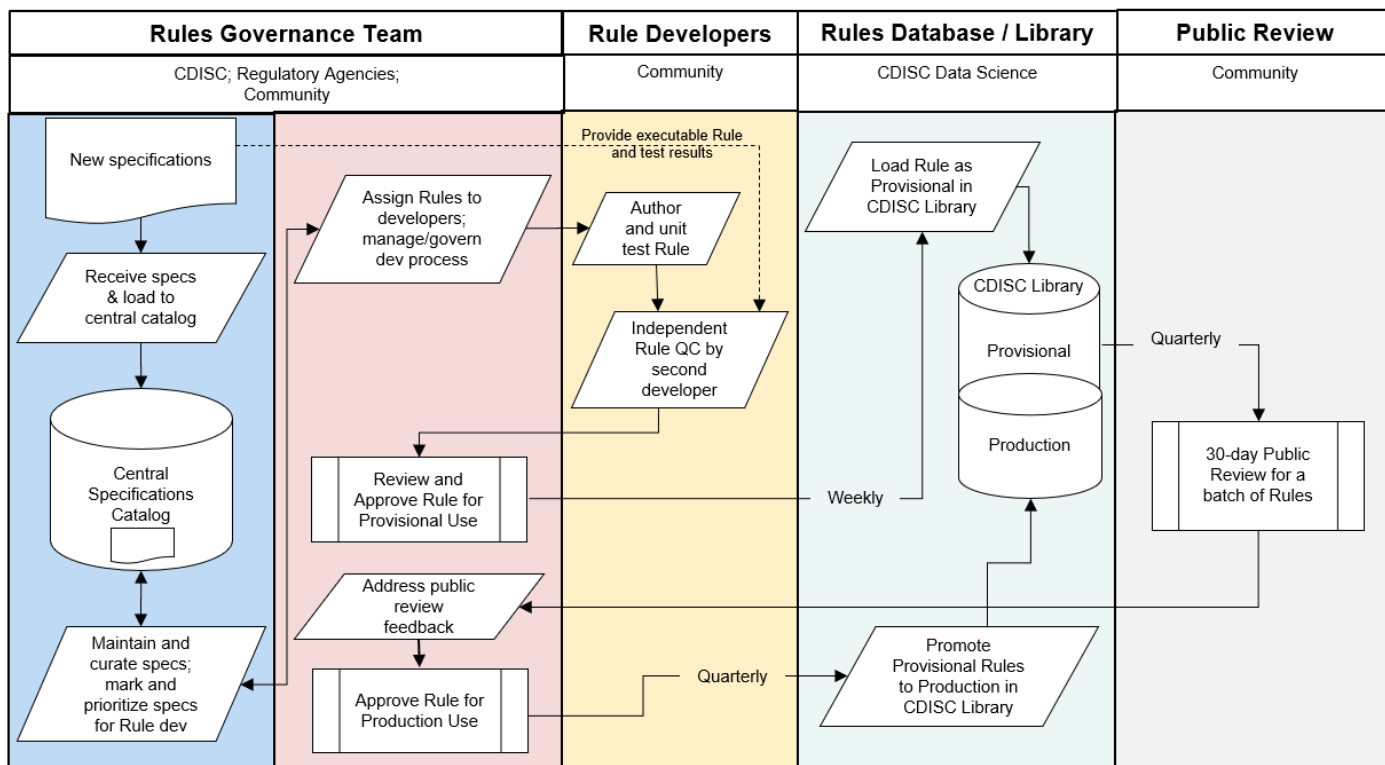


Rules Governance Team

(CDISC; Regulatory Agencies; Community)



Conformance Rules: Governed Development Process



➡ *Governance model is complete; implementation is in progress*



CORE Engine and Deployments

CORE Software: Engine and Rule Editor

- Each project
 - Has a public GitHub repository on the cdisc-org account and is listed on the COSA Directory
 - Has been released under the MIT open-source license
 - Development is led by CDISC
 - Still under development, but are being actively used
 - Can be extended (supports the development of software extensions)
- CORE Engine
 - Written in Python
 - Makes use of the Venmo Business Rule Engine
- CORE Rule Editor
 - Written in TypeScript
 - Makes use of the VSCode editor



Running the CORE Engine

- Source Code
 - Available on GitHub using the MIT open-source license
- CLI executable available in GitHub
 - Cached rules
 - Windows, Mac, and Linux install packages
 - Unzip and run
 - Will need datasets to validate
- Engine available on PyPI
 - Engine is a component that can be used in your own code
- Desktop versions
 - Vendor released versions of CORE
 - Includes a user-friendly UI
 - Easier for non-technical users to evaluate
- View a short CORE demonstration
 - <https://www.cdisc.org/core>
 - See **CORE on GitHub** tab



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
- First free, publicly available, vendor-provided CORE desktop version announced at the CDISC European Interchange
- CORE is a Reference Implementation
 - The principle is commonly used in the software industry
 - Provides a concrete example on how the standard should be implemented

 *Drive adoption*



CORE Registered Solution Provider

- Program purpose
 - For CORE vendors (solution providers)
 - Certify with CDISC that their solutions correctly use the Conformance Rules
 - For CDISC
 - Treat all CORE vendors equally
 - Achieve a level playing field regarding use of any Engine with the Conformance Rules
 - Inform the community which solutions have been certified
- Testing for certification will include
 - Generating results with Conformance Rules and test study data reflecting an “average study”
 - No system functionality testing



What's Next

Research Collaboration Agreement with US FDA CDER & CBER



CDISC and FDA working together to develop executable formats of the FDA Business Rules and on the development and ongoing governance of this set of executable rules within CORE that can be used by industry



The benefits of creating a single source of truth for all FDA validation needs increases transparency for all stakeholders on how FDA checks data for conformance to CDISC standards and to existing FDA Business Rules

CDISC is Proud to Announce a Research Collaboration to Incorporate FDA Business Rules into CORE

Austin, TX – January 16, 2024 – CDISC is proud to announce a research collaboration with the U.S. Food and Drug Administration's Office of Translational Sciences in the Center for Drug Evaluation and Research and Office of Regulatory Operations in the Center for Biologics Evaluation and Research to incorporate FDA Business Rules into CDISC's Open Rules Engine (CORE).

CDISC's CORE project provides an open-source version of the CDISC Conformance Rules in a machine-executable format. These rules, published and managed by CDISC, create a single source for conformance rules and allow external vendors and sponsor companies to implement and extend these rules within their tools. [FDA Business Rules](#) are currently written in a plain text, non-machine executable format and describe the business requirements for regulatory review to help ensure that clinical trial study data is compliant and useful and supports meaningful review and analysis.

The goal of this effort, which began on November 3, 2023 and has term of three years, is to collaborate on providing input on machine-executable formats of the FDA Business Rules and on the development and ongoing governance of this set of executable rules within CORE that can be used by sponsors of medical product applications.

FDA Business Rule ID		FDA Business Rule
Clinical and Nonclinical		
DAB008		All treatment exposure date/time should be between first and last study treatment date/time.
DAB009		All paired variables should have a one-to-one relationship. Examples include short name and name of test; parameter name and parameter code or number; variable name and variable label, etc.
DAB011		All trial design data should be submitted as specified in the FDA Study Data Technical Conformance Guide (TCG).
DAB012		Deprecated in v1.5.
DAB013		Deprecated in v1.5.
DAB015		Character values should not have leading spaces or only have a period character.
DAB016		Collection study day should be populated when date/time of collection is available.
DAB017		Controlled terms should use the exact term (case, spelling, and punctuation) used by the terminology maintenance organizations (e.g., MedDRA, CDISC controlled terminology).
DAB018		A variable's length across a study should be no longer than the maximum length of the actual data (except for SUPPQUAL).
DAB019		SUPPQUAL variable length should be no longer than the maximum length of the actual data.

Adoption by Industry

- TransCelerate Digital Data Flow
 - Conformance Rule Proof of Concept on Unified Study Definition Model (USDM)
- Tobacco Implementation Guide
 - Creating new TIG-specific rules
 - Aligning with existing conformance rules
- Various Implementations with Vendors, Sponsors, and CROs



Moving forward with additional implementations



Next Milestone

- The complete ruleset for
 - SDTM 3.3 and SDTM 3.4
 - Define.xml crosscheck rules
 - FDA business rules v1.5 (that apply to SDTM 3.3 and SDTM 3.4)
 - FDA Technical Rejection Criteria
- 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*



In Summary

- Rules
 - Full set of executable rules for submission standards (SDTM, SDTMIG, SENDIG, ADaMIG)
 - 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!

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