CDISC Conformance rules and the CORE engine

Progress and roadmap

Peter Van Reusel
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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**

**COMMUNITY GOVERNANCE**

- CDISC Community
- Specification
- Conformance rules
- Data Standards & rules
- 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

2022 - APR
EU Interchange
- CDISC Cloud Evaluation Deployment
- Rules Authoring Tool
- 210 of 336 executable rules in SDTMIG 3.4

2021 - JUL
Kick-off
- Kick-off meeting
- Start Microsoft engagement
- Sprint 0

2021 - APR
EU Interchange
- First notice
CORE Program Roadmap

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

Q3 2022 – Q2 2023

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

Q3 2021 – Q2 2022

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 2023 – Q2 2024

Establish CORE Roadmap Board
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

<table>
<thead>
<tr>
<th>Rule ID</th>
<th>SDTM/IG Version</th>
<th>Rule Version</th>
<th>Class</th>
<th>Domain</th>
<th>Variable</th>
<th>Condition</th>
<th>Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG0225</td>
<td>3.4</td>
<td>1</td>
<td>ALL</td>
<td>ALL</td>
<td>VISITDY</td>
<td>VISITNUM is NOT in TV:VISITNUM</td>
<td>VISITDY = null</td>
</tr>
</tbody>
</table>

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

```
1 Core
2 ID: CDISC_SOPGM.CG0225
3 Version: "1"
4 Authority: CDISC
5 Description: Trigger error if VISITDY is populated when VISITNUM is not in TV.
6 References:
7 Origin: SDTM and SDTM Conformance Rules
8 Rule Identifier
9 ID: VAMS
10 Version: "1"
11
12 Version: "3.8"
13 Severity: Warning
14 Rule Type: Value Present
15 Source
16 Include:
17 All
18 Domain:
19 Include:
20 All
21 Standards
22 Name: SDTM
23 Version: "3.4"
24 Operations:
25 domain: TV
26 if VISITNUM
27 name: VISITNUM
28 operator: =
29```
# Rule Count by Standard/Version

<table>
<thead>
<tr>
<th>Foundational Standard</th>
<th>Rule Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDTMIG v3.4</td>
<td>336 fully executable</td>
</tr>
<tr>
<td></td>
<td>445 total rules</td>
</tr>
<tr>
<td>SDTMIG v3.2</td>
<td>416 total rules</td>
</tr>
<tr>
<td>SDTMIG v3.3</td>
<td>450 total rules</td>
</tr>
<tr>
<td>SENDIG v3.1</td>
<td>303 total rules</td>
</tr>
<tr>
<td>ADaMIG v1.3</td>
<td>595 total rules</td>
</tr>
</tbody>
</table>

## 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

- SDTMIG 3.4
  - 210/336 rules
  - 245/336 rules
  - 261/336 rules

- SDTMIG 3.3
- SDTMIG 3.2
- SENDIG
- ADaMIG
- Define cross checks
- FDA rules
- PMDA rules

2021
- Q3
- Q4

2022
- Q1
- Q2
- Q3
- Q4

2023
- Q1
- Q2
- Q3
- Q4
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
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
# CORE Engine Deployments

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

- **Open-Source Engine**
  - Alpha version
  - CLI version

- **Third party deployments**
  - Vendor A: Free version
  - Vendor B: Commercial version
  - End-user integration C

- **Deployments**
  - CDISC Cloud Evaluation
  - Azure Marketplace Evaluation
  - Desktop deployment
  - Release on GitHub
  - Stable Releases
  - Beta Releases

- **Timeline**
  - Q1
  - Q2
  - Q3
  - Q4
  - 2021
  - 2022
  - 2023
CORE Roadmap Board
## CDISC Leadership

title: Roles & Responsibilities
- Establish CORE Roadmap & Technical Boards
- Provide strategic guidance to Roadmap Board
- Provide resources & staffing to CORE initiative
- Determine open-source licensing approach
- Liaise between CDISC Board and CORE Roadmap Board

## CDISC Standards Team

- **Roles & Responsibilities**
  - Develop conformance rules
  - Manage rules user feedback
  - Develop rules governance process
  - Apply rules versioning approach
  - Recruit & manage rules volunteer workforce

## COSA

- **Roles & Responsibilities**
  - Framework for CDISC to actively support open-source apps
  - Manage which applications are published in COSA program
  - Provide guidance on open-source licenses
  - Collaborate with other clinical research open-source initiatives

### Industry Stakeholders

- **Pharma-Biotech**
- **Independent Consultant**
- **Regulatory agency**

## CORE Development: Landscape of Participation & Responsibilities

### CORE Roadmap Board

- **Roles & Responsibilities**
  - Promote CORE and drive adoption
  - Set strategic vision
  - Oversee Roadmap development
  - Facilitate Reference Implementation development
  - Ensure open, unbiased interaction with vendor community
  - Direct and oversee Product Owner

### CORE Technical Committee

- **Roles & Responsibilities**
  - Function as the Architecture Review Board
  - Approve architecture decisions
  - Determine the technology stack
  - Resolve development / technology disputes
  - Recruit other developers
  - IP and security assessments

### CORE Registered Solution Providers

- **Roles & Responsibilities**
  - Software vendors who develop commercial CORE solutions
  - Communicate with Roadmap Board via CORE Product Owner and Roadmap Board chair/co-chair
  - Participate in CORE certification

### Maintainer and Contributor Technical Community

- **Pharma-Biotech**
- **Independent Consultant**
- **CDISC**
- **CRO**
- **Software vendor**
- **Service Provider**

### Requirements Working Group

- **Roles & Responsibilities**
  - Gather market requirements

### Testing Team

- **Roles & Responsibilities**
  - Develop and implement testing approach

### Developer Community

- **Roles & Responsibilities**
  - Develop CORE technical artifacts (e.g., code, test results, documentation, etc.).

### Validation Team

- **Roles & Responsibilities**
  - Develop and implement validation approach
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)
Next Steps
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!