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

End User

User Specific Rules

Configure and run

Report

Data & Metadata

Interface

Engine

CORE in COSA*

3rd Party application

API

COMMUNITY GOVERNANCE

CDISC Community

Executable

Specification

Conformance rules

Load

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 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

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

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

Q3 2021–Q2 2022

Q3 2022 –

Establish CORE Roadmap Board
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
CORE Rules
Rules Specifications and Executable Rules: Overview

Conformance Rule Specification Development

<table>
<thead>
<tr>
<th>Rule ID</th>
<th>SDTMIG 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.

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

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

Publish

CDISC Library
# Rules Development Progress

<table>
<thead>
<tr>
<th>Components</th>
<th>OPEN</th>
<th>DONE</th>
<th>BLOCKED</th>
<th>UNIT TESTING</th>
<th>QC IN PROGRESS</th>
<th>READY TO PUBLISH</th>
<th>PUBLISHED</th>
<th>Awaiting QC</th>
<th>Author In Progress</th>
<th>Back To Author</th>
</tr>
</thead>
</table>
| 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              | 440
| 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

Priority 1
- SDTMIG 3.2 + 3.3
- FDA SDTMIG 3.2 + 3.3
- Define cross checks

Priority 2
- SDTMIG 3.4
- PMDA SDTMIG 3.2

Priority 3
- SENDIG 3.0 + 3.1 + 3.1.1
- FDA SENDIG 3.0 + 3.1

Priority 4
- ADaMIG 1.1 + 1.2 + 1.3
- PMDA ADaMIG 1.1

Timelines depend on community engagement
How to sign up as a volunteer

• [https://www.cdisc.org/volunteer/form](https://www.cdisc.org/volunteer/form)
  • Select CORE Rules Team

Select the CDISC Standards Development team that you would like to join. (Please choose one)

- [ ] CORE Rules
- [ ] DDF
- [ ] Safety User Guide
- [ ] ADaM
- [ ] CDASH
- [ ] Controlled Terminology
- [ ] QRS
- [ ] SDS
- [ ] SEND
- [ ] Data Exchange (ODM, Define-XML)
- [ ] Medical Devices
- [ ] Tobacco Implementation Guide
- [ ] Genomics Subteam
- [ ] Other...

Additional standards information can be found on our [Standards Page](https://www.cdisc.org).
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

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* 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”
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
Engine and Deployments Overview

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

- **Third party deployments**
  - Vendor A
  - Vendor B

- **Deployments**
  - CDISC Cloud Evaluation
  - Azure Marketplace Evaluation
  - CLI deployment via GitHub
  - Release on GitHub
  - Beta Releases
  - Stable Releases
  - Free version
  - Commercial version
  - End-user integration C

- **Timeline**
  - Q1 2021
  - Q2 2021
  - Q3 2021
  - Q4 2021
  - Q1 2022
  - Q2 2022
  - Q3 2022
  - Q4 2022
  - Q1 2023
  - Q2 2023
  - Q3 2023
  - Q4 2023

- **Today**
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**

- **cdisc Standards**
  - Provide rule specs

- **Regulatory Agencies**
  - Provide validation rules

- **Community**
  - Propose new / updated rule specs

**Central Specifications Catalog**

- **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.

**CORE Rules (executable)**

- **Rules Gov Team Activities**
  - Govern CORE Rules dev. process
  - Assign Rules for development
  - Review/approve Rules for release

- **Rule Specifications**
  - CORE Engine
  - CDISC Library

- **3rd Party Applications**
  - API

- **Publish**

**Freely Available**
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

Rules Governance Team: CDISC; Regulatory Agencies, Community
- New specifications
- Receive specs & load to central catalog
- Central Specifications Catalog
- Maintain and curate specs; mark and prioritize specs for Rule dev

Rule Developers: Community
- Assign Rules to developers; manage/govern dev process
- Author and unit test Rule
- Independent Rule QC by second developer
- Review and Approve Rule for Provisional Use
- Approve Rule for Production Use

Rules Database / Library: CDISC Data Science
- Load Rule as Provisional in CDISC Library
- CDISC Library
- Provisional
- Production
- Promote Provisional Rules to Production in CDISC Library

Public Review: Community
- Quarterly
- 30-day Public Review for a batch of Rules

Governance model is complete; implementation is in progress
CORE Roadmap Board
CORE Development: Landscape of Participation & Responsibilities

**CDISC Leadership**

**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

**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
- Develop testing strategy
- Recruit other developers
- IP and security assessments

**Industry Stakeholders**

- Pharma-Biotech
- Independent Consultant
- Regulatory agency

**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
- Service Provider

**Requirements Working Group**

- Gather market requirements

**Testing Team**

- Develop and implement testing approach

**Developer Community**

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

**Validation Team**

- Develop and implement validation approach

**Information Exchange**

- Most-engaged members

**Most-engaged members**

- Chair
- Members

- Rules Development Plan

- Publish

- Information exchange
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
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