凯莱英临床(凯诺)
Asymchem Clinical (Clin-nov)

CDISC的一些新进展与数据验证

孙海泉 2024.11.15

凯莱英临床(凯诺)
Asymchem Clinical (Clin-nov)

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CDISC的一些新进展

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more

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There are no current Public Reviews.

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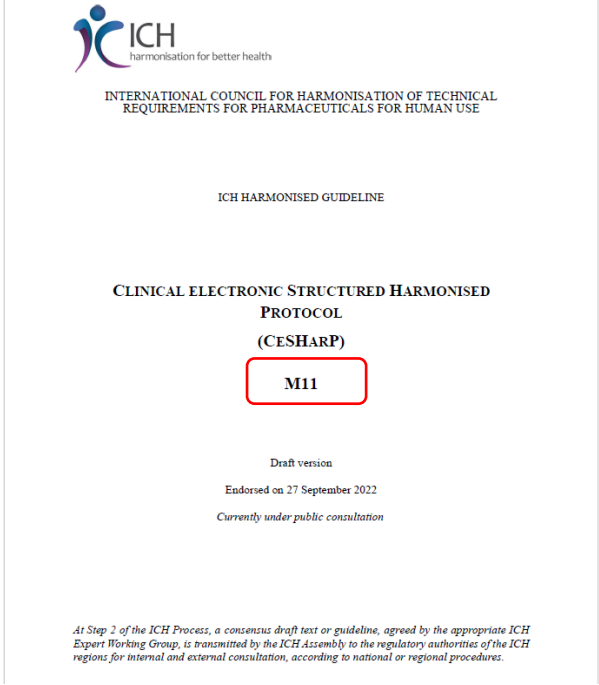
M11是什么

ICH CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CeSHarP)

ICH M11 is a new harmonised guideline on the clinical protocol that specifies comprehensive organization with standardized content (including both required and optional components).



ICH harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

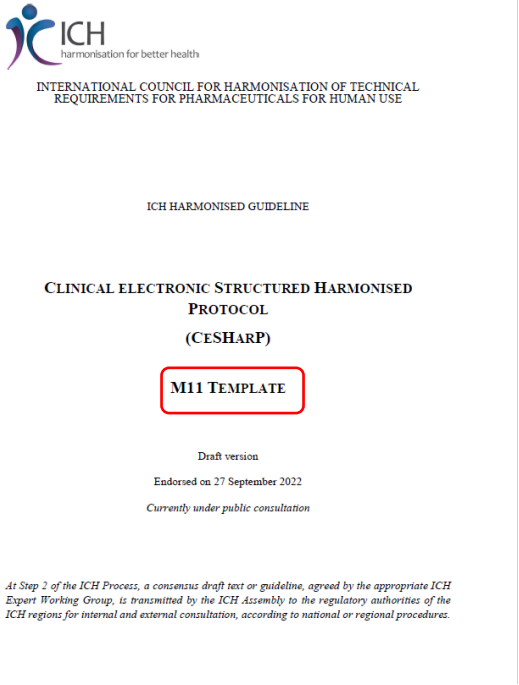
M11

Draft version

Endorsed on 27 September 2022

Currently under public consultation

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.



ICH harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

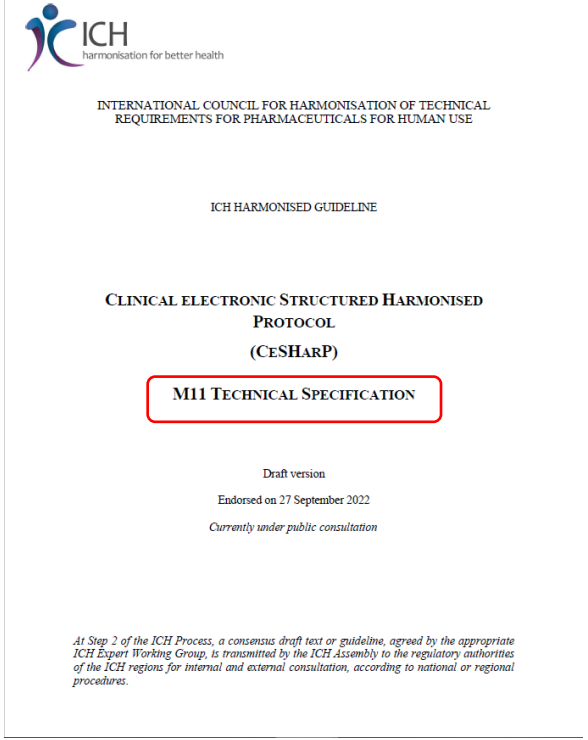
M11 TEMPLATE

Draft version

Endorsed on 27 September 2022

Currently under public consultation

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.



ICH harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11 TECHNICAL SPECIFICATION

Draft version

Endorsed on 27 September 2022

Currently under public consultation

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https://www.ich.org/page/multidisciplinary-guidelines.

M11 Simple Example

Template Specification

Protocol Full Title:	[Protocol Full Title] The protocol should have a descriptive title that identifies the scientific aspects of the trial sufficiently to ensure it is immediately evident what the trial is investigating and on whom, and to allow retrieval from literature or internet searches.
Sponsor Confidentiality Statement:	[Sponsor Confidentiality Statement] Insert the Sponsor's confidentiality statement, if applicable, otherwise delete.
Protocol Number:	[Protocol Number] A unique alphanumeric identifier for the trial, designated by the Sponsor, is a standard part of trial data, and should be included for most trials.
Version:	[Version] An optional field for use by the Sponsor at their discretion.
Amendment Number:	[Amendment Number] Enter the amendment number. If this is the original instance of
Trial Phase:	[Trial Phase] [Description of Trial Phase Other] Acceptable entries are: "Early Phase 1", "Phase 1", "Phase 1/Phase 2", "Phase 2", "Phase 2/Phase 3", "Phase 3", "Phase 4",
Compound Number(s):	[Compound Number] Enter the Sponsor's unique identifier for investigational compound(s) in the trial. Add or delete additional fields as needed.
Compound Name(s):	[Nonproprietary Name], [Proprietary Name], [Additional Proprietary Name] Delete this line from the table if a nonproprietary name has not yet been assigned. Omit proprietary name fields if not yet established.
Trial Phase:	[Trial Phase] [Description of Trial Phase Other] Acceptable entries are: "Early Phase 1", "Phase 1", "Phase 1/Phase 2", "Phase 2", "Phase 2/Phase 3", "Phase 3", "Phase 4",

Technical Specification

Term (Variable)	Trial Phase
Data Type	Pick list
Topic, Value or Header	D
Definition	
User Guidance	For trials combining investigational drugs or vaccines with devices, classify according to the phase of drug development.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
Relationship (reference to high level conceptual model)	
Value	Early Phase 1 Phase 1 Phase 1/Phase 2 Phase 2 Phase 2/Phase 3 Phase 3 Phase 4 Other
Business rules	**Value Allowed:** yes **Relationship:** n/a **Concept:** Protocol short title
Duplicate field in other sections	

Presented by Peter Van Reusel (Chief Standards Officer, CDISC), CDISC China Interchange 2024

Controlled Terms

Template Specification

Protocol Full Title:	[Protocol Full Title] The protocol should have a descriptive title that identifies the scientific aspects of the trial sufficiently to ensure it is immediately evident what the trial is investigating and on whom, and to allow retrieval from literature or internet searches.
Sponsor Confidentiality Statement:	[Sponsor Confidentiality Statement] Insert the Sponsor's confidentiality statement, if applicable, otherwise delete.
Protocol Number:	[Protocol Number] A unique alphanumeric identifier for the trial, designated by the Sponsor, is a standard part of trial data, and should be included for most trials.
Version:	[Version] An optional field for use by the Sponsor at their discretion.
Amendment Number:	[Amendment Number] Enter the amendment number. If this is the original instance of
Compound Number(s):	[Compound Number] Enter the Sponsor's unique identifier for investigational compound(s) in the trial. Add or delete additional fields as needed.
Compound Name(s):	[Nonproprietary Name]. [Proprietary Name]. [Additional Proprietary Name] Delete this line from the table if a nonproprietary name has not yet been assigned. Omit proprietary name fields if not yet established.
Trial Phase:	[Trial Phase] [Description of Trial Phase Other] Acceptable entries are: "Early Phase 1", "Phase 1", "Phase 1/Phase 2", "Phase 2", "Phase 2/Phase 3", "Phase 3", "Phase 4",

Trial Phase: [Trial Phase] [Description of Trial Phase Other]

Acceptable entries are: "Early Phase 1", "Phase 1", "Phase 1/Phase 2", "Phase 2", "Phase 2/Phase 3", "Phase 3", "Phase 4",

Technical Specification

Term (Variable)	Trial Phase
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Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
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Value	Early Phase 1 Phase 1 Phase 1/Phase 2 Phase 2 Phase 2/Phase 3 Phase 3 Phase 4 Other
Business rules	**Value Allowed:** yes **Relationship:** n/a **Concept:** Protocol short title
Duplicate field in other sections	

CDISC CT

Trial Phase Response (C66737)

NOT APPLICABLE
PHASE 0 TRIAL
PHASE I TRIAL
PHASE I/II TRIAL
PHASE II TRIAL
PHASE II/III TRIAL
PHASE IIA TRIAL
PHASE IIB TRIAL
PHASE III TRIAL
PHASE IIIA TRIAL
PHASE IIIB TRIAL
PHASE IV TRIAL
PHASE V TRIAL

Presented by Peter Van Reusel (Chief Standards Officer, CDISC), CDISC China Interchange 2024

M11 Work Plan

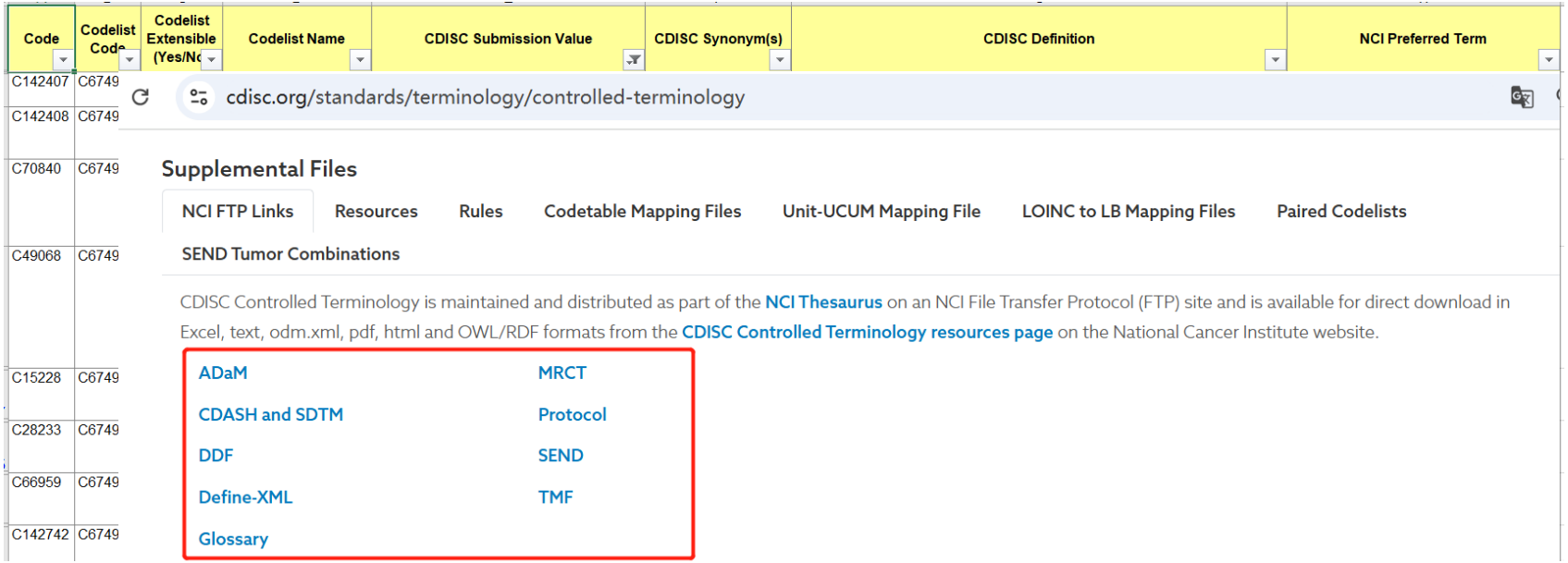
1.c. Future anticipated key milestones

Expected future completion date	Milestone
Oct. 2024	• *Regional Party Review of the Updated Guideline, Template, and Technical Specification* • *Clinical Data Interchange Standards Consortium (CDISC) Public Review of the M11 terms, definitions, and valid values*
Dec 2024	• *Adjudication of review comments* • *Updated Guideline, Template and Technical Specification*
Mar. 2025	*Regional Public Consultation Period on Technical Specification*
Jun 2025	*Adjudication of Public Comments on the Technical Specification*
Sep 2025	*Updated Guideline, Template and Technical Specification*
Oct. 2025	*Step 3 Sign-off Guideline, Template and Technical Specification*
Nov. 2025	*Step 4 adoption of Guideline, Template and Technical Specification*
Nov. 2025	*Final versioned training materials*
Feb 2026	*Step 2 (Testing) of the ICH Technical Implementation Guide for Fast Healthcare Interoperability Resources (FHIR)*
May 2026	*Step 4 adoption of ICH Technical Implementation Guide for FHIR*

Glossary v19.0

CDISC Glossary v19.0 contains 52 new terms, 76 changes to existing content, and many new, or changes to, existing “clusters” of related terms that, when their definitions are read together, help sharpen the semantic distinctions and optimize effective communication.

Glossary v19.0 can also be found in Excel, text, odm.xml, pdf, html, and OWL/RDF formats, along with CDISC Terminology Changes files on the NCI-EVS website with file date 2024-09-27.



Tobacco Implementation Guide v1.0

Release Date: 10 June 2024

Developed in partnership with the U.S. Food and Drug Administration Center for Tobacco Products (FDA CTP), the Tobacco Implementation Guide (TIG) v1.0 is a Foundational Standard that serves as a comprehensive resource for the collection, tabulation, analysis, and exchange of ***tobacco product*** data for submissions to FDA CTP. The TIG v1.0 implements the CDASH Model v1.2, SDTM v2.1 and ADaM v2.1, with references to standards such as the Define-XML v2.1, to standardize data for submission and facilitate tobacco product research, scientific review, and harm reduction. The TIG v1.0 focuses on implementation for use cases inherent to tobacco product data composed of concepts identified by one or more stakeholders as important in the context of tobacco product research.

Use cases addressed in the TIG v1.0 include:

- *Product Description*, which refers to concepts used to characterize tobacco products.
- *Nonclinical*, which refers to concepts used to identify potential risks and effects on biological processes for tobacco products via in vitro and in vivo nonclinical studies.
- *Product Impact on Individual Health*, which refers to concepts used to assess the impact of tobacco products on individuals.
- *Product Impact on Population Health*, which refers to concepts used to assess the impact of tobacco products on populations of individuals.

The TIG Conformance Rules Version 1.0 supports consistent implementation of TIG v1.0 standards.

Published Date: 10 June 2024

7 Changes from SDTM v2.0 to SDTM v2.1

The following new section was added:

- Section 6.8, Related References Dataset

New variables have been added to the following sections:

- Section 3.1.3 The Findings Observation Class
  - --CELLEV, Number of Cells Evaluated
- Section 3.1.4, Identifiers for All Classes
  - SPTOBID, Applicant-defined Tobacco Product Identifier
  - IGDCMPID, Ingredient or Component Identifier
  - STOCONID, Applicant-defined Storage Conditions ID

Many variable labels, notes, definitions, or examples were modified. In most cases, these modifications were to use the phrase "treatment or product" for the case when product use is not considered a treatment. In some cases a definition was added where there was none before. The type and location of revisions made are described in the following tables.

VARIABLES					
		Modifications made to existing Variable			
Variable	Section	Label	Notes	Definition	Examples
--TRT	Section 3.1.1, The Interventions Observation Class	X	X	X	
--RSDISC	Section 3.1.1, The Interventions Observation Class	X	X		
--DOSFRM	Section 3.1.1, The Interventions Observation Class			X	

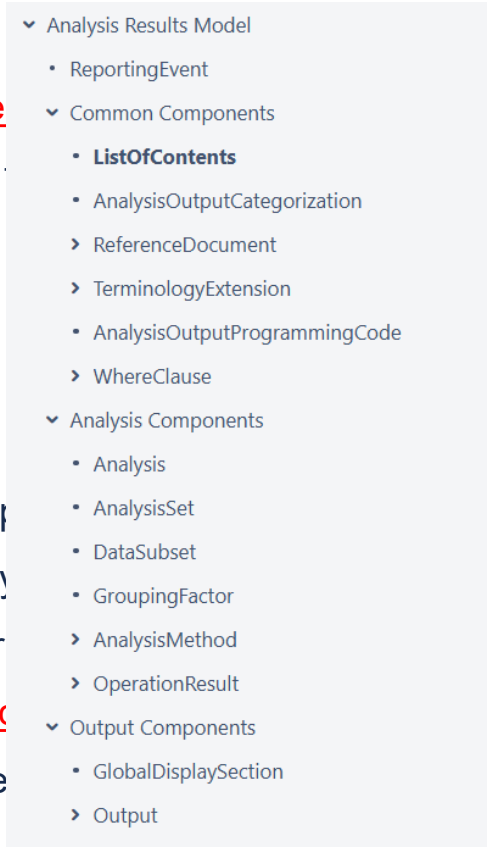
Analysis Results Standard v1.0

Published Date: 19 April 2024

The goal for the future state of analysis results is that they are machine-readable highly reusable. The aim in creating the ARS was to provide a logical model that analysis results and associated metadata to support

- automated generation of machine-readable results data;
- improved navigation and reusability of analysis and results data;
- storage, access, processing, and reproducibility of results data; and
- traceability to the study protocol, statistical analysis plan (SAP), and to the in

The ARS Model has several possible implementations, including leveraging analy aid in automation as well as representing analysis results as data in a dataset str ARS technical specification could be used to support automation, traceability, and displays. An analysis results dataset could support reuse and reproducibility of re



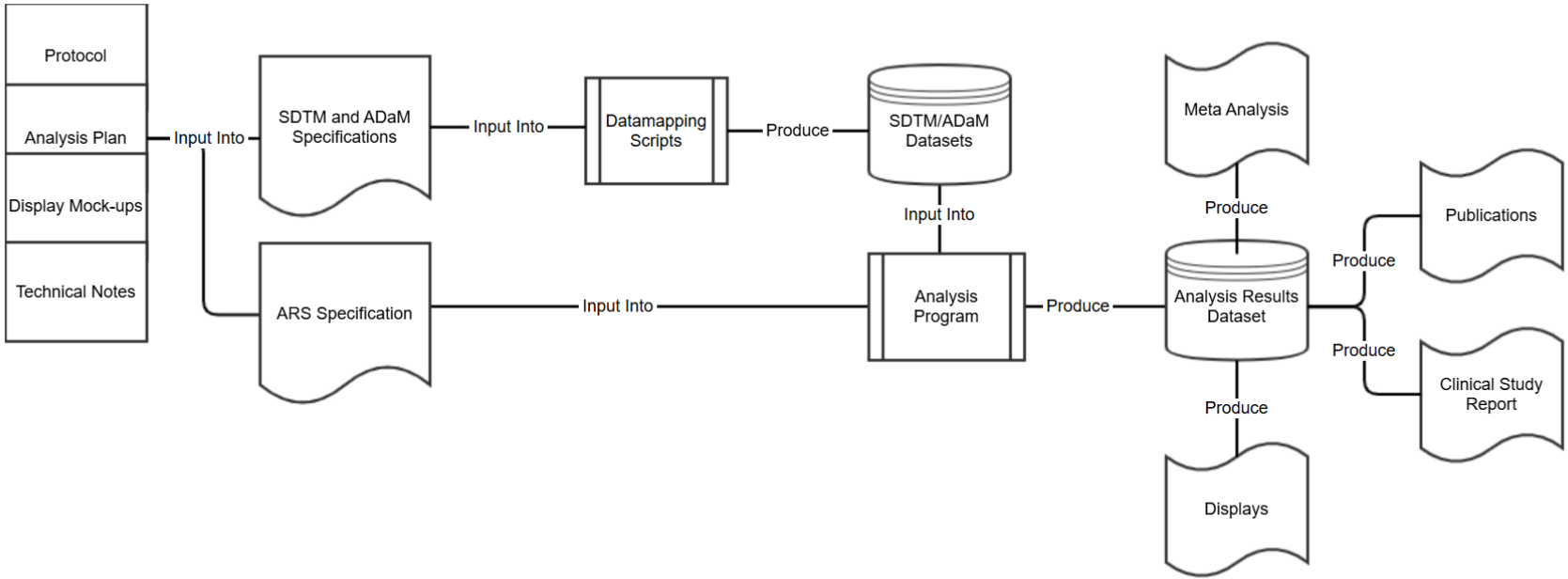
Relationship to Other CDISC Standards

由 Bess LeRoy创建, 最终由 Lorraine Sobson修改于 四月 18, 2024

The ARS Model is currently not considered to be a replacement for the ARM for Define-XML standard (available at https://www.cdisc.org/standards/foundational/define-xml/). The ARM for Define-XML meets a regulatory need and has not been modified. However, components have been added to the ARS Model to facilitate the creation of ARM for Define-XML, including the reason and purpose of each analysis and documentation references for both analyses and outputs. The ARM for Define-XML was developed for the purpose of submitting to regulatory agencies to provide traceability for a given analysis result to the specific ADaM data used as input to generating the analysis result. The ARM for Define-XML is often created retrospectively and only for key analyses. In contrast, the ARS Model is intended to leverage analysis results prospectively to enable automation, reusability, and traceability.

The creation and use of the ARS Model is based on the assumption that input analysis datasets will be "analysis-ready," as defined in ADaM v2.1 Section 3.1, Fundamental Principles (https://www.cdisc.org/standards/foundational/adam/). This means that ARS metadata components are designed only to define and describe the minimal additional processing needed to produce results from analysis-ready analysis datasets; they are not intended to describe more complex data manipulations (e.g., transformations, transpositions).

Example of Potential Future Workflow for ARS

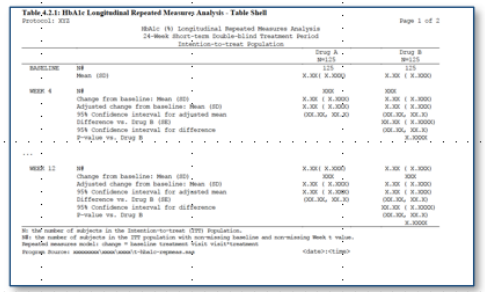


Analysis Results Current State

Table 3.1.1: ADHYPO Analysis Dataset

Row	STUDYID	USUBJID	MIDS	CEDECOD	WASAEYN	ASTDTM
1	XYZ	000001	HYPO 1	Hypoglycemia	Y	07Sep2012 22:29:00
2	XYZ	000001	HYPO 2	Hypoglycemia	N	10Sep2012 09:12:00
3	XYZ	000001	HYPO 3	Hypoglycemia	N	10Sep2012 23:05:00
4	XYZ	000001	HYPO 4	Hypoglycemia	N	11Sep2012 15:24:00
5	XYZ	000001	HYPO 5	Hypoglycemia	N	18Sep2012 11:39:00
6	XYZ	000002	HYPO 1	Hypoglycemia	N	22Oct2012 13:28:00
7	XYZ	000002	HYPO 2	Hypoglycemia	N	25Oct2012 13:59:00
8	XYZ	000002	HYPO 3	Hypoglycemia	N	17Nov2012 05:01:00

ADaM Dataset



Static Display

ARM for Define-XML

Table 4.2.2: HbA1c Longitudinal Repeated Measures Analysis Results Metadata

Metadata Field	Metadata
DISPLAY IDENTIFIER	Table 4.2.1/Figure 4.2.1
DISPLAY NAME	Mean Change from Baseline in HbA1c (Percent) Longitudinal Repeated Measures Analysis, 24-Week Short-term Double-blind Treatment Period, Intention-to-treat Population
RESULT IDENTIFIER	Treatment difference results (LSMean, confidence interval, p-value)
PARAM	HbA1c (%)
PARAMCD	HBA1C
ANALYSIS VARIABLE	CHG (Change from baseline)
ANALYSIS REASON	SPECIFIED IN SAP
ANALYSIS PURPOSE	PRIMARY OUTCOME MEASURE
ANALYSIS DATASET	ADHBA1C

ARM v1

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Analysis Results Future State

Shifting the Paradigm

Table 3.1.1: ADHYPO Analysis Dataset

Row	STUDYID	USUBJID	MIDS	CEDECOD	WASAEYN	ASTDTM
1	XYZ	000001	HYPO 1	Hypoglycemia	Y	07Sep2012 22:29:00
2	XYZ	000001	HYPO 2	Hypoglycemia	N	10Sep2012 09:12:00
3	XYZ	000001	HYPO 3	Hypoglycemia	N	10Sep2012 23:05:00
4	XYZ	000001	HYPO 4	Hypoglycemia	N	11Sep2012 15:24:00
5	XYZ	000001	HYPO 5	Hypoglycemia	N	18Sep2012 11:39:00
6	XYZ	000002	HYPO 1	Hypoglycemia	N	22Oct2012 13:28:00
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8	XYZ	000002	HYPO 3	Hypoglycemia	N	17Nov2012 05:01:00

ADaM Dataset

Table 4.2.2: HbA1c Longitudinal Repeated Measures Analysis Results Metadata

Metadata Field	Metadata
DISPLAY IDENTIFIER	Table 4.2.1/Figure 4.2.1
DISPLAY NAME	Mean Change from Baseline in HbA1c (Percent) Longitudinal Repeated Measures Ana Period, Intention-to-treat Population
RESULT IDENTIFIER	Treatment difference results (LSMean, confidence interval, p-value)
PARAM	HbA1c (%)
PARAMCD	HBA1C
ANALYSIS VARIABLE	CHG (Change from baseline)
ANALYSIS REASON	SPECIFIED IN SAP
ANALYSIS PURPOSE	PRIMARY OUTCOME MEASURE
ANALYSIS DATASET	ADHBA1C

ARM v1

ARM Extension Technical Specification

Automation

Reuse

Traceability

Analysis Results Dataset

Display

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数据验证规则

Definitions of Rule Sets

1. **Conformance Rules:** Conformance rules are created and maintained by CDISC. Conformance rules describe the criteria that must be met to be in compliance with the CDISC standard.
2. **Business Rules:** Business rules are created by a specific organization to describe the criteria that should be met to allow for the deliverable to be useful in the conduct of normal business practices. For example, FDA Business Rules describe criteria that should be met in order for datasets to be utilized internally for FDA business practices such as submission review.
3. **Technical Rejection Criteria for Study Data:** eCTD Technical Rejection Criteria describe the minimum requirements for eCTD submissions to be accepted by the agency at the gateway.
4. **Validator Rules:** Validator rules are rule sets utilized by validation tools. Each validator can have its own set of validation rules. For example:
   a. FDA Validator Rules describe the validation rules used by the FDA's in-house proprietary validator.
   b. Pinnacle 21 Validator Rules describe the validation rules used by the Pinnacle 21 Validator Tool.

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New to CDISC

Home / Standards / Foundational / SDTMIG / SDTM and SDTMIG Conformance Rules v2.0

SDTM and SDTMIG Conformance Rules v2.0

Release Information | Files & Links

ADaM Conformance Rules v5.0

Published Date: 29 November 2021

Release Information | Files & Links

Published Date: 6 October 2023

PharmaSUG 2023 – Paper SS-059

CDISC Conformance and Compliance: So Many Resources, So Little Time!

Jennifer Fulton and Stephen Black, Westat

FDA Business and Validator Rules

Validation activities occur at different times during submission and review of study data, including submission receipt and at the beginning of the regulatory review.

The rules below support regulatory review and analysis of study data:

- **FDA Business Rules**
  The Business Rules v1.5 (May 2019) help ensure that the study data are compliant, useful, and will support meaningful review and analysis. This applies to SDTM formatted clinical studies and SEND formatted non-clinical studies. For more information see Section 8 of the Technical Conformance Guide.
- **FDA Validator Rules**
  The Validator Rules v1.6 (December 2022) are used by the FDA to ensure data are standards compliant and support meaningful review and analysis.

FDA Data Standards Catalog v10.4，September 2024

Update of Data Standards Catalog and PMDA Validation Rules (on March 29, 2024)

Data Standards Catalog and Study Data Validation Rules

- Data Standards Catalog (2024-03-29) [24.6KB]
- Study Data Validation Rules

  Please note that when submitting electronic study data to the PMDA via the gateway system, only one version of the validation rules must be selected for a single application, even if it involves multiple studies. Also, when additionally submitting electronic study data after the application, the version of the validation rules at the time of the application must be selected.

  For the validation and the explanation of the results performed by applicant prior to submission, all versions of the validation rules, including those that have already been closed for acceptance, can be used for each study.

  - Version 1.0 (2015-11-18) [82.0KB] Acceptable from Oct 1, 2016 to Mar 31, 2021 (application date)
  - Version 2.0 (2019-09-27) [97.9KB] Acceptable from Apr 1, 2020 to Mar 31, 2023 (application date)
  - Version 3.0 (2021-12-15) [103KB] Acceptable from Jan 1, 2022 to Mar 31, 2025 (application date)
  - Version 4.0 (2023-02-28) [112KB] Acceptable from Apr 1, 2023 to Mar 31, 2026 (application date)
  - Version 5.0 (2024-03-29) [124KB] Acceptable from Apr 1, 2024 (application date)

https://www.pmda.go.jp/english/review-services/reviews/0002.html

FDA Data Submissions

FDA Guidance Documentations

- Study Data Standards Resources
- Technical Rejection Criteria for Study Data - Incorporated into Study Data Technical Conformance Guide
- Study Data Technical Conformance Guide v5.4 (June 2023)
- FDA Data Standards Catalog v9.0 (January 25, 2023)
- Business Rules v1.5 (May 2019)
- Validator Rules v1.6 (December 2022)
- PhUSE Clinical Study Data Reviewer's Guide v1.3, 2-Nov-2018
- PhUSE Analysis Data Reviewer's Guide v1.2, 18-Jul-2019
- Bioresearch Monitoring Technical Conformance Guide v3.0 (August 2022)
- PhUSE Bioresearch Monitoring Data Reviewers Guide (BDRG) Package v1.0 (June 22, 2022)

https://www.pinnacle21.com/documentation

PMDA Data Submissions

PMDA Guidance Documentations

- New Drug Review with Electronic Data
- Data Standards Catalog (2023-02-28)
- FAQs on Electronic Study Data Submission (English version, April 3, 2023)
- Study Data Validation Rules Version 4.0 (2023-02-28)
- FAQs on Electronic Study Data Submission (English version, June 27, 2022)
- Technical Conformance Guide (English version, April 1, 2022)
- Study Data Validation Rules Version 1.0 (2015-11-18)
- Study Data Validation Rules Version 2.0 (2019-09-27)
- Study Data Validation Rules Version 3.0 (2021-12-15)
- Explanation of Electronic Study Data (Form A)
- Explanation of Electronic Study Data (Form B)

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THANK YOU!