With Standards - Science Will Prevail!

2021 EUROPE INTERCHANGE



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Live Stream | 28-30 April

CDISC 360: What's in It for Me?

Peter Van Reusel CDISC European Interchange Session 7 - April 29, 2021





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. Common Implementation Challenges Addressed by CDISC 360
- 2. Four Pillars of CDISC 360 Implementation
- 3. Summary of Projects

Common Implementation Challenges

What is CDISC 360 trying to address?

Today we are here

CDISC Standards in the Clinical Research Process

PRE-CLINICAL CLINICAL COLLECT ORGANIZE **PLAN** ORGANIZE **ANALYZE** SUBMIT PUBLISH REPORT DATA EXCHANGE \bigotimes DATA EXCHANGE B ODM-XML Define - XML **ODM-XML** $\dot{\tau}$ SDM-XML Dataset - XML **SDTM SEND** PRM **CDASH** ADaM TAUGS

BRIDG, CONTROLLED TERMINOLOGY AND GLOSSARY



What is not in the standards?

- Lack comprehensive data meaning and relationships
- Do not describe the transformations and derivations
- Have flexibility that allows for inconsistencies, making automation difficult, allowing interpretation & unnecessary variability in using the standards
- Therapeut published as text instead of machine-readable content with machine executable transformation and derivation algorithms
- Therapeutic Area User Guides provide end-to-end knowledge standardization
 - From data collection to analysis
 - Analog documents, published as text



Therapeutic Area User Guide Overview

Therapeutic Area (TA) Standards extend the Foundational Standards to represent data that pertains to specific disease areas. TA Standards include disease-specific metadata, examples and guidance on implementing CDISC standards for a variety of uses, including global regulatory submission.

Autoimmune Psoriasis **Rheumatoid Arthritis** Cardiovascular Cardiovascular Heart Failure QT Studies Traditional Chinese Medicine - Coronary Artery Disease-Angina Endocrine Acute Kidney Injury Diabetes Diabetes - Type 1 **Diabetic Kidney Disease** Dyslipidemia **Kidney Transplant** Polycystic Kidney Disease Gastrointestinal CDAD Crohn's Disease

Infectious COVID-19 Ebola Hepatitis C HIV Influenza Malaria **Tuberculosis** Virology Mental Health Major Depressive Disorder Post Traumatic Stress Disorder **Schizophrenia** Neuroloay Alzheimer's Huntington's Disease **Multiple Sclerosis** Parkinson's Disease **Traumatic Brain Injury**

Oncology Breast Cancer Colorectal Cancer Lung Cancer Pancreatic Cancer **Prostate Cancer** Other Nutrition **Traditional Chinese Medicine - Acupuncture Rare Diseases Duchenne Muscular Dystrophy** Respiratory Asthma COPD COVID-19 Treatments Pain Vaccines

→ 44 Therapeutic Area User Guides in 8 years

cdisc

https://www.cdisc.org/standards/therapeutic-areas/disease-area



Therapeutic Area Concept Maps

- Provides scope and extent of TA User Guide
- Facilitates communication between scientists and data standards experts



Diagnostic Process

timing of ecent meals and medications

recipitating

Factors &

considers

as cause

→ "This is a picture for humans, this knowledge does not exist for machines"

TAUG CRFs and Datasets

Example CRF 5: Hypoglycemia

CETERM= Hypoglycemic Event CECAT= HYPO EVENTS		
Any Hypoglycemic Events Experienced?	No Yes (If yes complete for each event) CEYN	
Sponsor Defined ID CESPID	001	
Date/Time of Event CESTDTC	(DD-MMM-YYYY) (24 hour close	k) CESTDAT CESTTIM
When Did the Hypoglycemic Event Occur?	Between Bedtime and Waking QVAL when QNAM- Between Waking and Bedtime QLABEL="When Di	WHENOCC and d the Hypoglycemic Event Occur?"
In the Opinion of the Investigator Was This an Adverse Event?	No Yes WASAEYN FAORRES where FATESTCD	"WASAEYN", FATEST= "Was this
Was a Glucose Measurement Obtained at the Time of the Event? LBSTAT	No Yes (If yes enter result and unit below) LBPERF	
	Glucose Result LBORRES mg/dL, LBORRES	
To a Decide Model and an Talana	mmol/L	
Last Study Medication Taken	······Name Kelefence	
EXCAT- HIGHLIGHTED DOSE EXSTDTC	(DD-MMM-YYYY) (24 hour clos	k) EXSTDAT EXSTTIM
	dose EXDOSE EXDSTXT	
Last Concomitant Diabetic Medication Taken	Name Kelerence CMTRT	14
CMSCAT= HIGHLIGHTED DOSE CMSTDTC	(DD-MMM-YYYY) (24 hour close	k) CMSTDAT CMSTTIM
	dose CMDOSE CMDSTXT	2
Date/Time of Last Meal	units CMDOSU	MISTOAT
MLSTDTC	(Destablished 111) (24 hour clo	mLSTUMI mLSTIM
Were Signs/Symptoms Present? CECAT= HYPO SYMPTOMS	No Yes (If yes complete following) CEYN	
CETERM= SWEATING	Sweating	No Yes CEOCCUR with
CETERM= TREMORS/TREMBLING	Tremors/Trembling	No Yes CEPRESPEY
CETERM= DIZZINESS	Dizziness	No Yes
CETERM= COGNITIVE IMPAIRMENT	Cognitive Impairment	No Yes
CETERM= LOSS OF CONSCIOUSNESS	Loss of Consciousness	No Yes
GETERME CONVOLSIONS/SELECT	Convisions/Seizure	NO 165
GETERIA- COMA	Com	No Tes
FACATE PRECIPITATING FACTORS, FAOB JE HYPOGLY	CEMIC EVENT and:	(in yes enter below)
Ware Any Descinitation Fastory Reported?	Na	GETERON
were Any Freephaning Factors Reported	Yes (If yes complete following) HPFYN	
FATEST= Alcohol Consumption as a Precip Factor	Alcohol Consumption	No Yes
FATEST= Concurrent Illness as a Precip Factor	Concurrent filmess	No Yes FAORRES
FATEST= Dosing Deviation as a Precip Factor	Deviation from Dosing Instructions	No Yes
FATEST= Meal Variance as a Precip Factor	Missed, Delayed or Smaller Meal	No Yes
FATEST= Physical Activity as a Precip Factor	Physical Activity	No Yes
	Other (Specify)	NO Yes (if yes enter below)
CMCAT» MYPO TREATMENT		PATEST
Was Any Treatment Given for the Hypoglycemic Event?	Yes (If yes complete following) HTG YN	
CMTRT= DRINK	Drink	No Yes CMOCCUR with
CMTRT= FOOD	Food	No Yes CMPRESP= Y
CMTRT= OLLICOSE TABLETS	Glucose Tablets	No Yes
		No. Vac.
CMTRT= GLUCAGON INJECTION	Glucagon Injection	140 165
CMTRT= GLUCAGON INJECTION	Glucagon Injection Intravenous Glucose	No Yes
CMTRT=GLUCAGON INJECTION CMTRT=GLUCAGON INJECTION CMTRT=INTRAVENOUS GLUCOSE IfTreatment Given Indicate Assistance Needed?	Glucagon Injection Intravenous Ghacose None - Subject Treated Self	No Yes FAORRES when FAOBJa
CMITET GLUCAGON INJECTION CMITET GLUCAGON INJECTION CMITET BUTRAVENOUS GLUCOSE Il Treatment Given Indicate Assistance Needed?	Glucagon Injection Intravenous Glucose None - Subject Treated Self Subject was Capable of Treating Self, but Received Assistance	FAORRES when FAOBJa HYPOGLYCEMIC EVENT, FACAT TREATMENT ADMINISTRATION

1	Row	STUDYID	DOMAIN	USUBJID	CESEQ	CECAT	CETERM	CEDECOD	CEPRESP	CEOCCUR	CESTDTC	CESTDY
	2	XYZ	CE	XYZ-001-001	2	HYPO SYMPTOMS	SWEATING	Hyperhidrosis	Y	N		
	3	XYZ	CE	XYZ-001-001	3	HYPO SYMPTOMS	TREMORS/TREMBLING	Tremor	Y	N		
	4	XYZ	CE	XYZ-001-001	4	HYPO SYMPTOMS	DIZZINESS	Dizziness	Y	N		
	5	XYZ	CE	XYZ-001-001	5	HYPO SYMPTOMS	COGNITIVE IMPAIRMENT	Cognitive Disorder	Y	Y		
	6	XYZ	CE	XYZ-001-001	6	HYPO SYMPTOMS	LOSS OF CONSCIOUSNESS	Loss of Consciousness	Y	Y		
	7	XYZ	CE	XYZ-001-001	7	HYPO SYMPTOMS	CONVULSIONS/SEIZURES	Convulsion	Y	N		
	8	XYZ	CE	XYZ-001-001	8	HYPO SYMPTOMS	COMA	Coma	Y	N		
	9	XYZ	CE	XYZ-001-001	9	HYPO EVENTS	HYPOGLYCEMIC EVENT	Hypoglycaemia			2013-09-24T08:48	50

Row	RELMIDS	MIDS	MIDSDTC
1 (cont)		HYPO 1	
2 (cont)	DURING	HYPO 1	2013-09-01T11:00
3 (cont)	DURING	HYPO 1	2013-09-01T11:00
4 (cont)	DURING	HYPO 1	2013-09-01T11:00
5 (cont)	DURING	HYPO 1	2013-09-01T11:00
6 (cont)	DURING	HYPO 1	2013-09-01T11:00
7 (cont)	DURING	HYPO 1	2013-09-01T11:00
8 (cont)	DURING	HYPO 1	2013-09-01T11:00
9 (cont)		HYPO 2	

→ Human readable only

TAUG Analysis Datasets and Results

3.3 Hypoglycemic Episodes Summary Dataset

he analysis dataset ADHYSUM is built from an ADHYPO data set and supports both the statistical analysis of the hypophycemic epinodes (see Table 3.1.). The dataset includes one observation per combination of asubject, analysis parameter, time indov and indicator (e.g., treatment emergent flag). Each record is a summary of the type of hypophycemic epinodes (see Table 3.1.). The dataset includes one observation per combination of asubject, analysis parameter, then ch combination of parameter and the timing variable, AVISTI, records are created even if no hypophycemic epicodes occured. The statistical model presented elow is based on the actual treatment received (TRTA) and adjusted for unbject-level values of country and sex. Therefore, these variables are included in DIYSUM from ADSL to upport analysis redaines. The duration of exposure (TRTDRD) is added to the dataset in order to facilitate exposure adjusted incidence rates. For overall summaries the records which have "cumulative frequency count" within the text of PARAM and AVISTI = "End of treatment" can selected. In this example, parameters for each of the five ADA classification values are defined, ading with a derived parameter frate explore values of analysis parameters. The examples below of not attempt to have with data below in Table 3.3.1, yet is mock data have only a subset of the possible values of analysis parameters. The examples below do not attempt to have with data needed fully visualize to traceability between ADHYPO and ADHYSUM for a given subject since the volume of required mock data would be large. In practice, however, the counts reveal in ADHYSUM for a zime unbiect value of counts of the comblete the counts of individual rows for that subject towing a ADHYSUM for a zime and the comblete to the originate of required mock data have a subject value and the subject and the counts of individual rows for that aubject towing a DHYSUM for a zime and the counts of the rown of non-individual rows for that aubject addite and the subject and the cou

Tab	le 3.3.1: A	DHYSU	M Analysi	s Dataset							
Row	STUDYID	USUBJID	PARAMCD	PARAM	AVISIT	AVAL	TRTDURD	SEX	AGE	COUNTRY	TRTA
1	XYZ	000008	ASSYMP	Asymptomatic Hypoglycemia (frequency count)	Week 1	3	72	F	35	DZA	Drug B
2	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	Week 1	3	72	F	35	DZA	Drug B
3	XYZ	000008	ASSYMP	Asymptomatic Hypoglycemia (frequency count)	Week 2	1	72	F	35	DZA	Drug B
4	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	Week 2	4	72	F	35	DZA	Drug B
5	XYZ	000008	ASSYMP	Asymptomatic Hypoglycemia (frequency count)	Week 3	0	72	F	35	DZA	Drug B
6	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	Week 3	4	72	F	35	DZA	Drug B
7	XYZ	000008	ASSYMP	Asymptomatic Hypoglycemia (frequency count)	Week 4	1	72	F	35	DZA	Drug B
8	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	Week 4	5	72	F	35	DZA	Drug B
10	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	End of Treatment	7	72	F	35	DZA	Drug B

3.4 Hypoglycemic Episodes Summary Analysis Results

The summary statistics in Table 3.4.1 are presented for all hypoglycemic episodes as well as by ADA classification group. The statistics presented in the current example are number of subjects experiencing an event, the number of events, and the raw event rate. To estimate and present the event-rate information, exposure time is needed. Table 3.4.1 is based on the ADHYSUM dataset.

Table 3.4.1: Summary of Hypoglycemic Episodes by Classification – Table Shell

Hypoglycemic Episodes by	Classifica	tion - Tr	eatr	nent Eme	rgent	- Summar	у –	Safety	Analy	sis Set		
		Drug .	À			Drug	В			Tota	1	
	N	(%)	E	R	N	(8)	Е	R	N	(%)	Е	R
Number of subjects	XXX				xxx				xxx			
Total events	xx	(xx.x)	хх	xxx.x	XX	(xx.x)	хх	xxx.x	хх	(xx.x)	ххх	xxx.x
ADA												
Severe hypoglycemia	х	(x.x)	х	xx.x	х	(x.x)	х	х.х	х	(x.x)	х	х.х
Documented symptomatic hypoglycemia	XX	(xx.x)	хх	ххх.х	хх	(xx.x)	хх	ххх.х	хх	(xx.x)	XXX	ххх.х
Asymptomatic hypoglycemia	х	(x.x)	хх	xx.x	х	(x.x)	х	XX.X	XX	(x.x)	хх	xx.x
Probable symptomatic hypoglycemia	х	(x.x)	х	х.х	х	(x.x)	х	х.х	х	(x.x)	х	х.х
Pseudo-hypoglycemia	х				х				х			

N: Number of subjects; %: Percentage of subjects; E: Number of events; R: Event rate per 100 exposure years;

Severe: Subject unable to treat himself/herself and/or have a recorded PG < 3.1 mmol/ \hat{L} (56 mg/d \hat{L})

Treatment emergent episodes occur after trial product administration after randomization and no later than 1 day after last trial product administration.

Figure 3.4.1: Mean Cumulative Function Plot of Documented and Severe Symptomatic Hypoglycemic Episodes

Documented and Severe Symptomatic Hypoglycemic Episodes - Treatment Emergent - Mean Cumulative Function - Safety Analysis Set



➔ Only exists in PDF



Biomedical Concepts

The CDISC 360 Project: Adding a conceptual layer to standards

- Evolve from normative to informative standards
- Create and store standards as concepts which create meaning
- Electronically publish data standards as linked metadata
- Add computer executable process metadata which enables end to end automation
- Develop concept-based standard definitions, and test and demonstrate end-to-end automation of study specification, data processing, and analysis
 - → Test and demonstrate, but not building software



Four Pillars of CDISC 360 Implementation

Four Pillars of CDISC 360 Implementation

Four pillars of 360 implementation emerge from the 360 lessons learned:

- 1. **Complete** the E2E foundational standards where they are incomplete
- 2. Enrich the foundational standards with the additional metadata needed for full data meaning and relationships by creating a biomedical concept layer
- 3. Extend the CDISC Library model with implementation level metadata
- 4. Collaborate with industry to standup and curate biomedical concepts



Implementing 360: Projects

STANDARDS DEVELOPMENT

1. Complete E2E Foundational Standards

- Project: eCRF Portal
- Project: Analysis Results Standard
- Project: Safety User Guide

2. Enrich Foundational Standards

• Project: Mining Define.xml's

STANDARDS DELIVERY

3. Extend CDISC Library Model

- **Project:** Model concepts
- **Project:** Add QRS content

4. Collaborate with Industry

Project: Use mining Define.xml
 project as prototype for collaborative
 curation process



Implementing 360: Completing E2E Foundational Standards

STANDARDS DEVELOPMENT

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 project as prototype for collaborative
 curation process



eCRF Portal Project

eCRF Portal Project

Form	n AE - Adverse Events				
1 A	E - Adverse Events				t form (CRF) lay
1.1	Were any adverse events experienced?	O _M No O _M Yes		AEYN	
1.2	What is the adverse event term?			AETERM	
1.3	Start Date (DD-MMM-YYYY)			AESTDAT	
1.4	Ongoing (as of [the study- specific time point or period])	O _M No ^{<itemgr< sup=""> O_M Yes</itemgr<>}	<pre>oupDef OID="CDASH_2-1_IG_8" N</pre>	ame="AE - Adverse Ever lang="en">AE - Adverse	nts" Repeating="No" Domain="AE": e Events
1.5	End Date (DD-MMM-YYYY)		<itemref itemoid="IT.AEYN" m<br=""><itemref <br="" itemoid="IT.AETERM"><itemref it.aestdat<="" itemoid="IT.AESTDAT
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layout

eCRF Portal – What's in it for Me?

- Helps complete the end-to-end CDISC vision
- ODM XML file can be used directly in compliant EDC systems
- Comes with underlying CDASH metadata
- CDASH annotation is included

Reduce unnecessary variability in data collection <u>https://www.cdisc.org/kb/ecrf</u>



Analysis Results Standard Project

Analysis Results Standard

- **Extend** ARM to facilitate automated TFL generation
- **Create** a standardized structure for analysis results to support reuse and dynamic data display generation
- *Tighten* standardization around ADaM datasets for generally accepted analyses





Standardized analysis results support dynamic data display generation

:Observation	qb:Table	dim.population	dim.treatment	dim.parameter	dim.sex	dim.agecat	dim.statistic	analysisResult
1001	dm.summary	enrolled	Treatment.A	param.subjects	sex.ALL	agecat.ALL	stat.freq	100
1002	dm.summary	enrolled	Treatment.A	param.subjects	sex.F	agecat.ALL	stat.freq	60
1003	dm.summary	enrolled	Treatment.A	param.subjects	sex.F	agecat.ALL	stat.percent	60
1004	dm.summary	enrolled	Treatment.A	param.subjects	sex.M	agecat.ALL	stat.freq	40
1005	dm.summary	enrolled	Treatment.A	param.subjects	sex.M	agecat.ALL	stat.percent	40
1006	dm.summary	enrolled	Treatment.B	param.subjects	sex.ALL	agecat.ALL	stat.freq	50
1007	dm.summary	enrolled	Treatment.B	param.subjects	sex.F	agecat.ALL	stat.freq	30
1008	dm.summary	enrolled	Treatment.B	param.subjects	sex.F	agecat.ALL	stat.percent	60
1009	dm.summary	enrolled	Treatment.B	param.subjects	sex.M	agecat.ALL	stat.freq	20
1010	dm.summary	enrolled	Treatment.B	param.subjects	sex.M	agecat.ALL	stat.percent	40
1011	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.ALL	agecat.ALL	stat.freq	150
1012	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.F	agecat.ALL	stat.freq	90
1013	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.F	agecat.ALL	stat.percent	60
1014	dm.summarv	enrolled	Treatment.ALL	param.subjects	sex.M	agecat.ALL	stat.freq	60
1015	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.M	agecat.ALL	stat.percent	40
1016	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.freq	100
1017	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.mean	40.7
1018	dm.summarv	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.stdev	10.7
1019	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.median	37.0
1020	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.min	21.0
1021	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.max	66.0
1022	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.freg	50
1023	dm.summarv	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.mean	41.2
1024	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.stdev	10.3
1025	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.median	36.0
1026	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.min	23.0
1027	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.max	67.0
1028	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.freq	150
1029	dm.summarv	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.mean	40.9
1030	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.stdev	10.4
1031	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.median	37.0
1032	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.min	21.0
1033	dm.summary	itt	Treatment ALL	param.age	sex ALL	agecat ALL	stat.max	67.0

	Intention-to-treat Popula	tion	
		Drug A N=125	Drug B N=125
BASELINE	N# Mean (SD)	125 x.xx(x.xxx)	125 x.xx (x.xxx)
WEEK 4	384 Change from baseline: Mean (SD) Adjustad change from baseline: Mean (SD) 554 Confidence interval for diysted mean Difference vs. Erug B (SE) 554 Confidence interval for difference p-value vs. Erug B	300K X.30K (X.300K) X.30K (X.300K) (30K.30K, 30K.30)	3000 X.302 (X.3000) X.302 (X.3000) 005.305, 32X.30 305.305 (X.30000) (005.305, 32X.30) X.30000
122			
WEEK 12	all Charge from baseline: Mean (8D) Adjusted charge from baseline: Mean (8D) 584 confidence interval for adjusted mean Difference ve. Drug B (82) 584 confidence interval for difference P-value ve. Drug B	X.307 (X.3007) 3007 X.307 (X.3000) X.307 (X.3000) (307.307, 307.30)	X.XX (X.XXX) XXX (X.XXX) X.XX (X.XXX) X.XX (X.XXX) (XX.XX (X.XXX) (XX.XX) X.XXX X.XXX X.XXXX





Analysis Results Standard – What's in it for Me?



Add features that support automation of analysis results



Provide guidance on basic analysis structures towards analysis results generation



Provide greater traceability between analysis results and analysis data



Safety User Guide Project

Why Create a Safety User Guide?

Currently there is lack of a unified CDISC Safety User Guide that spans from data collection through analysis results



Each CDISC Foundational Standard has information on Safety Data that is commonly collected across studies of a wide-variety of indications



The TAUGs also often collect disease-specific safety information and examples



Will identify the most commonly performed safety analyses



Scope: From Analysis Results to Collection



Data Collection

cdisc

Row	STUDYID	DOMAIN	USUBJID	CESEQ	CECAT	CETERM	CEDECOD	CEPRESP	CEOCCUR	CESTDTC	CESTDY
2	XYZ	CE	XYZ-001-001	2	HYPO SYMPTOMS	SWEATING	Hyperhidrosis	Y	N		
3	XYZ	CE	XYZ-001-001	3	HYPO SYMPTOMS	TREMORS/TREMBLING	Tremor	Y	N		
4	XYZ	CE	XYZ-001-001	4	HYPO SYMPTOMS	DIZZINESS	Dizziness	Y	N		
5	XYZ	CE	XYZ-001-001	5	HYPO SYMPTOMS	COGNITIVE IMPAIRMENT	Cognitive Disorder	Y	Y		
6	XYZ	CE	XYZ-001-001	6	HYPO SYMPTOMS	LOSS OF CONSCIOUSNESS	Loss of Consciousness	Y	Y		
7	XYZ	CE	XYZ-001-001	7	HYPO SYMPTOMS	CONVULSIONS/SEIZURES	Convulsion	Y	N		
8	XYZ	CE	XYZ-001-001	8	HYPO SYMPTOMS	COMA	Coma	Y	N		
9	XYZ	CE	XYZ-001-001	9	HYPO EVENTS	HYPOGLYCEMIC EVENT	Hypoglycaemia			2013-09-24T08:48	50
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Safety User Guide – What's in it for Me?

- Standardize implementation of the most commonly performed Safety Analyses such as study drug exposure, adverse events, laboratory evaluations, vital signs, and others
- The Safety User Guide will provide:
 - Implementation guidance and examples using the new analysis results standards
 - Analysis datasets
 - Tabulation datasets
 - Data collection metadata
 - eCRFs in the eCRF portal

Provides common understanding of "how do we do safety"



Mining Biomedical Concepts from Define.xmls

Implementing 360: Standing Up Biomedical Concepts

STANDARDS DEVELOPMENT

1. Complete E2E Foundational Standards

- Project: eCRF Portal
- Project: Analysis Results Standard
- Project: Safety User Guide

STANDARDS DELIVERY

3. Extend CDISC Library Model

- Project: Model concepts
- Project: Add QRS content

2. Enrich Foundational Standards

• Project: Mining Define.xml's

4. Collaborate with Industry

• **Project:** Use mining Define.xml project as prototype for collaborative curation process



Mining Concepts from Define.xmls

- Retrieve metadata from Define.xmls to determine how standards are used in practice
- Curate the metadata (select best practice, standardize VLM) and stand up biomedical concepts
- Biomedical Concept modeling and load in CDISC Library

➔ The first biomedical concepts will be available in the CDISC Library and can be retrieved as an SDTM specification and Define.xml



Select and Identify the Concepts





Curate the Concepts

For the selected and identified concepts

- How are standards implemented in real studies?
- Determine the underlying SDTM structure for each concept
- Standardize the SDTM variable data types for each concept
 - e.g., Height STRESN is Float 4.1
- Standardize control terminology for each variable used in each concept
 - e.g., Height UNIT in CM or IN
- What do we consider?
 - Are there differences in how a concept is used across therapeutic areas?
 - Does this align with structure and business rules of the SDTMIG?
 - How do we compromise and reach consensus among different implementations?

Choose the best practice implementation





Load Concepts into CDISC Library

Dataset	Description	Class	Structure	Purpose	Keys	Location	Documentation
ТА	Trial Arms	TRIAL DESIGN	One record per planned Element per Arm	Tabulation	STUDYID, ARMCD, TAETORD	<u>ta.xpt</u>	
TE	Trial Elements	TRIAL DESIGN	One record per planned Element	Tabulation	STUDYID, ETCD	te.xot	
π	Trial Inclusion/Exclusion Criteria	TRIAL DESIGN	One record per I/E criterion	Tabulation	STUDYID, IETESTCD	ti.xpt	
TS	Trial Summary	TRIAL DESIGN	One record per trial summary parameter value	Tabulation	STUDYID, TSPARMCD, TSSEQ	ta.xpt	
τv	Trial Visits	TRIAL DESIGN	One record per planned Visit per Arm	Tabulation	STUDYID, VISITNUM, ARMCD	tv.xpt	
DM	Demographics	SPECIAL PURPOSE	One record per subject	Tabulation	STUDYID, USUBJID	dm.xpt	See Reviewer's Guide, Section 2. Demographics Reviewers Guide
SE	Subject Elements	SPECIAL PURPOSE	One record per actual Element per subject	Tabulation	STUDYID, USUBJID, SESTDTC, SEENDTC, TAETORD, ETCD	se.xpt	
sv	Subject Maits	SPECIAL PURPOSE	One record per actual visit per subject	Tabulation	STUDYID, USUBJID, SVSTDTC, VISITNUM	sy.xpt	
СМ	Concomitant Medications	INTERVENTIONS	One record per recorded medication occurrence or constant-dosing interval per subject	Tabulation	STUDYID, USUBID, CMSTDTC, CMENDTC, CMCAT, CMCAT, CMIRT, CMDOSTXT, CMDOSU, CMINDC, CMDOSEED	<u>cm.xpt</u>	



cdisc

Retrieve Concept Metadata from CDISC Library



SDTM Specifications



Define XML



"Mining Define.xmls" – What's in it for Me?

- Standardizing Value Level Metadata to increase consistency across studies
- Standardizing Data Types and Controlled Terminology per concept
- Linking concepts to SDTM structure to enable automation
 - Ability to Generate Define XML and SDTM Specifications from CDISC Library

This is just the first step of an open path to:

- Link lab concepts to unique LOINC codes
- Link concepts to how they are collected
- How concepts are used in analysis



Summary of Projects

Implementing 360: Projects' Summary

STANDARDS DEVELOPMENT

1. Complete E2E Foundational Standards

- Project: eCRF Portal
- Project: Analysis Results Standard
- Project: Safety User Guide

2. Enrich Foundational Standards

• Project: Mining Define.xml's

STANDARDS DELIVERY

3. Extend CDISC Library Model

- Project: Model concepts
- **Project:** Add QRS content

4. Collaborate with Industry

Project: Use mining Define.xml
 project as prototype for collaborative
 curation process



Biomedical Concept Layer



Biomedical Concept Layer

Presentation Layer





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eCRF Portal project



Biomedical Concept Layer

Presentation Layer

Data Flow





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"Analysis Results Standard" Project

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Biomedical Concept Layer

Presentation Layer



"Safety User Guide" Project



Biomedical Concept Layer







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"Mining Define.xml" Project

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We are on Our Way to

- Complete standards end-to-end (from analysis to collection)
- Content for standards implementation (e.g., value level metadata)
- Digitize therapeutic area user guides
- Extend the CDISC Library model to include biomedical concepts
- Set up a collaborative curation and governance process





Thank You!

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