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Incorporating the FDA BIMO and TransCelerate Guidance on Protocol Deviations into the DV Domain

Presented by Éanna Kiely, Head Clinical Data Standards, UCB and Daniil Teplitskii, Clinical Data Standards Manager, UCB

Meet the Speakers

Éanna Kiely

Title: Head Clinical Data Standards

Organization: UCB

Éanna Kiely is the Head of Clinical Data Standards in UCB, an authorized CDISC CDASH Instructor, a lecturer in CDISC/CDASH and CDISC consultant with ClinBuild. He is an author of CDASHIG 2.0 and SDTMIG 3.3, a long-term volunteer on CDISC teams and the E3C.
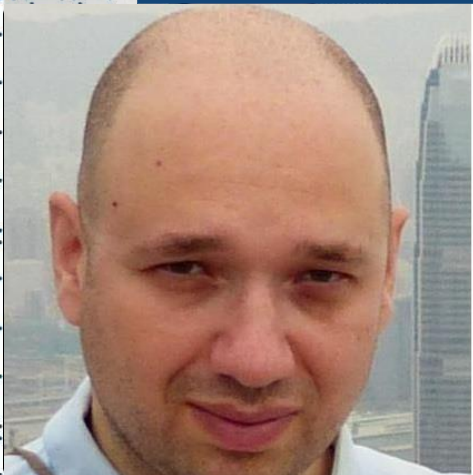
Daniil Teplitskii

Title: Clinical Data Standards Manager

Organization: UCB

Most of my career took place in CRO world, mostly in DM (but also in Clinical Ops as a CRA).

During the last several years I was being deep into clinical data standards.

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

- *The author(s) have no real or apparent conflicts of interest to report.*

Agenda

1. Introduction
2. New variable in DV dataset and its justification
3. The corresponding SDTM terminology (DVCAT, DVDECOD)
4. Publication and non-participant level deviations
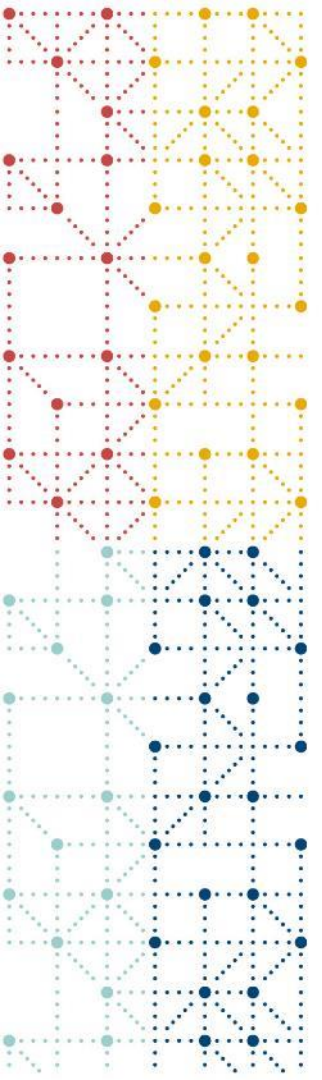
Introduction

The key concepts of the initiative

The key concepts of the initiative

- TransCelerate introduce **a new variable** (separate from DVCAT) **in DV domain** to contain information whether a Protocol deviation is Important / Non-important ("Important", "major", "critical" and "significant" are synonyms when referring to important protocol deviations).

- SDTM values for DVCAT codelist (corresponding to the categories developed by TransCelerate – please see the categories in TransCelerate_Protocol-Deviations_Process-Guide - *https://www.transceleratebiopharmainc.com/wp-content/uploads/2020/09/TransCelerate_Protocol-Deviations_Process-Guide_August-2020.pdf*).

- Aim to have other relevant controlled terminology (DVDECOD).

- Additional development: Site and country level PDs – CRAs or other roles identify every patient impacted at the time of PD identification. This is doable if the site only has a few patients, but is not scalable for sites or countries with larger number of patients;

  along with the consideration that a participant may change sites.

To meet BIMO TCG

7.   *Important Protocol Deviations*

This by-subject, by-clinical site listing should include all protocol deviations. The listing should include a description of the deviation and identify whether the sponsor considered the deviation to be an important or non-important protocol deviation.[4]

BIMO Technical Conformance Guide, July 2020, page 16

DV Domain (Protocol Deviations)

The DV domain should be included in your submission. It will be used by reviewers to examine protocol deviation trends of various study sites in order to facilitate the Bioresearch Monitoring Program (BIMO) clinical investigator site selection process, and once FDA tools are developed to extract and format needed data from SDTM, to populate line listings used by the Office of Regulatory Affairs (ORA) investigators during inspections. The following variables besides CDISC required variables should be included in the DV domain when submitting DV data: DVSPID, DVTERM, DVDECOD, DVCAT, DVSCAT, DVSTDTC, DVENDTC and EPOCH.

https://www.fda.gov/media/136460/download page 14

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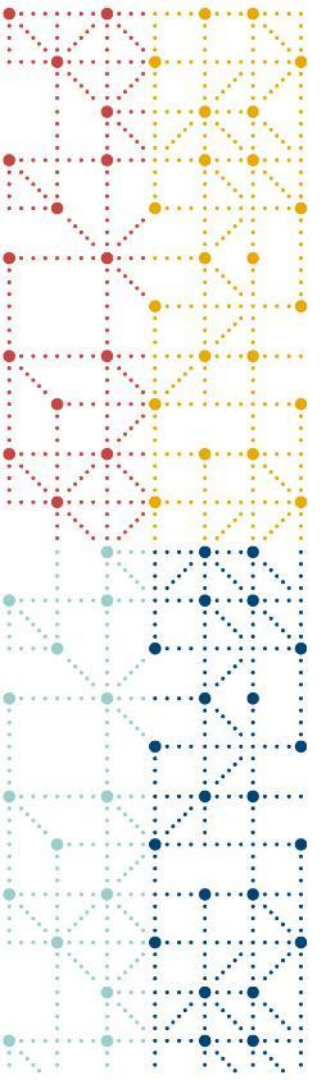
New variable in DV dataset and its justification

New variable in DV dataset and its justification

- Normal practice in many companies at the moment would be to enter such data into DVCAT variable in DV dataset, though TransCelerate suggest distinguishing between Categorization and Classification (Classification is to collect data whether Protocol deviation is important or non-important).

- *Rationale: to let DVCAT (Categorization) free to serve for splitting PDs into "big" categories.*

- We may name this new variable for Classification, say, DVCLASN (or, say, as an alternative, DVIMP with "Y" or "N" as flag – a good modeling topic to discuss) as possible values.

STUDYID	DOMAIN	USUBJID	DVSEQ	DVSPID	DVTERM	DVDECOD	DVCAT	DVCLASN	DVSTDTC	DVENDTC
ABC-1	DV	ABC-1futility - 101001	1	S101-PD01	NEW LAB TEST PERFORMED BEFORE PARTICIPANT WAS RECONSENTED	NEW CLINICAL STUDY PROCEDURES PERFORMED BEFORE PARTICIPANT WAS RECONSENTED	INFORMED CONSENT	IMPORTANT	2019-04-01	2019-04-01
ABC-1	DV	ABC-1-101001	2	S101-PD02	SUBJECT WAS DISPENSED DRUG THAT WAS 2 WEEKS AFTER EXPIRATION DATE AND WAS NOT TAKEN	SUBJECT WAS DISPENSED DRUG THAT WAS AFTER EXPIRATION DATE AND WAS NOT TAKEN	STUDY INTERVENTION	NON-IMPORTANT	2019-04-10	2019-04-10

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Important / Non-important Protocol Deviations

Important protocol deviations are a subset of protocol deviations that:

- may significantly impact the completeness, accuracy, and/or reliability of **key** study data

     or

- that may significantly affect a subject's rights, safety, or well-being

ICH E3 Guideline: Structure and content of Clinical Study Reports Questions & Answers (R1) July 2012 question 7

For example, important protocol deviations may include enrolling subjects in violation of key eligibility criteria or failing to collect data necessary to interpret primary endpoints, as this may compromise the scientific value of the trial.
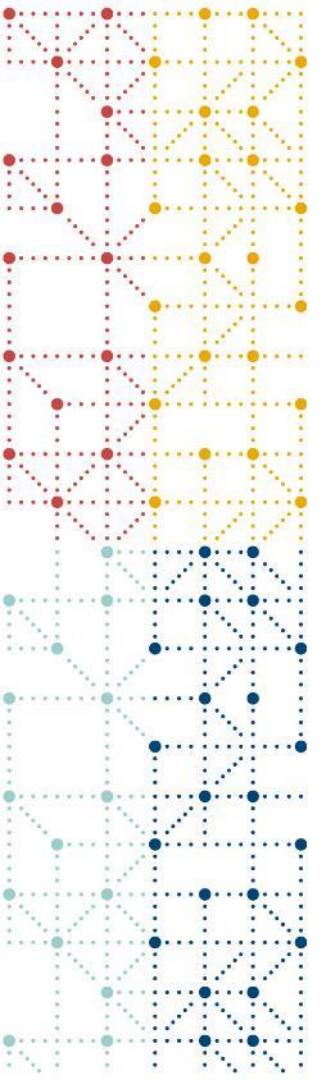
The corresponding SDTM terminology (DVCAT, DVDECOD)

SDTM values for DVCAT, the codelist

- The 4 ICH elements plus the 3 additional TransCelerate categories. See TransCelerate *"Protocol Deviation Process Guide"* Appendix 1.

Codelist Name	CDISC Submission Value	CDISC Synonym(s)
Category for Protocol Deviation	**DVCAT**	Category for Protocol Deviation
Category for Protocol Deviation	INFORMED CONSENT	Informed Consent
Category for Protocol Deviation	INCLUSION/ EXCLUSION	Inclusion/ Exclusion
Category for Protocol Deviation	STUDY INTERVENTION	Study Intervention
Category for Protocol Deviation	PROHIBITED CONCOMITANT MEDICATION	Prohibited Concomitant Medication
Category for Protocol Deviation	SAFETY REPORTING	Safety Reporting
Category for Protocol Deviation	TRIAL PROCEDURES	Trial Procedures
Category for Protocol Deviation	DISCONTINUATION	Discontinuation

SDTM values for DVDECOD, extensible codelist

- The further aim would be to develop extensible codelist for DVDECOD in CDISC Controlled terminology. *Examples (just one example for each Category).*

Codelist Name	CDISC Submission Value	CDISC Synonym(s)
Protocol Deviation Coded Term	**DVDECOD**	Protocol Deviation Coded Term
Protocol Deviation Coded Term	NEW CLINICAL STUDY PROCEDURES PERFORMED BEFORE PARTICIPANT WAS RECONSENTED	New clinical study procedures performed before participant was reconsented
Protocol Deviation Coded Term	SELECTION CRITERIA NOT MET	Selection criteria not met
Protocol Deviation Coded Term	INCORRECT DOSE	Incorrect dose
Protocol Deviation Coded Term	EXCLUDED CONCOMITANT MEDICATION	Excluded concomitant medication
Protocol Deviation Coded Term	PREGNANCY NOT REPORTED WITHIN THE EXPECTED TIME	Pregnancy not reported within the expected time
Protocol Deviation Coded Term	MISSED SAFETY OR EFFICACY ASSESSMENTS RELATED TO PRIMARY OR KEY SECONDARY ENDPOINTS	Missed safety or efficacy assessments related to primary or key secondary endpoints
Protocol Deviation Coded Term	SUBJECT NOT WITHDRAWN AS PER PROTOCOL	Subject not withdrawn as per protocol
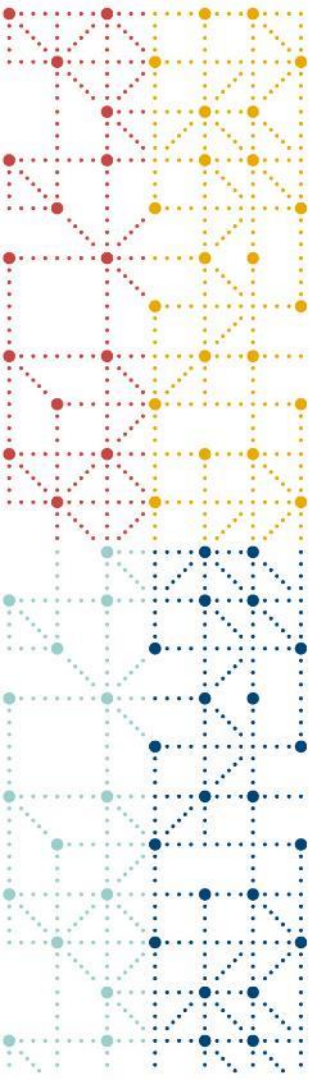
Publication in SDTM/IG 2.0/4.0

Non-Participant Level Deviations

New SDTMIG Major Version – New Possibilities

- Content produced by the Protocol Deviations Subteam is scheduled to be published in SDTMIG 4.0.

Target Year	Publication	Team	Project	Point of Contact
2023?	SDTMIG "v4.0"	Protocol Deviations Subteam	Further standardization of the DV domain and related terminology in alignment with TransCelerate.	@ Eanna Kiely @ Daniil Teplitskii Laura Galuchie

- SDTMIG 4.0 is planned to be a major update with potential additions of:
  - SUBJID as an Identifier for All Classes (+ SE/SV)
  - New Special Purpose Domain: Demographics as Collected (DC) for Rescreening and Reenrollment
  - Retirement of Supplemental Variables and Replacement with Non-Standard Variables
- Could the Protocol Deviations Subteam propose very new ways of reporting deviations?

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Non-Participant Level Data - POOLID

- In the CDISC Guidance for Ongoing Studies Disrupted by COVID-19 Pandemic Version 1.0 (2020-04-21) section 4 Protocol Deviations examples

Example 2

In this example, when a protocol deviation that affected subjects occurred at a site, the sponsor determined which subjects were affected by the deviation and used POOLDEF to define a pool for each deviation. The sponsor used DVCAT = "SITE DEVIATION" to identify site-level deviations.

pooldef.xpt

Row	STUDYID	POOLID	USUBJID
1	CVD-3	SITEDEV1	300
2	CVD-3	SITEDEV1	301
3	CVD-3	SITEDEV1	303
4	CVD-3	SITEDEV1	312
5	CVD-3	SITEDEV2	301
6	CVD-3	SITEDEV2	306
7	CVD-3	SITEDEV2	307
8	CVD-3	SITEDEV2	309
9	CVD-3	SITEDEV2	312

The pool identifier (POOLID) was then used in the DV domain.

Row 1:   Shows a protocol deviation for the pool of subjects given the identifier "SITEDEV1".

Row 2:   Shows a protocol deviation for the pool of subjects given the identifier "SITEDEV2".

dv.xpt

Row	STUDYID	DOMAIN	USUBJID	POOLID	DVSEQ	DVREFID	DVSPID	DVTERM	DVDECOD	DVCAT	DVSCAT	EPOCH	DVSTDTC	DVENDTC	DVREAS	DVEPRELI
1	CVD-3	DV		SITEDEV1				Site shut down		SITE DEVIATION		TREATMENT	2020-02-17	2020-02-20	Flooded basement	
2	CVD-3	DV		SITEDEV2				Site shut down		SITE DEVIATION		TREATMENT	2020-04-06	2020-04-18	All transportation in country down due to COVID-19.	Y

DV NSV Metadata

Variable	Label	Type	Codelist	Role	Origin	Comment
DVREAS	Reason for Deviation	text	DVCODES	Non-standard Record Qualifier	CRF	DVCODES is a sponsor-defined codelist.
DVEPRELI	Epi/Pandemic Related Indicator	text	NY	Non-standard Record Qualifier	CRF	

See Missed Visits for missed visits as protocol deviations and an alternative approach using a custom domain.

What is POOLID?

- POOLID is available for use in SDTM and is An Identifier for All Class.
- It is used commonly in SEND but had not been used in SDTM.

SDTM 1.7 - **2.2.4 Identifiers for All Classes**

All of the following identifier variables are available for use in any domain based on one of the 3 general observation classes. STUDYID, DOMAIN, and --SEQ are required in all domains based on one of the 3 general observation classes. Each general class domain must also include at least one of the following subject identifiers: USUBJID, APID, SPDEVID, or POOLID.

All identifier variables are allowed for all implementation guides.

Table 2.2.4.1 All Observation Classes - Identifiers

Variable Name	Variable Label	Type	Description
STUDYID	Study Identifier	Char	Unique identifier for a study.
DOMAIN	Domain Abbreviation	Char	2-character abbreviation for the domain most relevant to the observation. The domain abbreviation is also used as a prefix for variables to ensure uniqueness when datasets are merged.
USUBJID	Unique Subject Identifier	Char	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.
APID	Associated Persons Identifier	Char	Identifier for a single associated person, a group of associated persons, or a pool of associated persons. If APID identifies a pool, POOLDEF records must exist for each associated person. (See Table 4.1.3.1, Pool Definition Dataset and Section 6, Applying Model Fundamentals to Associated Persons).
POOLID	Pool Identifier	Char	An identifier used to identify a result from a group of subjects that is not assignable to a specific subject.
SPDEVID	Sponsor Device Identifier	Char	Sponsor-defined identifier for a device

1
2
3
4

Example Deviation – Incorrect Informed Consent

- Optional informed consent was not obtained for DNA extraction for gene expression profile of tumor (exploratory end-point) in some sites in Ireland and all sites in Germany.

Ireland

SITEID	Participants	Impacted
3001	199	Yes
3002	93	Yes
3003	124	Yes
3004	64	No
3005	119	No
3006	82	No
Total	**681**	**3**

Germany

SITEID	Participants	Impacted
6001	152	Yes
6002	94	Yes
6003	71	Yes
6004	94	Yes
6005	179	Yes
6006	124	Yes
Total	**714**	**6**

STUDYID	DOMAIN	USUBJID	DVSEQ	DVSPID	DVTERM	DVCAT	DVCLASN
PD01	DV	PD01-3001-0001	1	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
PD01	DV	PD01-3001-0002	2	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
PD01	DV	PD01-3001-0003	3	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
…	…	…	…	…	…	…	…
PD01	DV	PD01-3002-0001	292	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
…	…	…	…	…	…	…	…
PD01	DV	PD01-3003-0001	416	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
…	…	…	…	…	…	…	…
PD01	DV	PD01-6001-0001	568	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
…	…	…	…	…	…	…	…
PD01	DV	PD01-6002-0001	662	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
…	…	…	…	…	…	…	…
PD01	DV	PD01-6003-0001	733	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
…	…	…	…	…	…	…	…
PD01	DV	PD01-6004-0001	827	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
…	…	…	…	…	…	…	…
PD01	DV	PD01-6005-0001	1006	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
…	…	…	…	…	…	…	…
PD01	DV	PD01-6006-0124	1130	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT

STUDYID	DOMAIN	USUBJID	DVSEQ	DVSPID	DVTERM	DVCAT	DVCLASN
PD01	DV	PD01-3001-0001	1	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
PD01	DV	PD01-3001-0002	2	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
PD01	DV	PD01-3001-0003	3	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
...	...	...	...	...	...	...	...
PD01	DV	PD01-3002-0001	292	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
...	...	...	...	...	...	...	...
PD01	DV	PD01-3003-0001	416	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
...	...	...	...	...	...	...	...
PD01	DV	PD01-6001-0001	568	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
...	...	...	...	...	...	...	...
PD01	DV	PD01-6002-0001	662	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
...	...	...	...	...	...	...	...
PD01	DV	PD01-6003-0001	733	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
...	...	...	...	...	...	...	...
PD01	DV	PD01-6004-0001	827	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
...	...	...	...	...	...	...	...
PD01	DV	PD01-6005-0001	1006	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT
...	...	...	...	...	...	...	...
PD01	DV	PD01-6006-0124	1130	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	IMPORTANT

POOLID Can Reduce the DV Records from 1130 to …

- By using POOLID it is possible to reduce the number of records

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POOLID Can Reduce the DV Records from 1130 to 1

- By using POOLID it is possible to reduce the number of records

STUDYID	DOMAIN	USUBJID	POOLID	DVSEQ	DVSPID	DVTERM	DVDECOD	DVCAT	DVCLASN
PD01	DV		PD001-0001	1	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT

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POOLID Can Reduce the DV Records from 1130 to 1

- By using POOLID it is possible to reduce the number of records
- However, it is still necessary to create a POOLEF to describe the POOLID

STUDYID	DOMAIN	USUBJID	POOLID	DVSEQ	DVSPID	DVTERM	DVDECOD	DVCAT	DVCLASN
PD01	DV		PD001-0001	1	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT

POOLDEF adds 1130 records…

Row	STUDYID	POOLID	USUBJID
1	PD01	PD001-0001	PD01-3001-0001
…	…	…	…
292	PD01	PD001-0001	PD01-3002-0001
…	…	…	…
416	PD01	PD001-0001	PD01-3003-0001
…	…	…	…
568	PD01	PD001-0001	PD01-6001-0001
…	…	…	…
662	PD01	PD001-0001	PD01-6002-0001
…	…	…	…
733	PD01	PD001-0001	PD01-6003-0001
…	…	…	…
827	PD01	PD001-0001	PD01-6004-0001
…	…	…	…
1006	PD01	PD001-0001	PD01-6005-0001
…	…	…	…
1007	PD01	PD001-0001	PD01-6006-0001

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SDTM 2.0

- In draft SDTM 2.0 the tables include additional columns and additional identifiers are currently planned.

Variable Name	Variable Label	Type	Format	Role	Variable(s) Qualified	Usage Restrictions	Variable C-code	Definition	Notes	Examples
STUDYID	Study Identifier	Char		Identifier			C83082	A sequence of characters used by the sponsor to uniquely identify the study.		
DOMAIN	Domain Abbreviation	Char		Identifier			C49558	An abbreviation for a collection of observations, with a topic-specific commonality.	2-character abbreviation. The domain abbreviation is also used as a prefix for variables to ensure uniqueness when datasets are merged.	
USUBJID	Unique Subject Identifier	Char		Identifier			C69256	A sequence of characters used to uniquely identify a subject across all studies for all applications or submissions involving the product.		
POOLID	Pool Identifier	Char		Identifier			C117053	A sequence of characters used to uniquely identify a group of subjects that have been pooled together.	Used for results that are not assignable to a specific subject.	
SPDEVID	Sponsor Device Identifier	Char		Identifier			C117060	A sequence of characters used by the sponsor to uniquely identify a specific device.		

SDTM 2.0 – New Possibilities

- SUBJID may be promoted

Variable Name	Variable Label	Type	Format	Role	Variable(s) Qualified	Variable C-code	Definition	Notes
USUBJID	Unique Subject Identifier	Char		Identifier		C69256	A sequence of characters used to uniquely identify a subject across all studies for all applications or submissions involving the product.	
SUBJID	**Subject Identifier for the Study**	**Char**		**Identifier**				**Subject identifier, which must be unique within the study. Often the ID of the subject as recorded on a CRF**.
POOLID	Pool Identifier	Char		Identifier		C117053	A sequence of characters used to uniquely identify a group of subjects that have been pooled together.	Used for results that are not assignable to a specific subject.
SPDEVID	Sponsor Device Identifier	Char		Identifier		C117060	A sequence of characters used by the sponsor to uniquely identify a specific device.	

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SDTM 2.0 – New Possibilities

- SUBJID may be promoted

- Could SITEID?

Variable Name	Variable Label	Type	Format	Role	Variable(s) Qualified	Variable C-code	Definition	Notes
USUBJID	Unique Subject Identifier	Char		Identifier		C69256	A sequence of characters used to uniquely identify a subject across all studies for all applications or submissions involving the product.	
SUBJID	**Subject Identifier for the Study**	**Char**		**Identifier**				**Subject identifier, which must be unique within the study. Often the ID of the subject as recorded on a CRF**.
POOLID	Pool Identifier	Char		Identifier		C117053	A sequence of characters used to uniquely identify a group of subjects that have been pooled together.	Used for results that are not assignable to a specific subject.
SPDEVID	Sponsor Device Identifier	Char		Identifier		C117060	A sequence of characters used by the sponsor to uniquely identify a specific device.	
SITEID	Study Site Identifier	Char		Identifier			A sequence of characters used to uniquely identify the facility associated with study-specific activities.	

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SITEID Reduces the Records to 9 with no POOLDEF

STUDYID	DOMAIN	USUBJID	SITEID	DVSEQ	DVSPID	DVTERM	DVDECOD	DVCAT	DVCLASN
PD01	DV		3001	1	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT
PD01	DV		3002	2	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT
PD01	DV		3003	3	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT
PD01	DV		6001	4	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT
PD01	DV		6002	5	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT
PD01	DV		6003	6	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT
PD01	DV		6004	7	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT
PD01	DV		6005	8	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT
PD01	DV		6006	9	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT

SDTM 2.0 – New Possibilities

- SUBJID may be promoted

- Could SITEID and COUNTRY?

Variable Name	Variable Label	Type	Format	Role	Variable(s) Qualified	Variable C-code	Definition	Notes
USUBJID	Unique Subject Identifier	Char		Identifier		C69256	A sequence of characters used to uniquely identify a subject across all studies for all applications or submissions involving the product.	
SUBJID	**Subject Identifier for the Study**	**Char**		**Identifier**				**Subject identifier, which must be unique within the study. Often the ID of the subject as recorded on a CRF**.
POOLID	Pool Identifier	Char		Identifier		C117053	A sequence of characters used to uniquely identify a group of subjects that have been pooled together.	Used for results that are not assignable to a specific subject.
SPDEVID	Sponsor Device Identifier	Char		Identifier		C117060	A sequence of characters used by the sponsor to uniquely identify a specific device.	
SITEID	**Study Site Identifier**	**Char**		**Identifier**			**A sequence of characters used to uniquely identify the facility associated with study-specific activities.**	
COUNTRY	**Country**	**Char**	**ISO 3166-1 Alpha-3**	**Identifier**		**C170990**	**The country in which the investigational site is located.**	

SITEID and COUNTRY Reduces the Records to 4

STUDYID	DOMAIN	USUBJID	SITEID	COUNTRY	DVSEQ	DVSPID	DVTERM	DVDECOD	DVCAT	DVIMP
PD01	DV		3001		1	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	Y
PD01	DV		3002		2	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	Y
PD01	DV		3003		3	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	Y
PD01	DV			DEU	4	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	Y

Variable name still not set

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Why Stop There…

Example Deviation: Re-Consent Updated Risk Language Not Signed

Summary Product Characteristics/IB risk language update leads to updated Patient information sheet, reconsent required.

Country	ISO 3166-1 Alpha-3	Sites	Participants
Argentina	ARG	12	582
Australia	AUS	7	328
Austria	AUT	3	116
Belgium	BEL	3	149
Brazil	BRA	55	2,740
Bulgaria	BGR	2	89
Canada	CAN	10	486
Chile	CHL	5	246
China	CHN	372	18,558
Colombia	COL	14	656
Denmark	DNK	2	74
France	FRA	17	841
Germany	DEU	22	1,080
Greece	GRC	3	134
Hungary	HUN	3	124
Iceland	ISL	1	4
India	IND	356	17,793
Ireland	IRL	2	63
Israel	ISR	3	111
Italy	ITA	16	779
Japan	JPN	33	1,630
Lithuania	LTU	1	35
Luxembourg	LUX	1	8
Malawi	MWI	5	246
Malta	MLT	1	5
Mexico	MEX	34	1,662

Countries	
53	
Sites	
1,321	
Participants	
64,725	

Country	ISO 3166-1 Alpha-3	Sites	Participants
Morocco	MAR	10	475
Netherlands	NLD	5	220
New Zealand	NZL	2	62
Norway	NOR	2	69
Poland	POL	10	487
Portugal	PRT	3	131
Romania	ROU	5	248
Russia	RUS	38	1,881
Rwanda	RWA	4	167
Singapore	SGP	2	75
Slovakia	SVK	2	70
Slovenia	SVN	1	26
South Africa	ZAF	16	764
South Korea	KOR	14	661
Spain	ESP	13	602
Sri Lanka	LKA	6	276
Sweden	SWE	3	130
Switzerland	CHE	3	111
Thailand	THA	18	899
Tunisia	TUN	4	152
Turkey	TUR	22	1,087
Uganda	UGA	12	589
Ukraine	UKR	12	563
United Kingdom	GBR	18	875
United States of America	USA	86	4,267
Uruguay	URY	1	44
Vietnam	VNM	26	1,255

Why Stop There: Extending POOLDEF

- POOLID already includes USUBJID and APID.
- Should it also include: SUBJID, SPDEVID, SITEID and COUNTRY?

Variable Name	Variable Label	Type	Format	Role
STUDYID	Study Identifier	Char		Identifier
POOLID	Pool Identifier	Char		Identifier
USUBJID	Unique Subject Identifier	Char		Identifier
SUBJID	**Subject Identifier for the Study**	**Char**		**Identifier**
APID	Associated Persons Identifier	Char		Identifier
SPDEVID	**Sponsor Device Identifier**	**Char**		**Identifier**
SITEID	**Study Site Identifier**	**Char**		**Identifier**
COUNTRY	**Country**	**Char**		**Identifier**

Example Deviation: Re-Consent Updated Risk Language Not Signed

Row	STUDYID	POOLID	COUNTRY
1	PD02	PD002	ARG
2	PD02	PD002	AUS
3	PD02	PD002	AUT
4	PD02	PD002	BEL
5	PD02	PD002	BRA
6	PD02	PD002	BGR
7	PD02	PD002	CAN
8	PD02	PD002	CHL
9	PD02	PD002	CHN
10	PD02	PD002	COL
11	PD02	PD002	DNK
12	PD02	PD002	FRA
13	PD02	PD002	DEU
14	PD02	PD002	GRC
15	PD02	PD002	HUN
16	PD02	PD002	ISL
17	PD02	PD002	IND
18	PD02	PD002	IRL
19	PD02	PD002	ISR
20	PD02	PD002	ITA
21	PD02	PD002	JPN
22	PD02	PD002	LTU
23	PD02	PD002	LUX
24	PD02	PD002	MWI
25	PD02	PD002	MLT

Row	STUDYID	POOLID	COUNTRY
27	PD02	PD002	MAR
28	PD02	PD002	NLD
29	PD02	PD002	NZL
30	PD02	PD002	NOR
31	PD02	PD002	POL
32	PD02	PD002	PRT
33	PD02	PD002	ROU
34	PD02	PD002	RUS
35	PD02	PD002	RWA
36	PD02	PD002	SGP
37	PD02	PD002	SVK
38	PD02	PD002	SVN
39	PD02	PD002	ZAF
40	PD02	PD002	KOR
41	PD02	PD002	ESP
42	PD02	PD002	LKA
43	PD02	PD002	SWE
44	PD02	PD002	CHE
45	PD02	PD002	THA
46	PD02	PD002	TUN
47	PD02	PD002	TUR
48	PD02	PD002	UGA
49	PD02	PD002	UKR
50	PD02	PD002	GBR
51	PD02	PD002	USA

POOLDEF has been reduced from 64,725 participant records to 53 country records

STUDYID	DOMAIN	USUBJID	POOLID	DVSEQ	DVSPID
PD02	DV		PD02	1	PD02

DVTERM	DVDECOD	DVCAT	DVCLASN
WRONG INFORMED CONSENT VERSION SIGNED	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT

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POOLDEF Could be Reduced from 1130 to 4

- By extending the Identifiers in POOLDEF it could be possible to reduce the number of records from our previous example…

STUDYID	DOMAIN	USUBJID	POOLID	DVSEQ	DVSPID	DVTERM	DVDECOD	DVCAT	DVCLASN
PD01	DV		PD001-0001	1	PD001	OPTIONAL INFORMED CONSENT NOT OBTAINED FOR GENE EXPRESSION PROFILE (DNA EXTRACTION)	INFORMED CONSENT	INFORMED CONSENT	IMPORTANT

Row	STUDYID	POOLID	SITEID	COUNTRY
1	PD01	PD001-0001	3001	
2	PD01	PD001-0001	3002	
3	PD01	PD001-0001	3003	
4	PD01	PD001-0001		DEU

POOLDEF could be reduced from 1130 participant records to 4 records (3 site + 1 country)

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Supplemental Files

NCI FTP Links   Resources   Rules   **Codetable Mapping Files**

Unit-UCUM Mapping File   LOINC to LB Mapping Files   Paired Codelists

To address this issue, the Controlled Terminology Teams have created Codetable Mapping Files based on published Terminology, which show relationships between terms in different Controlled Terminology codelists. These supplemental files provide human and machine-readable linkages between published terms across multiple codelists and may be helpful for data QA/QC, CRF building, and data mapping. These files are for clinical use only.

The Controlled Terminology teams will continue to update these files as new Terminology is published, as well as develop new domain Codetable Mapping Files. If you are interested in seeing specific content developed, please submit the request through the **New Term Request Site**. CDISC is concurrently working on the development of electronically consumable formats of this content to be published out of **CDISC Library**.

SDTMIG3.2 Variable_Codelist

DD Codetable

DS Codetable

DV Codetable???

CV Codetable

The [CDISC Controlled Terminology](#) Team releases Codetable Mapping Files that link different CT together.

The Protocol Deviations Subteam could suggest/create Codetables.

Possible Codetable Mapping

| Category for Disposition Event (DSCAT)	For DSDECOD when DSCAT=DISPOSITION EVENT Completion/Reason for Non-Completion (NCOMPLT)	For DSDECOD when DSCAT=OTHER EVENT Other Disposition Event Response (OTHEVENT)	For DSDECOD when DSCAT=PROTOCOL MILESTONE Protocol Milestone (PROTMLST)
DISPOSITION EVENT	ADVERSE EVENT		
DISPOSITION EVENT	COMPLETED		
DISPOSITION EVENT	DEATH		
OTHER EVENT		TREATMENT UNBLINDED	
OTHER EVENT		WITHDRAWAL OF CONSENT FROM PROTOCOL-SPECIFIED ACTIVITY	
PROTOCOL MILESTONE			ELIGIBILITY CRITERIA MET
PROTOCOL MILESTONE			INFORMED CONSENT OBTAINED
PROTOCOL MILESTONE			RANDOMIZED

Category for Disposition Event (DVCAT)	For DVDECOD when DVCAT=INFORMED CONSENT	For DVDECOD when DVCAT=STUDY INTERVENTION	For DVDECOD when DVCAT= TRIAL PROCEDURES
INFORMED CONSENT	NEW CLINICAL STUDY PROCEDURES PERFORMED BEFORE PARTICIPANT WAS RECONSENTED		
STUDY INTERVENTION		INCORRECT DOSE	
TRIAL PROCEDURES			PREGNANCY NOT REPORTED WITHIN THE EXPECTED TIME
TRIAL PROCEDURES			MISSED EFFICACY ASSESSMENTS RELATED TO PRIMARY OR KEY SECONDARY ENDPOINTS

Please Volunteer on the Protocol Deviations Subteam!!!

- Volunteer on the protocol deviations subteam and you can:
  - draft and submit Controlled Terminology (~2021)
  - propose and draft Codetable Mapping Files (~2021)
  - collect and prepare modeling examples
    - could be used as NSV (~2021)
    - published SDTMIG 4.0 (~2023)
- please contact:

  Daniil (Dan) Teplitskii – Lead- (Daniil.Teplitskii@ucb.com)

  Éanna Kiely – (Co)Lead - (Eanna.Kiely@ucb.com)

cdisc   Kick-off meeting is scheduled for May!!!
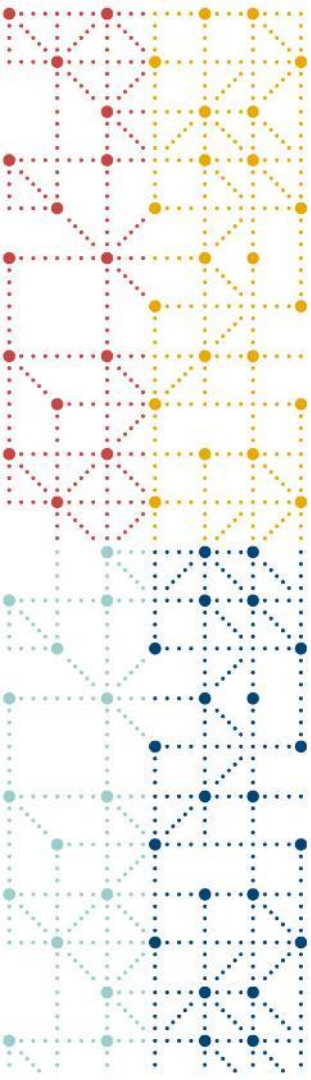
Thank You!

Any Questions?

(…please volunteer)

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