

PP10 DV Domain and the Classification of Protocol Deviations

Introduction

With the latest update of SDTM implementation guide 3.2 the DV domain has been proposed to capture the clinical information of subject-specific deviations from the clinical study protocol. The classification process of protocol deviations in a joint meeting between client, biostatistician and study project lead is a critical and integral part of most clinical studies.

To meet a high standard of consistency between SDTM on the one hand and analysis datasets and clinical study analyses and their reports on the other, ICON proposes the inclusion of the classification results within the DV domain dataset (SDTM IG 3.2).

- Process Flow
- Pros & Cons
- Next Step

Processing of Protocol Deviations I

1. Report of Protocol Deviations (PDs)

[illegible]

Protocol Deviation Criteria From: Reports by CRA/ClinOps into Protocol Deviation Criteria Form by type of PDs.

1a. Create Lists of Programmable Checks

2. Regular Reviews of PDs by ICON and Client Staff

3. Mapping of PDCF to DV Domain

3a. DV – Description/Overview for Protocol Deviations Domain Model (Section 6.2 SDTM IG 3.2)

	A	B	C	D	E	F	G	H	I	J	K	L
	Dataset	Variable Name	Label	Type	Length	Controlled Terminology	Origin	Role	Core	Comments	Source	Programming Notes
1	DV	STUDYID	Study Identifier	text	21		CRF Page 3	Identifier	Req	CPH-302-201030	EXT_PD.SPONSNO	
3	DV	DOMAIN	Domain Abbreviation	text	2	DOMAIN	Assigned	Identifier	Req	DV		
4	DV	USUBJID	Unique Subject Identifier	text	30		Assigned	Identifier	Req	Concatenate STUDYID, SITEID, and USUBID, separated by 7	EXT_PD.SCREENNO	
										Sequential number uniquely identifying the records within the domain by USUBJID and generated using the key sequence from the domain level metadata.		
5	DV	DVSEQ	Sequence Number	integer	8		Assigned	Identifier	Req			
6	DV	DVREFID	Reference ID	text		40	Assigned	Identifier	Perm		EXT_PD.DEVID	
7	DV	DVTERM	Protocol Deviation Term	text	200		eDT	Topic	Req	Populate only 200 characters. If more than 200 characters then move to SUPP Qual dataset.	EXT_PD.DEVCOM	
8	DV	DVDECO	Protocol Deviation Coded Term	text	200		eDT	Synonym Qualifier	Perm			Concatenate DVCAT and DVSCAT separated by '-'.
9	DV	DVCAT	Category for Protocol Deviation	text	40		eDT	Grouping Qualifier	Perm		EXT_PD.DEVTYPE	
10	DV	DVSCAT	Subcategory for Protocol Deviation	text	40		eDT	Grouping Qualifier	Perm		EXT_PD.DEVSUBTYPE	
11	DV	EPOCH	Epoch	text	40		Protocol	Timing	Perm	# SESTDTC <= DVNTDC < SEENDTC then use that EPOCH from SE domain		
12	DV	DVSTDTC	Start Date/Time of Deviation	datetime	19	ISO8601	eDT	Timing	Perm	ISO 8601 Calculation: If (DVSTDTC < DM.RFSTDTC) then DVSTDY=DVSTDTC-DM.RFSTDTC; Else if (DVSTDTC >= DM.RFSTDTC) then DVSTDY=DVSTDTC-DM.RFSTDTC+1.	EXT_PD.OCDATE	
13	DV	DVSTDY	Study Day of Start of Deviation	integer	8	Derived	Timing	Perm				

3b. DV Domain Example

Type of PD: Subject-related

VIEWTABLE: TMP1_dv_select												
	Study Identifier	Domain Abbreviation	Unique Subject Identifier	Sequence Number	Reference ID	Protocol Deviation Text	Protocol Deviation Coded Text	Category for Protocol Deviation	Subcategory for Protocol Deviation	Epoch	Start Date/Time of Deviation	Study Day of Start of Deviation
1	EXAMPLE1	DV	EXAMPLE1-1	1	85858701	VISIT CONDUCTED 12 DAYS OUT OF WINDOW (EXPECTED: 22NOV2016 +/- 2 DAYS) EVEN THOUGH SITE HAD SCHEDULED VISIT WITHIN WINDOW. SPECIFIED WINDOW DUE TO SUBJECT TRAVEL FOR HOLIDAY.	VISIT SCHEDULE VISIT OUTSIDE PROTOCOL WINDOW	VISIT SCHEDULE	VISIT OUTSIDE PROTOCOL WINDOW	OPEN LABEL TREATMENT	2016-12-06	21
2	EXAMPLE1	DV	EXAMPLE1-2	1	80173701	PAGE 16 OF 20 OF ICF WAS MISSING THE SIGNATURE OF THE PERSON OBTAINING CONSENT.	ICF ISSUES/ICF NOT DATED BY SUBJECT/SITE	ICF ISSUES	ICF NOT DATED BY SUBJECT/SITE	SCREENING	2016-06-29	4
3	EXAMPLE1	DV	EXAMPLE1-3	1	80173801	PAGE 16 OF 20 OF ICF WAS NOT SIGNED BY THE PERSON OBTAINING CONSENT AND PAGE 17 OF 20 WAS MISSING A SIGNATURE OF THE PERSON OBTAINING CONSENT. SUBJECT'S INITIALS IN THE BOX THAT REQUIRES THE INITIALS REGARDING PHOTOGRAPHS.	ICF ISSUES/ICF NOT DATED BY SUBJECT/SITE	ICF ISSUES	ICF NOT DATED BY SUBJECT/SITE	SCREENING	2016-06-29	4
4	EXAMPLE1	DV	EXAMPLE1-4	1	95726201	SUBJECT WAS ENROLLED IN STUDY WHILE TAKING PROHIBITED MEDICATION.	INCLUSION / EXCLUSION SUBJECT ON EXCLUDED MEDICATION(S)	INCLUSION / EXCLUSION	SUBJECT ON EXCLUDED MEDICATION(S)	SCREENING	2016-06-22	4

4. Export DV data into Excel to Prepare DCM

Proposal: Include here already novel classification variables as drop down-down menu with predefined values

Processing of Protocol Deviations II

Proposal: Identical Classification Variables in Excel and DV/SUPPDV domains?

5. Data Classification Meeting (DCM)

[illegible]

6a. DV Domain: Novel Variables Proposed

Unique Subject Identifier	Sequence Number	Reference ID	Protocol Deviation Term	Protocol Deviation Coded Term	Category for Protocol Deviation	Subcategory for Protocol Deviation	Epoch	Start Date/Time of Deviation	Study Day of Start of Deviation	Exclude From Analysis	Major/Minor
1	EXAMPLE-1	1 5858701	VISIT CONDUCTED 12 DAYS OUT OF WINDOW (EXPECTED 22NOV2016 +/- 2 DAYS) EVEN THOUGH SITE HAD SCHEDULED VISIT WITHIN PROTOCOL-SPECIFIED WINDOW DUE TO SUBJECT TRAVEL FOR HOLIDAY.	VISIT SCHEDULED/VISIT OUTSIDE PROTOCOL WINDOW	VISIT SCHEDULE	VISIT OUTSIDE PROTOCOL WINDOW	OPEN LABEL TREATMENT	2016-12-06	212		Minor
2	EXAMPLE-2	1 80173701	PAGE 16 OF 20 OF ICF WAS MISSING THE SIGNATURE OF THE PERSON OBTAINING CONSENT.	ICF ISSUES-ICF NOT DATED BY SUBJECT/SITE	ICF ISSUES	ICF NOT DATED BY SUBJECT/SITE	SCREENING	2016-06-29	6	IT/FAS/PP	Major
3	EXAMPLE-3	1 80173801	PAGE 16 OF 20 OF ICF WAS NOT SIGNED BY THE PERSON OBTAINING CONSENT AND PAGE 17 OF 20 WAS MISSING THE SUBJECT'S INITIALS IN THE BOX THAT REQUIRES THE INITIALS REGARDING PHOTOGRAPHS.	ICF ISSUES-ICF NOT DATED BY SUBJECT/SITE	ICF ISSUES	ICF NOT DATED BY SUBJECT/SITE	SCREENING	2016-06-29	6	IT/FAS/PP	Major
4	EXAMPLE-4	1 95762801	SUBJECT WAS ENROLLED IN STUDY WHILE TAKING PROHIBITED MEDICAL SUPPLEMENTS.	INCLUSION / EXCLUSION SUBJECT ON LIFE-IMPENDING MODIFICATIONS	INCLUSION / EXCLUSION SUBJECT ON LIFE-IMPENDING MODIFICATIONS	SUBJECT ON EXCLUDED MODIFICATIONS	SCREENING	2016-06-22	8	PP	Major

6b. SUPPDV Domain: Novel Variables Proposed

	Study Identifier	Related Domain Abbreviation	Unique Subject Identifier	Identifying Variable	Identifying Variable Value	Qualifier Variable Name	Qualifier Variable Label	Data Value
1	EXAMPLE1	DV	EXAMPLE1-1	DVSEQ	1	MAJMIN	Major or Minor	MINOR
2	EXAMPLE1	DV	EXAMPLE1-2	DVSEQ	1	MAJMIN	Major or Minor	MAJOR
3	EXAMPLE1	DV	EXAMPLE1-3	DVSEQ	1	MAJMIN	Major or Minor	MAJOR
4	EXAMPLE1	DV	EXAMPLE1-4	DVSEQ	1	MAJMIN	Major or Minor	MAJOR
5	EXAMPLE1	DV	EXAMPLE1-1	DVSEQ	1	EXANAL	EXCLUDE FROM ANALYSIS	NO
6	EXAMPLE1	DV	EXAMPLE1-2	DVSEQ	1	EXANAL	EXCLUDE FROM ANALYSIS	ITT/FAS/PP
7	EXAMPLE1	DV	EXAMPLE1-3	DVSEQ	1	EXANAL	EXCLUDE FROM ANALYSIS	ITT/FAS/PP
8	EXAMPLE1	DV	EXAMPLE1-4	DVSEQ	1	EXANAL	EXCLUDE FROM ANALYSIS	PP

Pros & Cons

Pros:

- High Standard of Consistency
- SDTM
- Analysis Dataset
- Tables/Figures/Listings
- CSR

Cons:

- DV domain not apt
- Process not feasible in real time
- Mapping classification back to SUPPDV
- Tight timing between events 5 and 6b

Next Step

As next step, to work on how to process site-related PDs:

- Attributed to subjects of a related site?
- In SDTM?
- In an Analysis Dataset

Open to discussion...

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