

Rescreened Subjects, Data Collection and Standard Domains Mapping

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June 14th – 18th, 2021

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Vamshi Matta Biography

Vamshi Matta holds a Master's degree in Computer Science, currently working at Covance as a Sr. Principal statistical programmer with extensive CDISC experience. She is part of the innovations team, building open source utilities using R and Python.

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Introduction

- ▶ In this paper we will discuss how we map the re-screened subjects data in SDTMs.
- ▶ These slides are created based on FDA TCG V4.5.1 and proposal from CDISC SDS Multiple Subject Instances (MSI) Team.

FDA TCG v4.5.1 (July 2020) section 4.1.1.3 SDTM Domain Specifications

Explains how subjects with multiple enrollments within a single study should be mapped

DM (Demographics)

- ▶ For subjects with multiple enrollments within a single study, the primary enrollment should be submitted in DM. Additional enrollments should be included in a custom domain with a similar structure to DM. Clarifying statements in the RG would be helpful.
- ▶ For subjects with multiple screenings and no subsequent enrollment, include the primary screening in DM with additional screenings in a custom domain with a structure similar to DM.
- ▶ For subjects with multiple screenings and subsequent enrollment, include the enrollment in DM with screenings in a custom domain with a structure similar to DM.

CDISC SDS Multiple Subject Instances (MSI) Team

- ▶ The MSI team proposes to create an additional Special Purpose domain called Demographics as Collected (DC) to act as the custom domain with a similar structure to DM.
- ▶ The DC domain is still under review within CDISC but has general support.
- ▶ It has not been directly reviewed by the FDA. Discuss with the relevant FDA review division before submitting the MSI team's approach.
- ▶ It will not be included in SDTMIG 3.4 possibly SDTMIG 4.0

Multiple Screen Failures: DC and DM

Row	STUDYID	DOMAIN	USUBJID	SUBJID	DCSEQ	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM
2	ABC123	DC	ABC12301002	1002	1	2006-01-12	2006-01-26	2006-01-12	2006-01-26	2006-01-04	2006-02-23	1	JOHNSON, M
4	ABC123	DC	ABC12301S005	S001	1					2005-11-14	2005-11-16	1	JOHNSON, M
5	ABC123	DC	ABC12301S005	S005	2					2006-01-07	2006-01-08	1	JOHNSON, M

Row	BRTHDTC	AGE	AGEU	SEX	RACE	ETHNIC	ARMCD	ARM	ACTARMCD	ACTARM	ARMNRS	ACTARMUD	COUNT
2	1955-03-22	50	YEARS	M	MULTIPLE	NOT HISPANIC OR LATINO	P	Placebo	P	Placebo			USA
4	1941-07-02			M	ASIAN	NOT HISPANIC OR LATINO					SCREEN FAILURE		USA
5											SCREEN FAILURE		USA

Row	STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM
2	ABC123	DM	ABC12301002	1002	2006-01-15	2006-02-28	2006-01-15	2006-02-28	2006-01-04	2006-03-26	1	JOHNSON, M
4	ABC123	DM	ABC12301S005	S005					2006-01-07	2006-01-08	1	JOHNSON, M

Row	BRTHDTC	AGE	AGEU	SEX	RACE	ETHNIC	ARMCD	ARM	ACTARMCD	ACTARM	ARMNRS	ACTARMUD	COUNT
2	1955-03-22	50	YEARS	M	MULTIPLE	NOT HISPANIC OR LATINO	P	Placebo	P	Placebo			U
4	1941-07-02			M	ASIAN	NOT HISPANIC OR LATINO					SCREEN FAILURE		U

Multiple Screen Failures: DC and DM

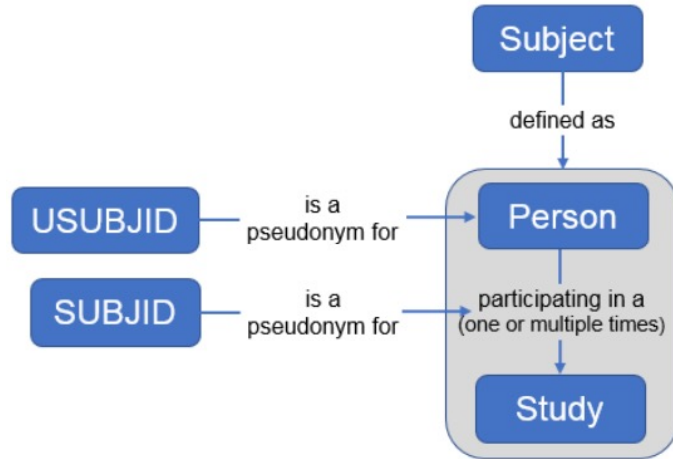
- ▶ Row 5 in DC Domain shows the second screening participation for USUBJID ABC12301S005. Note that per protocol, date of birth, sex, race, and ethnicity were not re-collected. Age has not been derived, as per protocol it is based on the date captured in RFSTDTC, which is null for a screen failure.
- ▶ Row 4: USUBJID ABC12301S005 is a merging of DC row 4 and 5. RFICDTC and RFPENDTC are from DC row 5 where as SITEID, INVNAM, BRTHDTC, AGE, AGEU, SEX, RACE, ETHNIC are from DC row 4

FDA Guidance on Linking Subject Participation Records to the USUBJID

- ▶ Subject Identifier (SUBJID) The variable SUBJID uniquely identifies each subject that participates in a study. If a single subject is screened and/or enrolled more than once in a study, then the subject's SUBJID should be different for each unique screening or enrollment. For a study with multiple screenings and/or multiple enrollments per subject, SUBJID should be included in other related domains besides DM **even though it may cause validation errors**. It is recommended to include a table linking each SUBJID for a single subject to that subject's USUBJID with any additional necessary explanation included in the relevant RG.

Linking SUBJID to USUBJID

Every subject participation in a study must have a unique subject participation identifier (SUBJID) (DC03). This is a refinement of any prior understanding of SUBJID and its relationship to USUBJID, which is summarized as follows:



FDA: DM Primary vs MSI: DM Summary

- ▶ The FDA states:
*“the **primary enrollment** should be submitted in DM. **Additional enrollments** should be included in a custom domain with a similar structure to DM.”*
- ▶ The MSI team modeled DM as a summary record
 - Draft DC Assumption 3:
When used, **DC represents all participations and/or foci for all subjects**, including the "primary" participation if such a concept is applicable.
 - It is best to **discuss with the relevant FDA review division before using the MSI's approach.**
 - The MSI team is aiming to have an FDA review of the approach.

Multiple Screens/Enroll: MSI Approach

The MSI team proposes to create an additional Special Purpose domain called Demographics as Collected (DC) to act as the custom domain with a similar structure to DM.

STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	ACTARM	ACTARM CD
XYZ123	DC	XYZ12301 S005	S001				
XYZ123	DC	XYZ12301 S005	S005	2016-01-01	2016-12-01	Drug A	A

Multiple Screens/Enroll: MSI Approach

STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	ACTARM	ACTARM CD
XYZ123	DM	XYZ12301 S005	S005	2016-01-01	2016-12-01	Drug A	A

EG Domain Example

The subject failed to meet the inclusion criteria and was rescreened again. Taking into consideration other domains, variables such as EGDY are null for records associated with the original screening, as the subject doesn't have a value for DM.RFSTDTC.

STUDYID	DOMAIN	USUBJID	SUBJID	EGTESTCD	EGORRES	EGDY
XYZ123	EG	XYZ12301S005	S001	DIABP	97	
XYZ123	EG	XYZ12301S005	S001	SYSBP	150	
XYZ123	EG	XYZ12301S005	S005	DIABP	98	XX
XYZ123	EG	XYZ12301S005	S005	SYSBP	130	XX

Multiple Screens/Enroll: FDA Approach

FDA DC or Custom Domain:

STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC
ABC123	DC	ABC12301S005	S001					2005-09-13
ABC123	DC	ABC12301S005	S012					2005-11-16

SITEID	BRTHDTC	AGE	AGEU	SEX	RACE	ETHNIC	ARMCD	ARMNRS
1	1941-07-02			M	ASIAN	NOT HISPANIC OR LATINO		SCREEN FAILURE
1								SCREEN FAILURE

FDA DM Domain:



Row	STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM
4	ABC123	DM	ABC12301004	1004	2006-01-16	2006-02-01	2006-01-16	2006-02-01	2006-01-07	2006-03-02	1	JOHNSON, M

Row	BRTHDTC	AGE	AGEU	SEX	RACE	ETHNIC	ARMCD	ARM	ACTARMCD	ACTARM	ARMNRS	ACTARMUD	COUNT
4	1941-07-02	64	YEARS	M	ASIAN	NOT HISPANIC OR LATINO	A	Drug A	A	Drug A			USA

In the FDA's approach DC has 2 records and DM has 1.

Multiple Screens/Enroll: DS

STUDYID	DOMAIN	USUBJID	SUBJID	DSSEQ	DSTERM	DSDECOD	DSCAT	EPOCH	DSSTDTC
XYZ123	DS	XYZ12304001	D001	1	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	SCREENING	2005-09-13
XYZ123	DS	XYZ12304001	D001	2	SCREEN FAILURE	SCREEN FAILURE	DISPOSITION EVENT	SCREENING	2005-09-21
XYZ123	DS	XYZ12304001	D002	3	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	SCREENING	2005-11-14
XYZ123	DS	XYZ12304001	D002	4	SCREEN FAILURE	SCREEN FAILURE	DISPOSITION EVENT	SCREENING	2005-11-16
XYZ123	DS	XYZ12304001	4001	5	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	SCREENING	2006-01-07
XYZ123	DS	XYZ12304001	4001	6	COMPLETED	COMPLETED	DISPOSITION EVENT	SCREENING	2006-01-16
XYZ123	DS	XYZ12304001	4001	7	COMPLETED	COMPLETED	DISPOSITION EVENT	TREATMENT	2006-02-01

SDTMIG 3.3 DM Assumptions

- ▶ DM Assumption 10.c:
 - RFICDTC should correspond to the date of the informed consent protocol milestone in DS, if that protocol milestone is documented in DS. In the event that there are multiple informed consents, this will be the date of the first one.

- ▶ DM Assumption 10.b:
 - RFXSTDTC and RFXENDTC always represent the date/time of first and last study exposure

MSI Trial Design Domains

- ▶ The multiple screening/enrollment are not seen as distinct elements.
- ▶ They can be seen as repeats of the same elements similar to cycles in an oncology trial

MSI Subject Elements

Row	STUDYID	DOMAIN	USUBJID	SUBJID	SESEQ	ETCD	ELEMENT	SESTDTC	SEENDTC	TAETORD	EPOCH
1	ABC123	SE	ABC12301004	S001	1	SCRN	Screening	2005-09-13	2005-09-21	1	SCREENING
2	ABC123	SE	ABC12301004	S012	2	SCRN	Screening	2005-11-14	2005-11-16	1	SCREENING
3	ABC123	SE	ABC12301004	1004	3	SCRN	Screening	2006-01-07	2006-01-16	1	SCREENING
4	ABC123	SE	ABC12301004	1004	4	A	Drug A	2006-01-16	2006-02-01	2	TREATMENT
5	ABC123	SE	ABC12301004	1004	5	FLUP	Follow-Up	2006-02-01	2006-03-02	3	FOLLOW-UP

MSI Subject Elements

- ▶ **Row 1:** Represents the initial screening element for USUBJID ABC12301004, with SUBJID S001. Note that SESEQ is unique per USUBJID, while TAETORD and EPOCH are unique within SUBJID. Each participation is treated as a distinct and independent interaction with the planned study elements. SUBJID in conjunction with the timing of the elements (SESTDTC/SEENDTC) allows for the participations to be distinguished.
- ▶ **Row 2:** Represents the second screening element for USUBJID ABC12301004, with SUBJID S012. Note that TAETORD and EPOCH are unique within SUBJID
- ▶ **Rows 3-5:** Represents the third screening element for USUBJID ABC12301004, with SUBJID 1004, followed by the "Drug A" and "Follow-Up" elements. Note that TAETORD and EPOCH are unique within SUBJID

SDTM Draft Domains: DC

- ▶ The draft DC domain is located in the SDTM Draft Domains wiki space
- ▶ It is currently available to SDS/CDISC team members with sufficient view access

Questions?

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References

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SDTMIG V 3.3
StudyDataTechnicalConformanceGuide v4.5.1



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