CDISC Italian User Network 2020

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Updates on Handling Multiple Enrollments and Screenings Subjects in SDTM

7th Italian CDISC User Group Network Annual Meeting

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Éanna Kiely

FDA

FDA Position on Multiple Enrollments / Screenings

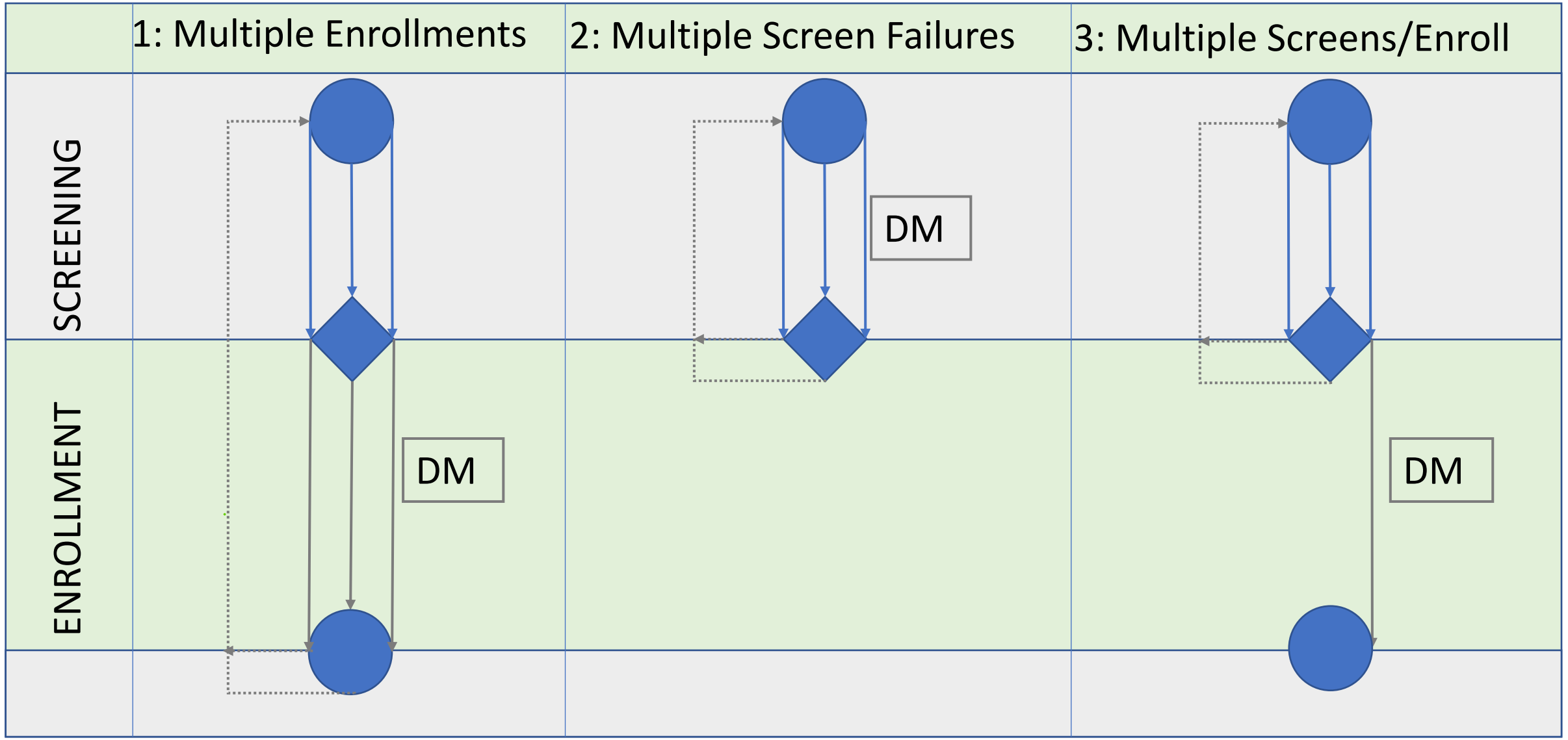
- The FDA position on multiple enrollments and multiple screenings was first described in the FDA Study Data Technical Conformance Guide (TCG) V4.2 (October 2018)

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

DM Domain (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.*

Multiple Subject Enrollment and Screening Graphic



CDISC SDS Multiple Subject Instances (MSI) Team

- The CDISC SDS Multiple Subject Instances (MSI) team created worked examples to describe and model the FDA position on multiple screening and multiple enrollment.
- 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

2: Multiple Screen Failures: DC Example 1

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 5: 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.

2: Multiple Screen Failures: DC Example 1

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

USUBJID ABC12301S005 is a merging of DC row 4 and 5.

Row 4: RFICDTC and RFPENDTC are from DC row 5

SITEID, INVNAM, BRTHDTC, AGE, AGEU, SEX, RACE, ETHNIC are from DC row 4

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			USA
4	1941-07-02			M	ASIAN	NOT HISPANIC OR LATINO					SCREEN FAILURE		USA

SDTMIG 3.3 DM Assumption 2. *...but only one DM record should be submitted for the subject.*

MSI Team: DC Contains All Records from DM

- If DC is used it should contain all records from DM even if they do not have multiple instances

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.
    a. DC must contain all subjects represented in DM (DC02). This may result in a record in DM duplicating a record in DC. This is appropriate, and supports the understanding that when DC is used, DM is generally considered to consist of derived records. How multiple participations and/or foci details are derived or summarized within a single DM record is to be described in the Define-XML and clinical Study Data Reviewer's Guide.

Discuss the MSI approach with the relevant FDA review division

- *include the enrollment in DM with screenings in a custom domain with a structure similar to DM.*

Restrictions on the Use of MULTIPLE in 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

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

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
1	ABC123	DC	ABC12301002	DCSEQ	1	RACE1	Race 1	ASIAN	CRF	
2	ABC123	DC	ABC12301002	DCSEQ	1	RACE2	Race 2	WHITE	CRF	

Row 1,2 SUPPDC show the RACE of multiple for USUBJID ABC12301002 Row 2: Show RACE repeated in SUPPDM

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

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

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
1	ABC123	DM	ABC12301002	DCSEQ	1	RACE1	Race 1	ASIAN	CRF	
2	ABC123	DM	ABC12301002	DCSEQ	1	RACE2	Race 2	WHITE	CRF	

Since RACE was only collected once we do not expect to have updates or changes between collection.
However with a number of demographics variables changes could occur due to actual changes or data entry errors.
The DM/CRA would need to check on the status of any differences.

SDTMIG 3.3 Section 4.2.8.3 Multiple Values for a Non-Result Qualifier Variable: Does Not Always Apply

Proposed DM Assumption 6:

- It is not allowed to use "MULTIPLE" in DM to indicate that more than a single value has been captured across participations. The use of "MULTIPLE" in DM is reserved for multiple values within a participation (e.g., a subject reports more than a single race). In other words, "MULTIPLE" cannot be used to indicate content captured in DC, but rather is only used to indicate content captured in SUPPDM.

Row	STUDYID	DOMAIN	USUBJID	SUBJID
2	ABC123	DC	ABC12301S005	S001
4	ABC123	DC	ABC12301S005	S005

Row	STUDYID	DOMAIN	USUBJID	SUBJID
2	ABC123	DM	ABC12301S005	1002

Row	STUDYID	DOMAIN	USUBJID	SUBJID
2	ABC123	DM	ABC12301S005	MULTIPLE

Row	STUDYID	DOMAIN	USUBJID	SUBJID	...	...	...	RACE
2	ABC123	DM	ABC12301002	S005				MULTIPLE

FDA

FDA Guidance on Linking Subject Participation Records to the USUBJID

- FDA TCG V4.2 did not provide guidance on linking the different subject participation records back to the parent USUBJID in study level domains.
- This was clarified in FDA TCG V4.4 (October 2019)

FDA TCG v4.5.1 (July 2020) section 4.1.1.2 SDTM General Considerations

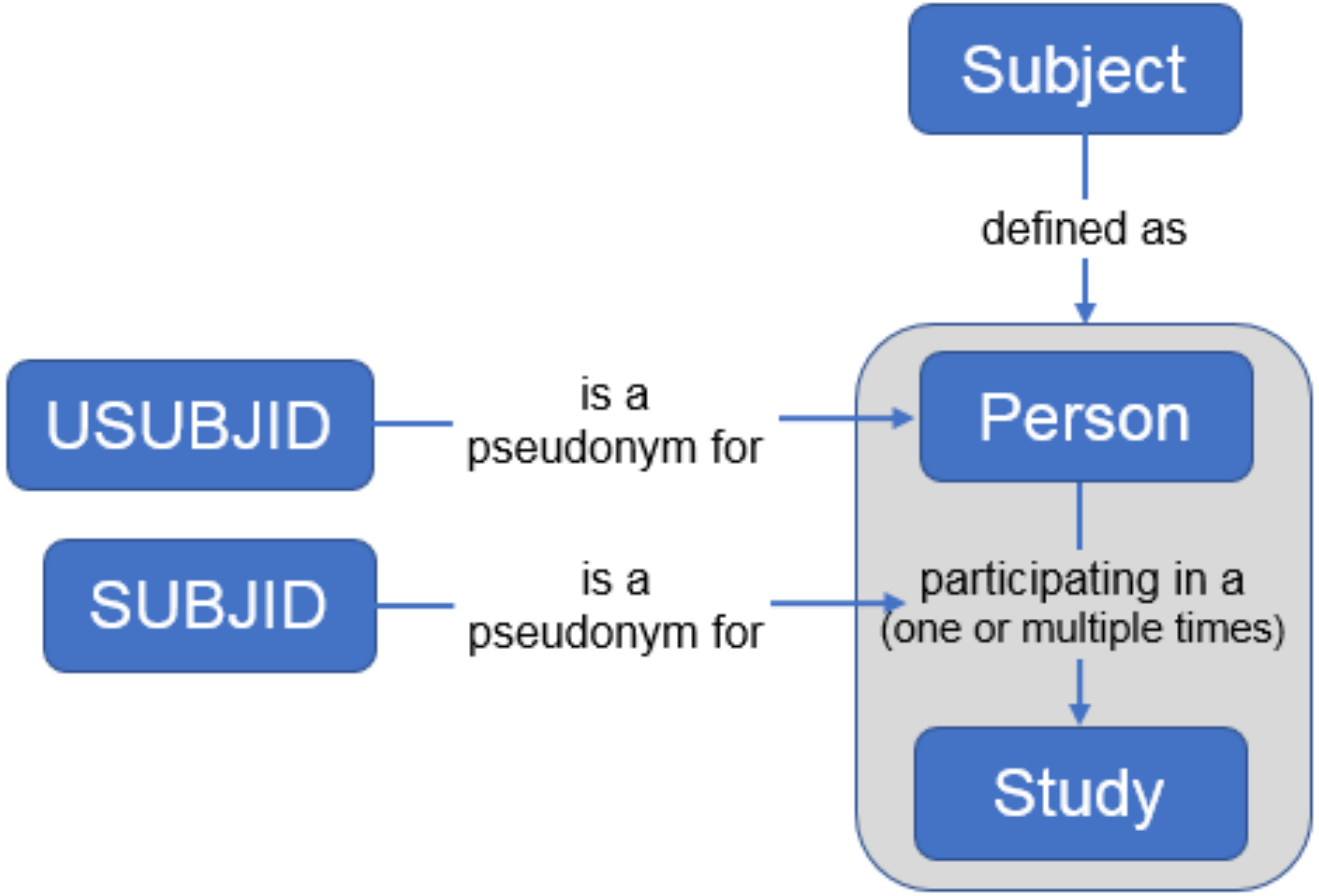
Subject Identifier (SUBJID)

- *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.*

Redefining SUBJID to be Unique Per Participation

Draft DC Assumption 3.b.

- *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:*



Linking SUBJID to USUBJID

Row	STUDYID	DOMAIN	USUBJID	SUBJID	VSTESTCD	VSTEST	VSORRES	VSORRESU	VSSTRESC	VSSTRESN	VSSTRESU
1	ABC123	VS	ABC12301S005	S001	DIABP	Diastolic Blood Pressure	97	mmHg	97	97	mmHg
2	ABC123	VS	ABC12301S005	S001	SYSBP	Systolic Blood Pressure	162	mmHg	162	162	mmHg
3	ABC123	VS	ABC12301S005	S001	PULSE	Pulse Rate	72	BEATS/MIN	72	72	BEATS/MIN
7	ABC123	VS	ABC12301S005	S005	DIABP	Diastolic Blood Pressure	90	mmHg	90	90	mmHg
8	ABC123	VS	ABC12301S005	S005	SYSBP	Systolic Blood Pressure	144	mmHg	144	144	mmHg
9	ABC123	VS	ABC12301S005	S005	PULSE	Pulse Rate	67	BEATS/MIN	67	67	BEATS/MIN

Row	VISITNUM	VISIT	EPOCH	VSDTC	VSDY
1	1	SCREENING	SCREENING	2005-11-14	
2	1	SCREENING	SCREENING	2005-11-14	
3	1	SCREENING	SCREENING	2005-11-14	
7	1	SCREENING	SCREENING	2006-01-07	
8	1	SCREENING	SCREENING	2006-01-07	
9	1	SCREENING	SCREENING	2006-01-07	

Row 1-3: The subject failed to meet the inclusion criteria due to hypertension.
VSDY is null for these records, as the subject doesn't have a value for DM.RFSTDTC.

Row 7-9: Blood pressure improved but the subject was still hypertensive. As only two screenings are allowed per protocol, the subject was not enrolled in the study.
EPOCH is 'SCREENING', reflecting the EPOCH of the data collection in relation to SUBJID.
VISITNUM and VISIT have been assigned values in relation to SUBJID.

Linking SUBJID to USUBJID

Row	STUDYID	DOMAIN	USUBJID	SUBJID	VSTESTCD	VSTEST	VSORRES	VSORRESU	VSSTRESC	VSSTRESN	VSSTRESU
1	ABC123	VS	ABC12301S005	S001	DIABP	Diastolic Blood Pressure	97	mmHg	97	97	mmHg
2	ABC123	VS	ABC12301S005	S001	SYSBP	Systolic Blood Pressure	162	mmHg	162	162	mmHg
3	ABC123	VS	ABC12301S005	S001	PULSE	Pulse Rate	72	BEATS/MIN	72	72	BEATS/MIN
7	ABC123	VS	ABC12301S005	S005	DIABP	Diastolic Blood Pressure	90	mmHg	90	90	mmHg
8	ABC123	VS	ABC12301S005	S005	SYSBP	Systolic Blood Pressure	144	mmHg	144	144	mmHg
9	ABC123	VS	ABC12301S005	S005	PULSE	Pulse Rate	67	BEATS/MIN	67	67	BEATS/MIN

Row	VISITNUM	VISIT	EPOCH	VSDTC	VSDY
1	1	SCREENING	SCREENING	2005-11-14	
2	1	SCREENING	SCREENING	2005-11-14	
3	1	SCREENING	SCREENING	2005-11-14	
7	1	SCREENING	SCREENING	2006-01-07	
8	1	SCREENING	SCREENING	2006-01-07	
9	1	SCREENING	SCREENING	2006-01-07	

Row 1-3: The subject failed to meet the inclusion criteria due to hypertension.
VSDY is null for these records, as the subject doesn't have a value for DM.RFSTDTC.

Row 7-9: Blood pressure improved but the subject was still hypertensive. As only two screenings are allowed per protocol, the subject was not enrolled in the study.
EPOCH is 'SCREENING', reflecting the EPOCH of the data collection in relation to SUBJID.
VISITNUM and VISIT have been assigned values in relation to SUBJID.

3: Multiple Screens/Enroll: DC

Row	STUDYID	DOMAIN	USUBJID	SUBJID	DCSEQ	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM
4	ABC123	DC	ABC12301004	S001	1					2005-09-13	2005-09-21	1	JOHNSON, M
5	ABC123	DC	ABC12301004	S012	2					2005-11-14	2005-11-16	1	JOHNSON, M
6	ABC123	DC	ABC12301004	1004	3	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			M	ASIAN	NOT HISPANIC OR LATINO					SCREEN FAILURE		USA
5											SCREEN FAILURE		USA
6		64	YEARS				A	Drug A	A	Drug A			USA

The subject with USUBJID ABC12301004 had two unsuccessful screening attempts before being successful on the third screening

Row 6: The screening number was updated to the subject number after enrollment.

3: Multiple Screens/Enroll: DC

Row	STUDYID	DOMAIN	USUBJID	SUBJID	DCSEQ	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM
4	ABC123	DC	ABC12301004	S001	1					2005-09-13	2005-09-21	1	JOHNSON, M
5	ABC123	DC	ABC12301004	S012	2					2005-11-14	2005-11-16	1	JOHNSON, M
6	ABC123	DC	ABC12301004	1004	3	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			M	ASIAN	NOT HISPANIC OR LATINO					SCREEN FAILURE		USA
5											SCREEN FAILURE		USA
6		64	YEARS				A	Drug A	A	Drug A			USA

Row 4: The DM record is based on the primary DC Row 6.
AGE is calculated from RFSTDTC

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

FDA

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.

3: Multiple Screens/Enroll: DM FDA Approach

Row	STUDYID	DOMAIN	USUBJID	SUBJID	DCSEQ	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM
4	ABC123	DC	ABC12301004	S001	1					2005-09-13	2005-09-21	1	JOHNSON, M
5	ABC123	DC	ABC12301004	S012	2					2005-11-14	2005-11-16	1	JOHNSON, M
6	ABC123	DC	ABC12301004	1004	3	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			M	ASIAN	NOT HISPANIC OR LATINO					SCREEN FAILURE		USA
5											SCREEN FAILURE		USA
6		64	YEARS				A	Drug A	A	Drug A			USA

Row 4: The DM record is primary with the *additional screenings in a custom domain with a structure similar to DM*

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 one.

Linking SUBJID to USUBJID with --DY Variables

Row	STUDYID	DOMAIN	USUBJID	SUBJID	VSTESTCD	VSTEST	VSORRES	VSORRESU	VSSTRESC	VSSTRESN	VSSTRESU
1	ABC123	VS	ABC12301004	S001	DIABP	Diastolic Blood Pressure	97	mmHg	97	97	mmHg
7	ABC123	VS	ABC12301004	S012	DIABP	Diastolic Blood Pressure	90	mmHg	90	90	mmHg
13	ABC123	VS	ABC12301004	1004	DIABP	Diastolic Blood Pressure	78	mmHg	78	78	mmHg

Row	VISITNUM	VISIT	EPOCH	VSDTC	VSDY
1	1	SCREENING	SCREENING	2005-09-13	-125
7	1	SCREENING	SCREENING	2005-11-14	-63
13	1	SCREENING	SCREENING	2006-01-07	-9

Row 1, 7,13: VSDY is based off the DM.RFSTDTC.

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

3: Multiple Screens/Enroll: DS

STUDYID	DOMAIN	USUBJID	SUBJID	DSSEQ	DSTERM	DSDECOD	DSCAT	EPOCH	DSSTDTC
ABC123	DS	ABC12301004	S001	1	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	SCREENING	2005-09-13
ABC123	DS	ABC12301004	S001	2	SCREEN FAILURE	SCREEN FAILURE	DISPOSITION EVENT	SCREENING	2005-09-21
ABC123	DS	ABC12301004	S012	3	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	SCREENING	2005-11-14
ABC123	DS	ABC12301004	S012	4	SCREEN FAILURE	SCREEN FAILURE	DISPOSITION EVENT	SCREENING	2005-11-16
ABC123	DS	ABC12301004	1004	5	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	SCREENING	2006-01-07
ABC123	DS	ABC12301004	1004	6	COMPLETED	COMPLETED	DISPOSITION EVENT	SCREENING	2006-01-16
ABC123	DS	ABC12301004	1004	7	COMPLETED	COMPLETED	DISPOSITION EVENT	TREATMENT	2006-02-01
ABC123	DS	ABC12301004	1004	8	COMPLETED	COMPLETED	DISPOSITION EVENT	FOLLOW-UP	2006-03-02

- SDTMIG 3.3 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.*

3: Multiple Screens/Enroll: DS

STUDYID	DOMAIN	USUBJID	SUBJID	DSSEQ	DSTERM	DSDECOD	DSCAT	EPOCH	DSSTDTC
ABC123	DS	ABC12301004	S001	1	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	SCREENING	2005-09-13
ABC123	DS	ABC12301004	S001	2	SCREEN FAILURE	SCREEN FAILURE	DISPOSITION EVENT	SCREENING	2005-09-21
ABC123	DS	ABC12301004	S012	3	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	SCREENING	2005-11-14
ABC123	DS	ABC12301004	S012	4	SCREEN FAILURE	SCREEN FAILURE	DISPOSITION EVENT	SCREENING	2005-11-16
ABC123	DS	ABC12301004	1004	5	INFORMED CONSENT OBTAINED	INFORMED CONSENT OBTAINED	PROTOCOL MILESTONE	SCREENING	2006-01-07
ABC123	DS	ABC12301004	1004	6	COMPLETED	COMPLETED	DISPOSITION EVENT	SCREENING	2006-01-16
ABC123	DS	ABC12301004	1004	7	COMPLETED	COMPLETED	DISPOSITION EVENT	TREATMENT	2006-02-01
ABC123	DS	ABC12301004	1004	8	COMPLETED	COMPLETED	DISPOSITION EVENT	FOLLOW-UP	2006-03-02

- SDTMIG 3.3 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.*
- Draft Update:
  - *DM.RFICDTC should correspond to the date of the informed consent protocol milestone in DS, if that protocol milestone is documented in DS. For subjects with only a single participation, DM.RFICDTC is the date of the earliest Date of Informed Consent should a subject have multiple consent dates (e.g., a distinct consent for genetic assays). For subjects with multiple participations, DM.RFICDTC is sponsor defined.*

1: Multiple Enrollments: DM

Row	STUDYID	DOMAIN	USUBJID	SUBJID	DCSEQ	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM
4	ABC123	DC	ABC12301004	1001	1	2005-09-22	2005-10-08	2005-09-22	2005-10-08	2005-09-13	2005-11-06	1	JOHNSON, M
5	ABC123	DC	ABC12301004	1003	2	2005-11-23	2005-12-09	2005-11-23	2005-12-09	2005-11-14	2006-01-07	1	JOHNSON, M
6	ABC123	DC	ABC12301004	1004	3	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
5	1941-07-02	64	YEARS	M	ASIAN	NOT HISPANIC OR LATINO	B	Drug B	B	Drug B			USA
6	1941-07-02	64	YEARS	M	ASIAN	NOT HISPANIC OR LATINO	A	Drug A	A	Drug A			USA

Row	STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM
4	ABC123	DM	ABC12301004	1004	2006-01-16	2006-02-01	2005-09-22	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

- SDTMIG 3.3 DM Assumption 10.b
  - *RFXSTDTC and RFXENDTC always represent the date/time of first and last study exposure.*
- Draft Update:
  - For studies that allow multiple enrollments, and therefore multiple exposure periods, RFXSTDTC represents the date/time of the first study exposure across all participations, and RFXENDTC represents the date/time of the last study exposure across all participations.

FDA USUBJID/SUBJID Linking Table

FDA TCG v4.5.1

Subject Identifier (SUBJID)

- *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.*

DOMAIN	USUBJID	SUBJID	DCSEQ
DC	ABC12301004	1001	1
DC	ABC12301004	1003	2

DOMAIN	USUBJID	SUBJID
DM	ABC12301004	1004

FDA USUBJID/SUBJID Linking Table

FDA TCG v4.5.1

Subject Identifier (SUBJID)

- *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.*

DOMAIN	USUBJID	SUBJID	DCSEQ
DC	ABC12301004	1001	1
DC	ABC12301004	1003	2
DC	ABC12301004	1004	3

DOMAIN	USUBJID	SUBJID	DCSEQ
DC	ABC12301004	1001	1
DC	ABC12301004	1003	2

DOMAIN	USUBJID	SUBJID
DM	ABC12301004	1004

- It is possible that by using the MSI DC domain the FDA USUBJID/SUBJID Linking Table may not be needed.

MSI Trial Design Domains Examples

Row	STUDYID	DOMAIN	ETCD	ELEMENT	TESTRL	TEENRL	TEDUR
1	ABC123	TE	SCRN	Screen	Informed consent	1 week after start of Element	P7D
2	ABC123	TE	A	Drug A	First dose of study drug, where drug is Drug A	2 weeks after start of Element	P14D
3	ABC123	TE	B	Drug B	First dose of study drug, where drug is Drug B	2 weeks after start of Element	P14D
4	ABC123	TE	FLUP	Follow-Up	Last dose of study drug	4 weeks after start of Element	P28D

Row	STUDYID	DOMAIN	ARMCD	ARM	TAETORD	ETCD	ELEMENT	TABRANCH	TATRANS	EPOCH
1	ABC123	TA	A	A	1	SCRN	Screen			SCREENING
2	ABC123	TA	A	A	2	A	Drug A			TREATMENT
3	ABC123	TA	A	A	3	FLUP	Follow-Up			FOLLOW-UP
4	ABC123	TA	B	B	1	SCRN	Screen			SCREENING
5	ABC123	TA	B	B	2	B	Drug B			TREATMENT
6	ABC123	TA	B	B	3	FLUP	Follow-Up			FOLLOW-UP

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

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,

Proposed SE Assumptions: 2

For studies that capture multiple participations per subject (i.e., the DC domain is present), ETCD will be unique per SUBJID. As this is critical for distinguishing elements for studies with multiple participations, if DC is present in a study then SE must contain SUBJID and SUBJID must be populated for all records for subjects with multiple participations.

- For studies with multiple participations / treatments
  - SUBJID becomes the primary identifier for participations
  - USUBJID the primary identifier for a person

Open Questions: DCSEQ: Chronological Order, DCDTC/DCDY

- Should the DCSEQ variable incorporate the chronological order of the subject instances?

Variable Name	Variable Label	Type	Role	CDISC Notes	Core
DCSEQ	Sequence Number	Num	Identifier	Sequence number to ensure uniqueness of subject records within DC. May be any valid number. When possible, it is recommended that the assigned values of DCSEQ reflect the chronological order of the subject participation.	Req

- DCDTC/DCDY are the permissible demographics timing variables.
  - Are they useful within the DC domain?

DOMAIN	USUBJID	SUBJID	DCSEQ	RFSTDTC	...	DCDTC	DCDY
DC	ABC12301004	1001	1	2005-09-22		2005-09-13	-125
DC	ABC12301004	1003	2	2005-11-23		2005-11-14	-63
DC	ABC12301004	1004	3	2006-01-16		2006-01-07	-9

Demographics as Collected (DC) Custom Domain Abbreviation Collisions

- The MSI team has chosen to use Demographics as Collected (DC) as the name to describe the domain since it is a summary/collected record concept similar to Exposure (EX)/ Exposure as Collected (EC)

Challenges: Disease Characteristics (DC)

- A number of years ago DC (Disease Characteristics) was used as a way to describe data that is now usually mapped to MH/FA and/or the specific findings domain
  - CDISC Non-Subject Data SDTM Implementation Guide (Draft 1.0 2011-06-17)

NSDC. xpt

STUDYID	DOMAIN	NSID	DCSEQ	USUBJID	DCRELSUB	DCTESTCD	DCTEST	DCORRES	DCSTRESC
2011-02-02	NSDC	2011-02-02-N125	1	2011-02-02-033	BROTHER, BIOLOGICAL	POMPEDX	Pompe Disease Diagnosis	CONFIRMED	CONFIRMED
2011-02-02	NSDC	2011-02-02-N125	2	2011-02-02-033	BROTHER, BIOLOGICAL	PHENTYP	Phenotype	JUVENILE	JUVENILE

SDTM Draft Domains

PAGE TREE

- List of Draft Domains
- Domain Template Instructions
- SDTM Draft Domains Under Construction
  - Cell Phenotype Findings (CP)
  - Integumentary System Findings (IG)
  - **Demographics as Collected (DC)**
    - DC Dataset Metadata
    - DC Specification
    - DC Assumptions
    - DC Examples
      - DC Example 1 Multiple screenings, no enrollment
      - DC Example 2 Multiple screenings with enrollment
      - DC Example 3 Multiple enrollments
    - DC Rule Candidates
  - SDTM Section 3.2.2(new) Demographics as Collected
  - QRS Reference (QX)

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

MSI Team Next Steps

- The MSI team is in the final stages of its development of the DC domain
- The MSI approach needs to be reviewed by the FDA
- It will not be included in SDTMIG 3.4
- The aim is to add it to SDTMIG 4.0
- The MSI team will prepare a considerations document for public review
- …

CDISC Next Steps: Alignment Between The Foundational Standards: SDTM & ADaM

- There is a CDISC Cross-functional team being setup to align the three different foundational standards
- There seems to be a consensus across the standards that the parent record e.g. DM / ADSL should not have more than one record per subject.
- In ADaM, an approach similar to DM/DC could be adopted where there is an ADSL and secondary ADSL for rescreening/reenrollment

FDA TCG 4.5.1 DM Domain (Demographics)

- *In the DM domain, each subject should have only one single record per study.*

ADaMIG 1.2 section 2.3.1 The ADaM Subject-Level Analysis Dataset (ADSL)

- *ADSL contains one record per subject, regardless of the type of clinical trial design*

CDISC Next Steps: Alignment Between The Foundational Standards: SEND

- In SEND this is complicated by the same subject being in more than one study with FOCID separating the different areas under study.
- 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.*

Re-Modeling the DM Domain

Identifiers

Trial: Reference & Arm

Site

STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	RFENDTC	RFXSTDTC	RFXENDTC	RFICDTC	RFPENDTC	SITEID	INVNAM
ABC123	DM	ABC12301004	1004	2006-01-16	2006-02-01	2005-09-22	2006-02-01	2006-01-07	2006-03-02	1	JOHNSON, M

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

Demographics

MSI Current Team Members

Name	Affiliation	Email
Carlo Radovsky	Immanant	carlo.radovsky@immanant.com
Tom Guinter	Nurocor	tom.guinter@nurocor.com
Janet Reich	Amgen	jroich@amgen.com
Éanna Kiely	ClinBuild	eanna.kiely@clinbuild.com
Varia Cartledge	Alexion	
Ilona Ayrapetova	GSK	
Mike Havener	Independent	
Madhavi Vemuri	Janssen Research	

- Team meets each Friday from 14:00 to 15:00 CEST (08:00 to 09:00 EDT)

MSI Current Team Members & You?

Name	Affiliation	Email
Carlo Radovsky	Immanant	carlo.radovsky@immanant.com
Tom Guinter	Nurocor	tom.guinter@nurocor.com
Janet Reich	Amgen	jroich@amgen.com
Éanna Kiely	ClinBuild	eanna.kiely@clinbuild.com
Varia Cartledge	Alexion	
Ilona Ayrapetova	GSK	
Mike Havener	Independent	
Madhavi Vemuri	Janssen Research	
You?	Your company?	Your email?

- A cross-functional team is being formed to investigate MSI across all of the foundational standards.

- Team meets each Friday from 14:00 to 15:00 CEST (08:00 to 09:00 EDT)

CDISC Volunteering

- CDISC is powered by volunteers reviewing/providing comments on standards and participating on teams and in the user community

Reviewer

Controlled terminology (CT)

Therapeutic Area User Guide

Standards

Other e.g. FHIR / COVID-19

Attend public webinars

Raise comments in JIRA

Teams

Join the foundational / CT team call

Participate in discussions

Add topics to the agenda and present

Join a project team

Join a sub-team

Lead a project team

Lead a sub-team

Take on a role: lab rep, Global Governance Group (GGG) rep, team lead

Community

Attend a User Group Event / CDISC Event

Join a User Group Committee

Join a x3C e.g. Europe CDISC Coordinating Committee (E3C)

SDS Laboratory Representative

Requirements

- Volunteer on the SDS and Laboratory sub-team.
- Participate on laboratory related projects/teams

Responsibilities

- Act as liaison between SDS Full Team and Lab Sub-Team
- Point of contact for questions on laboratory and SDTM modeling topics
- Triage of lab related JIRA tickets

SDS Support

- Ability to add topics to the SDS agenda

Current Lab Reps

- Glenn Barnes & Éanna Kiely

Any Questions?

eanna.kiely@clinbuild.com

Available Presentations:

Name	Affiliation	Presentation	Event
Éanna Kiely	*Syneos/ClinBuild*	Handling Multiple Enrollments and Screenings Subjects in SDTM: Are We There Yet?	2019 Europe Interchange
Carlo Radovsky	*Etera Solutions*	Handling Multiple Enrollments and Screenings Subjects in SDTM: Are We There Yet? (Paper)	2019 US Interchange
Kristin Kelly	Pinnacle 21	Considerations when Representing Multiple Subject Enrolments in SDTM	EU Connect 2019
Wafaa Jebert	*ichnos sciences*	Use case for multiple enrollments	2020 Europe Interchange