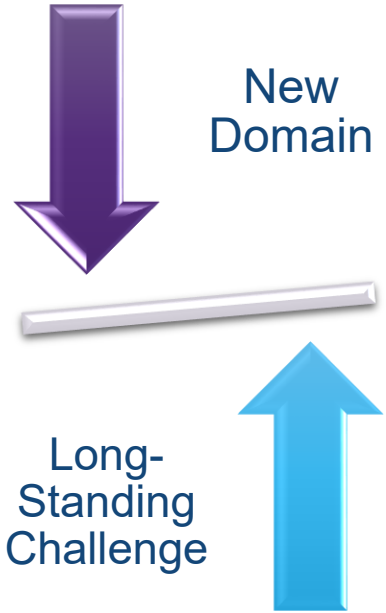
Demographics Domains:

Demographics (DM) and
Demographics for Multiple Participations (DC)

2025-10-14

Overview

- SDTMIG v4.0 introduces the Demographics for Multiple Participations (DC) domain
- Addresses a long-standing unmet need
- Establishes new definitions and modeling solutions related to subject participations
- Widely vetted and reviewed



History of DC

2014

PHUSE White Paper
- Called out challenge, considerations
- Catalyst, ultimately withdrawn

2015 - 2016

CDISC Sub-team developed and presented options to the FDA
- Defined problem space
- Modeled three structural options (preliminary use cases for evaluation purposes only)
- Initial model developed in alignment with FDA preference (Maintain DM and add a new dataset)

2017 - 2020

Working Team 1
- Not enough lead time to incorporate into SDTMIG v3.3
- Expanded use cases and ongoing internal evaluation bypassed SDTMIG v3.4
- Presented to industry in a range of forums

2020 - Present

Working Team 2
- Modelling and examples developed for all scoped use cases
- Evaluated by all CDISC foundational standards teams
- Presented to industry in a range of forums, and to FDA

Scope of DC

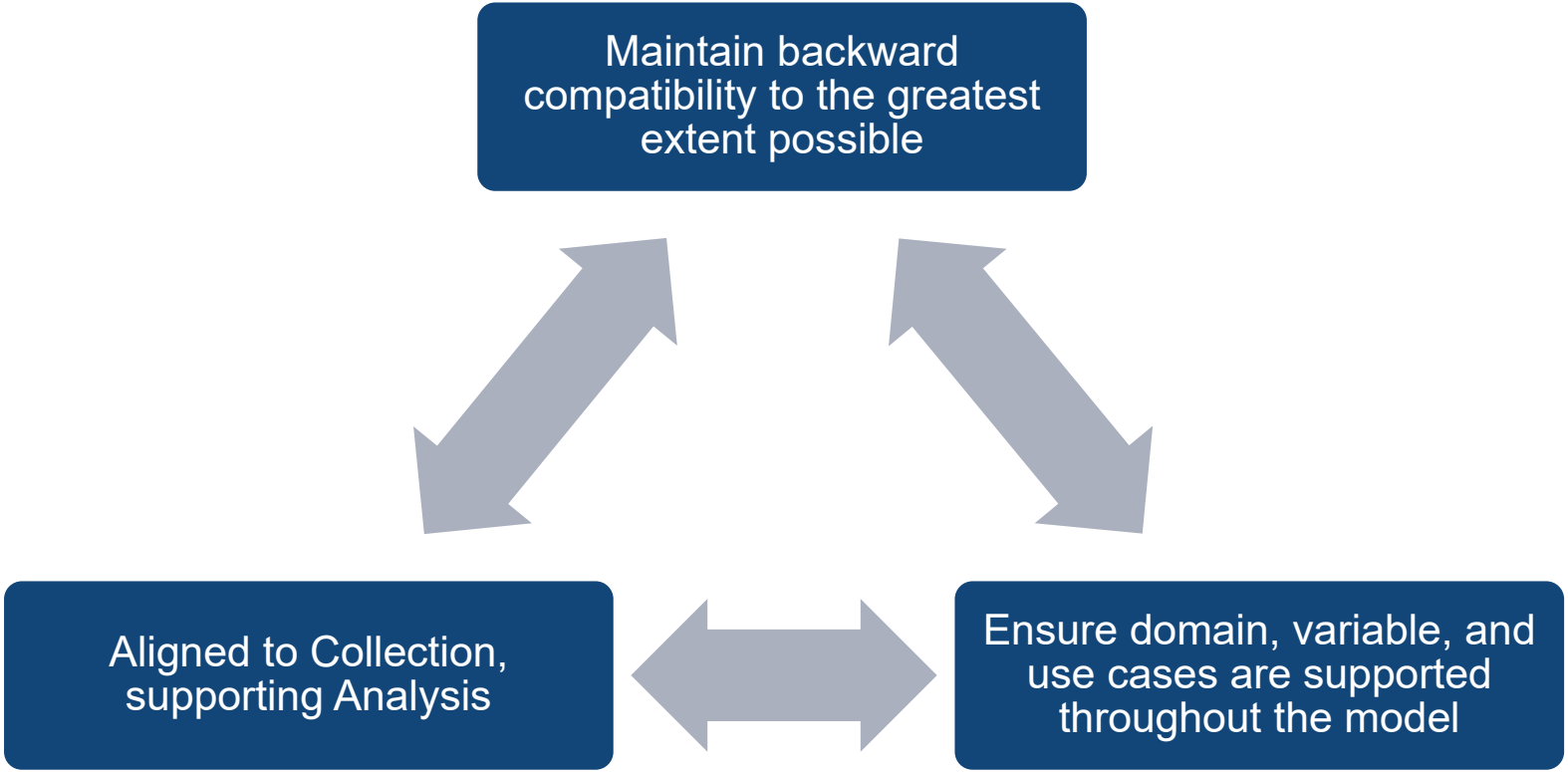
In Scope

- Addresses all known use cases
- Supports the use of FOCID
- Supports both SEND and SDTM

Out of Scope

Site transfers are NOT multiple participations

Primary Considerations for DM and DC



Backward Compatibility

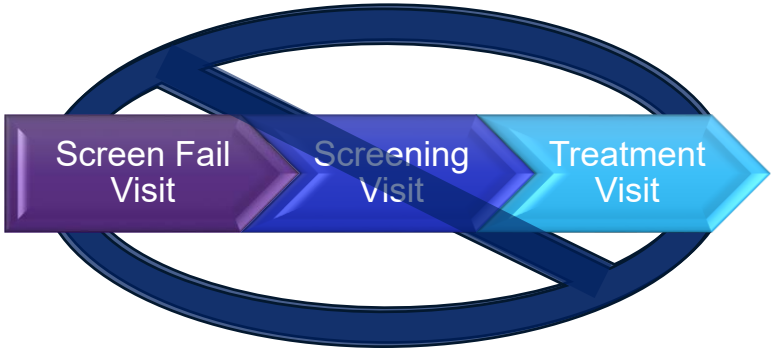
Demographics (DM) domain generally unchanged

- Domain model updated in support of SDTMIG v4.0 broader changes (e.g., addition of CRACE and CETHNIC)
- Domain remains restricted to one record per USUBJID
- SUBJID variable definition established as the unique identifier for a subject's participation
- All DM assumptions apply to DC as shared assumptions
  - The individual assumptions detail differences in usage between the domains
  - DC-only assumptions are identified separately

Backward Compatibility

Subject Timing Considerations only minimally impacted

- Visit and element representation remain aligned to the protocol
  - ADaM to address more nuanced representation



- A given visit uniquely defined per SUBJID

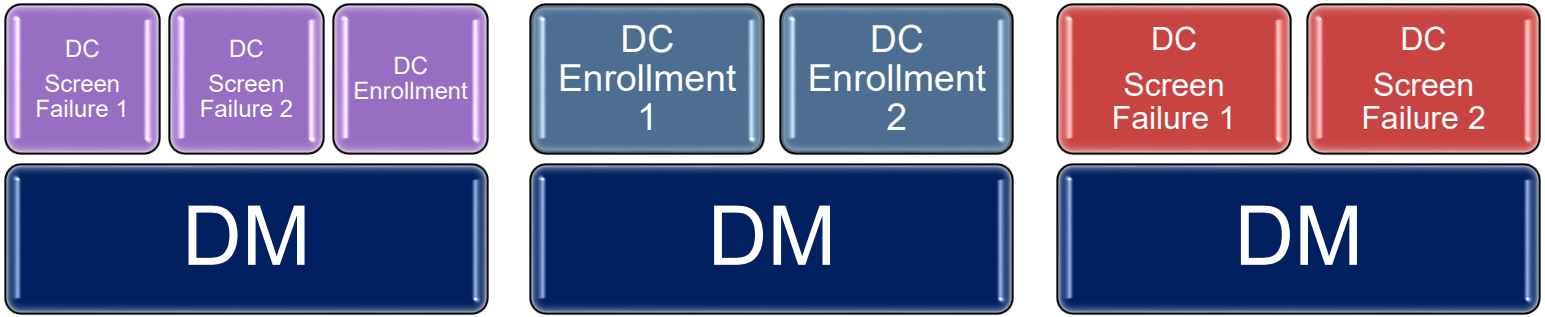
USUBJID	SUBJID	VISIT	--DTC
1001-01-003	01-003	Screening	2024-05-22
1001-01-003	01-012	Screening	2024-07-11

Model Support

- SUBJID now allowed in all subject-level (have USUBJID) domains
- Established assumptions and processes related to
  - Site ID values over time
  - Site transfers represented in DS
- Use FOCID
  - Relationship to multiple participations
  - Association with distinct treatment arms
    (e.g., left and right eyes randomized to different treatment arms)
- Impact on broader model
  - Special purpose domains (e.g., SE and SV)
  - General observation class domains

Aligned to Collection

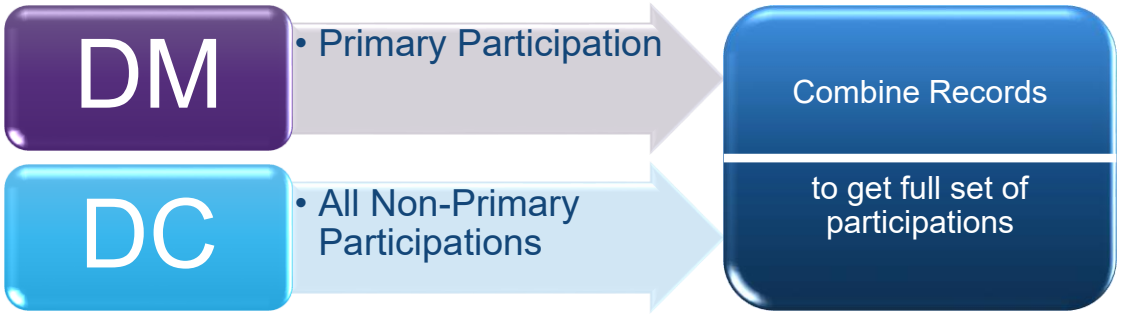
- Modelling and assumptions support distillation of DC to DM



- DC largely represents data as captured under a given participation
- DM values are determined based on protocol and analysis considerations
- Consideration of distinct analysis periods is not addressed, and is left to ADaM

Divergence from FDA TCG

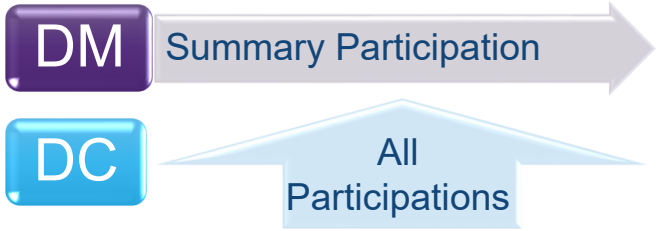
- The approach in SDTMIG v4.0 is broadly aligned to the FDA early preference when multiple participations are represented
- The language in the FDA Technical Conformance Guide, however, calls out a separation of the data:



Divergence from FDA TCG

- **When multiple participations are represented, the approach in SDTMIG v4.0 is as follows:**

- Per CDISC requirements
  - DM contains a single, “summary” record
  - DC contains the full set of participations



- Requires all subjects to have at least 1 record in DC when multiple participations are represented
- DC Record = DM Record when a subject has only a single participation
- DM record may be an amalgamation of records from DC when representing multiple participations for a subject

Divergence from FDA TCG

Why?

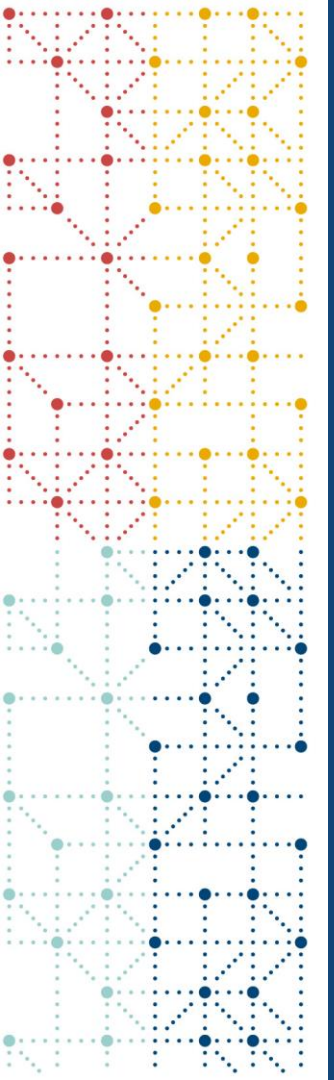
- Not all studies support the concept of a “primary” participation
- The source for any given variable may depend on protocol or analysis considerations

dc.xpt

USUBJID	SUBJID	RFICDTC	RFSTDTC	BRTHDTC	SEX	ARM	ARMNRS
02356-003-004	003-004	2024-03-25		1997-08-25	M		SCREEN FAILURE
02356-003-004	003-011	2024-07-12					SCREEN FAILURE
02356-003-004	003-027	2025-02-07	2025-03-10			TRT A	

dm.xpt

USUBJID	SUBJID	RFICDTC	RFSTDTC	BRTHDTC	SEX	ARM	ARMNRS
02356-003-004	003-004	2025-02-07	2025-03-10	1997-08-25	M	TRT A	



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Detailed Review

Structure and Assumptions

DM variables in DC	All DM variables except for –DY are in DC	Two new variables, CRACE and CETHNIC
		DCDY is disallowed, as it would require using reference dates from DM as input, when DC is the source for DM.
		Some variables such as BRTHDTC and DTHDTC were debated for inclusion in DC but were included for review and feedback, particularly by regulatory authorities
DC variable not in DM	FOCID is unique to DC	FOCID supports study designs with distinct body parts (e.g., each eye) and independently assigned to treatment as distinct arms. Works in conjunction with SUBJID
		DCSEQ can be used if helpful
Assumptions	There is a shared set of assumptions for both DM and DC	Details common usage, as well as how the two domains interact
	In addition, DC has its own set of assumptions	

Shared Assumption Highlights

- DC is used when there is at least 1 subject with more than 1 participation in a clinical study
- For regulatory purposes, DC must not be submitted when there are no subjects with multiple participations
- SUBJID must be populated for every row in DM and DC
- DM may include both collected and derived records when DC is used
- It is up to sponsors to determine how to populate variables in DM based on DC input
  - The specifics are driven by protocol and analysis considerations
  - Details should be described in Define-XML and/or the cSDRG

Shared Assumption Highlights

- Assumptions regarding reference dates largely unchanged, explicitly stating that all reference timing is relative to DM, not DC
  - For example, the derivation of study day values (LBDY, AESTDY, etc.) remains relative to DM.RFSTDTC
- While all DM variables are in DC, some may have their Core attribute shifted from Required to Expected
  - Recognizes that data (e.g., SEX, RACE) may not be collected after the first participation

Shared Assumption Highlights

- Arm-related variable assumptions mostly unchanged and apply to both DM and DC
- Subjects receiving multiple treatments as part of a single participation are managed per usual via the arm assignment
- If a subject has multiple participations with multiple treatments, meaning there is no “primary” treatment, then
  - DM variables ARM, ARMCD, ACTARM, and ACTARMCD are set to null
  - DC will capture the treatment assignments per participation or Focus ID
  - The DM variable ARMNRS is populated with “MULTIPLE PARTICIPATIONS WITH TREATMENT ASSIGNMENT”

Shared Assumption Highlights

- Managing MULTIPLE values for a variable WITHIN a participation unchanged, but more nuanced
- The algorithm used to represent multiple values for a variable in DM is described in Define-XML

dc.xpt

USUBJID	SUBJID	DCSEQ	RACE
02356-003-004	003-004	1	ASIAN
02356-003-004	003-011	2	ASIAN
02356-003-004	003-027	3	MULTIPLE

dm.xpt

USUBJID	SUBJID	RACE
02356-003-004	003-004	MULTIPLE

nsdc.xpt

USUBJID	DCSEQ	RACE1	RACE2
02356-003-004	3	ASIAN	WHITE

nsdm.xpt

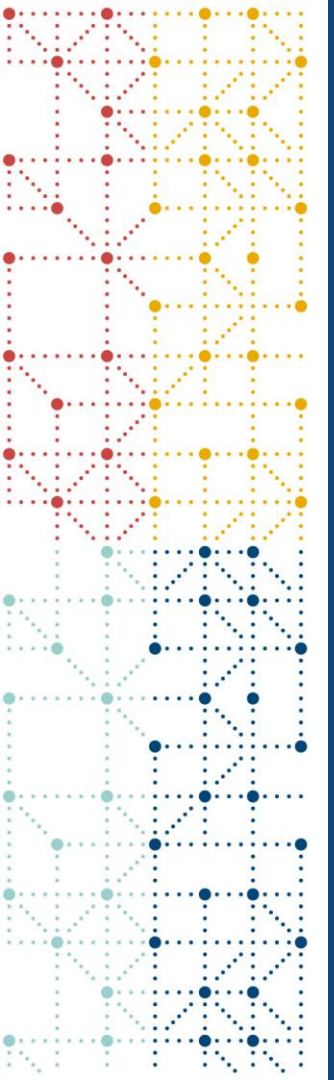
USUBJID	RACE1	RACE2
02356-003-004	ASIAN	WHITE

DC-Only Assumption Highlights

- Defines a participation
  - A participation is defined as engagement with the first element of a trial arm as defined in the Trial Arms domain (i.e., an element with TA.TAETORD=1).
  - This engagement could be by either an individual subject enrolling in a study or an individual subject enrolling a discrete part of their body (e.g., a subject's right eye) in a study.
  - When a subject enrolls a discrete part of their body, then the use of FOCID is required
- DC must contain all subjects in DM
- DC.RFSTDTC and DC.RFENDTC are permissible, but if one is needed, both must be present
- DCDY is not permitted in DC because it would lead to circular logic.

DC-Only Assumption Highlights

- Addresses AGE over multiple participations
  - DC.BRTHDTC could inadvertently reveal Personally Identifiable Information (PII) to someone who is blinded if it's collected per participation
  - Derivation of AGE may be impacted by multiple participations
  - cSDRG and Define-XML explanations warranted



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Summary

Summary

- DC is used when there is at least 1 subject with more than 1 participation in a clinical study
  - For regulatory purposes, DC must not be submitted when there are no subjects with multiple participations
- DC largely aligns with US federal guidance (i.e., sdTCG)
  - Exception – all participations included
- DM is largely unchanged
  - All variables in DM are in DC
  - DC does not have DCDY, and includes FOCID and DCSEQ
  - New CRACE/CETHNIC variables in both
- There is a shared set of demographics assumptions
  - DC has some assumptions that are DC-only

Thank You!

Dana Booth - Merck & Co., Inc., Rahway, NJ, USA
dana.booth@merck.com

Carlo Radovsky - Immanant
carlo.radovsky@immanant.com