

# **Multiple Subject Id/ Rescreened Subjects' Challenges in ADaM Programming?**

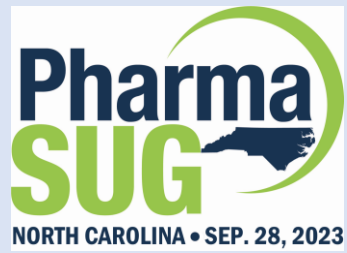


## Biography:

- Pradeep Bangalore has a diverse background in the Clinical Trial Industry, with almost 25 years of experience and an MBA from NC State. He has been independent since 2008 and has co-founded Cesta Inc, an analytics consulting firm that helps clients excel. He is also a serial entrepreneur and has been involved in several tech-startups throughout his career. Overall, Pradeep has a strong business acumen and a wealth of experience in the Clinical Trial industry.

## Why Multiple Screened/Repeat Subjects?

- Enrollment of patients in clinical trials for rare diseases is quite a challenge. This means that there are often only a small number of patients with a particular rare disease, making it difficult to find enough patients to enroll in a clinical trial. As a result of these challenges, the development of new treatments for these diseases slows and can leave patients without access to the latest therapies. To overcome this challenge, sometimes a patient is rolled over from another similar study if the eligibility criteria are met, or in some cases, the same patient is rescreened after failing for the first time. Per the norm, screen failed subjects' participation should be collected in the database. In subsequent attempts, the same patient might pass all the criteria and enroll in the study.



Legacy way :

Multiple Screened /Repeat Subjects information was included in SUPPDM.

ADSL Version 1:

STUDYID	USUBJID	SITEID	SUBJID	SUBJID1	SUBJID2
XXX	XXX-701-1002	701	MULTIPLE	1001	1002

ADSL Version 2:

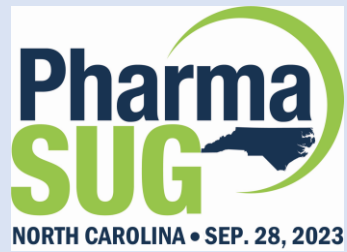
STUDYID	USUBJID	SITEID	SUBJID	ASUBJID
XXX	XXX-701-1002	701	1001	1002

As per FDA TCGv4.8 (Sep 2021) section 4.1.1.3 SDTM Domain Specifications

*DM Domain (Demographics) :*

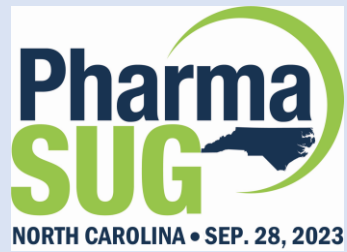
- *For subjects with multiple screenings and no subsequent enrollment, include the primary screening in DM with additional screenings in a **custom domain** with a structure similar to DM.*
- *For subjects with multiple screenings and subsequent enrollment, include the enrollment in DM with screenings in a custom domain with a structure similar to DM.*
- *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.*

- Client's SDTM team decided to call customized domain as DQ(Demographic Qualifiers) *to add the repeated/rolled/ over patients in Demog Qualifiers (DQ) to be compliant with SDTMIG.*
- *Subjects get issued a new subject ID for every screening/re-screening event*
- *For subjects with multiple screenings(without enrollment/ with enrollment), USUBJID reflects the Last Subject ID screened.*
- *For subjects with multiple enrollments within the same study. (Example: Subject received Drug A during the first enrollment, they received Drug B in the second) USUBJID reflects SUBJID associated with the first randomization/assignment to treatment.*
- *In all above 3 cases, DM.SUBJID='MULTIPLE' and multiple SUBJIDs in SUPPDM. SUBJID will be included in all domains(AE, LB, CM, RS,..).*
- *DM.RFICDTC is the earliest value while DS will hold all Inform Consent dates collected at multiple screenings/ multiple enrollments.*



## Created Analysis Data Demog Qualifiers - ADDQ

- Do we require ADDQ in all studies?
- ADDQ needed for these 3 cases happens:
  - 1) Multiple screenings and no subsequent enrollment (Screen Failures)
  - 2) Multiple screenings and subsequent enrollment (Initial SCRNFALL then Enrolled)
  - 3) Multiple enrollments(Rolled over from other similar studies).
- ADDQ should contain all SUBJIDS from DQ.
- ASEQ is created based on chronological order of the RFICDTC. ASEQ variable helps to identify multiple records for USUBJID.



# New Practice:

*ADDQ: ADSL + DQ (Source of ADDQ.SUBJID is always from DQ)*

## Scenario 1: Subjects with Multiple screenings and no subsequent enrollment

SDTM.DQ								
STUDYID	USUBJID	SUBJID	SITEID	RFICDTC	RFSTDTC	RFPENDTC	ARM	ACTARM
XXX	XXX-701-101	101	701	2010-01-04	2010-01-15	2010-02-24	Placebo	Placebo
XXX	XXX-701-103	102	701	2010-01-01		2010-01-08	Screen Failure	Screen Failure
XXX	XXX-701-103	103	701	2010-01-10		2010-01-15	Screen Failure	Screen Failure

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ADDQ								
STUDYID	USUBJID	SUBJID	ASEQ	ITTRFL	SAFRFL	PPROTRFL	COMPLRFL	FASRFL
XXX	XXX-701-101	101	1	Y	Y	Y	Y	Y
XXX	XXX-701-103	102	1					
XXX	XXX-701-103	103	2					

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ADSL									
STUDYID	USUBJID	SUBJID	ITTFL	SAFFL	PPROTFL	COMPLFL	FASFL	RFICDTC	RFPENDTC
XXX	XXX-701-101	101	Y	Y	Y	Y	Y	2010-01-04	2010-02-24
XXX	XXX-701-103	MULTIPLE	N	N	N	N	N	2010-01-01	2010-01-15



**Scenario 2:** Multiple screenings with subsequent enrollment.

Here ITTFL represents subject level population flag and ITTRFL represents records level flag.

**SDTM.DQ**

STUDYID	USUBJID	SUBJID	SITEID	RFICDTC	RFSTDTC	RFPENDTC	RFENDTC	ARM	ACTARM
XXX	XXX-701-107	107	701	2010-10-14	2010-10-25	2010-11-15	2010-11-01	Drug A	Drug A
XXX	XXX-701-110	108	701	2010-01-01		2010-01-08		Screen Failure	Screen Failure
XXX	XXX-701-110	109	701	2010-01-10		2010-01-15		Screen Failure	Screen Failure
XXX	XXX-701-110	110	701	2010-01-23	2010-02-01	2010-02-25	2010-02-18	Drug A	Drug A



**ADDQ**

STUDYID	USUBJID	SUBJID	ASEQ	ITTRFL	SAFRFL	PPROTRFL	COMPLRFL	FASRFL	ITTFL
XXX	XXX-701-107	107	1	Y	Y	Y	Y	Y	Y
XXX	XXX-701-110	108	1						Y
XXX	XXX-701-110	109	2						Y
XXX	XXX-701-110	110	3	Y	Y	Y	Y	Y	Y

**ADSL**

STUDYID	USUBJID	SUBJID	ITTFL	SAFFL	PPROTEFL	COMPLFL	FASFL	RFICDTC	RFSTDTC
XXX	XXX-701-107	107	Y	Y	Y	Y	Y	2010-10-14	2010-10-25
XXX	XXX-701-110	MULTIPLE	Y	Y	Y	Y	Y	2010-01-01	2010-02-01

### Scenario 3: Multiple enrollments

- USUBJID is from the earliest successful enrollment.
- ARM(CD), ACTARM(CD) – these two variables will be expressed as MULTIPLE in DM.
- SUPPDM will contain the actual treatment in QNAME/QVAL. For example, QNAME='ACTARM1", QVAL='DRUG A', QNAME='ACTARM2", QVAL='DRUG B".
- RFSTDTC - earliest value of multiple enrollments
- RFENDTC - latest value of multiple enrollments

#### SDTM.DQ

STUDYID	USUBJID	SUBJID	SITEID	RFICDTC	RFSTDTC	RFPENDTC	RFENDTC	ARM	ACTARM
XXX	XXX-701-112	112	701	2012-10-11	2012-10-25	2012-12-15	2012-12-10	Drug A	Drug A
XXX	XXX-701-112	113	701	2013-01-15	2013-01-20	2013-03-25	2013-03-12	Drug B	Drug B

#### ADDQ



STUDYID	USUBJID	SUBJID	ASEQ	ITTRFL	SAFRFL	PPROTRFL	COMPLRFL	FASRFL	ITTFLL
XXX	XXX-701-112	112	1						Y
XXX	XXX-701-112	113	2	Y	Y	Y	Y	Y	Y

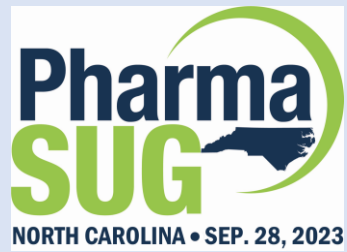
#### ADSL

STUDYID	USUBJID	SUBJID	SITEID	RFICDTC	RFSTDTC	RFPENDTC	RFENDTC	ARM	ACTARM
XXX	XXX-701-112	MULTIPLE	701	2012-10-11	2012-10-25	2013-03-25	2013-03-12	MULTIPLE	MULTIPLE

*LESSONS LEARNT :*

- Pre-programming was done with ADSL + other SDTM to create ADXXs Domains. When team decided to implement ADDQ, did not realize the amount of re-work required.
- ADSL was essentially replaced by ADDQ. However, using merge-by variables USUBJID SUBJID and creating ASEQ to maintain traceability was more time consuming.
- Discuss with the Team about potential delays that may cause to meet timelines.





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