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:

<table>
<thead>
<tr>
<th>STUDYID</th>
<th>USUBJID</th>
<th>SITEID</th>
<th>SUBJID</th>
<th>SUBJID1</th>
<th>SUBJID2</th>
</tr>
</thead>
<tbody>
<tr>
<td>XXX</td>
<td>XXX-701-1002</td>
<td>701</td>
<td>MULTIPLE</td>
<td>1001</td>
<td>1002</td>
</tr>
</tbody>
</table>

ADSL Version 2:

<table>
<thead>
<tr>
<th>STUDYID</th>
<th>USUBJID</th>
<th>SITEID</th>
<th>SUBJID</th>
<th>ASUBJID</th>
</tr>
</thead>
<tbody>
<tr>
<td>XXX</td>
<td>XXX-701-1002</td>
<td>701</td>
<td>1001</td>
<td>1002</td>
</tr>
</tbody>
</table>
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 SCRNFAIL 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.SUBLID is always from DQ)**

**Scenario 1:** Subjects with Multiple screenings and no subsequent enrollment
Scenario 2: Multiple screenings with subsequent enrollment.  

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