

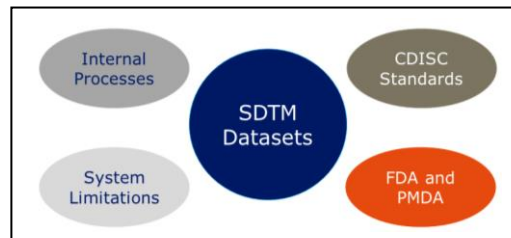
Top 5 challenges at Novo Nordisk complying with CDISC standards

Mikkel Traun, Novo Nordisk A/S, Copenhagen, Denmark
Trine Danø Klingberg, Novo Nordisk A/S, Copenhagen, Denmark

ABSTRACT /INTRODUCTION

Submission of SDTM datasets can be a challenge, as the SDTMIG gives options for interpretation and technical conformance guides differs between regulatory agencies. This presentation will explore below top five challenges at Novo Nordisk complying with CDISC SDTM requirements.

1. Race & Ethnicity
2. Pharmacokinetic Parameters (PP) domain
3. Standards units in SDTM
4. Event Adjudication Results
5. Associated Person (AP) domains



As a sponsor we spend a significant amount of time in our data standards teams addressing these types of issues when defining data collection and SDTM data standards. The aim of this presentation is to create awareness of how we as a sponsor would benefit from improved standardization and guidance within these areas.

1. RACE & ETHNICITY

Challenge number 1 is regarding collection of Race and Ethnicity data. A new recommendation from FDA to allow trial participants multiple selections of ethnicity and race, challenges established data collection standards and reporting. A summary of the challenges are shown in Figure 1.

Race and Ethnicity - Challenges

- The development of the standard is done backwards
 - FDA guidance -> 2 new code lists included in SDTM CT -> SDTMIG pending (Race & Ethnicity details have not changed in the draft version)
- FDA Guidance for Collection of Race & Ethnicity and SDTM code lists 'Race as collected' and 'Ethnicity as collected' are not aligned
 - Which concept to follow?
 - What about other authorities?

Figure 1: Summary of challenges regarding collection of Race and Ethnicity data

2. PHARMACOKINETIC PARAMETERS (PP) DOMAIN

Challenge number 2 is regarding pharmacokinetic data are considered derived data by most sponsors and this is reflected in the data analysis and internal processes. The inclusion of the PP definition in the SDTMIG reverses the situation by prescribing that derived data be treated as source data. This complicates the processes and programs for SDTM. A summary of the challenges are shown in Figure 2.

SDTM.PP - Challenges

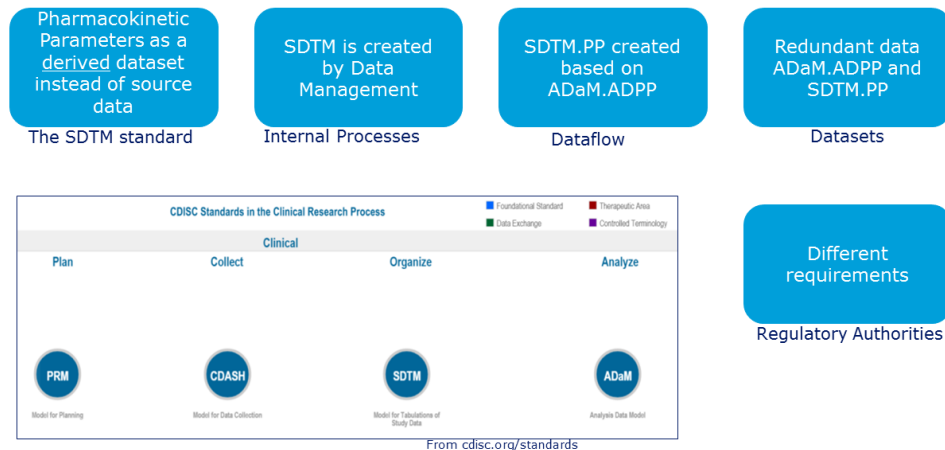


Figure 2: Summary of PP Domain challenge

3. STANDARDS UNITS IN SDTM

Challenge number 3 is regarding requirements for units differ between regulatory authorities. The definition of an SI unit depends on where you search. The internal process of converting collected units into conventional units or SI units is a continued effort due to PMDA requirements. Figure 3 shows our solution for “standardized” units in SDTM.

Our Solution for ‘Standardized’ Units in SDTM

- Duplicate data in additional sponsor defined domains
 - LB holds data in reported standardized units
 - XL/ZL in regulatory required standardized units
- This support simple traceability from SDTM, ADaM to CTR
 - But give redundant data in domains
 - Preferable compared to having SI unit in –STRESU and values in –STRESN and then have the conventional units and values in supplemental qualifiers
- Currently accepted by FDA and PMDA
 - But must be confirmed for each submission (not a general acceptance)

Figure 3: Solution for “standardized” units in SDTM

4. EVENT ADJUDICATION RESULTS

Challenge number 4 is regarding FDA Technical Conformance Guide specifies requirements to clearly identify investigator reported data from adjudication data. Different types of event data in different clinical settings are to be adjudicated. Currently the SDTMIG does not offer explicit guidance on how adjudication results are to be represented in SDTM. A summary of the Novo Nordisk considerations are shown in Figure 4.

Event Adjudication - Considerations

- Novo Nordisk has implemented a sponsor defined stand-alone domain based on the SDTM Findings About domain
- Flexible structure that can accommodate various types of adjudication data
- Only the final agreed assessments from the two independent adjudicators are submitted in our SDTM data set

Figure 4: Summary of PP Domain challenge

5. ASSOCIATED PERSON (AP) DOMAINS

Challenge number 5 is regarding many types of clinical studies collect information on people other than the person participating in the study. This has been formalized with the publication of the Associated Persons SDTM IG. As with any new requirements, there are challenges implementing data collection and SDTM standards for special types of studies, e.g. pregnancy studies. A summary of the challenges are shown in Figure 5.

AP Domain - Challenges

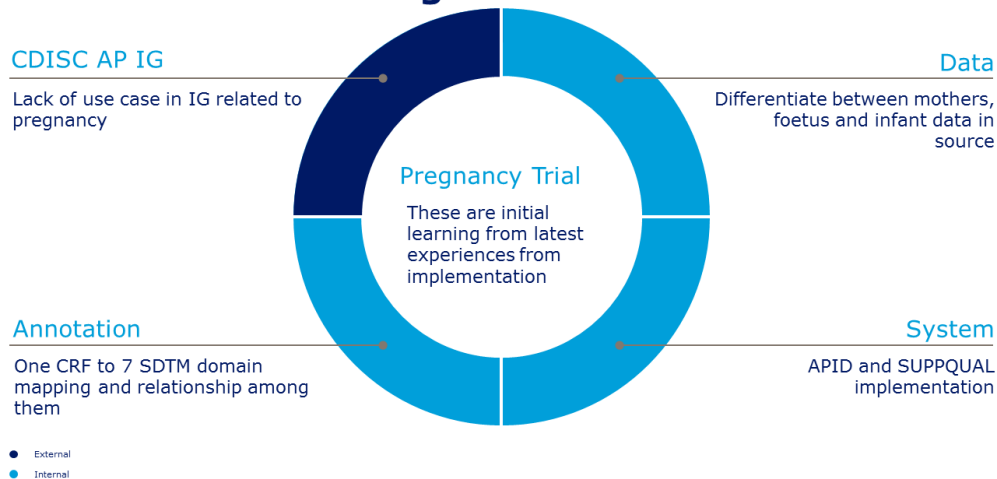


Figure 5: Summary of AP domain challenges

CONCLUSION/LEARNINGS

- CDISC standards are open for interpretation
- Regulatory guidance's are not always aligned with CDISC standards
- Using CDISC data standards should not be an implementation issue for pharmaceutical companies requiring individual case-by-case agreements at pre-NDA or e-data consultancy meetings
- CDISC standards should be specific and less open for interpretation
- Regulatory agencies should increase engagement in data standards development to ensure standards fulfil review needs
 - Limit data standard requirements in technical conformance guides

PhUSE 2018

CONTACT INFORMATION

Mikkel Traun
Principal System Developer
Novo Nordisk A/S
Vandtårnsvej 114
2860 Søborg
Work Phone: +45 3075 8200
Email: mt@novonordisk.com

Trine Danø Klingberg
Principal Standards Specialist
Novo Nordisk A/S
Vandtårnsvej 114
2860 Søborg
Work Phone: +45 3075 8756
Email: trdk@novonordisk.com