HOKKAIDO UNIVERSITY

Issues and Challenges between SDTM and ADaM

April 14, 2017 PhUSE Single Day Event

CDISC Japan User Group(CJUG) ADaM team

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Agenda

- Background
- Issues and Challenges
  - Similar Variables between SDTM and ADaM
  - Derived Values
  - Population Flags
  - ADaM source data other than SDTM datasets
  - Data listings
- Conclusions

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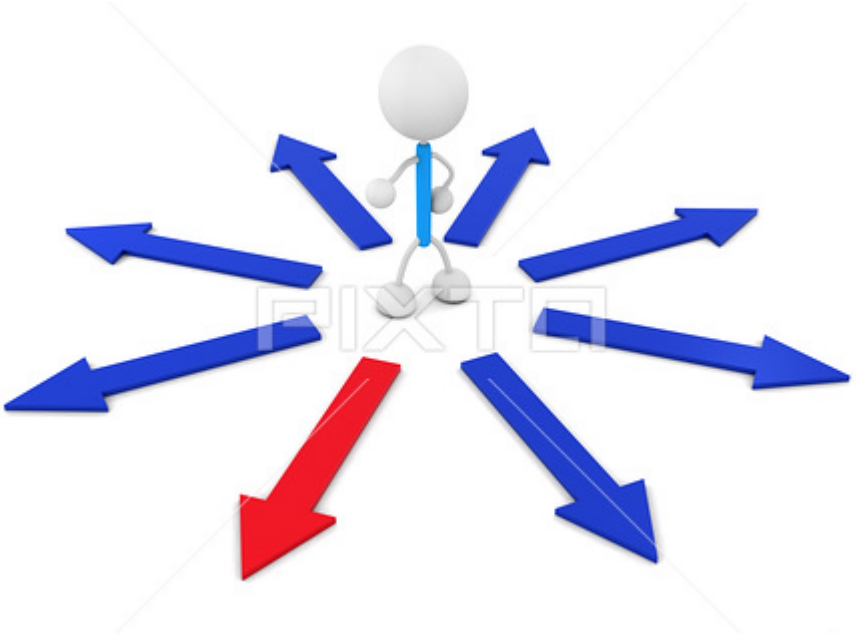
Background

- The CDISC-compliant e-Data submission to Pharmaceuticals and Medical Devices Agency (PMDA) has been required in Japan since 1st October 2016 with a three-and-a-half year transitional period.
- How to address some of practical issues are not clearly described in CDISC implementation guides.

- Flexibility produces variability...
- Little experience in CDISC...

Background

- The goal of this presentation is to provide recommendations for some of practical issues.



Background

- We assume the following:
  - SDTM aims at listings of individual data for subjects and reviewing data by using SDTM datasets.
    - Individual level and source of ADaM data
  - ADaM aims at statistical analyses and summarization of data.
- This presentation is based on the following documents:
  - SDTM IG Version 3.2, ADaM IG Version 1.1
  - Analysis Data Reviewer's Guide (ADRG) Completion Guidelines Version 1.1

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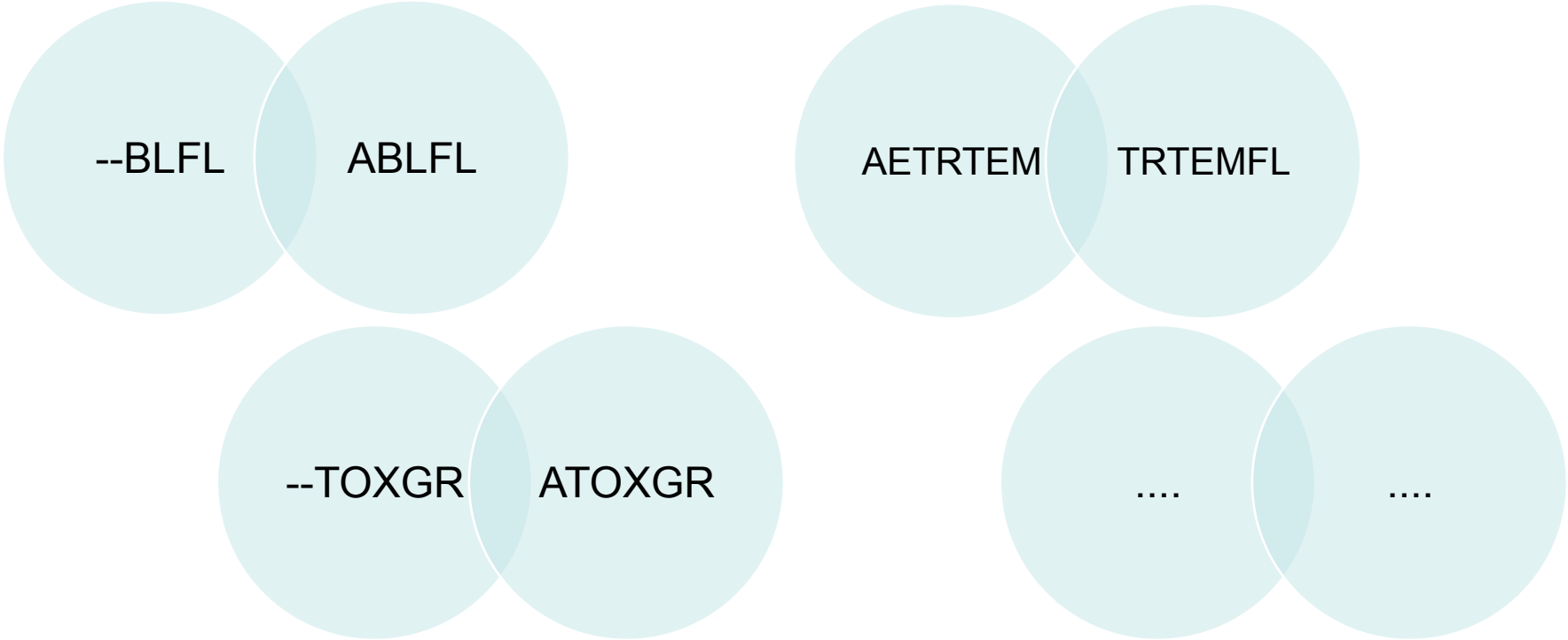
Similar Variables between SDTM and ADaM



- Discussion of any differences between SDTM and ADaM in the definitions of derived variable concepts should be described in ADRG.

Similar Variables between SDTM and ADaM

- If possible, match the definitions closely.
  - Reviewer-friendly, efficient, unambiguous
- It is impossible in some cases.
  - Separate baselines for different periods
  - Treatment-emergent flag when an AE start date is missing
- Discussion with members in relevant sections is essential.
  - ADaM members should offer variable definitions for analyses to SDTM members at an early stage of a study if matching the definitions is considered.

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Derived Values

- Derived values can be included in both SDTM and ADaM.
  - Should SDTM also have the derived values?

- SDTM purpose
  - listings of individual data for subjects and data review

Derived Values

1. Derived values whose derivation rules are specified in a protocol and which can be considered important in terms of data review
   - It is recommended to include them in SDTM.
   - QTcB, QTcF, certain type of QOL total score, etc

- We assume they do not require data handling such as analysis windows or imputation of missing values.

Derived Values

2. Derived values whose derivation rules require data handling for analyses, such as analysis windows or imputation of missing values
   - It is recommended to include them in ADaM.

- In both cases, if you decide to include derived values in both SDTM and ADaM, it is desirable to consider the first issue (Similar variables~).

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Population Flags

- Population flags can be regarded as derived variables.
- Subject-level population flags and record-level population flags
- Should these flags be included only in ADaM datasets?

Subject-level Population Flags

- Subject-level population flags can be included in SUPPDM/ADSL or ADSL.
  - Both are acceptable.
- ICH E3 says listing of patients excluded from the efficacy analysis are necessary.
  - Maybe useful for data review?
- ADaM IG explains differences between SDTM and ADaM population flags.
  - The difference may cause confusion.

Subject-level Population Flags

- Two derivation processes
  1. The population flags can be derived from SDTM data programatically.
  2. The data review meeting is held for deciding the handling of subjects in analysis.
     - The population flags are listed in certain type of file.
- In the second case, the population flags for ADSL are created from a non-SDTM file if the flags are decided not to be included in SUPPDM.
  - Traceability
  - The source for ADaM is a non-SDTM file...

Subject-level Population Flags

- It is recommended to include subject-level population flags in SUPPDM, at least in the second case.
  - Maybe the second case is Japan-specific...
  - Traceability
  - SDTM is the source for ADaM.

- It is desirable to consider the first and second issue.

Record-level Population Flags

- Record-level population flags are not illustrated in SDTM IG.
- The population flags may be used for data only in ADaM datasets.
  - Records for derived parameters, derived visits, etc.
- It is recommended to include record-level population flags only in ADaM datasets.

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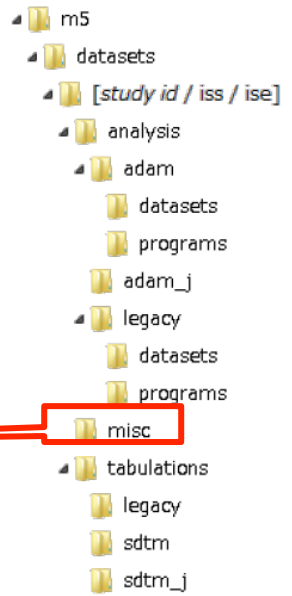
ADaM source data other than SDTM datasets

- In the ADaM model, it is assumed that the original data sources for ADaM datasets are SDTM datasets.

- ADRG Completion Guidelines say the source for ADaM may be a non-SDTM clinical database.
  - Customized lookup tables, adjudication information
  - Population flags

ADaM source data other than SDTM datasets

- If data sources for ADaM exist as non-SDTM files, it should be described in define.xml and ADRG section 1.4 and for submission to PMDA, the non-SDTM files are included in misc folder.



Folder for storing data which is not appropriate for storage in the analysis or tabulations folder.

Technical Conformance Guide on Electronic Study Data Submissions
https://www.pmda.go.jp/review-services/drug-reviews/about-reviews/p-drugs/0026.html

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Data listings

- ICH E3 says patient data listings are necessary as part of CSR.

http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html

Data listings

- ADaM is not intended to data listings.
- Given the purpose of SDTM, most of data listings can be created from SDTM datasets.
- If data are not included in SDTM datasets, data listings for such data are created from ADaM datasets.

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Conclusions

- Working with awareness of the following is important:
  - The purpose of SDTM and ADaM
  - Friendliness to reviewer/user/recipient of the data
  - Discussion with relevant sections

- Sharing knowledge and experience enable us to solve practical issues.

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