

DS08

OVERCOMING CHALLENGES OF YOUR INTEGRATED SUMMARY ISS/ISE SUBMISSIONS

Jenet C.P. (Lead – Statistical Programming, Genpro Research)
(jenet.cp@genproresearch.com)

Akhil Vijayan (Manager - Statistical Programming, Genpro Research)
(akhil.vijayan@genproresearch.com)

WHAT ARE INTEGRATED SUMMARIES (ISS/ISE)?

Documents comprised of integrated analyses used to analyze the efficacy and safety of an investigational product

These are significant components in the New Drug Application (NDA)

Include clinical trial results from different therapeutic areas which are combined, and analyses are done to get combined statistical results

INTEGRATED SUMMARIES USEFUL FOR:

Comparison of results
across multiple
studies

Identification of
common related
adverse events (AEs)

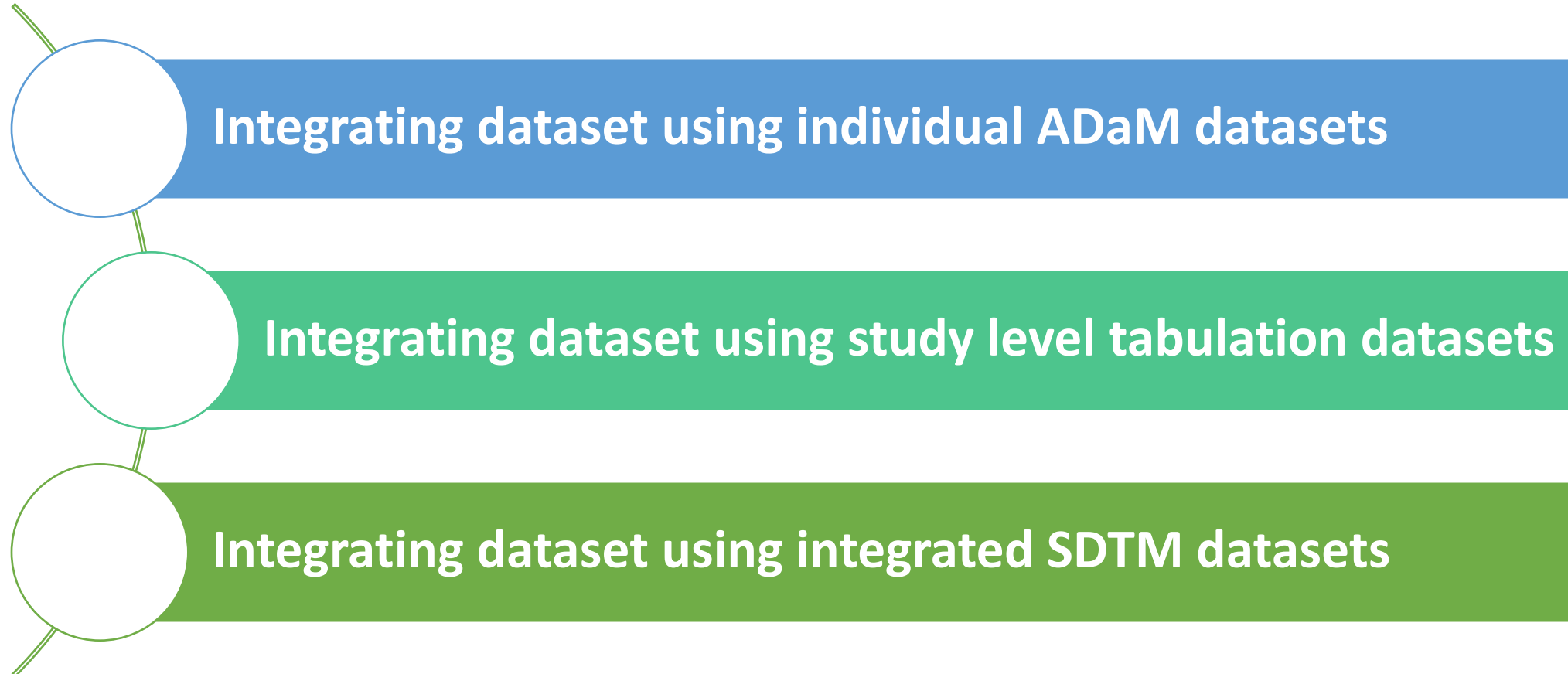
Identification of
common serious
adverse events
(SAEs)

Assessment of
efficacy in subgroups

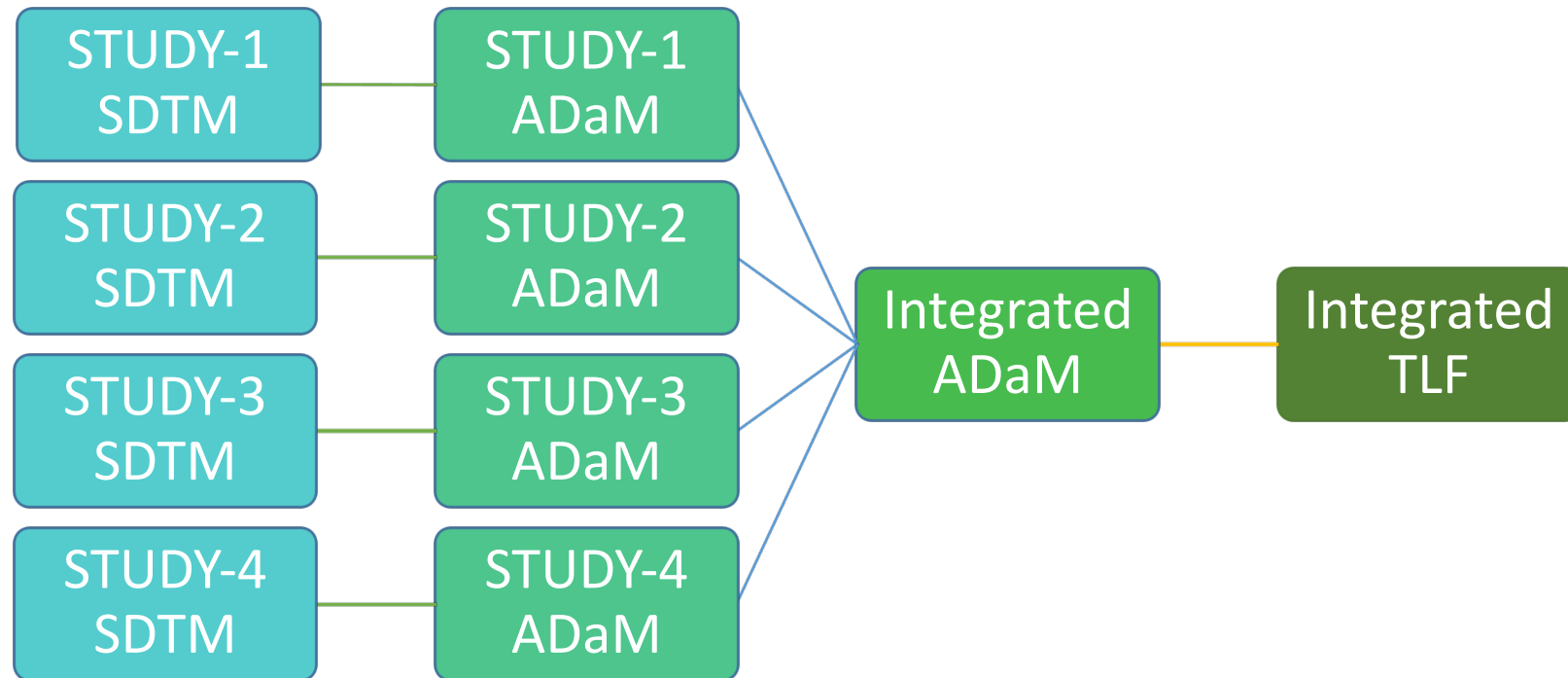
Identifying rare, or
unexpected trends in
different subgroups

Assessment of risks
and benefits of the
drug

DATASET INTEGRATION

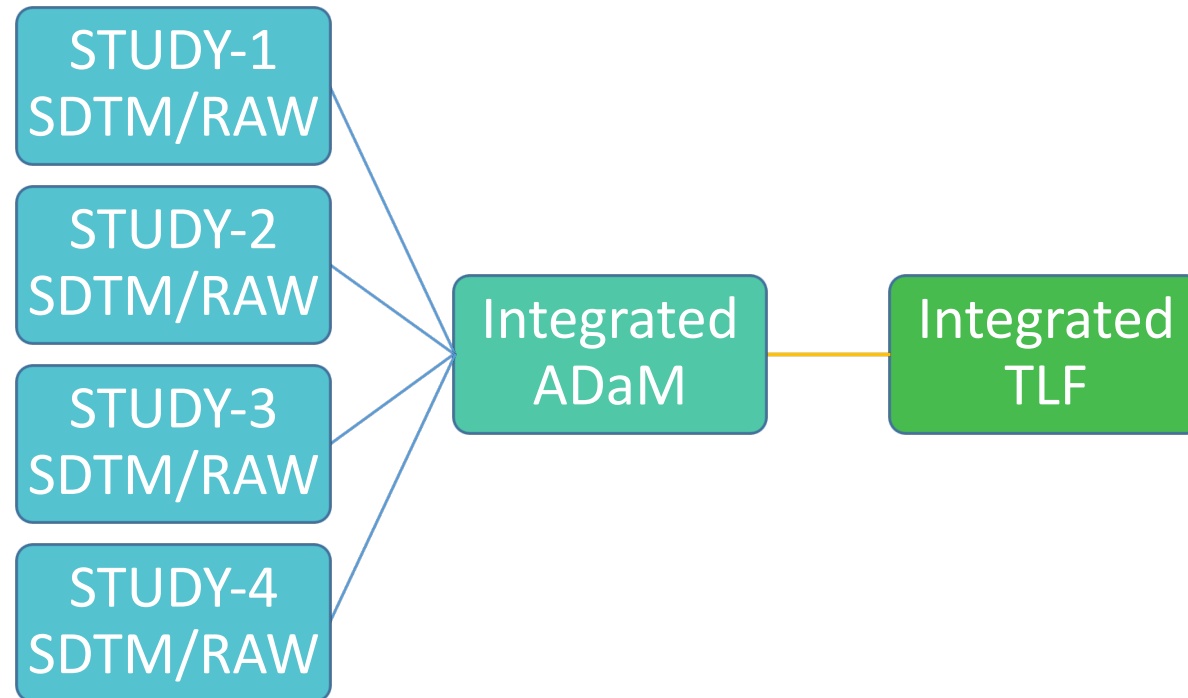


DATASET INTEGRATION – INTEGRATING DATASET USING INDIVIDUAL ADAM DATASETS



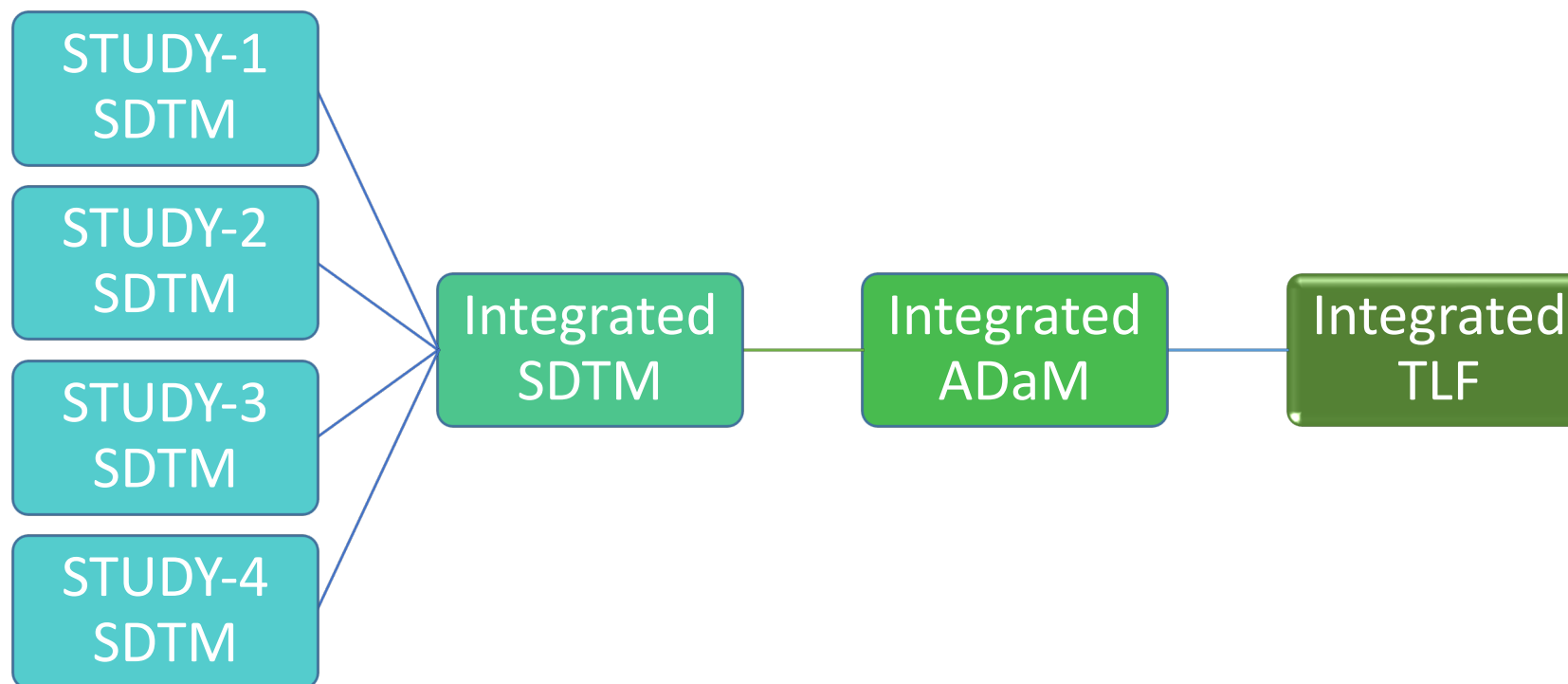
In this method, individual ADaM (Analysis Data Model) datasets are created from individual SDTM datasets, and thus created ADaM datasets will be used to create integrated analysis datasets

DATASET INTEGRATION – INTEGRATING DATASET USING STUDY LEVEL TABULATION DATASETS



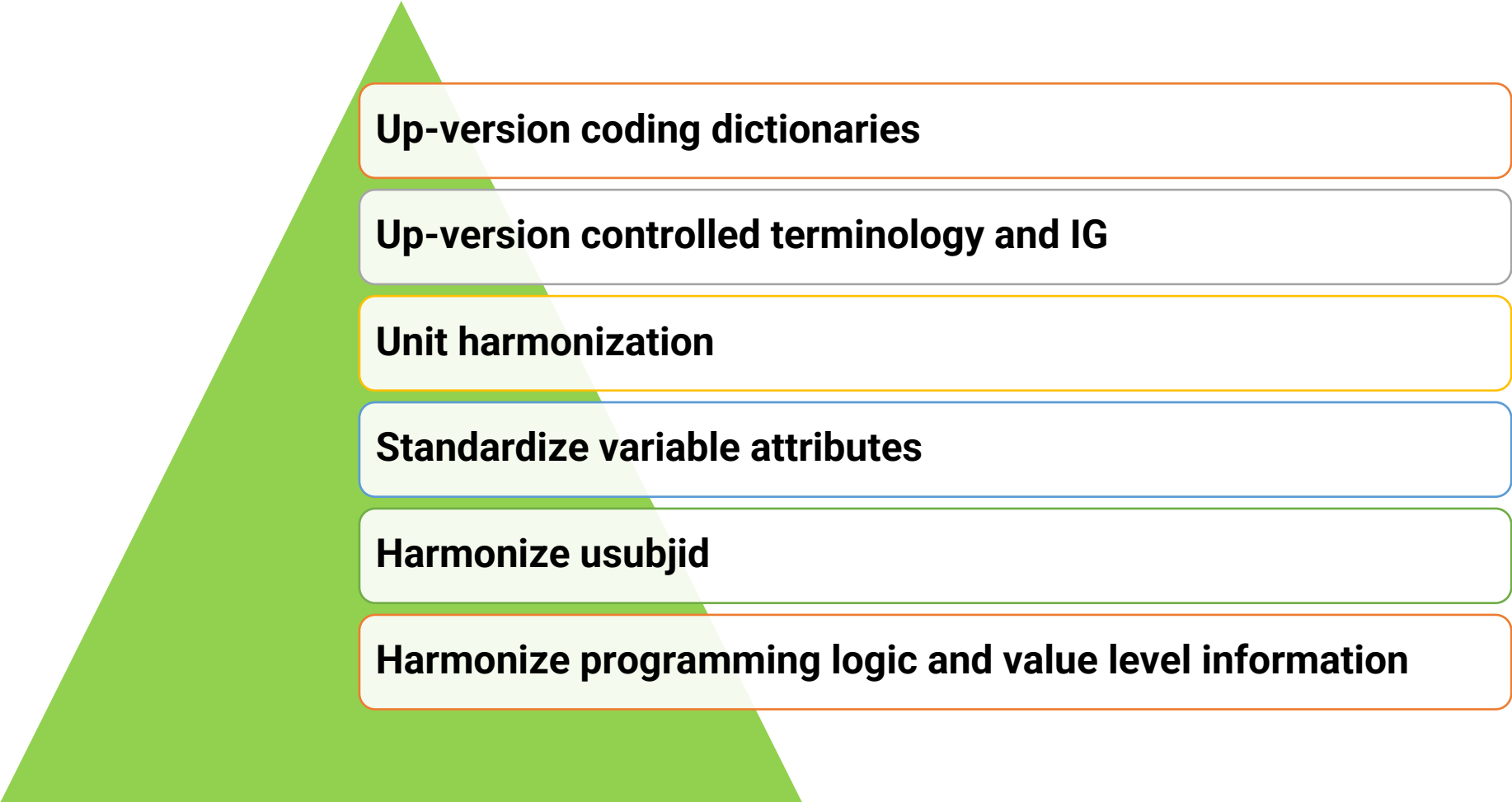
This approach is suggested when there are studies that are part of integration which are not CDISC compliant or if both standard and non-standard studies are included as study level tabulation datasets (SDTM datasets or RAW datasets), and are directly used to create integrated ADaM datasets

DATASET INTEGRATION – INTEGRATING DATASET USING INTEGRATED SDTM DATASETS



This approach is most recommended and most commonly used, as this provides more traceability to integrated ADaM datasets and SDTM datasets. Once individual SDTM datasets are ready, supplemental datasets are merged back with corresponding parent domains. Integrated SDTM datasets can be created by stacking these processed SDTM datasets.

DATA HARMONIZATION



Up-version coding dictionaries

Up-version controlled terminology and IG

Unit harmonization

Standardize variable attributes

Harmonize usubjid

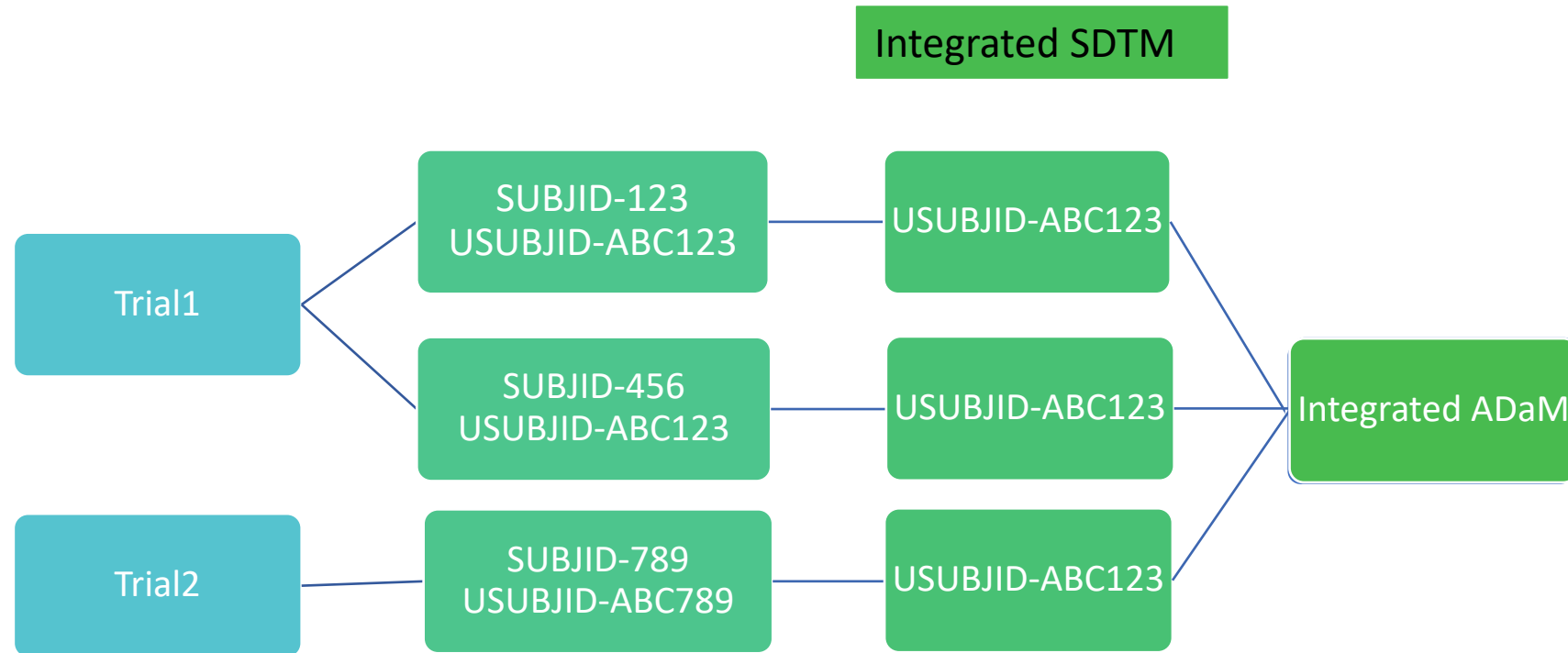
Harmonize programming logic and value level information

UP-VERSIONING STANDARDS AND CODING DICTIONARIES

Study	MedDRA v	WHO	SDTM IG v	SDTM CT v
STUDY-1	20	B3 SEP2017	3.2	2018-12-21
STUDY-2	17	B2 SEP2014	3.1.3	2017-12-22
STUDY-3	17	B2 SEP2014	3.1.3	2014-06-27
STUDY-4	21	GB3 MAR2018	3.2	2018-12-21
UP-VERSION	21	GB3 MAR2018	3.2	2018-12-21

This shows an example of up-versioning different coding dictionaries and controlled terminologies for four different studies.

HARMONIZE USUBJID



If the same subject participated in multiple studies, this subject will have a different SUBJID in each trial but USUBJID must be unique across studies

HARMONIZE PROGRAMMING LOGIC

Study	Variable Name	Variable Label	Programming Notes
ADaM 1	ANL01FL	Analysis Flag 1	Sort the USUBJID AVISITN CHG ATPTN and assign Y for the last record within each Visit (where ATPTN>0)
ADaM 2	ANL01FL	Analysis Flag 1	Sort the USUBJID AVISITN CHG ATPTN and assign Y for the last record within each Visit (where ATPTN>0 and CHG is not missing)
ADaM 3	ANL01FL	Analysis Flag 1	Sort the USUBJID AVISITN CHG ATPTN and assign Y for the last record within each Visit (where ATPTN>0 and DTYPE is missing)
ADaM 4	ANL01FL	Analysis Flag 1	Sort the USUBJID AVISITN CHG ATPTN and assign Y for the last record within each Visit (where ATPTN is not missing)

There is a possibility that derivation logic used for the same variables in individual studies (different datasets) can be different (eg: individual studies from multiple CRO/Sponsor). Different derivation logic can cause programming errors. This mostly happens in ADaM datasets

DATA VALIDATION

Compliance with CDISC/SDTM standards

Pinnacle 21 Validator

Cross check with SAP of Integrated analyses

Cross check with mapping specification of integrated SDTM and ADaM datasets

CONCLUSION

- Integrated Summaries of Effectiveness and Safety (ISE, ISS) are integral part of successful submission for New Drug Application (NDA).
- The most difficult and time-consuming part of the ISS/ISE process is creating the integrated datasets. We can choose different approach for dataset integration, depending on individual study standard.
- Up-versioning of coding dictionaries, controlled terminologies, harmonizing units, variable attributes etc. will help reducing programming effort.
- Validating individual SDTM/ADaM datasets before pooling and cross checking of mapping is recommended.



THANK YOU



Any Questions ?