

Authors Introduction



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Integrated SDTMs to Integrated ADaMs to TLFs – A Case study

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Why is there a need for integrated analysis?

Importance of ISS/ISE

- ❖ Important components of a submission required by the FDA (USA) for New Drug Applications (NDAs)
- ❖ Not required to be part of NDA submissions to MHLW (Japan) and EMA (Europe).
- ❖ However, submissions to MHLW and EMA must follow the common technical document (CTD) which contain sections in line with ISE and ISE

Importance of ISS/ISE

- ❖ Irrespective of a regulatory submission, integrated summaries are useful for:
 - ❖ Discerning trends in patient subgroups
 - ❖ Improving the precision of results with a larger population size when integrating studies
 - ❖ Understanding the risk and benefits by comparing the variation in study results
 - ❖ Reaching a statistical conclusion

Current state of affairs

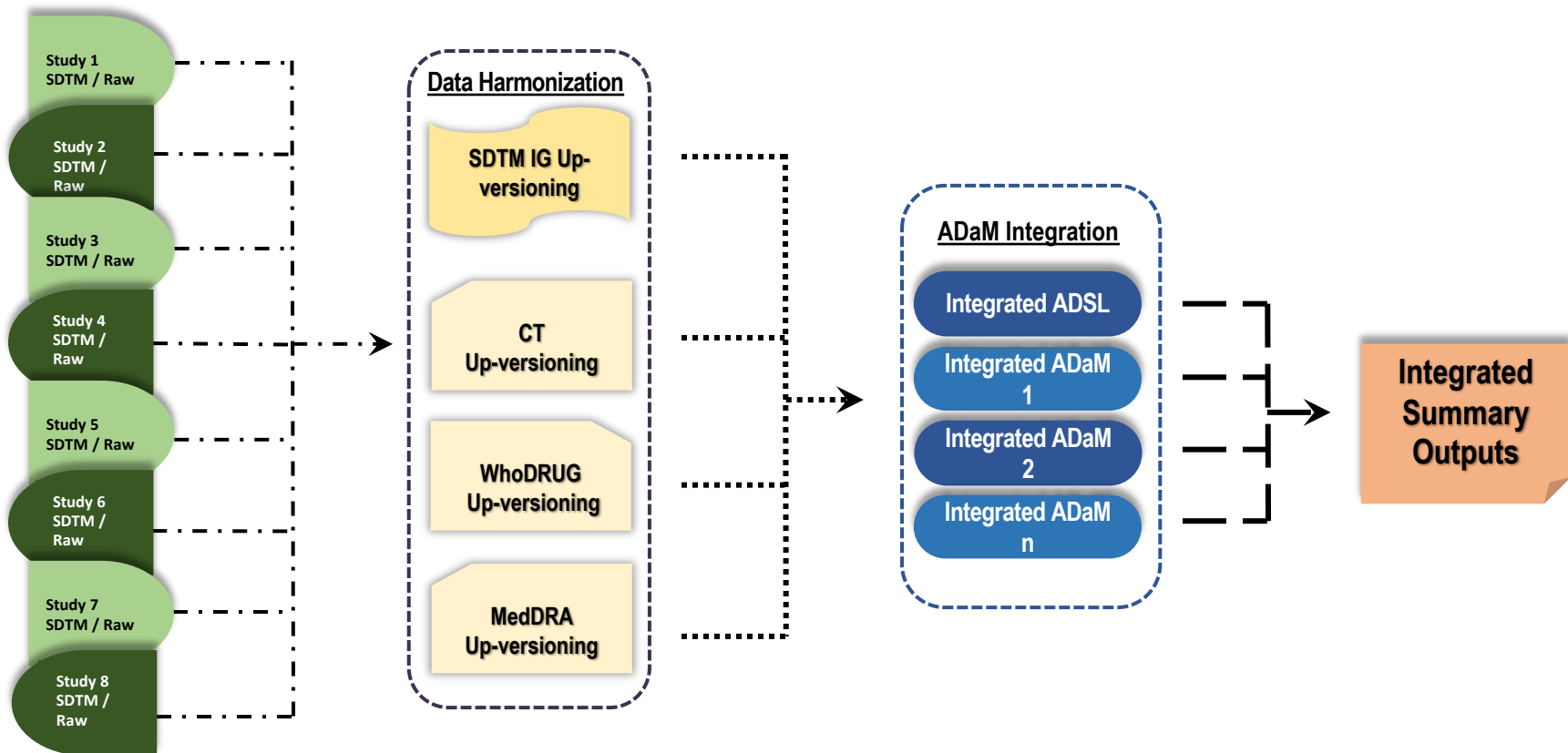
Current Scenario

- ❖ Many sponsor and vendor companies have a need for integrated analysis
- ❖ There is no established process or proven approach within the clinical industry or any strategy defined by regulatory agencies
- ❖ Continuous challenge

Approaches to integrated analysis

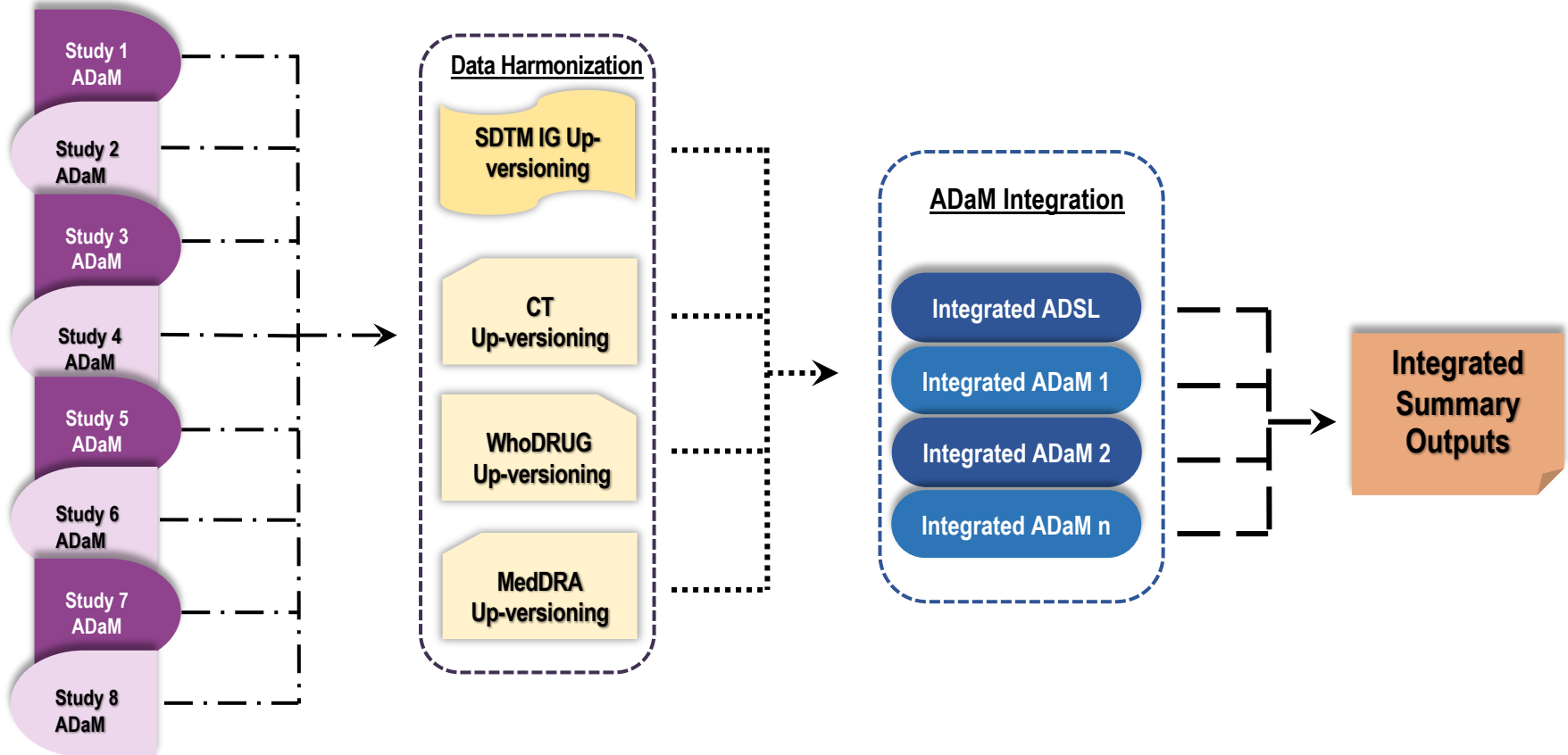
Approach #1:

❖ ADaM Integration using study-level Tabulation datasets



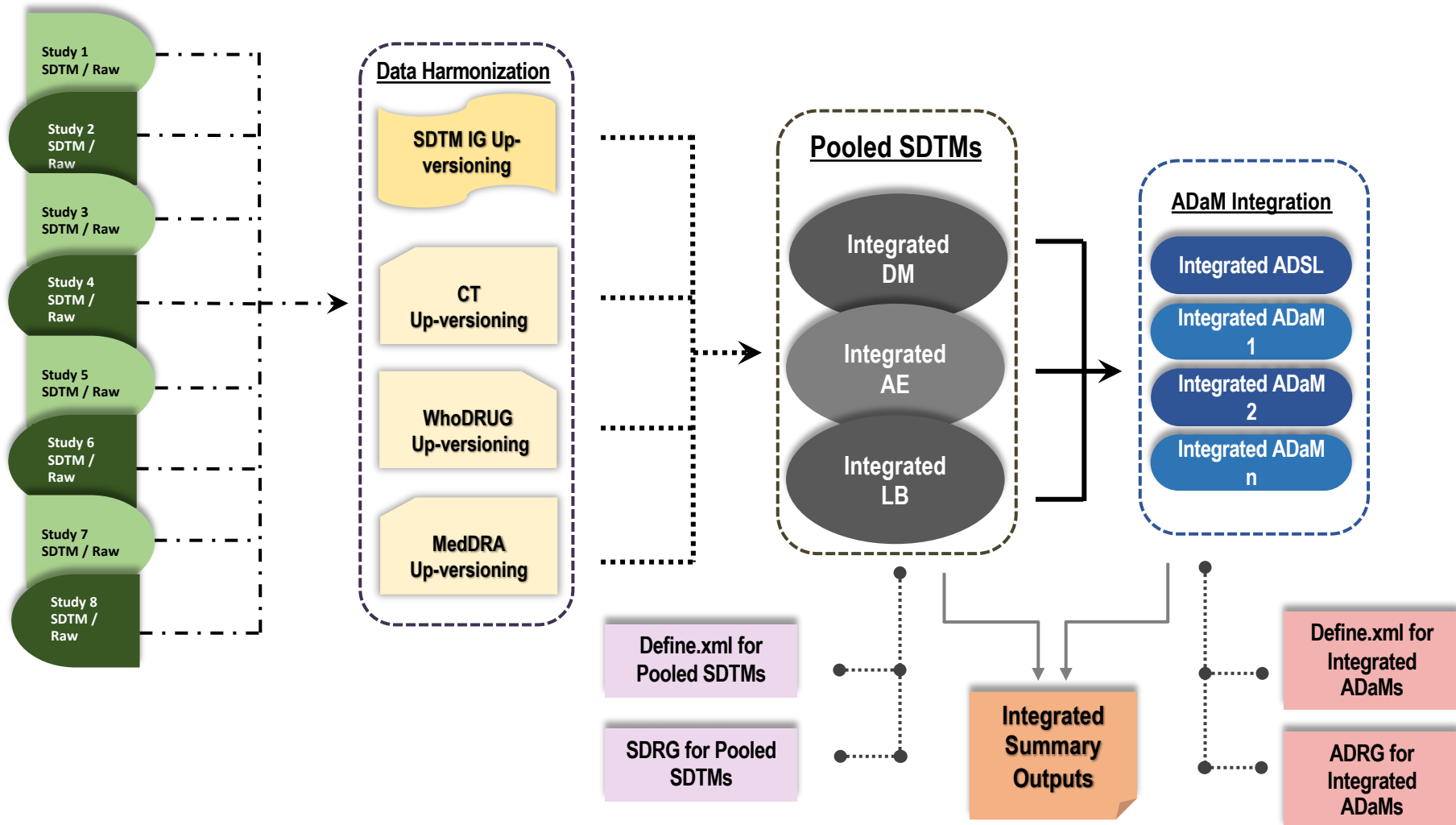
Approach #2:

❖ ADaM Integration using study-level Analysis datasets



Case Study

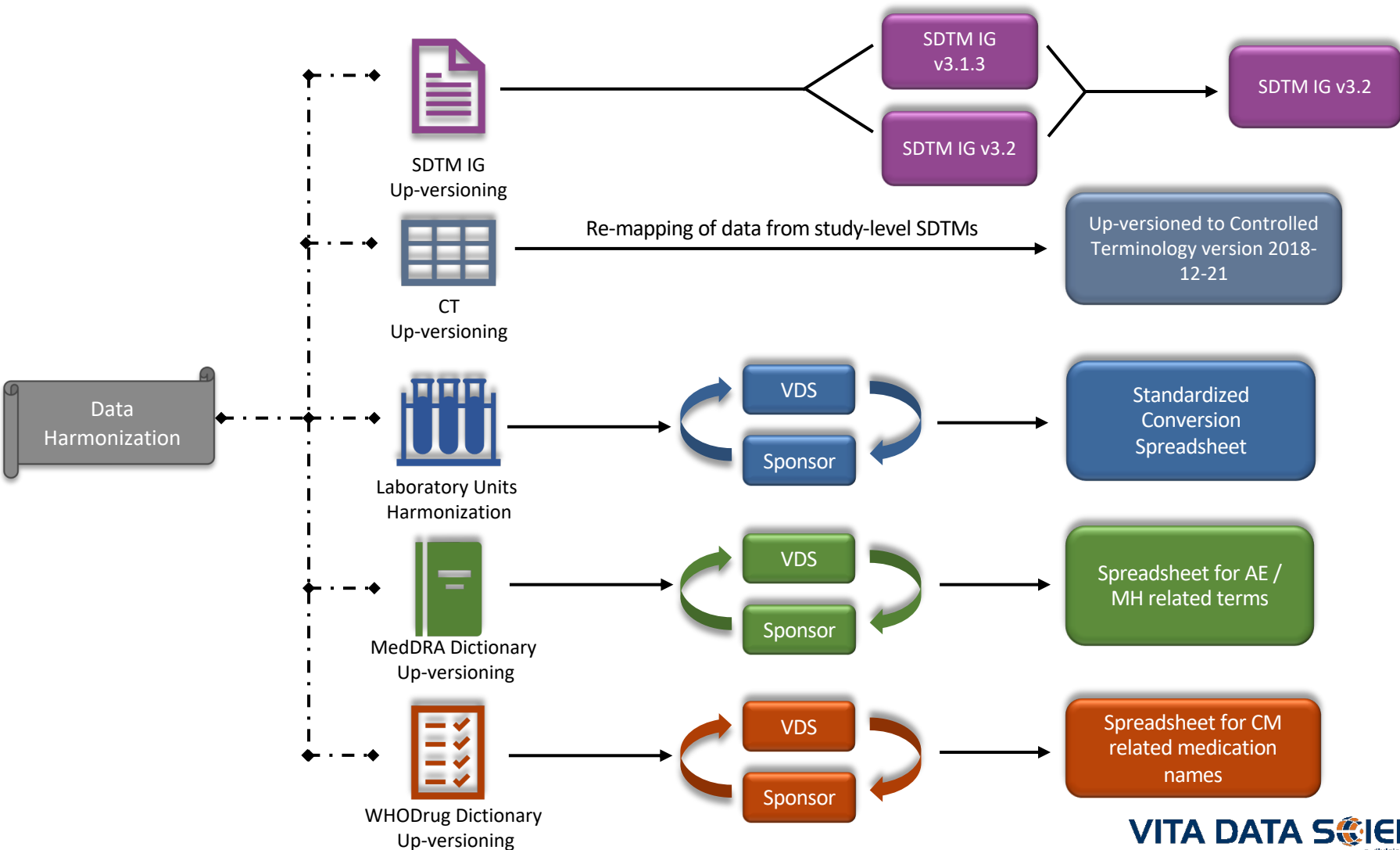
ADaM integration using pooled SDTMs:



Factors involved/Rationale

Study	SDTM IG Version used	SDTM CT Version used	MedDRA Version used	WHO Drug Version used	Vendor
STUDY 1	3.1.3	2014-03-28	17	WHO (World Health Organization) Drug Version September 2014 Enhanced Dictionary Version B2	VDS*
STUDY 2	3.2	2017-12-22	18.1	WHO Drug Dictionary Q2 2015	VDS*
STUDY 3	3.2	2017-12-22	18.1	WHO Drug Dictionary Q2 2015	VDS*
STUDY 4	3.1.3	2014-10-06	17	WHO (World Health Organization) Drug Version September 2014 Enhanced Dictionary Version B2	VDS*
STUDY 5	3.1.3	2014-06-27	17	WHO (World Health Organization) Drug Version September 2014 Enhanced Dictionary Version B2	VENDOR 1
STUDY 6	3.2	2017-12-22	20.1	WHODrug B3 Sep 2017	VDS*
STUDY 7	3.2	2017-12-22	21	WHODRUG B3 GLOBAL (MARCH 2018)	VDS*
STUDY 8	3.2	2018-12-21	21	WHO Drug Mar 2018G B3	VENDOR 2

Data Harmonization Schematic



Pros

- ❖ The need for study-level ADaM datasets was eliminated
- ❖ Majority of the variables were standardized and CDISC compliant at the study level facilitating the ease SDTM pooling
- ❖ The conversion and/or harmonization of the Lab units
- ❖ Up-versioning of the MedDRA and WHODrug dictionaries & harmonizing the Controlled terminologies (CT)

Cons

- ❖ Deriving new variables could not be done at the pooled SDTM level.
- ❖ Standardizing or harmonizing the Visit information – VISIT, VISITNUM and other variables such as --TPT (Planned time point name), --TPTNUM (Planned time point number) values, etc.
- ❖ In some cases, the traceability factor was impacted due to mapping decisions taken at an individual study level.
- ❖ Validation of the pooled SDTM and integrated ADaM datasets using pinnacle 21 validator tool.

Lessons Learned

- ❖ It is best that the decisions related to mapping and standards are made in a uniform manner upfront when mapping data to the study level SDTMs- this saves time and makes the process highly efficient when creating pooled SDTMs
- ❖ To facilitate consistent decision making throughout the integration process, avoid any misinterpretation of data etc., having the same team working is beneficial. From an operational perspective, this also ensures steady functioning of the team
- ❖ The approach can be further streamlined if all studies involved are handled by a single vendor to maintain consistency

To summarize

- ❖ Using the pooled SDTM dataset approach helped us streamline the ISS process
- ❖ It significantly reduced the time typically needed to program ADaM datasets using individual SDTM domains when multiple studies are involved



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