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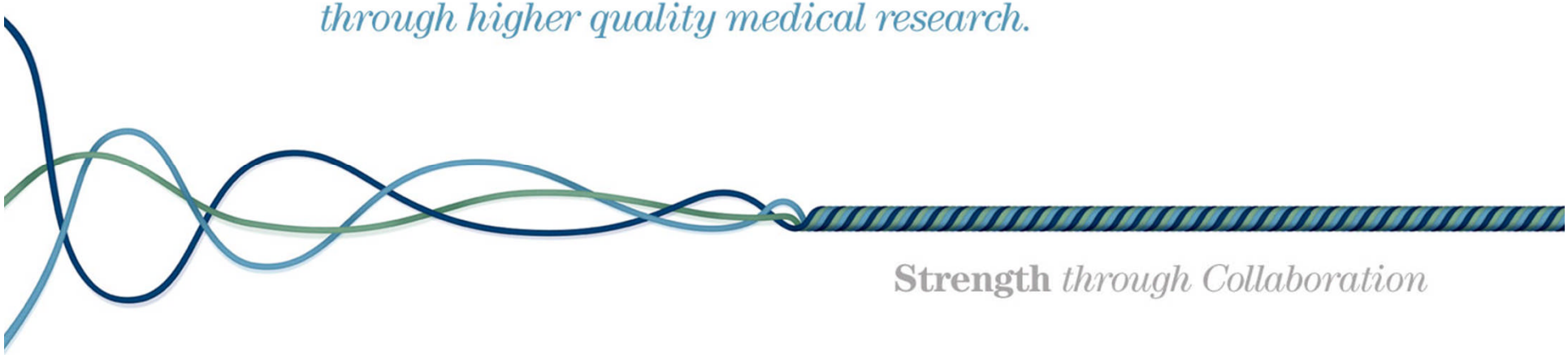
The CDISC vision is to inform patient care & safety through higher quality medical research.



Strength *through Collaboration*

Feasibility Study on Applying CDISC SDTM to Post-Marketing Surveillance

Presented by

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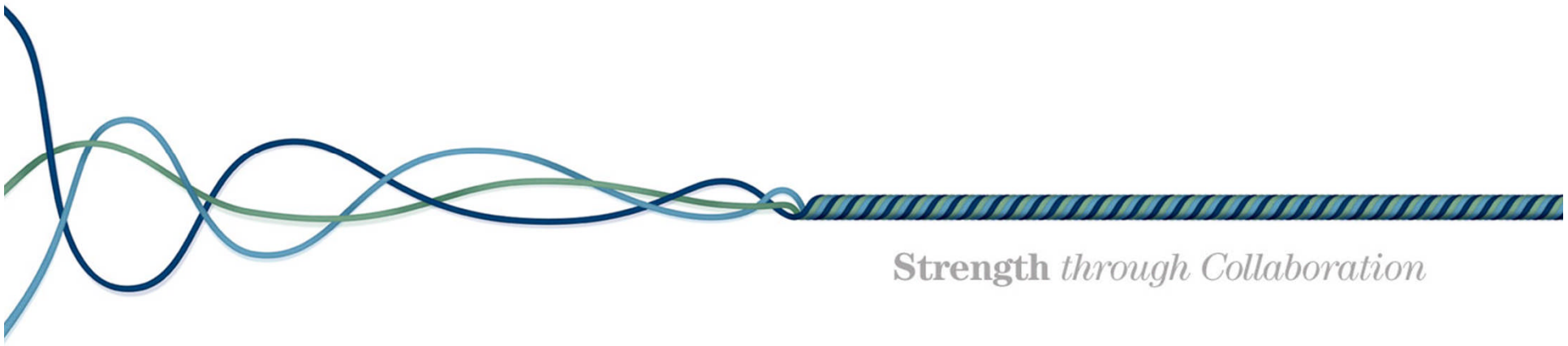


Contents

- Applying SDTM to Post-Marketing Surveillance
  - What it means
  - Values of SDTM in PMS
- Technical Approach and Considerations
  - Reliability and Trustworthiness of Records
  - Cost Effectiveness

Applying SDTM to Post-Marketing Surveillance

What is Post-Marketing Study

- Post-Marketing Studies in Japan are regulated by Good Post-marketing Study Practice (GPSP)
  - Phase VI Clinical Study
  - “使用成績調査” – Study of real-life uses of a new drug
    -> This is the topic of my presentation.

- Study of real-life uses of a new drug
  - Approximately 3,000 subjects
  - No placebo/comparators
  - Typically a specialized EDC and/or a paper CRF are used to capture patient records

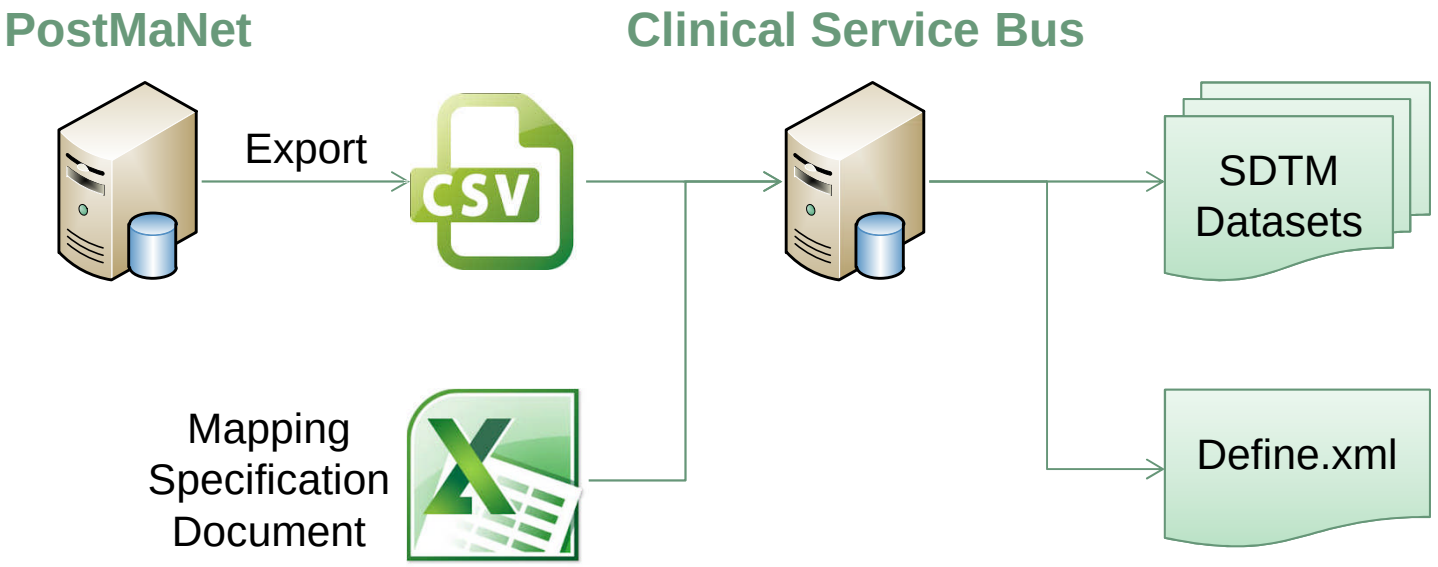
Why Applying SDTM to Post-Marketing Studies?

- Accelerate Studies and Reduce Costs
  - As fast and economy as clinical trials
  - Promote use of EDC for PMS
  - Standardize analytical datasets and programs
- Better comparison between clinical trial and PMS
  - Enhance data comparability between well-controlled clinical studies and real-life PMS
  - Enable sharing methods/resources in clinical and PMS
- Enabler of Healthcare-Link
  - Accelerate speed and improve data quality
  - Enable collecting more valuable information

Technical Approach and Considerations

Technical Architecture

- Tools
  - EDC – PostMaNet
  - ETL – Clinical Service Bus



Key Challenges

- How can we ensure that SDTM datasets are as reliable/trustworthy as PostMaNet source data while minimizing manual QCs on the SDTM datasets?
- To what extent can we standardize data transformation programs in order to minimize cost for SDTM transformation per protocol?

- **These are universal challenges with not limited to PMS data but including clinical trials data.**

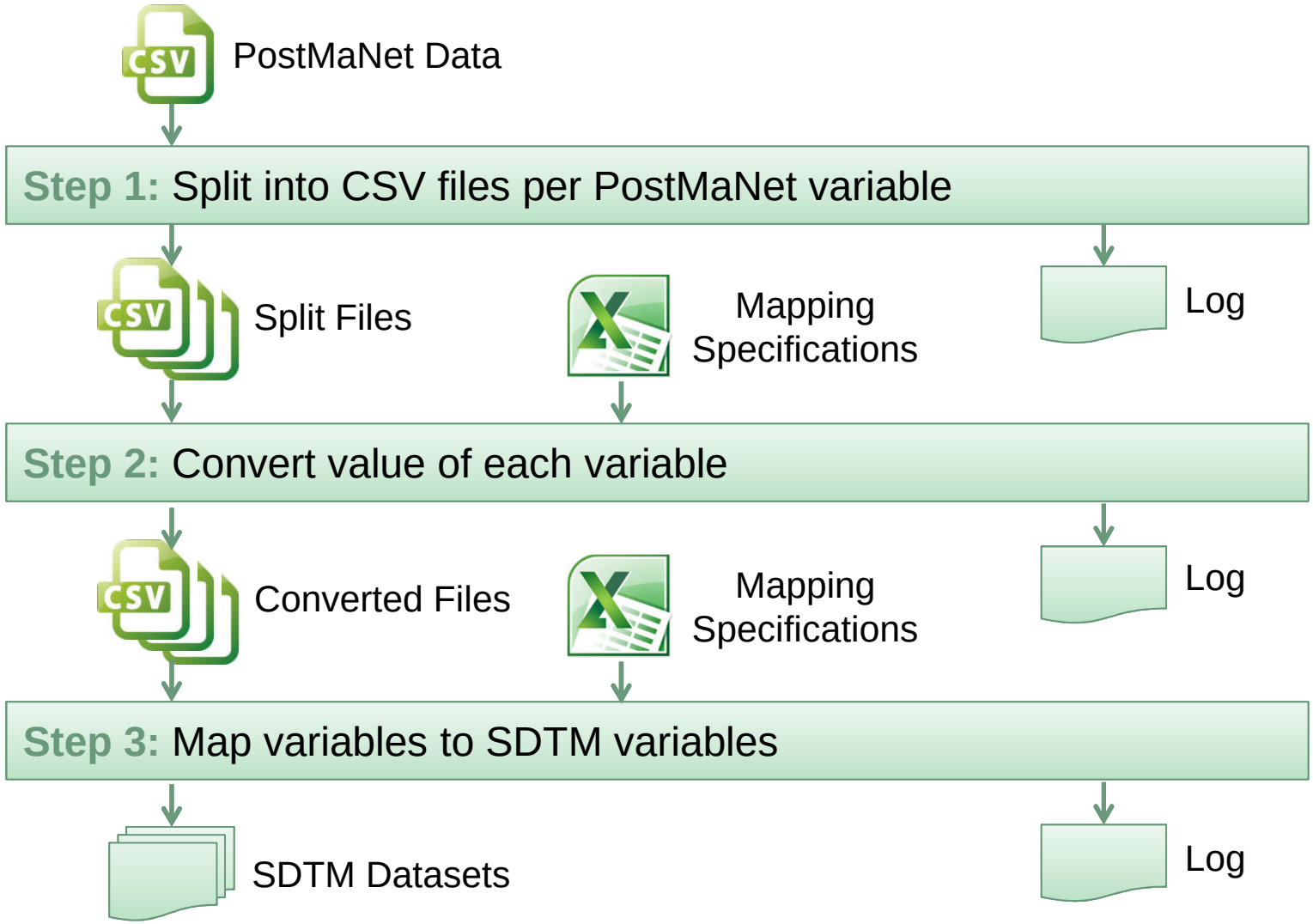
Reliability and Trustworthiness – Our Understanding

- **SDTM datasets** that are relied on to perform regulated activities or those submitted to a regulatory agency are considered to be **subject to Electronic Records requirements** in the region.
- A sponsor should make a decision on the **extent of the validation** taking into account the **impact on the reliability and trustworthiness** of the records.

Reliability and Trustworthiness – Validation Approach

- Mapping Specification Document
  - Including mapping between source system to SDTM, coding conversions, derivation formula, and so forth.
- Program Design & Test
  - Needed for each transformation program (could be for each transformation rule)
- Execution Records
  - Logs may substitute if SDTM datasets are produced in a fully systematic manner
- Qualification of SDTM Datasets
  - OpenCDISC may validate conformance to SDTM, but does not qualify all mapping specifications are met.
  - Manual QC may still be needed.

Transformation Steps



Reliability and Trustworthiness – Audit Trails

- A typical audit trail record contains who, when, and what (e.g. old value/new value) information.

- What are audit trails in terms of the following SDTM transformation?
  - when {0, 1} values are converted to {M, F}
  - when the minimum Exposure Date on CRF is calculated to derive SDTM Subject Reference Start Date
  - when a field on CRF is mapped to a different SDTM variable based on its context

Reliability and Trustworthiness – Our Logging Approach

- We identified that the following information should appear in the transformation log;
  - Execution user name
  - Date/time of execution
  - Input/output file names (i.e. variable names)
  - Number of records processed

- The logs will need to be retained along with input/output data during the required record retention period.

Cost Effectiveness – Our Findings

- Many transformation programs can be reused
  - Programs at step1 & 3
  - Common patterns of transformations at step 2

- SDTM transformation tend to require ad-hoc programs thus increase the cost, when;
  - Variable names and/or codelists in the source system are inconsistent across protocols.
  - Mapping is determined by the value of data
  - SUPP-- domains are used.

* Above is only a partial list.

Summary

- SDTM can be applied to post-marketing studies similarly to clinical studies.
- Maintaining reliability/trustworthiness and increasing cost effectiveness are the two key challenges in implementing transformation.
- Validation and logging approach should be defined clearly to ensure regulatory compliance.
- Use of ad-hoc programs should be minimized to reduce costs.

Thank you for listening!

Please feel free to send your questions to:

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