

ISS Experience and Expectation for Projects with Cross-company Cooperation



MSD

INVENTING FOR LIFE

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MSD

Today's Objectives

- Share experience of ISS for projects with cross-company cooperation
- Look forward to productive discussions

Agenda

- ISS introduction
- Cross-company project ISS background
- Challenges & Solutions
- Expectations & Discussion
- Contact information

ISS introduction

The integrated summary of safety (ISS) is a required section of a New Drug Application (NDA) and a supplemental New Drug Application (sNDA) that provides comprehensive safety outcomes of one or more clinical trials to agency reviewers.

With ISS, a single database is formed by pooling the results of all the clinical trials. This pool of database is much larger than those of individual studies, hence, it is easier to characterize the overall safety profile of the study drug and to identify risks that should be included on the product label.

Cross-company project ISS Background

- Experimental treatment:
Drug A (MSD) combination with Drug B (Partner company)
- Include pooled drug B data provided by Partner company in ISS analyses
- Take drug B safety profile into consideration

Challenges & Solutions

P R O C E S S

Drug B pooled data
transfer

Request Drug B pooled data by dedicated DM coordinator.
Submit IT request to download data from data exchange platform to production area by ISS programmer.

Drug B pooled data
pre-processing

Store partner's data transfer into dedicated ISS central area in computing platform for data reusability.
Prepare **complete** ADAE data for MeDRA version up-leveling.

Challenges & Solutions

A N A L Y S I S

Multiple data pools for multiple dosage forms

Multiple studies in each data pool

Multiple data transfer

Multiple supportive documents

Identify the difference of data pools

Find the right studies and phases according to documents

Investigate data contents & data structure
Key supportive documentations:
ADRG, ADaM define, Complex Algorithms

Challenges & Solutions

A N A L Y S I S

Different data structure between companies

Grab key variables such as AE action taken, causality, outcome, exposure duration, etc.

Normalize pooled data (ADSL, ADAE, ADLB, ADEXSUM) to MSD data structure.

Insufficient information in Lab data

Re-derive MSD required variables to generate MSD Lab analysis table

Challenges & Solutions

A N A L Y S I S

Present pivotal studies for both Drug A and Drug B

Different AESI for Drug A and Drug B

Different AESI for different data pools for Drug B

Present different layouts for different tables:

Derive corresponding population flags in ADSL;

Derive AESI flag variables in ADAE;
Set up multiple start up programs to display different layouts showing different column headers and different footnotes

AESI: Adverse Events of Special Interest

Challenges & Solutions

Present different layouts for different tables

ISS Table Presentation: General

Column A	Column B	Column C	Column D	Column E
Drug A pivotal study Arm 1 (N=XXX)	Drug A pivotal study Arm 2 (N=XXX)	Drug B pivotal study (N=XXX)	Drug B Tablet Pool (N=XXX)	Drug A Pool (N=XXX)

ISS Table Presentation: AESI for Drug A

Column A	Column B	Column E
Drug A pivotal study Arm 1 (N=XXX)	Drug A pivotal study Arm 2 (N=XXX)	Drug A Pool (N=XXX)

ISS Table Presentation: AESI for Drug B Tablet Pool

Column A	Column B	Column C	Column D
Drug A pivotal study Arm 1 (N=XXX)	Drug A pivotal study Arm 2 (N=XXX)	Drug B pivotal study (N=XXX)	Drug B Tablet Pool (N=XXX)

ISS Table Presentation: AESI for Drug B Tablet+Capsule Pool

Column A	Column B	Column C	Column D
Drug A pivotal study Arm 1 (N=XXX)	Drug A pivotal study Arm 2 (N=XXX)	Drug B pivotal study (N=XXX)	Drug B Tablet+Capsule Pool (N=XXX)

Challenges & Solutions

VALIDATION

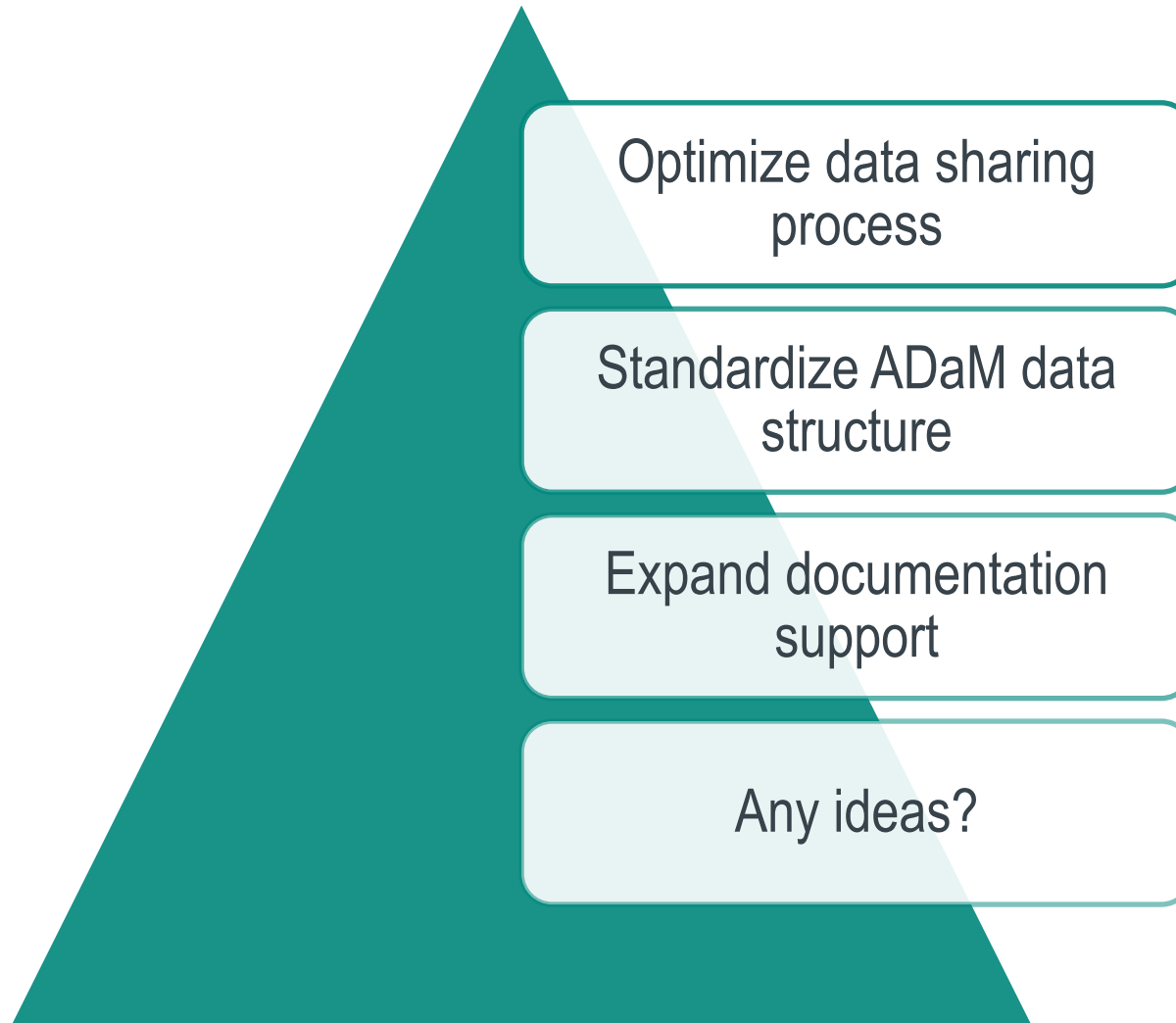
MUST do full
validation
BUT
Hard to validate
output table results

Perform double programming for ISS
analysis datasets internally

Manually compare MSD output results
with the published results for Drug B

NOT all information can be found due to
confidentiality reason

Expectations & Discussion



Contact Information

Your comments and questions are valuable and appreciated.

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THANK YOU

