

Interpreting ADaM Standards with OpenCDISC

Madhura Paranjape, Cytel
Trupti Bal, Cytel

Session CD04 - PhUSE 2012

Disclaimer

This presentation is based on first-hand experience of the presenters, their opinions and learnings.

However this is not to be construed as an official statement endorsed by Cytel

Agenda

- Introduction
- ADaM datasets workflow
- About OpenCDISC Validator
- Examples
 - ✓ Handling TRTP
 - ✓ ADaM for ISS
 - ✓ AVAL vs. AVALC
 - ✓ Additional cases
- Conclusion
- Discussion/Questions

Introduction

Analysis Dataset Model (ADaM)

- CDISC defined and FDA accepted standard
- Introduced in recent past
- Evolving

Introduction

Ensuring compliance may seem like a tightrope walk



© Ron Leishman * www.ClipartOf.com/437909

due to

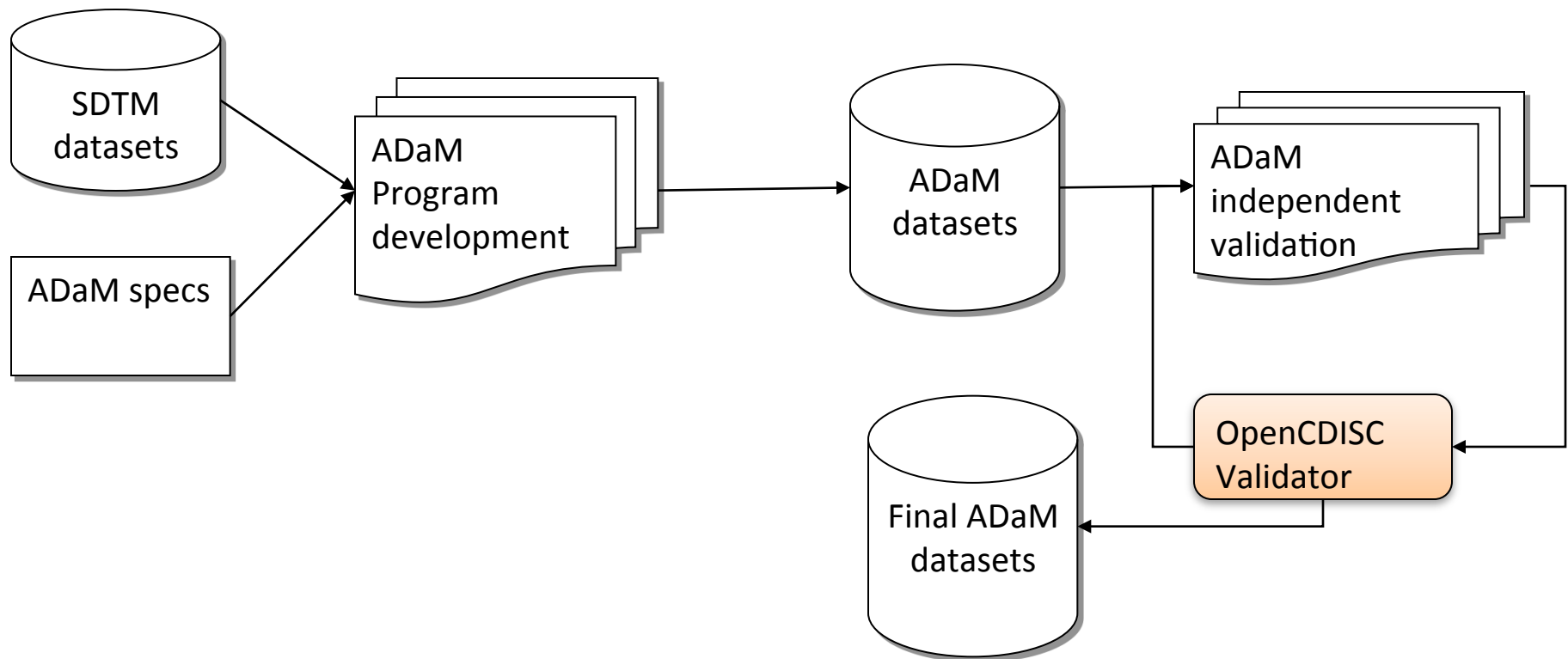
- a) Evolving standard – as yet unfamiliar
- b) Stringent timelines

Introduction

- Validation of datasets plays an important role



ADaM datasets workflow



OpenCDISC Validator is freely available and easy to use.

About OpenCDISC Validator

OpenCDISC Validator

File Help

What would you like to do? ☒ Validate Data ☐ Generate Define.xml

Standard: ADaM

Source Format: SAS® Transport (XPORT)

Source Data:

Browse
Remove
Clear

You can select multiple files or folders as sources

Configuration: config-adam-1.0.xml

Define.xml:

Browse

Optional

Report Format: Excel [Report Settings](#)

Progress:

Waiting to begin.

Start Stop

About OpenCDISC Validator

OpenCDISC Validator

File Help

The tool for ensuring clinical data compliance with CDISC standards

Source Format: SAS® Transport (XPORT) ▼

OpenCDISC

ADaM compliance check:

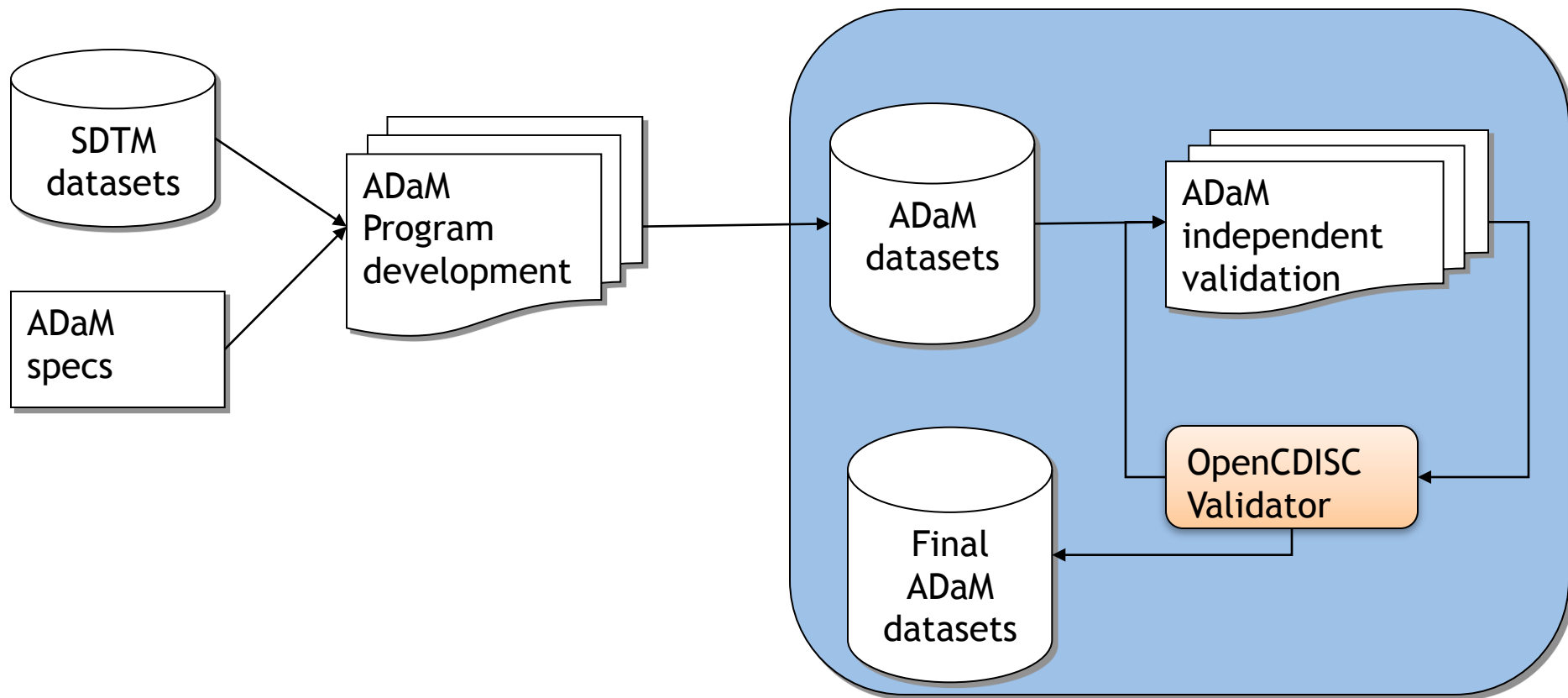
- 130 rules based on ADaM Validation Checks
- Gives a detailed report with issues categorized by
 - a) Severity: Error, Warning and Notice
 - b) Type: Consistency, Format, Limit, Metadata, Presence, System and Terminology

- Extra pair of eyes for ensuring compliance with ADaM

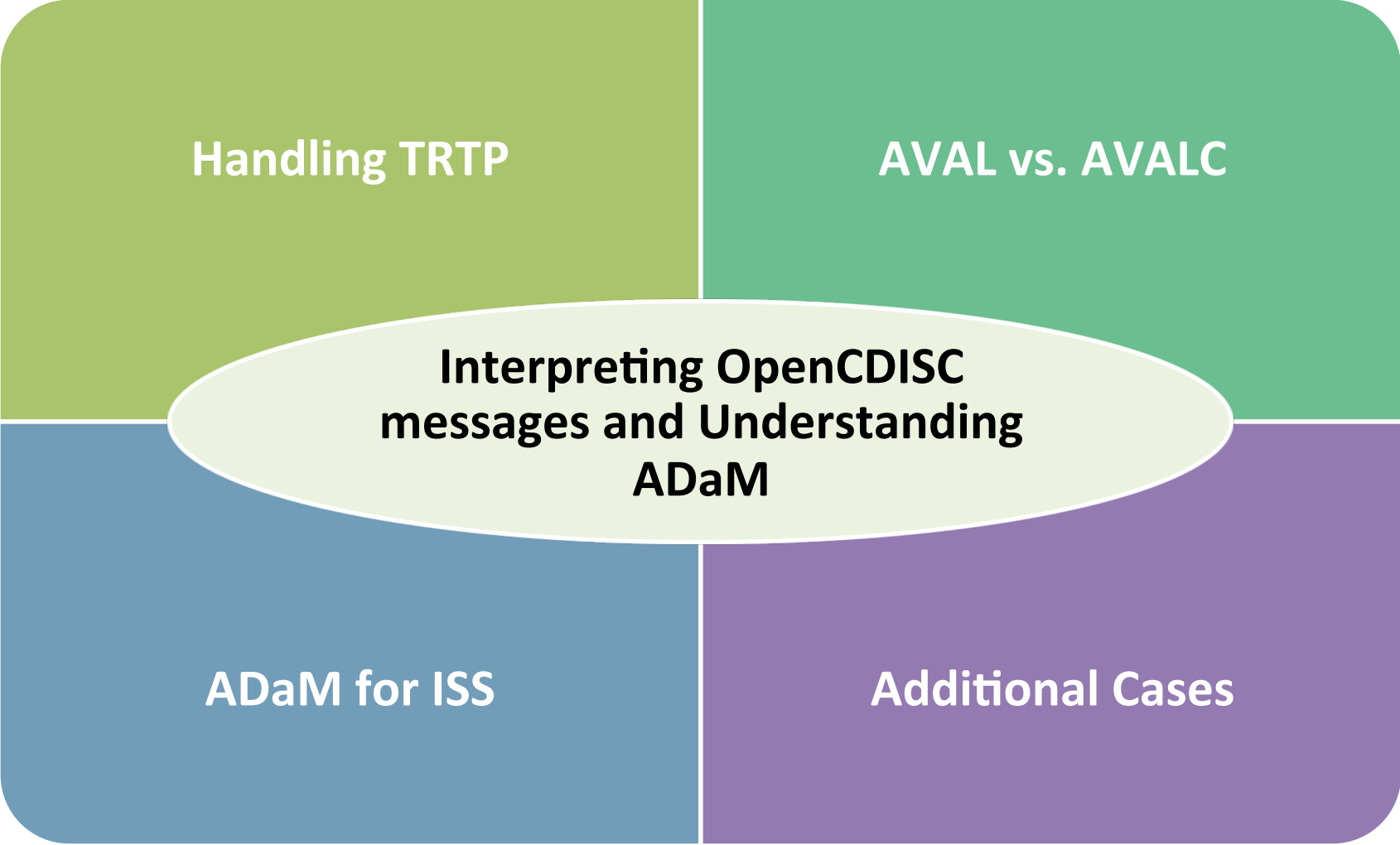
Progress:

Waiting to begin.

ADaM datasets workflow for examples



$$c_{ij}(z_i) = \Pr(Z_j \geq b_j | Z_i = z_i, \delta = 0)$$



Handling TRTP

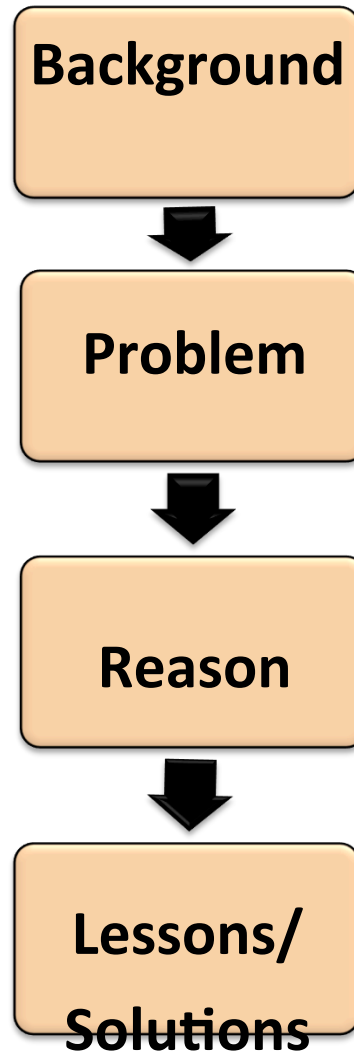
AVAL vs. AVALC

**Interpreting OpenCDISC
messages and Understanding
ADaM**

ADaM for ISS

Additional Cases

Steps to go through



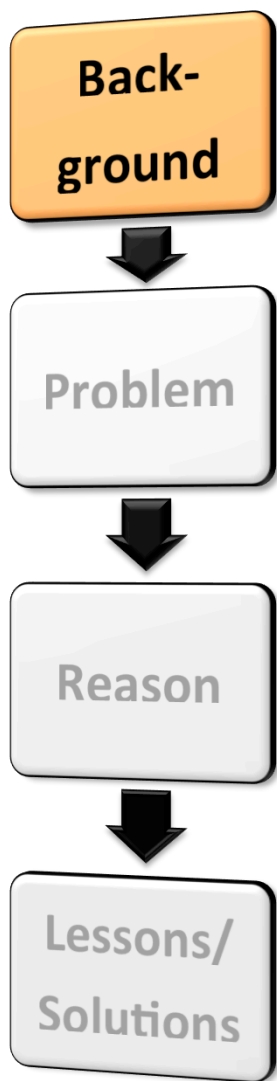
$$G_0(z_1) = \Pr(Z_2 \geq b_2 | Z_1 = z_1, \delta = 0)$$

$$G_1(z_1) = \Pr(Z_2 \geq b_2 | Z_1 = z_1, \delta = 1)$$

Case 1

Handling TRTP

Handling TRTP

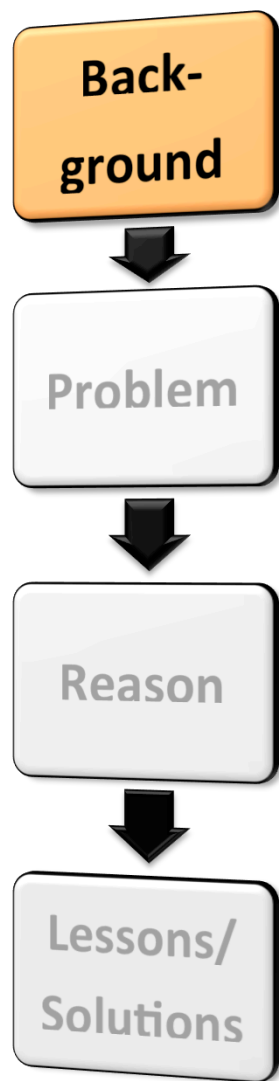


- Study Design: Randomized, parallel
- Phase: III
- Dataset: ADEG
- OpenCDISC version: 1.2.1

TRTP:

- Record level Identifier
- Represents planned Treatment for a record

Handling TRTP



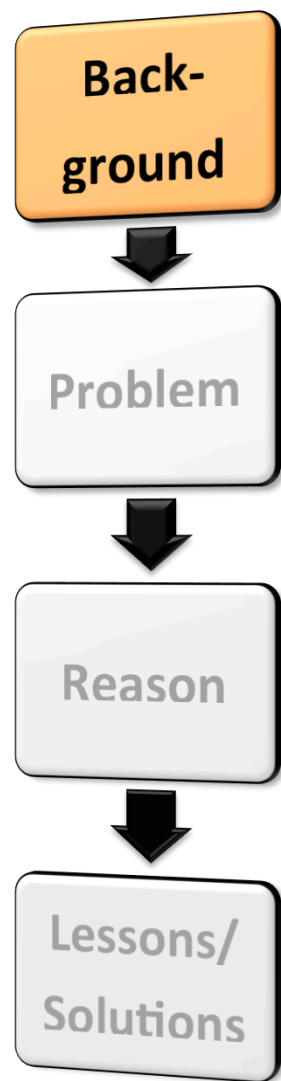
ECG Assessment

	Screening	Visit 1	Visit 5	Visit 9
TRT A	✓	✓	✓	✓
TRT B	✓	✓	✓	✓

SDTM EG Dataset

USUBJID	EGTESTCD	EGSTRESN	EGSTRESU	VISIT
ABC1201	HR	70	BEATS/MIN	Screening
ABC1201	HR	70	BEATS/MIN	Visit 1
ABC1201	HR	72	BEATS/MIN	Visit 5
ABC1201	HR	71	BEATS/MIN	Visit 9

Handling TRTP



SDTM EG Dataset

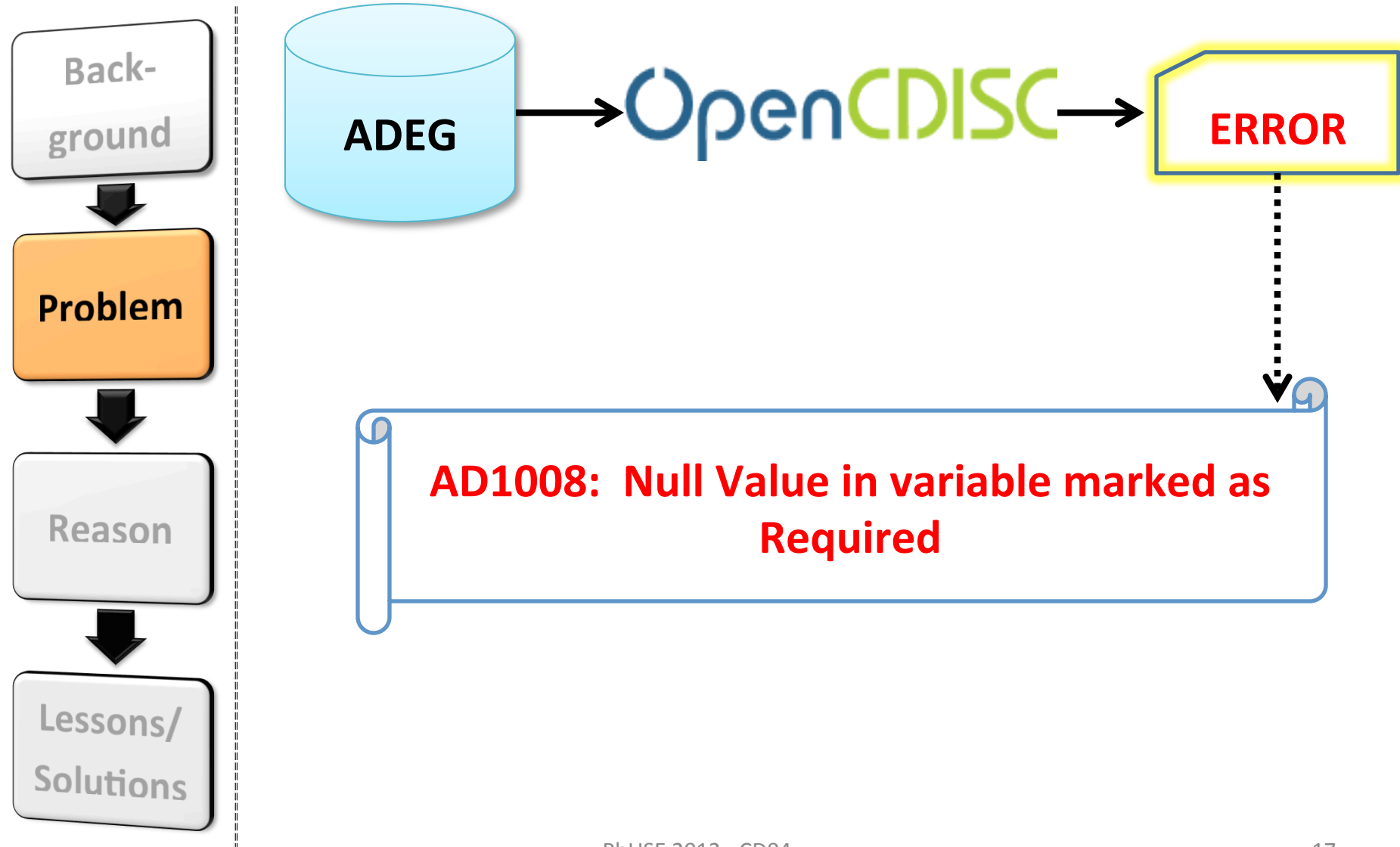
USUBJID	EGTESTCD	EGSTRESN	EGSTRESU	VISIT
ABC1201	HR	70	BEATS/MIN	Screening
ABC1201	HR	70	BEATS/MIN	Visit 1
ABC1201	HR	72	BEATS/MIN	Visit 5
ABC1201	HR	71	BEATS/MIN	Visit 9



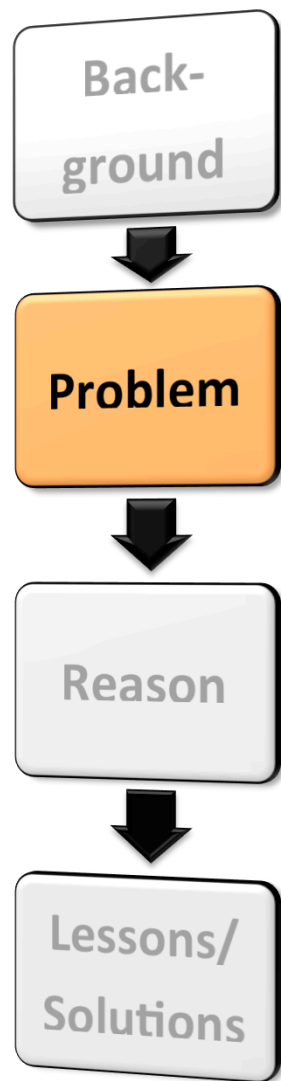
ADEG Dataset

USUBJID (Unique Subject Identifier)	TRTP (Planned Treatment)	PARAMCD (Parameter Code)	AVAL (Analysis Value)	AVISIT (Analysis Visit)
ABC1201		HR	70	Screening
ABC1201	TRT A	HR	70	Visit 1
ABC1201	TRT A	HR	72	Visit 5
ABC1201	TRT A	HR	71	Visit 9

Handling TRTP



Handling TRTP



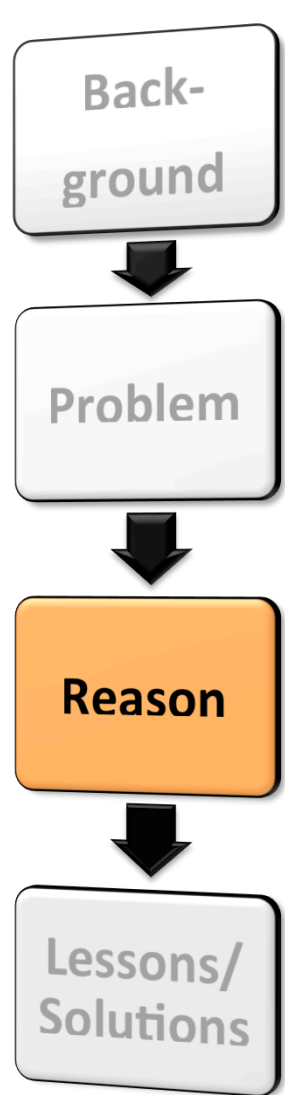
ADEG Dataset

USUBJID	TRTP	PARAMCD	AVAL	VISIT
ABC1201		HR	70	Screening
ABC1201	TRT A	HR	70	Visit 1
ABC1201	TRT A	HR	72	Visit 5
ABC1201	TRT A	HR	71	Visit 9

Details of Error:

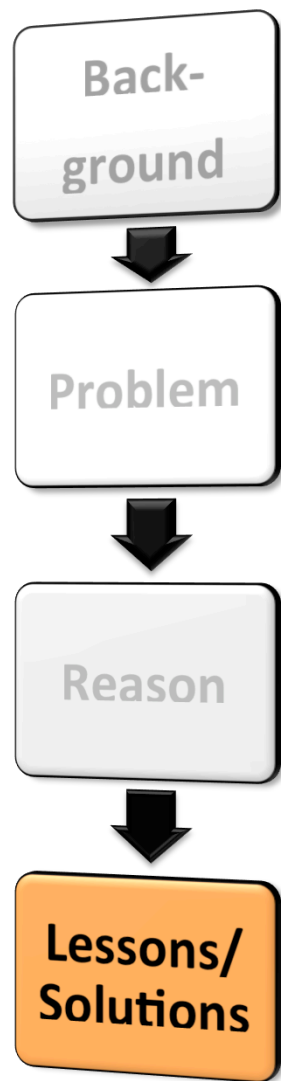
Record	Variables	Values	Rule ID	Message	Category
210	TRTP	null	AD1008	Null value in variable marked as Required	Presence

Handling TRTP



- The visit is screening
- No planned treatment at screening
- No valid value for TRTP
- Need to keep it blank

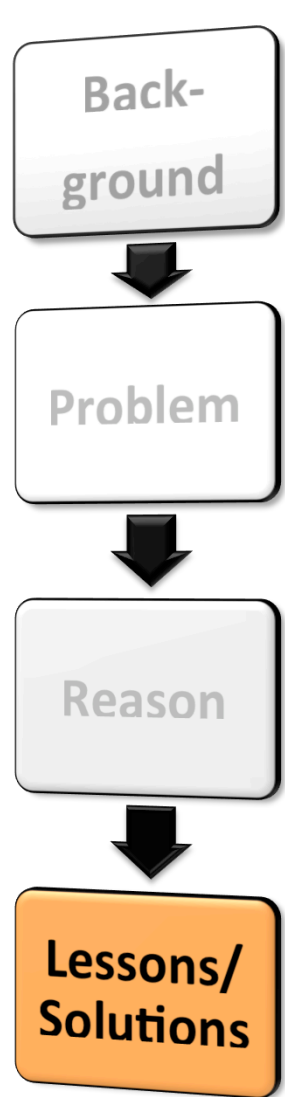
Handling TRTP



Solution

Override error because OpenCDISC Validator used SDTM definition

Handling TRTP



- Required variables can be null

SDTM ✗ ADaM ✓

- Required variables in ADaM

Can be Null	Can not be Null
TRTP	STUDYID
	USUBJID
	ARM
	PARAM

- Current version of OpenCDISC Validator allows null values in TRTP

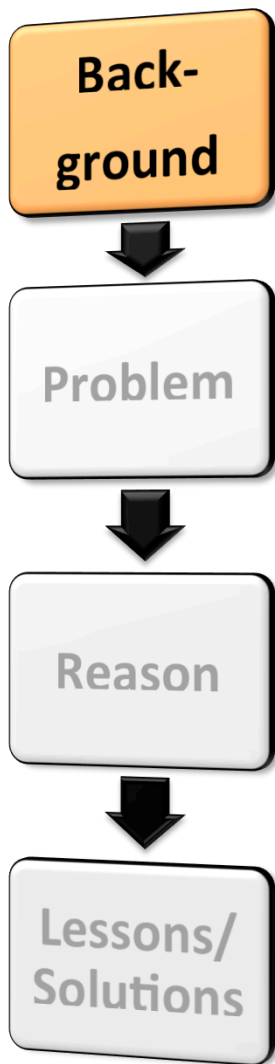
$$G_0(z_1) = \Pr(Z_2 \geq b_2 | Z_1 = z_1, \delta = 0)$$

$$G_0(z_1) = \Pr(Z_2 \geq b_2 | Z_1 = z_1, \delta = 0)$$

Case 2

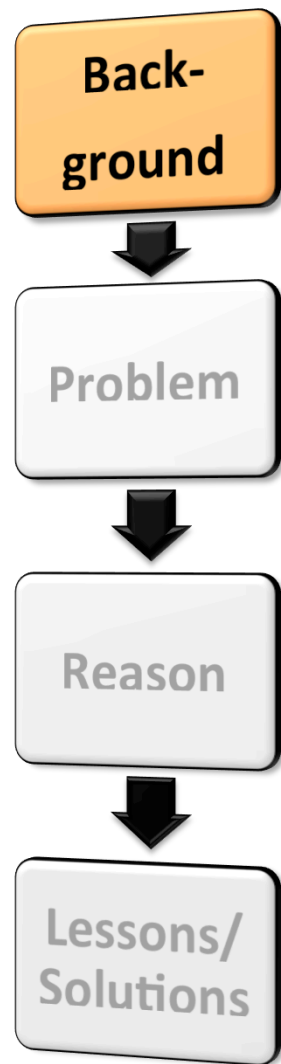
ADaM for ISS

ADaM for ISS

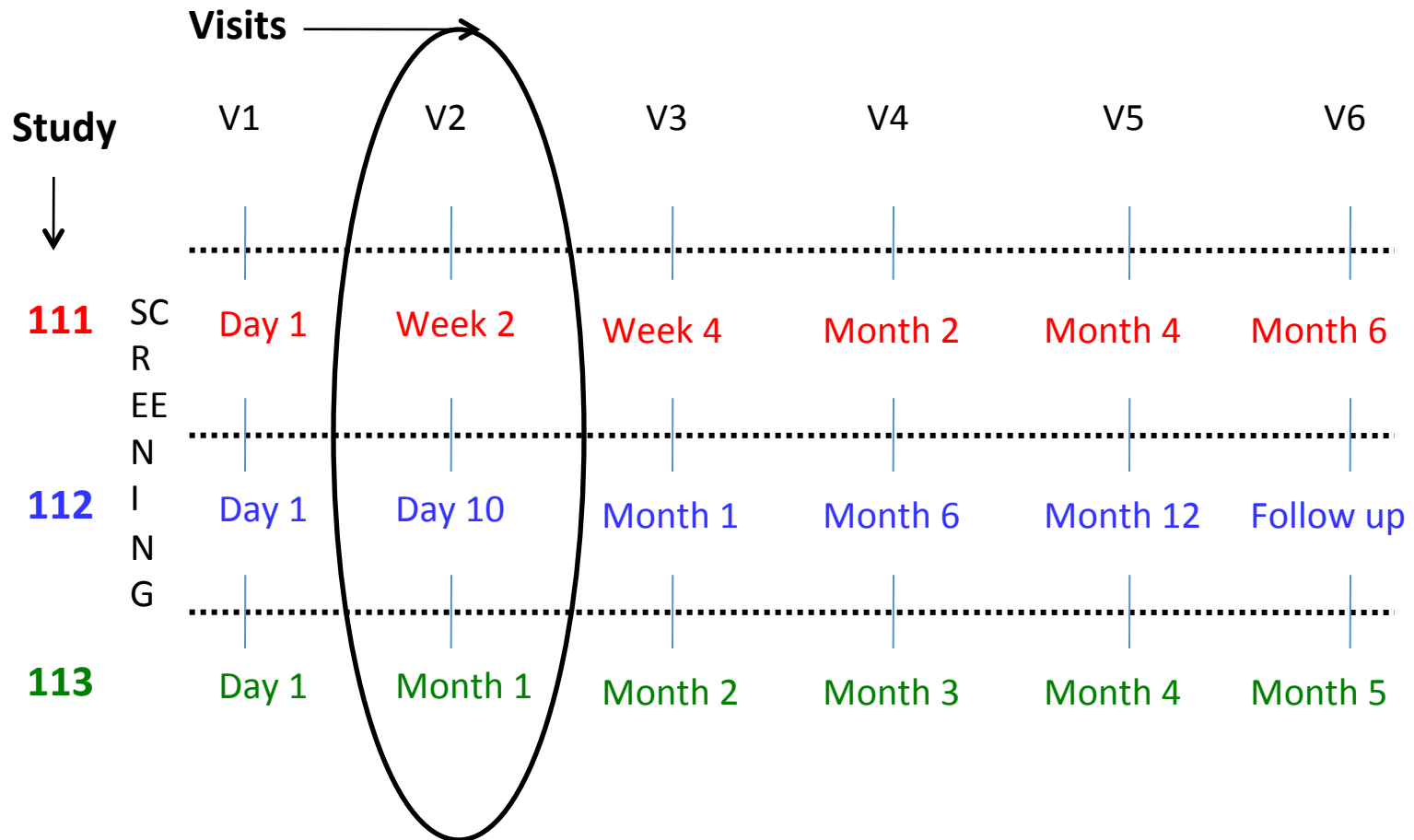


- Study Design:
Integrated Safety Summary (ISS) of 3 studies
- Dataset: ADLB
- OpenCDISC version: 1.3

ADaM for ISS



Laboratory schedule for 3 studies



ADaM for ISS

Back-ground

Problem

Reason

Lessons/
Solutions

SDTM to ADaM mapping

SDTM

Study	VISIT
111	Week 2
112	Day 10
113	Month 1

AVISITN
2

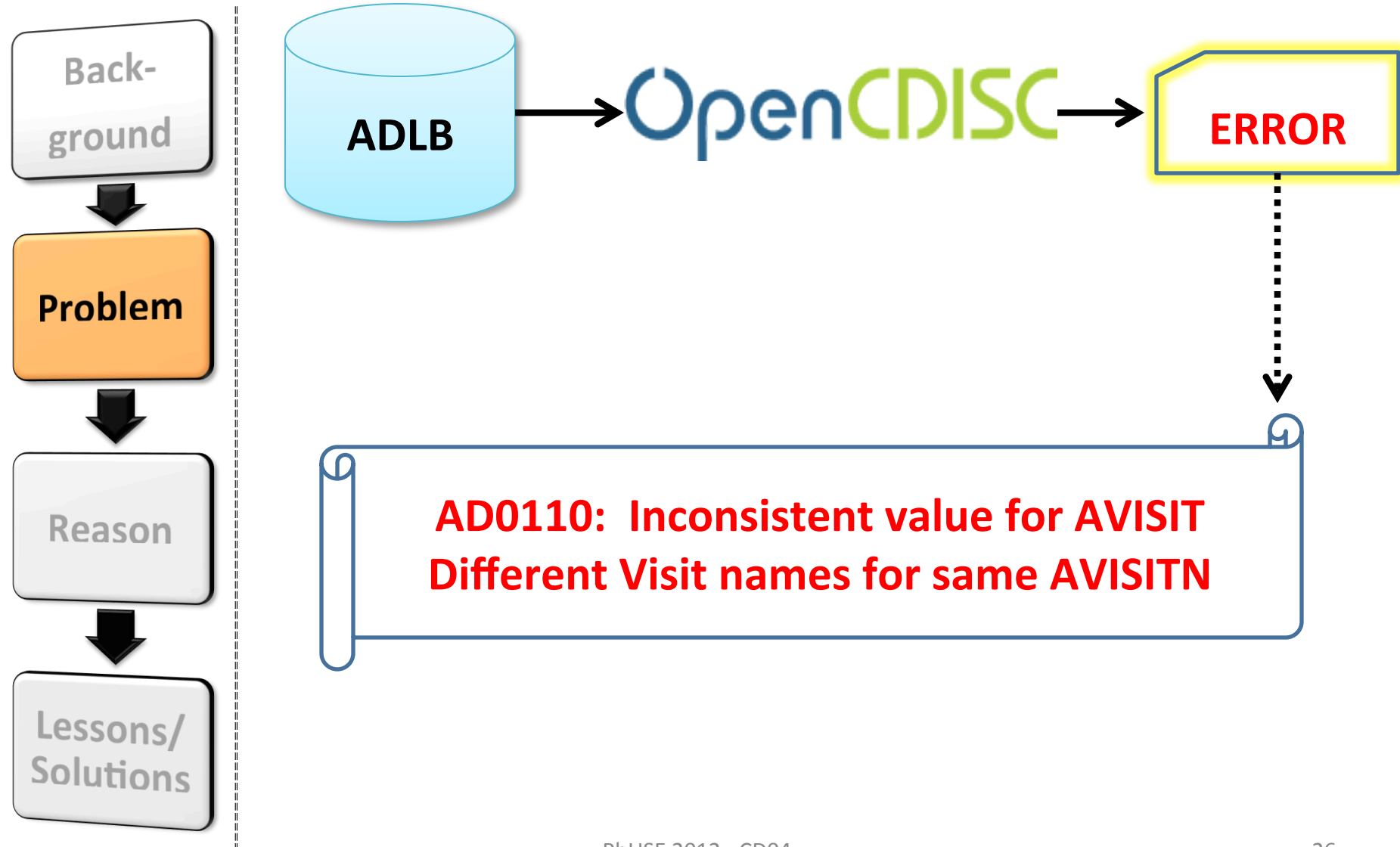
ADaM

AVISIT
Visit 2 (Week 2)
Visit 2 (Day 10)
Visit 2 (Month 1)

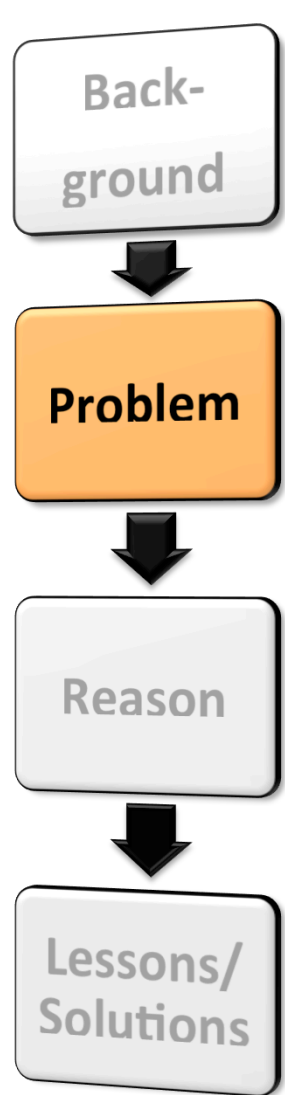
ADLB snapshot

STUDYID	PARAMCD	AVISIT	AVISITN
ABC111	ALT	VISIT 1 (DAY 1)	1
ABC111	ALT	VISIT 2 (WEEK 2)	2
ABC112	ALT	VISIT 1 (DAY 1)	1
ABC112	ALT	VISIT 2 (DAY 10)	2
ABC113	ALT	VISIT 1 (DAY 1)	1
ABC113	ALT	VISIT 1 (MONTH 1)	2

ADaM for ISS



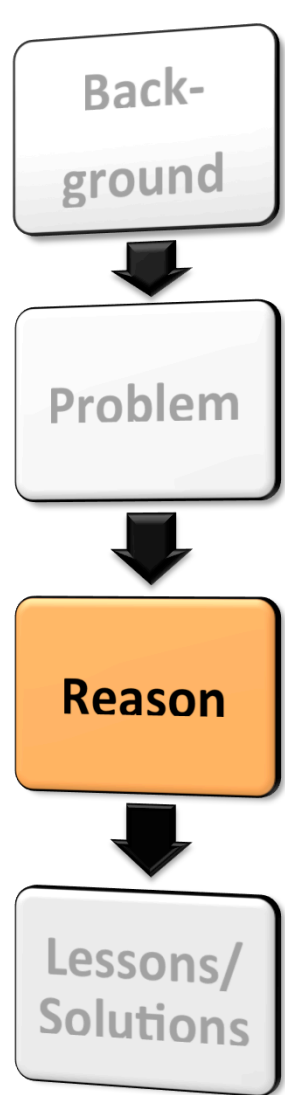
ADaM for ISS



ADaM consistency principle:

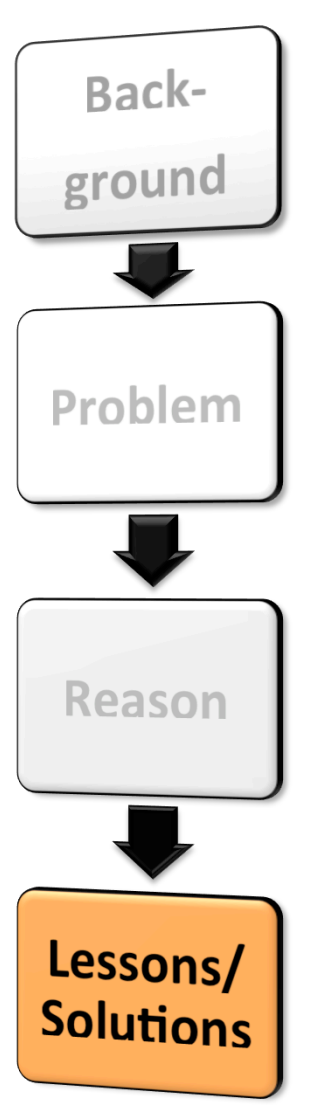
AVISIT and AVISITN should have consistent values
for a given PARAMCD

ADaM for ISS



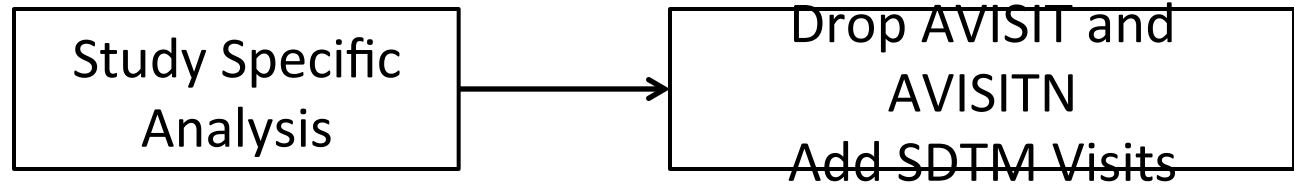
- Different visit schedule for 3 studies
- Analysis was study specific
- Analysis visits were not defined in ISS SAP

ADaM for ISS

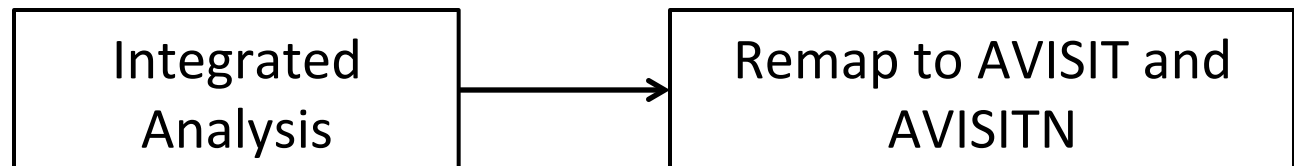


Need to have Consistency within visits

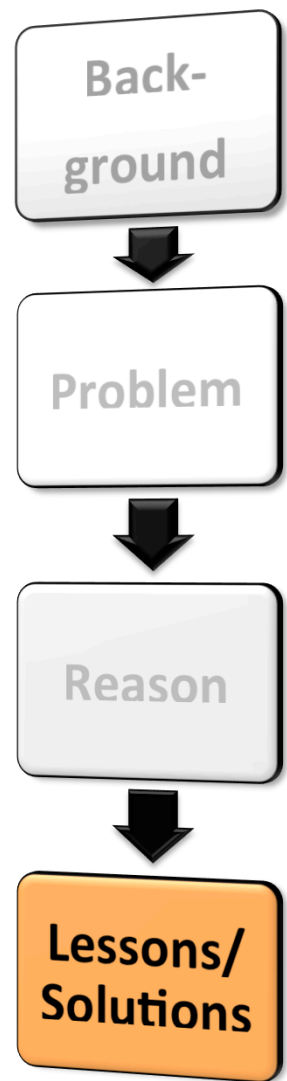
Solution 1:



Solution 2:



ADaM for ISS



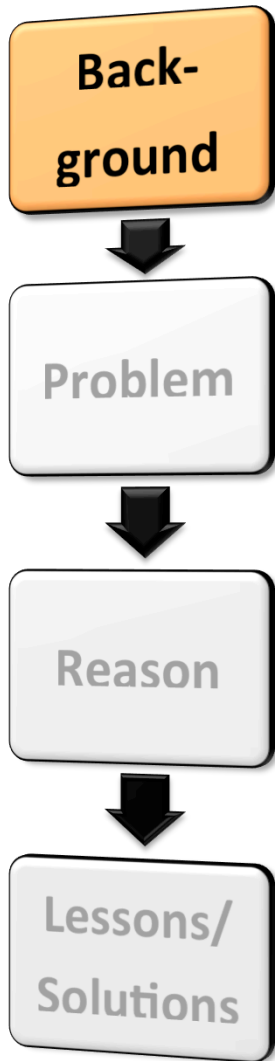
- ADaM IG does not strictly cover ISS/ ISE
- How much ADaM compliant datasets should be in such cases?



Case 3

AVAL vs. AVALC

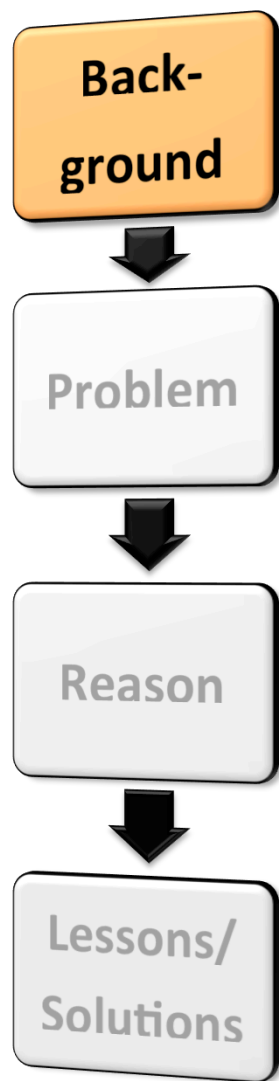
AVAL vs. AVALC



- Design: Placebo Controlled Study
- Phase: III
- Dataset: ADLB
- OpenCDISC version: v1.2.1

- AVAL: Analysis Value (Numeric)
- AVALC: Analysis Value (Character)
- AVAL and AVALC one to one relation

AVAL vs. AVALC



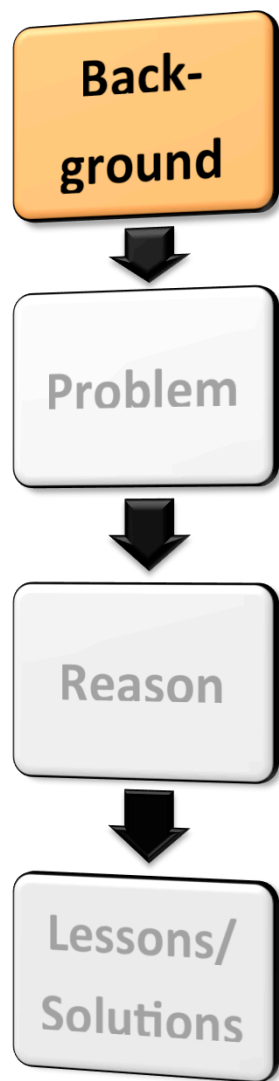
SDTM LB Dataset

USUBJID	LBTESTCD	VISIT	LBSTRESC	LBSTRESN
ABC01023	GGT	SCREENING	>4	.
ABC01023	GGT	VISIT 1	3	3
ABC01023	GGT	VISIT 3	>1	.

Snapshot of Statistical analysis Plan

For laboratory assessments if majority of results are indefinite, imputation of these values will be considered. Thus if the result has indefinite value, the upper limit, lower limit or median values need to be used in the summary. (for example, 0.1 can be used if the result is <0.1, >0.1, +0.1, or 0.1+)

AVAL vs. AVALC



SDTM LB Dataset

LBSTRESC
>4
3
>1

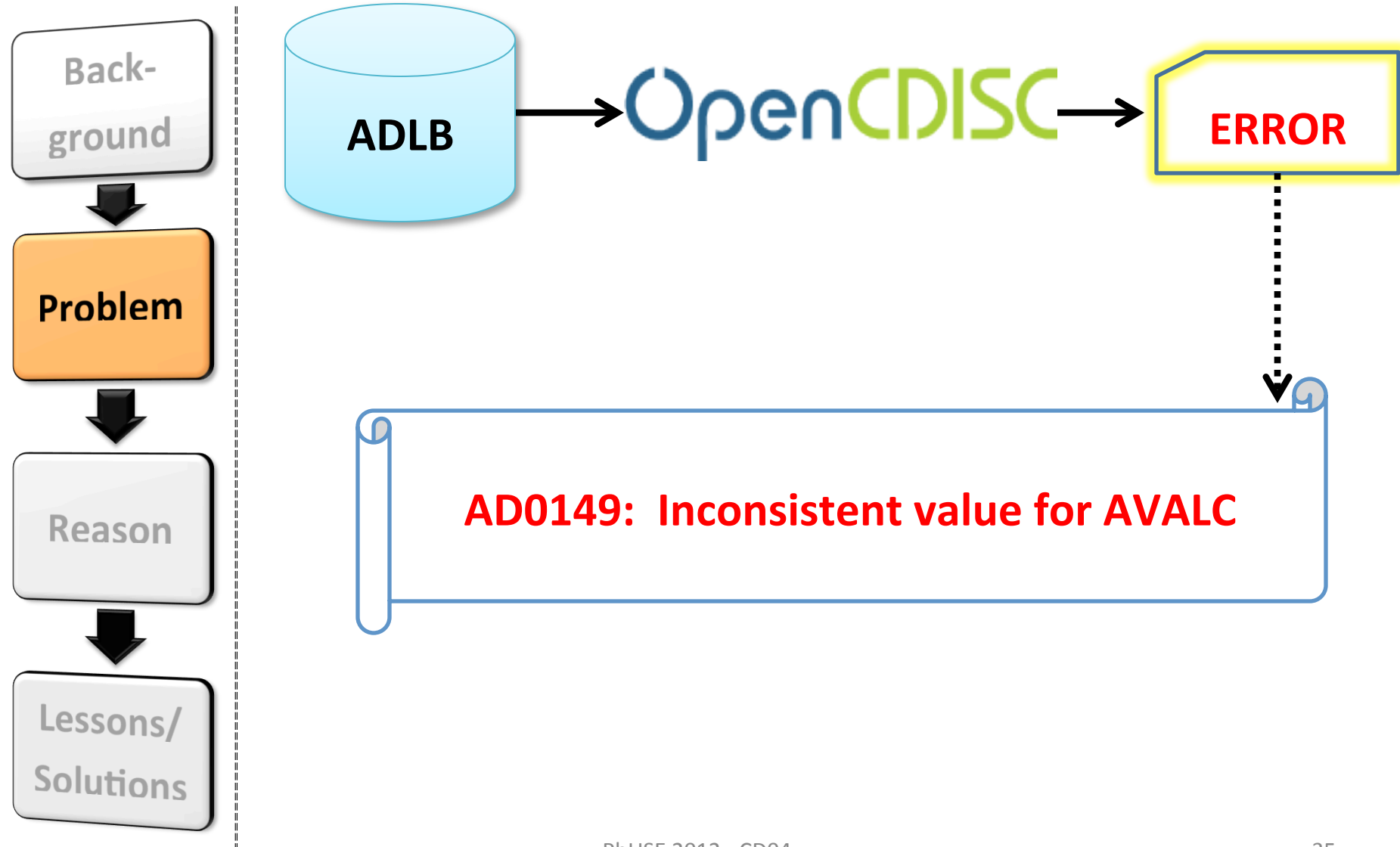
ADLB Dataset

AVAL	AVALC
4	>4
3	3
1	>1

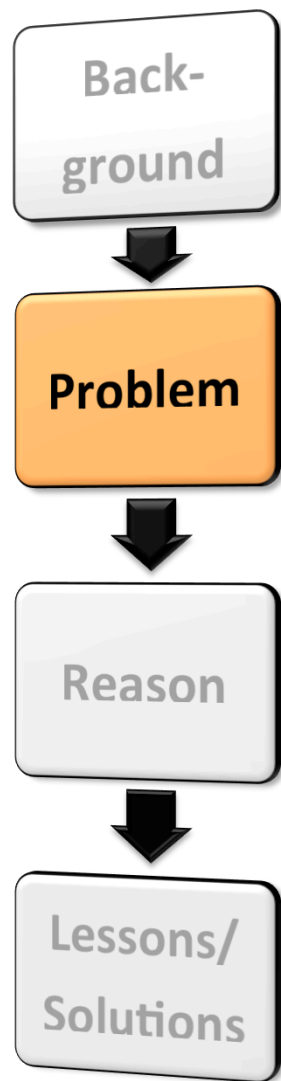
ADLB Dataset

USUBJID	PARAMCD	VISIT	AVALC	AVAL
ABC01023	GGT	SCREENING	>4	4
ABC01023	GGT	VISIT 1	3	3
ABC01023	GGT	VISIT 3	>1	1

AVAL vs. AVALC



AVAL vs. AVALC



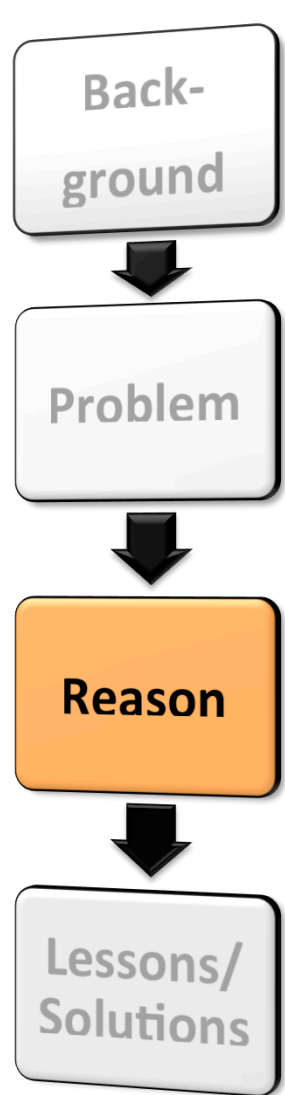
ADLB Dataset

USUBJID	PARAMCD	VISIT	AVALC	AVAL
ABC01023	GGT	SCREENING	>4	4
ABC01023	GGT	VISIT 1	3	3
ABC01023	GGT	VISIT 3	>1	1

Details of Error:

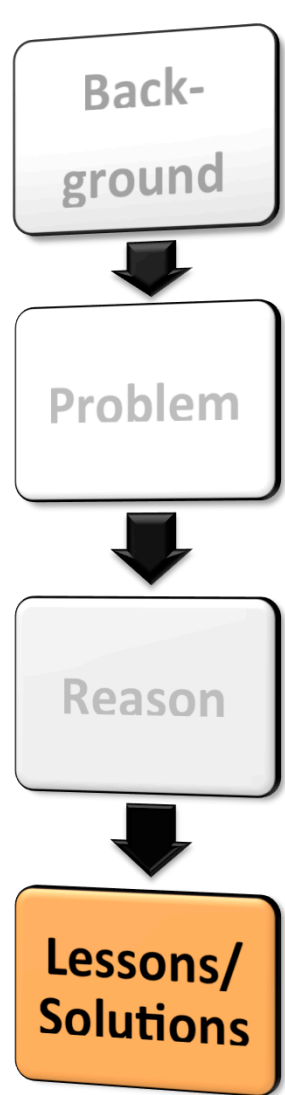
Record	Variables	Values	Rule ID	Message	Category
3019	AVALC, PARAMCD, AVAL	>4, GGT, 4	AD0149	Inconsistent value for AVALC	Consistency

AVAL vs. AVALC



- AVAL values derived as per SAP
- Integer portion of indefinite value is used
- Hence AVALC = AVAL not possible

AVAL vs. AVALC



Solution:

- Dropped AVALC
- Added LBSTRESC and LBSEQ

Lessons:

- Add LBSTRESC and LBSEQ for consistency
- Create different dataset with character and numeric results

Recap

Handling TRTP

Core Attributes of SDTM & ADaM are not 'interchangeable'

Null values allowed in ADaM "Required" variables

ADaM for ISS

AVISIT AND AVISITN have to be consistent with each other

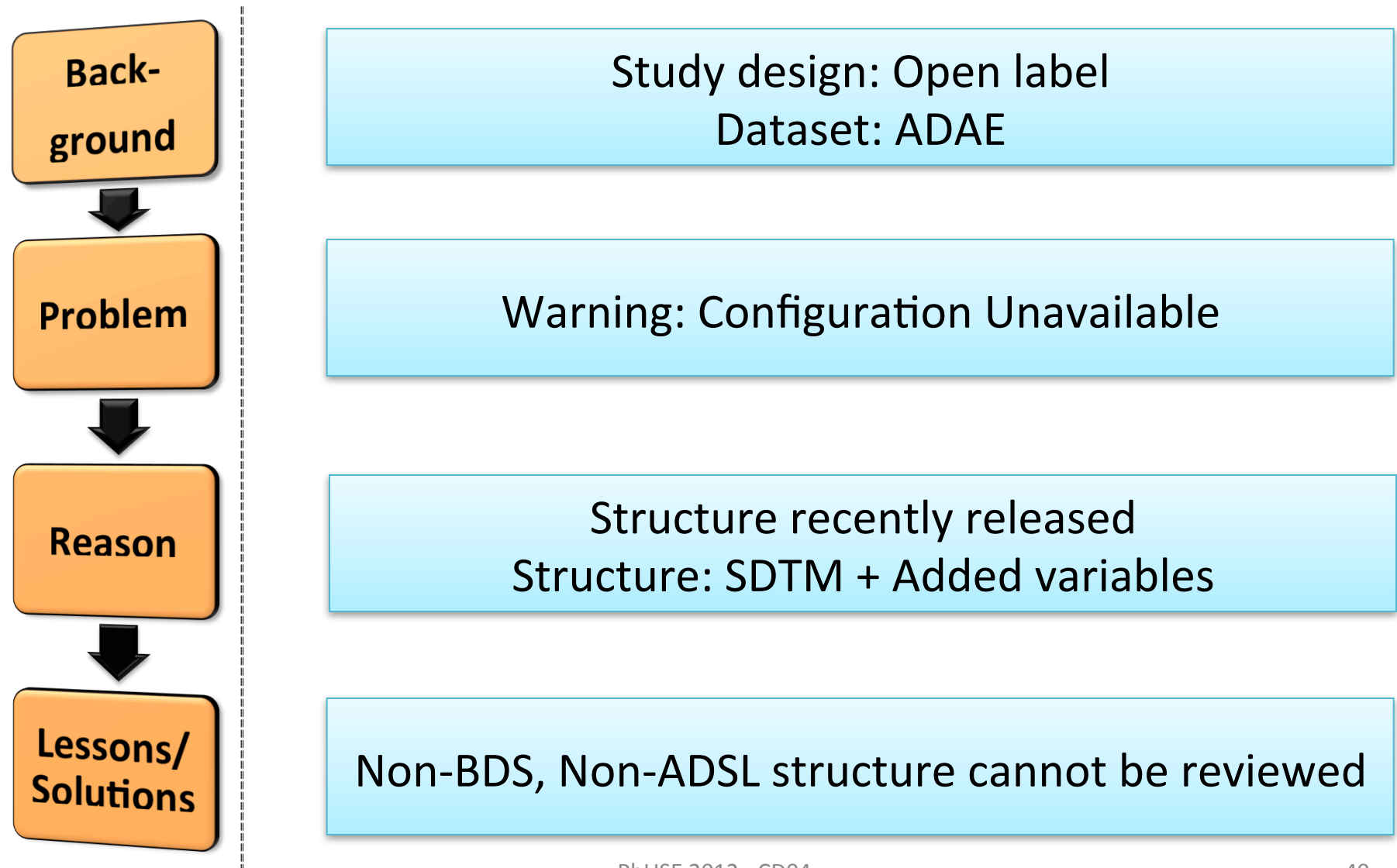
Need to determine how compliant ISS/ISE needs to be with ADaM

AVAL vs. AVALC

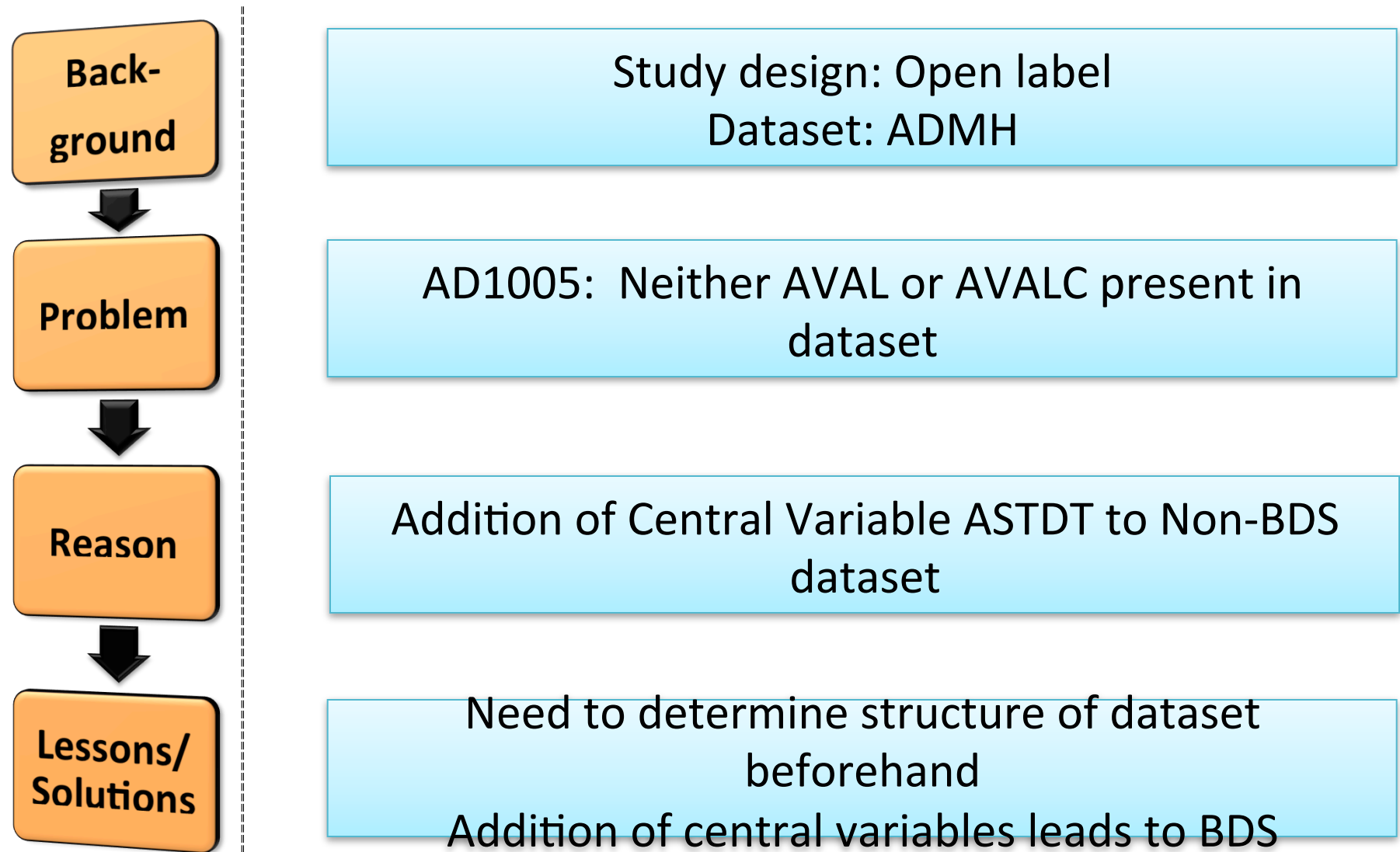
AVAL and AVALC need to have one to one relation

Addition of SDTM variables for consistency and traceability

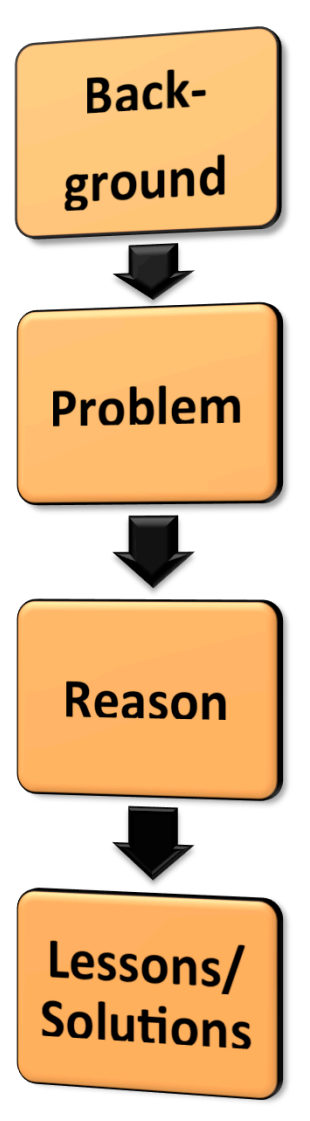
Additional Cases: 1



Additional Cases: 2



Additional Cases: 3



Study design: Any
Dataset: Any BDS where time is imputed

AD0040: Variable ending in *TMF not in TIMEF
codelist (described as D= Day, M= Month, Y= Year)

ASTMF flagged as 'Y'. Value should be either H=
Hours, M= Minutes, S= Seconds)

Correct Check, Incorrect Description!!!

Recap

- Non-BDS cannot be reviewed by OpenCDISC Validator yet
- Addition of Central Variables should be considered for BDS type datasets only
- Need to consult ADaM/Study specific guidelines before acting on a OpenCDISC Message



Conclusion

- ADaM
- Boon
- Bane
- Open
- Open
- Index

ysis needs

st/analysis

Walk the tightrope with OpenCDISC



Questions?

Thank you!

madhura.paranjape@cytel.com

trupti.bal@cytel.com