



Setting the
Global Standard
for Clinical Data

“Compliance” for Analysis Data

**CLINICAL DATA INTERCHANGE
STANDARDS CONSORTIUM**

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Overview

- Compliance within Clinical Research
- What is ADaM Compliance?
- ADaM Team Process for Defining Validation Document 1.0

Compliance? Validation?

- **com·pli·ance** *noun* \kəm-'plī-ən(t)s\
the act or process of complying to a desire, demand, proposal, or regimen or to coercion
- **val·i·da·tion** *noun* \,va-lə-'dā-shən\
the act of demonstrating that a procedure, process, and activity will consistently lead to the expected results

Different Definitions of Compliance

- **Software:** the process around the development of technical bits
- **Process:** process around the flow of information; much more imprecise
- **Data:** Both the structure and the content of the data

CDISC Compliance

Some compliance is easy and some is not

ODM - specification

```
<xs:simpleType name="TransactionType">
  <xs:restriction base="xs:string">
    <xs:enumeration value="Insert"/>
    <xs:enumeration value="Update"/>
    <xs:enumeration value="Remove"/>
    <xs:enumeration value="Upsert"/>
    <xs:enumeration value="Context"/>
    <xs:maxLength value="7"/>
  </xs:restriction>
</xs:simpleType>
```

```
<ClinicalData StudyOID="ABCDEF" MetaDataVersionOID="StudyVersion1.0">
  <SubjectData SubjectKey="39809" TransactionType="Upsert">
    <StudyEventData StudyEventOID="SCREENING" TransactionType="NOTAREALTYPE">
```

SDTM – standard

- Interpreting a doc
- Subjective
- Inconsistent rules get defined

What is ADaM Compliance?

- Perfect Structure + Bad Metadata = Bad ADaM
- Good Metadata + Bad Structure = Bad ADaM
- Good ADaM must include:

Perfect structure:

- Naming Conventions
- Labels/Types
- Terminology

Good metadata:

- Clear definition of algorithms
- Traceability to SDTM

But, not every ADaM submission should or will be identical

What is ADaM Compliance?

- Subjective
 - “Analysis datasets and their associated metadata should facilitate clear and unambiguous communication.”
 - What is clear to everyone?
- Objective
 - “ADSL contains one record per subject, regardless of the type of clinical trial design.”
 - Very black and white statement

Defining the Rules: The Process

- Why the ADaM team?
 - One gold standard
 - Reduce confusion
- When to define the rules?
 - During the IG review? Nope
 - Waited for a finalized document
- Sub-team with a short term goal

Extraction

- Pulling the rules out of a PDF file
 - Each team member tackled a section
 - Anything remotely resembling a rule was listed
- Initially had over 350 rules...ouch
- Collated in a spreadsheet for tracking
- Quickly realized we had some challenges

To Test or Not To Test?

- That is the question...
- Some rules could be clearly tested
 - *All ADaM variable labels must be no more than 40 characters in length*
- And some could be not be implemented with a machine (subjective)
 - *Analysis datasets and their associated metadata should facilitate clear and unambiguous communication*
- Some rules sounded logical but didn't exist

Rule Clarity

- Make sure that ADaM rules are clear & unambiguous
- Requirements:
 - Text based (no pseudo code)
 - Simple and clear

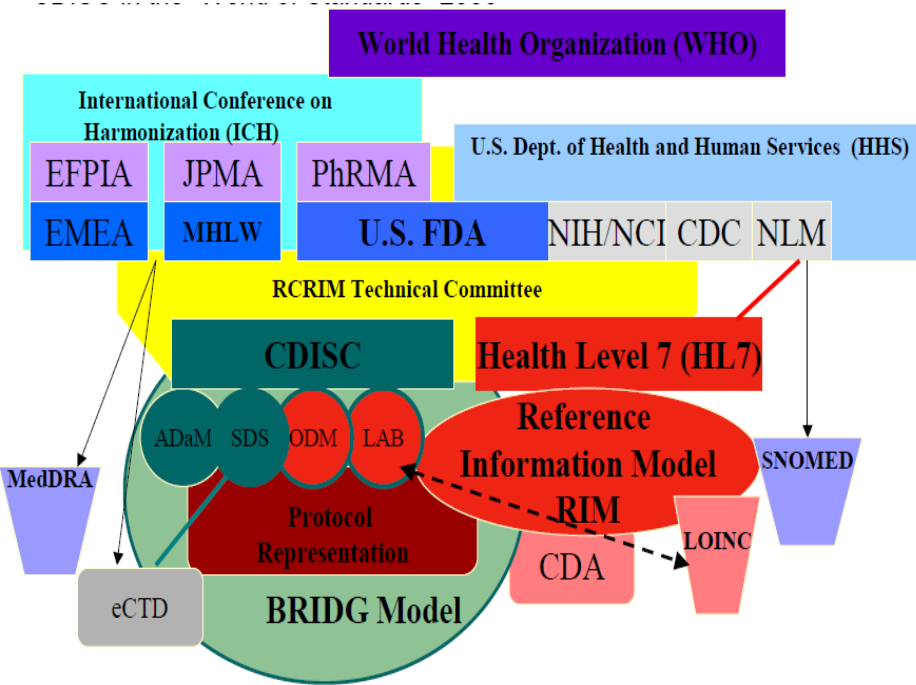
- Example:

Instead of: **FN and *FL must be a one-to-one mapping*

The team defined the following:

- There is more than one value of a variable with a suffix of FN for a given value of a variable with the same root name and a suffix of FL
 - There is more than one value of a variable with a suffix of FL for a given value of a variable with the same root name and a suffix of FN
 - A variable with a suffix of FL is equal to Y and a variable with the same root and a suffix of FN is not equal to 1
 - And a few more...
- Note: All checks were written in the ‘negative’

ADaM in a Box



- ADaM just a piece of the standards
- How to define cross model rules

Examples:

- SDTM: Clear and easy
 - identical metadata across variables with the same name
- Define: Did not include
 - An ADaM variable described in define.xml must be included in the dataset

Metadata about the Rules

- Always need metadata
- Team decided to describe the rules
- Structure Group: ADSL, BDS, ADSL to BDS
- Functional Group:
 - Metadata only
 - Value consistency
 - Presence/Population of variable
- ADaM Variable Group: Based on IG sections
 - Study Identifiers and Timing Variables
- Note: NO Severity ranking – they are all errors

Example of the Validation Rules

	A	B	C	D	E	F	G
	Check Num	ADaM IG 1.0 Section Num	Text from ADaM IG	ADaM Structure Group	Functional Group	ADaM Variable Group	Machine-Testable Failure Criteria
2	1	S2.3.1	There is only one ADSL per study	ADSL	Present/Populated	General	ADSL dataset does not exist
3	2	S3	Any ADaM variable whose name is the same as an SDTM variable must be a copy of the SDTM variable, and its label and values must not be modified	ALL:SDTM	Metadata	Data Point Traceability Variables	A variable is present in ADaM with the same name as a variable present in SDTM but the variables do not have identical labels
4	3	S3	Any ADaM variable whose name is the same as an SDTM variable must be a copy of the SDTM variable, and its label and values must not be modified	ALL:SDTM	Metadata	Data Point Traceability Variables	A variable is present in ADaM with the same name as a variable present in SDTM but the variables do not have identical formats
5	4	S3	Any ADaM variable whose name is the same as an SDTM variable must be a copy of the SDTM variable, and its label and values must not be modified	ALL:SDTM	Metadata	Data Point Traceability Variables	A variable is present in ADaM with the same name as a variable present in SDTM but the variables do not have identical lengths
6	5	S3	The names of all other character flag (or indicator) variables end in FL	ALL	Controlled Terminology	Flag Variables	A variable with a suffix of FL has a value that is not Y, N or null
7	6	S3	The names of the corresponding numeric flag (or indicator) variables end in FN	ALL	Controlled Terminology	Flag Variables	A variable with a suffix of FN has a value that is not 0, 1 or null
8	7	S3	If the numeric flag is used, the character version (*FL) is required	ALL	Present/Populated	Flag Variables	A variable with a suffix of FN is present but a variable with the same root and a suffix of FL is not present
9	8	S3	*FN and *FL must be a one-to-one mapping	ALL	Value Consistency	Flag Variables	There is more than one value of a variable with a suffix of FN for a given value of a variable with the same root name and a suffix of FL
10	9	S3	*FN and *FL must be a one-to-one mapping	ALL	Value Consistency	Flag Variables	There is more than one value of a variable with a suffix of FL for a given value of a variable with the same root name and a suffix of FN
11	10	S3	*FN and *FL must be a one-to-one mapping	ALL	Value Consistency	Flag Variables	A variable with a suffix of FL is equal to Y and a variable with the same root and a suffix of FN is not equal to 1
12	11	S3	*FN and *FL must be a one-to-one mapping	ALL	Value Consistency	Flag Variables	A variable with a suffix of FL is equal to N and a variable with the same root and a suffix of FN is not equal to 0

Summary

- ADaM Validation document timeline
 - Initiated February, 2010
 - Draft for public comment, July, 2010
 - Final version released September, 2010
- Extracting checks from a document is challenging
- Able to define 180 checks for ADaM
- Compliance is both the objective and subjective parts

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Strength *through* collaboration.