ADaM Conformance Rules: Bridging the Gap Between Standards and Practice

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AGENDA

Today's agenda is

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01

Introduction to ADaM Conformance Rules

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Let’s have a look

- **ADaM**: Ensures datasets are clear, traceable, and analysis-ready
- **Conformance Rules:**
  - Based on directive statements in the Implementation Guide (IG)
  - Identify potential issues and promote consistency
  - Exclude business rules outside IG or cross-study checks
- **Key Point:** Passing rules ≠ full compliance
- **True Compliance requires:**
  - Traceability
  - Clarity
  - Metadata integrity
  - Analysis readiness

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Question for Audience

Question: ADaM Conformance Rules takes priority over FDA business rules?

Answer

❌ **False** — No, ADaM Conformance Rules do not take priority over FDA business rules; both must be followed, and in case of a discrepancy, FDA business rules and other regulatory guidelines supersede ADaM conformance rules.

02

Conformance Rules Overview

As of Version 5.0, the catalog includes 1,000 rules

Key Component	Details
1. Rule Identification	**Rule ID** – Each rule is assigned a unique identifier for easy reference. **Version Information** – Rules are linked to specific versions of the ADaM Implementation Guide (e.g., ADaMIG v1.3).
2. Rule Classification	**Class** – General category of the rule (e.g., dataset structure, variable naming). **Domain** – The ADaM domain to which the rule applies (e.g., ADSL, BDS). **Variable** – The specific variable affected by the rule.
3. Rule Description	**Guidance** – Clear explanation of the rule's intent and application. **Compliance Criteria** – Conditions under which the dataset complies with the rule.
4. Implementation Notes	Additional context or examples to aid in understanding and applying the rule.

Importance

- **CONSISTENCY**
  Uniformity across studies
- **EFFICIENCY**
  Early detection of potential issues
- **TRANSPARENCY**
  Improve clarity and reproducibility

Gaps and Limitations:

- **Limited to machine-readable checks**
  Clear in naming, traceable to SDTM, analysis ready
- **Conflicts with other guidance**
  TAUG recommendations
- **No guarantee of alignment with the SAP**
  Meet study-specific analysis

The following are **out of scope** for Conformance Rules:

- Any rules **not supported by a definitive statement** in the IG
- **Business Rules**
- **Data validation logic** not specifically linked to the implementation guidance
- **Rules that check across studies** within a submission

03

Special Topics: PARQUAL, ADPL, NADIR

ADaM IG states:

PARAM must include all descriptive and qualifying information relevant to the analysis purpose.

PARAM	PARAMCD
Time to CV death (days), Adjudicated	TTCVDADJ
Time to CV death (days), Investigator	TTCVDINV

PARQUAL appeared in the draft ADaMIG v1.2 but was removed before finalization

PARCAT1	PARCAT2	PARQUAL	PARAM
Efficacy parameters	Primary endpoint and components	Adjudicated	Time to MACE (days)
Efficacy parameters	Primary endpoint and components	Adjudicated	Time to CV death (days)
Efficacy parameters	Primary endpoint and components	Adjudicated	Time to MI (days)
Efficacy parameters	Primary endpoint and components	Adjudicated	Time to stroke (days)
Efficacy parameters	Primary endpoint and components	Investigator	Time to MACE (days)
Efficacy parameters	Primary endpoint and components	Investigator	Time to CV death (days)

Due to confusion discovered during public review on when to use PARQUAL, the ADaM team has determined that PARQUAL needs more clarification and may be considered for a future release

The Breast Cancer TAUG offers a concrete example of how PARQUAL can be defined and applied:

	Variable Name	Variable Label	Type	Codelist/Controlled Terms	Notes
	USUBJID	Unique Subject Identifier	Char		ADSL.USUBJID
Proposed	*PARQUAL*	*Parameter Qualifier*	*Char*	*INVESTIGATOR; CENTRAL; PATHOLOGIC; PROTOCOL z*	*This identifies the source of the Parameter. Investigator for investigator based assessments; Central for central imaging assessments; Pathologic for an assessment by biopsy; and Protocol for events affecting assessment.*

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Proposed

Row	STUDYID	USUBJID	*PARQUAL*	PARAMCD	AVAL	AVALC	SRCSEQ
1	ABC-123	ABC-123-001	INVESTIGATOR	BOR	2	PR	7
2	ABC-123	ABC-123-001	CENTRAL	BOR	2	PR	8
3	ABC-123	ABC-123-002	INVESTIGATOR	BOR	3	SD	5
4	ABC-123	ABC-123-002	CENTRAL	BOR	3	SD	6

In such cases, the ADRG provides a mechanism to document and justify deviations.

Current Thoughts

ADaM v3.0 is expected to introduce PARQUAL in combination with a PARQTYPE

PARQUAL	PARQTYPE
Parameter Qualifier	Parameter Qualifier Type
Qualifying Text	Is one of the allowed types of qualifications
Not subject to CDISC CT	Uses CDISC Non-Extensible CT
Must be used with variable PARQTYPE	Must be one of the CDISC CTs

Addressing Multiple Participations with ADPL

Subjects participate multiple times - **Screen failures, re-enrollments, integrated study designs**

ADSL structure enforces one record per USUBJID

Proposed Solution:

The ADaM team has proposed a new dataset: **ADPL (Participation-Level Analysis Dataset).**

Key features include:

Feature	ADSL	ADPL
Record granularity	One record per subject (USUBJID)	One record per participation (SUBJID)
Purpose	Overall subject-level data	Participation-specific details (e.g., treatment arm, baseline characteristics)
Compatibility	Backward compatible with existing tools	Supplements ADSL; flexible for multi-participation studies
Use case	Standard analyses	Subjects with multiple enrollments, integrated studies, or re-screenings

Implement ADPL as an ADaM Other dataset, which:

- Supplements ADSL without violating current ADaM rules.
- Allows detailed participation-level reporting.
- Provides documentation via the ADRG to justify its use.
- Prepares organizations for potential official adoption of ADPL in ADaM v3.0.

➢ This separation allows sponsors to retain the ADSL dataset for tools expecting one-record-per-USUBJID, while ADPL captures participation-level information for more granular analyses.

Lowest observed value of a parameter

Derived measures: **Change from Nadir, Percent Change from Nadir**

ADaMIG v1.2 states: **4.2.1.1 Rule 1**

“A parameter-invariant function of AVAL and BASE on the same row that does not involve a transform of BASE should be added as a new column.”

- ➢ Nadir is not a function of AVAL and BASE

Solutions: **Compliant** BDS solution and **Non-compliant** BDS solution

Compliant BDS solution

Create additional records with BASETYPE = "Nadir"

PARAMCD	AVIISIT	AVAL	ABLFL	BASE	CHG	BASETYPE
XYZ	Day 1	12	Y	12	0	PRE-DOSE
XYZ	Week 1	14		12	2	PRE-DOSE
XYZ	Week 2	11		12	-1	PRE-DOSE
XYZ	Week 3	13		12	1	PRE-DOSE
XYZ	Day 1	15		11	4	NADIR
XYZ	Week 1	11	Y	11	0	NADIR
XYZ	Week 2	14		11	3	NADIR
XYZ	Week 3	13		11	2	NADIR

Fully compliant with BDS rules

Extra records per subject/parameter/basetype

Non-Compliant BDS solution

Nadir Variables in Columns

PARAMCD	AVIISIT	AVAL	ABLFL	BASE	CHG	NADIRFL	NADIR	NADRCHG
XYZ	Day 1	12	Y	12	0		11	1
XYZ	Week 1	14		12	2		11	3
XYZ	Week 2	11		12	-1	Y	11	0
XYZ	Week 3	13		11	2		11	2

Key variables are visible in one record

Not compliant with current BDS rules

Advantages and Limitations

Aspect	Compliant BDS Solution	Non-Compliant BDS Solution
Method	Create additional records with BASETYPE = "Nadir"	Add variables for *Nadir*, *Change from Nadir*, *Percent Change from Nadir*
Conformance	Fully compliant with BDS rules	Not compliant with current BDS rules
Dataset Size	Roughly doubled (extra records per subject/parameter/basetype)	Unchanged
Review Clarity	More complex; duplicated records can be confusing	More intuitive; key variables are visible in one record
Usability	Consistent with standards, but less practical	Easier for reviewers and statisticians
Documentation Needs	Standard ADRG notes on derivations	ADRG justification for deviation from rules

Future Direction

Formally address NADIR in ADaM v3.0

04

Principles vs. Rules

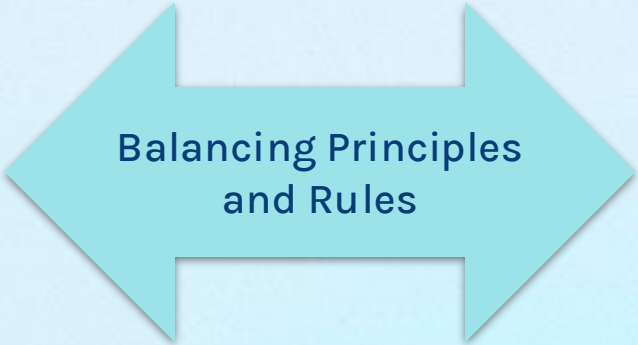
A key distinction within ADaM lies between its **fundamental principles** and its **rules.**

Aspect	Fundamental Principles (Non-Negotiable)	Rules (Important but Flexible)
Purpose	Ensure ADaM datasets are meaningful, interpretable, analysis-ready	Provides structure, consistency, and standardization
Core Requirements	• Clear and unambiguous communication • Traceability to SDTM/source • Usable by standard tools • Truly analysis-ready datasets • Metadata supports interpretation	• Dataset organization and structure • Variable naming standards • Controlled/allowable content • Conformance validation checks
Flexibility	No-flexibility	Some flexibility - deviations allowed if justified
Regulatory Acceptance	Violations -> Dataset cannot be considered ADaM	Acceptable if principles still fully met and justification is documented (e.g., ADRG)
Examples	Consistent with standards but less practical	Easier for reviewers and statisticians

Principles vs. Rules: A Hierarchy

Principles outweigh rules:

A dataset that violates principles (e.g., unclear, untraceable, or not analysis-ready) cannot be considered ADaM, regardless of conformance checks.



Rules are Flexible (not absolute).

A dataset that deviates from certain rules may still be considered valid ADaM if it continues to meet the fundamental principles.

Key Idea: Principles = Mandatory foundation
Rules = Guidelines supporting principles

Validity depends on adherence to principles, not strict rule compliance

05

Recommendations for Industry Practice

By following this approach, ADaM datasets will not only align with technical compliance requirements but also remain clear, traceable, and practically valuable for both regulators and statisticians

- Interpret findings thoughtfully
- Prioritize principles over rules
- Document deviations transparently
- Leverage conformance tools proactively
- Apply pragmatic solutions
- Anticipate upcoming standards

ADaM Conformance Rules are vital for ensuring automation, consistency, and transparency in standardized datasets. Yet true compliance is defined not by rules alone, but by ADaM's core principles: clarity, traceability, metadata, and analysis-readiness.

Rules provide structure, but principles set the standard. A balanced approach - combining automation with expert judgment and regulatory pragmatism - ensures datasets are both technically compliant and practically valuable. By focusing on principles while adapting to evolving guidance, organizations can deliver ADaM datasets that enable reliable, efficient, and meaningful regulatory decision-making.

Thank you

Do you have any questions?

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