Paper DS04

ADaM Conformance Rules: Bridging the Gap Between Standards and Practice

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ABSTRACT

The ADaM Conformance Rules provide a standardized framework for assessing the compliance of ADaM datasets with CDISC standards, helping to ensure quality, consistency, and transparency. Yet, passing conformance checks does not necessarily confirm full compliance, as true adherence depends on fundamental principles of traceability, clarity, metadata, and analysis readiness. This paper examines the purpose, structure, and limitations of ADaM Conformance Rules, drawing on regulatory context and practical experience. It highlights common challenges - such as misalignment with study-specific requirements or specific analysis needs - and identifies gaps between rule-based validation and broader CDISC standards. Finally, it emphasizes best practices for incorporating conformance checks into programming workflows and underscores the need to look beyond rule compliance to ensure datasets are reliable for all their intended uses.

INTRODUCTION

The Analysis Data Model (ADaM) is an important component of CDISC standards, designed to ensure that analysis datasets are clear, traceable, and analysis-ready. To help organizations achieve this, CDISC introduced ADaM Conformance Rules - checks, some of which can be run using validation tools, that are intended to identify potential issues in ADaM datasets and promote alignment with published standards. These Conformance Rules are specifically linked to declarative or directive statements within the Implementation Guide (IG) text. They are defined independently of their perceived programmability and are not derived from examples. Rules that fall outside this scope include those not supported by definitive IG statements, business rules, data validation logic not explicitly tied to implementation guidance, and rules that perform checks across multiple studies within a submission. By focusing on IG-based rules, Conformance Rules provide a structured approach to validating ADaM datasets while clarifying their limitations and intended scope. However, confusion persists in the industry: Does passing all conformance checks mean that a dataset is truly ADaM-compliant? How should programmers respond when regulatory requirements or Therapeutic Area User Guides (TAUGs) conflict with these rules? Addressing these questions requires understanding that conformance rules are a guide, not a guarantee, and that true compliance depends on adherence to the fundamental principles of traceability, clarity, metadata, and analysis-readiness.

ADaM Conformance Rules Overview

The ADaM Conformance Rules are organized into a comprehensive catalog designed to assess the compliance of ADaM datasets with the standards set forth in the ADaM Implementation Guide (ADaMIG). As of Version 5.0, the catalog includes over 1,000 rules, each identified by a unique ID and categorized to facilitate validation and tool development.

Key Components:

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:

ADaM Conformance Rules are important for several reasons:

- **Consistency:** They help maintain uniformity across studies by enforcing standardized dataset structures, variable naming conventions, and proper use of domain-specific elements.

- **Efficiency:** They support early detection of potential issues, enabling programmers to address inconsistencies before datasets reach reviewers.
- **Transparency:** They improve clarity and reproducibility, making it easier for reviewers to understand and trust the datasets.

In practice, these rules act as a shared framework among sponsors, CROs, and regulators. For example, rules that enforce unique and unambiguous values help prevent misinterpretation during analysis or review. Rules that ensure consistent handling of numeric and character variables support analysis readiness. Similarly, rules guiding the correct definition of analysis populations and derived variables help reduce errors and promote reproducible results across studies.

Usage in Practice

In day-to-day programming, ADaM Conformance Rules serve as checkpoints during dataset development and validation, helping to ensure alignment with CDISC standards. Validation tools incorporate these rules - often alongside regulatory business rules from agencies such as the FDA and PMDA - to generate detailed reports of potential findings. These outputs guide programmers and statisticians in determining whether issues require correction, further investigation, or formal justification.

An equally important element of the process is documentation. The Analysis Data Reviewer's Guide (ADRG) provides a structured venue for recording any rule violations, explaining the rationale behind deviations, and clarifying study-specific decisions. This not only facilitates regulatory review but also enhances transparency and reproducibility across stakeholders. In practice, the effective use of Conformance Rules, supported by clear documentation, helps organizations balance strict adherence to standards with the flexibility needed to address study-specific requirements.

Gaps and Limitations

Despite their value in promoting standardization and data quality, ADaM Conformance Rules have several important limitations.

1. **Limited to machine-readable checks**

   Conformance rules can only evaluate what is explicitly machine-readable. They cannot verify whether datasets are:

   - Clear and unambiguous in meaning (e.g., distinguishing between baseline and on-treatment values when the metadata is vague).
   - Fully traceable to SDTM or source data (e.g., ensuring that a derived variable such as "Time to Progression" can be accurately linked back to SDTM event dates).
   - Truly analysis-ready without further complex processing (e.g., datasets may require additional programming before being usable in statistical models).

2. **Conflicts with other guidance**

   Rules cannot always resolve inconsistencies between different industry documents or regulatory expectations. For example:

   - A Therapeutic Area User Guide (TAUG) may recommend a dataset structure that technically violates certain ADaM conformance rules.
   - Regulators might request the inclusion of custom variables or structures that do not conform to the standard, forcing sponsors to choose between strict adherence and regulatory compliance.

3. **No guarantee of alignment with the Statistical Analysis Plan (SAP)**

   Passing all conformance checks does not ensure that datasets meet study-specific analysis requirements. For example:

   - A dataset may pass every ADaM validation rule but still lack key derived variables specified in the SAP, such as "Duration of Response" or "NADIR value."
   - Similarly, variables may be technically valid but not coded in a way that supports the planned statistical analyses.

These limitations underscore an important distinction: **conformance is not the same as compliance.** While rules are essential for consistency, expert judgment and context-specific validation remain critical to ensuring datasets are truly fit for regulatory submission and statistical analysis.

Special Topics

PARQUAL

Parameter Qualifier

The role of **PARQUAL** has long been debated in the ADaM community. While ADaMIG states that *"PARAM must include all descriptive and qualifying information relevant to the analysis purpose,"* certain scenarios suggest value in a separate qualifier variable - for example differentiating **Investigator vs. Independent Assessor** evaluations, or distinguishing **study drug vs. comparator** in pharmacokinetic analyses.

PARQUAL appeared in the **draft ADaMIG v1.2** but was removed before finalization. Its current use is technically **non-compliant with BDS rules**, yet some TAUGs (e.g., **Oncology**) have included it in examples. In such cases, the **ADRG** provides a mechanism to document and justify deviations.

The **Breast Cancer TAUG** offers a concrete example of how PARQUAL can be defined and applied (see screenshots below).

	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.*

adresp.xpt **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

Expectation for the Future:

Looking ahead, ADaM v3.0 is expected to introduce PARQUAL in combination with a PARQTYPE variable, which would allow specific controlled use cases while limiting misuse through conformance checks.

Current Thoughts

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

Until then, sponsors face a range of options, from embedding all qualifiers in PARAM, to selectively using PARQUAL with clear ADRG documentation, to waiting for official standardization.

ADPL

Addressing Multiple Participations with ADPL

A recurring challenge in clinical trials occurs when subjects participate **multiple times** - for example, due to **screen failures**, **re-enrollments**, or **integrated study designs**. The current **ADSL** structure enforces **one record per USUBJID**, which can create conflicts or limitations for analyses involving multiple participations. Some reviewers insist on maintaining the single-record-per-subject approach, but this can restrict flexibility in reporting and analysis.

Proposed Solution: ADPL

To address this, 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

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.

Current Practical Implementation

Sponsors can already 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**.

NADIR

Nadir refers to the **lowest observed value of a parameter** and is widely used in oncology analyses. Derived measures such as *Change from Nadir* and *Percent Change from Nadir* are frequently required but present challenges under the current BDS framework.

However, there is no perfect way to present these within ADaM. According to Section 4.2.1.1 of the ADaM Implementation Guide, Rule 1 states:

"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."

But, NADIIR is not mathematically derived from BASE and AVAL on the same row. Therefore, there are two possible approaches to present NADIR within ADaM.

The first option is Compliant BDS solution, where additional records are created with BASETYPE = "Nadir". Each parameter then has its own set of records for baseline, post- baseline, and 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

And this fully aligns with BDS principles, supports automated checks and traceability, minimizes risk of data rejection.

The Second option is a Non-Compliant BDS solution. Instead of creating additional records, one record per parameter is retained with new variables added for Nadir, Change from Nadir, and Percent Change from Nadir.

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

While this aprroach may fail formal conformance checks due to inclusion of non-BDS variables; it offers a more compact and intuitive structure – all results for a perimeter are visible in one place.**Advantages and Limitations**

Both approaches have their advantages and limitation, summarized in the table below.

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

The ADaM team has recognized these challenges and plans to **formally address Nadir in ADaM v3.0**, potentially by introducing standard variables for this use case.

Until then, sponsors must weigh the trade-offs between **strict conformance** and **practical usability**, ensuring that whichever approach is selected is clearly justified in the **ADRG**.

Principles vs. Rules: A. Hierarchy

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

Fundamental Principles (Non-Negotiable)

ADaM datasets must always:

- Enable **clear and unambiguous communication**.
- Ensure **traceability** back to SDTM and, ultimately, source data.
- Be **usable by standard tools**.
- Include **metadata** that supports interpretation and use.
- Be truly **analysis-ready**, without requiring extensive additional processing.

Rules (Important but Flexible)

ADaM rules provide structure and consistency by defining:

- Dataset organization, variable naming, and allowable content.

- Conformance checks for **automation and validation**.

However, rules are **not absolute**. A dataset that deviates from certain rules may still be considered valid ADaM **if it continues to meet the fundamental principles**.

Balancing Principles and Rules

- **Principles outweigh rules**: A dataset that violates principles (e.g., unclear, untraceable, or not analysis-ready) cannot be considered ADaM, regardless of conformance checks.
- Conversely, a dataset that breaks some rules - such as through the use of **PARQUAL**, incorporation of **Nadir derivations**, or introduction of **ADPL** - may still be acceptable if it remains **clear, traceable, and analysis-ready**, with justification documented (e.g., in the ADRG).

Recommendations for Industry Practice

Drawing on insights from ADaM experts, CDISC discussions, and broad industry experience, we recommend the following best practices:

- **Prioritize principles over rules**: Ensure that fundamental principles (clarity, traceability, analysis readiness) always take precedence over strict rule adherence.
- **Leverage conformance tools proactively**: Use validation tools early and consistently to identify potential issues.
- **Interpret findings thoughtfully**: Treat automated validation results as guidance rather than definitive judgments.
- **Document deviations transparently**: Record any rule violations in the ADRG, providing clear rationale and justification.
- **Apply pragmatic solutions**: Where appropriate, implement practical approaches and document them thoroughly.
- **Anticipate upcoming standards**: Prepare for ADaM v3.0, which is expected to formalize approaches to these complex topics.

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.

CONCLUSION

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.

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