cdisc

2023
EUROPE
INTERCHANGE
COPENHAGEN | 26-27 APRIL

Proposal for New ADaM Paired Variables: PARQUAL/PARTYPE

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Meet the Speaker

Monika Kawohl

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Monika Kawohl is a Principal Statistical Programmer at the CRO mainanalytics GmbH in Germany and has 30 years of experience in the pharmaceutical industry. She joined the CDISC ADaM team in 2009 and has served as a CDISC authorized ADaM Instructor since 2012.

Meet the other Authors

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- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

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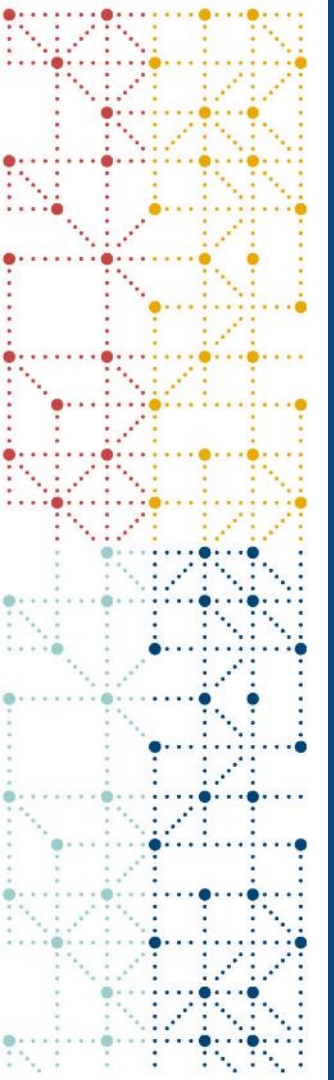


Current Requirements of ADaM Parameters

In the Basic Data Structure (BDS)

Current Requirement of ADaM Parameters

PARAM – Parameter

- The description of the analysis parameter.
- PARAM must include all descriptive and qualifying information relevant to the analysis purpose of the parameter.
- In contrast to SDTM --TEST, no additional variable is needed to further qualify PARAM.

PARAMCD – Parameter Code

- The short name of the analysis parameter in PARAM.
- There must be a one-to-one relationship between PARAM and PARAMCD within a dataset.

PARCATy - Parameter Category y

- A categorization of PARAM within a dataset.
- Note that PARCATy is not a qualifier for PARAM.
- PARAM to PARCATy is a many-to-one mapping;
  any given PARAM may be associated with at most one level of PARCATy.

Example of Incorrect and Correct Variable Usage

STUDYID	USUBJID	OESEQ	OETESTCD	OETEST	OESTRESN	OESTRESU	OELAT	OEDTC
AB-12	AB-12-01	1	IOP	Intraocular Pressure	18	mmHg	LEFT	2014-01-01
AB-12	AB-12-01	2	IOP	Intraocular Pressure	12	mmHg	RIGHT	2014-01-01

SDTM Dataset

STUDYID	USUBJID	ASEQ	PARCAT1	PARAMCD	PARAM	AVAL	ADT
AB-12	AB-12-01	1	Left	IOP	Intraocular Pressure (mmHg)	18	01Jan2014
AB-12	AB-12-01	2	Right	IOP	Intraocular Pressure (mmHg)	12	01Jan2014

Incorrect ADaM Implementation

STUDYID	USUBJID	ASEQ	PARCAT1	PARAMCD	PARAM	AVAL	ADT
AB-12	AB-12-01	1	Left	LIOP	Left Intraocular Pressure (mmHg)	18	01Jan2014
AB-12	AB-12-01	2	Right	RIOP	Right Intraocular Pressure (mmHg)	12	01Jan2014

ADaM Dataset corrected

History of Parameter Qualifiers

In Draft ADaM IG v1.2

PARQUAL In Draft ADaMIG V1.2

PARAM - Parameter

- The description of the analysis parameter.
- PARAM should include all descriptive and qualifying information relevant to the analysis purpose of the parameter.
- See the CDISC Notes for PARQUAL for possible exceptions regarding qualifying information.

PARAMCD – Parameter Code

- The short name of the analysis parameter in PARAM.
- There must be a one-to-one relationship between PARAM and PARAMCD within a dataset.

PARQUAL – Parameter Qualifier

- PARQUAL can be used in addition to PARAM, as an alternative to creating a distinct value of PARAM for each level of a separate, categorical concept.
- PARQUAL provides qualifying information pertaining to PARAM that does not affect the meaning of PARAM.
- PARAM must still uniquely and sufficiently describe what is contained in AVAL or AVALC.

PARQUAL Example from Draft ADaMIG v1.2

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)
Efficacy parameters	Primary endpoint and components	Investigator	Time to MI (days)
Efficacy parameters	Primary endpoint and components	Investigator	Time to stroke (days)
Efficacy parameters	Secondary endpoints	Adjudicated	Time to death (days)
Efficacy parameters	Secondary endpoints	Investigator	Time to death (days)
Efficacy parameters	Secondary endpoints		Time to hospitalization (days)
Safety parameters		Adjudicated	Time to major bleeding (days)
Safety parameters		Investigator	Time to major bleeding (days)

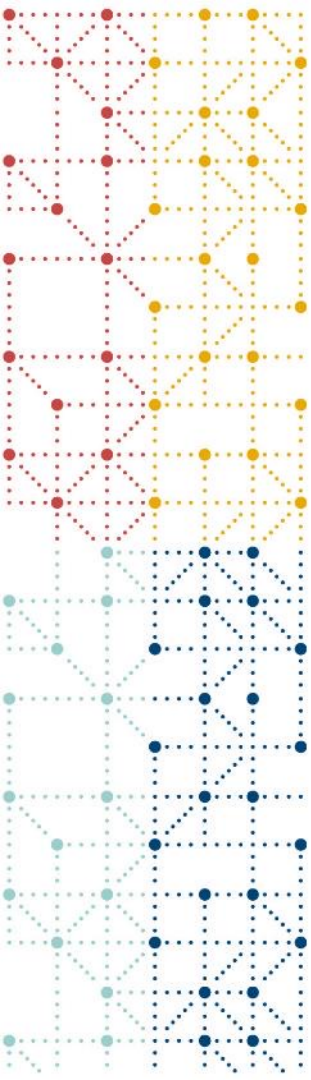
After Public Review

Based on public review comments, PARQUAL was not sufficiently clear.

Options to address these comments:

1) modifying the current text
2) restricting the use of PARQUAL to a small list of permissible use cases
3) exploring alternate ways to address the underlying issue PARQUAL was seeking to address.

➢ Ultimately, the ADaM team decided
- more time was required to evaluate PARQUAL
- ADaM IG v1.2 moved forward without it



Published Use Cases of PARQUAL

- Breast Cancer Therapeutic Area User Guide v1.0 (Provisional)
- FDA’s Pilot OCE/OOD Standard Safety Data Requests v1.3

Breast Cancer Therapeutic Area User Guide v1.0 (Provisional)

Row	STUDYID	USUBJID	ASEQ	ASTDT	ASTDY	PARQUAL	PARAMCD	AVALC
1	AB-12	AB-12-01	1	01JAN2014	20	INVESTIGATOR	ASSESS	SD
2	AB-12	AB-12-01	2	01JAN2014	20	CENTRAL	ASSESS	PR

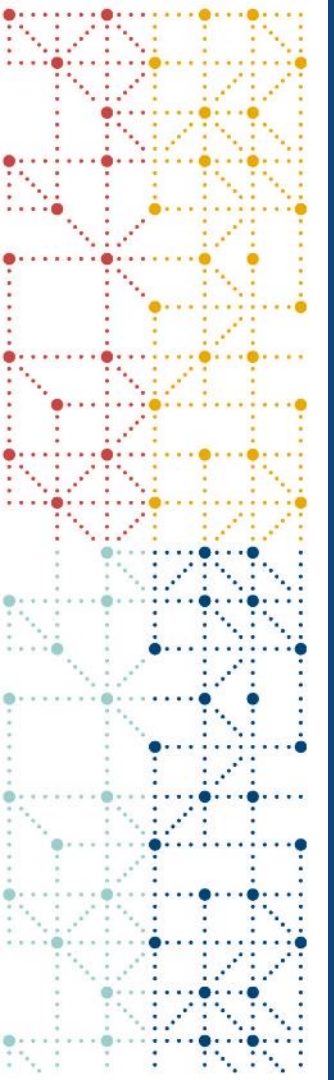
PARQUAL used to identify the source of the parameter

- INVESTIGATOR for investigator-based assessments
- CENTRAL for central imaging assessments
- PATHOLOGIC for an assessment by biopsy
- PROTOCOL for events affecting assessment

FDA's Pilot OCE/OOD Standard Safety Data Requests v1.3

PARQUAL	PARAMCD	PARAM	*OCE/OOD Notes*
<each value of EXTRT>	DOSRED	Any Dose Reductions	*Y if there were any dose reductions*
<each value of EXTRT>	NDOSRED	Number of Dose Reductions	*Number of dose reductions*
<each value of EXTRT>	DOSINT	Any Dose Interruptions	*Y if there were any dose interruptions*
<each value of EXTRT>	NDOSINT	Number of Dose Interruptions	*Number of dose interruptions*
ALL	TRTDCT	Treatment Discontinued	*Y if treatment permanently discontinued for all drugs*

Neither of these use cases for PARQUAL is currently supported by the ADaMIG v1.3.



Proposed Parameter Qualifiers

PARQUAL and PARTYPE

Proposal for Next ADaMIG Version

Allow PARQUAL but restrict use cases through addition of PARTYPE

PARTYPE governed by ADaM Controlled Terminology

- Starting with values "EVALUATOR" and "TREATMENT"
- Additions or changes to be requested via CDISC New Term Request Page

PARTYPE current working name and subject to change

- Other options: PARQTYPE, PQUALTYP
- Highlighting relationship to PARQUAL rather than PARAM

When PARTYPE and PARQUAL are used,
the combination of PARAM and PARQUAL must be sufficient to describe unambiguously the contents of AVAL/AVALC

In most cases PARAM/PARAMCD must be used alone

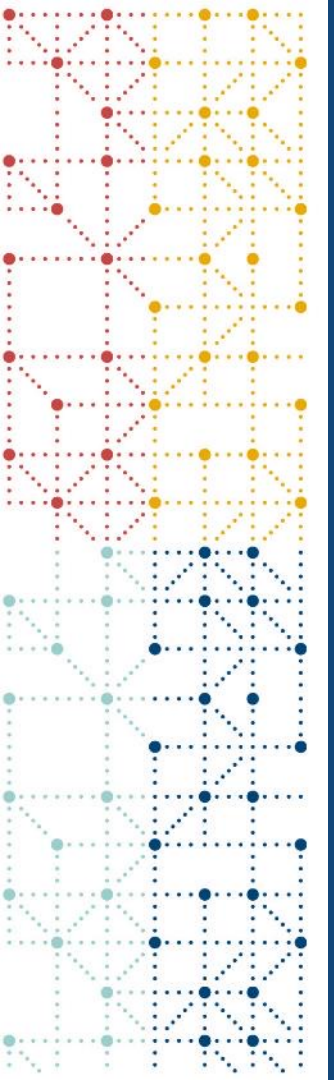
Published Examples with PARQUAL+PARTYPE

Breast Cancer TAUG including PARTYPE

Row	STUDYID	USUBJID	ASEQ	ASTDY	PARTYPE	PARQUAL	PARAMCD	AVALC
1	AB-12	AB-12-01	1	20	EVALUATOR	INVESTIGATOR	ASSESS	SD
2	AB-12	AB-12-01	2	20	EVALUATOR	CENTRAL	ASSESS	PR

FDA's OCE/OOD including PARTYPE

PARTYPE	PARQUAL	PARAMCD	*OCE/OOD Notes*
TREATMENT	<each value of EXTRT>	DOSRED	*Y if there were any dose reductions*
TREATMENT	<each value of EXTRT>	NDOSRED	*Number of dose reductions*
TREATMENT	<each value of EXTRT>	DOSINT	*Y if there were any dose interruptions*
TREATMENT	<each value of EXTRT>	NDOSINT	*Number of dose interruptions*
TREATMENT	ALL	TRTDCT	*Y if treatment permanently discontinued for all drugs*



Incorrect Usage

Examples of Incorrect Usage

PARTYPE	PARQUAL	PARAMCD	PARAM	AVALC
SEVERITY	MILD	AESI	Occurrence of AE of Special Interest	Y
SEVERITY	MODERATE	AESI	Occurrence of AE of Special Interest	Y
SEVERITY	SEVERE	AESI	Occurrence of AE of Special Interest	N

Invalid PARTYPE value, not in CT

PARTYPE	PARQUAL	PARAMCD	PARAM	AVAL
LBCAT	CHEMISTRY	GLUCOSE	Glucose (mmol/L)	5.48
LBCAT	URINALYSIS	GLUCOSE	Glucose (mmol/L)	0.6

PARTYPE	PARQUAL	PARAMCD	PARAM
TREATMENT	Sirolimus	TOTDOSE	Total dose across the study (mg)
TREATMENT	Gemcitabine	TOTDOSE	Total dose across the study (mg/m2)

Even with an allowed value of PARTYPE, PARQUAL cannot be used if PARAM is not the same across records

Documentation

Analysis Data Reviewer’s Guide (ADRG) and define.xml

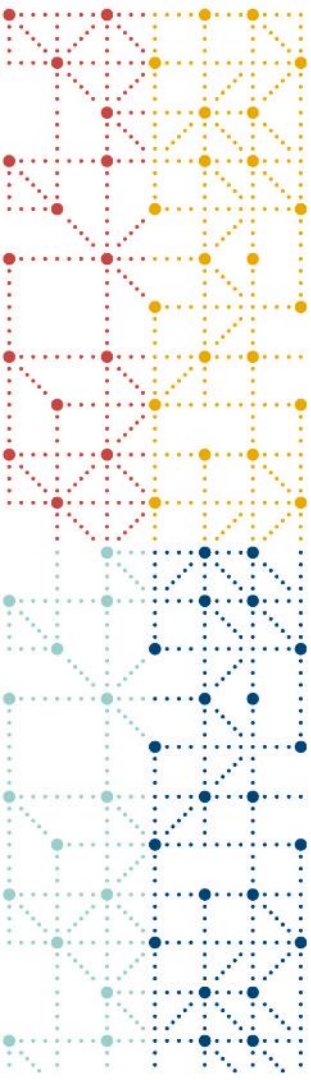
Documentation

5.2 ADEVENT – Event Analysis Dataset

ADEVENT is a sponsor-defined analysis dataset following the ADaM Basic Data Structure (BDS). It's used as an intermediate dataset to support the primary efficacy analysis. The PARAMCD 'ASSESS' applies to different evaluators, with the variable PARQUAL used to differentiate the evaluators (INVESTIGATOR, CENTRAL). Variables that make a record unique for this dataset are USUBJID PARQUAL PARAMCD.

- Describe usage of PARQUAL and PARTYPE in associated documentation
  - Analysis Data Reviewer's Guide (ADRG)
  - define.xml
- Highlight the variables that make a record unique

Variable	Label/ Description	Type	Codelist/ Controlled Terms	Origin / Source / Method / Comment
STUDYID	Study Identifier	text		Predecessor: ADSL.STUDYID
USUBJID	Unique Subject Identifier	text		Predecessor: ADSL.USUBJID
SUBJID	Subject Identifier for the Study	text		Predecessor: ADSL.SUBJID
ASEQ	Analysis Sequence Number	Integer		Derived: Sequential number for associating a record number in the dataset. Unique number per subject per parameter per parameter qualifier per analysis start date.
ASTDT	Analysis Start Date	integer		Derived: This is the date that the event occurred. RS.RSDTC when PARAMCD = 'ASSESS'. Convert –DTC variables to numeric date format.
ASTDY	Analysis Start Day	integer		Derived: RANDT – ASTDT + 1
PARTYPE	Parameter Qualifier Type	text		Assigned: Set to 'EVALUATOR'
PARQUAL	Parameter Qualifier	text		Predecessor: RS.RSEVAL
PARAMCD	Parameter Code	text		Assigned: Set to 'ASSESS'
PARAM	Parameter	text		Assigned: Set to 'Assessment'
AVALC	Analysis Value (C)	text		Predecessor: RS.RSSTRESC



Summary

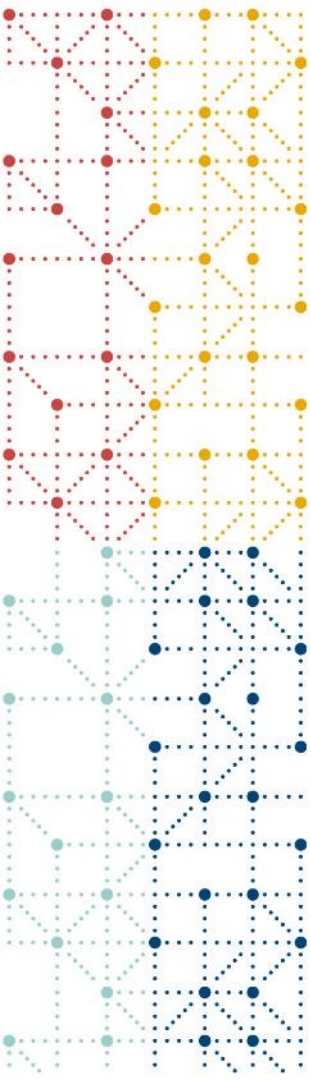
Summary

The conversation around possible PARAM qualifier variables has been around for years

Limited use will soon be allowed

Use will be restricted by the paired variable PARTYPE

PARTYPE will have non-extensible controlled terminology

ADRG and define.xml must document the use

Thank You!