Introducing the ADaM Implementation Guide v1.2

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Overview
The ADaM team is proposing a minor version update of the IG to provide clarifications and to introduce three significant changes:
- Addition of PARQUAL
- Addition of stratification variables
- Guidance for bi-directional toxicity grades

PARQUAL
New Permissible Variable within Basic Data Structure (BDS)
In some cases, an analysis parameter is defined the same (and AVAL or AVAŁC is derived in the same way) within each level of a single, separate, categorical concept. In such cases, it is permissible to use PARQUAL in addition to PARAM as an alternative to creating a distinct value of PARAM for each level of that separate categorical concept. PARQUAL provides qualifying information pertaining to PARAM that does not affect the meaning of PARAM. When using PARQUAL, PARAM must still uniquely and sufficiently describe what is contained in AVAL or AVAŁC.

PARQUAL may contain null values for some parameters within a dataset. If it is used for a parameter, PARQUAL must be populated for all records for that parameter within a dataset. The PARQUAL value cannot be included in the PARAM value. Invalid uses of PARQUAL include SDTM qualifiers (e.g., units), timepoints, and any other qualifying information that results in a change in the interpretation of AVAL or AVALC. All statements throughout all ADaM documents pertaining to PARAM alone also apply to the combination of PARQUAL plus PARAM.

Bi-Directional Toxicity Grades

Recommended Approach for Bi-Directional Toxicity Grades
The ADaM team discussed many options for handling lab limits that need to be assessed in more than one direction with different meaning. Rather than creating additional records, the ADaM team agreed to add guidance around the variables proposed to handle bi-directional information. Toxicity grades are the most common example of this, but other bi-directional examples can be applied to these new variables as needed.

Figure 1. Tumor Measurement without PARQUAL
In Figure 1 an example is shown using PARAM prior to the implementation of PARQUAL. In this case, PARAM and PARAMCD are unique for Investigator and Independent Reviewer. This is a good illustration of when the interpretation of AVAL does not change based on the individual who recorded the measurement.

Figure 2. Tumor Measurement with PARQUAL
Figure 2 shows an example using the new PARQUAL method. The source or evaluator is considered as qualifying information pertaining to a tumor measurement parameter. Therefore, a PARQUAL variable is created to contain this information. Table 4.9.1.2 in ADaM IG v1.2 provides a set of variables to allow maximum flexibility in representing the description of the prognostic factors as well as the values used for randomization and the values that were verified.

Figure 3. PARQUAL vs PARCATy
PARQUAL, designed to qualify parameters, is different from PARCATy, which is designed to group or categorize parameters. Figure 3 displays two examples of appropriate uses of PARCATy and PARQUAL. Note that the use of PARQUAL does not affect the meaning of the parameters.

Figure 4. Stratification Variables Within ADSL

Bi-Directional Lab Example
Figure 5 displays the bi-directional toxicity grading proposed in ADaM IG v1.2. The toxicity descriptions (ATOXDSCL and ATOXDSCH) can help to determine denominators. For example, if ATOXDSCL is populated then that record is counted in high toxicity grading. In some cases, a record can be counted for both since the record would be assessed in both directions.

Figure 6. Bi-Directional Lab Example
Figure 6 is an example of some of the variables in a dataset supporting bi-directional toxicity grades. *GRL and *GRH are included to indicate variables that pertain to low/high grading tables, and if ATOXDSCH is populated then that record is counted in high toxicity grading. In this example, hemoglobin is bidirectional (see red boxes), while SGOT and WBC are only in one direction (see orange box).