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LBTEST/LBSTRESU and ADaM lab parameters: The dilemma of mapping one-to-many or many-to-one

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ABSTRACT

Lab results for clinical trials need to be uniquely identified to allow them to be combined for analysis. Multiple source laboratories may have varying names or identifiers for the same test, so standardization is needed to identify lab tests that are the same. Industry wide, there are efforts to standardize lab codes via LOINC but that is still a work in progress and not a mandate. Many pharma companies have their own internal code system to uniquely identify lab tests. These internal codes are mapped to SDTM CDISC terms for LBTESTCD/LBTEST and associated units. Mapping those tests to ADaM parameters becomes a bit more complex because PARAMCD/PARAM must uniquely and unequivocally describe what is in AVAL or AVALC. It is not enough to just look at the SDTM LBTEST (and associated unit) to determine what your parameter should be. This paper will explain some of the levels of detail that needs to be assessed to correctly define an ADaM lab PARAMCD/PARAM. Examples will be provided showing labs that appear to be the same but are not, as well as labs whose names are different and yet can be combined for analysis.

INTRODUCTION

Pharma companies may have several hundred lab tests defined for use in clinical trials. Identifying unique parameters for hundreds of tests can be a daunting task. The ADaM lab data structure, ADLB, does not have qualifier variables that equate to the SDTM variables LBSPEC, LBMETHOD, LBFAST or LBSTRESU. All of the SDTM qualifiers that differentiate lab tests for analysis must be included in PARAM, and a unique PARAMCD has to be associated with it.

This paper will demonstrate two scenarios of mapping lab tests from SDTM to ADaM. The first scenario will be a one-to-many mapping of a single SDTM lab term to multiple ADaM lab parameters. The second will be a many-to-one mapping of multiple input lab tests to a single ADaM lab parameter.

The intent of this paper is to give you a better understanding of how to define ADaM lab parameters.

OVERVIEW OF RULES FOR PARAMCD AND PARAM

To provide a framework for the examples in this paper, please be aware of the CDISC rules for ADaM parameters and how company algorithms were defined to apply those rules for lab parameters.

Basic CDISC rules include the following:

- PARAM/PARAMCD must be a one-to-one map
- PARAM must be meaningful and must uniquely describe what is in AVAL or AVALC
- PARAMCD must be as meaningful as possible, yet not exceed 8 characters

Company algorithms were defined to consistently build PARAMCD and PARAM per CDISC rules. The algorithms incorporate SDTM CDISC terms, as well as company test codes associated with the collected source data. The company algorithms are below:

- PARAM = LBSPEC || LBTEST || LBMETHOD || (LBSTRESU)
- PARAMCD = 4-char of LBTESTCD || 3-char company code || 1-char for the system of units
    - For the system of units, “C” is for Conventional (CN) and “S” is for Standard International (SI)

SCENARIO 1: ONE-TO-MANY MAPPING

It is very common for there to be multiple source lab tests associated to one SDTM term for LBTEST. Depending on other SDTM qualifying variables, the one LBTEST may get mapped to many ADaM lab parameters. One-to-many mappings do not usually create challenges as long as the ADaM parameters include the information from the SDTM qualifying variables.

Table 1 is an example of this one-to-many mapping. All of the rows have one LBTEST term of "HDL Cholesterol" but each row has various values for LBSTRESU, LBSPEC, and LBMETHOD. Since these tests are meant to be analyzed separately, they need unique ADaM parameters.

Each PARAMCD was defined uniquely using the company algorithm to concatenate LBTESTCD with the source test code, and the 1-character suffix to represent the system of units. The PARAM was defined uniquely by concatenating the specimen, test, method, and units from SDTM.

Source test code	LBTEST CD	LBTEST	LBSTRESU	LBSPEC	LBMETHOD	PARAMCD	PARAM
F55	HDL	HDL Cholesterol	mg/dL	SERUM		HDLF55C	SERUM HDL Cholesterol (mg/dL)
F55	HDL	HDL Cholesterol	mmol/L	SERUM		HDLF55S	SERUM HDL Cholesterol (mmol/L)
HQ1	HDL	HDL Cholesterol	mg/dL	SERUM	ENZYMATIC	HDLHQ1C	SERUM HDL Cholesterol ENZYMATIC (mg/dL)
HQ1	HDL	HDL Cholesterol	mmol/L	SERUM	ENZYMATIC	HDLHQ1S	SERUM HDL Cholesterol ENZYMATIC (mmol/L)
L96	HDL	HDL Cholesterol	mg/dL	PLASMA	NMR	HDLL96C	PLASMA HDL Cholesterol NMR (mg/dL)
L96	HDL	HDL Cholesterol	mmol/L	PLASMA	NMR	HDLL96S	PLASMA HDL Cholesterol NMR (mmol/L)

Table 1. One LBTEST to many PARAM

SCENARIO 2: MANY-TO-ONE MAPPING

Many-to-one mappings can be a bit more challenging. The level of detail to which a company assigns internal test codes to individual lab tests can impact how those tests are defined in SDTM and ADaM. A company's internal coding system for central labs may use a different test code for each variation of a single lab test. For example, if one laboratory performs a test for ketones using reagent tablets but another laboratory uses a test-strip, each test could be assigned a unique code to distinguish between the variation in testing.

To explain how this can be a challenge, let's consider two source test codes, C09 and C58, which represent tests for ketones. Each has a different source code because of some slight variation, and both are mapped to the LBTEST term of "Ketones". Using the company algorithms for ADaM lab parameters, the test codes, C09 and C58, are incorporated into PARAMCD, generating two different parameter codes, both associated to the same PARAM as shown in Table 2. This violates the CDISC rule for PARAMCD and PARAM to be a one-to-one map. This is a problem which needs to be identified and resolved when building controlled terminology for lab parameters.

Source test code	LBTESTCD	LBTEST	LBSTRESU	LBSPEC	LBMETHOD	PARAMCD	PARAM
C09	KETONES	Ketones		URINE		KETOC09J	URINE Ketones
C58	KETONES	Ketones		URINE		KETOC58J	URINE Ketones

Table 2. Violation of 1:1 of PARAMCD to PARAM

RESOLVING VIOLATIONS OF 1:1 PARAMCD/PARAM

With appropriate checks in place, parameter problem records can be identified when they are being defined. If violations of the one-to-one mapping of PARAMCD to PARAM are found, the appropriate lab experts, clinicians, and/or statisticians should be consulted to gain a better understanding of the labs. Resolving problems with parameter definitions will be handled differently depending on whether or not the results from multiple tests can or cannot be analyzed together.

For the sake of discussion, the term "equivalent labs" will be used to refer to the tests that can be analyzed together. The term "non-equivalent labs" will refer to those that cannot be analyzed together. Examples will be provided on resolving parameter problems for each.

Parameters for equivalent labs

Equivalent labs are tests that are basically the same, such as the two different ketone tests described earlier. Although there may be slight differences in how the test is performed, usually the results are subjective, e.g. Positive or Negative, and can be analyzed together. You may not have to deal with this if your source data does not have unique test codes to distinguish slight variations of a test. However, if this situation exists then a solution is needed to map multiple tests to a single ADaM parameter.

Using the ketone tests as an example, let's take a look at how the problem was resolved. The problem parameters were reported and it was determined that the labs were equivalent. To get a single parameter code, test codes C09 and C58, were replaced with a common identifier of "15E", which allowed the generation of a single PARAMCD as shown in Table 3. Note that both source tests are mapped to single parameter, and the PARAMCD and PARAM maintain the 1:1 mapping required by CDISC.

Source test code	LBTESTCD	LBTEST	LBSTRESU	LBSPEC	LBMETHOD	PARAMCD	PARAM
C09	KETONES	Ketones		URINE		KETON15E	URINE Ketones
C58	KETONES	Ketones		URINE		KETON15E	URINE Ketones

Table 3. Corrected parameters for equivalent tests

Parameters for non-equivalent labs

Non-equivalent labs are tests with similar names but whose results cannot be combined for analysis. When these similar source tests get mapped to the same SDTM terminology, you can once again end up with parameter problem records.

After reviewing the problem records, if it is decided that the tests cannot be analyzed together then SDTM support staff and laboratory personnel should collaborate to determine how to make each test unique. Sometimes the solution is to update the company's test code dictionary with additional metadata, such as a laboratory method name. Other times, the solution is to map a test to a different CDISC term for LBTEST. Both solutions will be discussed.

Resolving non-equivalent labs via source metadata

This next example will go over the option of resolving the issue with an update to the company's test code dictionary. To further explain, look at Table 4 which shows two different source test codes mapped to the same SDTM terms and same PARAM, but two different PARAMCD terms.

Source test code	LBTESTCD	LBTEST	LBSTRESU	LBSPEC	LBMETHOD	PARAMCD	PARAM
E19	TSH	Thyrotropin	mU/L	SERUM		TSHE19S	SERUM Thyrotropin (mU/L)
E21	TSH	Thyrotropin	mU/L	SERUM		TSHE21S	SERUM Thyrotropin (mU/L)

Table 4. Non-equivalent labs with parameter problems

After investigation, lab personnel determined that the methodology was not the same and the results should not be analyzed together. To make the tests unique, an update was made to the company lab test code dictionary to include a method for one of the tests. The dictionary update triggered the population of LBMETHOD, which in turn allowed unique parameters for each PARAMCD as shown in Table 5.

Source test code	LBTESTCD	LBTEST	LBSTRESU	LBSPEC	LBMETHOD	PARAMCD	PARAM
E19	TSH	Thyrotropin	mU/L	SERUM		TSHE19S	SERUM Thyrotropin (mU/L)
E21	TSH	Thyrotropin	mU/L	SERUM	AXSYM	TSHE21S	SERUM Thyrotropin AXSYM (mU/L)

Table 5. Non-equivalent lab parameters resolved by adding method

Resolving non-equivalent labs via remapping to a different CDISC term

The last example will explain resolving the issue by remapping to different CDISC terms. This is another illustration of the many-to-one mapping of the source test code to a single LBTEST, creating parameter problem records. For this example, the different source test codes, YA3 and Y53, both were related to tests for cocaine. YA3 represents an initial screening test, and Y53 represents a confirmation test. Both provide results as positive or negative, and it was assumed that they would be analyzed together so they were initially mapped to the same CDISC term. The mapping created parameter problem records as shown in the first 2 rows of Table 6.

Additional discussions occurred to confirm whether or not these tests should be combined for analysis. Further investigation revealed that that the screening test, YA3, is less specific and can include the metabolites, whereas the confirmation test, Y53, is specific to cocaine. It was decided that these needed to be differentiated for analysis. In this case, the distinction was made by remapping the YA3 test to a CDISC term that described it more accurately. The unique mappings then allowed valid PARAMCD and PARAM values to be generated as shown in the last 2 rows.

Source test code	LBTESTCD	LBTEST	LBSPEC	LBMETHOD	PARAMCD	PARAM
YA3	COCAINE	Cocaine	URINE		COCAYA3J	URINE Cocaine
Y53	COCAINE	Cocaine	URINE		COCAY53J	URINE Cocaine
YA3	COCABNZL	Cocaine and/ or Benzoylecgonine	URINE		COCAYA3J	URINE Cocaine and/ or Benzoylecgonine
Y53	COCAINE	Cocaine	URINE		COCAY53J	URINE Cocaine

Table 6. Non-equivalent labs resolved by changing the CDISC term

CONCLUSION

Correctly defining ADaM lab parameters is essential for analysis. The method for defining parameters should be consistent and should include checks to ensure 1:1 mapping of PARAM to PARAMCD.

Lilly established an automated process for generating lab parameters and running validation checks on them. Considering the hundreds of parameters that are needed for labs, automation is highly recommended.

The author hopes that this paper aids in the creation of compliant and definitive ADaM lab parameters.

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

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