

Paper PP04

Novo Nordisk implementation of Logically Skipped Items for the QS=Questionnaires domain

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ABSTRACT

A Questionnaire may have some items that will be logically skipped per the instructions for the Questionnaire. Responses for logically skipped items (LSI) should as per the FDA Study Data Technical Conformance Guide be included in the submission dataset with the following: QSSTAT = "NOT DONE"; QSREASND = "LOGICALLY SKIPPED ITEM"; and QSORRES, QSSTRESC, and QSSTRESN all set to null. This paper will detail/explain how this has been implemented at Novo Nordisk. With a metadata-driven approach, the creation of LSI has been automated with standard programs; allowing maximum flexibility yet minimum maintenance and implementation effort.

INTRODUCTION

In FDA Study Data Technical Conformance Guide version 4.0 (October 2017), the concept of logically skipped items was introduced for the first time. Logically skipped items are currently only mentioned in relation to the Questionnaires (QS) domain. An example of a logically skipped item is, if in the first question, the subject is asked if currently employed and the subject answers No, then the subject should not answer the next 5 questions and skip to question 6.

FDA STUDY TECHNICAL CONFORMANCE GUIDE & EXAMPLES

The FDA Study Data Technical Conformance Guide provides technical recommendations to sponsors for the submission of animal and human study data and related information in a standardized electronic format in INDs, NDAs, ANDAs, and BLAs.

FDA STUDY TECHNICAL CONFORMANCE GUIDE

Text from the FDA Study Data Technical Conformance Guide:

4.1.1.3 SDTM Domain Specifications

QS Domain (Questionnaires)

Some items in an instrument may be logically skipped per the instrument's instructions. Responses for logically skipped items should be (1) recorded and/or scored according to the instructions provided in the instrument's user manual, scoring manual, or other documentation provided by the instrument developer and (2) included in the submission dataset.

If instructions on how to record and/or score responses to logically skipped items are available from the instrument developer, then records for logically skipped items should be included in the submission dataset with the following:

- QSSTAT = "NOT DONE";
- QSREASND = "LOGICALLY SKIPPED ITEM"; and
- QSORRES, QSSTRESC, and QSSTRESN would be assigned according to the instrument's instructions.

If instructions on how to record and/or score responses to logically skipped items are not available from the instrument developer, then records for logically skipped items should be included in the submission dataset with the following:

- QSSTAT = “NOT DONE”;
- QSREASND = “LOGICALLY SKIPPED ITEM”; and
- QSORRES, QSSTRESC, and QSSTRESN all set to null.

CRF EXAMPLES

Below are two examples where FDA would expect records for the logically skipped items.

Example 1:

QS = QUESTIONNAIRES **QSCAT=WPAI-SHP**
QSSCAT= abbreviation for PROBLEM TA, when TA-specific
 Work Productivity and Activity Impairment Questionnaire:
 Specific Health Problem V2.0 (WPAI:SHP)

The following questions ask about the effect of your PROBLEM on your ability to work and perform regular activities. Please fill in the blanks or circle a number, as indicated.

QSORRES for QSTESTCD=WPAI0101
 1. Are you currently employed (working for pay)? ____ NO ____ YES
 If NO, check “NO” and skip to question 6.

Question 2 to 5 (WPAI0101 to WPAI0105) are dependent on the answer to Question 1 (WPAI0101) and thereby in scope for logically skipped items. Question 2 to 5 (WPAI0101 to WPAI0105) are not shown.

Example 2:

QS=Questionnaires **QSCAT=PHQ-9**

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

FOR OFFICE CODING 0 + + + +
QSTESTCD= PHQ0111 =Total Score: **QSORRES/ QSSTRESC/ QSSTRESN**

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

QSTESTCD= PHQ0110

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

QSORRES/QSSTRESC

Question 10 (PHQ0110) is dependent on the answer to Question 11 (PHQ0111) and thereby in scope for logically skipped items. Question 1 to 9 (PHQ0101 to PHQ0109) are not shown.

SOLUTION & EXAMPLES

At the time of submitting this paper, Novo Nordisk has implemented the logically skipped items functionality on the following questionnaires:

- WPAI (WORK PRODUCTIVITY ACTIVITY IMPAIRMENT)
- PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)
- C-SSRS (COLUMBIA-SUICIDE SEVERITY RATING SCALE)

A METADATA DRIVEN SOLUTION

At Novo Nordisk, we have chosen to implement the logically skipped items functionality as a metadata driven solution. This can be done as we have a metadata repository (MDR) and that our data is collected based on what we call topic codes. A topic code identifies and classifies an observation with additional information linked to it. The concept of a topic code corresponds to the biometrical concept.

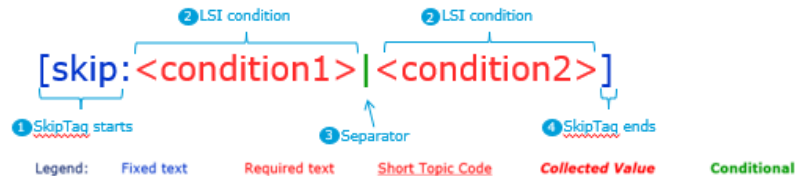
The steps for the solution:

- Define Questionnaires in scope for Logically Skipped Items
 - User Defined Codelist for questionnaire Category
- Define rule for when to apply 'logically skipped item' functionality
 - 'Tag' specified in the code definition

[skip:(qstestcd eq 'WPAI0101' and qsorres eq 'N')|(qstestcd eq 'WPAI0104' and qsorres eq '0')]

SKIPTAG SYNTAX: LSI CONDITION & EXAMPLES

Syntax for the logically skipped items.:



- 1 Fixed text that indicates SkipTag starts, required.
- 2 Condition upon which the question is skipped, required.
- 3 Separator, required when the question can be skipped upon multiple conditions.
- 4 Fixed text that indicates SkipTag ends, required.

Example 1: Single LSI condition with multiple requirements

[skip:(qstestcd eq 'CSS0101' and qsorres eq 'N') and (qstestcd eq 'CSS0102' and qsorres eq 'N'))]

Example 2: Multiple LSI conditions

[skip:(qstestcd eq 'CSS0112' and qsorres ne 'Y')|(qstestcd eq 'CSS0121B' and qsorres ne '0'))]

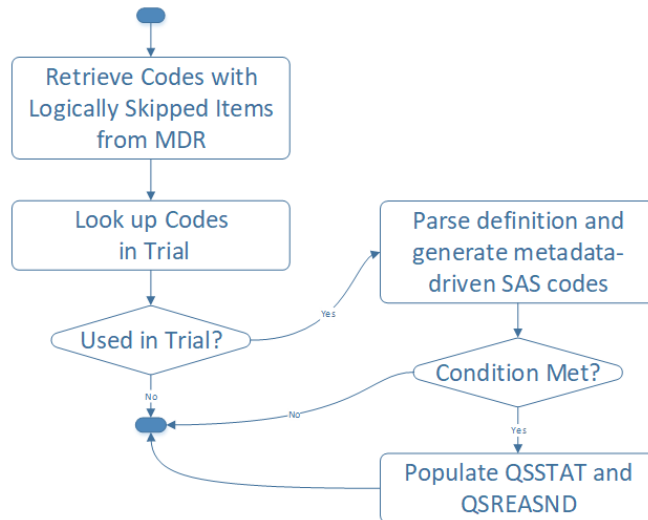
Legend: Fixed text (blue), Required text (red), Short Topic Code (green), Collected Value (orange), Conditional (green).

STANDARD PROGRAM

A standard program has been created to implement the defined rules.

The program will only apply 'logically skipped item' if:

- Record exists
- No data for QSORRES already
- 'Tag' rule fulfilled



When a question with LSI is used in a trial, the program will then retrieve the 'tag' defining LSI rule from the MDR and generate SAS code to process the records accordingly. A snippet of auto-generated codes is shown below.

```

if _n_=1 then do;
  declare hash qs4_1
    (dataset:"qs(where=((qstestcd eq 'WPAI0101' and qsorres eq 'N'))");
  qs4_1.definekey("usubjid","visitnum");
  qs4_1.definedone();
  declare hash qs4_2
    (dataset:"qs(where=((qstestcd eq 'WPAI0104' and qsorres eq '0'))");
  qs4_2.definekey("usubjid","visitnum");
  qs4_2.definedone();
end;
if qstestcd in ("WPAI0102" "WPAI0103" "WPAI0104" "WPAI0105") and
  qs4_1.find()=0 and missing(qsorres) then _lsi=1;
if qstestcd in ("WPAI0105") and qs4_2.find()=0 and missing(qsorres)
  then _lsi=1;
if _lsi=1 then do;
  qsstat="NOT DONE";
  qsreasnd="LOGICALLY SKIPPED ITEM";
end;

```

DATA EXAMPLES

In the Work Productivity and Activity Impairment Questionnaire - Specific Health Problem (WPAI-SHP) there are 6 questions – WPAI0101 to WPAI0106.

Whether or not question 2 to 5 should be answered, is dependent on the answer to question 1 (WPAI0101). Question 2 to 5 should not be answered if WPAI0101 = 'N'. Please refer to the tag examples below.

At the same time, question 5 is also dependent on the answer to question 4 (WPAI0104). Question 5 should not be answered if WPAI0104 = '0'. Please refer to the tag examples below.

WPAI0101: No tag

WPAI0102: [skip:(qstestcd eq 'WPAI0101' and qsorres eq 'N')]

WPAI0103: [skip:(qstestcd eq 'WPAI0101' and qsorres eq 'N')]

WPAI0104: [skip:(qstestcd eq 'WPAI0101' and qsorres eq 'N')]

WPAI0105: [skip:(qstestcd eq 'WPAI0101' and qsorres eq 'N')](qstestcd eq 'WPAI0104' and qsorres eq '0')]

WPAI0106: No tag

In the below example, the first question WPAI0101 (Currently employed) has been answered 'N' and question 6 (WPAI0106) has been answered '0'. Question 2 to 5 (WPAI0102 to WPAI01005) have not been answered, but the records exist. Question 2 to 5 are all in scope for logically skipped items. Question 2-4 have the same tag, but the tag for question 5 is different. The records with logically skipped items are shown in the red box.

QSTESTCD	QSTEST	QSORRES	QSSTAT	QSREASND
WPAI0101	WPAI01-Currently Employed	N		
WPAI0102	WPAI01-Missed Work Hours Due to Problem		NOT DONE	LOGICALLY SKIPPED ITEM
WPAI0103	WPAI01-Missed Work Hours Due to Other		NOT DONE	LOGICALLY SKIPPED ITEM
WPAI0104	WPAI01-Hours Actually Worked		NOT DONE	LOGICALLY SKIPPED ITEM
WPAI0105	WPAI01-Problem Affect Productivity		NOT DONE	LOGICALLY SKIPPED ITEM
WPAI0106	WPAI01-Problem Affect Reg Daily Activity	0		

```
WPAI0102: [skip:(qstestcd eq 'WPAI0101' and qsorres eq 'N')]
WPAI0103: [skip:(qstestcd eq 'WPAI0101' and qsorres eq 'N')]
WPAI0105: [skip:(qstestcd eq 'WPAI0101' and qsorres eq 'N')]
           [(qstestcd eq 'WPAI0104' and qsorres eq '0')]
```

In the below example, the first question WPAI0101 (Currently employed) has been answered 'Y' and question 4 (WPAI0104) has been answered '0'. Question 5 (WPAI0105) should therefore not be answered and are in scope for logically skipped items. The record with logically skipped items is shown in the red box.

QSTESTCD	QSTEST	QSORRES	QSORRESU	QSSTAT	QSREASND
WPAI0101	WPAI01-Currently Emp...	Y			
WPAI0102	WPAI01-Missed...Problem	0	HOURS		
WPAI0103	WPAI01-Missed...Other	20	HOURS		
WPAI0104	WPAI01-Hours...Worked	0	HOURS		
WPAI0105	WPAI01-Problem...Prod...			NOT DONE	LOGICALLY SKIPPED ITEM
WPAI0106	WPAI01-Problem...Activity	0			

CHALLENGES & REFLECTIONS

When trying to implement logically skipped items we have identified several challenges.

Interpretation

- When to logically skip and when not to?
 - If Yes, describe (If answered No, should the Description field be considered in scope for LSI?)
 - Suicidal Attempt=No, Total # of Attempts (If answered No, should 'Total # of Attempts' be considered in scope for LSI?)

Governance

- C-codes can be changed from CT version to CT version, so avoid basing the LSI implementation on this.

Version

- Topic code vs C-code

MDR - Operational

- Structure, topic codes, categories

Language

- English – US/UK, e.g. EQ-5D-5L

Storage

- A huge number of “NOT DONE” records

Why should data that is not captured be stored. The rules for not capturing data are already known.

Alternative solution could be to describe “skip rules” in the define.xml

- Add the “skip rules” in a human-readable way to each variable definition in the “Derivation/Comment” field
- QSTESTCD EQ WPAI0102: Logically skipped for QSTESTCD=WPAI0101 with QSORRES=N

REFERENCES

FDA Study Data Technical Conformance Guide on FDA site Study Data Standards Resources

<http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm>

<http://cdisc-end-to-end.blogspot.com/2019/03/logically-skipped-items-in-sdtm-qs.html>

CONTACT INFORMATION

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