

A Utility to Reconcile Report Numbers and Titles

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ABSTRACT

In clinical trials, analysis reports are generated in the form of tables, listings and figures (TLFs) for incorporation into Clinical Study Reports (CSRs) that are submitted to regulatory bodies for review and approval of a study drug or device. These TLFs are distinguished from one another by their unique report numbers and titles. A change either of these two important pieces of metadata conveys a completely different meaning to the output so it is very important that they are accurate. Lead programmers need to identify and fix cases of missing TLFs and/or incorrect TLF report numbers or titles, prior to CSR submission. A utility program was developed, to automate this process and reduce time required to reconcile the report header information.

INTRODUCTION

The purpose of the standard utility macro (LOT_TLF_Check.sas) is to check for discrepancies such as missing TLFs or mismatched output report numbers and title names between either the TLF List of Tables (LoT) excel file and the consolidated TLF output file (.csv) or the LoT excel file and the titles and footnotes .xml file and then generate a report with the differences. This paper will describe the features of the report number and titles reconciliation utility which can be used by clinical programmers at any level.

BACKGROUND

This utility program was developed on PC SAS and will work both in the Windows SAS 9.3/9.4 and Unix SAS 9.4 SAS GRID operating system environments. Files with extension .xlsx will work on SAS 9.3 or later versions and .xls files need to be used, when running on earlier versions of SAS. Also note that, working with excel files data import on SAS installed with 64-bit edition might result change in special characters (for example: μ to $\frac{1}{4}$). This is partly because 64-bit SAS process cannot use the Microsoft Excel, which is a 32-bit module. For LoT files, only a single column may be specified for report titles and a single column for report numbers. Consolidated TLFs output file (.csv) should have standard column names for the output title numbers (TABLENUM) and output title names (DSCRPT). Files with .xml and .map extensions should be located at the same drive path. In the .xml, the text defined with the elements TFLTYPE, TFLNUM represents the report number:

(Ex: <TFLTYPE>Table</TFLTYPE>, <TFLNUM>14.1.1</TFLNUM>)

The text defined with the element "TITLEx" represents report title, where suffix "x" represents sequential numbering.

SYNTAX

```
%LOT_TLF_Check
  (lot_path =
    ,lot_sheet_column =
    ,tlf_path =
    ,out_excel =
    ,condTLF =
    ,condLoT = );
```

MACRO PARAMETERS

1. lot_path = Mandatory parameter. Path and LoT excel file name with file extension. Only one file name at a time.

Ex: U:\output\ABCD_001.xls

2. lot_sheet_column = Mandatory parameter. Worksheet name, column names of output title numbers and output title names from the LoT excel file separated by "@" in that order. Only a single column may be specified for report titles and a single column for report numbers.

Ex: LOT@A@B

3. tlf_path = Mandatory parameter. Path and consolidated TLFs output file (.csv) with file extension (or) path and titles and footnotes file name with .xml extension. Only one file name at a time.

Ex: U:\output\stoutput.csv
U:\output\lsotop.xml

4. out_excel = Mandatory parameter. Name of output excel file, by default LOT_TLF_check.xls, created at path specified with tlf_path keyword parameter.

Ex: U:\output\out12346.xls

5. condTLF = Optional parameter. Filter condition for selecting outputs from consolidated TLFs output file (.csv) or .xml file to be compared.

Ex: where tablenum ne "Table 0.1"

6. condLOT = Optional parameter. Filter condition for selecting outputs from LoT excel file to be compared.

Ex: if a not in ("STUDY Standard Mocks", "Listings:")

Note: "a" in above example represents column name of LoT excel file.

INPUT FILES

LoT FILE

The LoT excel (.xls or .xlsx) file is the main input file and may have one or more worksheets containing the list of TLFs to be produced for a study. Only a single column should be specified for report titles and a single column for report numbers. If the data that is required exists in multiple LoT columns, users will need to concatenate those columns into a single column and assign the column header that is to be specified in the lot_sheet_column, before passing the LoT to lot_tlf_check.sas. For example, column G, in Figure 1 Sample LoT File below, the utility macro searches the LOT file for the worksheet name, column names of output title numbers and output title names concatenated with "@" e.g. table@a@g, in that specified order.

A	B	C	D	E	F	G
Table Number	Type	Table Title	Population			Table_title
Table 14.1.1.1	R	Summary of Subject Evaluation Groups	ITT Population	- ()		Summary of Subject Evaluation Groups - (ITT Population)
Table 14.1.1.2	R	Summary of Discontinuations from Study	ITT Population	- ()		Summary of Discontinuations from Study - (ITT Population)
Table 14.1.1.3	R	Summary of Discontinuations from Treatment Phase	Safety Population	- ()		Summary of Discontinuations from Treatment Phase - (Safety Population)
Table 14.1.2	R	Summary of Subject Accrual by Region, Country and Site	ITT Population	- ()		Summary of Subject Accrual by Region, Country and Site - (ITT Population)
Table 14.1.2.1	R	Summary of Demographic Characteristics	ITT Population	- ()		Summary of Demographic Characteristics - (ITT Population)
Table 14.1.2.1.2	R	Summary of Demographic Characteristics	Patients who were	- ()		Summary of Demographic Characteristics -

Figure 1. Sample LoT Excel File

CONSOLIDATED TLFs FILE

One of the comparison input files is a Consolidated TLFs (.csv) file, as shown in Figure 2. Sample Consolidated TLFs (.csv) File, which represents the list of all appended output files and comes with standard column names for the output title numbers (TABLENUM) and output title names (DSCRPT) or with .xml files and .map extension that should be located at the same drive path.

A	B
TITLE	TABLENUM
Treatment Related Adverse Events	Table 16.2.7.2.1
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (All Causalities) - Safety Population	Table 14.3.1.2.3.1
Summary of Serious Adverse Events by System Organ Class and Preferred Term (All Causalities) - Safety Population	Table 14.3.2.4.3.1
Summary of Serious Signs and Symptoms of Infusion Related Reactions by System Organ Class and Preferred Term (All Causalities) - Safety Population	Table 14.3.2.4.3.2
Treatment Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Safety Population	Table 14.3.1.3.3.1
Trastuzumab Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Safety Population	Table 14.3.1.3.3.2
Trastuzumab Related Signs and Symptoms of Infusion Related Reactions by System Organ Class and Preferred Term - Safety Population	Table 14.3.1.3.3.3
Signs and Symptoms of Infusion Related Reactions by System Organ Class and Preferred Term (All Causalities) - Safety Population	Table 14.3.1.2.3.2
Summary of Signs and Symptoms of Infusion Related Reactions by System Organ Class, Preferred Term and Maximum CTCAE Grade (All Causalities) - Safety Population	Table 14.3.1.2.9.1.2
Summary of Treatment-Emergent Cardiac Adverse Events by System Organ Class, High Level Group, Preferred Term and Maximum CTCAE Grade (All Causalities) - Safety Population	Table 14.3.1.2.9.1.1.2
Summary of Treatment-Emergent Adverse Events by System Organ Class, High Level Group, Preferred Term and Maximum CTCAE Grade (All Causalities) - Safety Population	Table 14.3.1.2.9.1.1.1

Figure 2. Sample Consolidated TLFs (.csv) File

The output file will have the following columns:

.csv columns	.xml tags
TABLENUM	<TFLTYPE> & <TFLNUM> for report number
DSCRPT	<TITLEx> for report titles
	Note: suffix "x" represents number associated with TITLE keyword defined in .xml file

TITLES AND FOOTNOTES FILE

The other type of comparison input file is an .xml file which contains report titles and footnotes, as shown in, Figure 3. Sample Titles And Footnotes .xml File, below.

```

<tfls>
  <PGMNAME>t_ae_socptincid</PGMNAME>
  <TFLTYPE>Table</TFLTYPE>
  <AREA>Report</AREA>
  <TFLNUM>14.X.X</TFLNUM>
  <SERIES>0</SERIES>
  <PGMED>-1</PGMED>
  <PGMDATE>17/11/2015</PGMDATE>
  <TESTED>0</TESTED>
  <SOURCE>Table 14.X.X</SOURCE>
  <TITLE1>Number (%) of Subjects Reporting Treatment Emergent Adverse Events (TEAE) with Incidence &gt;= X% in any</TITLE1>
  <TITLE2>Treatment Group - Safety Population</TITLE2>
  <FOOT2>Note: Classifications of adverse events are based on the MedDRA (version xx.X).</FOOT2>

```

Figure 3. Sample Titles And Footnotes .xml File

MACRO CALL

Assign the macro parameters as shown in Figure 4. Sample Macro Call.

- The location and filename of LoT to the macro parameter lot_path and the worksheet name and the columns of output title numbers and output title names for the macro parameter lot_sheet_column. Preprocessing might be required prior to using as input source file.

EX: Concatenation of columns done if title number data present in different columns.

- The location and filename of consolidated TLF file generated from bundle program (or) path of the .xml to macro parameter tlf_path.
- For optional parameters condlot and condtlf, specify any filter condition with “where” or “if” statement.
- For optional parameter, out_excel, by default will create LOT_TLF_Check.xls at the same location of tlf_path. Also the user can specify any name to output.

```

%lot_tlf_check
(tlf_path = U:\test01\tlf.csv
,lot_path = U:\test01\lot.xls
,out_excel =
,lot_sheet_column = lot @ a @ g */
,condtlf = where tablenum ne "Table 0.1"
,condlot = if a not in ("Table / Listing Number")

```

Figure 4. Sample Macro Call

PROGRAM CHECKS

The macro will generate messages such as those listed below, as part of its program checking. Programmers can take the appropriate action to address any errors, notes, or warnings.

- Missing value for lot_path/tlf_path macro parameters:
 - ERROR: <LOT_TLF_CHECK>: LOT file path cannot be blank or missing.
 - NOTE: <LOT_TLF_CHECK>: User Note: Macro expecting a valid LOT file path.
- Incorrect value for lot_path/tlf_path macro parameters:
 - ERROR: <LOT_TLF_CHECK>: LOT file does not exist at the given location.
 - NOTE: <LOT_TLF_CHECK>: User Note1: Macro expecting a valid LOT file with full path and extension
 - NOTE: <LOT_TLF_CHECK>: User Note2: Unix is case-sensitive. Check case if working with UNIX OS
 - Lot_path assigned with LOT file with .csv extension
 - ERROR: <LOT_TLF_CHECK>: LOT excel file should be .XLS or .XLSX files
 - NOTE: <LOT_TLF_CHECK>: User Note: please check the input LoT excel file extension
- Duplicate records (i.e same output title numbers or/and output title names) will be written to the log but removed from the output file.
 - ERROR: <LOT_TLF_CHECK>: Duplicate records with same output numbers present in LOT file
 - ERROR: <LOT_TLF_CHECK>: Duplicate records with same output numbers present in TLF consolidated file
 - Output number = Table 14.1.1.3 has duplicates. Please check LOT file.
 - Output number = Table Z0.3 has duplicates. Please check TLF consolidated file

OUTPUT FILE

This is the excel file generated by the lot_tlf_check.sas macro program with a list of the discrepancies that it identifies and containing columns for ‘LoT Title Number’, ‘LoT Title Name’, ‘TLF Title Number’, ‘TLF Title Name’, ‘Title Number Discrepancy’, and ‘Title Name Discrepancy’. See Figure 5. Sample Output Excel

File, below. The output excel file will be created at the same location of macro parameter tlf_path with all records read from both LoT and TLF files.

For matched records, the rows show white background with green color for text for column labels “Title number discrepancy” and “Title name discrepancy”. For records that have mismatches, the rows show yellow background with red color text for column labels “Title number discrepancy” and “Title name discrepancy”.

A	B	C	D	E	F
Summary of the comparison between LOT and consolidated TLF files of .csv or .xml					
LOT Title Number	LOT Title Name	TLF Title Number	TLF Title Name	Title Number Discrepancy	Title Name Discrepancy
Table 14.1.1.1	Subject Evaluation Groups	Table 14.1.1.1	Subject Evaluation Groups	Output numbers are same in both LOT and Consolidated TLF files	Output titles are same in both LOT and Consolidated TLF files
Table 14.1.1.3	Discontinuations from Treatment Phase - ITT Population	Table 14.1.1.3	Discontinuations from Treatment Phase - ITT Population	Output numbers are same in both LOT and Consolidated TLF files	Output titles are same in both LOT and Consolidated TLF files
Table 14.1.2.1	Demographic Characteristics – ITT Population	Table 14.1.2.1	Demographic Characteristics - ITT Population	Output numbers are same in both LOT and Consolidated TLF files	Discrepancies in output titles
Table 14.2.1	Population			Output number exist only in LOT file	Output titles exist only in LOT file
Table 14.2.2.1	Crough >20 µg/mL at Cycle 5 (Pre dose Cycle 6) – Per Protocol Population			Output number exist only in LOT file	Output titles exist only in LOT file
Table 14.2.2.2	Crough >20 µg/mL at Cycle 5 (Pre dose Cycle 6) - ITT Population	Table 14.2.2.2	Reporting Crough >20 µg/mL at Cycle 5 (Pre dose Cycle 6) - ITT Population	Output numbers are same in both LOT and Consolidated TLF files	Discrepancies in output titles

Figure 5. Sample Output Excel File

CONCLUSION

Reconciling report numbers and report titles can be a time-consuming task for programmers, if done manually. The lot_tlf_check.sas standard utility program is easy to use, platform independent, and automates the process, thereby reducing the amount of time required to prepare TLFs for CSR delivery and allowing programmers more time to focus on their priority tasks.

CONTACT INFORMATION

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