

A SAS Macro Application to Create Mock Tables in Statistical Analysis Plans for Phase I Clinical Studies

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ABSTRACT

A SAS macro %mock_table application is presented to easily and quickly generate mock tables for Phase I Statistical Analysis Plans (SAP). Mock tables are guides for programming final tables to present summaries of clinical study data. They are most commonly created using a word processor, e.g., Microsoft Word, and are often tedious to create from scratch or modify afterwards when columns and rows are added, deleted, or reformatted. By implementing with a simple excel template, macro %mock_table can be used to create almost all mock tables required by Phase I clinical studies efficiently. This paper will use an example Phase I oncology study to show how to prepare excel template sheets with minimal work and then use %mock_table to create mock tables immediately.

BACKGROUND

First in Human Phase I studies are designed to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of a drug. They are usually dose escalation studies with small sample sizes. In oncology, these studies are often used to identify a maximal tolerable dose (MTD). Therefore, the tables summarizing the clinical data generally fall into a fairly small number of types including numeric univariate statistics and counts of the number of unique subjects in certain categories, for example, univariate statistics are used for reporting lab chemistry results and some demographics such as age while counts are presenting to report the number of adverse events.

Good statistical practice dictates that a Statistical Analysis Plan (SAP) should be prepared for clinical studies (ICH E6, E9; references 1 and 2). The SAP describes statistical methods planned in more detail than in the study protocol and will include descriptions and mocks of the statistical data summaries. The mock tables focus on the layout of the rows and columns of each table and show arbitrary symbols such as an "X" to represent the unknown, future data.

Although this macro could be used for any clinical study, it provides the greatest advantage for a set of clinical studies that have similar design and endpoints. Unlike Phase I studies, later studies will often have many efficacy variables which are only common within a particular therapeutic area. These different study designs often have their own unique mock table layout due to different endpoints and multiple statistical analysis methods implemented. For example, late-stage oncology clinical trials generally have time-to-event endpoints while arthritis studies might instead have patient reported outcomes using a pain scale. Therefore, the mock tables can be quite different from one therapeutic area to another in later phases of drug development. It is not plausible to create one simple SAS macro to generate all mock tables for clinical trial studies in all phases but having a macro for a specific set of clinical studies with similar study objectives and endpoints would be beneficial.

No matter whether mock tables are created from scratch or by borrowing templates from a mock table library, the most tedious part of the task is modifying the number of columns and rows and resizing them so that all fit on the page in an aesthetically pleasing way. Labeling the column headers can also be time consuming. Under most circumstance, additional mock tables are created from scratch to satisfy needs unique to that study. However, using a word processor is not efficient to create many mock tables in a short time period. Modifying mock tables due to study amendments can also be especially time consuming using a word processor. The macro %mock_table and related excel sheet template were developed to meet such need.

MACRO %mock_table

There are three parameters in macro %mock_table:

Parameter	Purpose/Option
indata	Import the excel template data
pathout	Specify the location to save the mock table
tablename	Specify the mock table name in rtf format

EXAMPLE

The sample codes for calling the macro are shown below:

```
%mock_table ( indata=C:\Summary of Demographics.xlsx,  
              pathout=C:\,  
              tablename= t_14_1_5.rtf);
```

The mock table (t_14_1_5.rtf) shown below was generated using the above sample codes:

Table 14.1.5
Summary of Demographics
Full Analysis Set

Characteristics	Sample study Dose Cohort (mg/kg)							
	0.3 (N=xx)	0.6 (N=xx)	1.2 (N=xx)	1.8 (N=xx)	2.4 (N=xx)	3.0 (N=xx)	3.5 (N=xx)	Total (N=xx)
Age (years)								
N	xx	xx	xx	xx	xx	xx	xx	xx
Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Minimum	xx	xx	xx	xx	xx	xx	xx	xx
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Maximum	xx	xx	xx	xx	xx	xx	xx	xx
Missing	xx	xx	xx	xx	xx	xx	xx	xx
Age Group (years)								
<65	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>=65 [a]	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>=75 [a]	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Site								
<site 1>	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
<site 2>	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
...	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Percentages are based on the number of patients in each dose cohort.								
[a] Note that >=65 and >=75 age groups overlap and will result in double-counting of subjects.								
Note for Programmer: Missing not presented if no missing values.								

EXCEL TEMPLATE

The excel template is designed with great flexibility to create almost all possible layout of mock tables for phase I studies. Current template contains following five separate excel sheets: Tableinfo, Variables, DoseGroups, Continuous and Population.

Tableinfo sheet (7 columns):

Column	Value
Protocol	Protocol name
Pnote	Notes for programmers
Gnote	General footnotes
Tnumber	Table number
Ttitle	Table title
Stitle	Subtitle shown above the dose group columns
Col1name	First column label name

Variable sheet (7 columns):

Column	Value
Col1var	Main and subcategory variables display on the first column
Mainvar	Main category variables used to identify related subcategory variables
Page	Page number used to group main category variables together on the same page
Type	Variable type: continuous, categorical for main category variables and missing for sub category variables
Unit	Main category variable unit if applicable
Fsymbol	Footnote symbol in alphabetic or numeric order (i.e. a, b, c or 1,2,3) if applicable
Footnote	Footnotes if applicable for related variables

DoseGroups sheet (1 column):

Column	Value
Dose Groups	All dose groups and total (if needed)

Continuous sheet (2 columns):

Column	Value
Stat	Statistics for continuous variables
Stattype	Numeric format associated with these statistics

Population sheet (1 column):

Column	Value
Population	Population names (i.e. Full Analysis Set, Intend to Treat) shown under the table title

EXAMPLE (CONT.)

The example template (Summary of Demographics.xlsx) is shown below:

Tableinfo sheet:

Protocol	Pnote	Gnote	Tnumber	Ttitle	Stitle	Col1name
Sample Study	Missing not presented if no missing values.	Percentages are based on the number of patients in each dose cohort.	14.1.5	Summary of Demographics	Sample Study Dose Cohort (mg/kg)	Characteristics

Variable sheet:

Col1var	Mainvar	Page	Type	Unit	Fsymbol	Footnote
Age		1	continuous	Years		
Age Group		1	categorical	Years		
<65	Age Group					
>=65	Age Group				a	Note that >=65 and >=75 age groups overlap and will result in double-counting of subjects.
>=75	Age Group				a	Note that >=65 and >=75 age groups overlap and will result in double-counting of subjects.
Missing	Age Group					
Site		1	categorical			
<site 1>	Site					
<site 2>	Site					
...	Site					

DoseGroups sheet:

Dose Groups
0.3
0.6
1.2
1.8
2.4
3.0
3.5
Total

Continuous sheet:

Stat	Stattype
N	xx
Mean	xx.x
SD	xx.xx
Minimum	xx
Median	xx.x
Maximum	xx
Missing	xx

Population sheet:

Population
Full Analysis Set

CONCLUSION

%mock_table is a useful SAS macro to produce mock tables in SAPs for Phase I clinical studies. One more example was shown on the appendix to help further understanding how to use the macro and template. Instead of spending a lot time to create or modify each table using a word processor, statisticians or programmers can quickly run this macro using a pre-specified excel template to get the mock table they need. The excel template provides a lot of flexibility to generate common mock tables required by Phase I clinical studies. In practice, we use this macro to efficiently create all mock tables required for our Phase I oncology studies at Agensys. The macro and excel template method can be easily modified to create mock tables in other clinical studies with similar study objectives and endpoints.

REFERENCE

FDA Guidance for Industry: E3 Guideline for Industry: Structure and Content of Clinical Study Reports, July 1996.

FDA Guidance for Industry: E9 Statistical Principles for Clinical Trials, September 1998.

ACKNOWLEDGMENTS

I would like to thank Dr. Alan Hartford for coming up with the idea for a macro to generate mock tables and reviewing this paper.

CONTACT INFORMATION

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APPENDIX

The following example will show how to use the macro and template to create a shift table.

The sample codes for calling the macro are below:

```
%mock_table ( indata=C:\ Summary of Clinical Laboratory Shifts from Baseline.xlsx,
              pathout=C:\,
              tablename= t_14_3_12.rtf);
```

The sample codes create the following mock table (t_14_3_12.rtf):

Table 14.3.12
Summary of Clinical Laboratory Shifts from Baseline: Hematology, White Blood Cell Count
(cells/mm³)
Full Analysis Set

Sample Study Dose Cohort: 0.3 mg/kg	Baseline Grade[a]						
	Not Done	0	1	2	3	4	Total
Grade of Minimum Post-Baseline Value For Entire Study							
Not Done	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
0	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
4	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Total	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Note: [a] Baseline values are from pre-dose Day 1 if there is a value at pre-dose Day 1. Otherwise taken from Screening. Severity grade is based on NCI-CTCAE criteria (version 4.0). Note for Programmer: Repeat table for remaining dose cohorts. Repeat table for additional days and safety follow-up. Repeat for all hematology, coagulation, and chemistry.							

The example template (Summary of Clinical Laboratory Shifts from Baseline.xlsx) used to create mock table t_14_3_12.rtf is shown below:

Tableinfo sheet:

Protocol	Pnote	Gnote	Tnumber	Ttitle	Stitle	Col1name
Sample Study	Note for Programmer: Repeat table for remaining dose cohorts. Repeat table for additional days and safety follow-up.	Note: [a] Baseline values are from pre-dose Day 1 if there is a value at pre-dose Day 1. Otherwise taken from Screening.	14.3.12	Summary of Clinical Laboratory Shifts from Baseline: Hematology, White Blood Cell Count (cells/mm ³)	Baseline Grade[a]	Sample Study Dose Cohort: 0.3 mg/kg

	Repeat for all hematology, coagulation, and chemistry.	Severity grade is based on NCI-CTCAE criteria (version 4.0).				
--	--	--	--	--	--	--

Variable sheet:

Col1var	Mainvar*	Page	Type	Unit	Fsymbol	Footnote
Grade of Minimum Post-Baseline Value For Entire Study		1	categorical			
Not Done	Y					
0	Y					
1	Y					
2	Y					
3	Y					
4	Y					
Total	Y					

*note: 'Y' was used instead of 'Grade of Minimum Post-Baseline Value For Entire Study' in the Mainvar column to identify related subcategory variables for convenience concern.

DoseGroups sheet:

Dose Groups*
Not Done
0
1
2
3
4
Total

*note: Dose Groups name was used for consistence concern even though these values are not really dose groups.

Population sheet:

Population
Full Analysis Set

Note: the *Continuous* sheet is not included for this mock table since there is no summary for continuous variables.