



MODULAR MACROS FOR TFL PROGRAMMING

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WHY STANDARD?

- Reliable
- Good quality
- Cost saving
- Better Productivity
- Consistency
-



WHY SDTM?

- **FDA requires standards for their review**

- Universal platform for review of all data collected in clinical trials
- Data standards allow standard tools for FDA review of data
- Resolves challenges for review of atypical data

- **Sponsor advantages**

- Flexibility for in-stream changes to protocol and/or (e)CRF
- Efficient data submissions
- Shorter timelines for data submission and review
- Trial design standards and library for trial components
- Universal; allows for efficient sharing
- Cost and time benefits

SDTM DEVELOPMENT

- SDTMIG 3.1.1 – first usable version from AUG-2005, based on SDTM 1.1, having 15 domains plus the Trial Design and SUPP/RELREC structure described
- SDTMIG 3.1.2 – released in NOV-2008 , based on SDTM 1.2, many corrections for details, containing 24 domains, the FA domain plus the previous Trial Design and Related Records Domains
- SDTMIG 3.1.3 – released in JUL-2012 , based on SDTM 1.3, using the 3.1.2 version, new Oncology Disease-specific domains (RS, TR and TU), plus amendment for DM, coding of Event domains and TS
- SDTMIG 3.2 – released in NOV-2013, updated version with complete new design (portfolio-pdf, using imbedded files), 11 additional domains

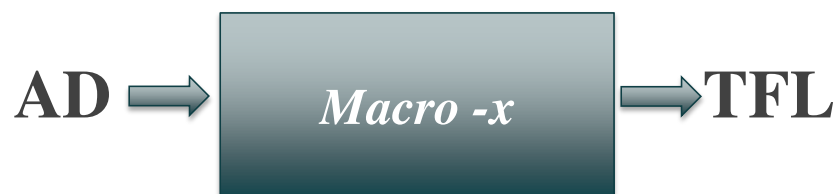
ARE TFL STANDARD IN PHARMA INDUSTRIES?



- **Company A / Company B /**



TYPICAL PHARMA – COMPANY X APPROACH



STANDARD LIBRARY& STANDARD MACROS

- **High efficiency**
- **High productivity**

**but, like the same iPhone may with several
different finish.....**

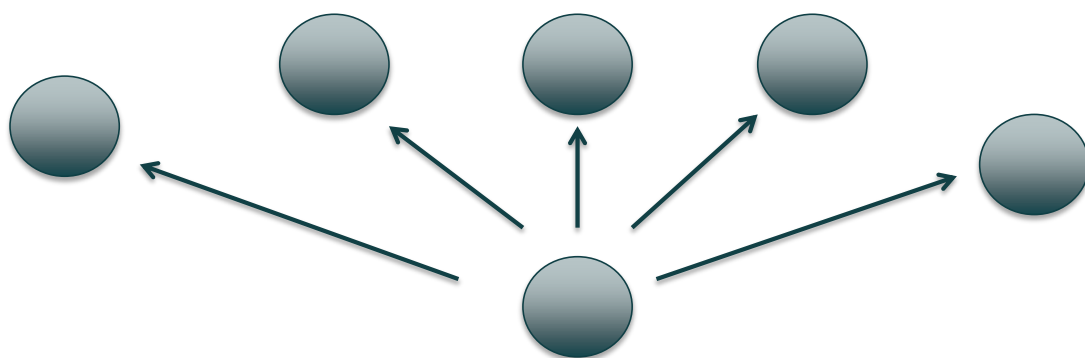


DIFFERENT FEASIBILITY

- Easy to reach agreement within one company



- But, when



INCREDIBLE LEGO



A TYPICAL STANDARD TABLE

System Organ Class Preferred Term	Trt A N=xx	Trt B N=xx	Total N=xx	P-value (Fisher's Exact Test)
Total Number of Treatment Emergent Adverse Events (TEAEs)	xx	xx	xx	N/A
Number of Subjects With at Least One TEAE N (%) (95% CI)	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	x.xxx
System Organ Class 1	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	x.xxx
Preferred Term 1	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	x.xxx
Preferred Term 2	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	x.xxx
System Organ Class 2	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	x.xxx
Preferred Term 1	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	x.xxx
Preferred Term 2	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	xx (xx.x) (xx, xx)	x.xxx

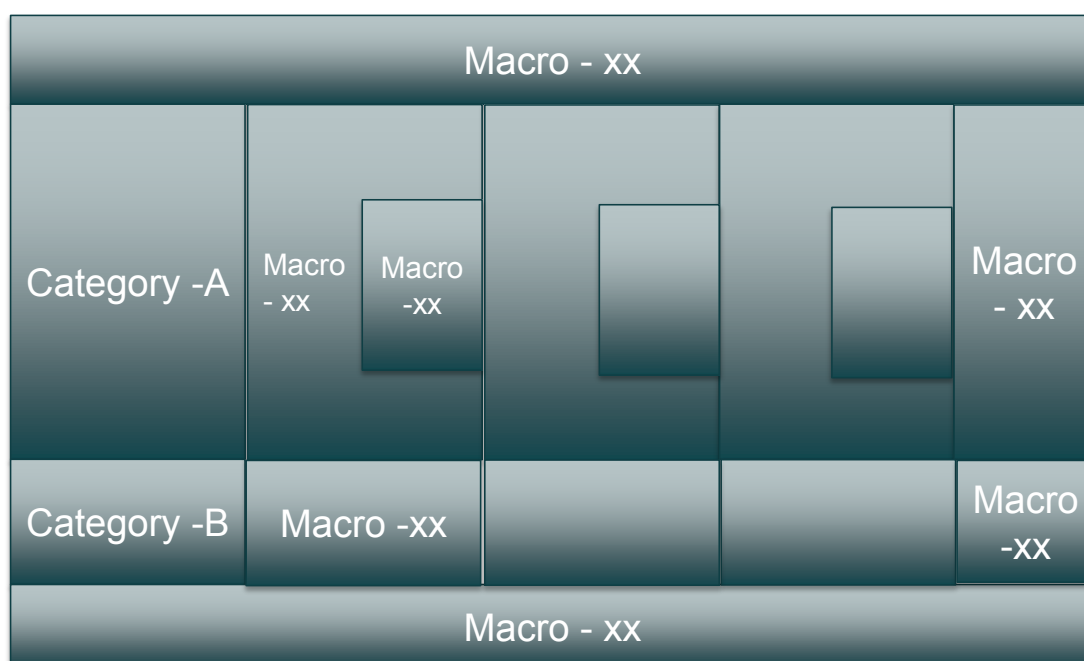
A TYPICAL STANDARD TABLE

Hematocrit (unit)	Trt A	Trt B	Total
Baseline			
N	XX	XX	XX
Mean (SD)	XX(XX.X)	XX(XX.X)	XX(XX.X)
Median	XX.X	XX.X	XX.X
IQR (Q1-Q3)	XX.X- XX.X	XX.X- XX.X	XX.X- XX.X
Range	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Week 1			
N	XX	XX	XX
Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Median	XX.X	XX.X	XX.X
IQR (Q1-Q3)	XX.X- XX.X	XX.X- XX.X	XX.X- XX.X
Range	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Change from Baseline			
N	XX	XX	XX
Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Median	XX.X	XX.X	XX.X
IQR (Q1-Q3)	XX.X- XX.X	XX.X- XX.X	XX.X- XX.X
Range	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value (Wilcoxon's Signed-rank Test Compare to baseline value)	X.XXX	X.XXX	X.XXX

A TYPICAL STANDARD TABLE

Timepoint Treatment	n/N	(%)	95% CI	95% DIFF CI
Time 1				
XXX	xx /xx	(xx.xx)	(xx.xx, xx.xx)	
YYY	xx /xx	(xx.xx)	(xx.xx, xx.xx)	(xx.xx, xx.xx)
Time 2				
XXX	xx /xx	(xx.xx)	(xx.xx, xx.xx)	
YYY	xx /xx	(xx.xx)	(xx.xx, xx.xx)	(xx.xx, xx.xx)
Time 3				
XXX	xx /xx	(xx.xx)	(xx.xx, xx.xx)	
YYY	xx /xx	(xx.xx)	(xx.xx, xx.xx)	(xx.xx, xx.xx)
Time 4				
XXX	xx /xx	(xx.xx)	(xx.xx, xx.xx)	
YYY	xx /xx	(xx.xx)	(xx.xx, xx.xx)	(xx.xx, xx.xx)

MODULAR MACROS



FEW POINTS TO CONSIDER

- AD with certain structure required (ADaM preferred)
- Not a simple replacement of certain procedure (e.g. proc summary, etc), good flexibility for the further-imputation required
- Easily to apply in constructing the general TFLs
- Robustness
- Macros to facilitate AD creation

MACRO TOOLKIT / USE

Example for Descriptive table

%Summary (Age,
Height, Weight, BMI)

%Freq (Sex, Race)

Prep4tab

%TitleFootnote

%Table

%Summary built up from the following blocks:

Sort macro: To prepare data for summary.

Univariate/mean procedures.

Transpose macro: To prepare data for output.

Alignment macro: Align data within columns e.g. correct number of d.p.

%Freq built up from the following blocks:

Sort macro: To prepare data for summary.

Frequency procedure.

Transpose macro: To prepare data for output.

Alignment macro: Align data within columns e.g. correct number of d.p.

Using these macros will gives us efficiency gains.

ESTIMATED EFFICIENCY GAINS

Example for Descriptive table: (conservative estimate)

Script without Modular Macros:

- Summary+Freq (incl. Align etc.)
- Other code(e.g. CI imputation)
- Titles/Footnotes
- Table (PROC REPORT)

Script including Modular Macros:

- %Summary+%Freq (incl. Align etc.) = 25% gain.
- Other code = 50% gain
- Titles/Footnotes = 75% gain
- Table (PROC REPORT) = 50% gain.

FLEXIBILITY AND ROBUSTNESS

To combine Calculation (Means/Freq/etc) with common data manipulation tasks
(sorting/transposing/alignment/concatination/etc.)

These Macros will cover the majority of the general TLF Programming tasks.

Each Macro offers the flexibility to be run in open code e.g.
%Summary+Statistical Code+%Table or %Summary+SGPLOT.

MACRO DEVELOPMENT

Various methods to calculate confidence interval CI Individual proportion, CI for difference of proportion with exact method, wilson score method, F-M method, CI for absolute value, etc (e.g. %wilson)

P value for different comparison

Template for efficacy endpoints involving statistical methods (Proc lifetest / Proc phreg / Proc mixed / Proc anova, etc)

FACILITY MACROS

Title footnote macro

Report macro

Sort macro (when multi-level involved, e.g. AE tables)

Unique event dataset filtering (e.g. maximum severity)

More.....

TEMPLATE PROGRAMS WITH MODULAR MACROS

Summary tables (demographic / CM / MH /DS, etc)

AE tables (SOC/PT, Maximum Intensity, etc)

Laboratory tables (summary / Shift Tables, etc)

Efficacy (Lifetest, Hazard ratio, etc)

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FUTURE CONSIDERATION

TFL Standard across industry

Key component library of TFLs

More modular macros with involvement of TA area
Standards

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THANK YOU!