



Pioneering science delivers vital medicines™

Using Metadata to Create Table Producing SAS® Programs at Amgen Inc.

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The Problem

Existing libraries of standard reporting code are 10+ years old

- They are difficult to use and maintain
- Requirements have been layered on
- Redundant code as functionality has been replaced
- AE tiered table macro has 9554 lines of code, a 60 page user manual, up to 76 input parameters with a log >100,000 lines!

Code is duplicated across programs leading to:

- Duplicated maintenance
- Inconsistency when a change is made in one program but not others

Bug fixes & enhancements are time consuming:

- Teams unnecessarily developing their own solutions

Staff can be hard to move between teams

The Solution

A suite of macros that have a single specific function

- Macros are combined and built upon to form modular macros that can be used to build any table

New problem...

- Lots of new macros that need to be understood

Requirements for a better solution

- Could we simplify the use of these new macros?
- Flexible enough to produce most tables?
- Maximize the re-use of information, reducing duplication of effort?
- Something intuitive?
- Maybe a nice WYSIWYG interface?
- Fully validated to reduce burden of QC?

TFLGen was born...

The Anatomy of a Table

Table 14-2.1.1. Baseline Demographics
(Primary Analysis Set)

	Comparator		AMG-Active	
	10 mg (N = 21)	20 mg (N = 25)	5 mg (N = 24)	10 mg (N = 24)
Sex - n(%)				
Male	13 (61.9)	12 (48.0)	10 (41.7)	13 (54.2)
Female	8 (38.1)	13 (52.0)	14 (58.3)	11 (45.8)
Age (years)				
n	21	25	24	24
Mean (SD)	55.2 (22.5)	53.6 (16.8)	56.1 (19.0)	52.5 (20.4)
Median	56.0	53.0	55.5	50.0
Q1, Q3	37.0, 69.0	44.0, 63.0	43.0, 71.5	40.0, 65.5
Min, Max	21, 88	20, 87	19, 87	21, 90
Age - n (%)				
< 65 years	14 (66.7)	20 (80.0)	15 (62.5)	18 (75.0)
≥ 65 years	7 (33.3)	5 (20.0)	9 (37.5)	6 (25.0)
Age by sex ¹				
Male subjects - n (%)				
< 65 years	8 (61.5)	11 (91.7)	6 (60.0)	10 (76.9)
≥ 65 years	5 (38.5)	1 (8.3)	4 (40.0)	3 (23.1)
Female subjects - n (%)				
< 65 years	6 (75.0)	9 (69.2)	9 (64.3)	8 (72.7)
≥ 65 years	2 (25.0)	4 (30.8)	5 (35.7)	3 (27.3)

N = number of subjects randomized and dosed in the safety analysis set.
¹ Percentages based on number of subjects of each sex.

Program: /home/nlyon/tflgen_training/exercise/tables/program/-dm-sum-pas.sas
Output: t14-02-001-001-dm-sum-pas.rtf (Date Generated: 25AUG15:07:45:42) Source: adam.adae

Titles
Footnotes
File names
Font size
Page orientation

Population and subsets
Treatment column headers
File locations

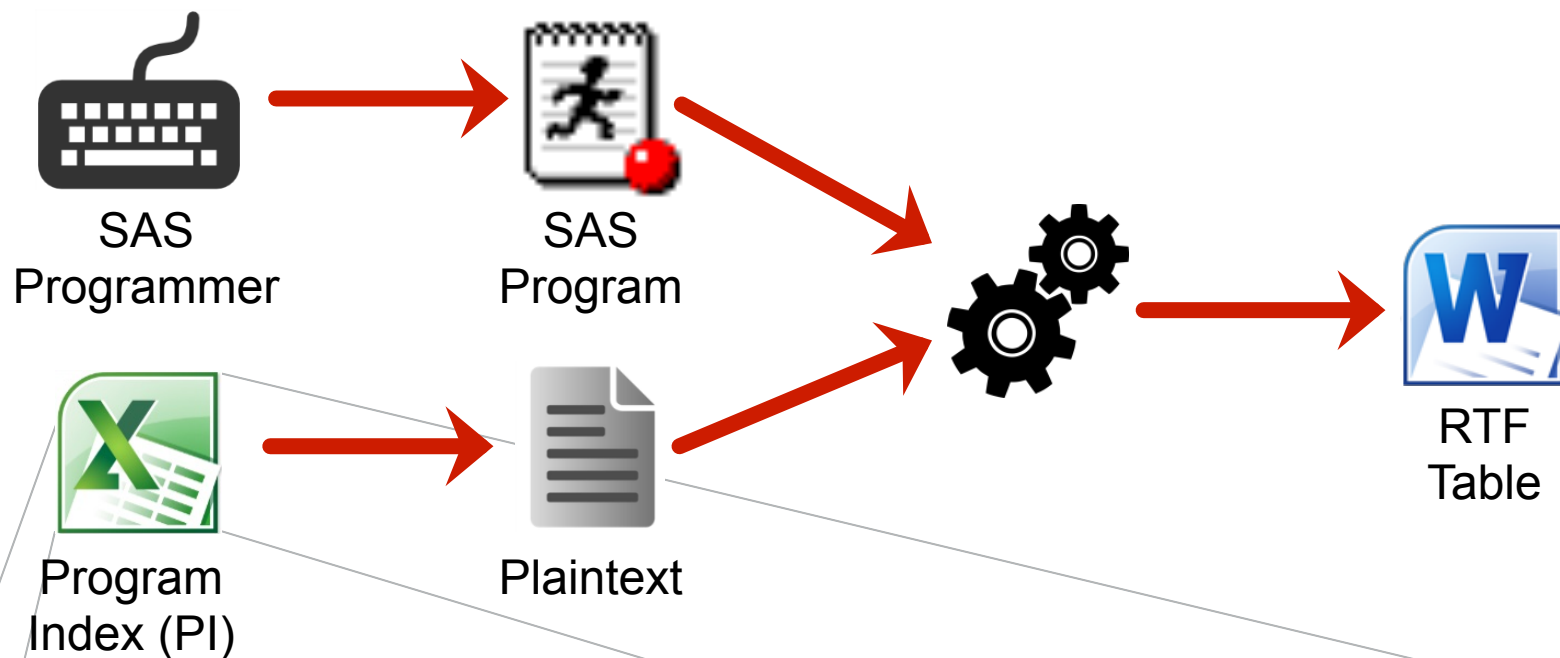
Statistics
Decimal precision
Labels
By-processing
Blank rows

Output
Specific

Analysis
Level

Table
Shell

Pre-TFLGen Process Flow



Output Number	Titles	Footnotes	Output Name	Program Name
14-2.1.1	Baseline Demographics{\\line}{Primary Analysis Set)	N = number of subjects randomized and dosed in the safety analysis set.{\\line} ¹ Percentages based on number of subjects of each sex.	t14-02-001-001-dm-sum-pas.rtf	t-dm-sum-pas.sas
14-6.2.1	Treatment Emergent Adverse Events by System Organ Class and Preferred Term{\\line}{Safety Analysis Set)	N = number of subjects randomized and dosed in the safety analysis set.{\\line}Coded using MedDRA version &meddrav..	t14-06-002-001-ae-soc-pref-saf.rtf	t-ae-soc-pref-saf.sas

Analysis Level: Populations/Subsets

Populations

Population	Where Clause
(Safety Analysis Set)	saffl = 'Y'
(Primary Analysis Set)	pasfl = 'Y'
(All Randomized Subjects)	n(randdt)

Subsets of Populations

Subset	Where Clause
Subjects with Anemia at Baseline	< blhgb < 10
Male subjects Only	sexn = 1
Female Subjects Only	sexn = 2

- **Population/Subset** = Names of populations and subsets
- **Where Clause** = SAS expressions to describe them

Analysis Level: Treatment Columns

Treatment Column Headers

Header	Upper Span Label	Lower Span Label	Treatment	Column Label	Data Set	Variable	Quant	Where Clause	Numerator Where	Column Width	Column Alignment
safety			1	Comparator	adam.adsl			trt01an in(1,2)		1	C
safety			2	AMG-Active	adam.adsl			trt01an in(3,4)		1	C
safety			3	Total	adam.adsl			trt01an in(1,2,3,4)		1	C
primary		Comparator	1	10 mg	adam.adsl	trt01an	1			1	C
primary		Comparator	2	20 mg	adam.adsl	trt01an	2			1	C
primary		AMG-Active	3	5 mg	adam.adsl	trt01an	3			1	C
primary		AMG-Active	4	10 mg	adam.adsl	trt01an	4			1	C

- **Header** = Name of header
- **Span Labels** = Labels above multiple treatment group columns
- **Treatment** = Number showing treatment group column order
- **Column Label** = Label for each treatment group column
- **Data Set** = Containing data that describes each treatment group
- **Variable/Quant** = Describes each treatment group
- **Where Clause** = Describes treatment group using SAS expressions
- **Numerator Where** = Limits subjects, but does not affect denominator
- **Column Width/Alignment** = Width in inches / centre, left or right alignment

Analysis Level: File Locations

Table Template Locations

Template Location	UNIX Directory
therapeutic_area	/home/therapeutic_area/docs/templates
product	/home/therapeutic_area/product/docs/templates
protocol	/home/therapeutic_area/product/protocol/docs/templates

- **Template Location** = Name given to template locations
- **UNIX Directory** = UNIX paths for each specified location

General Information

Item	Description	Value
table_program_dir	File location for table programs	/home/therapeutic_area/product/protocol/analysis/tables/program
table_metadata_dir	File location for table metadata sets	/home/therapeutic_area/product/protocol/analysis/tables/metadata
table_output_dir	File location for table outputs	/home/therapeutic_area/product/protocol/analysis/tables/output
custom_init_macro_dir1	First location searched for custom macros	/home/therapeutic_area/product/protocol/analysis/macros
custom_init_macro_dir2	Second location searched for custom macros	/home/therapeutic_area/product/macros
format_catalog1	First catalog searched for custom formats	/home/therapeutic_area/product/protocol/analysis/formats/formats.sas7bcat
format_catalog2	Second catalog searched for custom formats	/home/therapeutic_area/product/formats/formats.sas7bcat
adam_dir	File location for ADaM data sets	/home/therapeutic_area/product/protocol/analysis/datasets/adam
subject_var	Name of the subject/patient variable	usubjid

- **Item** = Keyword for metadata stored in the row
- **Description** = To let users know what the keywords refers to
- **Value** = Value of the metadata

Table Shell Information

Baseline Demographics

As metadata in Excel

[Headers]								
Metadata Item	Leftmost Table Column	Treatment Columns	Statistics	Leftmost Table Column Indent	Data Set	Variable	Variable Value	Where Clause
Label	Sex - n (%)			0				
Statistic	Male	x (x.x)	n percent	1	adam.adsl	sexn	1	
Statistic	Female	x (x.x)	n percent	1	adam.adsl	sexn	2	
Blank row								
Label	Age (years)			0				
Statistic	n	x	n	1	adam.adsl	age		
Statistic	Mean SD	x.x (x.x)	mean stdev	1	adam.adsl	age		
Statistic	Median	x.x	median	1	adam.adsl	age		
Statistic	Q1, Q3	x.x, x.x	q1 q3	1	adam.adsl	age		
Statistic	Min, Max	x, x	min max	1	adam.adsl	age		
Blank row								
Label	Age group - n (%)			0				
Statistic	< 65 years	x (x.x)	n percent	1	adam.adsl			.<age<65
Statistic	≥ 65 years	x (x.x)	n percent	1	adam.adsl			age>=65
Statistic	≥ 75 years	x (x.x)	n percent	1	adam.adsl			age>=75

Template Editor

Metadata Item	Leftmost Table Column	Treatment Columns	Statistics	Leftmost Table Column Indent	Data Set	Variable	Variable Value	Where Clause	Display Format	Alternative Denominator for Percentage [Where Clause]	By Display Variable	Sort Section ID Number	Sort Direction	Decimal Precision Variable
SPS root template name	root_standard_004													
Zero handling for geometric statistics	WARN													
Minimum % to report any column to														
Data set with subject-years data														
Subject-years exposure formula														
First event (in years) exposure formula														
Rate multiplier (in years)														
Drop rows if all categorical counts zero?	N													
Sections to wrap over page?	N													
Leftmost column width in inches	AUTO													
Leftmost column alignment	L													
Leftmost column label		[Headers]												
Treatment columns subject-years display														
Treatment columns big N display		(N = xx)												
Treatment columns statistic labels														
Blank row														
Label	Sex - n (%)			0										
Statistic	Male	x (x.x)	n percent	1	adam.adsl	sexn	1							
Statistic	Female	x (x.x)	n percent	1	adam.adsl	sexn	2							
Blank row														
Label	Age (years)			0										
Statistic	n	x	n	1	adam.adsl	age								
Statistic	Mean SD	x.x (x.x)	mean stdev	1	adam.adsl	age								
Statistic	Median	x.x	median	1	adam.adsl	age								
Statistic	Q1, Q3	x.x, x.x	q1 q3	1	adam.adsl	age								
Statistic	Min, Max	x, x	min max	1	adam.adsl	age								

- **General Metadata** = Captures metadata that applies to the whole of a generated table
- **Column Metadata** = Captures metadata that applies to leftmost table column and treatment column headers
- **Main Body Metadata** = Captures metadata to generate statistics

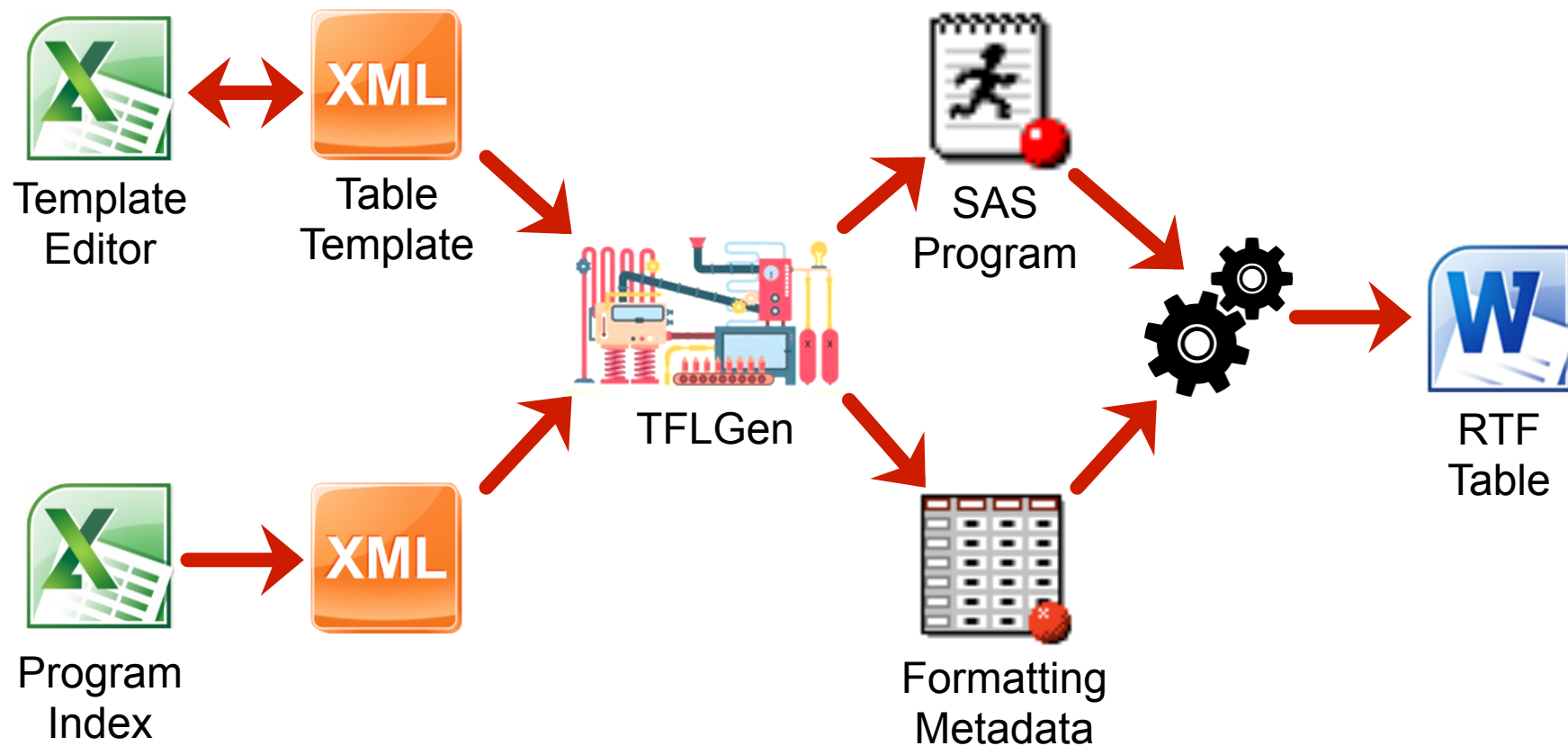
Extending the PI: Linking the Metadata

Linking TFLGen metadata with output level metadata

Population	Subset	Numerator Where	Header	Template Location	Template	Sort Section	Sort Source Treatment	Body Font Height	Orientation
(Safety Analysis Set)	Female Subjects Only	trtemfl = 'Y'	safety	therapeutic_area	t-ae-pt	1	3 2 1	10	Portrait
									Landscape Portrait

- **Population** = Drop-down list created from populations worksheet
- **Subset** = Drop-down list created from subsets worksheet
- **Numerator Where** = Limits all data used for statistic generation
- **Header** = Drop-down list created from headers worksheet
- **Template Location** = Drop-down list from template location worksheet
- **Template** = Name of the template required for the table
- **Sort Section** = Describes table sorting based on numbers
- **Sort Source Treatment** = Describes table sorting based on numbers
- **Body Font Height** = Font size to use in main body of table
- **Orientation** = Landscape or portrait

TFLGen Process Flow



Under the Hood

TFLGen application run against a specific Program Index

- Checks Program Index contents for validity against a schema
- Creates SAS data set of the Program Index
- Creates short SAS program for every record in the PI

TFLGen then runs each SAS program in parallel batches

- Checks table template contents for validity against a schema
- Creates SAS data set of the table template
- Combines the Program Index and table template data sets into a single table specific metadata data set
- Validates the metadata data set

If validation passes

- Compares the metadata data set against previous version, if present
- Saves metadata data set to permanent location
- Feeds metadata data set through macros that generate SAS program

Create TFLGen report of successes/failures

TFLGen Report

TFLGen Metadata Generation Report

PI: /home/nlyon/tflgen_training/exercise/docs/pi/PHUSE_PI_working.xlsm

Mode: CREATE Date: 26-Aug-2015 01:24:20 Requested Template: ALL

Requested TFLs: ALL

TFL Details

(14-6.2.1) t-ae-soc-pref-saf.rtf (Allow Code Generation: Yes)

Template: /home/nlyon/tflgen_training/exercise/docs/templates/phuse-ae-real.xlsm Location Name: protocol

NOTICE: Metadata data set does not currently exist.

NOTICE: Metadata data set requires generation.

NOTICE: SAS program requires generation.

NOTICE: Metadata data set has been generated.

NOTICE: SAS program has been generated.

(14-2.1.1) t-dm-sum-pas.rtf (Allow Code Generation: Yes)

Template: /home/nlyon/tflgen_training/exercise/docs/templates/phuse-dm-real.xlsm Location Name: protocol

ERROR: File ADAM.ADXL.DATA does not exist.

ERROR: [Template, Row 31] DENOMINATOR (sexn = 1) is not valid when applied to the DATA_SET adam.adxl

ERROR: [Template, Row 20] VARIABLE age does not exist in the specified DATA_SET adam.adxl

ERROR: [Template, Row 23] STATISTIC 'mn max' contains the invalid value 'mn'

ERROR: [Template, Row 31] DATA_SET adam.adxl does not exist in the specified library

ERROR: Previous errors prevent metadata data set generation. Please fix these errors and rerun TFLGen.

ERROR: Previous errors prevent program generation. Please fix these errors and rerun TFLGen.

Report created on 26-Aug-2015 01:24:20 by TFLGen version: 01.02.00

Problem 1: Too Many Templates

Too many near-identical table templates being generated

- Changeable parameters similar to SAS macro variables
- New worksheet on Program Index

Metadata Item	Leftmost Table Column	Treatment Columns	Statistics	Leftmost Table Column Indent	Data Set	Variable	Sort Section ID Number	Sort Direction
Leftmost column label	System Organ Class Preferred Term	[Headers]						
Treatment columns subject-years display								
Treatment columns big N display		(N = xx)						
Treatment columns statistic labels		n (%)						
Blank row								
Tier level 0 (statistic)	Subjects experiencing &level_0_text	x (x.x)	n percent	0				
Blank row								
Tier level 1 (statistic)	System Organ Class	x (x.x)	n percent	0	adam.adae	aebodsys	1	descending
Tier level 2 (statistic)	Preferred Terms	x (x.x)	n percent	1	adam.adae	aedecod	2	descending

Base Output Name	Parameter	Value
t-ae-soc-pref-fas.rtf	level_0_text	an adverse event
t-ae-soc-pref-ser-fas.rtf	level_0_text	a serious adverse event
t-ae-soc-pref-disc-fas.rtf	level_0_text	an adverse event leading to discontinuation

- **Base Output Name** = Output that parameter to be resolved in
- **Parameter** = Name of parameter to be resolved
- **Value** = String to replace parameter with

Problems 2: TFLGen Too Rigid

Users limited to using data sets directly from a library

- Allow users to enter custom code that runs at start of generated program
- Create work data sets for use within generated program
- Create macro variables that can resolve when program runs

Base Output Name	Custom Code to Include at Start of Program
t-dm-sum-pas.rtf	<pre>*--- Derive BMI ---; data bmi; set adam.adsl; if n(wgt,hgt) = 2 then bmi = wgt / (hgt**2); run;</pre>

- **Base Output Name** = Output that custom code required for
- **Custom Code to Include at Start of Program** = Custom code

Problem 3: Simplifying QC

How to QC programs generated by TFLGen?

- Black text shows data that is displayed
- Red text shows underlying metadata
- Blue highlighting shows changes to metadata since last created

Table 14-2.1.1. Baseline Demographics
(Primary Analysis Set)
Population: pasfl = 'Y'

	Comparator		AMG-Active	
	10 mg adam.adsl. (trt01an=1) (N = xx)	20 mg adam.adsl. (trt01an=2) (N = xx)	5 mg adam.adsl. (trt01an=3) (N = xx)	10 mg adam.adsl. (trt01an=4) (N = xx)
drop_zero_row_flag:N subject_var:usubjid				
Sex - n(%)				
Male adam.adsl.(sexn=1)	x (x.x) n percent	x (x.x)	x (x.x)	x (x.x)
Female adam.adsl.(sexn=2)	x (x.x) n percent	x (x.x)	x (x.x)	x (x.x)
Age (years)				
n adam.adsl.age	x n	x	x	x
Mean (SD) adam.adsl.age	x.x (x.x) mean stdev	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median adam.adsl.age	x.x median	x.x	x.x	x.x
Q1, Q3 adam.adsl.age	x.x, x.x q1 q3	x.x, x.x	x.x, x.x	x.x, x.x
Min, Max adam.adsl.age	x, x min max	x, x	x, x	x, x
Age - n (%)				
< 65 years adam.adsl(<age<65)	x (x.x) n percent	x (x.x)	x (x.x)	x (x.x)
≥ 65 years adam.adsl(age>=65)	x (x.x) n percent	x (x.x)	x (x.x)	x (x.x)
Age by sex ¹				
!adam.adsl.sexnl subjects - n (%)				
< 65 years adam.adsl(<age<65)	x (x.x) n percent(sexn>.)	x (x.x)	x (x.x)	x (x.x)
≥ 65 years adam.adsl(age>=65)	x (x.x) n percent(sexn>.)	x (x.x)	x (x.x)	x (x.x)

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N = number of subjects randomized and dosed in the safety analysis set.
¹ Percentages based on number of subjects of each sex.

Program: /t-dm-sum-pas.sas
Output: t_dm_sum_pas.rtf (Date Generated: 25AUG15:07:44:30) Source: adam.adsl



Problem 4: Programming and Testing

Developing many interconnected macros

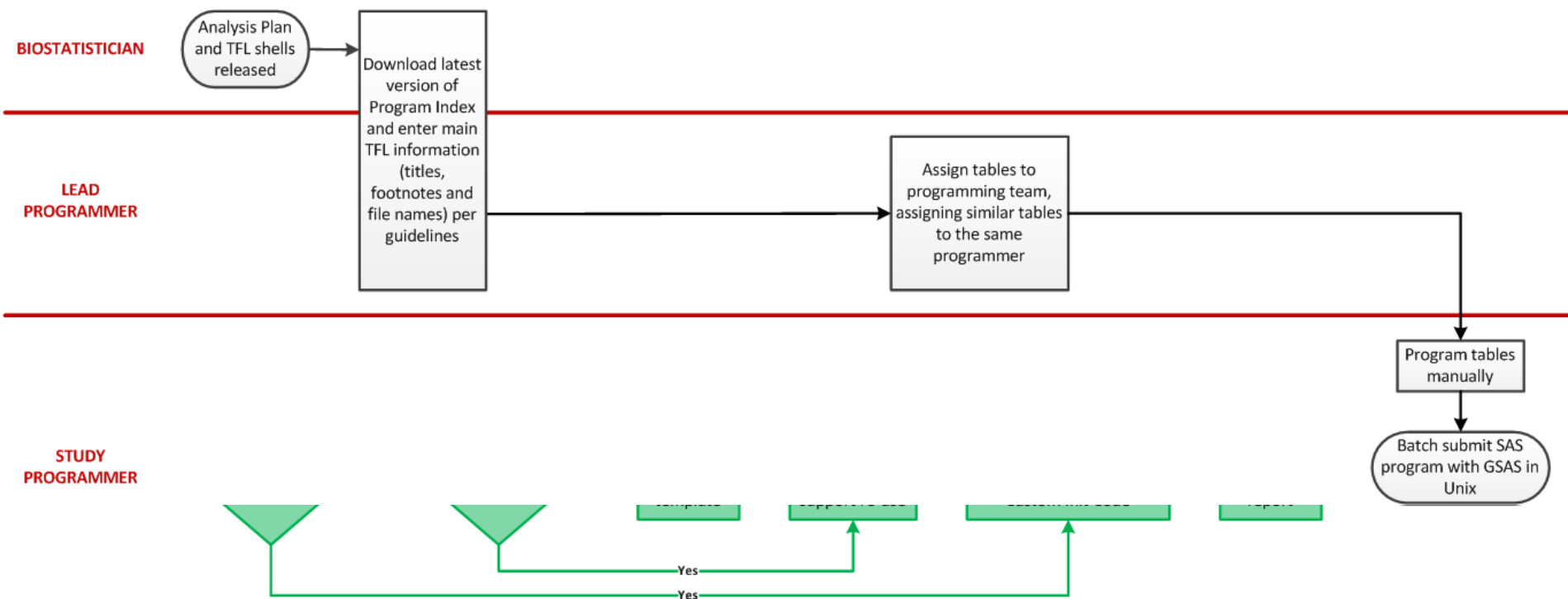
- Hard for multiple developers to work on modules
 - Decisions have ramifications for other developers' work
- One programmer oversaw the primary development
- Avoid tramping macro parameters
 - Data sets were used to pass information across macros
- Areas of commonality identified and distributed amongst team

Testing TFLGen for robustness, reliability and validity

- It must run without problems, generating the expected numbers every time
- Every module is unit tested to ensure that it follows requirements
- Once complete, integration testing was performed
 - Program Index and table templates to test all functions
 - The results were dual-programmed for validity
- Limited production roll-out

Integrating TFLGen into a Study

Pre-TFLGen



TFLGen Table Coverage

TFLGen can generate programs for:

- Demography / Patient disposition
- Analysis set inclusion and exclusion
- Baseline characteristics
- Medical history
- Protocol deviations
- Adverse events (n %)
- Exposure-adjusted adverse events
- Concomitant medications
- Safety summaries by visit (Labs/Vitals/ECG)
- Lab shift tables
- Pretty much any table with n, % or continuous summary statistics

TFLGen does not cover:

- Treatment differences
- Inferential statistics

Example 1: Baseline Demography

Metadata Item	Leftmost Table Column	Treatment Columns	Statistics	Leftmost Table Column Indent	Data Set	Variable	Variable Value	Where Clause
SPS root template name	root_standard_004							
Zero handling for geometric statistics	WARN							
Minimum % to report any column to								
Data set with subject-years data								
Subject-years exposure formula								
First event (in years) exposure formula								
Rate multiplier (in years)								
Drop rows if all categorical counts zero?	N							
Sections to wrap over page?	N							
Leftmost column width in inches	AUTO							
Leftmost column alignment	L							
Leftmost column label		[Headers]						
Treatment columns subject-years display								
Treatment columns big N display		(N = xx)						
Treatment columns statistic labels		n (%)						
Blank row								
Label	Sex - n (%)			0				
Statistic	Male	x (x.x)	n percent	1	adam.adsl	sexn	1	
Statistic	Female	x (x.x)	n percent	1	adam.adsl	sexn	2	
Blank row								
Label	Age (years)			0				
Statistic	n	x.x	n	1	adam.adsl	age		
Statistic	Mean (SD)	x.x (x.x)	mean stdev	1	adam.adsl	age		
Statistic	Median	x.x	median	1	adam.adsl	age		
Statistic	Q1, Q3	x.x, x.x	q1 q3	1	adam.adsl	age		
Statistic	Min, Max	x, x	min max	1	adam.adsl	age		
Blank row								
Label	Age group - n (%)			0				
Statistic	< 65 years	x (x.x)	n percent	1	adam.adsl			.<age<65
Statistic	≥ 65 years	x (x.x)	n percent	1	adam.adsl			age>=65
Statistic	≥ 75 years	x (x.x)	n percent	1	adam.adsl			age>=75

Example 1: Baseline Demography

**Table 14-2.1.1. Baseline Demographics
(Full Analysis Set)**

	Comparator (N = 50) n (%)	AMG-Active (N = 49) n (%)	Total (N = 99) n (%)
Sex - n (%)			
Male	26 (52.0)	27 (55.1)	53 (53.5)
Female	24 (48.0)	22 (44.9)	46 (46.5)
Age (years)			
n	50.0	49.0	99.0
Mean (SD)	51.8 (17.9)	55.1 (17.1)	53.4 (17.5)
Median	51.0	53.0	53.0
Q1, Q3	41.0, 66.0	43.0, 64.0	42.0, 66.0
Min, Max	19, 87	22, 90	19, 90
Age group - n (%)			
< 65 years	35 (70.0)	37 (75.5)	72 (72.7)
≥ 65 years	15 (30.0)	12 (24.5)	27 (27.3)
≥ 75 years	7 (14.0)	8 (16.3)	15 (15.2)

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N = Number of subjects in the analysis set.

Program: /home/nlyon/tflgen_training/exercise/tables/program/t-dm-sum-base-fas.sas
Output: t-dm-sum-base-fas.rtf (Date Generated: 11MAY16:06:31:15) Source: adam.adsl

Example 2: Safety Summary

Metadata Item	Leftmost Table Column	Treatment Columns	Statistics	Leftmost Table Column Indent	Data Set	Variable	Where Clause	Display Format	Decimal Precision Variable
SPS root template name	root_standard_004								
Zero handling for geometric statistics	WARN								
Minimum % to report any column to									
Data set with subject-years data									
Subject-years exposure formula									
First event (in years) exposure formula									
Rate multiplier (in years)									
Drop rows if all categorical counts zero?	N								
Sections to wrap over page?	N								
Leftmost column width in inches	AUTO								
Leftmost column alignment	L								
Leftmost column label		[Headers]							
Treatment columns subject-years display									
Treatment columns big N display		(N = xx)							
Treatment columns statistic labels									
Blank row									
Label	Baseline			0					
Statistic	n	x	n	1	&ds_name	aval	ablfl = 'Y'		anumdec
Statistic	Mean (SD)	x.x (x.x)	mean stdev	1	&ds_name	aval	ablfl = 'Y'		anumdec
Statistic	Median	x.x	median	1	&ds_name	aval	ablfl = 'Y'		anumdec
Statistic	Q1, Q3	x.x, x.x	q1 q3	1	&ds_name	aval	ablfl = 'Y'		anumdec
Statistic	Min, Max	x, x	min max	1	&ds_name	aval	ablfl = 'Y'		anumdec
Blank row									
By start (label)	!BY_VARIABLE!			0	&ds_name	avisitn	1 < avisitn < 99	visfmt.	
Statistic	n	x	n	1	&ds_name	aval			anumdec
Statistic	Mean (SD)	x.x (x.x)	mean stdev	1	&ds_name	aval			anumdec
Statistic	Median	x.x	median	1	&ds_name	aval			anumdec
Statistic	Q1, Q3	x.x, x.x	q1 q3	1	&ds_name	aval			anumdec
Statistic	Min, Max	x, x	min max	1	&ds_name	aval			anumdec
By end (blank row)									

Example 2: Safety Summary

Table 14-7.1.1. Summary of Hemoglobin (g/dL) by Scheduled Visit (Full analysis Set)

	Comparator (N = 50)	AMG-Active (N = 49)	Total (N = 99)
Baseline			
n	50	49	99
Mean (SD)	10.74 (1.14)	10.54 (1.29)	10.64 (1.22)
Median	10.65	10.40	10.60
Q1, Q3	9.70, 11.50	9.70, 11.10	9.70, 11.50
Min, Max	8.1, 13.6	8.1, 13.4	8.1, 13.6
Week 2			
n	50	49	99
Mean (SD)	10.96 (1.09)	10.91 (1.26)	10.94 (1.17)
Median	11.00	11.00	11.00
Q1, Q3	10.20, 11.60	10.10, 11.80	10.10, 11.70
Min, Max	9.1, 14.5	7.5, 13.7	7.5, 14.5
Week 4			
n	50	49	99
Mean (SD)	10.80 (1.18)	11.20 (1.10)	11.00 (1.15)
Median	10.90	11.30	11.10
Q1, Q3	10.30, 11.50	10.50, 11.70	10.40, 11.70
Min, Max	7.6, 13.0	8.4, 13.4	7.6, 13.4

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N = Number of subjects in the analysis set.

Program: /home/nlyon/tflgen_training/exercise/tables/program/t-lb-sum-hgb-fas.sas
Output: t-lb-sum-hgb-fas.rtf (Date Generated: 11MAY16:06:44:40) Source: adam.adlb

Example 3: AE 2 Level Summary

Required?	Metadata Item	Leftmost Table Column	Treatment Columns	Statistics	Leftmost Table Column Indent	Data Set	Variable	Sort Section ID Number	Sort Direction
Yes	SPS root template name	root_standard_004							
Yes	Zero handling for geometric statistics	WARN							
Yes	Minimum % to report any column to								
Yes	Data set with subject-years data								
Yes	Subject-years exposure formula								
Yes	First event (in years) exposure formula								
Yes	Rate multiplier (in years)								
Yes	Drop rows if all categorical counts zero?	N							
Yes	Sections to wrap over page?	N							
Yes	Leftmost column width in inches	AUTO							
Yes	Leftmost column alignment	L							
Yes	Leftmost column label	System Organ Class Preferred Term	[Headers]						
Yes	Treatment columns subject-years display								
Yes	Treatment columns big N display		(N = xx)						
Yes	Treatment columns statistic labels		n (%)						
Yes	Blank row								
Yes	Tier level 0 (statistic)	Number of subjects reporting AEs	x (x.x)	n percent	0				
Yes	Blank row								
Yes	Tier level 1 (statistic)	System Organ Class	x (x.x)	n percent	0	adam.adae	aebodsys	1	descending
Yes	Tier level 2 (statistic)	Preferred Term	x (x.x)	n percent	1	adam.adae	aedecod	2	descending

Example 3: AE 2 Level Summary

Table 14-6.1.1. Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Full Analysis Set)

System Organ Class Preferred Term	Comparator (N = 50) n (%)	AMG-Active (N = 49) n (%)	Total (N = 99) n (%)
Number of subjects reporting AEs	41 (82.0)	43 (87.8)	84 (84.8)
Gastrointestinal disorders	17 (34.0)	19 (38.8)	36 (36.4)
Dyspepsia	4 (8.0)	3 (6.1)	7 (7.1)
Abdominal pain	0 (0.0)	5 (10.2)	5 (5.1)
Abdominal discomfort	4 (8.0)	1 (2.0)	5 (5.1)
Flatulence	1 (2.0)	3 (6.1)	4 (4.0)
Gingival inflammation	2 (4.0)	1 (2.0)	3 (3.0)
Abdominal pain upper	0 (0.0)	2 (4.1)	2 (2.0)
Dry mouth	0 (0.0)	2 (4.1)	2 (2.0)
Abdominal distension	1 (2.0)	1 (2.0)	2 (2.0)
Enterocolitis	0 (0.0)	1 (2.0)	1 (1.0)
Hiatus hernia	0 (0.0)	1 (2.0)	1 (1.0)
Hypoaesthesia oral	0 (0.0)	1 (2.0)	1 (1.0)
Toothache	0 (0.0)	1 (2.0)	1 (1.0)
Diarrhoea	1 (2.0)	0 (0.0)	1 (1.0)
Diverticulum	1 (2.0)	0 (0.0)	1 (1.0)
Gastric mucosa erythema	1 (2.0)	0 (0.0)	1 (1.0)
Gastritis	1 (2.0)	0 (0.0)	1 (1.0)
Gastrointestinal disorder	1 (2.0)	0 (0.0)	1 (1.0)
Gastrointestinal pain	1 (2.0)	0 (0.0)	1 (1.0)

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Coded using MedDRA version 16.1.
N = Number of subjects in the analysis set.

Program: /home/nlyon/tfigen_training/exercise/tables/program/t-ae-sum-soc-pref-fas.sas
Output: t-ae-sum-soc-pref-fas.rtf (Date Generated: 11MAY16:07:57:36) Source: adam.adae

Example 4: Exposure-adjusted AEs

Metadata Item	Leftmost Table Column	Treatment Columns	Statistics	Leftmost Table Column Indent	Data Set	Variable	Sort Section ID Number	Sort Direction
SPS root template name	root_standard_004							
Zero handling for geometric statistics	WARN							
Minimum % to report any column to								
Data set with subject-years data	adam.adsl							
Subject-years exposure formula	eosdy / 365.25							
First event (in years) exposure formula	aesdy / 365.25							
Rate multiplier (in years)	100							
Drop rows if all categorical counts zero?	N							
Sections to wrap over page?	Y							
Leftmost column width in inches	AUTO							
Leftmost column alignment	L							
Leftmost column label	System Organ Class Preferred Term	[Headers]						
Treatment columns subject-years display								
Treatment columns big N display		(N = xx)						
Treatment columns statistic labels		n / e (r)						
Blank row								
Tier level 0 (statistic)	Number of subjects reporting AEs	x / x.x (x.x)	n exposure rate	0				
Blank row								
Tier level 1 (statistic)	System Organ Class	x / x.x (x.x)	n exposure rate	0	adam.adae	aebodsys	1	descending
Tier level 2 (statistic)	Preferred Term	x / x.x (x.x)	n exposure rate	1	adam.adae	aedecod	2	descending

Example 4: Exposure-adjusted AEs

Table 14-6.5.1. Exposure-adjusted Subject Rate for Treatment emergent Adverse Events by System Organ Class and Preferred Term (Full Analysis Set)

System Organ Class Preferred Term	Comparator (N = 50) n / e (r)	AMG-Active (N = 49) n / e (r)	Total (N = 99) n / e (r)
Number of subjects reporting AEs	41 / 8.8 (464.5)	43 / 8.0 (536.6)	84 / 16.8 (498.8)
Gastrointestinal disorders	17 / 16.1 (105.4)	19 / 14.9 (127.5)	36 / 31.0 (116.1)
Dyspepsia	4 / 19.6 (20.4)	3 / 19.3 (15.5)	7 / 38.9 (18.0)
Abdominal pain	0 / 20.7 (0.0)	5 / 18.8 (26.6)	5 / 39.5 (12.7)
Abdominal discomfort	4 / 19.7 (20.3)	1 / 19.9 (5.0)	5 / 39.6 (12.6)
Flatulence	1 / 20.5 (4.9)	3 / 19.3 (15.5)	4 / 39.8 (10.0)
Gingival inflammation	2 / 20.2 (9.9)	1 / 19.9 (5.0)	3 / 40.0 (7.5)
Abdominal pain upper	0 / 20.7 (0.0)	2 / 19.6 (10.2)	2 / 40.3 (5.0)
Dry mouth	0 / 20.7 (0.0)	2 / 19.6 (10.2)	2 / 40.3 (5.0)
Abdominal distension	1 / 20.4 (4.9)	1 / 19.8 (5.0)	2 / 40.3 (5.0)
Enterocolitis	0 / 20.7 (0.0)	1 / 19.8 (5.0)	1 / 40.6 (2.5)
Hiatus hernia	0 / 20.7 (0.0)	1 / 19.8 (5.0)	1 / 40.6 (2.5)
Hypoaesthesia oral	0 / 20.7 (0.0)	1 / 19.9 (5.0)	1 / 40.6 (2.5)
Toothache	0 / 20.7 (0.0)	1 / 19.9 (5.0)	1 / 40.6 (2.5)
Diarrhoea	1 / 20.4 (4.9)	0 / 20.1 (0.0)	1 / 40.6 (2.5)
Diverticulum	1 / 20.4 (4.9)	0 / 20.1 (0.0)	1 / 40.6 (2.5)
Gastric mucosa erythema	1 / 20.4 (4.9)	0 / 20.1 (0.0)	1 / 40.6 (2.5)
Gastritis	1 / 20.5 (4.9)	0 / 20.1 (0.0)	1 / 40.6 (2.5)
Gastrointestinal disorder	1 / 20.5 (4.9)	0 / 20.1 (0.0)	1 / 40.6 (2.5)

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Coded using MedDRA version 16.1.

N = Number of subjects in the analysis set.

e = Sum across all subjects, the total time to first event or total exposure if no event (years).

r = Exposure-adjusted subject rate per 100 subject years (n/e*100).

Program: /home/nlyon/tfigen_training/exercise/tables/program/t-ae-subject-rate-soc-pref-fas.sas

Output: t-ae-subject-rate-soc-pref-fas.rtf (Date Generated: 11MAY16:06:19:33) Source: adam.adae

Example Headers

Header	Upper Span Label	Lower Span Label	Treatment	Column Label	Data Set	Variable	Quant	Where Clause	Numerator Where	Column Width	Column Alignment
safety			1	Comparator	adam.adsl			trt01an in(1,2)		1	C
safety			2	AMG-Active	adam.adsl			trt01an in(3,4)		1	C
safety			3	Total	adam.adsl			trt01an in(1,2,3,4)		1	C
lb-shift-dec		Maximum Grade for Decreased Value	1	NA	adam.adsl			trt01an in(1,2,3,4)	missing(lbtoxlow)	1	C
lb-shift-dec		Maximum Grade for Decreased Value	2	0	adam.adsl			trt01an in(1,2,3,4)	lbtoxlow = 0	1	C
lb-shift-dec		Maximum Grade for Decreased Value	3	1	adam.adsl			trt01an in(1,2,3,4)	lbtoxlow = 1	1	C
lb-shift-dec		Maximum Grade for Decreased Value	4	2	adam.adsl			trt01an in(1,2,3,4)	lbtoxlow = 2	1	C
lb-shift-dec		Maximum Grade for Decreased Value	5	3	adam.adsl			trt01an in(1,2,3,4)	lbtoxlow = 3	1	C
lb-shift-dec		Maximum Grade for Decreased Value	6	4	adam.adsl			trt01an in(1,2,3,4)	lbtoxlow = 4	1	C
lb-shift-dec		Maximum Grade for Decreased Value	7	Total	adam.adsl			trt01an in(1,2,3,4)		1	C

safety header:

- Used for all the previous examples

lb-shift-dec header:

- Used for all the next example
- All subjects are included in all columns (denominator)
- Limit the counts, but not denominator with Numerator Where

Example 5: Lab Shift

Metadata Item	Leftmost Table Column	Treatment Columns	Statistics	Leftmost Table Column Indent	Data Set	Variable	Variable Value	Where Clause	Alternative Denominator for Percentage [Where Clause]
SPS root template name	root_standard_004								
Zero handling for geometric statistics	WARN								
Minimum % to report any column to									
Data set with subject-years data									
Subject-years exposure formula									
First event (in years) exposure formula									
Rate multiplier (in years)									
Drop rows if all categorical counts zero?	N								
Sections to wrap over page?	N								
Leftmost column width in inches	AUTO								
Leftmost column alignment	L								
Leftmost column label	Baseline Grade	[Headers]							
Treatment columns subject-years display									
Treatment columns big N display									
Treatment columns statistic labels		n (%)							
Blank row									
Label	Comparator (N = &n_cmp)			0					
Statistic	NA	x (x.x)	n percent	1	adam.adlb	lbtolob	!MISSING!		trt01an in(1,2)
Statistic	0	x (x.x)	n percent	1	adam.adlb	lbtolob	0		trt01an in(1,2)
Statistic	1	x (x.x)	n percent	1	adam.adlb	lbtolob	1		trt01an in(1,2)
Statistic	2	x (x.x)	n percent	1	adam.adlb	lbtolob	2		trt01an in(1,2)
Statistic	3	x (x.x)	n percent	1	adam.adlb	lbtolob	3		trt01an in(1,2)
Statistic	4	x (x.x)	n percent	1	adam.adlb	lbtolob	4		trt01an in(1,2)
Statistic	Total	x (x.x)	n percent	1	adam.adlb			.<=lbtolob	trt01an in(1,2)
Blank row									
Label	AMG-Active (N = &n_amg)			0					
Statistic	NA	x (x.x)	n percent	1	adam.adlb	lbtolob	!MISSING!		trt01an in(3,4)
Statistic	0	x (x.x)	n percent	1	adam.adlb	lbtolob	0		trt01an in(3,4)
Statistic	1	x (x.x)	n percent	1	adam.adlb	lbtolob	1		trt01an in(3,4)
Statistic	2	x (x.x)	n percent	1	adam.adlb	lbtolob	2		trt01an in(3,4)
Statistic	3	x (x.x)	n percent	1	adam.adlb	lbtolob	3		trt01an in(3,4)
Statistic	4	x (x.x)	n percent	1	adam.adlb	lbtolob	4		trt01an in(3,4)
Statistic	Total	x (x.x)	n percent	1	adam.adlb			.<=lbtolob	trt01an in(3,4)

Example 5: Lab Shift

**Table 14-7.2.1. Shift of Hemoglobin (g/dL)
(Full analysis Set)**

Baseline Grade	Maximum Grade for Decreased Value						Total n (%)
	NA n (%)	0 n (%)	1 n (%)	2 n (%)	3 n (%)	4 n (%)	
Comparator (N = 50)							
NA	0 (0.0)	0 (0.0)	2 (4.0)	2 (4.0)	0 (0.0)	0 (0.0)	4 (8.0)
0	0 (0.0)	0 (0.0)	12 (24.0)	12 (24.0)	0 (0.0)	0 (0.0)	24 (48.0)
1	0 (0.0)	0 (0.0)	7 (14.0)	9 (18.0)	1 (2.0)	0 (0.0)	17 (34.0)
2	0 (0.0)	0 (0.0)	0 (0.0)	4 (8.0)	1 (2.0)	0 (0.0)	5 (10.0)
3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	0 (0.0)	0 (0.0)	21 (42.0)	27 (54.0)	2 (4.0)	0 (0.0)	50 (100.0)
AMG-Active (N = 49)							
NA	0 (0.0)	0 (0.0)	4 (8.2)	1 (2.0)	0 (0.0)	0 (0.0)	5 (10.2)
0	0 (0.0)	0 (0.0)	11 (22.4)	9 (18.4)	1 (2.0)	0 (0.0)	21 (42.9)
1	0 (0.0)	0 (0.0)	8 (16.3)	12 (24.5)	0 (0.0)	0 (0.0)	20 (40.8)
2	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.1)	1 (2.0)	0 (0.0)	3 (6.1)
3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	0 (0.0)	0 (0.0)	23 (46.9)	24 (49.0)	2 (4.1)	0 (0.0)	49 (100.0)

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N = Number of subjects in the analysis set.

Program: /home/nlyon/tflgen_training/exercise/tables/program/t-lb-shift-hgb-fas.sas
Output: t-lb-shift-hgb-fas.rtf (Date Generated: 11MAY16:07:31:28) Source: adam.adlb

Conclusion

- TFLGen increases consistency, maintainability, reusability, and extensibility through modularization
- Table templates can be re-used across analyses
- QC requirements have been minimized
- Increases resource portability between teams
- TFLGen is expected to produce > 65% of tables
 - Single programmer
 - 462 out 697 (66%) tables
 - only 3 days
 - 37 templates
- Feedback for TFLGen has been overwhelmingly positive
 - Teams reporting quicker table production and QC

Q&A

