

Get a Jump Start on Clinical Data Analysis and Visualization with Standard Scripts

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ABSTRACT

The FDA has implemented the JumpStart service to help reviewers better understand submission data more quickly, and detect opportunities for clarification or areas of concern, early in the submission review process. Wouldn't it be nice to know what content the reviewers are seeing as a result of this service? Better yet, produce similar outputs from your submission for internal review before sending it to the FDA. Several scripts that are used by the FDA as part of their JumpStart service can be found in the GitHub code repository, which was built and is maintained by the Pharmaceutical Users Software Exchange (PhUSE), Standard Analyses & Code Sharing Working Group, alongside a wealth of other content, which is delivered through the collaboration of pharmaceutical companies, contract research organizations (CROs), contractors, and government regulators.

BACKGROUND

The PhUSE Standard Analyses & Code Sharing Working Group began in 2012 with a vision to, "Fill the Gap on Analysis Standards." An early gap was identified in the Industry Standards Alignment with the Clinical Data Flow in that there are no existing standards for tables, figures, listings (TFLs), even though TFLs represent the most common scenario of reviewer interaction with Clinical Data. The working group split into 3 separate focus areas; one devoted to producing white papers recommending industry standards, with respect to analysis and reporting for measurements that are common across clinical trials and therapeutic areas; another one aimed at creating and managing a script repository (i.e., shared reusable code library) to hold any code related to medical research including code to produce the displays recommended in the white papers; and third, one whose mission is to communicate, promote, and educate about the activities of the other 2 focus areas. In the four years since the Working Group began, several white papers have been produced, the content repository has been created on GitHub, and scripts are available in the repository. While much has been accomplished, even more work remains to be done to fulfill the original vision.

INTRODUCTION

Prior to CSS 2015, the Working Group received the first few contributions that are used in the JumpStart service and received more again prior to CSS this year. The programs are all written in SAS and are meant to be run against Study Data Tabulation Model (SDTM) datasets. They have been uploaded to the Working Group's GitHub repository, and many have been tested by Working Group members. Most of the programs analyze and report adverse events or demographics data, and instructions, as well as other documentation related to the qualification and use of the code, are stored in the repository. Down the road, the Working Group hopes to qualify the scripts that it has received from the FDA along with the other code generated as part of the project; however, this is a herculean task with limited volunteer resources currently at the group's disposal.

SCRIPTS BEING TESTED

The Working Group received 7 scripts from the FDA that are used as part of the JumpStart service. Volunteers from three major companies Lilly, Merck and Accenture are reviewing the scripts. Here is a list of the scripts being reviewed and tested:

Script Name ¹	Script File Name ²
AE Severity	ae_v1.sas
AE Toxicity	ae_oncology_v1.sas
Demographics	demographics_v1.sas
Disposition	disposition_v2.sas
Exposure	exposure_v1.sas
Liver Labs	liver_v2.sas

¹ Clicking on the script name will open the GitHub folder containing the script and related documentation.

² Clicking on the Script File Name will open the script's code.

PhUSE 2016

Script Name ¹	Script File Name ²
MedDRA at a Glance	ae_meddra_w_flag_generation_v1.sas

A discussion of each script is presented below.

AE Severity

The ae_v1.sas program creates a series of Adverse Events (AE) Severity panels and was programmed using SAS 9.2. It relies on the following files that can also be downloaded from the PhUSE GitHub repository:

Category	File Name	Function
Utilities	ae_setup.sas	Merges AE, DM, and EX
Macros	ae_aggregate.sas	Finds the subject/event counts
Macros	ae_output.sas	Creates the Excel XML output
Macros	ae_rror.sas	Relative risk/odds ratio analysis
Utilities	xml_output.sas	XML formatting macros
Utilities	data_checks.sas	Generic variable checks
Utilities	sl_gs_output.sas	Script Launcher settings output
Utilities	err_output.sas	Error output when missing required variables
Templates	AE_OR_Template.xls	Odds ratio Excel template
Templates	AE_RR_Template.xls	Relative risk Excel template

AE Severity runs on SDTM domain files that have been converted to SAS7BDAT format. The following variables from the following domains are required or used when available:

Necessity	Domain	Variable
Required	AE	AEBODSYS
Required	AE	AEDECOD
Required	AE	USUBJID
Required	DM	ACTARM or ARM
Required	DM	USUBJID
Required	EX	USUBJID
Used when available	AE	AESTDTC
Used when available	AE	AESER
Used when available	AE	AESEV
Used when available	DM	RFSTDTC
Used when available	DM	RFENDTC
Used when available	DM	ARMCD
Used when available	EX	EXSTDTC
Used when available	EX	EXENDTC

It requires the following parameters to be set depending on whether the script is run locally or through Script Launcher*:

Necessity	Parameter	Description
Always Required	saspath	Location of the SAS programs designated as Macros
Always Required	utilpath	Location of the SAS programs designated as Utilities
Always Required	aeout1	Filename of the Excel output to contain the data tables
Always Required	aeout2	Filename of the Excel output to contain the Odds Ratio analysis
Always Required	aeout3	Filename of the Excel output to contain the Relative Risk analysis
Always Required	study_lag	Window in days after last exposure where AEs should be kept in analysis
Always Required	cc	Continuity correction value
Required when run locally	studypath	Location of the drug study datasets in SAS7BDAT format
Required when run locally	templatepath	Location of the Excel templates.

* The FDA uses "Script Launcher," a utility internal to the FDA, to run the JumpStart scripts, and the script still contains references to it. Part of the current work being done is to remove all references to the Script Launcher so that the script runs and produces the same results on multiple platforms.

Necessity	Parameter	Description
Required when run locally	outpath	Location of the output

Screenprints of example output are below.

AE Data Tables:

B38 Chest Pain											
Adverse Events by Organ Class and Term											
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46											
NDAB/LA: Study: CDISC Analysis run date: 2016-03-07 11:15:12 AM											
Where subject count is the number of subjects in the treatment arm experiencing at least one adverse event per organ class and term and greater than 2% of subjects in any arm experienced at least one adverse event											
Body System or Organ Class		Dictionary-Derived Term		Placebo N=86		Xanomeline High Dose N=84		Xanomeline Low Dose N=84		Total N=254	
				Subject Count	%	Subject Count	%	Subject Count	%	Subject Count	%
		Sinus Bradycardia	2	2.3	8	9.5	7	8.3	17	6.7	
		Myocardial Infarction	4	4.7	4	4.8	2	2.4	10	3.9	
		Atrial Fibrillation	1	1.2	3	3.6	1	1.2	5	2.0	
		Ventricular Extrasystoles	0	0.0	1	1.2	2	2.4	3	1.2	
		Palpitations	0	0.0	0	0.0	2	2.4	2	0.8	
		Ventricular Septal Defect	0	0.0	2	2.4	1	1.2	3	1.2	
		Diarrhoea	9	10.5	4	4.8	4	4.8	17	6.7	
		Vomiting	3	3.5	7	8.3	3	3.6	13	5.1	
		Nausea	3	3.5	6	7.1	3	3.6	12	4.7	
		Abdominal Pain	1	1.2	1	1.2	3	3.6	5	2.0	
		Salivary Hypersecretion	0	0.0	4	4.8	0	0.0	4	1.6	
		Application Site Pruritus	6	7.0	22	26.2	22	26.2	50	19.7	
		Application Site Erythema	3	3.5	15	17.9	12	14.3	30	11.8	
		Application Site Dermatitis	5	5.8	7	8.3	9	10.7	21	8.3	
		Application Site Irritation	3	3.5	9	10.7	9	10.7	21	8.3	
		Application Site Vesicles	1	1.2	6	7.1	4	4.8	11	4.3	
		Fatigue	1	1.2	5	6.0	5	6.0	11	4.3	
		Oedema Peripheral	2	2.3	2	2.4	1	1.2	5	2.0	
		Application Site Swelling	0	0.0	2	2.4	1	1.2	3	1.2	
		Application Site Urticaria	0	0.0	1	1.2	2	2.4	3	1.2	
		Malaise	0	0.0	2	2.4	1	1.2	3	1.2	
		Pyrexia	2	2.3	1	1.2	0	0.0	3	1.2	
		Application Site Pain	0	0.0	2	2.4	0	0.0	2	0.8	
		Application Site Perspiration	0	0.0	2	2.4	0	0.0	2	0.8	
		Chest Discomfort	0	0.0	2	2.4	0	0.0	2	0.8	
		Chest Pain	0	0.0	2	2.4	0	0.0	2	0.8	
		Oedema	0	0.0	0	0.0	2	2.4	2	0.8	
		Nasopharyngitis	2	2.3	6	7.1	4	4.8	12	4.7	
		Upper Respiratory Tract Infection	6	7.0	3	3.6	1	1.2	10	3.9	
		Urinary Tract Infection	2	2.3	1	1.2	0	0.0	3	1.2	
		Ear Infection	2	2.3	0	0.0	0	0.0	2	0.8	
		Contusion	1	1.2	2	2.4	1	1.2	4	1.6	
		Excoriation	2	2.3	1	1.2	1	1.2	4	1.6	
		Fall	1	1.2	1	1.2	2	2.4	4	1.6	
1 AEs by Arm 2 Serious AEs by Arm 3 AEs by Severity 4 Serious AEs by Severity Data Check Summary Grouping and Subsetting											

4

[illegible]

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AE Severity was reviewed by PhUSE members last year, and feedback was incorporated into the ae_v1upd.sas version of the program. The Working Group continues to review the script this year, and more updates are possible in the future.

AE Toxicity

The ae_oncology_v1.sas program creates a series of AE Toxicity panels and was programmed using SAS 9.2. It relies on the following files, most of which can also be downloaded from the PhUSE GitHub repository:

Category	File Name	Function
Utilities	ae_setup.sas	Merges AE, DM, and EX
Macros	ae_oncology_aggregate.sas	Performs the analysis
Macros	ae_oncology_output.sas	Creates the Excel output
Utilities	xml_output.sas	XML formatting macros
Utilities	data_checks.sas	Generic variable checks
Utilities	sl_gs_output.sas	Script Launcher settings output
Utilities	err_output.sas	Error output when missing required variables
User-supplied	mdhier_x_y.sas7bdat	MedDRA hierarchy version X.Y

AE Toxicity runs on SDTM domain files that have been converted to SAS7BDAT format. The following variables from the following domains are required or used when available:

Necessity	Domain	Variable
Required	AE	AEBODSYS
Required	AE	AEDECOD
Required	AE	USUBJID
Required	DM	ACTARM or ARM
Required	DM	USUBJID
Required	EX	USUBJID
Used when available	AE	AESTDTC
Used when available	AE	AETOXGR
Used when available	DM	RFSTDTC
Used when available	DM	RFENDTC
Used when available	DM	ARMCD
Used when available	EX	EXSTDTC
Used when available	EX	EXENDTC

It requires the following parameters to be set depending on whether the script is run locally or through Script Launcher*:

Necessity	Parameter	Description
Always Required	meddrapath	Location of MedDRA hierarchy datasets
Always Required	saspath	Location of the SAS programs designated as Macros
Always Required	utilpath	Location of the SAS programs designated as Utilities
Always Required	study_lag	Window in days after last exposure where AEs should be kept in analysis
Always Required	toxgr_min	Minimum valid toxicity grade
Always Required	toxgr_max	Maximum valid toxicity grade
Always Required	toxgr_grp5_sw	Group toxgrade 5 with 3&4?
Always Required	ver	MedDRA version
Always Required	exp	Comparison treatment arm number
Always Required	ctl	Comparison control arm number

* The FDA uses "Script Launcher," a utility internal to the FDA, to run the JumpStart scripts, and the script still contains references to it. Part of the current work being done is to remove all references to the Script Launcher so that the script runs and produces the same results on multiple platforms.

Necessity	Parameter	Description
Always Required	cmptrm	MedDRA levels to compare
Always Required	cmpgr	Toxicity grades to compare
Always Required	cmpsort	Variable by which to sort formatted output
Always Required	cc	Continuity correction value
Required when run locally	studypath	Location of the drug study datasets in SAS7BDAT format
Required when run locally	outpath	Location of the output

A screenprint of example output is below.

AE Toxicity Analysis:

A1		A		B		C		D		E		F		G		H		I		J		K		L		M		N		O		P		Q		R		S			
1		Adverse Events Two-Term Analysis		by Body System or Organ Class and Dictionary-Derived Term: Sorted by Relative Risk																																					
2		Adverse Events Two-Term Analysis		by Body System or Organ Class and Dictionary-Derived Term: Sorted by Relative Risk																																					
3		by Body System or Organ Class and Dictionary-Derived Term: Sorted by Relative Risk																																							
4		HDA-BLA																																							
5		Study: DED																																							
6		Analysis run date: 2016-03-08 05:17 AM																																							
7		Where subject count is the number of subjects experiencing at least one adverse event at the stated toxicity grade using the maximum																																							
8		toxicity grade per subject, body system or organ class, and dictionary-derived term																																							
9																																									
10																																									
11																																									
12																																									
13																																									
14		Investigations																																							
15		Electrocardiogram ST Segment Depression		4	4.7	(1.28, 11.48)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				4.7	(0.20, 9.10)		8.8*		(0.48, 160.64)		9.2*		(0.49, 173.93)						0.12				
16		Blood Alkaline Phosphatase Increased		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
17		Blood Creatine Phosphokinase Increased		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
18		Blood Creatine Phosphokinase Present		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
19		Cystoscopy		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
20		Electrocardiogram T Wave Amplitude Decreased		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
21		Heart Rate Increased		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
22		Heart Rate Irregular		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
23		Electrocardiogram T Wave Inversion		2	2.3	(0.28, 8.15)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				1.1	(-2.81, 5.08)		2.0		(0.10, 117.97)		2.0		(0.10, 117.97)						1.00				
24		Blepharitis		0	0.0	(0.00, 4.20)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				-1.2	(-3.51, 1.13)		0.3*		(0.01, 7.88)		0.3*		(0.01, 8.01)						0.49				
25		Blepharitis		0	0.0	(0.00, 4.20)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				-1.2	(-3.51, 1.13)		0.3*		(0.01, 7.88)		0.3*		(0.01, 8.01)						0.49				
26		Blood Glucose Increased		0	0.0	(0.00, 4.20)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				-1.2	(-3.51, 1.13)		0.3*		(0.01, 7.88)		0.3*		(0.01, 8.01)						0.49				
27		Blood Glucose Increased		0	0.0	(0.00, 4.20)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				-1.2	(-3.51, 1.13)		0.3*		(0.01, 7.88)		0.3*		(0.01, 8.01)						0.49				
28		Weight Decreased		0	0.0	(0.00, 4.20)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				-1.2	(-3.51, 1.13)		0.3*		(0.01, 7.88)		0.3*		(0.01, 8.01)						0.49				
29		Weight Decreased		0	0.0	(0.00, 4.20)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				-1.2	(-3.51, 1.13)		0.3*		(0.01, 7.88)		0.3*		(0.01, 8.01)						0.49				
30		Infections and Infestations																																							
31		Ear Infection		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				2.3	(-0.98, 5.51)		4.9*		(0.24, 100.26)		5.0*		(0.24, 106.71)						0.50				
32		Bronchitis		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
33		Cervicitis		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
34		Gastroenteritis Viral		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
35		Localised Infection		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
36		Vaginal Mycosis		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)						1.00				
37		Upper Respiratory Tract Infection		6	7.0	(2.60, 14.57)				3	3.6	(0.74, 10.08)				3	3.6	(0.74, 10.08)				3.4	(3.28, 10.09)		2.0		(0.50, 7.56)		2.0		(0.50, 7.56)				0.50						
38		Urinary Tract Infection		2	2.3	(0.28, 8.15)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				1.1	(-2.81, 5.08)		2.0		(0.10, 117.97)		2.0		(0.10, 117.97)				1.00						
39		Urinary Tract Infection		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)				1.00						
40		Influenza		1	1.2	(0.03, 6.31)				0	0.0	(0.00, 4.30)				0	0.0	(0.00, 4.30)				1.2	(-1.10, 3.43)		2.9*		(0.12, 70.95)		3.0*		(0.12, 73.81)				1.00						
41		Herdulium		0	0.0	(0.00, 4.20)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				-1.2	(-3.51, 1.13)		0.3*		(0.01, 7.88)		0.3*		(0.01, 8.01)				0.49						
42		Lower Respiratory Tract Infection		0	0.0	(0.00, 4.20)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				-1.2	(-3.51, 1.13)		0.3*		(0.01, 7.88)		0.3*		(0.01, 8.01)				0.49						
43		Rhinitis		0	0.0	(0.00, 4.20)				1	1.2	(0.03, 6.46)				1	1.2	(0.03, 6.46)				-1.2	(-3.51, 1.13)		0.3*		(0.01, 7.88)		0.3*		(0.01, 8.01)				0.49						
44		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
45		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
46		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
47		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
48		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
49		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
50		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
51		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
52		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
53		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)				6	7.1	(2.67, 14.90)				-4.8	(-11.8, 1.55)		0.3		(0.07, 1.57)		0.3		(0.03, 1.81)				0.17						
54		Nasopharyngitis		2	2.3	(0.28, 8.15)				0	0.0	(0.00, 4.20)																													

PhUSE 2016

AE Toxicity was reviewed by PhUSE members last year, and feedback was incorporated into the ae_oncology_v1upd.sas version of the program. The Working Group continues to review the script this year, and more updates are possible in the future.

Demographics

The demographics_v1.sas program summarizes study data based on the demographics of study participants and was programmed using SAS 9.2. It relies on the following files that can also be downloaded from the PhUSE GitHub repository:

Category	File Name	Function
Utilities	data_checks.sas	Generic variable checks
Utilities	sl_gs_output.sas	Script Launcher settings output
Utilities	err_output.sas	Error output when missing required variables
Templates	Demographics_Template.xls	Demographics Excel template

Demographics runs on SDTM domain files that have been converted to SAS7BDAT format. The following variables from the following domains are required or used when available:

Necessity	Domain	Variable
Required	DM	ACTARM or ARM
Required	DM	USUBJID
Required	DS	DSDECOD
Required	DS	USUBJID
Required	DS	DSSTDTC or DSTDDY
Used when available	DM	ARMCD
Used when available	DM	AGE
Used when available	DM	COUNTRY
Used when available	DM	ETHNIC
Used when available	DM	RACE
Used when available	DM	SEX
Used when available	DM	SITEID
Used when available	DS	DSCAT
Used when available	DS	DSSCAT
Used when available	DS	DSSEQ

It requires the following parameters to be set depending on whether the script is run locally or through Script Launcher*:

Necessity	Parameter	Description
Always Required	utilpath	Location of the SAS programs designated as Utilities
Always Required	ndabla	NDA or BLA number
Always Required	studyid	Study Number
Always Required	age1 - age8	Upper bound of age bucket
Always Required	ageunit	Unit of time age buckets are in
Always Required	demout	Filename and path of output
Required when run locally	studypath	Location of the drug study datasets in SAS7BDAT format
Required when run locally	templatepath	Location of the Excel templates.
Required when run locally	outputpath	Location of the output
Required when run locally	outfile	Filename of the output
Required when run locally	template	Filename of the template

A screenprint of example output is below.

* The FDA uses "Script Launcher," a utility internal to the FDA, to run the JumpStart scripts, and the script still contains references to it. Part of the current work being done is to remove all references to the Script Launcher so that the script runs and produces the same results on multiple platforms.

PhUSE 2016

Demographics Analysis:

A1	B	C	D	E	F	G	H	I	J
1	A								
2	Demographic Baseline Characteristics by Disposition Term: Age Groups								
3									
4									
5	NDARBLA:								
6	Study:								
7	Analysis run date:								
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Ready									

The Count column shows the count of subjects in each demographic group per arm whose last disposition event is the disposition term shown. See the front page for further information. The % column shows the proportion of the demographic group in each arm that the count represents.

Standard Disposition Term	Age Group	Count		%					
		Count	%						
Adverse Event	Age between 1 year and 35 years	0	0.0	0.0	0	0.0	0	0.0	0.0
	Age between 35 and 65	1	0.5	1.0	1	1.0	2	0.7	0.7
	Age 65 and over	1	0.9	3.7	2	3.7	3	1.8	1.8
Completed	Age between 1 year and 35 years	0	0.0	2	66.7	2	2	66.7	66.7
	Age between 35 and 65	176	94.6	91	89.2	267	92.7	92.7	92.7
	Age 65 and over	112	96.6	50	92.6	162	95.3	95.3	95.3
Death	Age between 1 year and 35 years	0	0.0	0	0.0	0	0	0.0	0.0
	Age between 35 and 65	2	1.1	3	2.9	5	1.7	1.7	1.7
	Age 65 and over	1	0.9	0	0.0	1	0.6	0.6	0.6
Informed Consent Obtained	Age between 1 year and 35 years	0	0.0	3	100.0	3	100.0	100.0	100.0
	Age between 35 and 65	186	100.0	102	100.0	288	100.0	100.0	100.0
	Age 65 and over	116	100.0	54	100.0	170	100.0	100.0	100.0
Lost To Follow-Up	Age between 1 year and 35 years	0	0.0	1	33.3	1	33.3	33.3	33.3
	Age between 35 and 65	0	0.0	1	1.0	1	0.3	0.3	0.3
	Age 65 and over	0	0.0	0	0.0	0	0.0	0.0	0.0
Physician Decision	Age between 1 year and 35 years	0	0.0	0	0.0	0	0.0	0.0	0.0
	Age between 35 and 65	1	0.5	0	0.0	1	0.3	0.3	0.3
	Age 65 and over	2	1.7	0	0.0	2	1.2	1.2	1.2
Protocol Violation	Age between 1 year and 35 years	0	0.0	0	0.0	0	0.0	0.0	0.0
	Age between 35 and 65	6	3.2	3	2.9	9	3.1	3.1	3.1
	Age 65 and over	4	3.4	0	0.0	4	2.4	2.4	2.4
Randomized	Age between 1 year and 35 years	0	0.0	3	100.0	3	100.0	100.0	100.0
	Age between 35 and 65	186	100.0	102	100.0	288	100.0	100.0	100.0
	Age 65 and over	116	100.0	54	100.0	170	100.0	100.0	100.0
Sponsor Decision	Age between 1 year and 35 years	0	0.0	0	0.0	0	0.0	0.0	0.0
	Age between 35 and 65	0	0.0	0	0.0	0	0.0	0.0	0.0
	Age 65 and over	1	0.9	0	0.0	1	0.6	0.6	0.6
Withdrawal By Subject	Age between 1 year and 35 years	0	0.0	0	0.0	0	0.0	0.0	0.0
	Age between 35 and 65	8	4.3	7	6.9	15	5.2	5.2	5.2
	Age 65 and over	4	3.4	3	5.6	7	4.1	4.1	4.1

Demographics was reviewed by PhUSE members last year, and the Working Group continues to review the script this year with the hope of creating an updated, more user-friendly version.

Disposition

The disposition_v2.sas program charts the time to disposition event for all subjects and for exposed subjects and was programmed using SAS 9.2. It relies on the following files that can also be downloaded from the PhUSE GitHub repository:

Category	File Name	Function
Macros	data_checks_disposition.sas	DS data checks
Utilities	data_checks.sas	Generic variable checks

PhUSE 2016

Category	File Name	Function
Utilities	sl_gs_output.sas	Script Launcher settings output
Utilities	err_output.sas	Error output when missing required variables
Templates	Disposition_Template.xls	Disposition Excel template

Disposition runs on SDTM domain files that have been converted to SAS7BDAT format. The following variables from the following domains are required or used when available:

Necessity	Domain	Variable
Required	DM	ACTARM or ARM
Required	DM	USUBJID
Required	DM	RFSTDTC if no DSSTDY in DS Domain
Required	DS	DSDECOD
Required	DS	USUBJID
Required	DS	DSSTDY or DSSTDTC
Required	EX	USUBJID
Used when available	DM	ARMCD
Used when available	DS	DSCAT
Used when available	DS	DSSCAT
Used when available	DS	DSSEQ

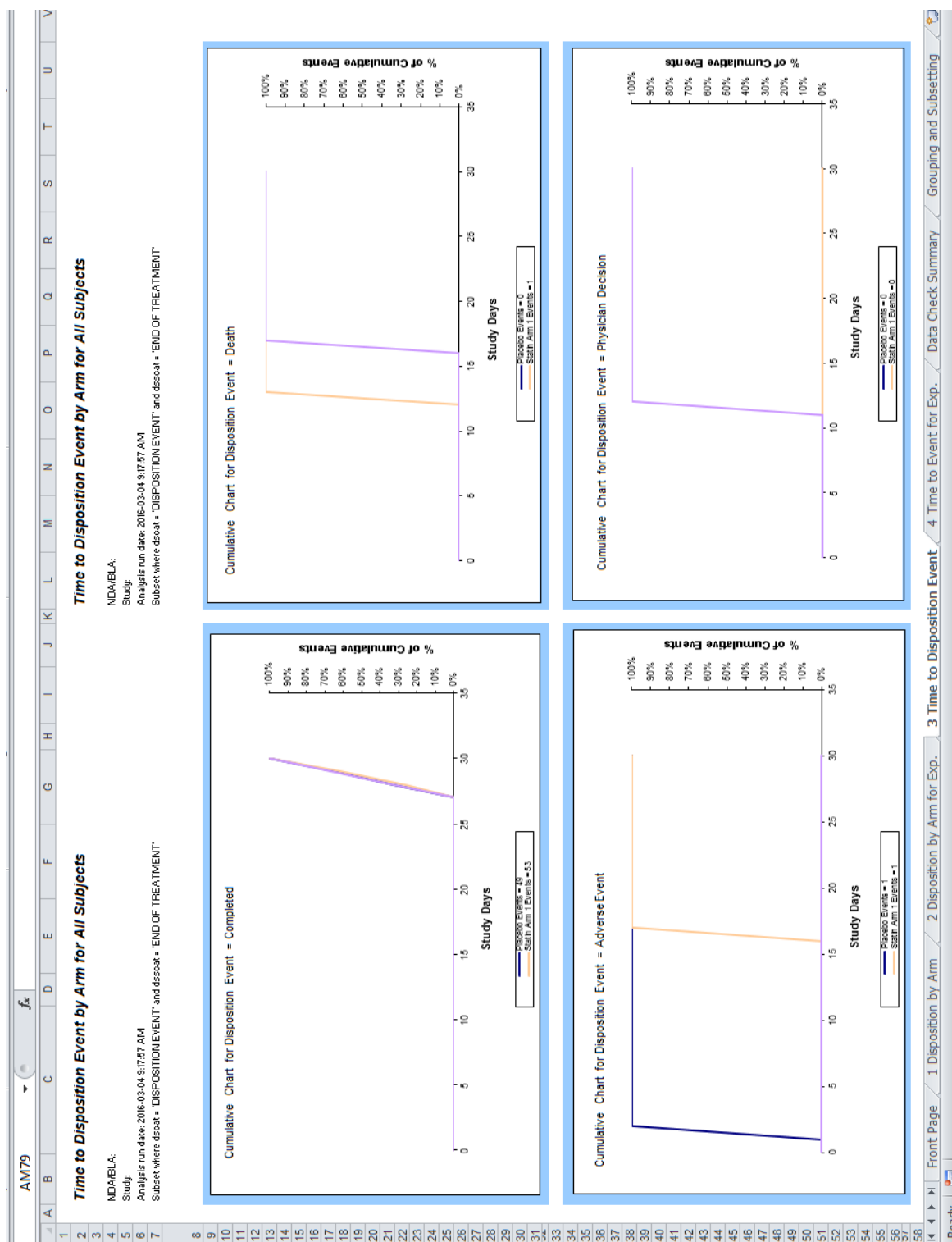
It requires the following parameters to be set depending on whether the script is run locally or through Script Launcher*:

Necessity	Parameter	Description
Always Required	saspath	Location of the SAS programs designated as Macros
Always Required	utilpath	Location of the SAS programs designated as Utilities
Always Required	ndabla	NDA or BLA number
Always Required	studyid	Study Number
Required when run locally	studypath	Location of the drug study datasets in SAS7BDAT format
Required when run locally	outpath	Location of the output
Required when run locally	templatepath	Location of the Excel templates.
Required when run locally	outfile	Filename of the output
Required when run locally	template	Filename of the template

A screenprint of example output is below.

* The FDA uses "Script Launcher," a utility internal to the FDA, to run the JumpStart scripts, and the script still contains references to it. Part of the current work being done is to remove all references to the Script Launcher so that the script runs and produces the same results on multiple platforms.

Disposition Analysis:



Disposition was reviewed by PhUSE members last year, and the Working Group continues to review the script this year with the hope of creating an updated, more user-friendly version.

PhUSE 2016

Exposure

The exposure_v1.sas program performs an analysis of the exposure events for subjects in the study and was programmed using SAS 9.2. It relies on the following files that can also be downloaded from the PhUSE GitHub repository:

Category	File Name	Function
Utilities	data_checks.sas	Generic variable checks
Utilities	sl_gs_output.sas	Script Launcher settings output
Utilities	err_output.sas	Error output when missing required variables
Macros	data_checks_exposure.sas	Exposure data checks
Templates	Exposure_Template.xls	Exposure Excel template
Input ³	exposure_exdosfrq.csv	Exposure dose frequency codes

Exposure runs on SDTM domain files that have been converted to SAS7BDAT format. The following variables from the following domains are required or used when available:

Necessity	Domain	Variable
Required	DM	ACTARM or ARM
Required	DM	USUBJID
Required	DM	RFSTDTC
Required	EX	USUBJID
Required	EX	EXENDTC or EXSTDTC
Used when available	DM	ARMCD
Used when available	EX	EXTRT
Used when available	EX	EXDOSE
Used when available	EX	EXDOSU
Used when available	EX	EXDOSFRQ
Used when available	EX	EXDOSFRM
Used when available	EX	EXADJ

It requires the following parameters to be set depending on whether the script is run locally or through Script Launcher^{*}:

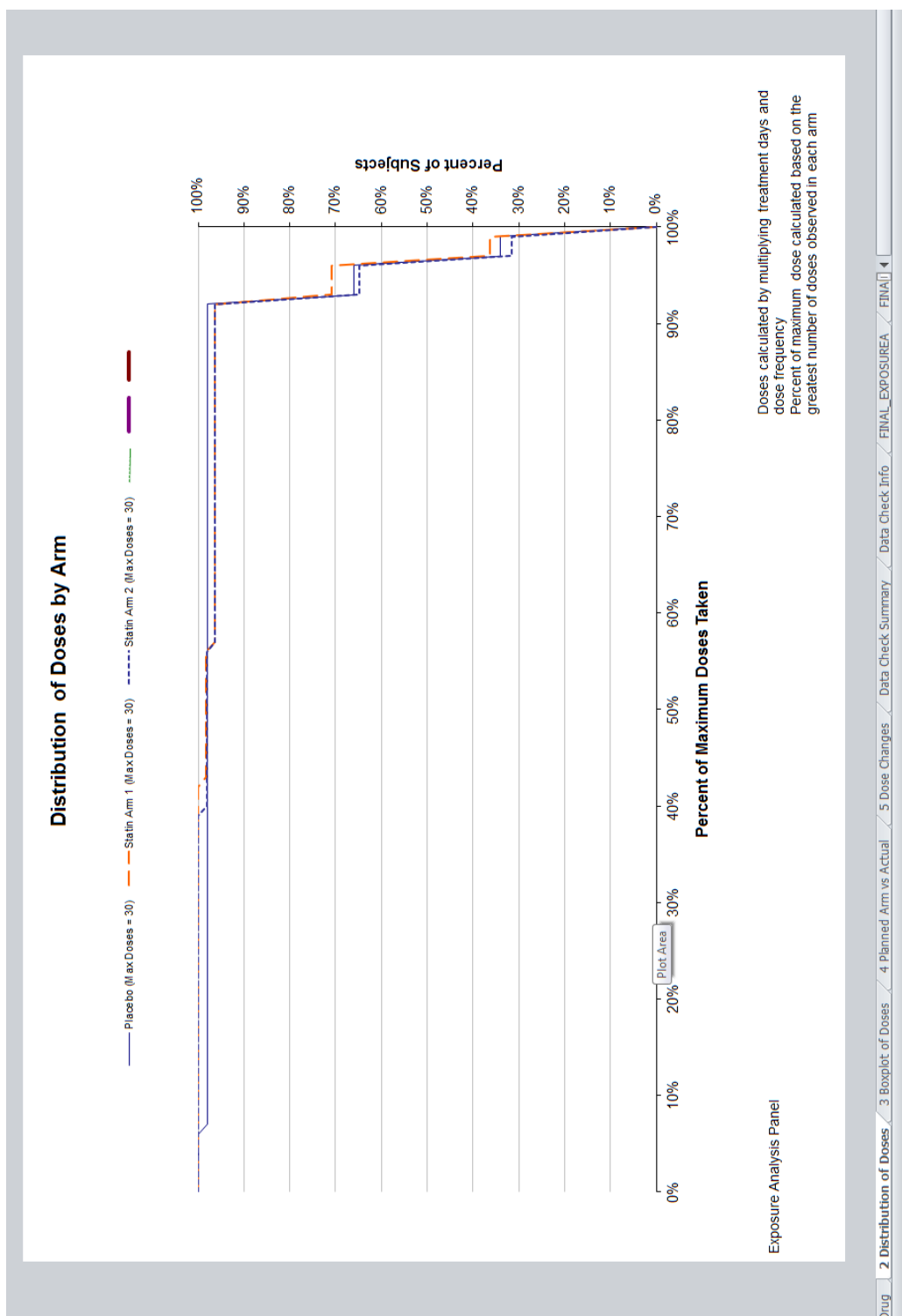
Necessity	Parameter	Description
Always Required	saspath	Location of the SAS programs designated as Macros
Always Required	utilpath	Location of the SAS programs designated as Utilities
Always Required	dosfrqpath	Location of the Exposure dose frequency code list
Always Required	ndabla	NDA or BLA number
Always Required	studyid	Study Number
Required when run locally	studypath	Location of the drug study datasets in SAS7BDAT format
Required when run locally	outputpath	Location of the output
Required when run locally	templatepath	Location of the Excel templates.
Required when run locally	outfile	Filename of the output
Required when run locally	template	Filename of the template

Screenprints of example output are below.

³ The file developed for use with the program is available for download in the same PhUSE GitHub folder as the main program.

* The FDA uses "Script Launcher," a utility internal to the FDA, to run the JumpStart scripts, and the script still contains references to it. Part of the current work being done is to remove all references to the Script Launcher so that the script runs and produces the same results on multiple platforms.

Dosing Distribution Figure:



Planned to Actual Dosing Comparison:

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f _k											
A											
Planned Arm to Actual Treatment Comparison											
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52											
Front Page / 1 Number of Days on Drug / 2 Distribution of Doses / 3 Boxplot of Doses / 4 Planned Arm vs Actual / 5 Dose Changes / Data Check Summary / Data Check Info / FINAL Ex											
Ready											

Exposure was reviewed by PhUSE members last year, and the Working Group continues to review the script this year with the hope of creating an updated, more user-friendly version.

Liver Labs

The liver_v2.sas program creates a series of liver lab analysis panels and was programmed using SAS 9.2. It relies on the following files that can also be downloaded from the PhUSE GitHub repository:

PhUSE 2016

Category	File Name	Function
Utilities	data_checks.sas	Generic variable checks
Utilities	sl_gs_output.sas	Script Launcher settings output
Macros	data_checks_liver.sas	Liver lab data checks
Templates	Liver_Labs_Template.xls	Liver lab Excel template

Liver Labs runs on SDTM domain files that have been converted to SAS7BDAT format. The following variables from the following domains are required or used when available:

Necessity	Domain	Variable
Required	DM	ACTARM or ARM
Required	DM	USUBJID
Required	LB	USUBJID
Required	LB	LBDTC
Required	LB	LBTESTCD
Required	LB	LBSTNRHI
Required	LB	LBSTRESN
Required	LB	LBSTRESU
Required	LB	LBSTNRLO
Used when available	DM	RFSTDTC
Used when available	DM	ARMCD
Used when available	LB	LBDY
Used when available	LB	LBBLFL
Used when available	LB	VISITNUM

It requires the following parameters to be set depending on whether the script is run locally or through Script Launcher*:

Necessity	Parameter	Description
Always Required	saspath	Location of the SAS programs designated as Macros
Always Required	utilpath	Location of the SAS programs designated as Utilities
Always Required	ndabla	NDA or BLA number
Always Required	studyid	Study Number
Required when run locally	studypath	Location of the drug study datasets in SAS7BDAT format
Required when run locally	outputpath	Location of the output
Required when run locally	templatepath	Location of the Excel templates.
Required when run locally	outfile	Filename of the output
Required when run locally	template	Filename of the template

Screenprints of example output are below.

* The FDA uses "Script Launcher," a utility internal to the FDA, to run the JumpStart scripts, and the script still contains references to it. Part of the current work being done is to remove all references to the Script Launcher so that the script runs and produces the same results on multiple platforms.

PhUSE 2016

Possible Hy's Law Cases:

A1					
A	B	C	D	E	F
1					
2	Possible Hy's Law Cases				
3					
4					
5	NDA/BLA:				
6	Study:				
7	Analysis run date:				
8					
9					
10	Combinations for Possible Hy's Law Cases: At the Same Visit				
11					
12	Liver Lab Test At Same Visit	0 N =			
13		Event Count	Subject Count	% of Subjects	
14					
15	ALT or AST $\geq$ 3 ULN, TB $\geq$ 1.5 ULN & ALP normal	0	0	0.00	
16	ALT or AST $\geq$ 3 ULN, TB $\geq$ 2 ULN & ALP normal	0	0	0.00	
17	ALT or AST $\geq$ 5 ULN, TB $\geq$ 3 ULN & ALP normal	0	0	0.00	
18	ALT or AST $\geq$ 3 ULN, TB $\geq$ 1.5 ULN & ALP > normal	0	0	0.00	
19	ALT or AST $\geq$ 3 ULN, TB $\geq$ 2 ULN & ALP > normal	0	0	0.00	
20	ALT or AST $\geq$ 5 ULN, TB $\geq$ 3 ULN & ALP > normal	0	0	0.00	
21	ALT or AST $\geq$ 3 ULN, TB $\geq$ 1.5 ULN & ALP missing	0	0	0.00	
22	ALT or AST $\geq$ 3 ULN, TB $\geq$ 2 ULN & ALP missing	0	0	0.00	
23	ALT or AST $\geq$ 5 ULN, TB $\geq$ 3 ULN & ALP missing	0	0	0.00	
24					
25	Notes: All scores are post-baseline. Cases that have the lab combinations occurring at the same visit.				
26					
27					
28	Combinations for Possible Hy's Law Cases: At Any Time During the Study				
29					
30	Liver Lab Test Any Time During Study	0 N =			
31		Subject Count	% of Subjects		
32					
33	ALT or AST $\geq$ 3 ULN, TB $\geq$ 1.5 ULN & ALP normal	0	0.00		
34	ALT or AST $\geq$ 3 ULN, TB $\geq$ 2 ULN & ALP normal	0	0.00		
35	ALT or AST $\geq$ 5 ULN, TB $\geq$ 3 ULN & ALP normal	0	0.00		
36	ALT or AST $\geq$ 3 ULN, TB $\geq$ 1.5 ULN & ALP > normal	0	0.00		
37	ALT or AST $\geq$ 3 ULN, TB $\geq$ 2 ULN & ALP > normal	0	0.00		
38	ALT or AST $\geq$ 5 ULN, TB $\geq$ 3 ULN & ALP > normal	0	0.00		
39	ALT or AST $\geq$ 3 ULN, TB $\geq$ 1.5 ULN & ALP missing	0	0.00		
40	ALT or AST $\geq$ 3 ULN, TB $\geq$ 2 ULN & ALP missing	0	0.00		
41	ALT or AST $\geq$ 5 ULN, TB $\geq$ 3 ULN & ALP missing	0	0.00		
42					
43	Notes: All scores are post-baseline. Subjects that have the lab combinations occurring at any point during the study.				
44					
45					
46					
Front Page 1 Labs Greater Than ULN 2 Possible Hy's Law 3 Max vs BL 4 AST & ALT vs TB Charts 5 Max L					
Ready					

Maximum Post-Baseline Lab Tests vs Baseline Lab Tests:

A1	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ	BA	BB	BC	BD	BE	BF	BG	BH	BI	BJ	BK	BL	BM	BN	BO	BP	BQ	BR	BS	BT	BU	BV	BW	BX	BY	BZ	CA	CB	CC	CD	CE	CF	CG	CH	CI	CJ	CK	CL	CM	CN	CO	CP	CQ	CR	CS	CT	CU	CV	CW	CX	CY	CZ	DA	DB	DC	DD	DE	DF	DG	DH	DI	DJ	DK	DL	DM	DN	DO	DP	DQ	DR	DS	DT	DU	DV	DW	DX	DY	DZ	EA	EB	EC	ED	EE	EF	EG	EH	EI	EJ	EK	EL	EM	EN	EO	EP	EQ	ER	ES	ET	EU	EV	EW	EX	EY	EZ	FA	FB	FC	FD	FE	FF	FG	FH	FI	FJ	FK	FL	FM	FN	FO	FP	FQ	FR	FS	FT	FU	FV	FW	FX	FY	FZ	GA	GB	GC	GD	GE	GF	GG	GH	GI	GJ	GK	GL	GM	GN	GO	GP	GQ	GR	GS	GT	GU	GV	GW	GX	GY	GZ	HA	HB	HC	HD	HE	HF	HG	HH	HI	HJ	HK	HL	HM	HN	HO	HP	HQ	HR	HS	HT	HU	HV	HW	HX	HY	HZ	IA	IB	IC	ID	IE	IF	IG	IH	II	IJ	IK	IL	IM	IN	IO	IP	IQ	IR
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PhUSE 2016

Liver Labs was reviewed by PhUSE members last year, and the Working Group continues to review the script this year with the hope of creating an updated, more user-friendly version.

MedDRA at a Glance

The `ae_meddra_w_flag_generation_v1.sas` program creates a series of AE panels by MedDRA level and was programmed using SAS 9.2. It relies on the following files, most of which can also be downloaded from the PhUSE GitHub repository:

Category	File Name	Function
Utilities	ae_setup.sas	Merges AE, DM, and EX
Macros	ae_meddra.sas	Performs the analysis by MedDRA level
Macros	ae_meddra_output.sas	Creates the Excel XML output
Utilities	xml_output.sas	XML formatting macros
Utilities	data_checks.sas	Generic variable checks
Utilities	sl_gs_output.sas	Script Launcher settings output
Utilities	err_output.sas	Error output when missing required variables
User-supplied	<code>mdhier_x_y.sas7bdat</code>	MedDRA hierarchy version X.Y
User-supplied	<code>dme.sas7bdat</code>	Designated Medical Events (DME) list

MedDRA at a Glance runs on SDTM domain files that have been converted to SAS7BDAT format. The following variables from the following domains are required or used when available:

Necessity	Domain	Variable
Required	AE	AEBODSYS
Required	AE	AEDECOD
Required	AE	USUBJID
Required	DM	ACTARM or ARM
Required	DM	USUBJID
Required	EX	USUBJID
Used when available	AE	AESTDTC
Used when available	DM	RFSTDTC
Used when available	DM	RFENDTC
Used when available	DM	ARMCD
Used when available	EX	EXSTDTC
Used when available	EX	EXENDTC

It requires the following parameters to be set depending on whether the script is run locally or through Script Launcher*:

Necessity	Parameter	Description
Always Required	<code>meddrapath</code>	Location of MedDRA hierarchy datasets
Always Required	<code>saspath</code>	Location of the SAS programs designated as Macros
Always Required	<code>utilpath</code>	Location of the SAS programs designated as Utilities
Always Required	<code>dmepath</code>	Location of the DME list dataset
Always Required	<code>aemedout</code>	Filename and path of output
Always Required	<code>study_lag</code>	Window in days after last exposure where AEs should be kept in analysis
Always Required	<code>ver</code>	MedDRA version
Always Required	<code>cc</code>	Continuity correction value
Required when run locally	<code>studypath</code>	Location of the drug study datasets in SAS7BDAT format
Required when run locally	<code>outputpath</code>	Location of the output

A screenprint of example output is below.

* The FDA uses "Script Launcher," a utility internal to the FDA, to run the JumpStart scripts, and the script still contains references to it. Part of the current work being done is to remove all references to the Script Launcher so that the script runs and produces the same results on multiple platforms.

Error Summary:

Clipboard		Font	Alignment	Number	Styles	
A1	A	f _x				
1	MedDRA at a Glance Error Summary					
2						
3						
4	NDA/BLA: xxx					
5	Study: fdatadata					
6	Analysis run date: 2016-03-08 2:11:22 PM					
7						
8	There were zero adverse events with matching MedDRA descriptions.					
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Ready		Error Summary				

MedDRA at a Glance was reviewed by PhUSE members last year. The program did not perform as expected in that “MedDRA at a Glance Error Summary.xls” was created but did not reflect the known errors in the input file, and no output for “MedDRA at a Glance Analysis Panel.xls” was created. The Working Group members found that the program was expecting input files that were not detailed in the requirements, and work is continuing on this script to identify the necessary structure of the additional input files so that an updated, functioning version can be created.

PhUSE 2016

CONCLUSION

Although the size of the Working Group's ranks has grown steadily over the last four years, so has the amount of work yet to be completed. There are many ways for people to become involved in this group, whether it is by reviewing the white papers, writing code, testing code, or promoting the repository. Even receiving feedback on how the code performs in the various computing environments used by different organizations would be of immense benefit to these projects. Having open-source, qualified, industry-standard scripts to analyze and display results from common endpoints will fill in a critical gap that is missing in the flow of Clinical Data from CRO to Sponsor to reviewer.

RELATED LINKS

Here is a list of links providing you a quick access to the related scripts and documents:

- Working Group:
 - ✓ Main Page: http://www.phusewiki.org/wiki/index.php?title=Standard_Scripts
- Repository:
 - ✓ Github: <https://github.com/phuse-org/phuse-scripts>
- Index Pages:
 - ✓ Simple Index: <https://github.com/phuse-org/phuse-scripts/wiki/Simple-Index>.
 - ✓ Standard Index: <https://github.com/phuse-org/phuse-scripts/wiki/Standard-Script-Index>
 - ✓ Mirrored Index: http://www.phusewiki.org/wiki/index.php?title=Standard_Script_Index
- White Papers
 - ✓ CS Deliverables Catalog: <http://www.phuse.eu/CSS-deliverables.aspx>

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