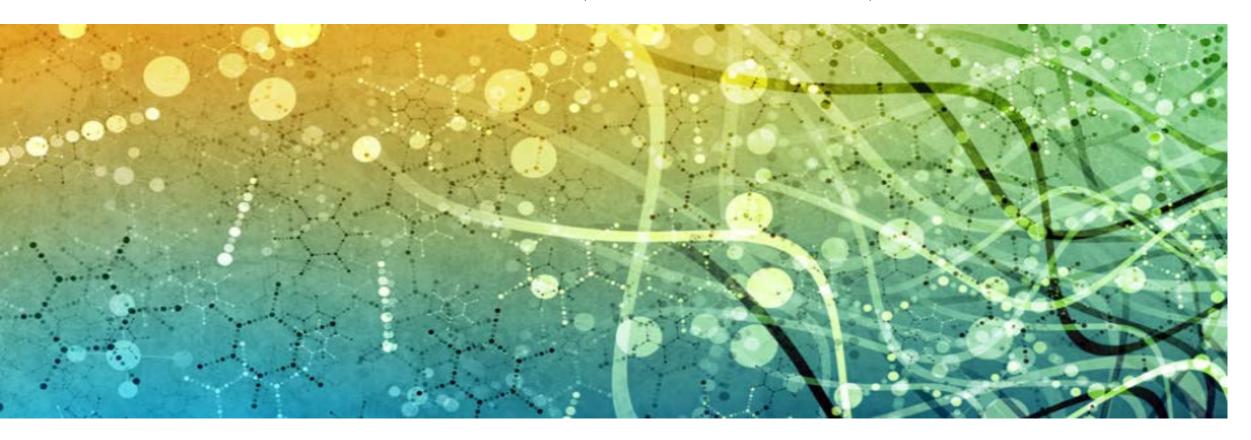
### **PHARMASTAT LLC**

SPECIALIZING IN CLINICAL TRIAL DATA ANALYSIS, DATA STANDARDIZATION, AND FDA SUBMISSIONS





# ANALYSIS RESULTS METADATA: WHY TO DO IT AND HOW TO DO IT

- What's new in Define-XML V2.1
- Overview of Define-XML Analysis Results Metadata (ARM)
- ARM Examples
- Creating ARM from Analysis Tables



### WHAT'S NEW IN DEFINE 2.1

- Define and reference standards
- Highlight non-standard elements
- Document planned domains that were not included
- Indicate variables with only null values
- Changes to Origin



# **STANDARDS**

Standard	Туре	Status	Documentation
SDTMIG 3.1.2	IG	Final	The CDISC01 study was modeled on a very old SDTMIG and no attempt was done yet to upversion it to a newer SDTMIG
SDTMIG 3.2	IG	Final	As an example, the CDISC01 study was adjusted to include a new Domain available in SDTM IG 3.2
SDTMIG-MD 1.0	IG	Final	As an example, the CDISC01 study was adjusted to include a new Domain available in SDTMIG-MD 1.0. The XS Domain is expected to reference the device used with variable SPDEVID.
CDISC/NCI SDTM 2011-12-09	ст	Final	Assuming the CT was not upversioned for this study
CDISC/NCI SDTM 2015-12-18	СТ	Final	The CT version applicable for the new Domain is the 2015-12-18 version



# **STANDARDS**

DI [SDTMIG-MD 1.0]	Device Identifiers	SPECIAL PURPOSE	One record per device identifier per device	Tabulation	STUDYID, SPDEVID, DIPARMCD	The DI domain is included to illustrate the use of a separate complementary SDTMIG. In this example, the device ID is referenced from a Findings Domain (XS).	di.xpt &
DM [SDTMIG 3.1.2]	Demographics	SPECIAL PURPOSE	One record per subject	Tabulation	STUDYID, USUBJID	See Reviewer's Guide, Section 2.1 Demographics Reviewers Guide [section2.1 🗗]	dm.xpt &
EC [SDTMIG 3.2]	Exposure as Collected	INTERVENTIONS	One record per constant dosing interval per subject	Tabulation	STUDYID, USUBJID, ECSTDTC, ECENDTC, ECTRT, ECDOSE		ec.xpt &



### **STANDARDS**

Ethnic Group [*C*66790] [CDISC/NCI SDTM 2011-12-09]

Permitted Value (Code)

HISPANIC OR LATINO [C17459]

NOT HISPANIC OR LATINO [C41222]

Domain Abbreviation (EX) [C66734] [CDISC/NCI SDTM 2011-12-09]

Permitted Value (Code)	Display Value (Decode)
EX [C49587]	Exposure

Treatment [CDISC/NCI SDTM 2011-12-09] [Non Standard]

Permitted Value (Code)

Miracle Drug

Placebo



### WHAT'S NEW IN DEFINE 2.1

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# **NON-STANDARD ELEMENTS**

XS [Non Standard] S Finding	FINDINGS	One record per finding per visit per subject	Tabulation	STUDYID, USUBJID, XSTESTCD, XSDTC, VISITNUM		xs.xpt &
-----------------------------	----------	---	------------	---	--	----------

Variable	Label / Description	Туре		Format	Origin / Source / Method / Comment
STUDYID [Non Standard]	Study Identifier	text	7		Protocol (Source: Sponsor)
DOMAIN	Domain Abbreviation	text		<u>Domain Abbreviation (DM)</u> • "DM" = "Demographics"	Assigned (Source: Sponsor)

### WHAT'S NEW IN DEFINE 2.1

- Define and reference standards
- Highlight non-standard elements
- Document planned domains that were not included
- Indicate variables with only null values
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# **NULL DATA**

[Non Standard] [No Data]	X Findings	FINDINGS	One record per finding per visit per subject	Tabulation	STUDYID, USUBJID, XXTESTCD, XXDTC, VISITNUM	Special domain contingent on rare conditions observed.	&		
--------------------------	------------	----------	---	------------	---	--	---	--	--

[No Data] Original Units text 2	Units for S Findings Results  • "g/dL" =  "g/dL"  • "mg/dL" =  "mg/dL"	Collected (Source: Vendor) Planned Numeric tests were not performed.
---------------------------------	---	--

### WHAT'S NEW IN DEFINE 2.1

- Define and reference standards
- Highlight non-standard elements
- Document planned domains that were not included
- Indicate variables with only null values
- Changes to Origin



### **CHANGES TO ORIGIN**

#### Origin / Source / Method / Comment

Protocol (Source: Sponsor)

Assigned (Source: Sponsor)

Collected (Source: Vendor)

Derived (Source: Sponsor)

Sequential number identifying records within each  $% \label{eq:condition}%$ 

USUBJID in the domain.

Assigned (Source: Vendor)

Assigned (Source: Vendor)

Collected (Source: Vendor)

Derived (Source: Investigator)

Collected (Source: Investigator)

Annotated CRF [20 ₺ ]



### **DEFINE 2.1 SDTM ORIGINS**

The following table lists the allowed Origin Type and Source values for SDTM datasets. Type and Source values that do not apply to SDTM datasets are not listed. Table cells include examples that highlight cases where the specific combination of Type and Source attributes apply. Cells that include only an  $\mathbf{X}$  indicate that the combination of Type and Source attributes is not valid. The Notes provide additional information about use of the Origin attributes for SDTM datasets.

Т	Source				Notes
Type	Subject	Investigator	Vendor	Sponsor	Notes
Collected	ePro	CRF	Lab data, ECG	X	This term should be used for clinical data that were actually observed or recorded by a person or received from an instrument; it should not be used for data that have been interpreted, calculated, or derived from other information.
Derived	X	X	Lab data, ECG	SDTM	Derivation examples include calculations performed during data collection (e.g.,DY). Other derivation examples: calculations within ePRO (e.g., questionnaire section scores) and calculations within EDC (e.g., BMI, BSA).
Assigned	X	X	Adjudicator	SDTM	Examples of this include third-party attributions by an adjudicator, coded terms that are supplied as part of a coding process, and values that are set independently of any subject-related data values in order to complete SDTM fields such as DOMAIN andTESTCD
Protocol	X	X	X	SDTM	An example would be VSPOS (Vital Signs Position), which could be specified in the protocol and be provided by other means (e.g. CRF, eDT).
Predecessor	X	X	X	X	Use when a value is an exact copy of another value in an SDTM dataset.



### **DEFINE 2.1 ADAM ORIGINS**

Teme	Source	Notes				
Type Sponsor		Notes				
Derived	ADaM	For sponsor-performed analysis derivations in ADaM				
Assigned	ADaM					
Predecessor	X	Use when a value is an exact copy of another value in either SDTM or ADaM dataset.				

### **OVERVIEW OF ARM**

- Draft standard released 2014 for public comment
- Final standard released 2015 with support for Define-XML V2.0 and V2.1
- Define-XML 2.0 required for NDA studies starting after 2016-12-17
- Define-XML 2.1 required for NDA studies starting after 2022-03-15
- Define ARM is currently optional, no date for future requirement



### THE STYLESHEETS

There are 2 stylesheets available for use with ARM:

define 2-0-0.xls modified 2015-01-16 (Analysis Results Metadata

Final Package)

define2-1.xls modified 2019-05-08 (Final Define 2.1 release)



### WHY USE ARM?

Highlight Key Tables or Findings

Provide Additional Analysis Details

Enhance Traceability



### WHAT ARE WE DOCUMENTING?

Primary, secondary, or exploratory outcome measures

- Driven by the SAP and study design
- NOT every table or result



### ARM CONCEPT - ANALYSIS DISPLAY

PharmaStat LLC CDISC Pilot Data Dummy Product Page of

	Plac	ebo	All Active Drug		
Time Point	Observed Value	Change from Baseline	Observed Value	Change from Baseline	
End of Treatment					
n	80	78	80	80	
Mean (SD)	9.833 (4.2890)	0.460 (3.0772)	11.07 (5.3592)	021 (3.1554)	
Median	8.550	0.000	10.26	0.000	
Min Max	3.42 , 23.94	-10.3, 8.55	3.42,30.78	-8.55, 11.97	
Within Group Least Square Mean Change	e				
LSM (SE) a		0.201 (0.3437)		0.230 (0.3398)	
95% CI for LSM <sup>a</sup>		-0.479 , 0.880		-0.442 , 0.901	
Between Group Least Square Mean Difference					
LSMD (Active-Placebo) (SE) <sup>a</sup>				0.029 (0.4859)	
95% CI for LSMD a				-0.931 , 0.989	
P-value <sup>a</sup>				0.9523	

<sup>&</sup>lt;sup>1</sup>Intent-to-treat population includes subjects who meet all enrollment criteria or who have been given an exemption.

<sup>&</sup>lt;sup>a</sup> Results are based on a MMRM model including the change from baseline value as the dependent variable; treatment, visit (Week 2, EOT), and treatment by visit interaction, and the continuous covariates of baseline value, as fixed effects; and subject as a random effect.



### ARM CONCEPT - ANALYSIS DISPLAY

#### **Analysis Results Metadata - Summary**

Table 14.2.2 Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population

Individual treatment groups vs. Placebo on Hy's law criteria by Visit

Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin|Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.



PharmaStat LLC CDISC Pilot Data Dummy Product Page of

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Median	8.550	0.000	10.26	0.000		
Min Max	3.42, 23.94	-10.3, 8.55	3.42,30.78	-8.55, 11.97		
Within Group Least Square Mean Change						
LSM (SE) a		0.201 (0.3437)		0.230 (0.3398)		
95% CI for LSM <sup>a</sup>		-0.479 , 0.880		-0.442 , 0.901		
Between Group Least Square Mean						
Difference						
LSMD (Active-Placebo) (SE) a				0.029 (0.4859)		
95% CI for LSMD <sup>a</sup>				-0.931, 0.989		
P-value <sup>a</sup>				0.9523		

<sup>&</sup>lt;sup>1</sup>Intent-to-treat population includes subjects who meet all enrollment criteria or who have been given an exemption.

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PharmaStat LLC CDISC Pilot Data Dummy Product Page of

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LSM (SE) <sup>a</sup>		0.201 (0.3437)		0.230 (0.3398)		
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Between Group Least Square Mean						
Difference				0.000 (0.4050)		
LSMD (Active-Placebo) (SE) a				0.029 (0.4859)		
95% CI for LSMD <sup>a</sup>				-0.931 , 0.989		
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PharmaStat LLC CDISC Pilot Data Dummy Product Page of

	Plac	ebo	All Activ	ve Drug
Time Point	Observed Value	Change from Baseline	Observed Value	Change from Baseline
End of Treatment				
n	80	78	80	80
Mean (SD)	9.833 (4.2890)	0.460 (3.0772)	11.07 (5.3592)	021 (3.1554)
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Between Group Least Square Mean				
Difference				
LSMD (Active-Placebo) (SE) a				0.029 (0.4859)
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#### Analysis Results Metadata - Summary

Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit|Intent to Treat Population

Individual treatment groups vs. Placebo on Hy's law criteria by Visit

Table 14.2.3 Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.



#### Analysis Results Metadata - Summary

<u>Table 14.2.2</u> Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit|Intent to Treat Population <u>Individual treatment groups vs. Placebo on Hy's law criteria by Visit</u>



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Dummy Product Page of

Table 14.2.2 Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population

				_		her alue
		Placebo	Xanomeline Low Dose	Xanomeline High Dose	Placebo	Placebo
		(N=86)	(N=84)	(N=84)	v. Low	v. High
ummary of Hy's Lav	v Status by Visit					
Baseline	- Total -	86	82	84		
	N	86 (100.0%)	82 (100.0%)	84 (100.0%)		
	Y	0	0	0		
Week 2	- Total -	83	80	78		
	N	82 (98.8%)	80 (100.0%)	78 (100.0%)	1.0000	1.0000
	Y	1 (1.2%)	0	0		
Week 4	- Total -	79	72	72		
	N	78 (98.7%)	72 (100.0%)	72 (100.0%)	1.0000	1.0000
	Y	1 (1.3%)	0	0		
Week 6	- Total -	73	62	66		

<sup>&</sup>lt;sup>1</sup>Intent-to-treat population includes subjects who meet all enrollment criteria or who have been given an exemption.



#### Table 14.2.2

Display	Clinical Study Report [1 🗗 Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population	
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit	
Analysis Parameter(s)	PARAMCD = "HYLAW" (Total Bili 1.5 x ULN and Transaminase 1.5 x ULN)	
Analysis Variable(s)	ADLBHY.AVALC (Analysis Value (C))	
Analysis Reason	SPECIFIED IN SAP	
Analysis Purpose	PRIMARY OUTCOME MEASURE	
Data References (incl. Selection Criteria)	ADLBHY [PARAMCD = "HYLAW"]  Subset ADSL and ADLBHY per selection criteria. Merge subsetted ADSL and ADLBHY by USUBJID, keeping only subjects that exist in the ADSL subset.	
Documentation	Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.  Statistical Analysis Plan [5 8 8 7]	
Programming Statements	[SAS version 9.4]  proc freq data = adlbhy;  where trt01pn in (1,2);  by avisitn;  tables trt01pn * avalc / chisq sparse exact alpha = .05;  run;  * Repeat for trt01pn in (1,3) *;  Laboratory Table Program - Hy's Law	



Table 14.2.2				
Display	Clinical Study Report [1 & ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population			
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Analysis Parameter(s)	PARAMCD = "HYLAW" (Total Bili 1.5 x ULN and Transaminase 1.5 x ULN)			
Analysis Variable(s)	ADLBHY.AVALC (Analysis Value (C))			
Analysis Reason	SPECIFIED IN SAP			
Analysis Purpose	PRIMARY OUTCOME MEASURE			
Data References (incl. Selection Criteria)	ADLBHY [PARAMCD = "HYLAW"]  Subset ADSL and ADLBHY per selection criteria. Merge subsetted ADSL and ADLBHY by USUBJID, keeping only subjects that exist in the ADSL subset.			
Documentation	Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.  Statistical Analysis Plan [5 8 8]			
Programming Statements	[SAS version 9.4]  proc freq data = adlbhy;  where trt01pn in (1,2);  by avisitn;  tables trt01pn * avalc / chisq sparse exact alpha = .05;  run;  * Repeat for trt01pn in (1,3) *;  Laboratory Table Program - Hy's Law ©			



#### Table 14.2.2

Display	Clinical Study Report [1 &] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population		
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Analysis Variable(s)	ADLBHY.AVALC (Analysis Value (C))		
Analysis Reason	SPECIFIED IN SAP		
Analysis Purpose	PRIMARY OUTCOME MEASURE		
Data References (incl. Selection Criteria)	ADLBHY [PARAMCD = "HYLAW"]  Subset ADSL and ADLBHY per selection criteria. Merge subsetted ADSL and ADLBHY by USUBJID, keeping only subjects that exist in the ADSL subset.		
Documentation	Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.  Statistical Analysis Plan [5 & 8 & 7]		
Programming Statements	[SAS version 9.4]  proc freq data = adlbhy;  where trt01pn in (1,2);  by avisitn;  tables trt01pn * avalc / chisq sparse exact alpha = .05;  run;  * Repeat for trt01pn in (1,3) *;  Laboratory Table Program - Hy's Law		



Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin|Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.



Table 14.2.3	able 14.2.3			
Display	Clinical Study Report [1 & ] Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin Intent to Treat Population			
Analysis Result	Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).	7		
Analysis Parameter (s)	PARAMCD = "BILI" (Bilirubin (umol/L))	(		
Analysis Variable(s)	ADLBC.AVAL (Analysis Value) ADLBC.CHG (Change from Baseline)	_		
Analysis Reason	SPECIFIED IN SAP	4		
Analysis Purpose	PRIMARY OUTCOME MEASURE	4		
Data References (incl. Selection Criteria)	ADLBC [AVISITN IN (0, 2, 99) and PARAMCD = "BILI"]  Subset ADSL and ADLBC per selection criteria. Merge subsetted ADSL and ADLBC by USUBJID, keeping only subjects that exist in the ADSL subset. Generate column number (COLNUM) as: 1=AVAL where TRT01P='Placebo', 2=CHG where TRT01P= any treated, 3=AVAL where TRT01P='Placebo', 4=CHG where TRT01P=any treated.			
Documentation	Calculate mixed model between groups over all visits Statistical Analysis Plan [건 단 9 단 ]			
Programming Statements	[SAS version 9.4] ods output lsmestimates = _tests3; proc mixed data=_aptmix2 method=reml noclprint=20 covtest; where colnum in (2,4); class colnum avisitn usubjid; model chg = colnum base colnum*avisitn /s chisq ddfm=kr; repeated avisitn /subject= usubjid type=un; lsmestimate &_column*avisitn "Between treatments 0.05" 0 1 0 -1	F		

		Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.
	Analysis Parameter (s)	PARAMCD = "BILI" (Bilirubin (umol/L))
	Analysis Variable(s)	ADLBC.AVAL (Analysis Value) ADLBC.CHG (Change from Baseline)
-	Analysis Reason	SPECIFIED IN SAP
	Analysis Purpose	PRIMARY OUTCOME MEASURE
	Data References (incl. Selection Criteria)	ADLBC [AVISITN IN (0, 2, 99) and PARAMCD = "BILI"] Subset ADSL and ADLBC per selection criteria. Merge subsetted ADSL and ADLBC by USUBJID, keeping only subjects that exist in the ADSL subset. Generate column number (COLNUM) as: 1=AVAL where TRT01P='Placebo', 2=CHG where TRT01P= any treated, 3=AVAL where TRT01P='Placebo', 4=CHG where TRT01P=any treated.
	Documentation	Calculate mixed model within group LS Means and comparison between groups per visit Statistical Analysis Plan [7 단 9 단 ]
	Programming Statements	[SAS version 9.4] ods output lsmeans = _lsmeans; ods output diffs = _diffs; proc mixed data=_mix method=reml noclprint=20 covtest; where colnum in (2,4); class colnum avisitn usubjid; model chg = colnum base colnum*avisitn /s chisq ddfm=kr; repeated avisitn /subject= usubjid type=un; lsmeans colnum*avisitn /cl pdiff e; run;  Laboratory Table Program - Mixed Model &

#### Table 14.2.3

Display	Clinical Study Report [1 🖗 ] Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin Intent to Treat Population	Analysis Result	Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between		
Analysis Result	Mixed model repeated measures of lab values change from baseline. Least square mean		groups (estimate, 95% CI) by visit.		
	difference between-group statistics over all visits (p-value).	Analysis Parameter	PARAMCD = "BILI" (Bilirubin (umol/L))		
Analysis Parameter (s)	PARAMCD = "BILI" (Bilirubin (umol/L))	(s)	FARMICE - DIE (UIII (UIII))))))))))		
		Analysis Variable(s)	ADLBC.AVAL (Analysis Value)		
Analysis Variable(s)	ADLBC.AVAL (Analysis Value)		ADLBC.CHG (Change from Baseline)		
	ADLBC.CHG (Change from Baseline)		ADLBC.CHG (Change Holli Baseline)		
Analysis Reason	SPECIFIED IN SAP	Analysis Reason	SPECIFIED IN SAP		
Analysis Purpose	PRIMARY OUTCOME MEASURE	Analysis Purpose	PRIMARY OUTCOME MEASURE		
Data References (incl. Selection Criteria)	rences ADLBC [AVISITN IN (0, 2, 99) and PARAMCD = "BILI"]		ADLBC [AVISITN IN (0, 2, 99) and PARAMCD = "BILI"] Subset ADSL and ADLBC per selection criteria. Merge subsetted ADSL and ADLBC by USUBJID, keeping only subjects that exist in the ADSL subset. Generate column number (COLNUM) as: 1=AVAL where TRT01P='Placebo', 2=CHG where TRT01P= any treated, 3=AVAL where TRT01P='Placebo', 4=CHG where TRT01P=any treated.		
Documentation	Calculate mixed model between groups over all visits Statistical Analysis Plan [7 당 9 당 ]	Documentation	Calculate mixed model within group LS Means and comparison between groups per visit Statistical Analysis Plan [7 당 9 당 ]		
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	Laboratory Table Program - Mixed Model &		Laboratory Table Program - Mixed Model &		

# **ARM SUMMARY STRUCTURE**

# Table 14.2.2: Laboratory Summary - Hy's Law Status by ARD.Table14.2.2 Table 14.2.3: Laboratory Summary - Mixed Model Analysis ARD.Table14.2.3 of Bilirubin | Intent to Treat Population CSR 1 CSR 1

### **Define Stylesheet**

Analysis Results Metadata - Summary

Table 14.2.2 Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit|Intent to Treat Population
Individual treatment groups vs. Placebo on Hy's law criteria by Visit

Table 14.2.3 Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin|Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

<u>Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.</u>

### Pinnacle21 Analysis Displays

Display	▼ ID ▼	Description
ARD.Table14.2.2	t_lab.01_itt	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
ARD.Table14.2.3	t_labmmrm.01_itt	Mixed model repeated measures of lab values change from baseline.  Least square mean difference between-group statistics over all visits (p-value).
ARD.Table14.2.3	t labmmrm.02 itt	Mixed model repeated measures of lab values change from baseline per visit.  Least square mean within group (estimate, 95% CI) by visit.  Least square mean difference between groups (estimate, 95% CI) by visit.



### **ARM STRUCTURE**

### **Define Stylesheet**

Analysis Results Metadata - Summary



Table 14.2.2 Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit|Intent to Treat Population

Individual treatment groups vs. Placebo on Hy's law criteria by Visit

Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin|Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.

### Pinnacle21 Analysis Displays

Display	▼ ID	Description
ARD.Table14.2.2	t_lab.01_itt	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
ARD.Table14.2.3	t_labmmrm.01_itt	Mixed model repeated measures of lab values change from baseline.  Least square mean difference between-group statistics over all visits (p-value).
ARD.Table14.2.3	t_labmmrm.02_itt	Mixed model repeated measures of lab values change from baseline per visit.  Least square mean within group (estimate, 95% CI) by visit.  Least square mean difference between groups (estimate, 95% CI) by visit.



# **ARM SUMMARY STRUCTURE**

# Table 14.2.2: Laboratory Summary - Hy's Law Status by ARD.Table14.2.2 Table 14.2.3: Laboratory Summary - Mixed Model Analysis ARD.Table14.2.3 Of Bilirubin | Intent to Treat Population CSR 1

### **Define Stylesheet**

Analysis Results Metadata - Summary

Table 14.2.2 Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit|Intent to Treat Population

Individual treatment groups vs. Placebo on Hy's law criteria by Visit

Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin|Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.

### Pinnacle21 Analysis Displays

Display	<b>▼ ID</b>	▼ Description
ARD.Table14.2.2	t_lab.01_itt	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
ARD.Table14.2.3	t_labmmrm.01_itt	Mixed model repeated measures of lab values change from baseline.  Least square mean difference between-group statistics over all visits (p-value).
ARD.Table14.2.3	t_labmmrm.02_itt	Mixed model repeated measures of lab values change from baseline per visit.  Least square mean within group (estimate, 95% CI) by visit.  Least square mean difference between groups (estimate, 95% CI) by visit.



# **ARM SUMMARY STRUCTURE**

# Table 14.2.2: Laboratory Summary - Hy's Law Status by ARD.Table14.2.2 Visit | Intent to Treat Population Table 14.2.3: Laboratory Summary - Mixed Model Analysis ARD.Table14.2.3 of Bilirubin | Intent to Treat Population CSR 1

### **Define Stylesheet**

Analysis Results Metadata - Summary

<u>Table 14.2.2</u> Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit|Intent to Treat Population <u>Individual treatment groups vs. Placebo on Hy's law criteria by Visit</u>

Table 14.2.3 Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

<u>Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.</u>

### Pinnacle21 Analysis Displays

Display	¥	ID	▼ Description
ARD.Table14.2.2		t_lab.01_itt	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
ARD.Table14.2.3	1	t labmmrm.01 itt	Mixed model repeated measures of lab values change from baseline.  Least square mean difference between-group statistics over all visits (p-value).
			Mixed model repeated measures of lab values change from baseline per visit.  Least square mean within group (estimate, 95% CI) by visit.
ARD.Table14.2.3		t_labmmrm.02_itt	Least square mean difference between groups (estimate, 95% CI) by visit.



### **ARM SUMMARY STRUCTURE**

# Define Stylesheet ARD.Table14.2.2 ARD.Table14.2.3

Analysis Results Metadata - Summary

Table 14.2.2: Laboratory Summary - Hy's Law Status by

Visit Intent to Treat Population

ARD.Table14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin Intent to Treat Population

CSR

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CSR

1

<u>Table 14.2.2</u> Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit|Intent to Treat Population <u>Individual treatment groups vs. Placebo on Hy's law criteria by Visit</u>

Table 14.2.3 Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin|Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.

#### Pinnacle21 Analysis Displays

#### Pinnacle21 Analysis Results

Display	▼ ID	Description
ARD.Table14.2.2	t_lab.01_itt	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
ARD.Table14.2.3	t_labmmrm.01_itt	Mixed model repeated measures of lab values change from baseline.  Least square mean difference between-group statistics over all visits (p-value).
Mixed model repeated measures of lab values change from baseline per Least square mean within group (estimate, 95% CI) by visit.		Mixed model repeated measures of lab values change from baseline per visit.  Least square mean within group (estimate, 95% CI) by visit.  Least square mean difference between groups (estimate, 95% CI) by visit.



#### **ARM SUMMARY STRUCTURE**

# Table 14.2.2: Laboratory Summary - Hy's Law Status by ARD.Table14.2.2 Visit | Intent to Treat Population Table 14.2.3: Laboratory Summary - Mixed Model Analysis ARD.Table14.2.3 of Bilirubin | Intent to Treat Population CSR 1

#### **Define Stylesheet**

Analysis Results Metadata - Summary

<u>Table 14.2.2</u> Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit|Intent to Treat Population Individual treatment groups vs. Placebo on Hy's law criteria by Visit

Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin|Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.

#### Pinnacle21 Analysis Displays

#### Pinnacle21 Analysis Results

Display	▼ ID	Description	
ARD.Table14.2.2	t_lab.01_itt	Individual treatment groups vs. Placebo on Hy's law criteria by Visit	
		Mixed model repeated measures of lab values change from baseline.	
ARD.Table14.2.3	t_labmmrm.01_itt	Least square mean difference between-group statistics over all visits (p-value).	
		Mixed model repeated measures of lab values change from baseline per visit.	
		Least square mean within group (estimate, 95% CI) by visit.	
ARD.Table14.2.3	t_labmmrm.02_itt	Least square mean difference between groups (estimate, 95% CI) by visit.	



### **ARM SUMMARY STRUCTURE**

# Table 14.2.2: Laboratory Summary - Hy's Law Status by ARD.Table14.2.2 Visit | Intent to Treat Population Table 14.2.3: Laboratory Summary - Mixed Model Analysis ARD.Table14.2.3 of Bilirubin | Intent to Treat Population CSR 1

#### **Define Stylesheet**

Analysis Results Metadata - Summary

<u>Table 14.2.2</u> Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit|Intent to Treat Population Individual treatment groups vs. Placebo on Hy's law criteria by Visit

Table 14.2.3 Table 14.2.3: Laboratory Summary - Mixed Model Analysis of Bilirubin|Intent to Treat Population

Mixed model repeated measures of lab values change from baseline. Least square mean difference between-group statistics over all visits (p-value).

Mixed model repeated measures of lab values change from baseline per visit. Least square mean within group (estimate, 95% CI) by visit. Least square mean difference between groups (estimate, 95% CI) by visit.

#### Pinnacle21 Analysis Displays

#### Pinnacle21 Analysis Results

Display	▼ ID	▼ Description
ARD.Table14.2.2	t_lab.01_itt	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
		Mixed model repeated measures of lab values change from baseline.
ARD.Table14.2.3	t_labmmrm.01_itt	Least square mean difference between-group statistics over all visits (p-value).
		Mixed model repeated measures of lab values change from baseline per visit.
		Least square mean within group (estimate, 95% CI) by visit.
ARD.Table14.2.3	t_labmmrm.02_itt	Least square mean difference between groups (estimate, 95% CI) by visit.



Table 14.2.2	able 14.2.2		
Display	Clinical Study Report [1 & ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population		
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit		
Analysis Parameter(s)	PARAMCD = "HYLAW" (Total Bili 1.5 x ULN and Transaminase 1.5 x ULN)		
Analysis Variable(s)	ADSL.ITTFL (Intent-To-Treat Population Flag) ADLBHY.AVALC (Analysis Value (C))		
Analysis Reason	SPECIFIED IN SAP		
Analysis Purpose	PRIMARY OUTCOME MEASURE		
Data References (incl. Selection Criteria)	ADSL [ITTFL = "Y"]  ADLBHY [PARAMCD = "HYLAW"]  Subset ADSL and ADLBHY per selection criteria. Merge subsetted ADSL and ADLBHY by USUBJID, keeping only subjects that exist in the ADSL subset.		
Documentation	Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.  Statistical Analysis Plan [5 & 8 & 7]		
Programming Statements	[SAS version 9.4]  proc freq data = adlbhy;  where trt01pn in (1,2);  by avisitn;  tables trt01pn * avalc / chisq sparse exact alpha = .05;  run;  * Repeat for trt01pn in (1,3) *;  Laboratory Table Program - Hy's Law		

ID JT	Title
	Table 14.2.2: Laboratory Summary - Hy's Law Status by
ARD.Table14.2.2	Visit   Intent to Treat Population



 Clinical Study Report [1 🗗 ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population
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ID 5	Title	▼ Document	▼ Pages
	Table 14.2.2: Laboratory Summary - Hy's Law Status by		
ARD.Table14.2.2	Visit Intent to Treat Population	CSR	1



Clinical Study Report [1 🗗 ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population

ID J	Title	▼ Document	▼ Pages
	Table 14.2.2: Laboratory Summary - Hy's Law Status by		
ARD.Table14.2.2	Visit   Intent to Treat Population	CSR	1



Clinical Study Report [1 &] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population

ID J	Title	~	Document	¥	Pages
	Table 14.2.2: Laboratory Summary - Hy's Law Status by			_	
ARD.Table14.2.2	Visit   Intent to Treat Population		CSR		1



### **ANALYSIS RESULT STRUCTURE**

Display	Clinical Study Report [1 🗗 ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
Analysis Parameter(s)	PARAMCD = "HYLAW" (Total Bili 1.5 x ULN and Transaminase 1.5 x ULN)
Analysis Variable(s)	ADSL.ITTFL (Intent-To-Treat Population Flag) ADLBHY.AVALC (Analysis Value (C))
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE
Data References (incl. Selection Criteria)	ADSL [ITTFL = "Y"]  ADLBHY [PARAMCD = "HYLAW"]  Subset ADSL and ADLBHY per selection criteria. Merge subsetted ADSL and ADLBHY by USUBJID, keeping only subjects that exist in the ADSL subset.
Documentation	Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.  Statistical Analysis Plan [5 & 8 & 7]
Programming Statements	[SAS version 9.4]  proc freq data = adlbhy;  where trt01pn in (1,2);  by avisitn;  tables trt01pn * avalc / chisq sparse exact alpha = .05;  run;  * Repeat for trt01pn in (1,3) *;  Laboratory Table Program - Hy's Law

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				Individ	ual treatme	ent	groups vs.
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Variables	¥	Reason		¥	Purpose		~
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Selection Crite	ria		ŀ	Join	Comment		
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	-	EQ HYLAV	V]	t_lab	.01_itt		
ADSL[ITTFL EQ	-	) EQ HYLAV	V]	t_lab	.01_itt	<b>v</b>	<b>Documentation</b>
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Table 14.2.2	
Display	Clinical Study Report [1 & ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
Analysis Parameter(s)	PARAMCD = "HYLAW" (Total Bili 1.5 x ULN and Transaminase 1.5 x ULN)
Analysis Variable(s)	ADSL.ITTFL (Intent-To-Treat Population Flag) ADLBHY.AVALC (Analysis Value (C))
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE
Data References (incl. Selection Criteria)	ADSL [ITTFL = "Y"]  ADLBHY [PARAMCD = "HYLAW"]  Subset ADSL and ADLBHY per selection criteria. Merge subsetted ADSL and ADLBHY by USUBJID, keeping only subjects that exist in the ADSL subset.
Documentation	Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.  Statistical Analysis Plan [5 8 8]
Programming Statements	[SAS version 9.4]  proc freq data = adlbhy;  where trt01pn in (1,2);  by avisitn;  tables trt01pn * avalc / chisq sparse exact alpha = .05;  run;  * Repeat for trt01pn in (1,3) *;  Laboratory Table Program - Hy's Law

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			Indiv	/idu	ual treatmer	it groups vs.
ARD.Table14.2	.2	t_lab.01_itt	Place	ebo	on Hy's lav	v criteria by Visi
Variables	¥	Reason		*	Purpose	₩
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ADLBHY.AVAL	.C	SPECIFIED I	N SAP	•	MEASURE	
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ADLBHY[PARA	MCI	D EQ HYLAW	] t la	ab.	01 itt	
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Documentation						Documentation
Calculate Fisher's	exa	ct test of each	active	gro	up vs placebo	,
on the categorica					-	
law criteria. Fishe	er's e	exact test of Hy	's law s	stat	tus by visit.	SAP (5 8)
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Display	Clinical Study Report [1 🗗 ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit

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				Individual treatment groups vs.
ARD.Table14.2.2		t_lab.01_it	tt	Placebo on Hy's law criteria by Visit



Display	Clinical Study Report [1 🗗 ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit



Display	Clinical Study Report [1 🗗 ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit

Display	Ţ	ID	¥	Description
				Individual treatment groups vs.
ARD.Table14.2.2	2	t_lab.01_it	t	Placebo on Hy's law criteria by Visit

### **ANALYSIS PARAMETERS**

Display	Clinical Study Report [1 & ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
Analysis Parameter(s)	PARAMCD = "HYLAW" (Total Bili 1.5 x ULN and Transaminase 1.5 x ULN)
Analysis Variable(s)	ADSL.ITTFL (Intent-To-Treat Population Flag) ADLBHY.AVALC (Analysis Value (C))
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE
Data References (incl. Selection Criteria)	ADSL [ITTFL = "Y"]  ADLBHY [PARAMCD = "HYLAW"]  Subset ADSL and ADLBHY per selection criteria. Merge subsetted ADSL and ADLBHY by USUBJID, keeping only subjects that exist in the ADSL subset.
Documentation	Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.  Statistical Analysis Plan [5 8 8]
Programming Statements	[SAS version 9.4]  proc freq data = adlbhy;  where trt01pn in (1,2);  by avisitn;  tables trt01pn * avalc / chisq sparse exact alpha = .05;  run;  * Repeat for trt01pn in (1,3) *;  Laboratory Table Program - Hy's Law &

Display	,τ ID		Ŧ	Descri	ption			
				Individ	lual trea	tment	groups	vs.
ARD.Table14.2	.2 t la	b.01 i	tt	Placeb	o on Hy	's law	criteria	by Visit
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Variables	<b>▼</b> Rea	son		¥	Purpo	se		₩
ADSL.ITTFL,					PRIMA	RY O	UTCON	IE
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_	•	( HYLA)	W]	t_lab	.01_itt		Docum	entation
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### **ANALYSIS PARAMETERS**

Analysis Parameter(s) PARAMCD = "HYLAW" (Total Bili 1.5 x ULN and Transaminase 1.5 x ULN)

ID	्र Term	¥	Decoded Value
PARAMCD_ADLBHY	ALT		Alanine Aminotransferase (U/L)
PARAMCD_ADLBHY	AST		Aspartate Aminotransferase (U/L)
PARAMCD_ADLBHY	BILI		Bilirubin (umol/L)
PARAMCD_ADLBHY	BILIH	Y	Bilirubin 1.5 x ULN
PARAMCD_ADLBHY	TRAN	SHY	Transaminase 1.5 x ULN
PARAMCD_ADLBHY	HYLA	N	Total Bili 1.5 x ULN and Transaminase 1.5 x ULN



Display	Clinical Study Report [ $\frac{1}{2}$ $^{\circ}$ ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population							
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit							
Analysis Parameter(s)	PARAMCD = "HYLAW" (Total Bili 1.5 x ULN and Transaminase 1.5 x ULN)							
Analysis Variable(s)	ADSL.ITTFL (Intent-To-Treat Population Flag) ADLBHY.AVALC (Analysis Value (C))							
Analysis Reason	SPECIFIED IN SAP							
Analysis Purpose	PRIMARY OUTCOME MEASURE							
Data References (incl. Selection Criteria)	ADSL [ITTFL = "Y"]  ADLBHY [PARAMCD = "HYLAW"]  Subset ADSL and ADLBHY per selection criteria USUBJID, keeping only subjects that exist in the	-						
Documentation	Calculate Fisher's exact test of each active grou whether subject met Hy's law criteria. Fisher's Statistical Analysis Plan [5 양 8 양 ]	up vs placebo, on the categorical status (Y/N) of exact test of Hy's law status by visit.						
Programming Statements	[SAS version 9.4]  proc freq data = adlbhy;  where trt01pn in (1,2);  by avisitn;  tables trt01pn * avalc / chisq sp  run;  * Repeat for trt01pn in (1,3) *;  Laboratory Table Program - Hy's Law 6							

Display	Ţ,	ID	~	Descri	otion		
				Individ	ual treatme	nt groups	vs.
ARD.Table14.2	.2	t_lab.01_	_itt	Placeb	o on Hy's la	w criteria	by Visit
		_			_		
Variables	¥	Reason		▼	Purpose		▼
ADSL.ITTFL,					PRIMARY (	DUTCOM	E
ADLBHY.AVAL	C	SPECIFIE	DIN	N SAP	MEASURE		
Selection Crite	ria			√ Join (	Comment		
ADSL[ITTFL EQ	[Y]						
ADLBHY[PARAI	MCD	EQ HYL	AW]	t lab	.01 itt		
ADLBHY[PARAI	MCD	EQ HYL	AW]	t_lab	.01_itt		
-	MCD	EQ HYL	AW]	t_lab	.01_itt	<b>▼</b> Docume	entation l
ADLBHY[PARAI  Documentation  Calculate Fisher's					_		entation l
<b>Documentation</b> Calculate Fisher's on the categorica	exac	t test of e	ach a	active gro	oup vs placebo	ο,	entation l
<b>Documentation</b> Calculate Fisher's on the categorica	exac	t test of e	ach a	active gro	oup vs placebo	ο,	
Documentation Calculate Fisher's on the categorica law criteria. Fishe	exad al stat er's ex	et test of e tus (Y/N) o kact test o	ach a f who	active gro ether suk s law sta	oup vs placebo	ο,	
Documentation Calculate Fisher's on the categorica law criteria. Fishe	exac al stat er's ex	et test of e tus (Y/N) o kact test o	ach a f who f Hy's	active gro ether sub s law sta	oup vs placebo	ο,	
Documentation Calculate Fisher's on the categorica	s exactal state er's ex	et test of e tus (Y/N) o kact test o Programmin proc freq dat where trt01p	ach a f who f Hy's g Code	active gro ether sub s law sta e lbhy;	oup vs placebo	ο,	
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	ADSL.ITTFL (Intent-To-Treat Population Flag) ADLBHY.AVALC (Analysis Value (C))
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE





Analysis Variable(s)	ADSL.ITTFL (Intent-To-Treat Population Flag) ADLBHY.AVALC (Analysis Value (C))
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE

Variables -	Reason	7	Purpose -	ĺ
ADSL.ITTFL,			PRIMARY OUTCOME	
ADLBHY.AVALC	SPECIFIED IN SAP		MEASURE	



Analysis Variable(s)	ADSL.ITTFL (Intent-To-Treat Population Flag) ADLBHY.AVALC (Analysis Value (C))
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE

Variables <b>▼</b>	Reason	Ŧ	Purpose 🔻
ADSL.ITTFL,			PRIMARY OUTCOME
ADLBHY.AVALC	SPECIFIED IN SAP		MEASURE



### DATA REFERENCES

Display	Clinical Study Report [1 & ] Table 14.2.2: Laboratory Summary - Hy's Law Status by Visit Intent to Treat Population
Analysis Result	Individual treatment groups vs. Placebo on Hy's law criteria by Visit
Analysis Parameter(s)	PARAMCD = "HYLAW" (Total Bili 1.5 x ULN and Transaminase 1.5 x ULN)
Analysis Variable(s)	ADSL.ITTFL (Intent-To-Treat Population Flag) ADLBHY.AVALC (Analysis Value (C))
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE
Data References (incl. Selection Criteria)	ADSL [ITTFL = "Y"]  ADLBHY [PARAMCD = "HYLAW"]  Subset ADSL and ADLBHY per selection criteria. Merge subsetted ADSL and ADLBHY by USUBJID, keeping only subjects that exist in the ADSL subset.
Documentation	Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.  Statistical Analysis Plan [5 & 8 & 7]
Programming Statements	[SAS version 9.4]  proc freq data = adlbhy;  where trt01pn in (1,2);  by avisitn;  tables trt01pn * avalc / chisq sparse exact alpha = .05;  run;  * Repeat for trt01pn in (1,3) *;  Laboratory Table Program - Hy's Law

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#### DATA REFERENCES

Data References (incl. Selection Criteria)

<u>ADSL</u> [<u>ITTFL</u> = "Y"] <u>ADLBHY</u> [<u>PARAMCD</u> = "HYLAW"]

Subset ADSL and ADLBHY per selection criteria. Merge subsetted ADSL and ADLBHY by USUBJID, keeping only subjects that exist in the ADSL subset.

Selection Criteria 

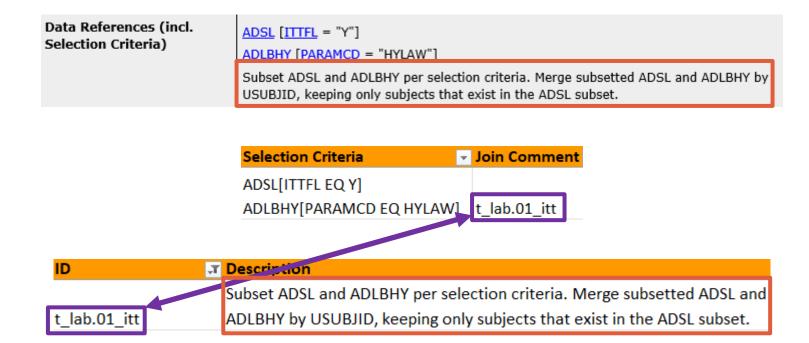
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ADSL[ITTFL EQ Y]

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#### DATA REFERENCES





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#### Documentation

Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.

Statistical Analysis Plan [FISH 🗗 ]

#### **Documentation**

▼ Documentation Refs

Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.

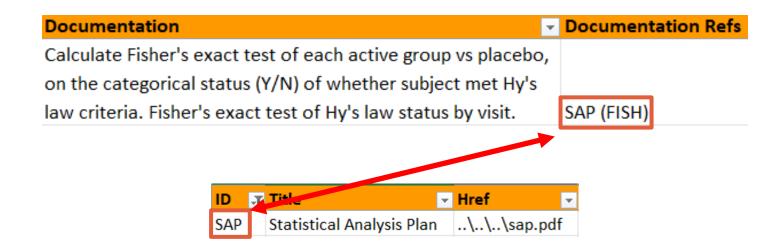
SAP (FISH)



#### Documentation

Calculate Fisher's exact test of each active group vs placebo, on the categorical status (Y/N) of whether subject met Hy's law criteria. Fisher's exact test of Hy's law status by visit.

Statistical Analysis Plan [FISH 🚱 ]





#### Documentation

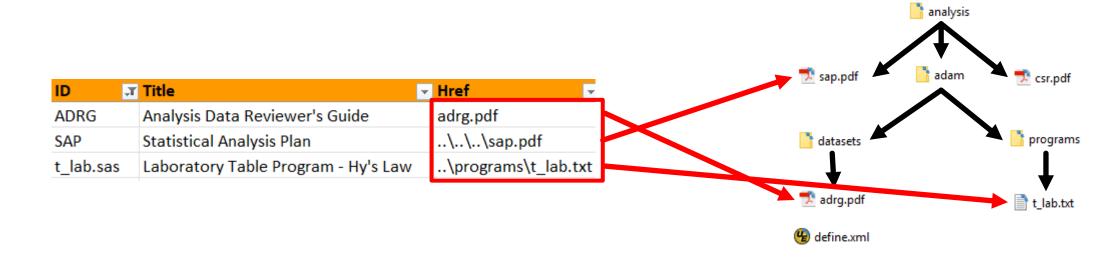
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Statistical Analysis Plan [FISH 🚱]

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Calculate Fisher's exact test of each active group vs placebo,	
on the categorical status (Y/N) of whether subject met Hy's	
law criteria. Fisher's exact test of Hy's law status by visit.	SAP (FISH)

ID "Ţ	Title -	Href -
ADRG	Analysis Data Reviewer's Guide	adrg.pdf
SAP	Statistical Analysis Plan	\\sap.pdf
t_lab.sas	Laboratory Table Program - Hy's Law	\programs\t_lab.txt

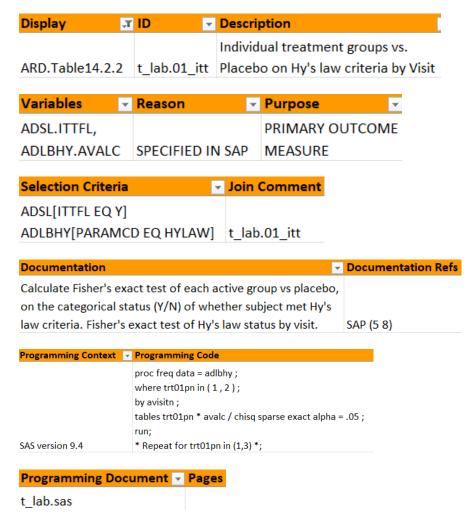






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Programming Context -	Programming Code	Programming Document 🔻	Pages -
	proc freq data = adlbhy ;		
	where trt01pn in (1,2);		
	by avisitn ;		
	tables trt01pn * avalc / chisq sparse exact alpha = .05;		
	run;		
SAS version 9.4	* Repeat for trt01pn in (1,3) *;	t_lab.sas	



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Programming Statements

[SAS version 9.4]

proc freq data = adlbhy;
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Laboratory Table Program - Hy's Law
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Programming Context Programming Code

proc freq data = adlbhy;
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tables trt01pn * avalc / chisq sparse exact alpha = .05;
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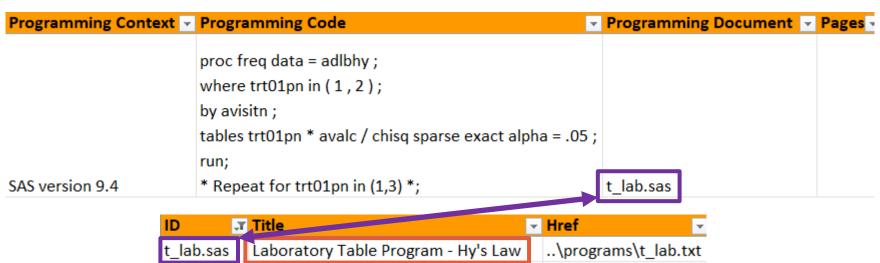
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| SAS version 9.4 | proc freq data = adlbhy; where trt01pn in (1,2); by avisitn; tables trt01pn * avalc / chisq sparse exact alpha = .05; run; * Repeat for trt01pn in (1,3) *; | Laboratory Table Program - Hy's Law & |
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#### IN SUMMARY

Help your reviewer – provide ARM

- Describe Primary, Secondary, and Exploratory outcome measures
- Use plain language descriptions

Provide additional detail with links to the SAP and programs



#### **CONTACT INFORMATION**

For questions, contact: David Brega, dbrega@pharmastat.com

For professional inquiries, contact info@pharmastat.com

