

Metadata Submission Guidelines

Document for ADaM:

Implementation in Define v 1.0

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Background

Analysis Data Model (ADaM)-
Metadata Submission Guidelines
(MSG)

Resources

CDISC website: <http://www.cdisc.org/>

ADaMIG CDISC ADaM Implementation Guide Version 1.0:

<http://www.cdisc.org/extranet/index.php?a=1067>

ADaM Analysis Data Model (ADaM) Final Version 2.1:

<http://www.cdisc.org/extranet/index.php?a=1067>

CRT-DDS Case Report Tabulation Data Definition Specification (define.xml) Version

1.0: <http://www.cdisc.org/models/def/v1.0/index.html>

FDA eCTD Guidance [Electronic Common Technical Document \(eCTD\)](#)

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm>

Controlled Terminology:

<http://www.cancer.gov/cancertopics/cancerlibrary/terminologyresources/cdisc>

CDISC ADaM update

- <http://www.cdisc.org/adam>
- Analysis Data Model Implementation Guide v 1.0
- Analysis Data Model v 2.1 Document
- ADaM v 2.1 Validation Checks
- Examples Document*
- Metadata Submission Guidelines Document**
 - ADaM Metadata subteam

ADaM Metadata Team Members

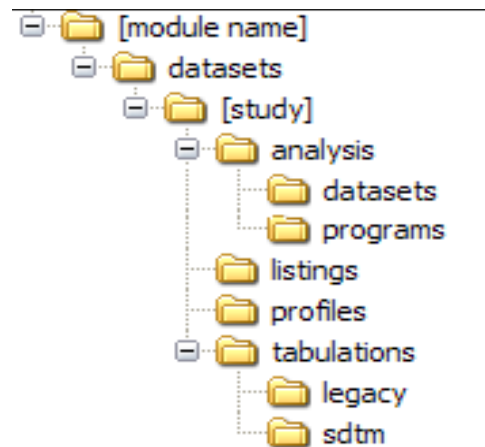
- Monika Kawohl
- Randall Austin
- Terek Peterson
- Stephen Hamburg
- Kim Minkalis
- Geoffrey Mann
- Chris Decker
- Jian Chen
- Jeff Abolafia
- Lin Yan
- David Smith*
- Lex Jansen (XML Tech)
- Sally cassells (XML Tech)
- Jack Shostak
- Susan Kenny
- Cathy Barrows
- Nate Freimark

Progress

ADaM-MSG

ADaM Metadata Submission Guidelines Document

- Guidance for compiling the eCTD module 5 “analysis” folder.



- Create example submission components for ADaM data and metadata.
- Illustrate acceptable practices and formats that sponsors should incorporate into their submissions.

ADaM-MSG Submission Components

- Submission datasets
- Submission programs
- Submission results
- define.xml (v 1.0) file
- Analysis Results Metadata Schema Extension
- Standard ADaM Stylesheet
- Optional Reviewers' Guide

Dataset Metadata

ADaM-MSG

Dataset Metadata

- Almost Identical to SDTM
- ADaM Attributes: *Name, Description, Location, Structure, Keys, Class, and Documentation*
- SDTM Attributes: *Name, Description, Location, Structure, Keys, Class, Purpose*, and Comments*

Variable Metadata

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Variable Metadata

- Very Similar to SDTM
- ADaM Attributes: ***Dataset Name****, *Name*, *Label*, *Type*, ***Display Format****, *Codelist/Controlled Terms*, and *Source/Derivation**
- SDTM Attributes: *Name*, *Label*, *Key*, *Type*, *Length*, *Codelist/Controlled Terms*, *Derivation*, *Origin*, *Role*, *Comments*

Analysis Results Metadata (ARM)

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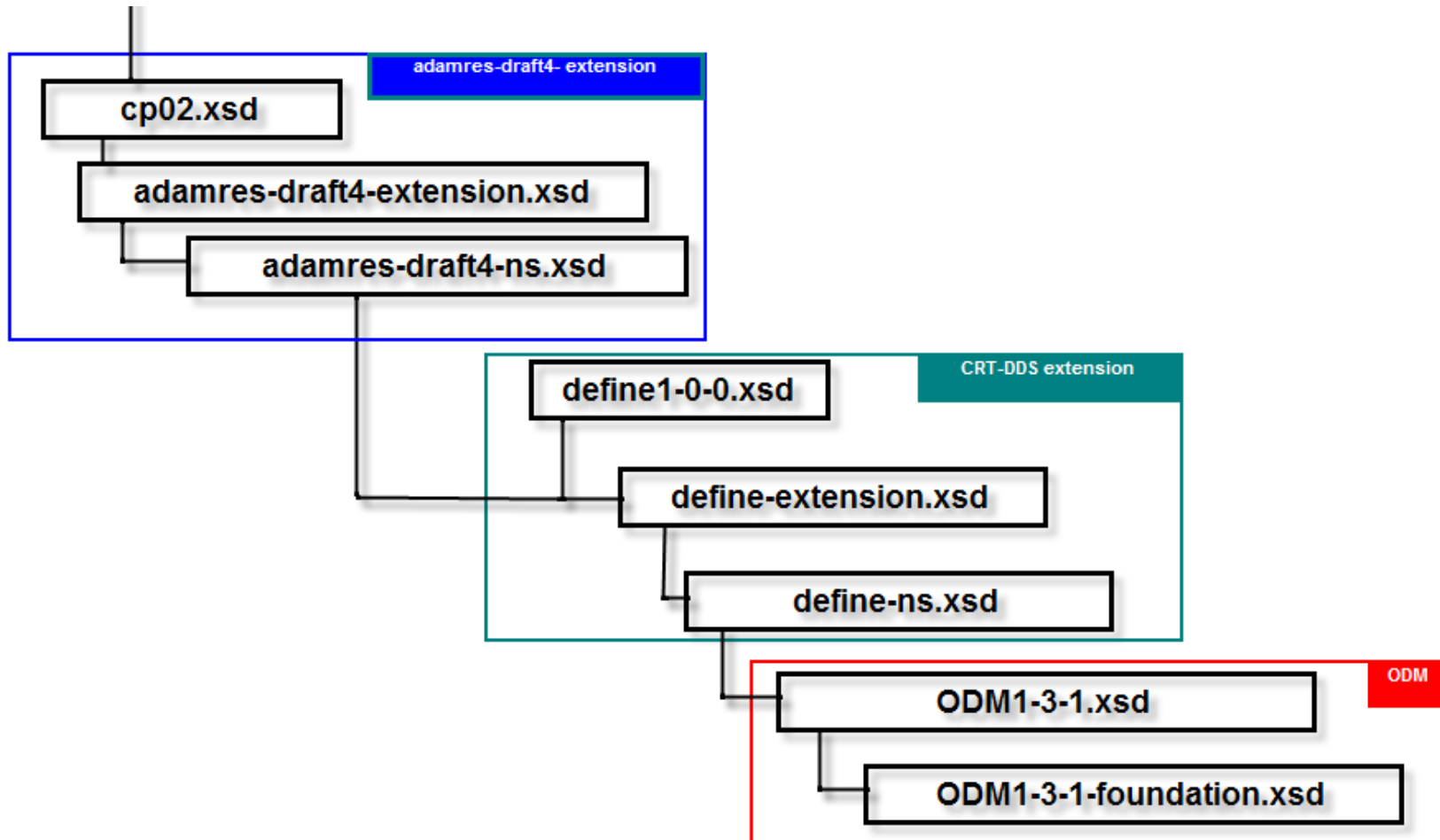
Table 5.3.1.1 in ADaM Model Document v 2.1

Metadata Field	Definition of field	Metadata
DISPLAY IDENTIFIER	Unique identifier for the specific analysis display	Table 14-3.01
DISPLAY NAME	Title of display	Primary Endpoint Analysis: ADAS Cog (11) - Change from Baseline to Week 24 – LOCF
RESULT IDENTIFIER	Identifies the specific analysis result within a display	Analysis of dose response
PARAM	Parameter	ADAS-Cog (11) Total Score
PARAMCD	Parameter code	ACTOT11
ANALYSIS VARIABLE	Analysis variable being analyzed	CHG
REASON	Rationale for performing this analysis	Primary efficacy analysis as pre-specified in protocol
DATASET	Dataset(s) used in the analysis.	ADQSADAS
SELECTION CRITERIA	Specific and sufficient selection criteria for analysis subset and / or numerator	ITTFL='Y' and AVISIT='Week 24' and PARAMCD='ACTOT11'
DOCUMENTATION	Textual description of the analysis performed	SAP Section 10.1.1. Linear model analysis of dose response for the ADAS-Cog(11) total score change from baseline at Week 24 - missing values imputed using LOCF, Efficacy population. Used PROC GLM in SAS to produce p-value (from Type III SS for treatment dose); Independent terms in model are TRTDOSE (randomized dose: 0 for placebo; 54 for low dose; 81 for high dose) SITEGR1 (site group, as a class variable) and BASE (baseline ADAS-Cog score).
PROGRAMMING STATEMENTS	The analysis syntax used to perform the analysis.	

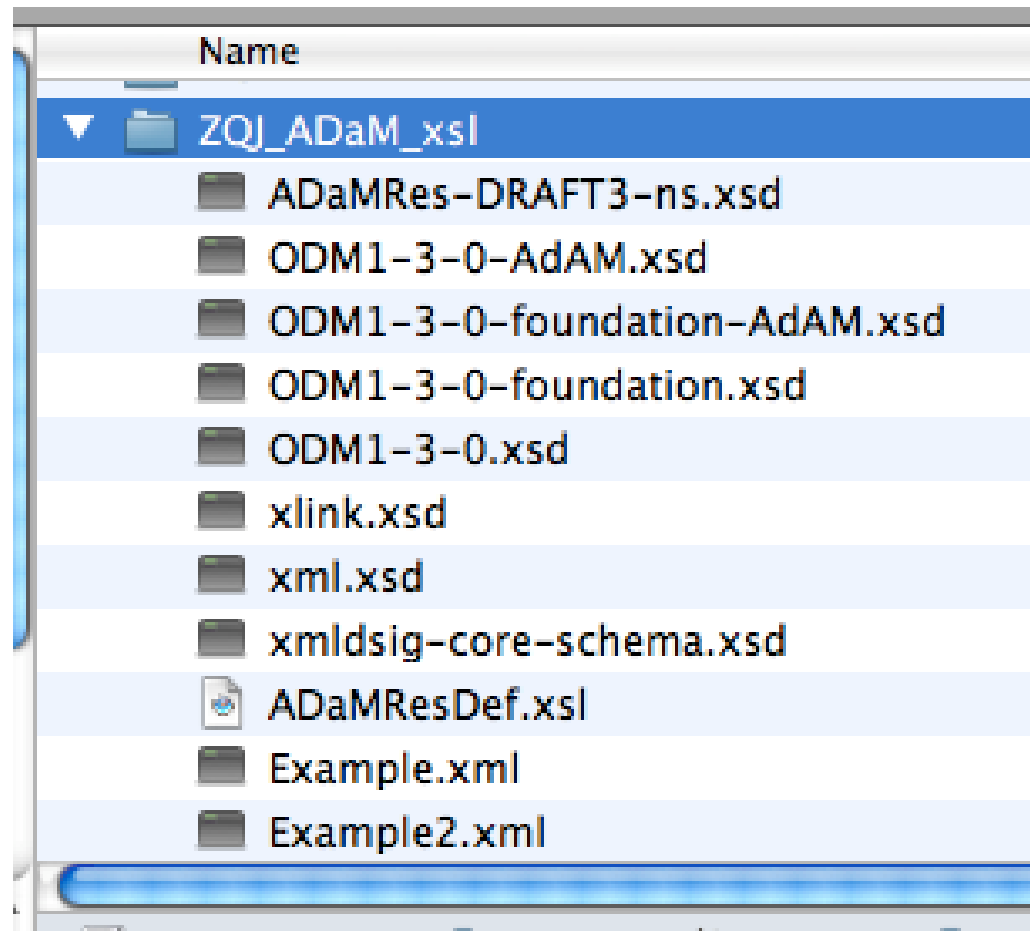
Analysis Results Metadata Schema

- XML Technologies team, working with Sally Cassells and members created three draft schemas from the Analysis Results Metadata section of a draft ADaM 2.1 Model Document in 2009.
- Implemented as an extension, not built into define specification itself.

Analysis Results Metadata (ARM) Schema Extension



ARM Schema and dependencies



ARM Stylesheet

Analysis Results Metadata (Detail) for Study XXX

Display	Table 1 : Multivariate Analysis of Variance Testing the Hypothesis of No Overall Treatment Effect at Week 6 (ITT Population)
Result Identifier	Test for Overall Treatment Effect Considering All Subscales
Analysis Parameter(s) (PARAMCD/PARAM)	SUBSCOR1=Sub Score 1 SUBSCOR2=Sub Score 2
Analysis Variable(s)	AVAL
Reason	Secondary efficacy analysis as pre-specified in SAP
Data References (incl. Selection Criteria)	Sample Analysis Topic (ADSAMPLE) [ITTFL="Y" and PARAMCD not ="TOTAL" and AVISITN=4]
Documentation	SAP Section X.X , t-program1-sas.txt , Wilks' Lambda multivariate test of treatment effect. The MANOVA statement in PROC GLM is used to generate the result after first transposing ADSAMPLE. The two subscale scores are the dependent variables in the model, with treatment being the only independent variable.
Programming Statements	(SAS 9.2 code) PROC TRANSPOSE DATA=ADSAMPLE(WHERE=(ITTFL="Y" AND AVISITN=4 AND PARAMCD NE "TOTAL")) OUT=ADSAMPLZ; VAR AVAL; ID PARAMCD; BY USUBJID TRTPN; RUN; PROC GLM DATA=ADSAMPLZ; CLASS TRTPN; MODEL SUBSCOR1 SUBSCOR2 = TRTPN / NOUNI; MANOVA H=TRTPN; RUN;

Prototype Schema changes

- Change Model Specification to Programming Statements
- Remove XML attributes from schema for determining required status of any of the given ARM Fields.
- Linkage to other elements in the define file?

Parameter Value-Level Metadata: ADaM Basic Data Structure (BDS)

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Background: ADaM Basic Data Structure (BDS)

- BDS can contain multiple analysis parameters.
- In BDS, the variable PARAM contains a unique description for every analysis parameter included in that dataset. This is similar to LBTEST or VSTEST in SDTM.
- Each value of PARAM identifies a set of one or more rows in the dataset.

Background: Parameter Value-Level Metadata Controlled Terminology

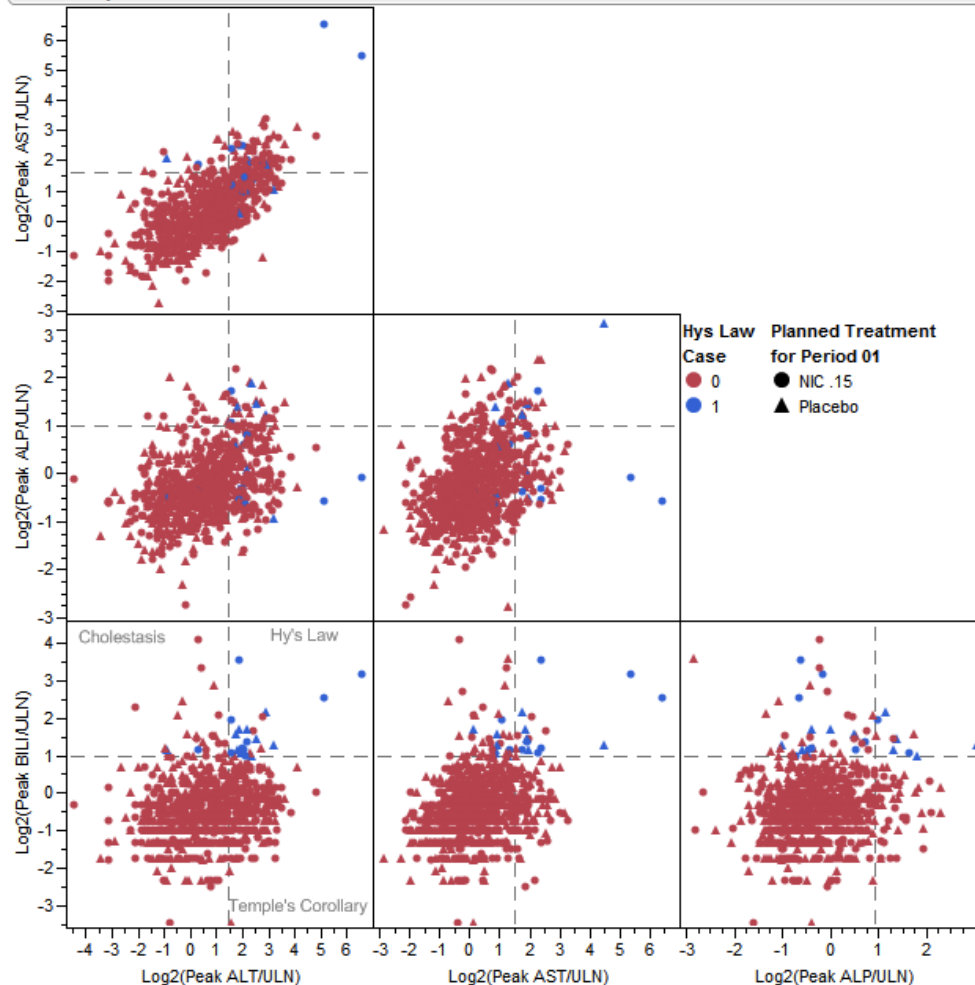
- ***ALL*** - Used when the variable metadata applies to all analysis parameters in the dataset.
- ***DEFAULT*** - Used when the variable metadata applies to all analysis parameters in the dataset except for those specifically listed within the metadata.

Background: Hy's Law

Hy's Law Screening 3D Scatterplot Missing Lab Test Summary

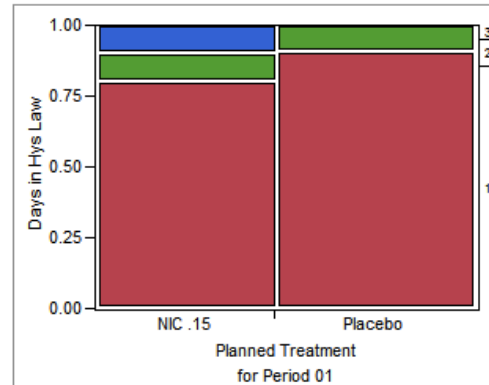
Frame Size Hys Law Cases are flagged if ALT or AST $\geq 3 \times \text{ULN}$ and BILI $\geq 2 \times \text{ULN}$ within 30 Days of ALT/AST peak.

Scatterplot Matrix



Contingency Analysis of Days in Hys Law By Planned Treatment for Period 01

Mosaic Plot



Contingency Table

	Days in Hys Law			
	1	2	3	
Count	8	1	1	10
Total %	38.10	4.76	4.76	47.62
Col %	44.44	50.00	100.00	
Row %	80.00	10.00	10.00	
NIC .15				
Count	10	1	0	11
Total %	47.62	4.76	0.00	52.38
Col %	55.56	50.00	0.00	
Row %	90.91	9.09	0.00	
Placebo				
Count	18	2	1	21
Total %	85.71	9.52	4.76	

Tests

	N	DF	-LogLike	RSquare (U)
	21	2	0.78066952	0.0742
Test	ChiSquare ProbChiSq			

Background: Example Document

- Currently Example 8 from the Examples Document.
- Categorical Analysis of Subjects Meeting Hy's Law Criteria (ADLBHY).
- Shift of Transaminase and Bilirubin levels.
- Focus on Parameter Value-Level Metadata Issues.

Example ADLBHY: Analysis Results

Summary E.8 Shifts of Hy's Law Values During Treatment (Safety Population)							
			Placebo (N=xxx)	Drug XYZ (N=xxx)			
Modified Hy’s Law Criteria	Visit	Shift [1]	Normal at Baseline	Met Criteria at Baseline	Normal at Baseline	Met Criteria at Baseline	p-value
Elevated Transminase [3]	Week 2	n	xxx	xxx	xxx	xxx	x.xx
		Normal	xxx (x.x%)	xxx (x.x%)	xxx (x.x%)	xxx (x.x%)	
		Met Criteria	xxx (x.x%)	xxx (x.x%)	xxx (x.x%)	xxx (x.x%)	
Elevated Transminase and Elevated Bilirubin [4]		n	xxx	xxx	xxx	xxx	x.xx
		Normal	xxx (x.x%)	xxx (x.x%)	xxx (x.x%)	xxx (x.x%)	
		Met Criteria	xxx (x.x%)	xxx (x.x%)	xxx (x.x%)	xxx (x.x%)	
		Etc.					

Page 1

N=Safety Population
Only subjects with baseline results are included in the summary.
[1] A change will be considered shifting from normal at baseline to met criteria or from met criteria at baseline to normal at each visit during the treatment.
[2] CMH test for general association.
[3] Transaminase 1.5 x ULN (i.e., ALT or AST)
[4] Transaminase 1.5 x ULN (i.e., ALT or AST) and Total Bili 1.5 x ULN

Example ADLBHY Parameters

- PARAM (PARAMCD)
- Elevated Transaminase (HYS1FL)
- Elevated Transaminase and Elevated Bilirubin (HYS2FL)

ADLBHY Example

PARAMCD HYS1FL and HYS2FL
at BASELINE and WEEK 2

Row	STUDYID	USUBJID	SAFFL	TRTP	TRTPN	AVISIT	AVISITN	PARAM	PARAMCD	PARAMTYP	AVAL	AVALC	BASE	BASEC	ANRHIN
1	AZY389	101-001	Y	Drug XYZ	1	BASELINE	1	Total Bilirubin umol/L	BIL		32	32	32	32	21
2	AZY389	101-001	Y	Drug XYZ	1	BASELINE	1	Alanine Aminotransferase U/L	ALT		30	30	30	30	34
3	AZY389	101-001	Y	Drug XYZ	1	BASELINE	1	Aspartate Aminotransferase U/L	AST		31	31	31	31	34
4	AZY389	101-001	Y	Drug XYZ	1	BASELINE	1	Elevated Transminase	HYS1FL	DERIVED		N		N	
5	AZY389	101-001	Y	Drug XYZ	1	BASELINE	1	Elevated Transminase and Elevated Bilirubin	HYS2FL	DERIVED		N		N	
6	AZY389	101-001	Y	Drug XYZ	1	WEEK 2	2	Total Bilirubin umol/L	BIL		24	24	32	32	21
7	AZY389	101-001	Y	Drug XYZ	1	WEEK 2	2	Alanine Aminotransferase U/L	ALT		54	54	30	30	34
8	AZY389	101-001	Y	Drug XYZ	1	WEEK 2	2	Aspartate Aminotransferase U/L	AST		45	45	31	31	34
9	AZY389	101-001	Y	Drug XYZ	1	WEEK 2	2	Elevated Transminase	HYS1FL	DERIVED		Y		N	

ADLBHY Example, continued

10	AZY389	101-001	Y	Drug XYZ	1	WEEK 2	2	Elevated Transminase and Elevated Bilirubin	HYS2FL	DERIVED		N		N	
11	AZY389	101-001	Y	Drug XYZ	1	WEEK 4	3	Total Bilirubin umol/L	BIL		33	33	32	32	21
12	AZY389	101-001	Y	Drug XYZ	1	WEEK 4	3	Alanine Aminotransferase U/L	ALT		52	52	30	30	34
13	AZY389	101-001	Y	Drug XYZ	1	WEEK 4	3	Aspartate Aminotransferase U/L	AST		47	47	31	31	34
14	AZY389	101-001	Y	Drug XYZ	1	WEEK 4	3	Elevated Transminase	HYS1FL	DERIVED		Y		N	
15	AZY389	101-001	Y	Drug XYZ	1	WEEK 4	3	Elevated Transminase and Elevated Bilirubin	HYS2FL	DERIVED		Y		N	

ADLBHY Example, continued

Row	ABLFL	CRIT1	CRIT1FL	CRIT1FN	SHIFT1	SHIFT1N
1	Y	BIL(AVAL)>1.5*ULN	Y	1		
2	Y	ALT(AVAL)>1.5*ULN	N	0		
3	Y	AST(AVAL)>1.5*ULN	N	0		
4	Y					
5	Y					
6		BIL(AVAL)>1.5*ULN	N	0		
7		ALT(AVAL)>1.5*ULN	Y	1		
8		AST(AVAL)>1.5*ULN	N	0		
9					Normal to Met Criteria	2
10					Normal to Normal	1
11		BIL(AVAL)>1.5*ULN	Y	1		
12		ALT(AVAL)>1.5*ULN	Y	1		
13		AST(AVAL)>1.5*ULN	N	0		
14					Normal to Met Criteria	2
15					Normal to Met Criteria	2

Variables are changing with PARAM

Dataset Name	Parameter Identifier	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADLBHY	*ALL*	STUDYID	Study Identifier	Text	\$10		ADSL.STUDYID
ADLBHY	*ALL*	USUBJID	Unique Subject Identifier	Text	\$10		ADSL.USUBJID
ADLBHY	*ALL*	SAFFL	Safety Population Flag	Text	\$1	Y, N	ADSL.SAFFL
ADLBHY	*ALL*	TRTP	Planned Treatment	Text	\$10	Drug XYZ Placebo	ADSL.TRT01P
ADLBHY	*ALL*	TRTPN	Planned Treatment Number	Integer	1.0	1=Drug XYZ 0=Placebo	ADSL.TRT01PN
ADLBHY	*ALL*	AVISIT	Analysis Visit	Text	\$40	BASELINE WEEK 2 WEEK 4	ADLB.AVISIT
ADLBHY	*ALL*	AVISITN	Analysis Visit (N)	Integer	1.0	1=BASELINE 2=WEEK 2 3=WEEK 4	ADLB.AVISITN
ADLBHY	*DEFAULT*	PARAM	Parameter	Text	\$100	Total Bilirubin umol/L, Alanine Aminotransferase U/L, Aspartate Aminotransferase U/L	For records with a corresponding record in ADLB, populate with the value of ADLB.PARAM
ADLBHY	HYS1FL	PARAM	Parameter	Text	\$100	Elevated Transminase	For records created to contain the Hy's Law Elevated Transminase criteria result, populate with "Elevated Transminase"
ADLBHY	HYS2FL	PARAM	Parameter	Text	\$100	Elevated Transminase and Elevated Bilirubin	For records created to contain the Hy's Law Elevated Transminase and Elevated Bilirubin criteria result, populate with "Elevated Transminase and Elevated Bilirubin"
ADLBHY	PARAMCD	PARAMCD	Parameter Code	Text	\$8	BIL, ALT, AST, HYS1FL, HYS2FL	One-to-one correspondence with PARAM For records with a corresponding record in ADLB, ADLBHY.PARAMCD=ADLB.PARAMCD If PARAM="Elevated Transminase", ADLBHY.PARAMCD="HYS1FL" If PARAM="Elevated Transminase and Elevated Bilirubin", ADLBHY.PARAMCD="HYS2FL"
ADLBHY	*ALL*	PARAMTYP	Parameter Type	Text	\$7	DERIVED	Populated with "DERIVED" for records created to contain the Elevated Transminase or the Elevated Transminase and Elevated Bilirubin, blank otherwise
ADLBHY	*DEFAULT*	AVAL	Analysis Value	Float	7.3		ADLB.AVAL
ADLBHY	HYS1FL	AVAL	Analysis Value	Float	7.3		blank

HYS1FL and HYS2FL are changing context

Dataset Name	Parameter Identifier	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADLBHY	HYS2FL	AVAL	Analysis Value	Float	7.3		blank
ADLBHY	DEFAULT	AVALC	Analysis Value (C)	Text	\$7		ADLB.AVALC
ADLBHY	HYS1FL	AVALC	Analysis Value (C)	Text	\$7	Y, N	Considering the ADLBHY records for which ADLBHY.USUBJID and ADLBHY.AVISIT match those for this record, set AVALC to "Y" if at least one of the records with ADLBHY.PARAMCD in ("ALT","AST") have CRIT1FL="Y", set AVALC to "N" otherwise
ADLBHY	HYS2FL	AVALC	Analysis Value (C)	Text	\$7	Y, N	Considering the ADLBHY records for which ADLBHY.USUBJID and ADLBHY.AVISIT match those for this record, set AVALC to "Y" if at least one of the records with ADLBHY.PARAMCD in ("ALT","AST") have CRIT1FL="Y" and if the record with ADLBHY.PARAMCD="BIL" has CRIT1FL="Y", set AVALC to "N" otherwise
ADLBHY	*DEFAULT*	BASE	Baseline Value	Float	7.3		ADLB.BASE
ADLBHY	HYS1FL	BASE	Baseline Value	Float	7.3		blank
ADLBHY	HYS2FL	BASE	Baseline Value	Float	7.3		blank
ADLBHY	*ALL*	BASEC	Baseline Value(C)	Text	\$7		ADLBHY.AVALC from record where ADLBHY.USUBJID and ADLBHY.AVISIT match those for this record and ADLBHY.ABLFL="Y"
ADLBHY	*DEFAULT*	ANRHIN	Analysis Normal Range Upper Limit (N)	Float	7.3		ADLB.ANRHIN
ADLBHY	HYS1FL	ANRHIN	Analysis Normal Range Upper Limit (N)	Float	7.3		blank
ADLBHY	HYS2FL	ANRHIN	Analysis Normal Range Upper Limit (N)	Float	7.3		blank
ADLBHY	*ALL*	ABLFL	Baseline Record Flag	Text	\$1	Y	"Y" if record contains the baseline value, i.e., if ADLBHY.AVISITN=1; blank otherwise
ADLBHY	*DEFAULT*	CRIT1	Analysis Criterion 1	Text	\$100		Blank if ADLBHY.PARAMTYP="DERIVED"
ADLBHY	BIL	CRIT1	Analysis Criterion 1	Text	\$100	BIL(AVAL)>1.5*ULN	Populate when ADLBHY.PARAMCD="BIL"

HYS1FL and HYS2FL have no context with AVAL

Value Level Metadata (VL.ADLBHY.AVAL)							
Source Variable	Value	Label	Type	Controlled Terms or Format	Origin	Role	Comment
AVAL	BIL	Total Bilirubin umol/L	float		ADLB.AVAL		ADLB.AVAL
AVAL	ALT	Alanine Aminotransferase U/L	float		ADLB.AVAL		ADLB.AVAL
AVAL	AST	Aspartate Aminotransferase U/L	float		ADLB.AVAL		ADLB.AVAL
AVAL	HYS1FL	Elevated Transminase	float				Blank 
AVAL	HYS2FL	Elevated Transminase and Elevated Bilirubin	float				Blank 

HYS1FL and HYS2FL have context with AVALC

Value Level Metadata (VL.ADLBHY.AVALC)							
Source Variable	Value	Label	Type	Controlled Terms or Format	Origin	Role	Comment
AVALC	BIL	Total Bilirubin umol/L	text		ADLB.AVALC		ADLB.AVALC
AVALC	ALT	Alanine Aminotransferase U/L	text		ADLB.AVALC		ADLB.AVALC
AVALC	AST	Aspartate Aminotransferase U/L	text		ADLB.AVALC		ADLB.AVALC
AVALC	HYS1FL	Elevated Transminase	text	CL.YN	Derived		Considering the ADLBHY records for which ADLBHY.USUBJID and ADLBHY.AVISIT match those for this record, set AVALC to 'Y' if at least one of the records with ADLBHY.PARAMCD in ('ALT','AST') have CRIT1FL='Y', set AVALC to 'N' otherwise.
AVALC	HYS2FL	Elevated Transminase and Elevated Bilirubin	text	CL.YN	Derived		Considering the ADLBHY records for which ADLBHY.USUBJID and ADLBHY.AVISIT match those for this record, set AVALC to 'Y' if at least one of the records with ADLBHY.PARAMCD in ('ALT','AST') have CRIT1FL='Y' and if the record with ADLBHY.PARAMCD='BIL' has CRIT1FL='Y', set AVALC to 'N' otherwise.

ADLBHY Example, continued

Row	ABLFL	CRIT1	CRIT1FL	CRIT1FN	SHIFT1	SHIFT1N
1	Y	BIL(AVAL)>1.5*ULN	Y	1		
2	Y	ALT(AVAL)>1.5*ULN	N	0		
3	Y	AST(AVAL)>1.5*ULN	N	0		
4	Y					
5	Y					
6		BIL(AVAL)>1.5*ULN	N	0		
7		ALT(AVAL)>1.5*ULN	Y	1		
8		AST(AVAL)>1.5*ULN	N	0		
9					Normal to Met Criteria	2
10					Normal to Normal	1
11		BIL(AVAL)>1.5*ULN	Y	1		
12		ALT(AVAL)>1.5*ULN	Y	1		
13		AST(AVAL)>1.5*ULN	N	0		
14					Normal to Met Criteria	2
15					Normal to Met Criteria	2

Analysis Data Metadata

Dataset Name	Parameter Identifier	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADLBHY	ALT	CRIT1	Analysis Criterion 1	Text	\$100	ALT(AVAL)>1.5*ULN	Populate when ADLBHY.PARAMCD="ALT"
ADLBHY	AST	CRIT1	Analysis Criterion 1	Text	\$100	AST(AVAL)>1.5*ULN	Populate when ADLBHY.PARAMCD="AST"
ADLBHY	*DEFAULT*	CRIT1FL	Criterion 1 Evaluation Result Flag	Text	\$1		Blank if ADLBHY.PARAMTYP="DERIVED"
ADLBHY	BIL	CRIT1FL	Criterion 1 Evaluation Result Flag	Text	\$1	Y, N	"Y" if ADLBHY.AVAL>1.5*ADLBHY.ANRHIN, "N" otherwise
ADLBHY	ALT	CRIT1FL	Criterion 1 Evaluation Result Flag	Text	\$1	Y, N	"Y" if ADLBHY.AVAL>1.5*ADLBHY.ANRHIN, "N" otherwise
ADLBHY	AST	CRIT1FL	Criterion 1 Evaluation Result Flag	Text	\$1	Y, N	"Y" if ADLBHY.AVAL>1.5*ADLBHY.ANRHIN, "N" otherwise
ADLBHY	*ALL*	CRIT1FN	Criterion 1 Evaluation Result Flag (N)	Integer	1.0	1=Y, 0=N	From ADLBHY.CRIT1FL
ADLBHY	*DEFAULT*	SHIFT1	Shift 1	Text	\$20		Blank if ADLBHY.PARAMTYP="DERIVED" or if ADLBHY.ABLFL="Y"
ADLBHY	HYS1FL	SHIFT1	Shift 1	Text	\$30	Normal to Normal, Normal to Met Criteria, Met Criteria to Normal, Met Criteria to Met Criteria	Using values on this record: "Normal to Normal" if ADLBHY.BASEC="N" and ADLBHY.AVALC="N", "Normal to Met Criteria" if ADLBHY.BASEC="N" and ADLBHY.AVALC="Y", "Met Criteria to Normal" if ADLBHY.BASEC="Y" and ADLBHY.AVALC="N", "Met Criteria to Met Criteria" if ADLBHY.BASEC="Y" and ADLBHY.AVALC="Y"
ADLBHY	HYS2FL	SHIFT1	Shift 1	Text	\$20	Normal to Normal, Normal to Met Criteria, Met Criteria to Normal, Met Criteria to Met Criteria	Using values on this record: "Normal to Normal" if ADLBHY.BASEC="N" and ADLBHY.AVALC="N", "Normal to Met Criteria" if ADLBHY.BASEC="N" and ADLBHY.AVALC="Y", "Met Criteria to Normal" if ADLBHY.BASEC="Y" and ADLBHY.AVALC="N", "Met Criteria to Met Criteria" if ADLBHY.BASEC="Y" and ADLBHY.AVALC="Y"
ADLBHY	*ALL*	SHIFT1N	Shift 1 (N)	Integer		1=Normal to Normal, 2=Normal to Met Criteria, 3=Met Criteria to Normal, 4=Met Criteria to Met Criteria	From ADLBHY.SHIFT1

HYS1FL and HYS2FL have context with SHIFT1

Value Level Metadata (VL.ADLBHY.SHIFT1)							
Source Variable	Value	Label	Type	Controlled Terms or Format	Origin	Role	Comment
SHIFT1	BIL	Total Bilirubin umol/L	text				Blank
SHIFT1	ALT	Alanine Aminotransferase U/L	text				Blank
SHIFT1	AST	Aspartate Aminotransferase U/L	text				Blank
SHIFT1	HYS1FL	Elevated Transminase	text	CL.ADLBHY.SHIFT	Derived		Using values on this record: 'Normal to Normal' if ADLBHY.BASEC='N' and ADLBHY.AVALC='N'; 'Normal to Met Criteria' if ADLBHY.BASEC='N' and ADLBHY.AVALC='Y'; 'Met Criteria to Normal' if ADLBHY.BASEC='Y' and ADLBHY.AVALC='N'; 'Met Criteria to Met Criteria' if ADLBHY.BASEC='Y' and ADLBHY.AVALC='Y'
SHIFT1	HYS2FL	Elevated Transminase and Elevated Bilirubin	text	CL.ADLBHY.SHIFT	Derived		Using values on this record: 'Normal to Normal' if ADLBHY.BASEC='N' and ADLBHY.AVALC='N'; 'Normal to Met Criteria' if ADLBHY.BASEC='N' and ADLBHY.AVALC='Y'; 'Met Criteria to Normal' if ADLBHY.BASEC='Y' and ADLBHY.AVALC='N'; 'Met Criteria to Met Criteria' if ADLBHY.BASEC='Y' and ADLBHY.AVALC='Y'

Draft Document in Q1 of 2012

ADaM-MSG

Questions?
Suggestions?

ADaM-MSG

Extra Slides for background, if
necessary

ADaM-MSG

Analysis Data Metadata

Dataset Name	Dataset Description	Dataset Location	Dataset Structure	Key Variables of Dataset	Class of Dataset	Documentation
ADLBHY	Hy's Law analysis data, including lab data used to assess Hy's Law criteria	<u>adlbhy.xpt</u>	One record per subject per parameter per analysis visit	STUDYID, USUBJID, PARAMCD, AVISIT	BDS	adlbhy.sas

Datasets for Study ADAM_Example_8						
Dataset	Description	Class	Structure	Purpose	Keys	Location
	Hy's Law Criteria	Analysis	One record per subject per parameter per analysis visit	Analysis	STUDYID, USUBJID, PARAMCD, AVISIT	adlbhy.xpt

Analysis Results Metadata

Metadata Field	Metadata
DISPLAY IDENTIFIER	<u>Summary E.8</u>
DISPLAY NAME	Shifts of Hy's Law Values During Treatment (Safety Population)
RESULT IDENTIFIER	CMH Test for general association
PARAM	Elevated Transminase, Elevated Transminase and Elevated Bilirubin
PARAMCD	HYS1FL, HYS2FL
ANALYSIS VARIABLE	SHIFT1N
REASON	Secondary safety analysis as pre-specified in SAP
DATASET	<u>ADLBHY</u>
SELECTION CRITERIA	SAFFL="Y" and PARAMCD in ("HYS1FL", "HYS2FL")
DOCUMENTATION	Shift table summarizing whether or not a subject's status changed from baseline during the treatment period for changes based on threshold ranges and changes based on Hy's Law. Comparisons between Placebo and Treatment are illustrated by Cochran-Mantel-Haenszel (CMH) test.
PROGRAMMING STATEMENTS	PROC FREQ DATA=ADLBHY; TABLES SHIFT1N*TRTPN / LIST MISSING CMH; BY AVISITN PARAMCD; OUT = RSLTS OUTPCT MISSPRINT; OUTPUT OUT=CMHRSLT CMH; RUN;

SHIFT1 and SHIFT1N Codelists

ADLBHY Shift 1, Reference Name (CL.ADLBHY.SHIFT)	
Code Value	Code Text
Normal to Normal	Normal to Normal
Normal to Met Criteria	Normal to Met Criteria
Met Criteria to Normal	Met Criteria to Normal
Met Criteria to Met Criteria	Normal to Abnormal
ADLBHY Shift 1 (N), Reference Name (CL.ADLBHY.SHIFTN)	
Code Value	Code Text
1	Normal to Normal
2	Normal to Met Criteria
3	Met Criteria to Normal
4	Normal to Abnormal