ADaMIG v1.2 & ADaM Integration

Presented by

Brian Harris - Dir. of Biometrics Operations at Medimmune (AstraZeneca)
Deborah Bauer- Associate Director, Biostatistics, Sanofi

18 APR 2019

Agenda

1. Presenter Bios + Panelists
2. Housekeeping
3. Feature Presentation
4. Question & Answer Session
5. Upcoming Learning Opportunities + Resources

Our Presenters

- Brian Harris - Dir. of Biometrics Operations at Medimmune (AstraZeneca)
- Deborah Bauer- Associate Director, Biostatistics, Sanofi

Our Panelists

- Nate Friemark
- Kimberly Minalis
- Sandra Minjoe
- Wayne Zhong

Housekeeping

Housekeeping

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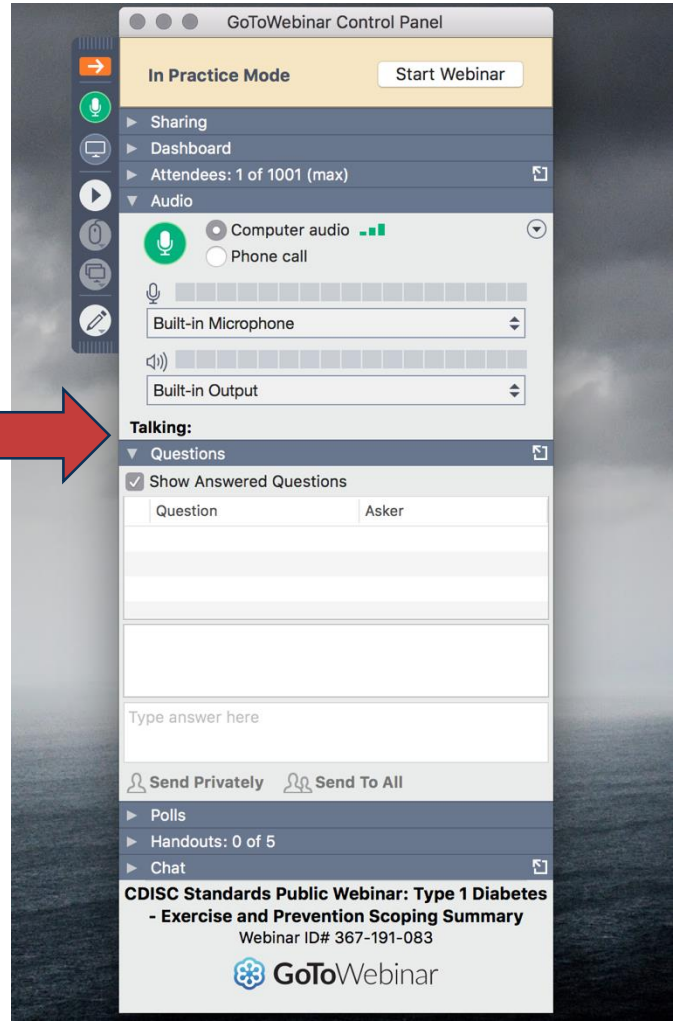
  - Examples:
    - Sam: ‘Question’
    - Anthony: ‘Question’



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18 APR 2019

ADaM Implementation Guide v1.2

Publication pending

Presented by Brian Harris
Director of Biometrics Operations, AstraZeneca

04.18.2019

Agenda

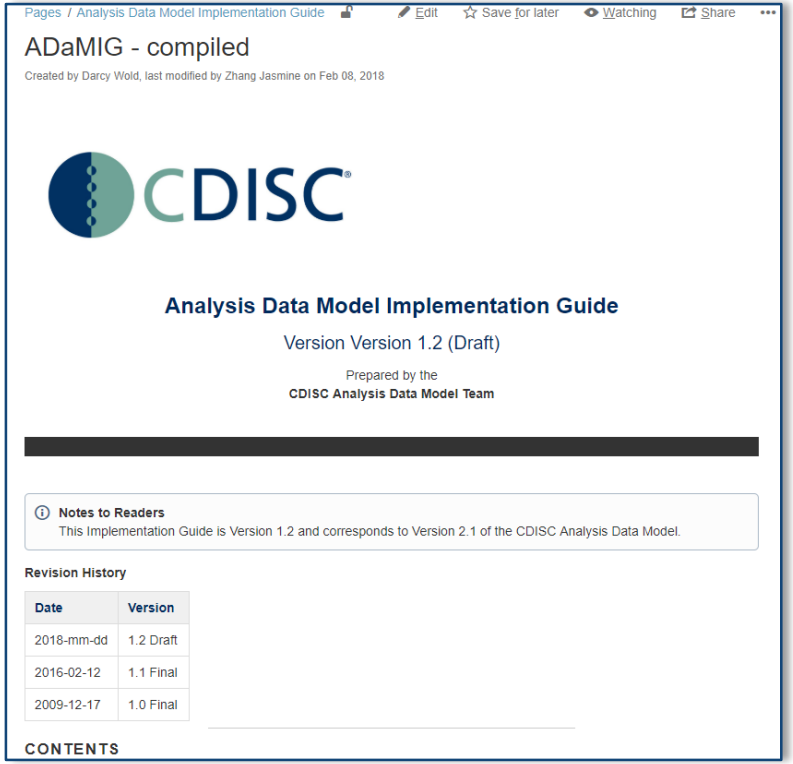
1. Brief History of the ADaM Implementation Guide (ADaMIG)
2. Overview of Additions & Clarifications in ADaMIG v1.2
3. Addition: Stratification Variables in ADSL
4. Addition: Bi-directional Toxicity Variables in BDS
5. Clarification: Pre-ADSL Dataset Concept
6. Other Changes
   - ❖ PARQUAL
   - ❖ BASETYPE
   - ❖ Relationship between Primary & Secondary Variables

Brief History of the ADaMIG

- ADaMIG v1.0 released late 2009
  - Two data structures were described
    - Subject Level Dataset (ADSL)
    - Basic Data Structure (BDS)
- Supplemental documents for specific analyses
  - BDS TTE v1.0 released mid 2012
  - ADAE v1.0 released mid 2012
- ADaMIG v1.1 released early 2016
  - OCCDS v1.0 concurrently released as final

Overview of Additions & Clarifications in ADaMIG v1.2

- Nomenclature for stratification variables in ADSL
- Recommended approach for bi-directional toxicity grades in BDS
- Clarifications allowing the use of a pre-ADSL dataset
- Additional descriptions, clarifications, refinement of text, and examples



Addition: Stratification Variables in ADSL

Stratification Variables in ADSL

- A prognostic factor is an aspect of the disease or a characteristic of the subject that may influence treatment response
- Stratified randomization is used to ensure balance of treatment assignments across one or more prognostic factors
- The prognostic factors used to stratify the randomization are specified in the protocol
- For analysis, we may need
  - Stratification values that were used for randomization
  - Stratification values that come from verification source
- Table 3.2.9 in the IG provides a set of variables to allow maximum flexibility in representing the description of the prognostic factors used for stratification

Stratification Variables within ADSL

Variable Name	Variable Label	Type	Core	Example
STRATAR	Strata Used for Randomization	Char	Perm	STRATAR = ">=50, Treatment experienced, N"
STRATARN	Strata Used for Randomization (N)	Num	Perm	STRATARN = 3 when STRATAR = ">=50, Treatment experienced, N"
STRATwD	Description of Stratification Factor w	Char	Perm	STRAT3D = "Hypertension"
STRATwR	Strat Factor w Value Used for Rand	Char	Perm	STRAT3R = "N“
STRATwRN	Strat Factor w Value Used for Rand (N)	Num	Perm	STRAT3RN = 0 when STRAT3R = "N"
STRATAV	Strata from Verification Source	Char	Perm	STRATAV = ">=50, Treatment experienced, Y"
STRATAVN	Strata from Verification Source (N)	Num	Perm	STRATAVN = 4 when STRATAV = ">=50, Treatment experienced, Y"
STRATwV	Strat Factor w Value from Verif Source	Char	Perm	STRAT3V = "Y"
STRATwVN	Strat Fact w Val from Verif Source (N)	Num	Perm	STRAT3VN = 1 when STRAT3V = "Y"

The examples are based on the combination of three stratification factors: Age Group (“<50” or “>=50”), Prior Treatment Status (“Treatment naïve”, “Treatment experienced”), and Hypertension (“Y” or “N”).

Addition: Bi-directional Toxicity Variables

Handling lab limits assessed in more than one direction

- Lab values may need to be assessed for toxicity in more than one direction
  - both abnormally low values as well as abnormally high values are of concern
- The ADaM team decided to provide guidance around additional variables that can be added to handle bi-directional toxicity grading
- The examples are based on CTC Toxicity Grades; however, the bi-directional variables can also be used if there is sponsor-specific toxicity grading

Bi-directional Variables

Variable Name	Variable Label	Type	Core	Description
ATOXGRL	Analysis Toxicity Grade Low	Char	Perm	Low Toxicity grade of AVAL or AVALC for analysis
ATOXGRLN	Analysis Toxicity Grade Low (N)	Num	Perm	Numeric representation of ATOXGRL
ATOXGRH	Analysis Toxicity Grade High	Char	Perm	High Toxicity grade of AVAL or AVALC for analysis
ATOXGRHN	Analysis Toxicity Grade High (N)	Num	Perm	Numeric representation of ATOXGRH
BTOXGRL	Baseline Toxicity Grade Low	Char	Perm	ATOXGRL of the baseline record identified by ABLFL
BTOXGRLN	Baseline Toxicity Grade Low (N)	Num	Perm	Numeric representation of BTOXGRL.
BTOXGRH	Baseline Toxicity Grade High	Char	Perm	ATOXGRH of the baseline record identified by ABLFL
BTOXGRHN	Baseline Toxicity Grade High (N)	Num	Perm	Numeric representation of BTOXGRH.
ATOXDSCL	Analysis Toxicity Description Low	Char	Perm	The analysis toxicity term used to describe toxicity in the low direction.
ATOXDSCH	Analysis Toxicity Description High	Char	Perm	The analysis toxicity term used to describe toxicity in the high direction.

Bi-directional Lab Example

Legend
Yellow box → bi-directional grading
Red box → grading in only 1 direction

Row	USUBJID	PARAMCD	AVISITN	AVAL	BASE	ABLFL	ANRLO	ANRHI
1	001-0001	HGB	1	7.4	7.4	Y	11	16.1
2	001-0001	HGB	2	20.5	7.4		11	16.1
3	001-0001	AST	1	33	33	Y	5	25
4	001-0001	AST	2	55	33		5	25
5	001-0001	AST	3	60	33		5	25
6	001-0001	AST	4	77	33		5	25
7	001-0001	PLAT	1	250	250	Y	150	450
8	001-0001	PLAT	2	100	250		150	450
9	001-0001	PLAT	3	99	250		150	450
10	001-0001	PLAT	4	75	250		150	450
11	001-0001	PLAT	5	49	250		150	450
12	001-0002	HGB	1	21.1	21.1	Y	11	16.1

Row	ATOXDSCL	ATOXGRL	BTOXGRL	ATOXDSCH	ATOXGRH	BTOXGRH
1	Anemia	Grade 3	Grade 3	Hemoglobin increased	Grade 0	Grade 0
2	Anemia	Grade 0	Grade 3	Hemoglobin increased	Grade 3	Grade 0
3				Aspartate aminotransferase increased	Grade 1	Grade 1
4				Aspartate aminotransferase increased	Grade 1	Grade 1
5				Aspartate aminotransferase increased	Grade 1	Grade 1
6				Aspartate aminotransferase increased	Grade 2	Grade 1
7	Platelet count decreased	Grade 0	Grade 0			
8	Platelet count decreased	Grade 1	Grade 0			
9	Platelet count decreased	Grade 1	Grade 0			
10	Platelet count decreased	Grade 1	Grade 0			
11	Platelet count decreased	Grade 3	Grade 0			
12	Anemia	Grade 0	Grade 0	Hemoglobin increased	Grade 3	Grade 3

Bi-directional Lab Example

- Example on previous slide has variables supporting bi-directional toxicity grades
- Variables with suffixes *GRL and *GRH as well as ATOXDSCL and ATOXDSCH are used to indicate if that record is assessed in the low or high direction
- The Yellow box demonstrates the following:
  - ATOXDSCL is populated whenever AVAL is not null and grading is in the LOW direction, even if ATOXGRL is null
  - ATOXDSCH is populated whenever AVAL is not null and grading is in the HIGH direction, even if ATOXGRH is null
- The Red box demonstrates the following:
  - PARAMCD PLAT has toxicity grading only in the low direction, only BTOXGRL, ATOXGRL, and other toxicity variables in the low direction are populated
  - None of the high direction toxicity variables for PARAMCD PLAT are ever populated, even if the value is out of range in the high direction (ANRIND=HIGH)

Bi-directional Example using SHIFTy

USUBJID	AVAL	BASE	ABLFL	ATOXGRL	BTOXGRL	ATOXGRH	BTOXGRH	SHIFT1	SHIFT2
001-0001	7.4	7.4	Y	Grade 3	Grade 3	Grade 0	Grade 0		
001-0001	20.5	7.4		Grade 0	Grade 3	Grade 3	Grade 0	Grade 3 to Grade 0	Grade 0 to Grade 3
001-0001	33	33	Y			Grade 1	Grade 1		
001-0001	55	33				Grade 1	Grade 1		Grade 1 to Grade 1
001-0001	60	33				Grade 1	Grade 1		Grade 1 to Grade 1
001-0001	77	33				Grade 2	Grade 1		Grade 1 to Grade 2
001-0001	250	250	Y	Grade 0	Grade 0				
001-0001	100	250		Grade 1	Grade 0			Grade 0 to Grade 1	
001-0001	99	250		Grade 1	Grade 0			Grade 0 to Grade 1	
001-0001	75	250		Grade 1	Grade 0			Grade 0 to Grade 1	
001-0001	49	250		Grade 3	Grade 0			Grade 0 to Grade 3	
001-0002	21.1	21.1	Y	Grade 0	Grade 0	Grade 3	Grade 3		

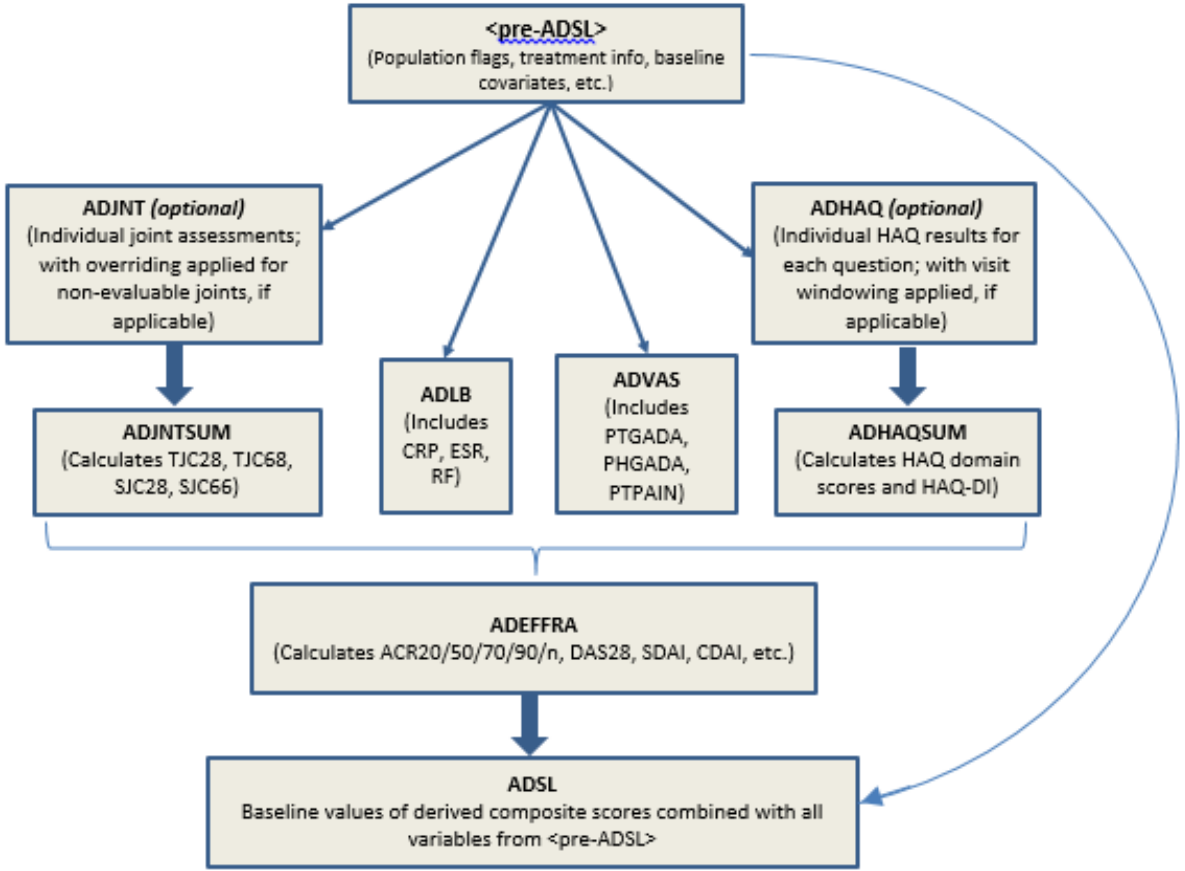
Bi-directional Shift Variables Example

- ATOXGRL, ATOXGRH, and the corresponding baseline toxicity variables were used to derive shifts in toxicity grade
- In this example, SHIFT1 is the shift from baseline in low direction toxicity
  - Derived from BTOXGRL and ATOXGRL
- In this example, SHIFT2 is the shift from baseline in high direction toxicity
  - Derived from BTOXGRH and ATOXGRH

Clarification: Pre-ADSL Dataset Concept

Pre-ADSL Dataset Concept

Example of a possible dataset creation flow
(As proposed in the Rheumatoid Arthritis Therapeutic Area User's Guide (RA TAUG))



ADaMIG v1.2 text was clarified to remove any prescribed method of creating ADSL

cdisc

Other Changes

PARQUAL

- In the draft version of ADaMIG v1.2 that went through public review, PARQUAL was included as a new permissible variable in BDS
- Due to confusion discovered during public review on when to use PARQUAL, the ADaM team has determined that PARQUAL needs more clarification and may be considered for a future release
- PARQUAL is not part of this release
- As in prior releases, there are no qualifiers allowed for PARAM

BASETYPE Should be Populated for a PARAM if Used

USUBJID	PARAMCD	AVISIT	AVAL	BASE	ABLFL	BASETYPE
001-0001	ALT	Screening 1	20	20	Y	MIN
001-0001	ALT	Screening 2	25	25	Y	MAX
001-0001	ALT	Week 1	19	20		MIN
001-0001	ALT	Week 1	19	25		MAX
001-0001	ALT	Week 2	21	20		MIN
001-0001	ALT	Week 2	21	25		MAX
001-0001	ALP	Screening 1	25	27		
001-0001	ALP	Screening 2	27	27	Y	
001-0001	ALP	Week 1	26	27		
001-0001	ALP	Week 2	24	27		

- In ADaMIG v1.1, the BASETYPE CDISC notes stated the following:
  - *If used for any PARAM within a dataset, should be non-null for all records of that dataset.*
- BASETYPE is only defined for some of the parameters within a dataset
- In ADaMIG v1.2, the BASETYPE CDISC notes now state the following:
  - *If used for any PARAM within a dataset, should be non-null for all records for that PARAM within that dataset*

Relationship between Primary & Secondary Variables

The text within the CDISC notes for secondary variables was expanded to clarify its relationship to the primary variable. Below is a typical example of this change.

Primary Variable CDISC Notes (v1.1 & v1.2) for AGEGRy	Secondary Variable CDISC Notes (v1.1) for AGEGRyN	Secondary Variable CDISC Notes (v1.2) for AGEGRyN
Character description of a grouping or pooling of the subject's age for analysis purposes. For example, AGEGR1 might have values of "<18", "18-65", and ">65"; AGEGR2 might have values of "Less than 35 y old" and "At least 35 y old".	The numeric code for AGEGRy. Orders the grouping or pooling of subject age for analysis and reporting. One-to-one mapping to AGEGRy within a study	**N**umeric **representation of** AGEGRy. Orders the grouping or pooling of subject age for analysis and reporting. **There must be** a one-to-one **relationship between AGEGRyN and** AGEGRy within a study. **AGEGRyN cannot be present unless AGEGRy is also present. When AGEGRy and AGEGRyN are present, then on a given record, either both must be populated or both must be null.**

Acknowledgements

Thank you to the ADaMIG v1.2 sub-team

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Alana St. Clair
Steve Wilson

Thank You!

ADaM Structures for Integration

Draft version currently out for public review (through 21-May-2019)

Presented by Deborah Bauer
Associate Director, Biostatistics, Sanofi

04.18.2019

Agenda

1. Integration, Simple and Complex
2. Structures for Simple Integration
3. Simple Integration Example (ISE)
4. Structures for Complex Integration
   - Model for Integrated ADSL (IADSL)
   - Model for Integrated OCCDS (IOCCDS)
   - Model for Integrated BDS (IBDS)
5. Complex Integration Example (ISS)
6. FAQs & Conclusion

Team Rules

- Use published ADaM standards when possible
- Do not recommend a data flow
- Achieve harmonization of integrated ADaM data
- Consistent variable names, labels, definitions

Section 1: Integration, Simple and Complex

Integration, Simple and Complex

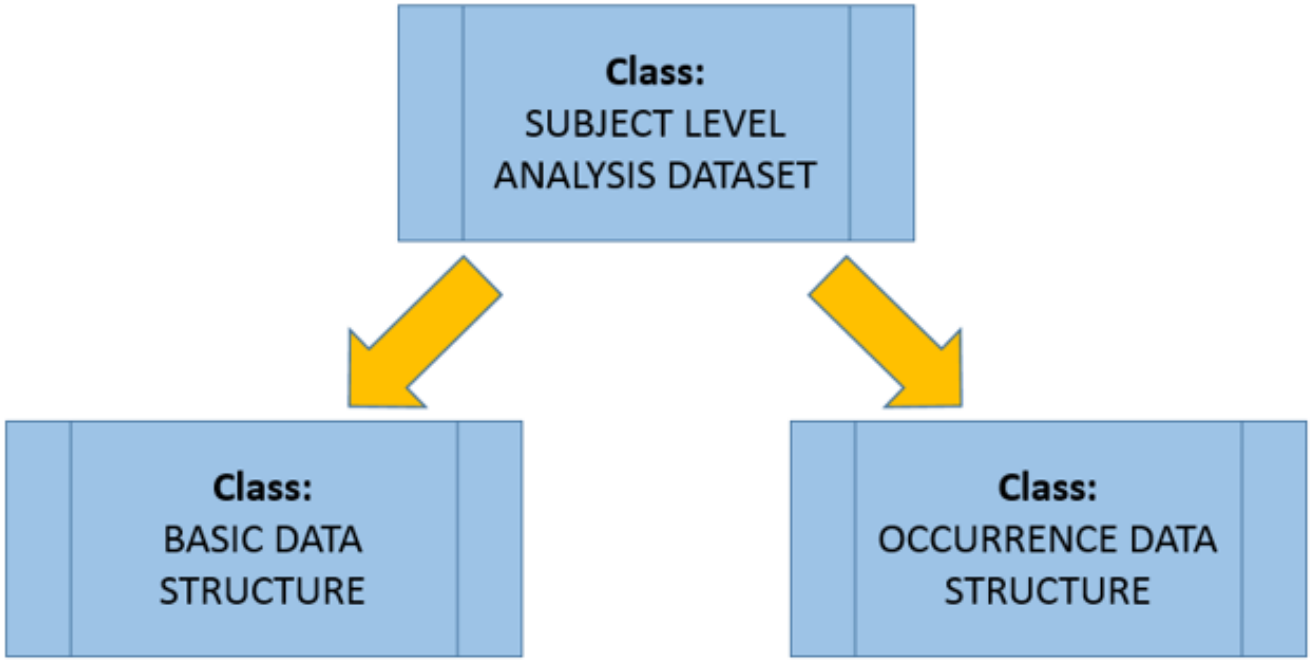
- Pool
  - A term used in integration, typically in Statistical Analysis Plans (SAPs), to define a combination of subjects' clinical trial experience which will be the focus of analysis
  - Pools may include/exclude certain treatment periods
  - Pools may define unique baseline and covariate values
  - For example: A subject participates in both a double-blind (DB) study and an open-label (OL) study. The integration SAP defines both a DB Pool and an active drug Pool. The analysis for each pool will examine a different slice of this subject’s clinical trial experience

Integration, Simple and Complex

	Simple	Complex
Number of studies in which a subject was enrolled	1	> 1
Multiple pools defined in SAP	No	Yes

Section 2: Structures for Simple Integration

Structures for Simple Integration



Structures for Simple Integration

- Subjects enroll in one study, the SAP does not define pools
- Only one set of treatment periods analyzed
- Only one definition for baselines and covariates

- Conclusion: ADSL, BDS, OCCDS classes sufficient

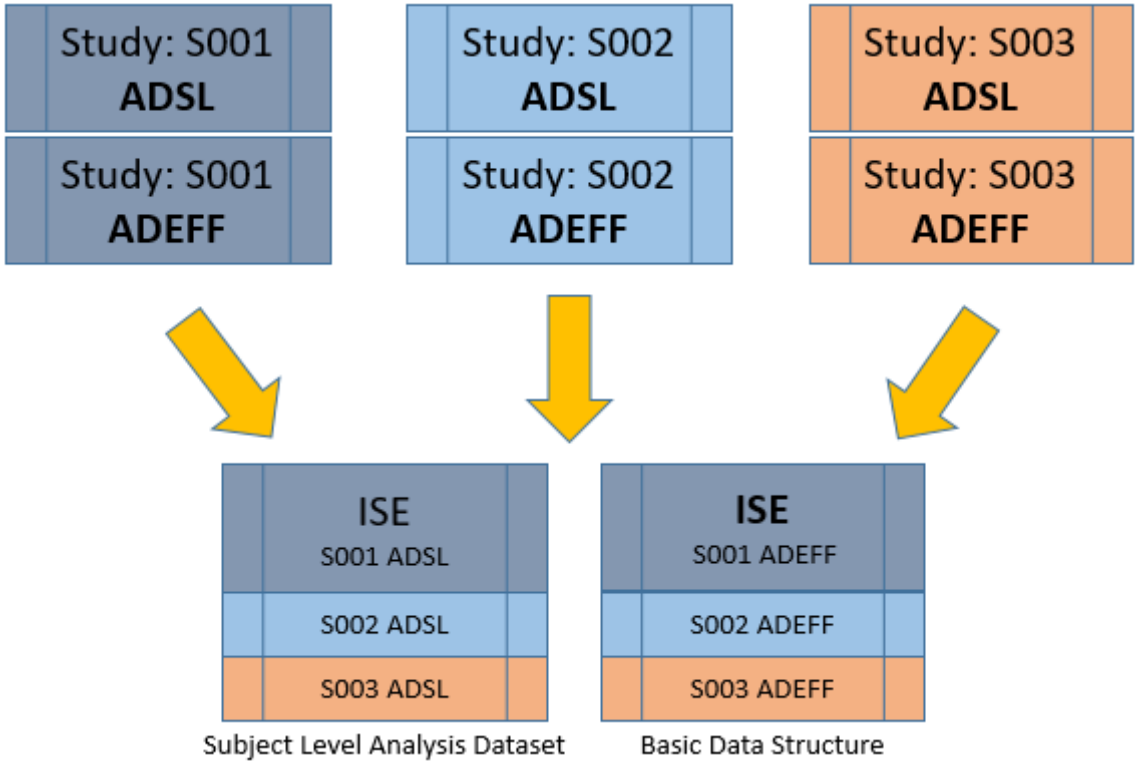
- Differences are minor
  - STUDYID variable has more than one value
  - Population flags that don’t apply for a study may be left missing and explained in the ADRG

Section 3: Simple Integration Example (ISE)

Simple Integration Example (ISE)

- 3 phase III studies
  - Similar study design and statistical analysis
  - No re-enrollment between studies
  - Study-level ADaM datasets used consistent design
- Integration using study-level ADaM as the source
  - Stacking
- Minimal harmonization efforts were needed

Simple Integration Example (ISE)



Section 4: Structures for Complex Integration

Structures for Complex Integration

- Subjects enrolled in multiple studies and phases
- SAP defines Pools

- Pools may include/exclude certain treatment periods
- Pools may define unique baseline and covariate values

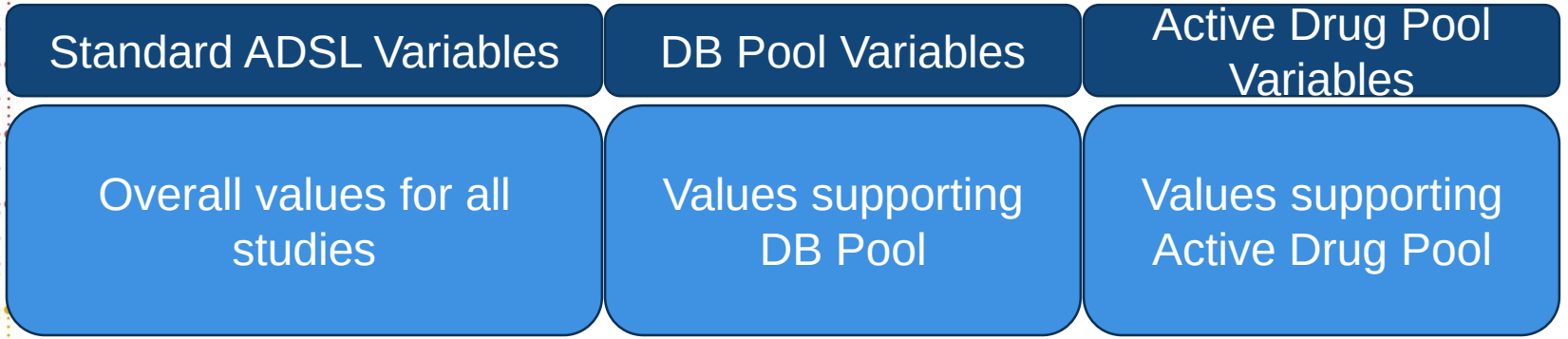
Structures for Complex Integration

- Two Studies: DB and OL
- Two Pools: DB and Active Drug
- Subjects may participate in one or both studies

- ADSL Affected?
  - Treatment Variables, e.g. TRTSDT, TRT01P
  - Population Flags, e.g. ITTFL, SAFFL
  - Covariates, e.g. AGE
  - Baselines, e.g. BMIBL

Structures for Complex Integration

- ADSL dataset using ADSL class:



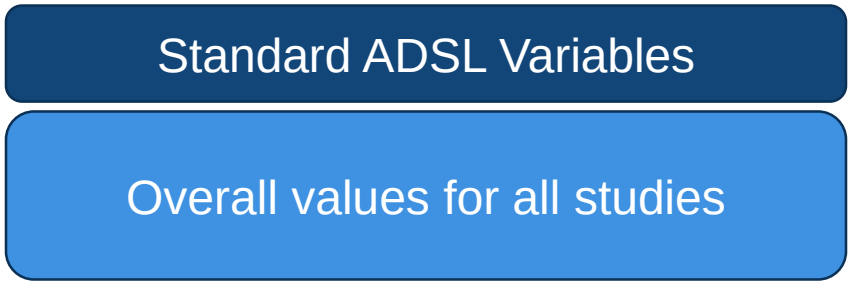
Structures for Complex Integration

- Is this approach doable?
- Challenges
  - Variable naming/labeling
  - Using correct variables for each pool
- Implication for the Integration Standard (ADSL)
  - For impacted variables, create new standard variables names with index
- Feedback – Is there a simpler way?

IADSL Structure

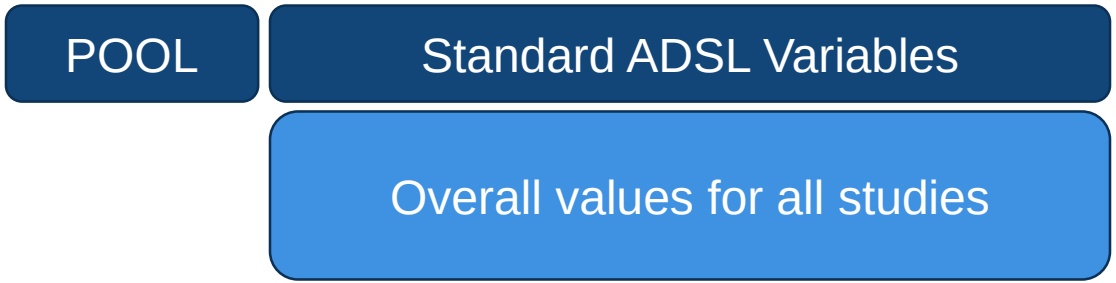
IADSL Structure

- ADSL using IADSL class:



IADSL Structure

- ADSL using IADSL class:



IADSL Structure

- ADSL using IADSL class:

POOL	Standard ADSL Variables
‘OVERALL’	Overall values for all studies
‘DB’	Values supporting DB Pool
‘ACTIVE DRUG’	Values supporting Active Drug Pool

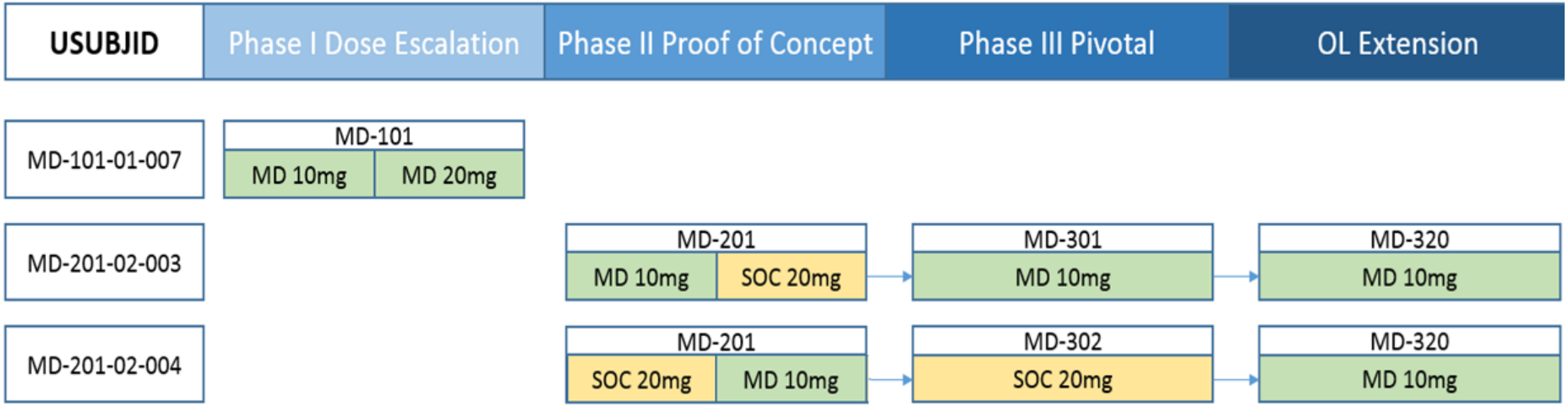
IADSL Structure

- Original one-record-per-subject ADSL preserved in the Overall pool
  - One record for each subject in the Integration
- For other pools, create records only for subjects in pool
  - Examine overall pool record to see why a subject is not in a pool
- Variables only populated when needed
  - If a covariate or baseline variable is not needed for a pool, there is no requirement to populate it

Section 5: ISS Example (IADSL)

ISS Example (IADSL)

- Multiple Studies, Phases



ISS Example (IADSL)

- Multiple Pools, Unique Periods, Baselines, Covariates

Pool	Studies	Definition	Purpose
1	101, 201, 301, 302, 320	Overall Pool: Includes all periods.	Support treatment overview of all enrolled subjects, demographics and disposition
2	301, 302	Pivotal Pool: Includes all periods. Re-enrollers counted as distinct subjects for each enrollment.	Support pooled safety and efficacy analysis of pivotal studies
3	201, 301, 302	Comparison Pool: Includes all periods.	Support pooled safety analysis between study drug and comparators

ISS Example (IADSL)

- ADSL using IADSL class

ROW	USUBJID	POOLN	POOL	STUDIES	TRT01P	TR01SDT	TR01EDT
1	**MD-101-01-007**	**1**	**OVERALL**	**MD-101**	**MD 10mg**	**2000-02-01**	**2000-02-07**
2	MD-201-02-003	1	OVERALL	MD-201, MD-301, MD-320	MD 10mg	2000-08-10	2000-09-02
3	MD-201-02-003	2	PIVOTAL	MD-301	MD 10mg	2001-08-21	2002-04-11
4	MD-201-02-003	3	COMPARISON	MD-201, MD-301	MD 10mg	2000-08-10	2000-09-02
5	MD-201-02-004	1	OVERALL	MD-201, MD-302, MD-320	SOC 20mg	2000-08-29	2000-09-24
6	MD-201-02-004	2	PIVOTAL	MD-302	SOC 20mg	2001-09-06	2002-04-27
7	MD-201-02-004	3	COMPARISON	MD-201, MD-302	SOC 20mg	2000-08-29	2000-09-24

ISS Example (IADSL)

- ADSL using IADSL class

ROW	USUBJID	POOLN	POOL	STUDIES	TRT01P	TR01SDT	TR01EDT
1	MD-101-01-007	1	OVERALL	MD-101	MD 10mg	2000-02-01	2000-02-07
2	**MD-201-02-003**	**1**	**OVERALL**	**MD-201, MD-301, MD-320**	**MD 10mg**	**2000-08-10**	**2000-09-02**
3	**MD-201-02-003**	**2**	**PIVOTAL**	**MD-301**	**MD 10mg**	**2001-08-21**	**2002-04-11**
4	**MD-201-02-003**	**3**	**COMPARISON**	**MD-201, MD-301**	**MD 10mg**	**2000-08-10**	**2000-09-02**
5	MD-201-02-004	1	OVERALL	MD-201, MD-302, MD-320	SOC 20mg	2000-08-29	2000-09-24
6	MD-201-02-004	2	PIVOTAL	MD-302	SOC 20mg	2001-09-06	2002-04-27
7	MD-201-02-004	3	COMPARISON	MD-201, MD-302	SOC 20mg	2000-08-29	2000-09-24

ISS Example (IADSL)

- ADSL using IADSL class

ROW	USUBJID	POOLN	POOL	STUDIES	TRT01P	TR01SDT	TR01EDT
1	MD-101-01-007	1	OVERALL	MD-101	MD 10mg	2000-02-01	2000-02-07
2	MD-201-02-003	1	OVERALL	MD-201, MD-301, MD-320	MD 10mg	2000-08-10	2000-09-02
3	MD-201-02-003	2	PIVOTAL	MD-301	MD 10mg	2001-08-21	2002-04-11
4	MD-201-02-003	3	COMPARISON	MD-201, MD-301	MD 10mg	2000-08-10	2000-09-02
5	**MD-201-02-004**	**1**	**OVERALL**	**MD-201, MD-302, MD-320**	**SOC 20mg**	**2000-08-29**	**2000-09-24**
6	**MD-201-02-004**	**2**	**PIVOTAL**	**MD-302**	**SOC 20mg**	**2001-09-06**	**2002-04-27**
7	**MD-201-02-004**	**3**	**COMPARISON**	**MD-201, MD-302**	**SOC 20mg**	**2000-08-29**	**2000-09-24**

IBDS & IOCCDS Structure

IBDS & IOCCDS Structure

- IBDS & IOCCDS:

POOL	Standard BDS/OCCDS Variables	ADSL variables
'OVERALL'	Overall values for all studies	Values for Overall
'DB'	Values supporting DB Pool	Values for DB Pool
'ACTIVE DRUG'	Values supporting Active Drug Pool	Values for Active Drug Pool

IBDS & IOCCDS Structure

- Create a set of records for a pool if needed
  - if there are pools 1, 2, & 3, AE analysis is done only for pools 2, 3, there is no need to create pool 1 records in ADAE.
- Keep relevant records for a pool
  - If there are studies A, B, C, and pool 2 only analyzes study B, it is fine to keep only records from study B for pool 2

IBDS & IOCCDS Structure

- Benefits
  - Timing variables values may change by pool
    - Analysis visit (AVISIT)
    - AE start study day (ASTDY)
  - Baseline record may change by pool
    - Baseline flag, baseline value, change from baseline (ABLFL, BASE, CHG)
  - Slotting of date values may change by pool
    - Treatment emergence, concomitance (TRTEMFL, ONTRTFL)
  - Right covariates merged in from ADSL for each pool
    - for analysis on pool X, subset by POOL=X

Section 5: ISS Example (IBDS)

ISS Example (IBDS)

- ADLB using IBDS class

USUBJID	POOL	STUDYID	LBSEQ	PARAM	AVAL	ADT	ADY	AVISIT	ABLFL	TRTP
MD-201-02-003	**PIVOTAL**	**MD-301**	**1**	**Glucose (mg/dL)**	**96**	**2001-08-21**	**1**	**Baseline**	**Y**	**MD 10mg**
MD-201-02-003	**PIVOTAL**	**MD-301**	**2**	**Glucose (mg/dL)**	**87**	**2001-08-29**	**9**	**Week 1**		**MD 10mg**
MD-201-02-003	COMPARISON	MD-201	1	Glucose (mg/dL)	98	2000-08-10	1	Baseline	Y	MD 10mg
MD-201-02-003	COMPARISON	MD-201	2	Glucose (mg/dL)	78	2000-08-17	8	Days 2-30		MD 10mg
MD-201-02-003	COMPARISON	MD-301	1	Glucose (mg/dL)	96	2001-08-21	377	Days 151-380		MD 10mg
MD-201-02-003	COMPARISON	MD-301	2	Glucose (mg/dL)	87	2001-08-29	385	Days 381-500		MD 10mg

ISS Example (IBDS)

- ADLB using IBDS class

USUBJID	POOL	STUDYID	LBSEQ	PARAM	AVAL	ADT	ADY	AVISIT	ABLFL	TRTP
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Section 6: FAQs and Conclusion

Frequently Asked Questions

- Is the IADSL class required?
  - No
- Is there additional ADSL class support for Integration?
  - No
- Is the dataset name still ADSL?
  - Yes
- What about compliance checks/validation rules?
  - New ADaM compliance checks will be developed for IADSL, IBDS, and IOCCDS classes once document is final

Frequently Asked Questions (2)

- What if USUBJID wasn't correct and unique across studies?
  - Sponsor is expected to have a process to identify the same person across studies, and to consistently assign the same USUBJID value
  - Integration document does not provide a way to handle incorrect USUBJID
- What if I have re-enrollers in different studies or other complicated scenarios?
  - See the Integration document for additional variables, suggestions, and detailed examples
- What about dataset size?
  - Large datasets can be split using variables such as POOL
- Can I implement these new structures now?
  - This is a draft document and possibly subject to change. Has not yet been included in any regulatory agency data standards catalogs

Conclusion

- Draft Version 1.0 ADaM Data Structures for Integration is now out for Public Review
  - Register with CDISC
  - Review the Document
  - **Review period closes May 21**

- We look forward to your review and comments!

Acknowledgements

- Wayne Zhong – PharmaSUG presentation
- The entire ADaM Integration Subteam

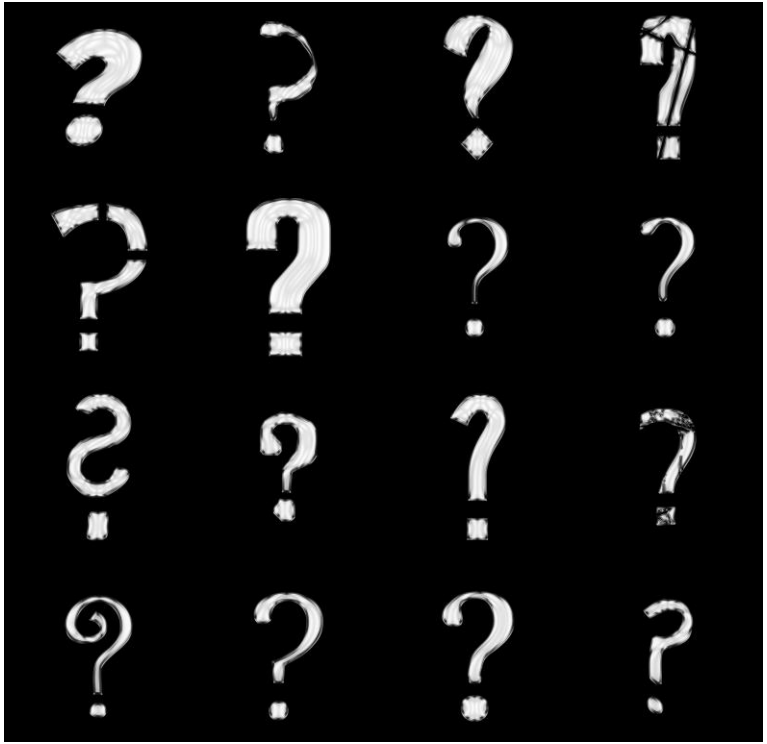
Thank You!

Questions & Answers

This is an SDTM related question - in regards to stratification variables coming from verification source, where might you expect to find that data in SDTM (would it be represented in SDTM)?

Questions & Answers

in ADaM datasets that are a combination of parameters with bi-directional toxicity grading together with parameters that only graded in one direction, how are you storing the one direction grading: in ATOXGR or ATOXGRL or ATOXGRH (depending on the direction)



Questions & Answers

Should the second record you had shown in your slides for anemia have been decreased?

Questions & Answers

Is there a naming convention to be followed for pre-ADSL?

Questions & Answers

How can pre-ADSL be incorporated into a Define.xml and an ADRG?

Questions & Answers

When creating Pre-ADSL, will this need to be kept in the final ADAM package, define, etc.?

ADaMIG v1.2 & ADaM Integration

Presented by

Brian Harris - Dir. of Biometrics Operations at Medimmune (AstraZeneca)
Deborah Bauer- Associate Director, Biostatistics, Sanofi

18 APR 2019

Questions & Answers

Can you give an example for PARQUAL

Questions & Answers

If we do ADSL at end for complicated variables that depend on other ADaM datasets and if those variables are 'core' variables for analysis then those core would not be in ADaM datasets (other than ADSL). It makes sense to so, but TCG recommends that all Core variables should be in ADaMs that need them for analysis. Any comments?

Here is the TCG text ... Core variables, which include covariates presented in the study protocol that are necessary to analyze data, should be included in each ADaM dataset, and are typically already included in the ADSL dataset (See section 4.1.2.4).

Questions & Answers

What is the recommended name for pre-ADSL?

Questions & Answers

would the V(erification) variables be only filled in case of deviation from original stratification?

Questions & Answers

Does a pre-ADSL have to be submitted, or is only referenced in the adrg?

Questions & Answers

Should all ADaM and ADaM Other datasets start with AD?

Questions & Answers

Pre-ADSL will cause P21 failure; what should be done about it?

Questions & Answers

Would we specify in the ADRG in what order analysis datasets should be run in cases where a pre-ADSL is used?

Questions & Answers

Is this version of IG included in pinnacle 21 directly after release

Questions & Answers

Is data integration done in the ADaM, not in the SDTM?

Questions & Answers

We have a case a subject participates in a feeder and extension study; in the feeder the subject he/she is exposed to drug A+ drug b and in the extension only drug b. the pooling aims to find the cumulative exposure to both drugA and B . how will this handled in the iss?

Questions & Answers

For IADSL: How do we represnt if same subject recieved different dose in different study\?

Questions & Answers

Question on ASEQ: Should it be unique within USUBJID over all pools or unique within each pool?

Questions & Answers

Can we apply these guidances even though the documents have not been published? will they be accepted by regulatory agencies?

Questions & Answers

Can we use it to keep multiple records per subject for different cutoffs of the same study?

Questions & Answers

Slide 27 - How would NUMSTUDY and UADSLFL be populated for the new structure (one record per subject per pool). Woulld NUMSTUDY follow STUDIES and be per the pool for that record?

Questions & Answers

Will detailed specification document needed for I- datasets? If so, any example?

Questions & Answers

Have there been extensive discussions with the FDA and PMDA about the iADSL structure?

Has it been taken (adopted?) by them?

Questions & Answers

Will splitted package for different pools still be an option?

Questions & Answers

The defination of TRTAE in adae may be different?

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2019 Public Courses in North America

Location:	Dates:	Courses Offered:	Discount period ends:	Host:
Bridgewater, NJ	20-24 MAY	SEND, CDASH, SDTM, Define-XML, ADaM	18 FEB 2019	Janssen Pharmaceutical Companies of Johnson & Johnson
Seattle, WA	3-7 JUN	CDASH, SDTM, ADaM	4 MAR 2019	Axio Partners in Research
Indianapolis, IN	3-7 JUN	CDASH, SDTM, Define-XML, SDTM Changes and Updates, ADaM Primer, ADaM Theory & Application	4 MAR 2019	Syneos Health
Gaithersburg, MD	9-13 SEP	CDASH, SDTM, Define-XML, ADaM	10 JUN 2019	MedImmune, A member of the AstraZeneca Group

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Frankfurt, Germany	3-7 JUN	SDTM, CDASH, ADaM Primer + Theory & Application, Define-XML	4 MAR	Analytical Software
Brussels Belgium	9-13 SEP	CDASH, SDTM, Define-XML, ADaM Primer + Theory & Application	6 JUN	Business & Decision Life Sciences
Paris, France	7-11 OCT	CDASH, SDTM, Define-XML, ADaM Primer + Theory & Application	8 JUL	SERVIER
Copenhagen, DK	30-31 OCT + 4-8 NOV	SEND, CDASH, SDTM, Define-XML, ADaM Primer, ADaM Theory & Application		

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Tokyo, Japan	2-6 SEP	SDTM, CDASH, ADaM Primer + Theory & Application, Define-XML	2 JUN	Croit

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19 APR	CDISC Public Webinar: Highlights of Define-XML 2.0 Implementation & FAQ
25 APR	CDISC Public Webinar: Membership Benefits
23 MAY	CDISC Public Webinar: Relative Timing Variables in CRFs
9 JUL	CDISC Public Webinar: Quarterly Controlled Terminology Updates
25 JUL	CDISC Public Webinar: ODM v2.0 Demo Tech

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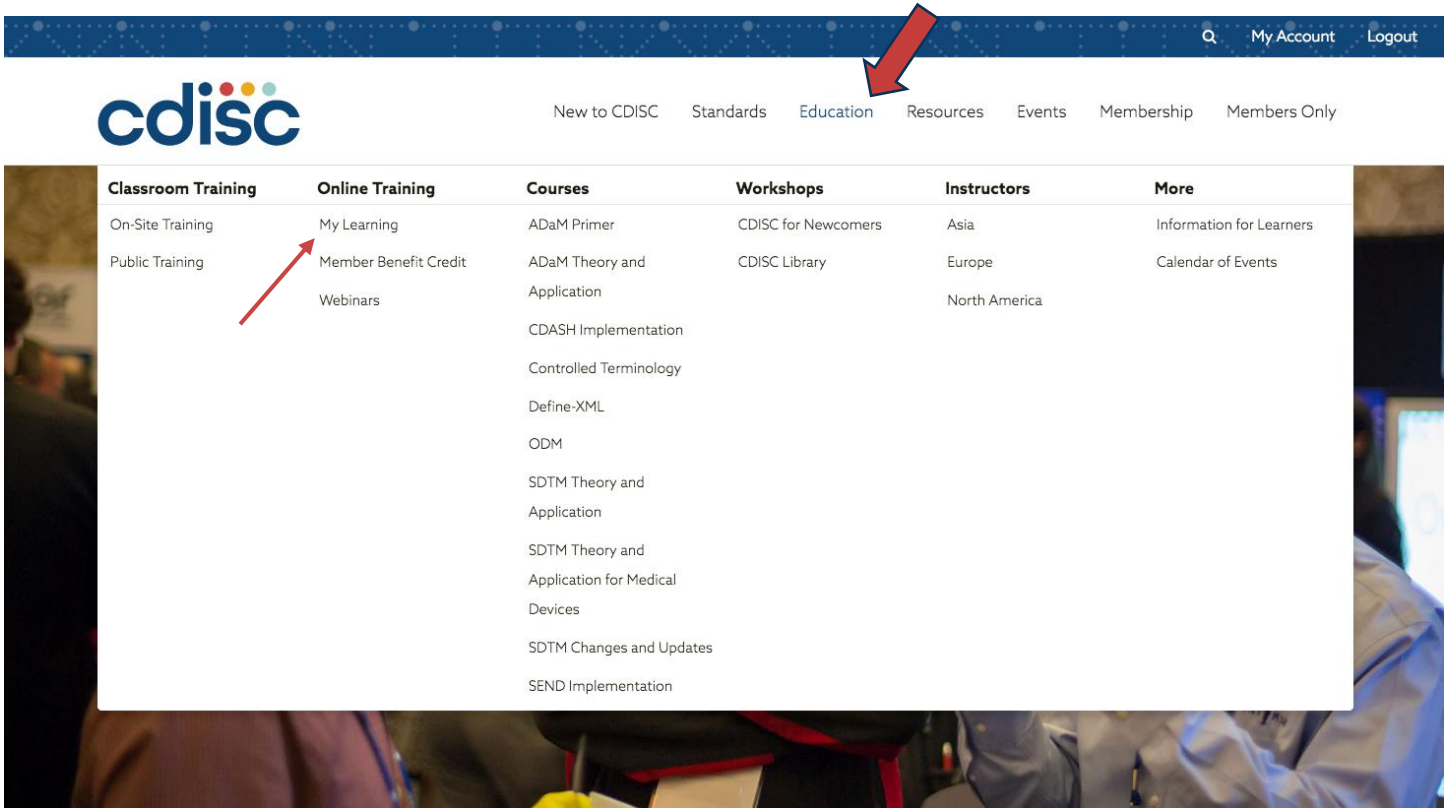
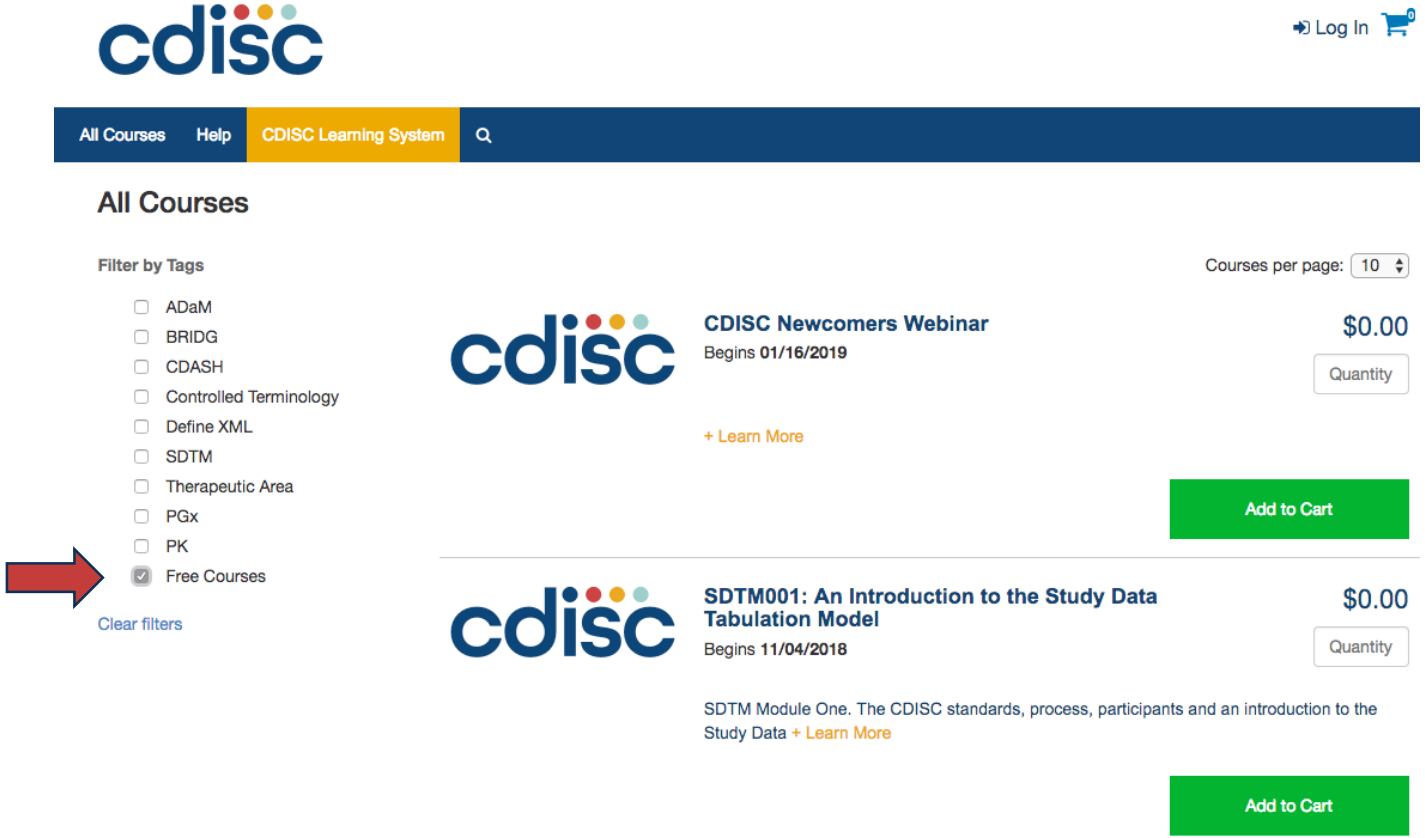


Online Learning Management System Courses



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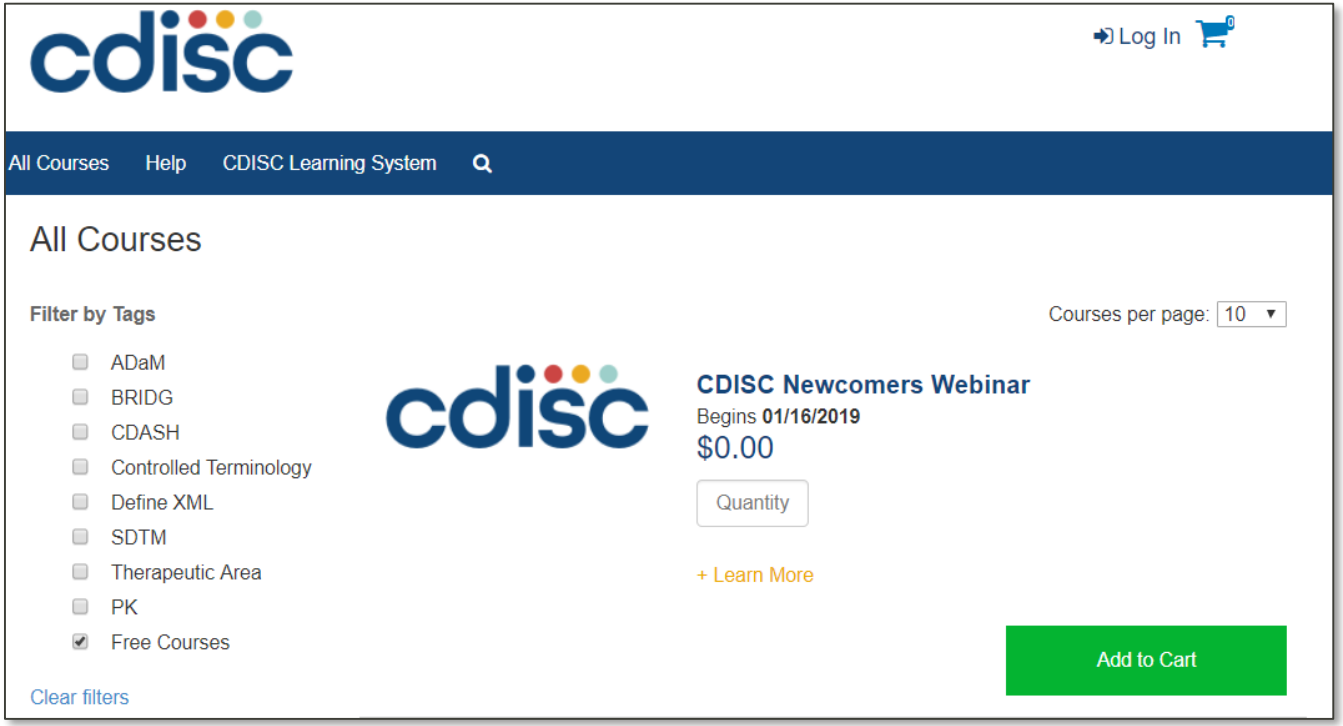

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Questions & Answers

Thank You!

Questions, comments, concerns? Email bklinke@cdisc.org