Introducing the Analysis Results Standard: Project Start Up and Call for Volunteers

Jeffrey Abolafia, Chief Strategist, Data Standards, Rho Inc.
Nancy Brucken, Standards Engineer, Clinical Solutions Group (CSG, Inc.)
Bhavin Busa, VP, Clinical Data Services & Operations, Vita Data Sciences
Sally Cassells, Sr. Director, Data Exchange Standards and Certification, CDISC
Nate Freimark, Vice President, Clinical Programming and Data Standards, The Griesser Group
Hansjörg Frenzel, Sr. Principal Clinical Data Standards Consultant, PRA Health Sciences
Brian Harris, Director, Biometrics Operations and Clinical Data Standards, AstraZeneca
Bess LeRoy, Head of Standards Development, CDISC
Kent Letourneau, Executive Director, Global Head, Data Standards, PRA Health Sciences
Jon Neville, Sr. Standards Developer, CDISC
Peter Van Reusel, CSO, CDISC

Thursday, 22 OCT 2020
11:00AM – 12:30PM EDT

Today’s Agenda

1. Housekeeping
2. Presenter Introductions
3. Feature Presentations
4. Question & Answer Session
5. Upcoming Learning Opportunities + Resources

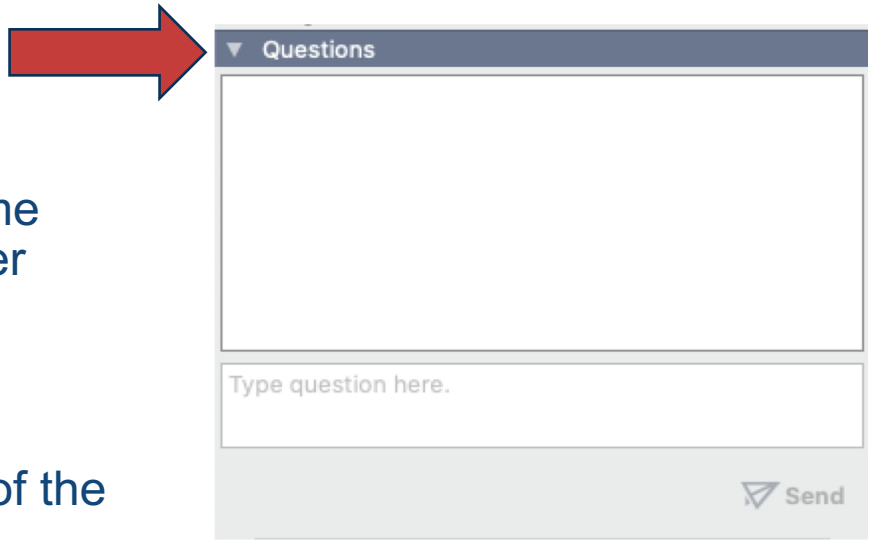
Housekeeping

Housekeeping

- You will remain on **mute** for the entirety of the webinar
- There will be a Q&A after all of the presentations are finished
- Audio issues? Shut down and restart the GoToWebinar app
- The slides from the presentation and a recording of this webinar will be available in the Members Only section of the CDISC website
  - To access – make sure that you create a login for the CDISC website if you haven't already
  - If you are employed by a CDISC member organization, please ensure you use your employer-issued email address with your employer's domain name, so we can verify membership for the purpose of applying discounts to purchasing event tickets, online courses, and more!

Submitting Questions

- To send a question, use the “QUESTIONS” function on your GoToWebinar app. (See red arrow)
- You can submit questions at any time during the presentation, we’ll answer them during the Q&A.
- If you have a question for a specific presenter, please indicate the presenter’s name at the beginning of the question
  - Examples:
    - John: ‘Question’
    - Alana: ‘Question’



Content Disclaimer

- The purpose of this webinar is to provide examples of implementation and should not be considered official recommendations by CDISC unless otherwise stated in the presentation.
- This webinar is not an authorized CDISC course, is not developed or delivered under CDISC Operating Procedures, and should not replace a published standard. Please refer to the latest published standards for the most authoritative implementation information.

Our Presenters

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CDISC Analysis Results Standard Kick-off Meeting

Bess LeRoy
Head of Standards Development, CDISC

27 October 2020

Agenda

1. Background
2. Enhancing CDISC ADaM standards
3. Leveraging existing work
4. Scope
5. Timelines

Background

ADaM currently provides ***standardized inputs*** to enable analysis

- Subject-Level Analysis Dataset (ADSL)
- Basic Data Structure (BDS)
  - Time to Event (TTE)
- Occurrence Data Structure (OCCDS)
  - Adverse Events (ADAE)
- Limited Controlled Terminology

Background

- Analysis Results Metadata (ARM) ***extension to the Define-XML 2.0 model***
  - Provides traceability for a given analysis result to the specific ADaM data that were used as input to generating the analysis result
  - Provides standard metadata fields to represent analysis method used and the reason the analysis was performed

Table 4.2.2: HbA1c Longitudinal Repeated Measures Analysis Results Metadata

Metadata Field	Metadata
DISPLAY IDENTIFIER	Table 4.2.1/Figure 4.2.1
DISPLAY NAME	Mean Change from Baseline in HbA1c (Percent) Longitudinal Repeated Measures Analysis, 24-Week Short-term Double-blind Treatment Period, Intention-to-treat Population
RESULT IDENTIFIER	Treatment difference results (LSMean, confidence interval, p-value)
PARAM	HbA1c (%)
PARAMCD	HBA1C
ANALYSIS VARIABLE	CHG (Change from baseline)
ANALYSIS REASON	SPECIFIED IN SAP
ANALYSIS PURPOSE	PRIMARY OUTCOME MEASURE
ANALYSIS DATASET	ADHBA1C
SELECTION CRITERIA	ITTFL= "Y" and PARAMCD = "HBA1C" and CHG ne . and ANL01FL = "Y" and DTYPE = " "
DOCUMENTATION	See SAP Section XX for details. Program: t-hba1c-repmeas.sas LS means and 95% CIs are based on repeated measures model adjusting for planned treatment, baseline HbA1c value, avisit, avisit*baseline and avisit*treatment interaction.
PROGRAMMING STATEMENTS	[SAS version 9.2] PROC MIXED DATA = ADHBA1C; WHERE ITTFL = "Y" and PARAMCD = "HBA1C" and CHG ne . and ANL01FL = "Y" and DTYPE = " " CLASS TRTP AVISIT; MODEL CHG = TRTP BASE AVISIT BASE*AVISIT AVISIT*TRTP / DDFM=KR; LSMEANS TRTP / CL DIFF; REPEATED usubjid / subject = USUBJID TYPE=UN; RUN ;

Challenges

- ARM provides limited traceability from analysis results to analysis data and does not currently support the capture of actual results
- Limited standardization of analysis results metadata and conceptual layer of TFLs

Enhancing and extending ADaM standards is key to help achieve end to end automation and improve consistent use of the standards

Enhancing ADaM standards

Add features that support automation of analysis results

Provide guidance on basic analysis structures towards analysis results generation

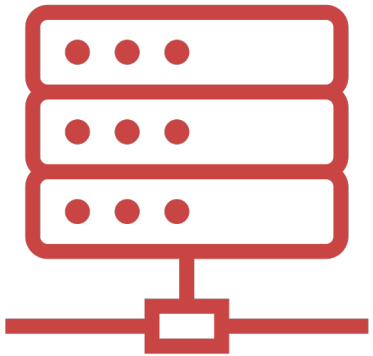
Provide greater traceability between analysis results and analysis data

What could this look like?

- Concept-based standards development for ***generally accepted analyses***
- Analysis dataset examples including relevant controlled terminology
- Expansion of the standardization that is provide by the ARM specification for Define.xml
  - Methodology guidance examples
  - Pseudo code for transformations and derivations
- Standardized analysis results metadata for TFL generation
  - Structure
  - Terminology
  - Enhancing traceability and documentation of the results

Analysis dataset structure including relevant controlled terminology

- Provide ADaM dataset structure examples that are used to produce TFLs
- Challenges with variation in ADaM dataset that are generated for submission
  - Provide feedback to relevant ADaM teams to work towards a more consistent implementation for biomedical concepts



Expansion of the standardization that is provide by the ARM specification for Define.xml

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CDISC

Analysis Results Metadata Specification
Version 1.0
for
Define-XML Version 2

Need for standard analysis definition

The ARM specification standardizes the metadata structure for the define.xml

Standardized analysis results metadata for TFL generation

qb:Observation	qb:Table	dim.population	dim.treatment	dim.parameter	dim.sex	dim.agecat	dim.statistic	analysisResult
1002	dm.summary	enrolled	Treatment.A	param.subjects	sex.F	agecat.ALL	stat.freq	60
1003	dm.summary	enrolled	Treatment.A	param.subjects	sex.F	agecat.ALL	stat.percent	60
1004	dm.summary	enrolled	Treatment.A	param.subjects	sex.M	agecat.ALL	stat.freq	40
1005	dm.summary	enrolled	Treatment.A	param.subjects	sex.M	agecat.ALL	stat.percent	40
1006	dm.summary	enrolled	Treatment.B	param.subjects	sex.ALL	agecat.ALL	stat.freq	50
1007	dm.summary	enrolled	Treatment.B	param.subjects	sex.F	agecat.ALL	stat.freq	30
1008	dm.summary	enrolled	Treatment.B	param.subjects	sex.F	agecat.ALL	stat.percent	60
1009	dm.summary	enrolled	Treatment.B	param.subjects	sex.M	agecat.ALL	stat.freq	20
1010	dm.summary	enrolled	Treatment.B	param.subjects	sex.M	agecat.ALL	stat.percent	40
1011	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.ALL	agecat.ALL	stat.freq	150
1012	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.F	agecat.ALL	stat.freq	90
1013	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.F	agecat.ALL	stat.percent	60
1014	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.M	agecat.ALL	stat.freq	60
1015	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.M	agecat.ALL	stat.percent	40
1016	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.freq	100
1017	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.mean	40.7
1018	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.stdev	10.7
1019	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.median	37.0
1020	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.min	21.0
1021	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.max	66.0
1022	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.freq	50
1023	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.mean	41.2
1024	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.stdev	10.3
1025	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.median	36.0
1026	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.min	23.0
1027	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.max	67.0
1028	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.freq	150
1029	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.mean	40.9
1030	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.stdev	10.4
1031	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.median	37.0
1032	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.min	21.0
1033	dm.summary	itt	Treatment.ALL	param.age	sex.ALL	agecat.ALL	stat.max	67.0

Reference: *'Analysis Results that Save Trees - #KillTFLs'*, Chris Decker, DH12 PHUSE US Connect 2019

Standardized analysis results metadata for TFL generation

qb:Observation	qb:Table	dim.population	dim.treatment	dim.parameter	dim.sex	dim.agecat	dim.statistic	analysisResult
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1005	dm.summary	enrolled	Treatment.A	param.subjects	sex.M	agecat.ALL	stat.percent	40
1006	dm.summary	enrolled	Treatment.B	param.subjects	sex.ALL	agecat.ALL	stat.freq	50
1007	dm.summary	enrolled	Treatment.B	param.subjects	sex.F	agecat.ALL	stat.freq	30
1008	dm.summary	enrolled	Treatment.B	param.subjects	sex.F	agecat.ALL	stat.percent	60
1009	dm.summary	enrolled	Treatment.B	param.subjects	sex.M	agecat.ALL	stat.freq	20
1010	dm.summary	enrolled	Treatment.B	param.subjects	sex.M	agecat.ALL	stat.percent	40
1011	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.ALL	agecat.ALL	stat.freq	150
1012	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.F	agecat.ALL	stat.freq	90
1013	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.F	agecat.ALL	stat.percent	60
1014	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.M	agecat.ALL	stat.freq	60
1015	dm.summary	enrolled	Treatment.ALL	param.subjects	sex.M	agecat.ALL	stat.percent	40
1016	dm.summary	itt	Treatment.A	param.age	sex.ALL	agecat.ALL	stat.freq	100
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1022	dm.summary	itt	Treatment.B	param.age	sex.ALL	agecat.ALL	stat.freq	50
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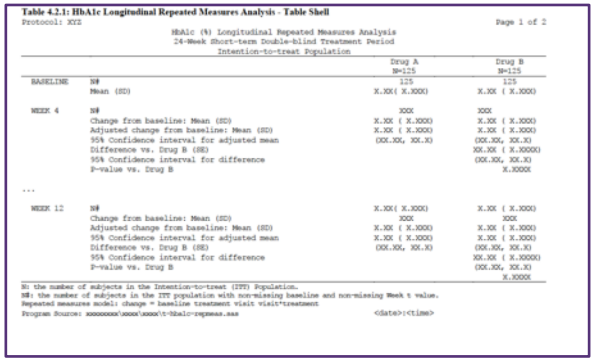


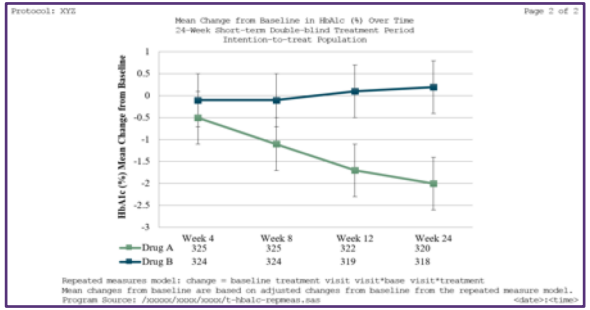
Table 4.2.1: HbA1c Longitudinal Repeated Measures Analysis - Table Shell

Protocol: XYZ — Page 1 of 2

HbA1c (%) Longitudinal Repeated Measures Analysis
24-Week Short-term Double-blind Treatment Period
Intention-to-treat Population

		Drug A N=125	Drug B N=125
BASELINE	N#	125	125
	Mean (SD)	X.XX(X.XXX)	X.XX (X.XXX)
WEEK 4	N#	XXX	XXX
	Change from baseline: Mean (SD)	X.XX (X.XXX)	X.XX (X.XXX)
	Adjusted change from baseline: Mean (SD)	X.XX (X.XXX)	X.XX (X.XXX)
	95% Confidence interval for adjusted mean	(XX.XX, XX.X)	(XX.XX, XX.X)
	Difference vs. Drug B (SE)		XX.XX (X.XXXX)
	95% Confidence interval for difference		(XX.XX, XX.X)
	P-value vs. Drug B		X.XXXX
...			
WEEK 12	N#	X.XX(X.XXX)	X.XX (X.XXX)
	Change from baseline: Mean (SD)	XXX	XXX
	Adjusted change from baseline: Mean (SD)	X.XX (X.XXX)	X.XX (X.XXX)
	95% Confidence interval for adjusted mean	X.XX (X.XXX)	X.XX (X.XXX)
	Difference vs. Drug B (SE)	(XX.XX, XX.X)	(XX.XX, XX.X)
	95% Confidence interval for difference		XX.XX (X.XXXX)
	P-value vs. Drug B		(XX.XX, XX.X)
			X.XXXX

N: the number of subjects in the Intention-to-treat (ITT) Population.
N#: the number of subjects in the ITT population with non-missing baseline and non-missing Week t value.
Repeated measures model: change = baseline treatment visit visit*treatment
Program Source: xxxxxxxx\xxxx\xxxx\t-hba1c-regmeas.sas <date>:<time>



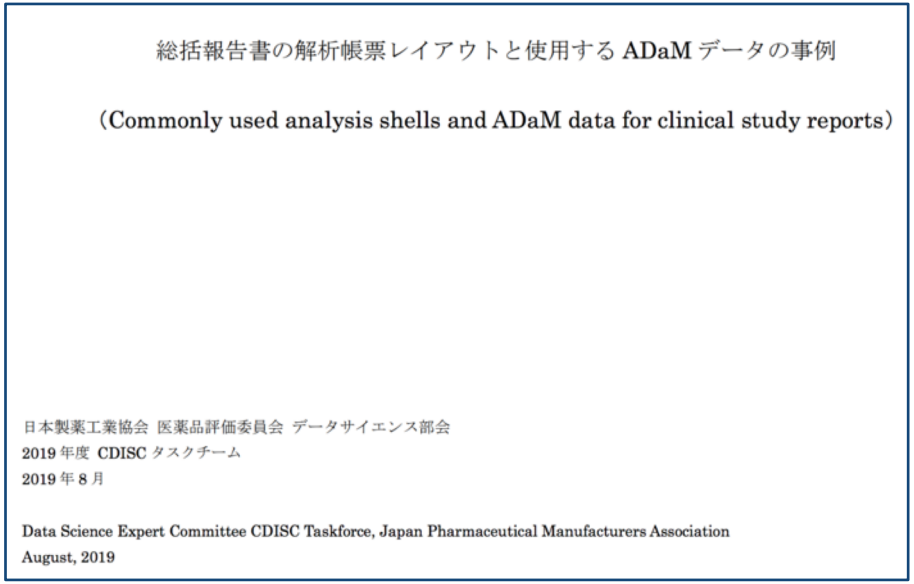
Protocol: XYZ — Page 2 of 2

Mean Change from Baseline in HbA1c (%) Over Time
24-Week Short-term Double-blind Treatment Period
Intention-to-treat Population

Repeated measures model: change = baseline treatment visit visit*base visit*treatment
Mean changes from baseline are based on adjusted changes from baseline from the repeated measure model.
Program Source: /xxxxx/xxxx/xxxx/t-hba1c-regmeas.sas <date>:<time>

What existing work can we leverage?

JPMA: Commonly used analysis shells and ADaM data for clinical study reports



総括報告書の解析帳票レイアウトと使用する ADaM データの事例

（Commonly used analysis shells and ADaM data for clinical study reports）

日本製薬工業協会 医薬品評価委員会 データサイエンス部会
2019 年度 CDISC タスクチーム
2019 年 8 月

Data Science Expert Committee CDISC Taskforce, Japan Pharmaceutical Manufacturers Association
August, 2019

http://www.jpma.or.jp/english/reports/drug_evaluation_committee/expert_committees/adam_data.html

JPMA: Commonly used analysis shells and ADaM data for clinical study reports

- Data Science Expert Committee CDISC Taskforce of JPMA conducted survey in 2019
- 40 member companies responded to the survey, and the Taskforce identified the standard TFLs commonly used for clinical study reports
- Proposed TFL Shells and ADaM data structures were defined based on the identified standard TFLs
- Document describes analysis shells for clinical study reports with annotation of CDISC ADaM datasets/variables commonly used for statistical analysis of clinical trials
- It will support data science functions in pharmaceutical companies, CROs and academia, etc., when they create statistical analysis deliverables

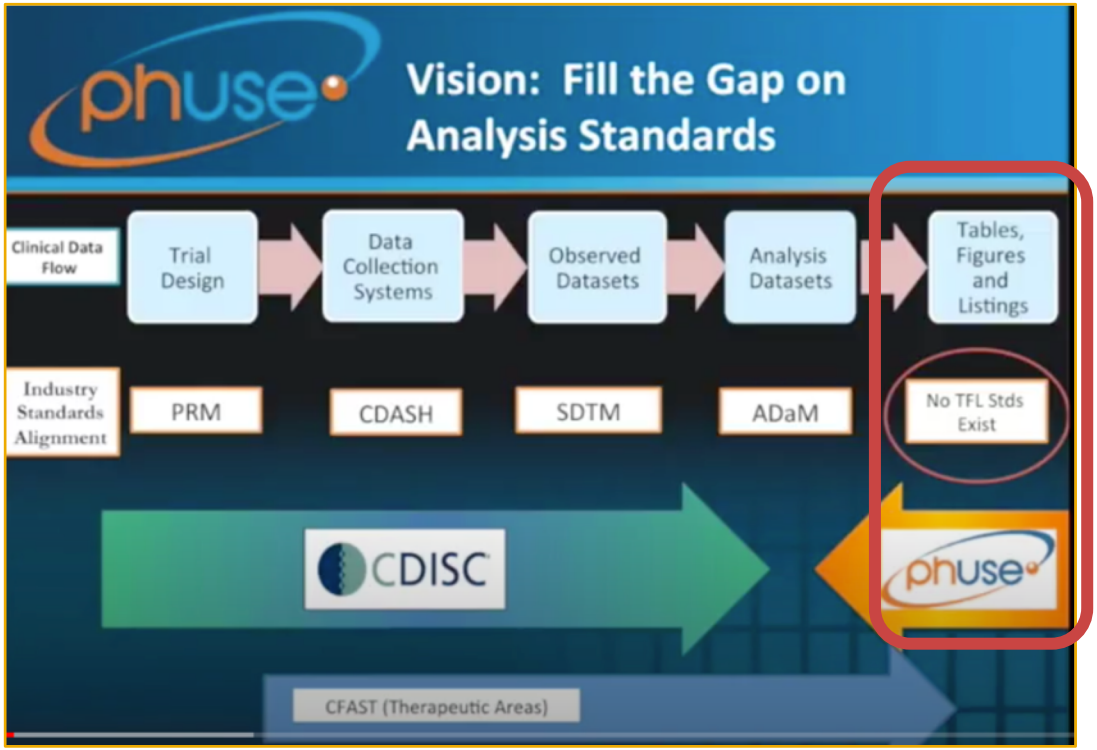
Analysis shells for clinical study reports with annotation of CDISC ADaM datasets/variables

Table summary of subject incidence of treatment-emergent adverse events

ADSL.TRTxxP/ADSL.TRTxxA

ADAE.TRTEMFL (= 'Y')	Treatment A N=XX n(%)	Treatment B N=XX n(%)
TEAE	xx (xxx.x)	xx (xxx.x)
AE related to study treatment — ADAE.AEREL/ADAE.AREL (= 'Y' or '')	xx (xxx.x)	xx (xxx.x)
Serious TEAE — ADAE.AESER (= 'Y')	xx (xxx.x)	xx (xxx.x)
Serious TEAE related to study treatment — ADAE.AESER (= 'Y') and ADAE.AEREL/ADAE.AREL (= 'Y' or '')	xx (xxx.x)	xx (xxx.x)
TEAE leading to death — ADAE.AEOUT (= 'FATAL')	xx (xxx.x)	xx (xxx.x)
AE related to study treatment leading to death — ADAE.AEOUT (= 'FATAL') and ADAE.AEREL/ADAE.AREL (= 'Y' or '')		
Other important TEAE	xx (xxx.x)	xx (xxx.x)
Other important AE related to study treatment	xx (xxx.x)	xx (xxx.x)
TEAE: Treatment emergent adverse events — ADAE.AESER (= 'N') and ADAE.AEACN (= 'DOSE REDUCED' or 'DRUG WITHDRAWN')		
ADAE.AESER (= 'N') and ADAE.AEREL/ADAE.AREL (= 'Y' or '') and ADAE.AEACN (= 'DOSE REDUCED' or 'DRUG WITHDRAWN')		

PHUSE Working Group: Standard Analyses and Code Sharing



PHUSE Working Group: Standard Analyses and Code Sharing

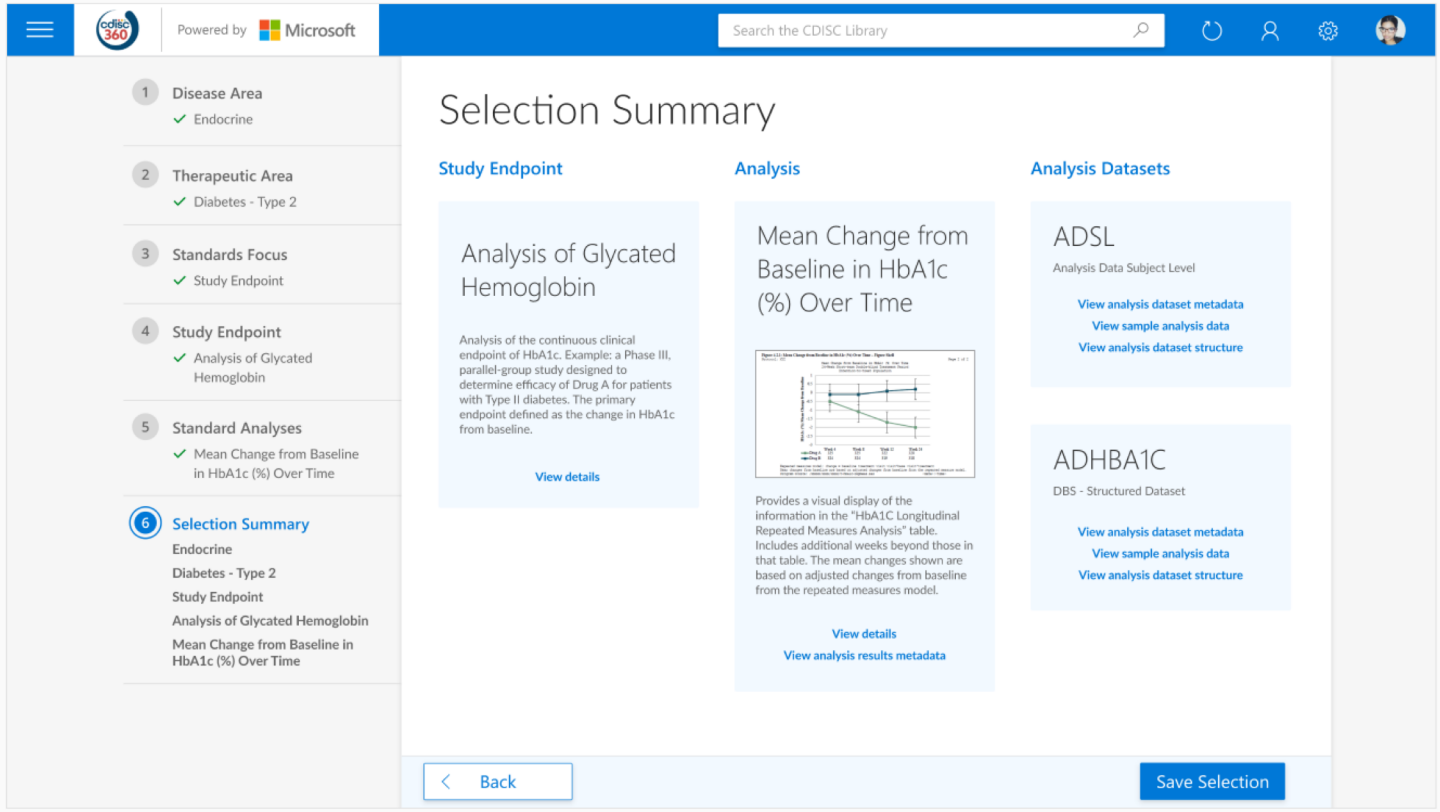
- Vision: Leverage crowd-sourcing to improve the content and implementation of analyses for medical research, leading to better data interpretations and increased efficiency in the clinical drug development and review processes.

- Goals:
  - Establish and maintain a publicly available repository for storing program code to be used as analytical tools for medical research.
  - Where gaps exist, develop recommendations for analyses and displays in areas that could benefit from crowd-sourcing.
  - Where gaps exist, develop code for recommended analyses and displays that could benefit from crowd-sourcing (to reside in the repository).

PHUSE analysis & display white papers

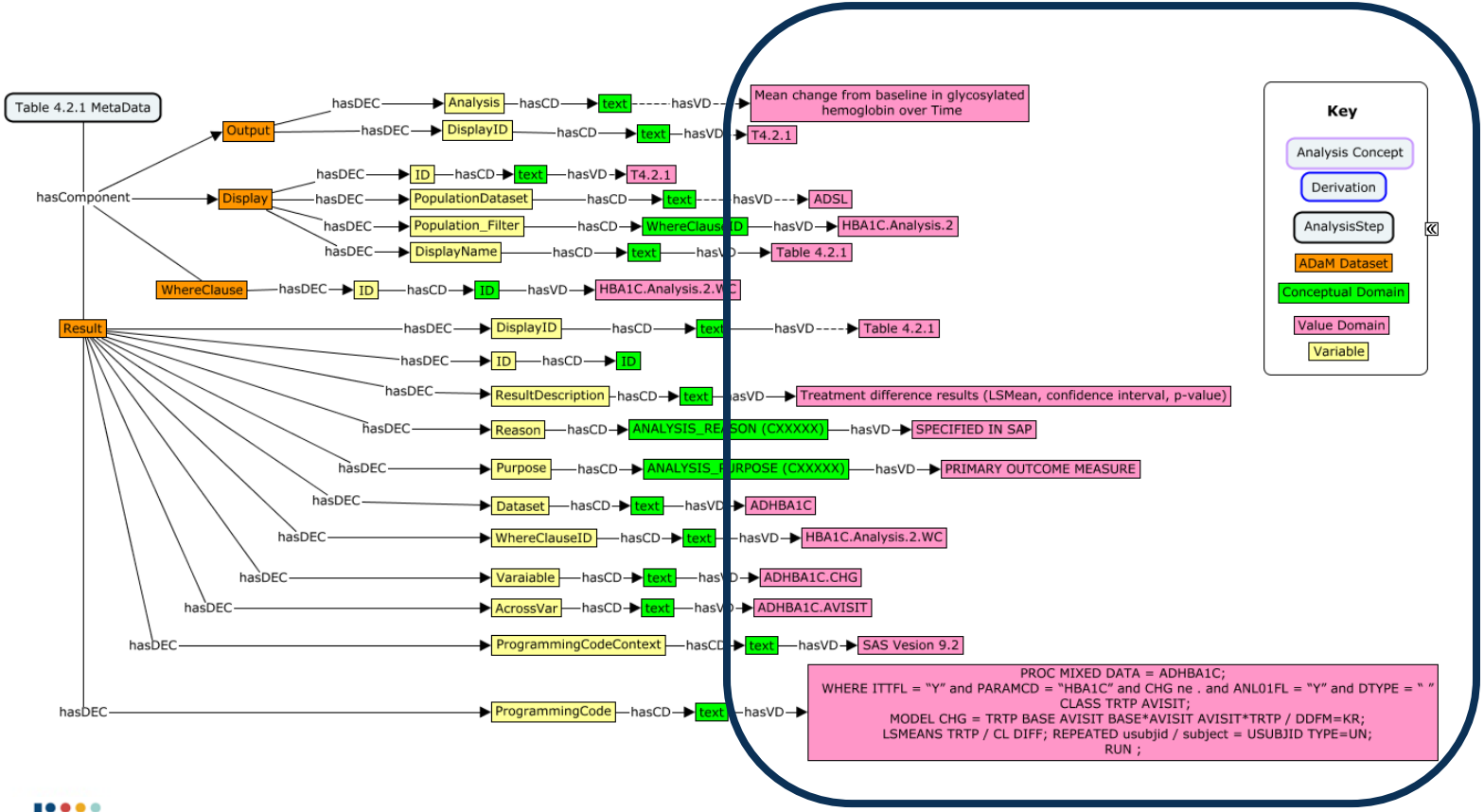
	Version 1		Version 2	
	Review	Publish (ed)	Review	Publish (ed)
Vital Signs, Labs, ECG – Central Tendency		Oct 2013 ✓		
Non-Compartmental PK		March 2014 ✓		
Demographics, Disposition, Medications		Oct 2014 ✓	Q4 2017 ✓	Q1 2018 ✓
Vital Signs, Labs, ECG – Outliers / Shifts		Sept 2015 ✓		
QT/QTc Studies		March 2016 ✓		
Adverse Events		Feb 2017 ✓		
General Output Tips and Considerations (Karin)	Q1 2020	Q2 2020 🎯		
Treatment-Emergent Definitions (Survey Results)	Q2 2020	Q3 2020 🎯		
Labs (Wei)	Q3 2020	Q1 2021 🎯		
Hepatotoxicity (Terry)	Q3 2020	Q1 2021 🎯		
Questionnaires (Karin)	Q3 2020	Q1 2021 🎯		
Listings	Q3 2020	Q4 2020 🎯		
Safety Topics of Interest (Brenda)	Q3 2020	Q4 2020 🎯		
Vital Signs	Q3 2021	Q4 2021 🎯		
ECG's	Q3 2021	Q4 2021 🎯		
Treatment-Emergent Definitions (Recommendations on Definition)	Q3 2021	Q1 2022 🎯		
Interactive Displays for Clinical Safety Data (Wei)	Q4 2021	Q1 2022 🎯		

CDISC 360: The Art of the Possible



Reference: '*CDISC 360 - The Journey so Far and the Road Ahead', Peter Van Reusel, 28th April 2020*

Analysis Result Concept



Reference: '*CDISC 360 - The Journey so Far and the Road Ahead', Peter Van Reusel, 28th April 2020*

CDISC ARM v1 Metadata

Result

- ResultOID
- Description
- Reason
- Purpose
- Dataset
- WhereClause
- AnalysisVariable
- Documentation
- ProgrammingCode

Study – CDISC 360

Table 14.1.1.1
Demographic characteristics (Safety Population)

Characteristics	METFORMIN (N=XX)	HUMAN INSULIN (N=XX)
Age (years)		
n	XX	XX
Mean	XX.X	XX.X
SD	XX.XX	XX.XX
Min	XX	XX
Q25	XX.X	XX.X
Median	XX.X	XX.X
Q75	XX.X	XX.X
Max	XX	XX
Age Group - n (%)		
15 - <30 years	XX (XX.X)	XX (XX.X)
30 - <45 years	XX (XX.X)	XX (XX.X)
>=45 years	XX (XX.X)	XX (XX.X)
Gender - n (%)		
Male	XX (XX.X)	XX (XX.X)
Female	XX (XX.X)	XX (XX.X)

Max = Maximum. Min = Minimum. N = Number of subjects in treatment group. n = Number of subjects included in analysis. SD = Standard deviation.
Datasets used - adsl
Executed by <Username> on DDMONYYYY:HH:MM

Display

- DisplayOID
- Name
- Title
- Document

CDISC ARM v1 Metadata Extensions

Output (Study, Analysis, Group, Filename/Type, Style)

Study - CDISC 360

Table 14.1.1.1
Demographic characteristics (Safety Population)

Characteristics	METFORMIN (N=XX)	HUMAN INSULIN (N=XX)
Age (years)		
n	XX	XX
Mean	XX.X	XX.X
SD	XX.XX	XX.XX
Min	XX	XX
Q25	XX.X	XX.X
Median	XX.X	XX.X
Q75	XX.X	XX.X
Max	XX	XX
Age Group - n (%)		
15 - <30 years	XX (XX.X)	XX (XX.X)
30 - <45 years	XX (XX.X)	XX (XX.X)
>=45 years	XX (XX.X)	XX (XX.X)
Gender - n (%)		
Male	XX (XX.X)	XX (XX.X)
Female	XX (XX.X)	XX (XX.X)

Max = Maximum. Min = Minimum. N = Number of subjects in treatment group. n = Number of subjects included in analysis. SD = Standard deviation.
Datasets used - adsl
Executed by <Username> on DDMONYYYY:HH:MM

Result

Version
DisplayPattern
Grouping
- AnalysisVar
- ByVar
CodeReference

Display

Parent
Version
Grouping:
- Dataset
- WhereClause
- AnalysisVar
- ByVar
Template
Title 1..N
RowLabelHeader
Header 1..N
Footer 1..N

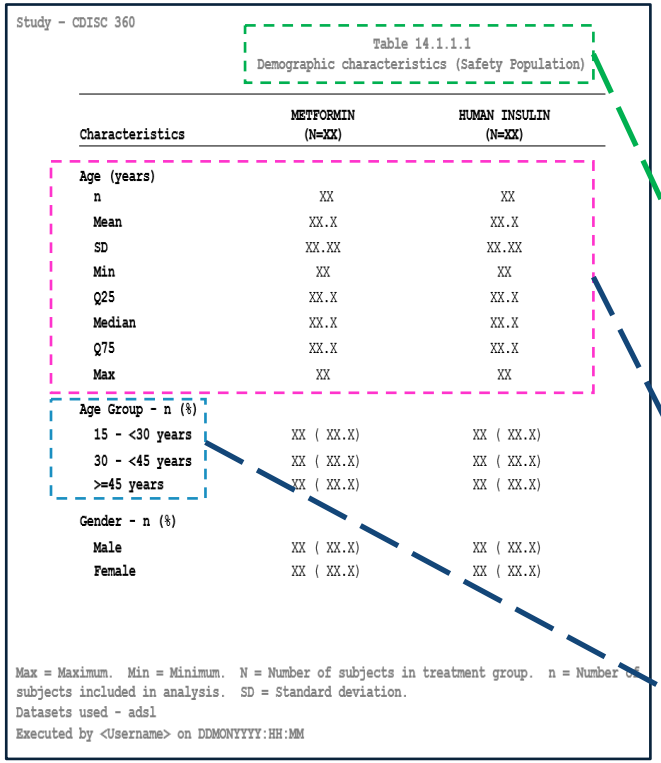
Reference: '*Automation of TFL Generation using CDISC 360 Enriched Metadata' ; Bhavin Busa, Prasanna Murugesan, Stuart Malcom; CDISC US Interchange 2020*

CDISC 360 Enriched TFL Metadata (ARM++)

- Based on CDISC ARM v1
- Added OUTPUT & STYLE
- Extended DISPLAY and RESULT
  - Parent
  - Version
  - Grouping and ByVar
  - CodeReference
- Use-cases for production TFL automation

Reference: '*Automation of TFL Generation using CDISC 360 Enriched Metadata' ; Bhavin Busa, Prasanna Murugesan, Stuart Malcom; CDISC US Interchange 2020*

CDISC 360 Enriched TFL Metadata (ARM++): Sample



Study - CDISC 360

Table 14.1.1.1
Demographic characteristics (Safety Population)

Characteristics	METFORMIN (N=XX)	HUMAN INSULIN (N=XX)
Age (years)		
n	XX	XX
Mean	XX.X	XX.X
SD	XX.XX	XX.XX
Min	XX	XX
Q25	XX.X	XX.X
Median	XX.X	XX.X
Q75	XX.X	XX.X
Max	XX	XX
Age Group - n (%)		
15 - <30 years	XX (XX.X)	XX (XX.X)
30 - <45 years	XX (XX.X)	XX (XX.X)
>=45 years	XX (XX.X)	XX (XX.X)
Gender - n (%)		
Male	XX (XX.X)	XX (XX.X)
Female	XX (XX.X)	XX (XX.X)

Max = Maximum. Min = Minimum. N = Number of subjects in treatment group. n = Number of subjects included in analysis. SD = Standard deviation.
Datasets used - adsl
Executed by <Username> on DDMONYYYY:HH:MM

Study	Analysis	Group	Order	DisplayID	DisplayVersion	Filename	Type	StyleID
CDISC	CDISC 360	Safety	1	T14111_SAF_DEMOG	1	tdemog_saf	rtf	table_rtf
CDISC	CDISC 360	Safety	2	T14131_SAF_AE2TIER	1	tae_soc_pt_saf	rtf	table_rtf
CDISC	CDISC 360	Efficacy	3	T1421_EFF	1	tmace_edpt_fas	rtf	table_rtf

Output | Display | Result | WhereClause | Style | TFL Metadata Tables | TFL Metadata ...

DisplayID	DisplayName	DisplayTitle	Title1	Title2	Title3
T14111_SAF_DEMOG	Table 14.1.1.1	Demographic characteristics (SAF)	Study - CDISC 360	Table 14.1.1.1	Demographic characteristics (Safety Population)

Output | Display | Result | WhereClause | Style | TFL Metadata Tables | TFL Metadata Variables ...

ResultDisplayOID	AnalysisResultOID	Version	ResultDescription	DisplayPattern
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	n	xxx
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	Mean	xx.x
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	SD	xx.xx
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	Min	xx
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	Q25	xx.x
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	Median	xx.x

Output | Display | Result | WhereClause | Style | TFL Metadata Tables | TFL Metadata Variables ...

WhereClauseOID	Dataset	Variable	Comparator	Value
T14111_02_SAF_DEMOG_01	ADSL	AGEGR1	EQ	15<= to <30 years
T14111_02_SAF_DEMOG_02	ADSL	AGEGR1	EQ	30<= to <45 years
T14111_02_SAF_DEMOG_03	ADSL	AGEGR1	EQ	>=45 years
T14111_03_SAF_DEMOG_01	ADSL	SEX	EQ	M
T14111_03_SAF_DEMOG_02	ADSL		EQ	F

Output | Display | Result | WhereClause | Style | TFL Metadata Tables | TFL Me...

Reference: *'Automation of TFL Generation using CDISC 360 Enriched Metadata' ; Bhavin Busa, Prasanna Murugesan, Stuart Malcom; CDISC US Interchange 2020*

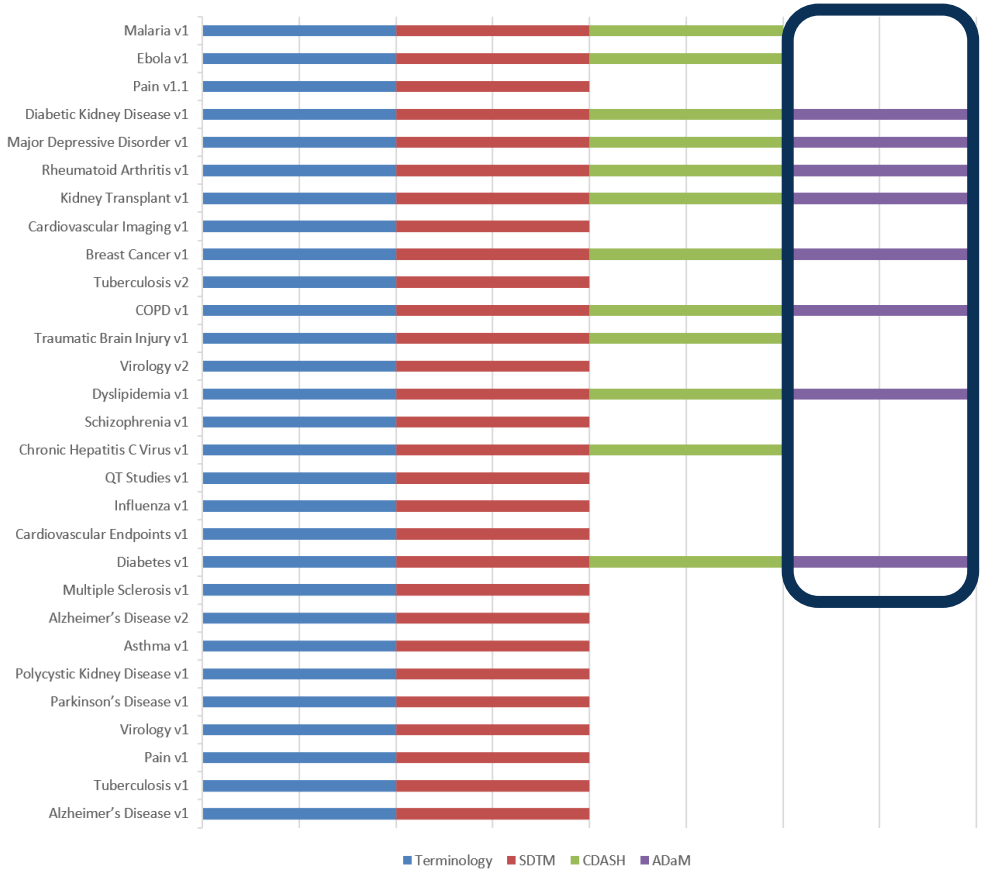
What content will be the focus?

- Most common safety analyses
- TAUGs with analysis components
- TAUGs without analysis components
- Community generated content
- Will not focus on TFL layout
  - Example options for layouts for illustration purposes

What common safety analyses do we start with?

	Version 1		Version 2	
	Review	Publish (ed)	Review	Publish (ed)
Vital Signs, Labs, ECG – Central Tendency		Oct 2013 ✓		
Non-Compartmental PK		March 2014 ✓		
Demographics, Disposition, Medications		Oct 2014 ✓	Q4 2017 ✓	Q1 2018 ✓
Vital Signs, Labs, ECG – Outliers / Shifts		Sept 2015 ✓		
QT/QTc Studies		March 2016 ✓		
Adverse Events		Feb 2017 ✓		
General Output Tips and Considerations (Karin)	Q1 2020	Q2 2020		
Treatment-Emergent Definitions (Survey Results)	Q2 2020	Q3 2020		
Labs (Wei)	Q3 2020	Q1 2021		
Hepatotoxicity (Terry)	Q3 2020	Q1 2021		
Questionnaires (Karin)	Q3 2020	Q1 2021		
Listings	Q3 2020	Q4 2020		
Safety Topics of Interest (Brenda)	Q3 2020	Q4 2020		
Vital Signs	Q3 2021	Q4 2021		
ECG's	Q3 2021	Q4 2021		
Treatment-Emergent Definitions (Recommendations on Definition)	Q3 2021	Q1 2022		
Interactive Displays for Clinical Safety Data (Wei)	Q4 2021	Q1 2022		

TAUGs with and without ADaM components



TAUG Tables, Listings, and Figures

Table 4.2.1: HbA1c Longitudinal Repeated Measures Analysis - Table Shell

Protocol: XYZ — Page 1 of 2

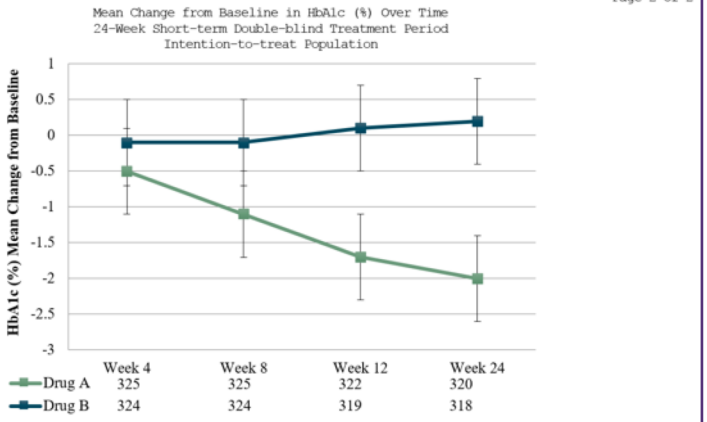
HbA1c (%) Longitudinal Repeated Measures Analysis
24-Week Short-term Double-blind Treatment Period
Intention-to-treat Population

		Drug A N=125	Drug B N=125
BASELINE	N♯	125	125
	Mean (SD)	X.XX(X.XXX)	X.XX (X.XXX)
WEEK 4	N♯	XXX	XXX
	Change from baseline: Mean (SD)	X.XX (X.XXX)	X.XX (X.XXX)
	Adjusted change from baseline: Mean (SD)	X.XX (X.XXX)	X.XX (X.XXX)
	95% Confidence interval for adjusted mean	(XX.XX, XX.X)	(XX.XX, XX.X)
	Difference vs. Drug B (SE)		XX.XX (X.XXXX)
	95% Confidence interval for difference		(XX.XX, XX.X)
	P-value vs. Drug B		X.XXXX
...			
WEEK 12	N♯	X.XX(X.XXX)	X.XX (X.XXX)
	Change from baseline: Mean (SD)	XXX	XXX
	Adjusted change from baseline: Mean (SD)	X.XX (X.XXX)	X.XX (X.XXX)
	95% Confidence interval for adjusted mean	X.XX (X.XXX)	X.XX (X.XXX)
	Difference vs. Drug B (SE)	(XX.XX, XX.X)	(XX.XX, XX.X)
	95% Confidence interval for difference		XX.XX (X.XXXX)
	P-value vs. Drug B		(XX.XX, XX.X)
			X.XXXX

N: the number of subjects in the Intention-to-treat (ITT) Population.
N♯: the number of subjects in the ITT population with non-missing baseline and non-missing Week t value.
Repeated measures model: change = baseline treatment visit visit*treatment
Program Source: xxxxxxxx\xxxx\xxxx\t-hbalc-repmeas.sas <date>:<time>

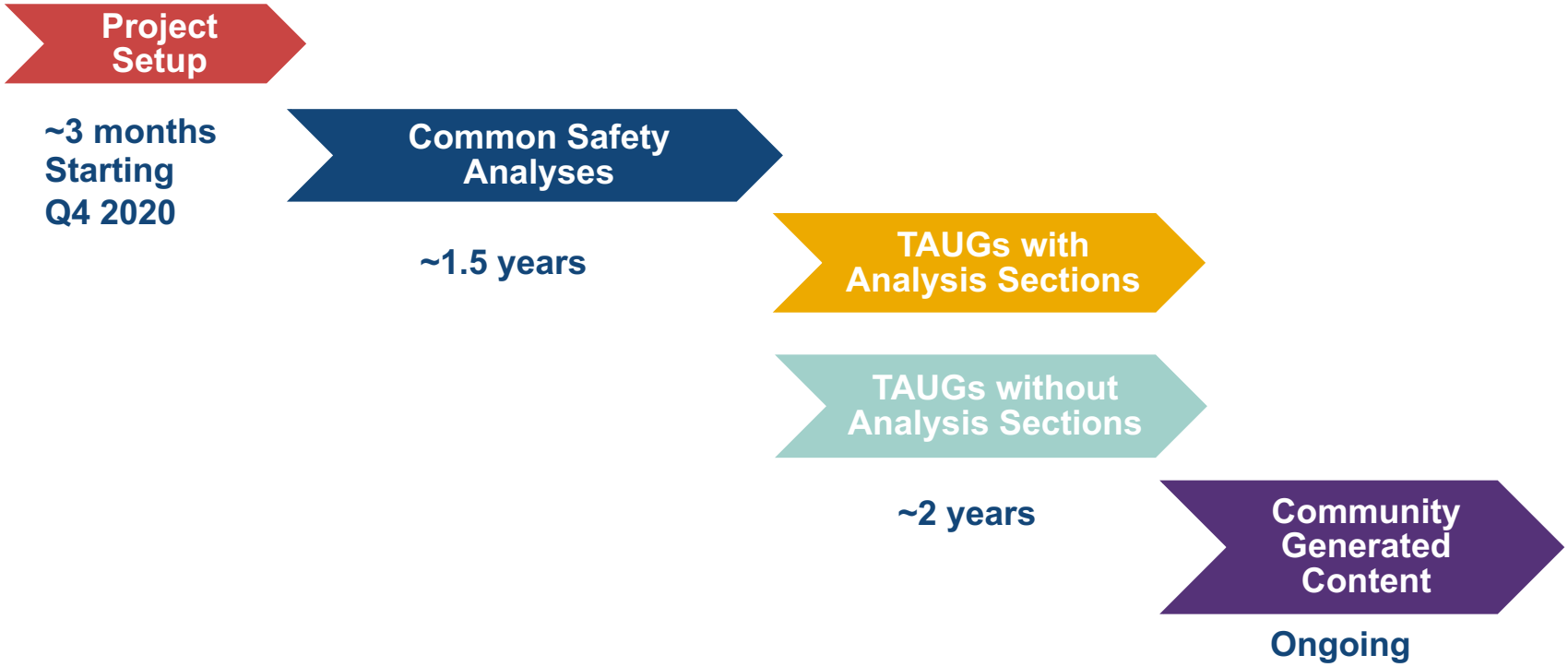
Some examples exist in the TAUGs for various disease areas but not all analysis sections have the same level of detail

Protocol: XYZ — Page 2 of 2



Repeated measures model: change = baseline treatment visit visit*base visit*treatment
Mean changes from baseline are based on adjusted changes from baseline from the repeated measure model.
Program Source: /xxxxx/xxxx/xxxx/t-hbalc-repmeas.sas <date>:<time>

Anticipated Project Timeline



Interested? Join our team!

- Looking for additional team members
- Meet weekly on Friday at 10:00 am Eastern
- Contact Bess LeRoy at bleroy@cdisc.org

Thank you to the current team!

- Jeff Abolafia
- Brian Harris
- Nate Freimark
- Mary Nilsson
- Maria Matilde Kam
- Yumiko Asami
- Kent Letourneau
- Hansjoerg Frenzel
- Nancy Brucken
- Bhavin Busa
- Sally Cassells
- Jon Neville
- Peter Van Reusel
- Azusa Tsukida
- Chenoa Conley

Audience Questions

How can I get involved in the project?

Audience Questions

The paper by Chris Decker that you mentioned builds on the PhUSE working group: PhUSE Analysis Results Model Project, (2016, Marc Andersen and Tim Williams, https://www.phusewiki.org/wiki/index.php?title=Analysis_Results_Model).

Audience Questions

I'm excited to hear about this project. One thing that has always bothered me about the current ARM standard is the one-to-one coupling of results with displays, which leads to unnecessary repetition, e.g. when the same result appears in multiple tables. Will this project consider the whole data model behind ARM, so the relationship between results and displays can be normalised? It sounds like it probably will but confirmation would be great!

Audience Questions

Why can't ARM currently be used to help generate reesults. Instead of being produced after results are generated?

Audience Questions

Nice presentation. Is there an online form to be filled become an volunteer?

Answer:

https://www.cdisc.org/volunteer

Audience Questions

Is a development of ODM-XML-based standard for TLFs (based on ARM/ARM++) is part of the project scope?

Audience Questions

Is this a CDISC initiative or will the results datasets be requested soon by the FDA?

Upcoming Learning Opportunities

2021 CDISC Upcoming Events

February 2021 – TechniCon Virtual Events

TechniCon

- Tuesday, 2 February: Asia-Pacific Rim
- Wednesday, 3 February: EMEA
- Friday, 5 February: India
- Monday, 8 February: Americas

Submit Abstracts Now. Registration Open Soon!

April 2021 – Europe Virtual Event

2021 Europe Interchange

28-29 April

February 2021 – Abstract Submissions and Registration Coming Soon.

Free Upcoming Webinar Lineup – Registration Open!

CDASH SAE v2.0 Public Review

10 NOV 2020, 11:00 AM - 12:30 PM EDT

- CDISC, with support from our partner TransCelerate Biopharma, is developing version 2.0 of the CDASH SAE Supplement, which will capture how to structure serious adverse events (SAE) concepts for regulated clinical trials.

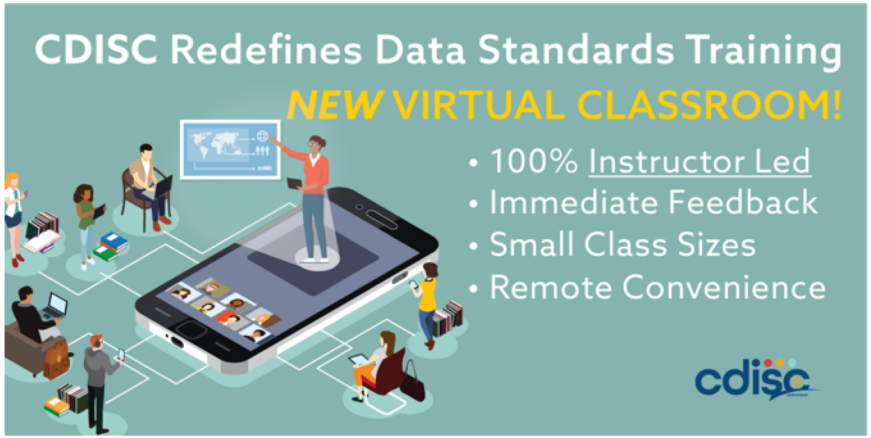
CDISC Tabulate Certification Launch

16 NOV 2020, 11:00 AM - 12:30 PM EDT

- Announcing the new CDISC Certification program: why you should take it, and how you can do it.

New Virtual Training Methods

- CDISC Provides Many Ways to Begin or Continue Growing Your Standards Knowledge.
  - Popular self-paced training plus new Blended Learning and Virtual Classroom settings.



Thank You!

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

Don’t forget to fill out the feedback survey!