

PINNACLE²¹

CDISC ANALYSIS RESULTS STANDARD

Jeff Abolafia – Director of Product Innovation

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JEFF ABOLAFIA

DIRECTOR OF PRODUCT INNOVATION

- ▶ 50% at FDA > RWE and Analysis Projects
- ▶ CDISC ADAM Team 15+ years
- ▶ CDISC Analysis Results Team
- ▶ CDISC E-2C Team
- ▶ PhUSE Real World Evidence Team
- ▶ PhUSE Research on FHIR Team

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AGENDA

Background

What We Have Accomplished

What's Next

Q&A

THANK YOU!



BACKGROUND

Analysis Results Current State

Table 3.1.1: ADHYPO Analysis Dataset

Row	STUDYID	USUBJID	MIDS	CEDECOD	WASAEYN	ASTDTM
1	XYZ	000001	HYP0 1	Hypoglycemia	Y	07Sep2012 22:29:00
2	XYZ	000001	HYP0 2	Hypoglycemia	N	10Sep2012 09:12:00
3	XYZ	000001	HYP0 3	Hypoglycemia	N	10Sep2012 23:05:00
4	XYZ	000001	HYP0 4	Hypoglycemia	N	11Sep2012 15:24:00
5	XYZ	000001	HYP0 5	Hypoglycemia	N	18Sep2012 11:39:00
6	XYZ	000002	HYP0 1	Hypoglycemia	N	22Oct2012 13:28:00
7	XYZ	000002	HYP0 2	Hypoglycemia	N	25Oct2012 13:59:00
8	XYZ	000002	HYP0 3	Hypoglycemia	N	17Nov2012 05:01:00

ADaM Dataset

Table	Parameter	Estimate	95% CI	p-value
Table 4.2.1	Mean (95%)	0.000	[-0.000, 0.000]	0.000
Table 4.2.1	95% CI (Lower)	-0.000	[-0.000, -0.000]	0.000
Table 4.2.1	95% CI (Upper)	0.000	[0.000, 0.000]	0.000

Analysis Results

Table 4.2.2: HbA1c Longitudinal Repeated Measures Analysis Results Metadata

Table	Parameter	Value
Table	RESULT IDENTIFIER	Table 4.2.1 Figure 4.2.1
Table	DISPLAY NAME	Mean Change from Baseline in HbA1c (Percent) Longitudinal Repeated Measures Analysis, 24-Week Short-term Double-blind Treatment
Table	PARAM	CHG (Change from baseline)
Table	PARAMCD	HBA1C
Table	ANALYSIS REASON	SPECIFIED IN SAP
Table	ANALYSIS PURPOSE	PRIMARY OUTCOME MEASURE
Table	ANALYSIS DATASET	ADHBA1C

ARM for define.xml

ANALYSIS RESULTS CURRENT STATE

- ▶ Static results created for Clinical Study Report
- ▶ May be hundred of tables in PDF format, often difficult to navigate
- ▶ No or limited traceability (e.g., to protocol, SAP, ADaM data)
- ▶ Expensive to generate and only used once, no or limited reusability
- ▶ ARM v1.0 describes *metadata* about displays (PDF) and results (at high level), no formal analysis and results model or results data.
- ▶ Lack of features to drive automation
- ▶ Limited regulatory use cases

CDISC ANALYSIS RESULTS STANDARD SHIFTING THE PARADIGM

Table 3.1.1: ADHYPO Analysis Dataset

Row	STUDYID	USUBJID	MIDS	CEDECOD	WASAEYN	ASTDTM
1	XYZ	000001	HYP0 1	Hypoglycemia	Y	07Sep2012 22:29:00
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4	XYZ	000001	HYP0 4	Hypoglycemia	N	11Sep2012 15:24:00
5	XYZ	000001	HYP0 5	Hypoglycemia	N	18Sep2012 11:39:00
6	XYZ	000002	HYP0 1	Hypoglycemia	N	22Oct2012 13:28:00
7	XYZ	000002	HYP0 2	Hypoglycemia	N	25Oct2012 13:59:00
8	XYZ	000002	HYP0 3	Hypoglycemia	N	17Nov2012 05:01:00

ADaM Dataset

qb:Observation	qb:Table	dim.population	dim.treatment	dim.parameter	dim.sex	dim.agecat	dim.statistic	analysisResult
1001	dm.summary	enrolled	Treatment.A	param.subjects	sex.ALL	agecat.ALL	stat.freq	100
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

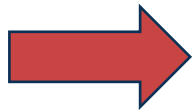
Analysis Results Dataset

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, 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

ARM v1

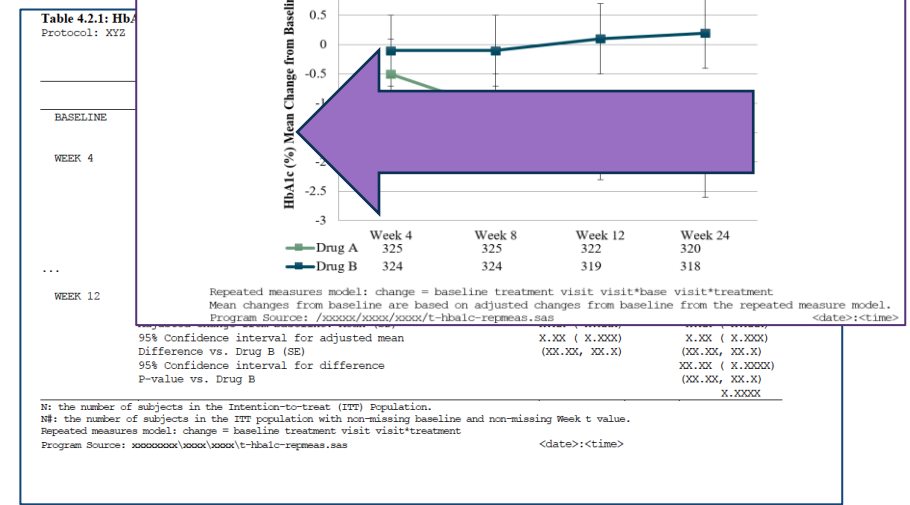
ARM Extensions



Automation



Reuse



Display Traceability

ANALYSIS RESULTS DESIRED FUTURE STATE

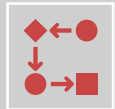
- ▶ Formal model for describing analyses and results as data
- ▶ Facilitate automated generation of results
- ▶ From electronic (PDF) to machine readable results, with context and metadata to source
- ▶ Improved navigation and reusability of analyses and results
- ▶ Support storage, access, processing and reproducibility of results
- ▶ Traceability to Protocol/SAP and to input ADaM data
- ▶ Open-source tools to design, specify, build and generate analysis results



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PROJECT UPDATE

ANALYSIS RESULTS STANDARDS GOALS



Formal model that describes analysis results metadata



Analysis Results Metadata Technical Specification (ARM-TS), to support automation, traceability, and creation of data displays



Define an Analysis Results Data (ARD) structure, to support reuse and reproducibility of results data



Illustrate and exercise ARD and ARM-TS with a set of machine-readable common safety displays

LIST OF INITIAL WORKING DATA DISPLAYS, CONCEPTS

- ▶ Analysis Populations and Subject Disposition
- ◀ Protocol Deviations
- ▶ Demographics and Other Baseline Characteristics
- ◀ Medical History
- ▶ Prior and Concomitant Medications
- ◀ Subject Incidence of Adverse Events
- ◀ Treatment Emergent Adverse Events by SOC and PT
- ▶ TEAE SOC and PT by Maximum Severity
- ◀ Laboratory Tests by Visit
- ◀ Change in Vital Signs by Visit

EXTEND ARM

- Prospective focus on automation, traceability, and creation of data displays
- Linked, modular, flexible and tool agnostics
- Supports meta-programming
- Serves a different purpose than ARM for Define-XML

Output	StudyID	Display	DisplayID	Display Section	DisplaySectionID	
	AnalysisTask		ReferenceDisplayID		ReferenceDisplayID	
	AnalysisSetLabel		Version		Section	
	OutputOrder		Name		SectionSubID	
	DisplayID		Title		Order	
	Filename		DisplaySectionID		Label	
	OutputVersion		AnalysisSetID		Text	
	FileType		AnalysisGroupID		Reference	
	StyleID		DisplayTemplateID			
	Document					
		Result	DisplayID	Analysis Set	AnalysisSetID	
	AnalysisResultID		Dataset		Order	
	Version		Variable		Comparator	
	ResultDescription		Value		Label	
	DisplayPattern		CompoundExpression			
	Reason					
	Purpose		Analysis Group		AnalysisGroupID	
	Dataset				Dataset	Order
	AnalysisVariable				Variable	Comparator
	AnalysisGroupID				Value	Label
	WhereClauseID				CompoundExpression	
	GroupingByVar					
	GroupingByOrdFmt				Template	DisplayTemplateID
	Documentation	TemplateContext		ElementName		
	ProgrammingCodeContext	ElementValue				
	ProgrammingCode					
	CodeReference					
		Where Clause		WhereClauseID		
	StyleID			Dataset		Order
Style	StyleContext		Variable	Comparator		
	ElementName		Value	Label		
	ElementValue		Compound Expression			

*Work in progress

CDISC 360: Extended Analysis Results Metadata 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

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)

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
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	Q75	xx.x

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	SEX	EQ	F

Draft Analysis Results Dataset Specification (ARDS)

Metadata Describing the ARDS

Analysis Results Dataset Specification – One record per result

Variable Name	Variable Label	Type	Code list/ Controlled Terms	Core	CDISC Notes	PARAMCD	Analysis Parameter	C			
STUDYID	Study Identifier	C			Unique identifier for a study						The description of the analysis parameter (i.e., Supine Systolic Blood Pressure (mm Hg)). Typically, only used with BDS datasets.
RESULTID	Result Identifier	C			Unique identifier for a result	ANAL_VAR	Analysis Variable	C			Analysis variable needed to create the respective analysis result.
TABLEID	Display Identifier	C			Sponsor defined identifier to tie a group of related results together	AVAR_VAL	Analysis Variable Value	C			Value of analysis. Typically, only used for categorical variables
ADSNS	Source Datasets	C			List of source datasets separated by commas (i.e., ADSL, ADAE)	STATNAME	Name of Statistic	C			
POPULATION	Analysis Population	C			Description of population (i.e., Safety Population)	STATVAL	Value of Statistic	Float			
TIME	Description of Time Frame	C			Time frame used in analysis (i.e., Visit 1 or 12 weeks)	STATDESC	Description of Statistic	C			
WHERE	Description of Subsetting Criteria	C			selection criterion needed to select the required subset of records from the specified analysis dataset						
<u>BYVARz</u>	Name of <u>BYVARz</u>	C			The lower-case letter "z" in the variable name is the <u>z</u> th By-Variable, where "z" is replaced with a one-digit integer between 1 and 9.						
<u>BYVALz</u>	Value of <u>BYVARz</u>				The lower-case letter "z" in the variable name is the <u>z</u> th By-Variable, where "z" is replaced with a one-digit integer between 1 and 9.						
TRTVAR	Treatment variable name	C			Name of treatment variable used in analysis (i.e. TRTP, TRT01P)						
TRTVAL	Treatment value	C			Value of TRTVAR for a given record						

Analysis Result Dataset: OCCDS Structure Example

Protocol: CDISPILOT01
Population: Safety

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Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

System Organ Class/ Preferred Term	Placebo (N=86)		Xanomeline Low (N=84)		Xanomeline High (N=84)		Fisher's Exact p-values Placebo vs. vs. Low Dose High Dose	
	n (%)	[AEs]	n (%)	[AEs]	n (%)	[AEs]	Low Dose	High Dose
ANY BODY SYSTEM	65 (75.6%)	[281]	77 (91.7%)	[412]	76 (90.5%)	[433]	0.007*	0.014*
CARDIAC DISORDERS	12 (14.0%)	[26]	13 (15.5%)	[30]	15 (17.9%)	[30]	0.831	0.534
SINUS BRADYCARDIA	2 (2.3%)	[2]	7 (8.3%)	[10]	8 (9.5%)	[12]	0.097*	0.056*
MYOCARDIAL INFARCTION	4 (4.7%)	[4]	2 (2.4%)	[4]	4 (4.8%)	[8]	0.682	>0.99
ATRIAL FIBRILLATION	1 (1.2%)	[1]	1 (1.2%)	[1]	3 (3.6%)	[5]	>0.99	0.365
ATRIAL FLUTTER	0		1 (1.2%)	[1]	1 (1.2%)	[2]	0.494	0.494
CARDIAC DISORDER	0		0		1 (1.2%)	[1]		0.494
SUPRAVENTRICULAR	1 (1.2%)	[2]	1 (1.2%)	[2]	1 (1.2%)	[1]	>0.99	>0.99
EXTRASYSTOLES								
VENTRICULAR EXTRASYSTOLES	0		2 (2.4%)	[4]	1 (1.2%)	[1]	0.243	0.494
ATRIAL HYPERTROPHY	1 (1.2%)	[2]	0		0		>0.99	>0.99
ATRIOVENTRICULAR BLOCK	1 (1.2%)	[1]	1 (1.2%)	[1]	0		>0.99	>0.99
FIRST DEGREE								
ATRIOVENTRICULAR BLOCK	1 (1.2%)	[1]	0		0		>0.99	>0.99
SECOND DEGREE								
BRADYCARDIA	1 (1.2%)	[4]	0		0		>0.99	>0.99
BUNDLE BRANCH BLOCK LEFT	1 (1.2%)	[1]	0		0		>0.99	>0.99
BUNDLE BRANCH BLOCK RIGHT	1 (1.2%)	[2]	1 (1.2%)	[1]	0		>0.99	>0.99

Analysis Result Dataset: OCCDS Structure Example

IDENTIFIERS			DATA / POPULATION				BY VARIABLES					ANALYSIS VARIABLES			STATISTICS			
StudyID	ResultID	TableID	ADSNs	Population	Where	Time	ByVar1	ByVal1	ByVar2	ByVal2	TrtVar	TrtVal	ParamCD	Anal_Var	Anal_Var_Val	Stat_Name	Stat_Val	Stat_Desc
1234	AE01a1	AE01a	ADAE, ADSL Safety								TRTP	D1		AE Incidence		N	xx	# subjects with event
1234	AE01a2	AE01a	ADAE, ADSL Safety								TRTP	P1		AE Incidence		N	xx	
1234	AE01a3	AE01a	ADAE, ADSL Safety								TRTP	D1		AE Incidence		Percent	xx.xx	% of subjects in treatment group with event
1234	AE01a4	AE01a	ADAE, ADSL Safety								TRTP	P1		AE Incidence		Percent	xx.xx	
1234	AE01a5	AE01a	ADAE, ADSL Safety				Body System	Blood and lymphatic system disorders			TRTP	D1		AE Incidence		N	xx	# subjects with event
1234	AE01a6	AE01a	ADAE, ADSL Safety				Body System	Blood and lymphatic system disorders			TRTP	P1		AE Incidence		N	xx	
1234	AE01a7	AE01a	ADAE, ADSL Safety				Body System	Blood and lymphatic system disorders			TRTP	D1		AE Incidence		Percent	xx.xx	% of subjects in treatment group with event
1234	AE01a8	AE01a	ADAE, ADSL Safety				Body System	Blood and lymphatic system disorders			TRTP	P1		AE Incidence		Percent	xx.xx	
1234	AE01a9	AE01a	ADAE, ADSL Safety				Body System	Blood and lymphatic system disorders	PT	Anaemia	TRTP	D1		AE Incidence		N	xx	# subjects with event
1234	AE01a10	AE01a	ADAE, ADSL Safety				Body System	Blood and lymphatic system disorders	PT	Anaemia	TRTP	P1		AE Incidence		N	xx	
1234	AE01a11	AE01a	ADAE, ADSL Safety				Body System	Blood and lymphatic system disorders	PT	Anaemia	TRTP	D1		AE Incidence		Percent	xx.xx	% of subjects in treatment group with event
1234	AE01a12	AE01a	ADAE, ADSL Safety				Body System	Blood and lymphatic system disorders	PT	Anaemia	TRTP	P1		AE Incidence		Percent	xx.xx	



WHAT'S NEXT

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FUTURE DELIVERABLES

Formal model/technical specification
that describes analysis results metadata

Analysis Results Dataset Specification

New Model and Implementation Guide
to represent analysis results

Terminology

Identification of Conformance Rules

FUTURE DELIVERABLES: SUPPORT NEW FDA GUIDANCE “FDA STANDARD SAFETY TABLES AND FIGURES INTEGRATED GUIDE”

For a selection of FDA tables and figures, create packages containing

Machine readable displays

Associated analysis results metadata

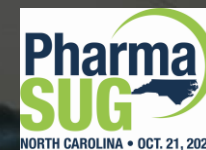
Analysis results dataset examples

Underlying ADaM datasets

Make packages freely available on the CDISC website

QUESTIONS?

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THANK YOU ;)

KEEP IN TOUCH!



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