CDISC Analysis Results Standards – Approach and Development Update

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Analysis Results Current State

- Static results created for Clinical Study Report
- May be hundred of tables in PDF format, often difficult to navigate
- Variability between sponsors
- Expensive to generate and only used once, no or limited reusability

Analysis Ready ADaM Dataset

Table 3.1.1: ADHYPO Analysis Dataset

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

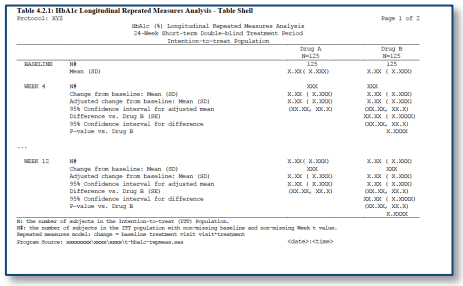

Table 4.2.1: HbA1c Longitudinal Repeated Measures Analysis - Table Shell

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-rpgmeas.sas — <date>:<time>

Static Display

Analysis Results Current State

Table 3.1.1: ADHYPO Analysis Dataset

Row	STUDYID	USUBJID	MIDS	CEDECOD	WASAEYN	ASTDTM
1	XYZ	000001	HYPO 1	Hypoglycemia	Y	07Sep2012 22:29:00
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6	XYZ	000002	HYPO 1	Hypoglycemia	N	22Oct2012 13:28:00
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ADaM Dataset

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\xxx\xxxx\t-hbalc-rmanal.sas — <date>:<time>

Static Display

ARM for Define-XML

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

ARM v1

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Analysis Results Current State

- ARM v1.0 describes *metadata* about analysis displays and results (at a high level), no formal analysis and results model or results data
- Lack of features to drive automation
- Limited regulatory use cases
- Limited traceability

Table 4.2.2: HbA1c Longitudinal Repeated Measures Analysis Results Metadata

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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

Shifting the Paradigm

Table 3.1.1: ADHYPO Analysis Dataset

Row	STUDYID	USUBJID	MIDS	CEDECOD	WASAEYN	ASTDTM
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ADaM Dataset

Shifting the Paradigm

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ADaM 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 Ana 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

ARM v1

ARM Extension Technical Specification

Shifting the Paradigm

Table 3.1.1: ADHYPO Analysis Dataset

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1	XYZ	000001	HYPO 1	Hypoglycemia	Y	07Sep2012 22:29:00
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ADaM 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 Ana 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

ARM v1

ARM Extension Technical Specification

Automation

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

Reuse

Traceability

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-repmeas.sas <date>:<time>

Display

Analysis Results Desired Future State

- Formal model for describing analyses and results as data
- Facilitate automated generation of results
- From static to machine readable results
- 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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Analysis Results Standards Goals

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

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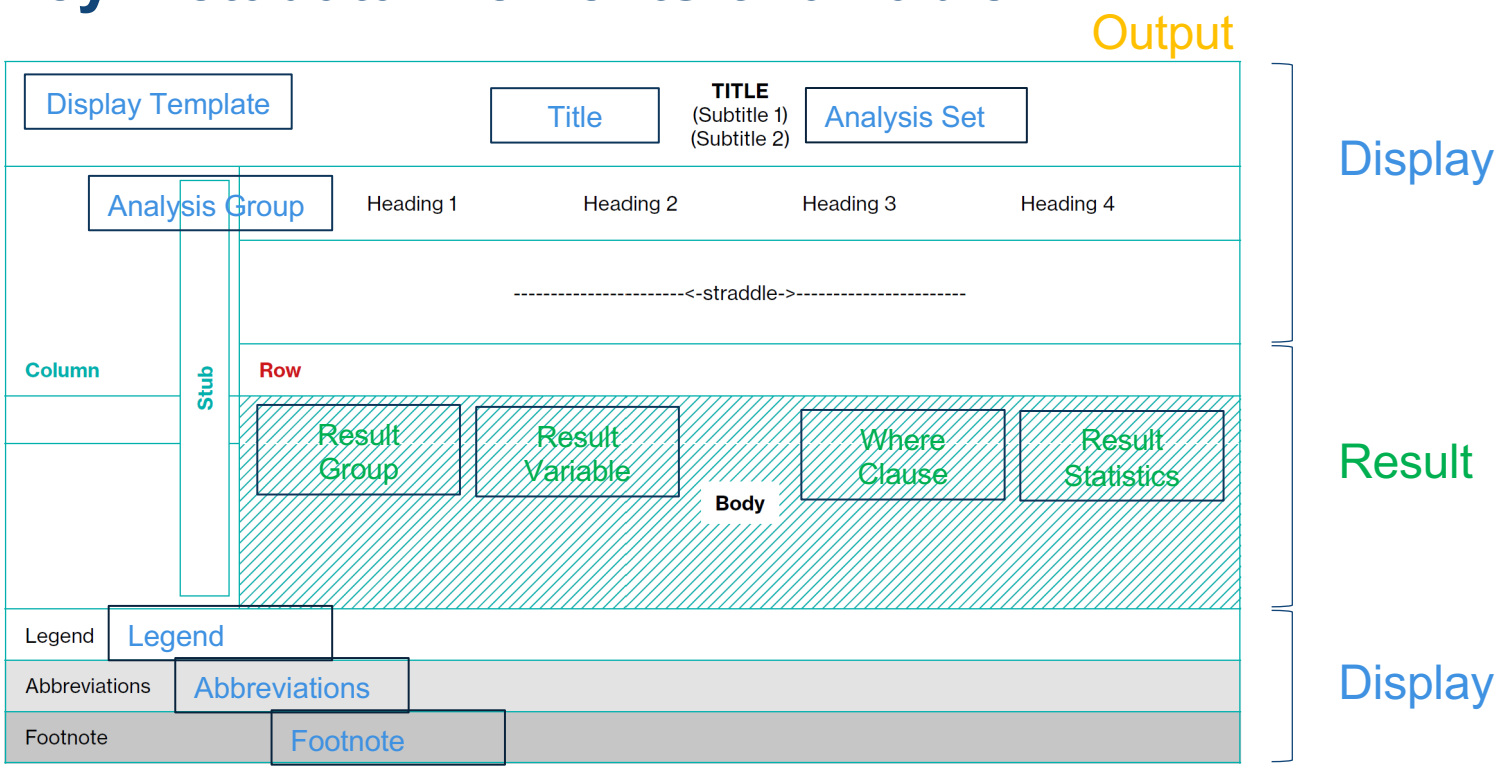
Key Metadata Elements of a Table



Reference: PHUSE White Paper "*General Output Tips and Considerations*", Doc ID: WP-034, Version 1.0, Aug 2020

Demographics Analysis Results and Metadata

Display Template | Title | Analysis Set

Table 2. Baseline Demographic and Clinical Characteristics, Safety Population, Pooled Analyses (or Trial X)

Characteristic	Drug Name Dosage X N = XXX	Drug Name Dosage Y N = XXX	Placebo N = XXX	Active Control N = XXX	Total Population N = XXX
	n (%)	n (%)	n (%)	n (%)	n (%)
Sex, n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Male	n (%)	n (%)	n (%)	n (%)	n (%)
Female	n (%)	n (%)	n (%)	n (%)	n (%)
Age, years	**X.X (Y.Y)**	**X.X (Y.Y)**	**X.X (Y.Y)**	**X.X (Y.Y)**	**X.X (Y.Y)**
Mean (SD)	X.X (Y.Y)	X.X (Y.Y)	X.X (Y.Y)	X.X (Y.Y)	X.X (Y.Y)
Median (min, max)	X.X (Y.Y, Z.Z)	X.X (Y.Y, Z.Z)	X.X (Y.Y, Z.Z)	X.X (Y.Y, Z.Z)	X.X (Y.Y, Z.Z)
Age groups (years), n (%)					**n (%)**
≥17 to <65					n (%)
≥65					n (%)
≥65 to <75					n (%)
≥75	n (%)	n (%)	n (%)	n (%)	n (%)
Race, n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
American Indian or Alaska Native Asian	n (%)	n (%)	n (%)	n (%)	n (%)
Black or African American	n (%)	n (%)	n (%)	n (%)	n (%)
Native Hawaiian or Other Pacific Islander	n (%)	n (%)	n (%)	n (%)	n (%)
White	n (%)	n (%)	n (%)	n (%)	n (%)
Other	n (%)	n (%)	n (%)	n (%)	n (%)

Analysis Group

Result Group | Result Variable | Where Clause | Result Statistics

Source: [include Applicant source, datasets and/or software tools used].
[1] Difference is shown between [treatment arms] (e.g., difference is shown between Drug Name dosage X vs. placebo).
Abbreviations: N, number of patients in treatment arm; n, number of patients with given characteristic; SD, standard deviation

Footnote | Abbreviations | Legend

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Analysis Results Dataset Example: Demographics

Identifiers		Analysis Group			Result Variable			Results Statistic		
Name	Title	Dataset	Variable	Value	Variable	Value	Label	Value	Name	Label
Table 2	Baseline Demographics and Clinical Characteristics, Safety Population	ADSL	TR01X	Drug Name Dosage X	SEX	M	Male	53	Count	n
Table 2	Baseline Demographics and Clinical Characteristics, Safety Population	ADSL	TR01X	Drug Name Dosage X	SEX	M	Male	61.6	Percent	%
Table 2	Baseline Demographics and Clinical Characteristics, Safety Population	ADSL	TR01X	Drug Name Dosage X	SEX	F	Female	33	Count	n
Table 2	Baseline Demographics and Clinical Characteristics, Safety Population	ADSL	TR01X	Drug Name Dosage X	SEX	F	Female	38.4	Percent	%

Analysis Results Dataset Example: Demographics

Identifiers		Analysis Group			Result Variable			Results Statistic		
Name	Title	Dataset	Variable	Value	Variable	Value	Label	Value	Name	Label
Table 2	Baseline Demographics and Clinical Characteristics, Safety Population	ADSL	TR01X	Drug Name Dosage X	SEX	M	Male	53	Count	n
Table 2	Baseline Demographics and Clinical Characteristics, Safety Population	ADSL	TR01X	Drug Name Dosage X	SEX	M	Male	61.6	Percent	%
Table 2	Baseline Demographics and Clinical Characteristics, Safety Population	ADSL	TR01X	Drug Name Dosage X	SEX	F	Female	33	Count	n
Table 2	Baseline Demographics and Clinical Characteristics, Safety Population	ADSL	TR01X	Drug Name Dosage X	SEX	F	Female	38.4	Percent	%

Traceability to the underlying ADaM dataset

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Machine Readable TFL Shells

```
<?xml version="1.0" encoding="UTF-8"?>
<TableShell>
    <ID>TEAE.01</ID>
    <Ordinal>1</Ordinal>
    <Type>Table</Type>
    <Name>TEAE-Overall</Name>
    <Title>Overall Summary of Treatment Emergent Adverse Events</Title>
    <Population>Safety Population</Population>
    <ColDefs>
        <TreatmentVar Name="TRT01" Num="4" StatOID="ST.01"/>
        <ComputeCols>
            <ComputeCol Name="Overall" StatOID="ST.01"/>
        </ComputeCols>
    </ColDefs>
    <ResultGroupDef OID="EAE.01.GRP.01" OrderNumber="1"> [3 lines]
    <ResultGroupDef OID="TEAE.01.GRP.02" OrderNumber="2"> [2 lines]
    <ResultDef OID="TEAE.01.GRP.01.RES.01"> [4 lines]
    <ResultDef OID="TEAE.01.GRP.01.RES.02">
        <Label>Subjects with a related AE</Label>
        <StatRef StatOID="ST.01"/>
        <StatRef StatOID="ST.02"/>
    </ResultDef>
    <ResultDef OID="TEAE.01.GRP.02.RES.01">
        <Label>Number of AEs</Label>
        <StatRef StatOID="ST.01"/>
    </ResultDef>
    <StatDef OID="ST.01" Name="N">
        <Label>Number of Subjects</Label>
        <Format>XX</Format>
    </StatDef>
    <StatDef OID="ST.02" Name="PCT">
        <Label>Percentage of Subjects</Label>
        <Format>(XX.X%)</Format>
    </StatDef>
</TableShell>
```

Adverse Events

Table 35. Patients With Adverse Events[1] by System Organ Class, Safety Population, Pooled Analysis (or Trial X)[2]

System Organ Class	Drug Name Dosage X N = XXX n (%)	Drug Name Dosage Y N = XXX n (%)	Active Control N = XXX n (%)	Placebo N = XXX n (%)	Risk Difference (%) (95% CI)[3,4]
Blood and lymphatic system	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Cardiac disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Ear and labyrinth disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Endocrine disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Eye disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Gastrointestinal disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Hepatobiliary disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Immune system disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Infections and infestations	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Injury, poisoning and procedural complications	n (%)	n (%)	n (%)	n (%)	X (Y, Z)

Source: [include Applicant source, datasets and/or software tools used].
[1] Treatment-emergent adverse event defined as [definition].
[2] Duration = [e.g., X week double-blind treatment period or median and a range indicating pooled trial durations].
[3] Difference is shown between [treatment arms] (e.g., difference is shown between Drug Name dosage X vs. placebo).
[4] Table display is ordered by the risk difference.
Abbreviations: CI, confidence interval; N, number of patients in treatment arm; n, number of patients with at least one event

Develop schema for machine readable TFL shells

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Current Analysis Data Flow

Adverse Events

Table 35. Patients With Adverse Events[1] by System Organ Class, Safety Population, Pooled Analysis (or Trial X)[2]

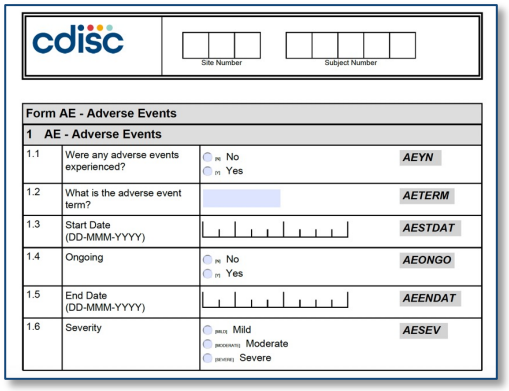
System Organ Class	Drug Name Dosage X N = XXX n (%)	Drug Name Dosage Y N = XXX n (%)	Active Control N = XXX n (%)	Placebo N = XXX n (%)	Risk Difference (%) (95% CI)[3,4]
Blood and lymphatic system	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Cardiac disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Ear and labyrinth disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Endocrine disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Eye disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Gastrointestinal disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Hepatobiliary disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Immune system disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Infections and infestations	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Injury, poisoning and procedural complications	n (%)	n (%)	n (%)	n (%)	X (Y, Z)

Source: [include Applicant source, datasets and/or software tools used].
[1] Treatment-emergent adverse event defined as [definition].
[2] Duration = [e.g., X week double-blind treatment period or median and a range indicating pooled trial durations].
[3] Difference is shown between [treatment arms] (e.g., difference is shown between Drug Name dosage X vs. placebo).
[4] Table display is ordered by the risk difference.
Abbreviations: CI, confidence interval; N, number of patients in treatment arm; n, number of patients with at least one event

End Goals: Streamline Analysis Data Flow and Reducing Unnecessary Variability

Standardized Metadata

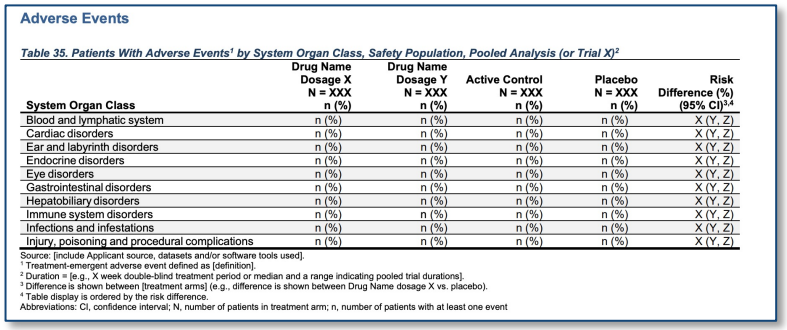
CDASH (Collection) ← SDTM (Tabulation) ← ADaM (Analysis) ← Analysis Results ← TFL



cdisc

Site Number | Subject Number

Form AE - Adverse Events			
1 AE - Adverse Events			
1.1	Were any adverse events experienced?	No / Yes	AEYN
1.2	What is the adverse event term?		AETERM
1.3	Start Date (DD-MMM-YYYY)		AESTDAT
1.4	Ongoing	No / Yes	AEONGO
1.5	End Date (DD-MMM-YYYY)		AEENDAT
1.6	Severity	Mild / Moderate / Severe	AESEV



Adverse Events

Table 35. Patients With Adverse Events[1] by System Organ Class, Safety Population, Pooled Analysis (or Trial X)[2]

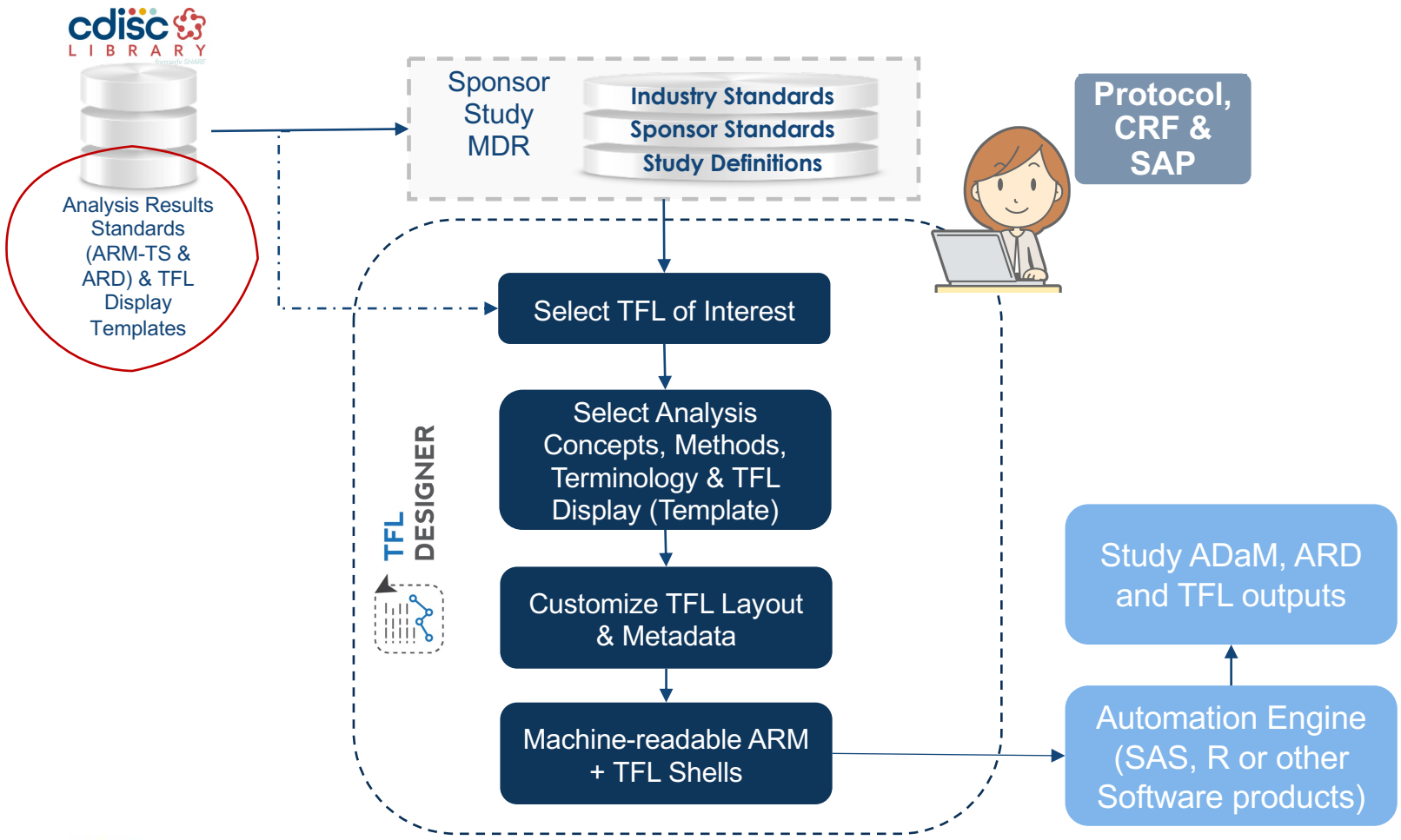
System Organ Class	Drug Name Dosage X N = XXX n (%)	Drug Name Dosage Y N = XXX n (%)	Active Control N = XXX n (%)	Placebo N = XXX n (%)	Risk Difference (%) (95% CI)[3,4]
Blood and lymphatic system	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Cardiac disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Ear and labyrinth disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Endocrine disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Eye disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Gastrointestinal disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Hepatobiliary disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Immune system disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Infections and infestations	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Injury, poisoning and procedural complications	n (%)	n (%)	n (%)	n (%)	X (Y, Z)

Source: [include Applicant source, datasets and/or software tools used].
[1] Treatment-emergent adverse event defined as [definition].
[2] Duration = [e.g., X week double-blind treatment period or median and a range indicating pooled trial durations].
[3] Difference is shown between [treatment arms] (e.g., difference is shown between Drug Name dosage X vs. placebo).
[4] Table display is ordered by the risk difference.
Abbreviations: CI, confidence interval; N, number of patients in treatment arm; n, number of patients with at least one event

ARS will drive automation and open-source tool development

TFL Designer

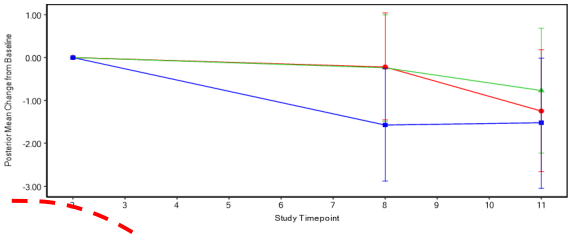
- Open-source tool to design tables, figures, and listings (TFL) and generate associated metadata to support clinical trial data analysis and reporting
- MIT license
- CDISC COSA approved



* Open-Source TFL Designer, Bhavin Busa
Link to GitHub: https://github.com/bhavinbusa/tfldesigner

Sponsor Use Case
Current TFL Process

Treatment	Timepoint	n	Observed Mean(SD)	Posterior Mean(SE*)	Posterior Mean Change(95% CrI)	Treatment Difference (Trt vs PBO) Posterior Mean Change Difference (95% CrI)	P(LY - PBO <0)	Effect Size
Placebo	Week 2	XX	XX.XX(X.XX)	XX.XX(X.XX)				
(N=XX)	Week 8	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)			
	Week 11	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)			
Trt A	Week 2	XX	XX.XX(X.XX)	XX.XX(X.XX)				
(N=XX)	Week 8	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX
	Week 11	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX
Trt B	Week 2	XX	XX.XX(X.XX)	XX.XX(X.XX)				
(N=XX)	Week 8	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX
	Week 11	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX



SDTM

ADAM (ADSL and ADTTE)

Bayesian Table

Bayesian Graph

CSR

In-Text Table

Exploratory Analysis

Journal Publication

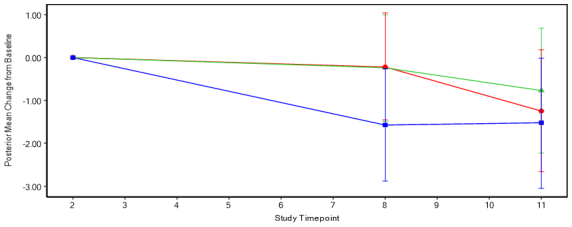
Labeling

Sponsor Use Case
Current Process

- Downstream groups must rely on programming needs to create all outputs
- Must re-create complex analysis each time from ADAM datasets
- Increased chance for error, added time, and bottleneck in programming group

Sponsor Use Case ARD Process

Treatment	Timepoint	n	Observed Mean(SD)	Posterior Mean(SE*)	Posterior Mean Change(95% CrI)	Treatment Difference (Trt vs PBO) Posterior Mean Change Difference (95% CrI)	P(LY - PBO <0)	Effect Size
Placebo	Week 2	XX	XX.XX(X.XX)	XX.XX(X.XX)				
(N=XX)	Week 8	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)			
	Week 11	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)			
Trt A	Week 2	XX	XX.XX(X.XX)	XX.XX(X.XX)				
(N=XX)	Week 8	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX
	Week 11	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX
Trt B	Week 2	XX	XX.XX(X.XX)	XX.XX(X.XX)				
(N=XX)	Week 8	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX
	Week 11	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX



SDTM

ADAM (ADSL and ADTTE)

ARM TS and Analysis Results Dataset

In-Text Table

Bayesian Table

Bayesian Graph

Journal Publication

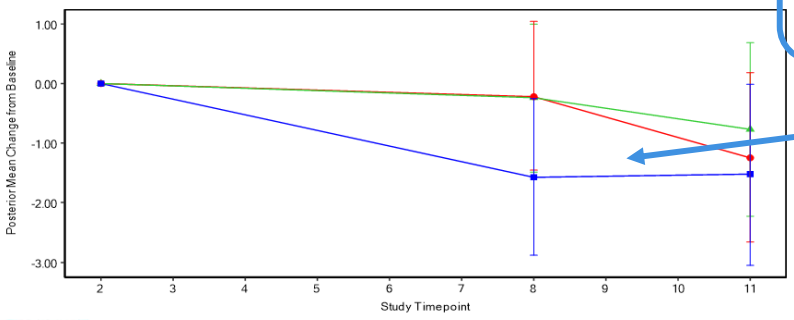
CSR

Exploratory Analysis

Labeling

Sponsor Use Case
ARD Process

Treatment	Timepoint	n	Observed Mean(SD)	Posterior Mean(SE*)	Posterior Mean Change(95% CrI)	Treatment Difference (Trt vs PBO) Posterior Mean Change Difference (95% CrI)	P(LY - PBO <0)	Effect Size
Placebo (N=XX)	Week 2	XX	XX.XX(X.XX)	XX.XX(X.XX)				
	Week 8	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)			
	Week 11	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)			
Trt A (N=XX)	Week 2	XX	XX.XX(X.XX)	XX.XX(X.XX)				
	Week 8	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX
	Week 11	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX
Trt B (N=XX)	Week 2	XX	XX.XX(X.XX)	XX.XX(X.XX)				
	Week 8	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX
	Week 11	XX	XX.XX(X.XX)	XX.XX(X.XX)	XX.XX(XX.XX, X.XX)	(XX.XX, X.XX)	X.XXX	XX.XXX



8	Week 8	1	Trt A		Change from Baseline	95% CI High	Response Rate	Posterior		XXX
8	Week 8	2	Trt B		Change from Baseline	95% CI High	Response Rate	Posterior		XXX
8	Week 8	3	PBO		Change from Baseline	95% CI High	Response Rate	Posterior		XXX
8	Week 8	1	Trt A		Change from Baseline	95% CI Low	Response Rate	Posterior		XXX
8	Week 8	2	Trt B		Change from Baseline	95% CI Low	Response Rate	Posterior		XXX
8	Week 8	3	PBO		Change from Baseline	95% CI Low	Response Rate	Posterior		XXX
8	Week 8	1	Trt A		Change from Baseline	Mean	Response Rate	Posterior		XXX
8	Week 8	2	Trt B		Change from Baseline	Mean	Response Rate	Posterior		XXX
8	Week 8	3	PBO		Change from Baseline	Mean	Response Rate	Posterior		XXX
8	Week 8	1	Trt A	3	PBO	Change from Baseline	95% CI High	Response Rate	Posterior	Difference	XXX
8	Week 8	2	Trt B	3	PBO	Change from Baseline	95% CI High	Response Rate	Posterior	Difference	XXX
8	Week 8	1	Trt A	3	PBO	Change from Baseline	95% CI Low	Response Rate	Posterior	Difference	XXX
8	Week 8	2	Trt B	3	PBO	Change from Baseline	95% CI Low	Response Rate	Posterior	Difference	XXX
8	Week 8	1	Trt A	3	PBO	Change from Baseline	Difference	Response Rate	Posterior	Difference	XXX
8	Week 8	2	Trt B	3	PBO	Change from Baseline	Difference	Response Rate	Posterior	Difference	XXX
8	Week 8	1	Trt A	3	PBO	Change from Baseline	Effect Size	Response Rate	Posterior	Effect Size	XXX
8	Week 8	2	Trt B	3	PBO	Change from Baseline	Effect Size	Response Rate	Posterior	Effect Size	XXX
8	Week 8	1	Trt A	3	PBO	Change from Baseline	EOI < 0	Response Rate	Posterior	Probability	XXX
8	Week 8	2	Trt B	3	PBO	Change from Baseline	EOI < 0	Response Rate	Posterior	Probability	XXX

RESULTTYPE2	RESULTTYPE3	RESULTTYPE4	RESUI
Observed			XXX
Observed			XXX
Observed			XXX
Observed			XXX
Observed			XXX
Observed			XXX
Observed			XXX
Observed			XXX
Observed			XXX
Response Rate	Posterior		XXX
Response Rate	Posterior		XXX
Response Rate	Posterior		XXX
Response Rate	Posterior		XXX
Response Rate	Posterior		XXX
Response Rate	Posterior		XXX

Sponsor Use Case
ARD Process

- Downstream groups can easily consume Analysis Result Dataset directly without relying on programming group
- Complex analyses done once
- Decreased chance for error, more efficient use of time, and less reliance on programming group for downstream activities

In Conclusion

- Industry-wide CDISC model to support analysis results metadata technical specification (ARM-TS) and analysis results data (ARD)
- Streamlined analysis data flow – keeping end in mind (TFL → ADaM → SDTM → CRF)
- Perform each analysis once
- Pro-actively discuss with Regulatory agency if ARD is intended
- Open-source tool development