

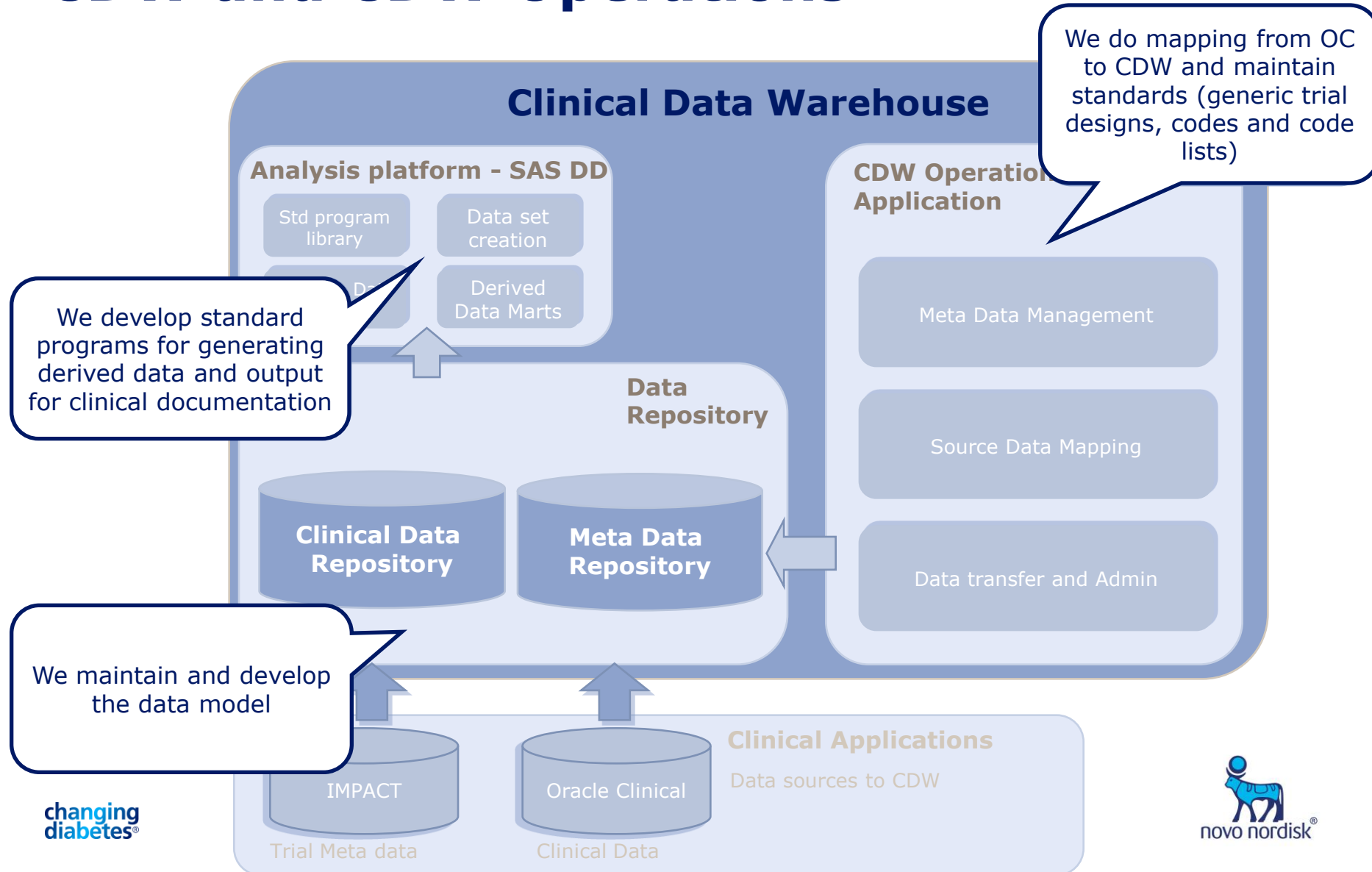
Metadata and Standard Programs

By Martin Lindhard
and Marianne Caramés
CDW Operations and Biostatistics
Novo Nordisk A/S

Novo Nordisk at a glance

- 
- More than 27,000 employees in 81 countries
 - A world leader in diabetes care since 1923
 - Also leading positions in:
 - Haemostasis management
 - Growth hormone therapy
 - Hormone replacement therapy
 - Total net turnover (2008): 8.64 billion USD
 - Committed to financial, environmental and social results

CDW and CDW Operations



Metadata

- What is metadata?
- Metadata is data about data
- Example: For visit we can have:
 - a visit code
 - different labels to use in reports and plots
 - information of planned time
 - information of allowed visit windows
 - and a lot more



Sources for metadata

Internal standards

**Std
CRFs**

**Oracle
Clinical
code lists**

**Mapping
Standards**

**Protocol
Metadata
Template**

**Std
templates
and
reports**

**Business
Rules**

External standards

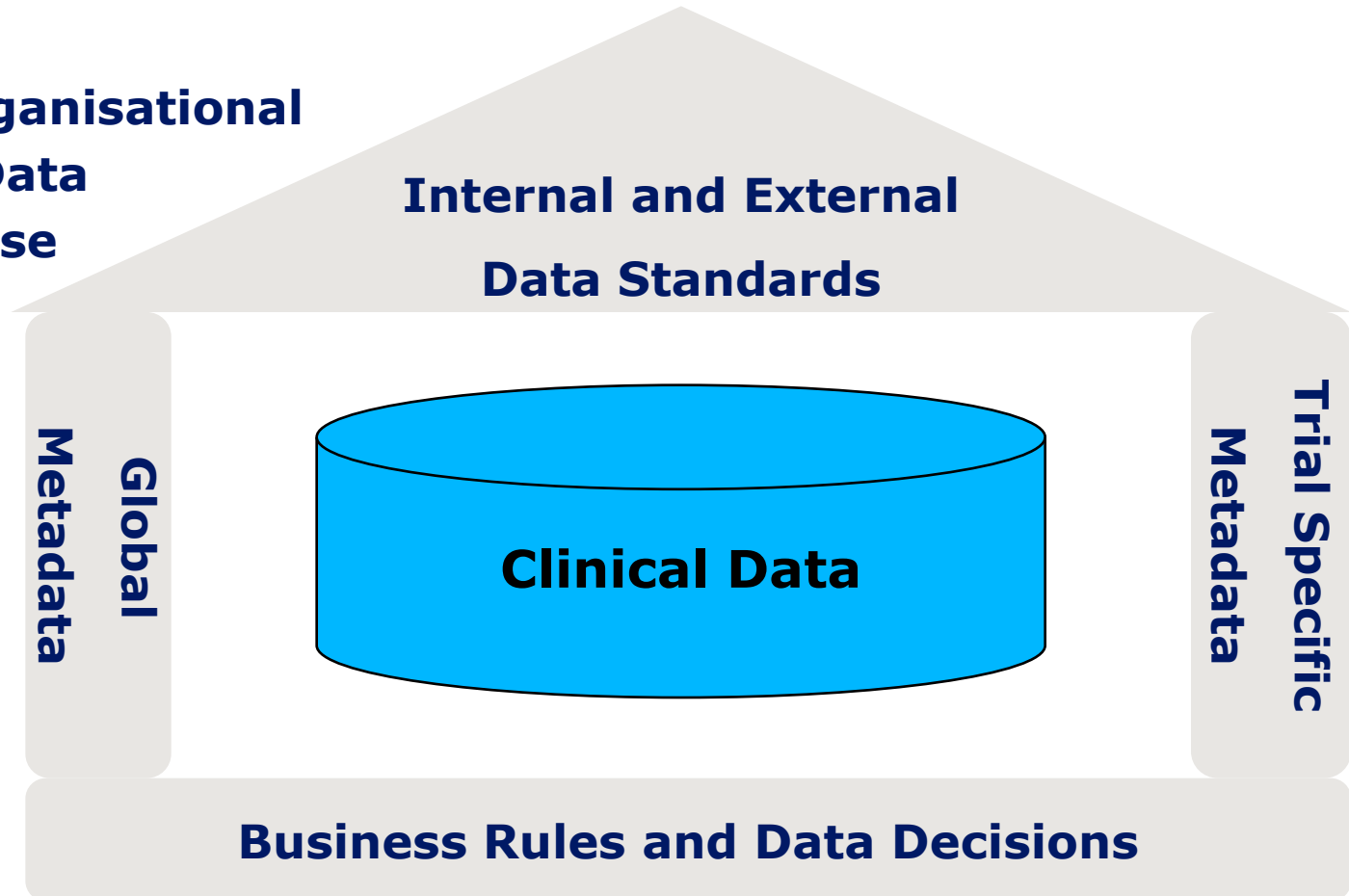
**CDISC
Standards**



Metadata

Data is not limited to Clinical Data

**Cross-organisational
Clinical Data
Warehouse**



Global Metadata

- Defined across all project and trials
- Generic Trial Designs
 - Trial arms
 - Branches
 - Epochs
 - Elements

Global Metadata

Define Generic Trial Design

Add Arms, Epochs, Elements and Branches, and define relations between epochs, arms and elements

No. of All Elements: 5
No. of Treatment Elements: 2
No. of All Epochs: 6
No. of Treatment Epochs: 2
No. of Trial Arms: 2
Status: Active

Arm	Branch	Screening Epoch	Wash-out Epoch 1	Treatment Epoch 1	Wash-out Epoch 2	Treatment Epoch 2
Arm 1	Arm 1	Screening ▼	Wash-out ▼	Treatment A ▼	Wash-out ▼	Treatment B ▼
Arm 2	Arm 2	Screening ▼	Wash-out ▼	Treatment B ▼	Wash-out ▼	Treatment A ▼

< >

Elements Add Epoch Add Arm Branch Edit Delete Return Save Cancel

Global Metadata

- Topic codes
 - Units
 - Display formats
 - Unit conversion metadata
 - Labels
- Site and Investigator metadata
- Code lists

Trial Specific Metadata

- Defined within the trial
- Trial Design
- Visits
 - Association to Oracle Clinical visit
 - Labels
 - Planned time
 - Windows
 - Visit type

Trial Specific Metadata

- Trial Flowchart
 - Shows planned findings
 - Contains connection between topic codes and visits
 - Allocation of Business Rules for each topic code/visit combination

Trial Specific Metadata

Flowchart

Assessment	Visit Short Label	V1	V2	V3	V4	V5
		Screening visit	Baseline/Randomisation visit	Treatment visit	Treatment visit	Treatment visit
EFFICACY						
Insulin						
Basal Insulin						
Bolus Insulin						
Premix insulin						
Glucose metabolism						
Fasting plasma glucose level		X				
Blood HbA1c		X				
Self measured plasma glucose						
Self Measured Plasma Glucose level			X	X	X	X
EXCLUSION CRITERIA						
Exclusion criteria						
Clin Sign Active Diseases		X				
Positive HIV Antibodies		X				
Clin Sign Abnorm LAB Screening Tests		X				
Hepatitis B Antigen or C Antibody "+"		X				
Impaired hepatic ASAT/ALAT > 2.5 normal		X				
Predict change eating, exercise habits		X				
Disease/condi interfering with trial		X				
Mental Incapacity, Unwillingness		X				
Proliferative Retinopathy or Maculopathy		X				
Impaired Renal fun MF		X				
Cardiac problems within 12 months		X				
Cancer (except basal/squamous cell skin)		X				
Severe hypertension		X				
Allergy To Trial Products		X				
Hypoglycaemia Unawareness/Hosp		X				

Trial Specific Metadata

Collection Attributes

Flowchart Group: Glucose metabolism
Assessment: Blood HbA1c
Visit ID: 10
Visit Short Label: V1

Treatment Allocation: ■ 

Assessment Type: 

Mandatory for PP Population: ☐

Qualify for FAS Population: ☐

Pre Visit Date Time Window: Days

Post Visit Date Time Window: Days

Pre First Drug Date Time Window: Days

Post First Drug Date Time Window: Days

Pre Last Drug Date Time Window: Days

Post Last Drug Date Time Window: Days

Retest Rule: 

Missing Finding Value Rule: 

Visit Reallocation Rule: 

Missing Finding Date Rule: 

Missing Finding Time Rule: 

Trial Specific Metadata

Assessment Attributes

Flowchart Group: Efficacy
Assessment: Blood HbA1c
Finding Topic Code: HBA1C_BLOOD

Protocol Attributes

Planned Finding Group:
Planned Finding Sub Group:
Profile Name:

Statistical Attributes

Lower Limit Type:
Lower Limit Value:
Lower Limit Rule:
Lower Limit Value Censored: ☐
Lower Limit Unit:

Data derivations and enrichments

- Performed by the DVE Framework
- Program complex composed of a shell and a lot of building block components
- Purpose:
 - Conversions (date, time, character to numeric)
 - Blinding (subject level, fake randomisation, blinded treatment, specific topic codes)
 - Treatment allocation
 - Populations, flags and derived variables
 - And a lot more ..

Standard Analysis Reporting

- Standard Program Library
 - Macros
 - Tables
 - Figures
 - Listings

Metadata in Standard Analysis Reporting UI's

Parameter Resolution

Report Selections1 | Report Selections2 | Layout Selections | Statistics | EOT Specific | 1

*Instance
/SDD/Test Data/Test0/Current from SDD [Browse...] [Clear]

Trial Population
<no selection> [?]

Trial Sub Group
<no selection> [?]
<no selection> [?]
Sex=M [?]

ui_arm_elem.sas7bdat
• TRL_BRANCH_ARM_SHORT_LB
• TRL_ELEM_SHORT_LB
+ User-generated columns [Clear]

Treatment
available: <no selection>, BIAsp 50, BIAsp 70, Follow-up, Screening
selected: [?]
> < << >> ^ v

[OK] [Cancel] [Apply]

Data Explorer - trl_pop.sas7bdat */SDD/Test Data/Test...

File View Tools Help

#	POP	TRL_...	TRL_ID	POP_VAR...
1	FT	PQ SD...	1526	INTEN_TO...
2	PP	PQ SD...	1526	PER_PRO...

trl_pop.sas7bdat
• CDW_EXEC_NUM
• CLINICAL_STUDY_ID
• CONTR_PARTITION_KEY
• ERROR_MARK
• POP
• TRL_CONTR
• TRL_DEF_ID
• TRL_ID
• TRL_METADATA_VER
• POP_VAR_NM
+ User-generated columns

Add Remove

Rounding: OFF. Total Rows: 2 Filtered Rows: 2 Vari

Data Explorer - plnd_trl_sub_grp.sas7bdat */SDD/Priva...

File View Tools Help

#	TRL_ID	TRL_SUB...	TRL_SUB...
1	BIAsp-1526	Sex=M	Sex = M

plnd_trl_sub_grp.sas7bdat
• TRL_SUB_GRP_ABB
• TRL_ID
• TRL_CONTAINER
• TRL_DEF_ID
• TRL_METADATA_VE
• TRL_SUB_GRP_DOM

Add Remove

Rounding: OFF. Total Rows: 1 Filtered Rows: 1 Vari

Metadata in Standard Analysis Reporting UI's

Parameter Resolution

Report Selections1 Report Selections2 Layout Selections Statistics EOT Specific 1

*Instance
/SDD/Test Data/Test0/Current from SDD Browse... Clear

Trial Population
<no selection>

Trial Sub Group
<no selection>

Treatment Variable
ui_arm_elem.sas7bdat
• TRL_BRANCH_ARM_SHORT_LB
• TRL_ELEM_SHORT_LB
• TRL_ARM_SHORT_LB
User-generated columns
Clear

Treatment
available selected
<no selection>
BlAsp 50
BlAsp 70
Follow-up
Screening
> < << >> ^ v
OK Cancel Apply

- ddm.plnd_trl_arm
ddm.plnd_trl_branch_arm
ddm.plnd_trl_elem

Metadata in Standard Analysis Reporting UI's

Parameter Resolution

Report Selections1 Report Selections2 Layout Selections Statistics EOT Specific 1

*Select change type
Absolute

*Topic Code

ui_topic_cd_to_vis_id_num.sas7bdat

- ALT_SERUM
- AP_SERUM
- BMI
- BMI_DERIVED
- BODY_WEIGHT
- BP_DIASTOLIC
- BP_SYSTOLIC
- CREATININE_SERUM
- C_PEPTIDE_SERUM
- GLUCOSE_PLASMA
- GLUCOSE_SERUM
- HAEMOGLOBIN_BLOOD
- URIC_ACID_BLOOD

Clear

Visit ID

available selected

<no selection>

10
20
60
80
120
140

> < << >>

Change Visit ID

available selected

<no selection>

10
20
60
80
120
140

> < << >>

OK Cancel Apply

- ddm.plnd_trl_arm
ddm.plnd_trl_branch_arm
ddm.plnd_trl_elem
- ddm.plnd_flowch_item_coll
Topic Code
Visit ID

Data Explorer - plnd_flowch_item_coll.sas7bdat

File View Tools Help

plnd_flowch_item_coll.sas7bdat

- TOPIC_CD
- TRL_ID
- TRL_CONTAINER
- TRL_DEF_ID
- TRL_METADATA_VER
- VIS_ID
- FLOWCH_ITEM_TYPE
- STRATA_SPEC
- STRATA_LIST
- SUBJ_GRP_SPEC
- SUBJ_GRP_LIST
- User-generated columns

#	TOPIC_CD	TRL_CON...	VIS_ID
9	BP_DIASTOLIC	BIAsp-1526	120
10	BP_DIASTOLIC	BIAsp-1526	140
11	BP_SYSTOLIC	BIAsp-1526	10
12	BP_SYSTOLIC	BIAsp-1526	20
13	BP_SYSTOLIC	BIAsp-1526	60
14	BP_SYSTOLIC	BIAsp-1526	80
15	BP_SYSTOLIC	BIAsp-1526	120
16	BP_SYSTOLIC	BIAsp-1526	140
17	GLUCOSE_PLASMA	BIAsp-1526	60
18	GLUCOSE_PLASMA	BIAsp-1526	80
19	GLUCOSE_PLASMA	BIAsp-1526	120
20	GLUCOSE_PLASMA	BIAsp-1526	140
21	HEIGHT	BIAsp-1526	10
22	PULSE	BIAsp-1526	10
23	PULSE	BIAsp-1526	20
24	PULSE	BIAsp-1526	60

Rounding: OFF. Total Rows: 58 Filtered Rows: 58 Variables: 3 Excl

Metadata in Standard Analysis Reporting UI's

Parameter Resolution

Report Selections1 Report Selections2 Layout Selections Statistics EOT Specific 1

*Paper Orientation ?

port

User Defined Footnote ?

User Footnote Delimiter ?

~

*Include Reference ranges ?

no

Output Format for Parallel Output ?

<no selection>

*Font Size ?

9

Row Label Width ?

(Integer 18 - 40)

Spacing ?

(Integer 1 - 100)

ID columns ?

1

*Visit ID Presentation ?

Visit Label and Visit Description

Visit Label

Visit Description

Visit Type

Visit Short Label

Visit Label and Visit Description

Visit Label and Visit Type

Planned Trial Duration Time Unit and Planned Trial Duration Time

Planned Trial Duration Time and Planned Trial Duration Time Unit

OK Cancel Apply

as7bdat-*(/SDD/Private Folders/HQ/MRL/DDM) from SAS Drug Development Domain

#	TRL_ID	VIS_ID	VIS_TYPE	VIS_LB	VIS_SHO...	VIS_DESC	PLN...	PLND_TR...
1	BIAsp-1526	10	SCREENIN...	Screening Visit	Screen	Visit Descr	-8	DAYS
2	BIAsp-1526	20	BASELINE/...	Baseline visit	Baseline	Visit Descr	0	DAYS
3	BIAsp-1526	30	TELEPHO...	Visit 3	V3	Visit Descr	2	DAYS
4	BIAsp-1526	40	TELEPHO...	Visit 4	V4	Visit Descr	6	DAYS
5	BIAsp-1526	50	TELEPHO...	Visit 5	V5	Visit Descr	10	DAYS
6	BIAsp-1526	60	TREATEM...	Visit 6	V6	Visit Descr	14	DAYS
7	BIAsp-1526	70	TELEPHO...	Visit 7	V7	Visit Descr	22	DAYS
8	BIAsp-1526	80	TREATEM...	Visit 8	V8	Visit Descr	30	DAYS
9	BIAsp-1526	90	TELEPHO...	Visit 9	V9	Visit Descr	40	DAYS
0	BIAsp-1526	100	TELEPHO...	Visit 10	V10	Visit Descr	52	DAYS
1	BIAsp-1526	110	TELEPHO...	Visit 11	V11	Visit Descr	64	DAYS
2	BIAsp-1526	120	TREATEM...	Visit 12	V12	Visit Descr	78	DAYS
3	BIAsp-1526	130	TELEPHO...	Visit 13	V13	Visit Descr	90	DAYS
4	BIAsp-1526	140	TREATEM...	Visit 14	V14	Visit Descr	100	DAYS
5	BIAsp-1526	150	SCREENIN...	Screening Visit	Screen	Visit Descr	-8	DAYS

How are the metadata displayed

Summary of Blood pressure (Systolic) (mmHg) by Visit and Treatment - All Subjects

	BIAsp 50 /70	BIAsp 70 /50	Total
Number of Subjects	37	37	74
Screen			
Mean (SD)	142 (16)	144 (14)	143 (15)
Median	143	145	145
Min ; Max	115 ; 175	120 ; 171	115 ; 175
Baseline			
N	37	38	75
Mean (SD)	141 (14)	144 (15)	142 (15)
Median	140	143	140
Min ; Max	113 ; 166	116 ; 172	113 ; 172
V6			
N	37	38	75
Mean (SD)	141 (13)	144 (14)	143 (13)
Median	141	146	145
Min ; Max	113 ; 170	109 ; 173	109 ; 173
V8			
N	37	37	74
Mean (SD)	137 (15)	141 (14)	139 (15)
Median	135	140	140
Min ; Max	110 ; 185	110 ; 178	110 ; 185
V12			
N	37	34	71
Mean (SD)	137 (12)	141 (14)	138 (13)
Median	136	140	139
Min ; Max	111 ; 165	108 ; 175	108 ; 175
V14			
N	37	36	73
Mean (SD)	133 (15)	134 (15)	133 (15)
Median	135	134	135
Min ; Max	100 ; 160	100 ; 160	100 ; 160
Change (absolute) from Baseline to V14			
N	37	36	73
Mean (SD)	8 (14)	9 (12)	9 (13)
Median	6	10	9
Min ; Max	-18 ; 45	-10 ; 40	-18 ; 45

Topic codes and units

Population
(and sub-group)

Treatment metadata

Visit metadata

Statistics

Display formats

How much is metadata controlled?

Summary of Blood pressure (Systolic) (mmHg) by Visit and Treatment - All Subjects

	BIAsp 50 /70	BIAsp 70 /50	Total
Number of Subjects	37	37	74
Screen			
N	37	38	75
Mean (SD)	142 (16)	144 (14)	143 (15)
Median	143	145	145
Min ; Max	115 ; 175	120 ; 171	115 ; 175
Baseline			
N	37	38	75
Mean (SD)	141 (14)	144 (15)	142 (15)
Median	140	143	140
Min ; Max	113 ; 166	116 ; 172	113 ; 172
V6			
N	37	38	75
Mean (SD)	141 (13)	144 (14)	143 (13)
Median	141	146	145
Min ; Max	113 ; 170	109 ; 173	109 ; 173
V8			
N	37	37	74
Mean (SD)	137 (15)	141 (14)	139 (15)
Median	135	140	140
Min ; Max	110 ; 185	110 ; 178	110 ; 185
V12			
N	37	34	71
Mean (SD)	137 (12)	141 (14)	138 (13)
Median	136	140	139
Min ; Max	111 ; 165	108 ; 175	108 ; 175
V14			
N	37	36	73
Mean (SD)	133 (15)	134 (15)	133 (15)
Median	135	134	135
Min ; Max	100 ; 160	100 ; 160	100 ; 160
Change (absolute) from Baseline to V14			
N	37	36	73
Mean (SD)	8 (14)	9 (12)	9 (13)
Median	6	10	9
Min ; Max	-18 ; 45	-10 ; 40	-18 ; 45

Conclusion

The use of metadata and standard programs have given us a lot of benefits:

- Business Rules and Data Decisions are defined in a standardised way
- Business Rules and Data Decisions no longer embedded in SAS program code
- By separating the definition and the implementation/use of the business rules it is possible to make enrichment and derivations data driven
- Data driven data checking
- Data driven use of business rules and application of data decisions
- Transparency and easy documentation
- Consistent presentation of data

