



Easing Your Pain with Biomedical Concepts

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Previously Presented

PhUSE EU Connect 2018



- The talk was originally presented as “Presentation SI13” at the PhUSE EU Connect in Frankfurt, 4th-7th November 2018.
- **Kirsten Langendorf** presented the work and wrote the associated paper.
- Paper is available <https://www.lexjansen.com/phuse/2018/si/SI13.pdf>
- It was a 20 minute talk, 5 minute Q&A.
- This version is the 45 minute directors cut! 😊

Outline

- Challenges in study setup
- Biomedical Concepts: What are they?
- Why bother?
- How can it help?
- Questions



Study Setup

Translating study specifications to reality

Which units to use – do we allow for multiple units or just one? Which ones are applicable for the test?

Which SDTM domains are needed for this study – do we need a new or where does this information belong in SDTM domains? Do we need a new annotation?

Is the blood pressure to be measured STANDING, SITTING or SUPINE – what should be on the CRF? Do we need a new CRF?

Which tests are being measured in BLOOD, SERUM, or PLASMA

Protocol

Measurements	V1	V2	V3	V4
Demographics	x			
Vital signs	x			x
CT Scan		x		
Dosing		x	x	x
EQ-5D	x			x
Lipids	x			x
Haemoglobin	x			x
Adverse Events	x	x	x	x

VS=Vital Signs

CDISC Study: CDISC01 Assessment Date: [DATE]

VITAL SIGNS

HEIGHT cm in
(CDISCRES / VSORRESU when VSTESTCD = HEIGHT)

Weight kg lbs
(CDISCRES / VSORRESU when VSTESTCD = WEIGHT)

Body Frame Size Small Medium Large

Sitting Blood Pressure (CDISCRES / VSORRESU when VSTESTCD = SYSBP, DIABP)
 Systolic / Diastolic mmHg

Radial Pulse Rate (CDISCRES / VSORRESU when VSTESTCD = PULSE)
 bpm

(CDISCRES when VSTESTCD = FRMSIZE)

EDC, Labs etc.

Datasets for Study CDISC01

Dataset	Description	Class	Structure	Purpose	Keys	Location
TA	Final Arms	Trial Design	One record per planned Element per Arm	Tabulation	STUDYID, ARMCID, TACTORD	ts.xml
TE	Final Elements	Trial Design	One record per planned Element	Tabulation	STUDYID, ETCD	te.xml
TI	Final Techniques/Technique Criteria	Trial Design	One record per TE criterion	Tabulation	STUDYID, BETESTCD	ti.xml
TS	Final Summaries	Trial Design	One record per trial summary parameter value	Tabulation	STUDYID, TSPARMCD, TSSEQ	ts.xml
TV	Final Visits	Trial Design	One record per planned Visit per Arm	Tabulation	STUDYID, VISITNUM, ARMCD	tv.xml
DM	Demographics	Special Purpose	One record per subject	Tabulation	STUDYID, USUBID	dm.xml
SE	Subject Elements	Special Purpose	One record per actual Element per subject	Tabulation	STUDYID, USUBID, SESTDTC, SEENDTC, TACTORD, ETCD	se.xml
SV	Subject Visits	Special Purpose	One record per actual visit per subject	Tabulation	STUDYID, USUBID, SVSTDTC, VENTNUM	sv.xml

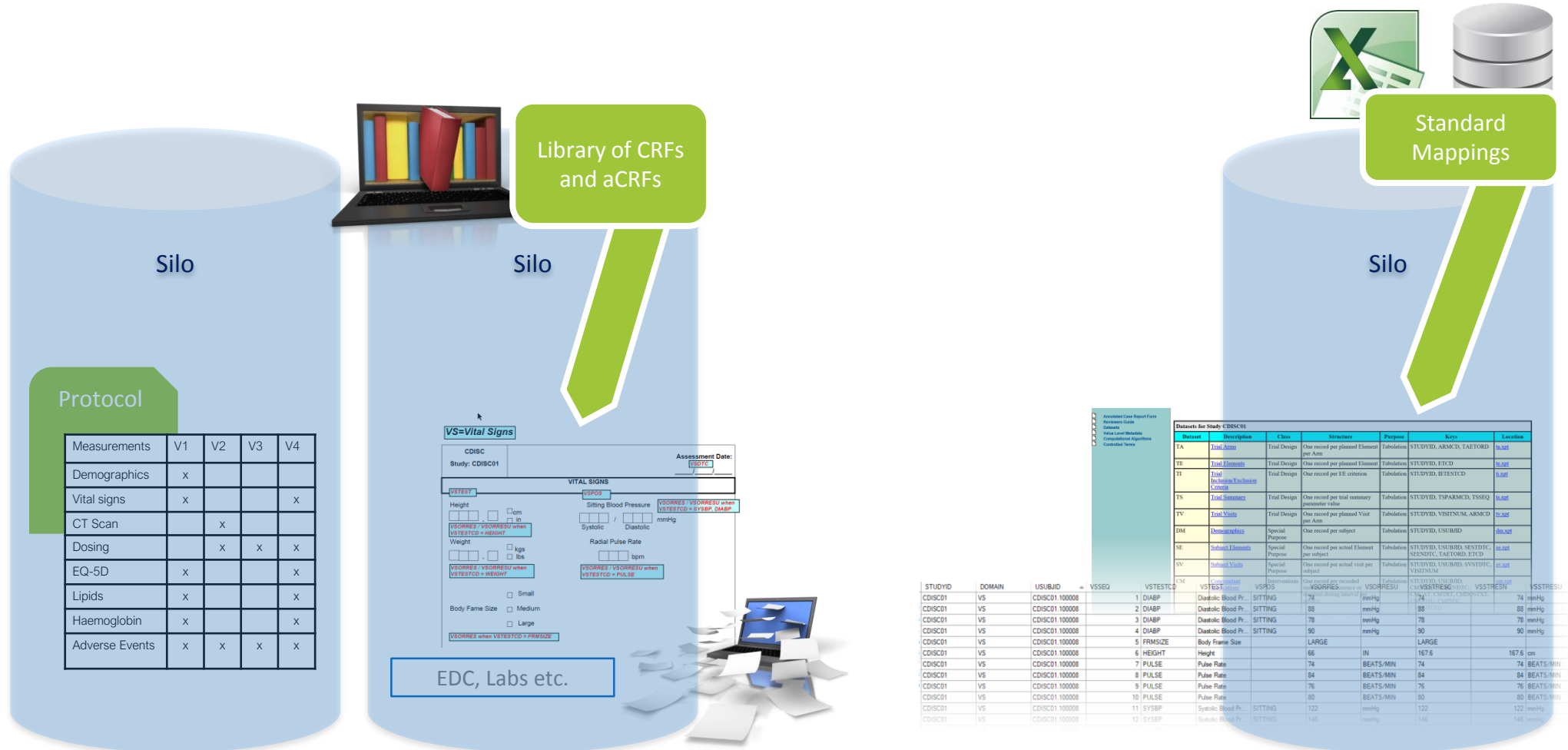
STUDYID	DOMAIN	USUBID	VSSEQ	VSTESTCD	CM	VSPOS	VSORRESU	VSORRESU	VSORRESU	VSORRESU	VSORRESU	VSORRESU
CDISC01	VS	CDISC01.100008	1	DIABP	CM	SITTING	mmHg	74	74	74	74	74 mmHg
CDISC01	VS	CDISC01.100008	2	DIABP	CM	SITTING	mmHg	88	88	88	88	88 mmHg
CDISC01	VS	CDISC01.100008	3	DIABP	CM	SITTING	mmHg	78	78	78	78	78 mmHg
CDISC01	VS	CDISC01.100008	4	DIABP	CM	SITTING	mmHg	90	90	90	90	90 mmHg
CDISC01	VS	CDISC01.100008	5	FRMSIZE	CM		LARGE	LARGE	LARGE	LARGE	LARGE	LARGE
CDISC01	VS	CDISC01.100008	6	HEIGHT	CM		IN	167.6	167.6	167.6	167.6	167.6 cm
CDISC01	VS	CDISC01.100008	7	PULSE	CM		BEATS/MIN	74	74	74	74	74 BEATS/MIN
CDISC01	VS	CDISC01.100008	8	PULSE	CM		BEATS/MIN	84	84	84	84	84 BEATS/MIN
CDISC01	VS	CDISC01.100008	9	PULSE	CM		BEATS/MIN	76	76	76	76	76 BEATS/MIN
CDISC01	VS	CDISC01.100008	10	PULSE	CM		BEATS/MIN	80	80	80	80	80 BEATS/MIN
CDISC01	VS	CDISC01.100008	11	SYSBP	CM	SITTING	mmHg	122	122	122	122	122 mmHg
CDISC01	VS	CDISC01.100008	12	SYSBP	CM	SITTING	mmHg	148	148	148	148	148 mmHg

protocol -> data collection -> reporting



Study Setup

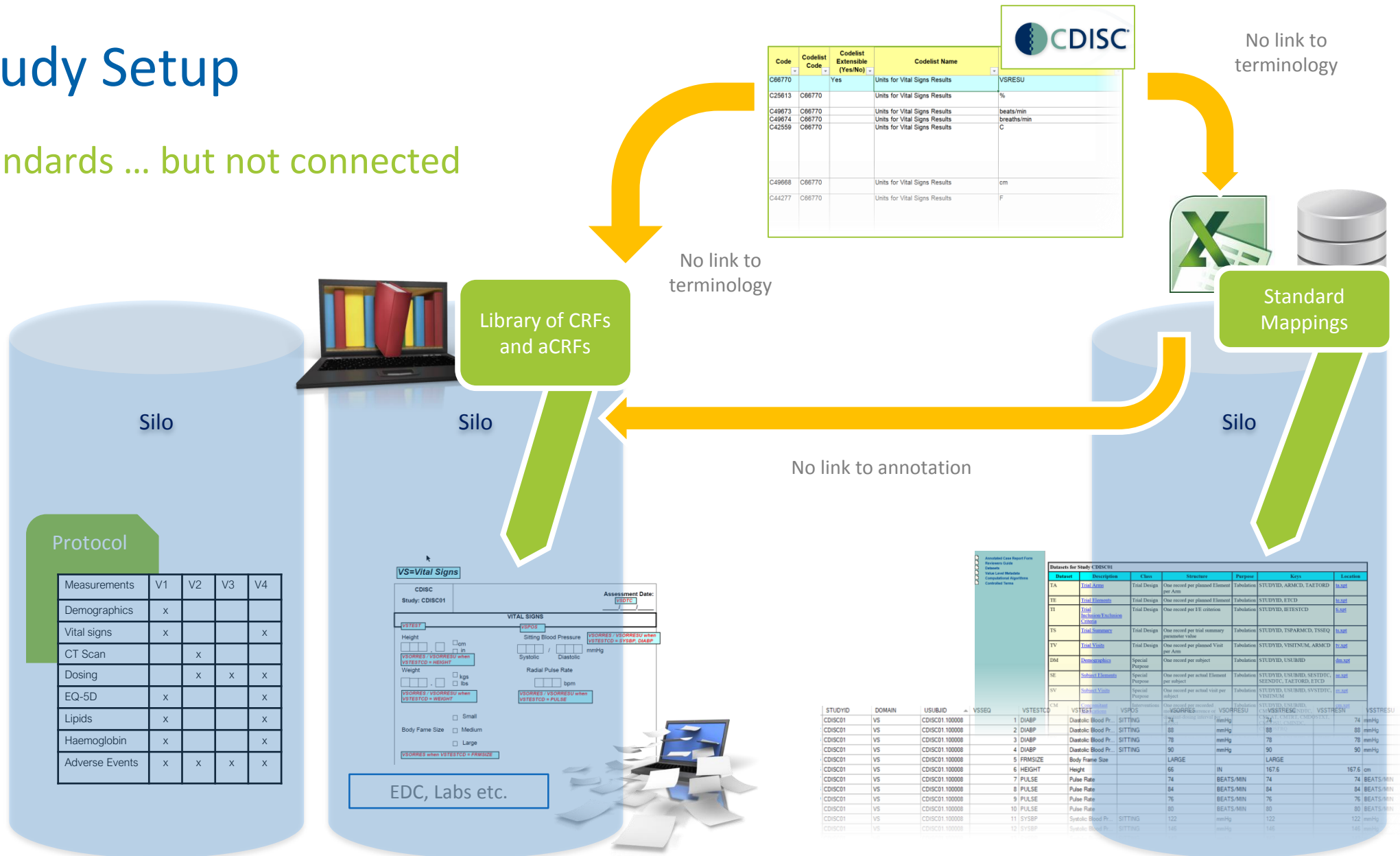
Standards ... but not connected



protocol -> data collection -> reporting

Study Setup

Standards ... but not connected

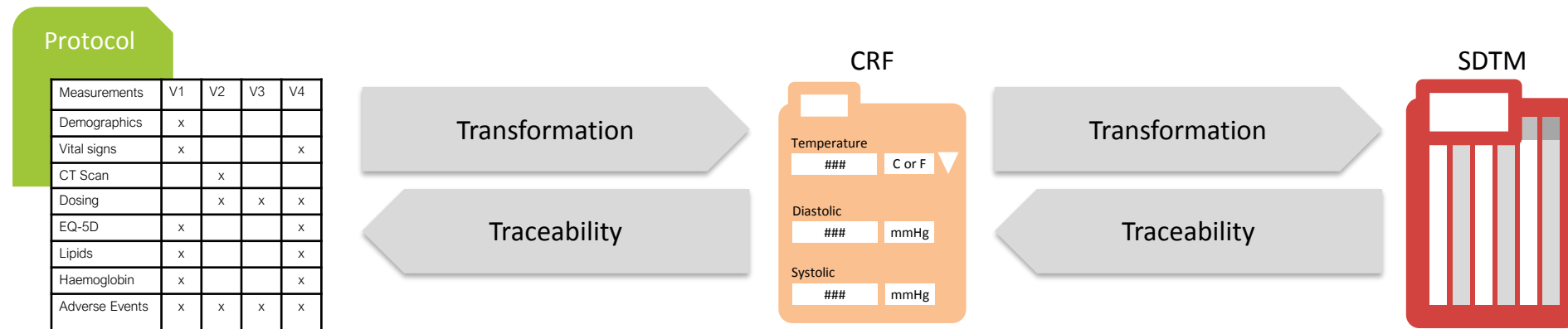


protocol -> data collection -> reporting



Study Setup

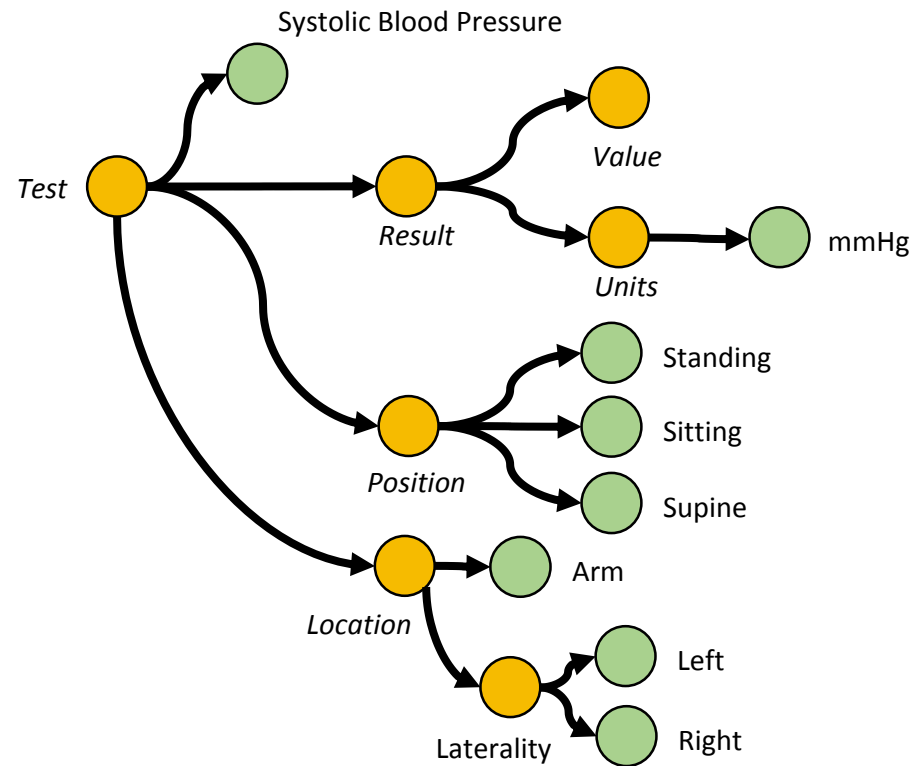
Challenge – maintaining transformations and traceability effectively



Biomedical Concepts (BCs) break down the “silos” and facilitate a consistent way of collecting the data across studies

What is a Biomedical Concept?

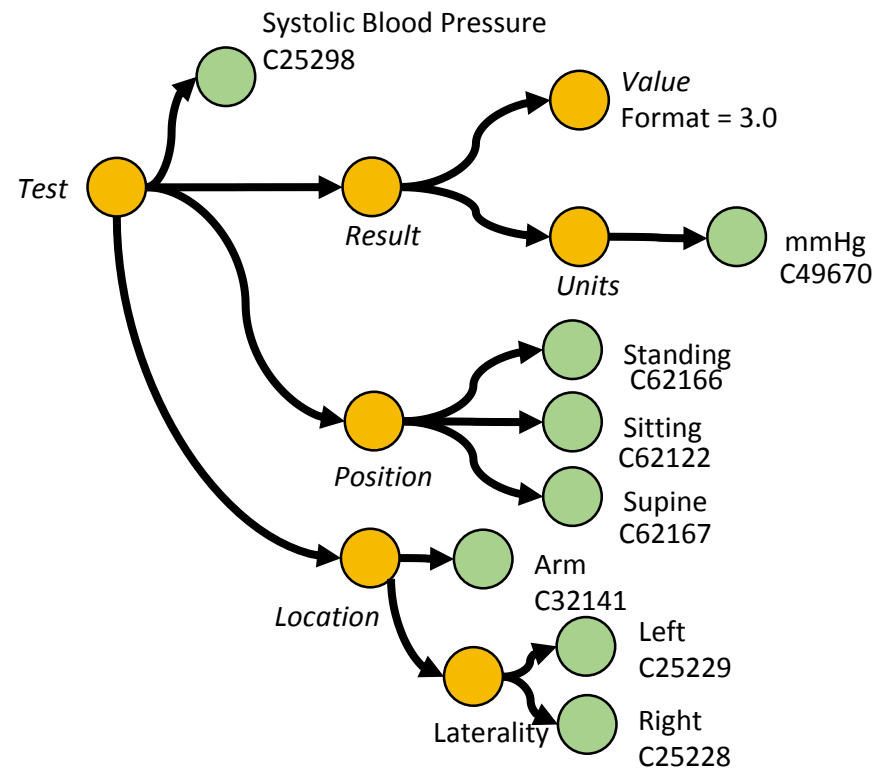
Clinical view



- A collection of variables
- A real-world entity
- Something a physician would recognize

What is a Biomedical Concept?

Data Manager / Programmer view



- Some more detail
- Linked to the CDISC terminology
- Consistent information with views tailored to user
- Present in a way that is meaningful to the consumer

Biomedical Concepts

Implementation

Show: Systolic Blood Pressure (BC C25298) BC C25298 (V3.1.0, 4, Incomplete)

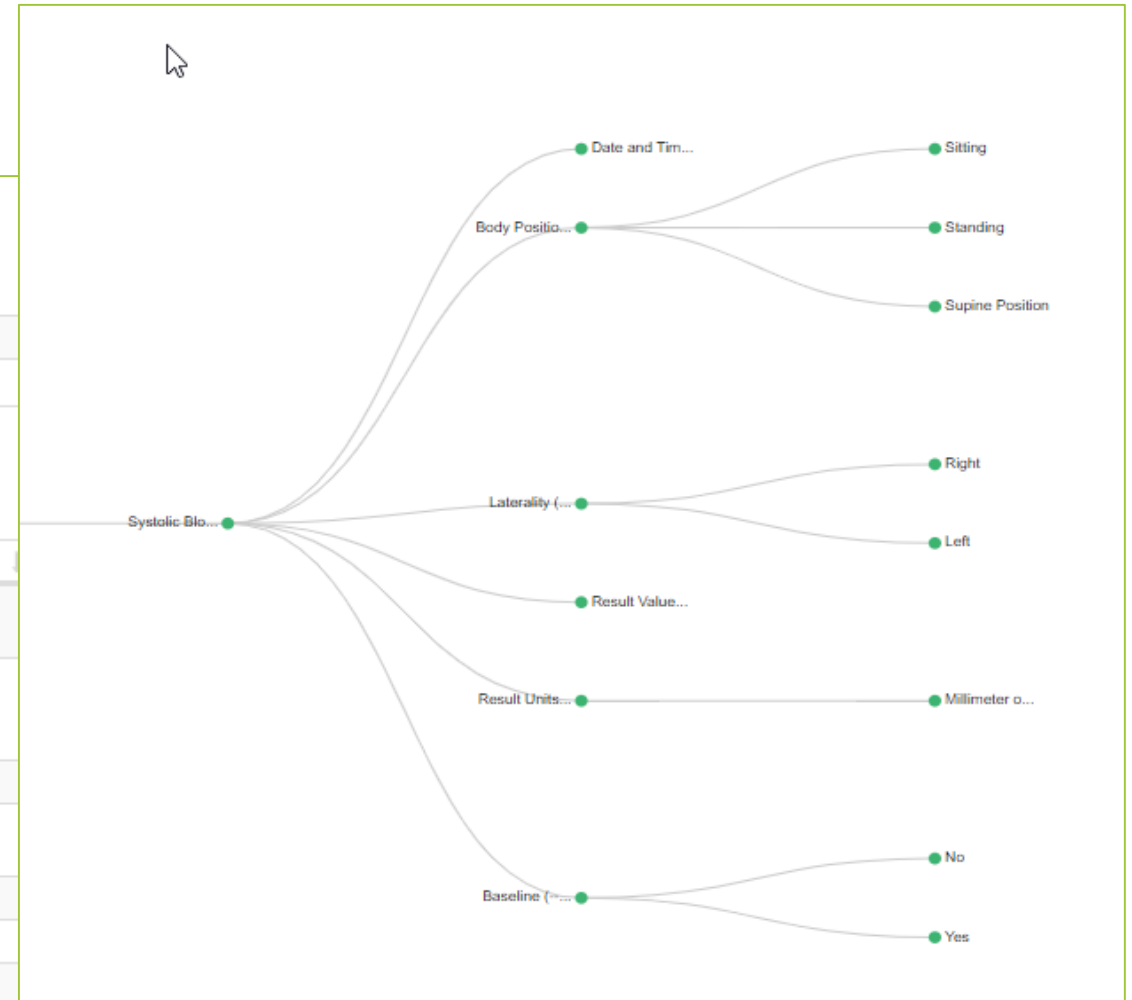
Details

Identifier	Label	Owner
BC C25298	Systolic Blood Pressure (BC C25298)	ACME

Items

Show entries

Alias	Question Text	Prompt Text
Baseline (--BLFL)	Is this a baseline value?	Baseline
Body Position (--POS)	In what position was the subject during the measurement?	Position
Date and Time (--DTC)	On what date were the measurement performed?	Date
Laterality (--LAT)	Which arm?	Arm
Location (--LOC)	The location of the measurement	Location
Method Code (--METHOD)		
Result Units (--ORRESU)	The unit of the measurement	Units
Result Value (--ORRES)	What was the result of the measurement?	Result
Test Code (--TESTCD)		
Test Name (--TEST)		



	✓	✓	float	3	
	✓	✗	string		SYSBP (C25298)
	✓	✗	string		Systolic Blood Pressure (C25298)

Refer domains to Biomedical Concepts

Where does the collected information belong?

- Multiple domains can refer to the same BC.
- The context of the study will then determine which domain is used
- **IMPORTANT:** The domain refers to the BC. They BC DOES NOT refer to the domain. Can be used with any appropriate SDTM domain of the correct class

Show: Vital Signs VS Domain (V1.0.0, 2, Standard)

Details

Identifier	Label	Owner	Internal Version	Version
VS Domain	Vital Signs	ACME	1.0.0	

Notes

Used Variables

Show 10 entries Search:

Ordinal	Name	Label	Datatype	CT	Format	Role	Sub Role	IG Notes	Notes	Core
1	STUDYID	Study Identifier	Char			Identifier		Unique identifier for a study.		Required
2	DOMAIN	Domain Abbreviation	Char	DOMAIN		Identifier		Two-character abbreviation for the domain.		Required
3	USUBJID	Unique Subject Identifier	Char			Identifier		Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.		Required
4	VSSEQ	Sequence Number	Num			Identifier		Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.		Required
5	VSGRPID	Group ID	Char			Identifier		Used to tie together a block of related records in a single domain for a subject.		Permissible
6	VSSPID	Sponsor-Defined Identifier	Char			Identifier		Sponsor-defined reference number. Perhaps pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database.		Permissible
7	VSTESTCD	Vital Signs Test Short Name	Char	VSTESTCD		Topic		Short name of the measurement, test, or examination described in VSTEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in VSTESTCD cannot be longer than 8 characters, nor can it start with a number (e.g. "1TEST"). VSTESTCD cannot contain characters other than letters, numbers, or underscores. Examples: SYSBP, DIABP, BMI.		Required
8	VSTEST	Vital Signs Test Name	Char	VSTEST		Qualifier	Synonym Qualifier	Verbatim name of the test or examination used to obtain the measurement or finding. The value in VSTEST cannot be longer than 40 characters. Examples: Systolic Blood Pressure, Diastolic Blood Pressure, Body Mass Index.		Required
9	VSCAT	Category for Vital Signs	Char			Qualifier	Grouping Qualifier	Used to define a category of related records.		Permissible
10	VSSCAT	Subcategory for Vital Signs	Char			Qualifier	Grouping Qualifier	A further categorization of a measurement or examination.		Permissible

Showing 1 to 10 of 32 entries Previous 1 2 3 4 Next

Unused Variables

Show 10 entries Search:

Ordinal	Name	Label	Datatype	CT	Format	Role	Sub Role	IG Notes	Notes	Core
No data available in table										

Showing 0 to 0 of 0 entries Previous Next

Biomedical Concepts

Show 10 entries Search: pressure

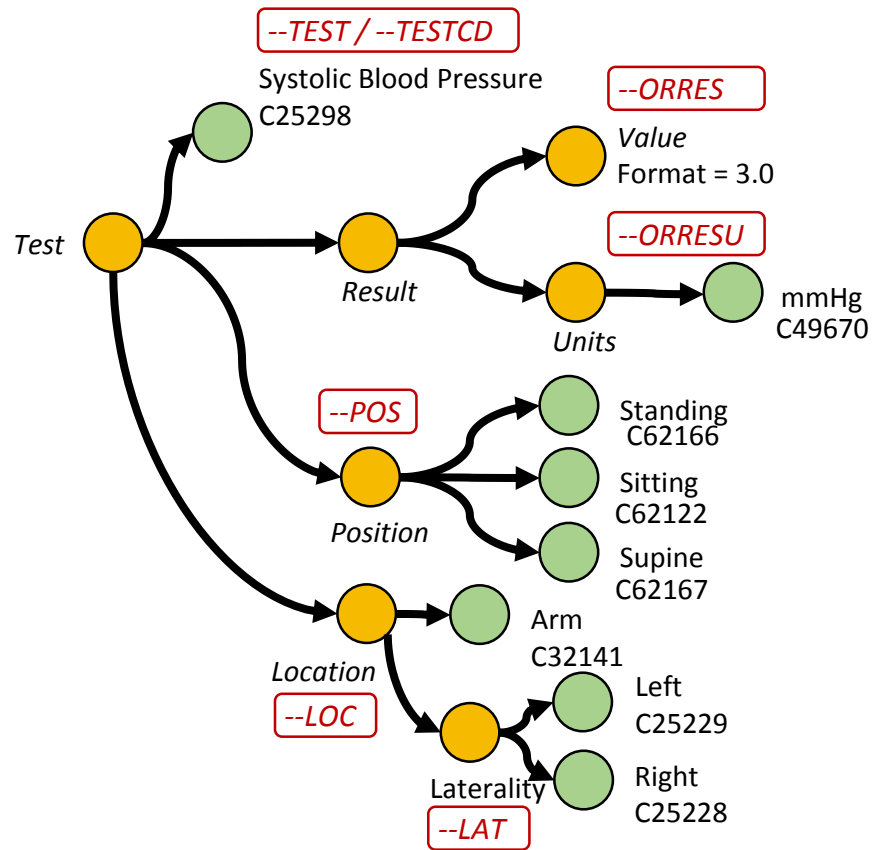
Identifier	Label	Owner	Version	Version Label
BC C25298	Systolic Blood Pressure (BC C25298)	ACME	2.0.0	0.2
BC C25298	Systolic Blood Pressure (BC C25298)	ACME	3.0.0	0.3
BC C25299	Diastolic Blood Pressure (BC C25299)	ACME	2.0.0	0.2

BCs added to the VS domain

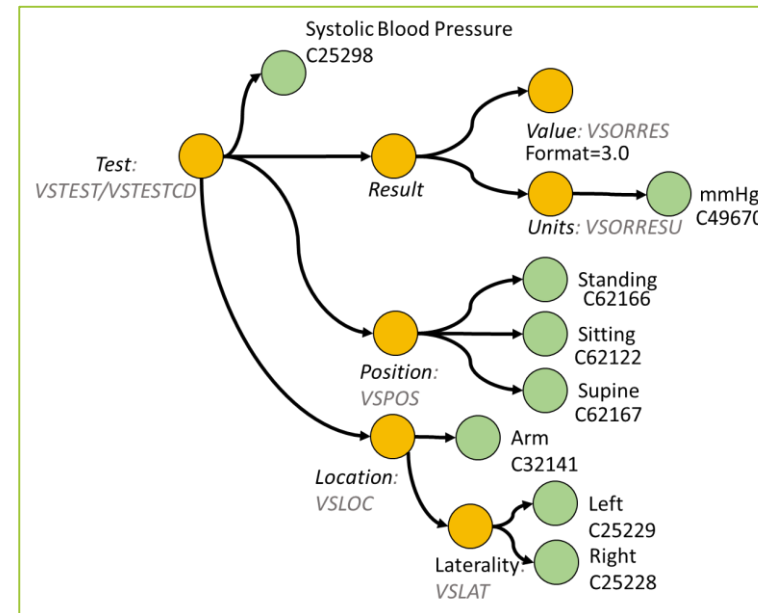


Biomedical Concepts

Domain relationship

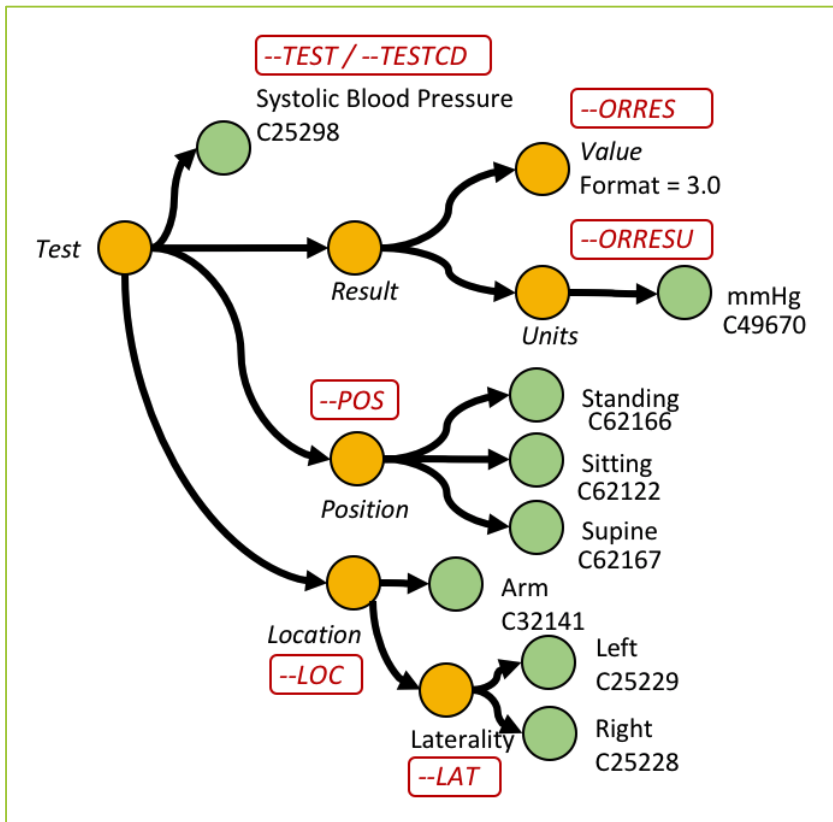


- We can automatically add these “mappings” because the BC is linked to a domain
- In reality linked to a class hence the “--” rather than “VS”

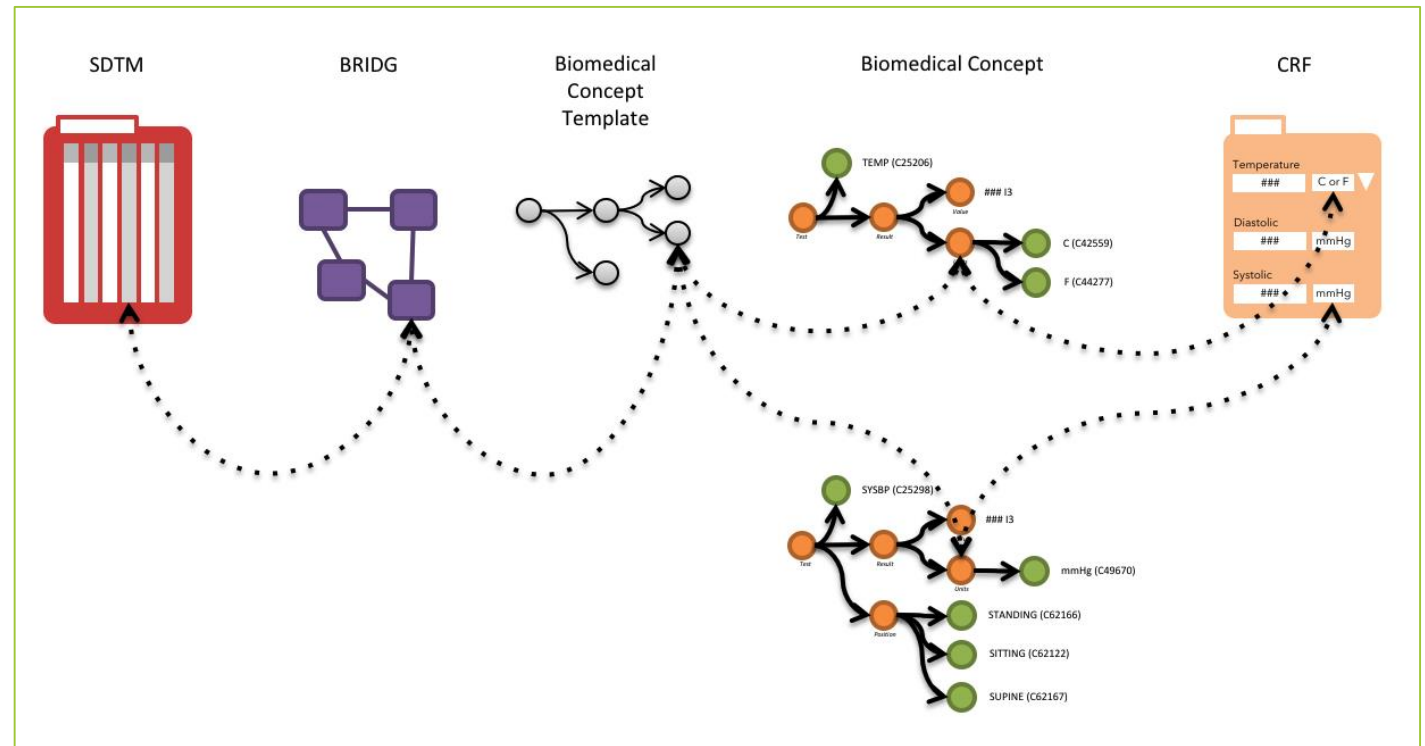


Biomedical Concepts

Domain relationship

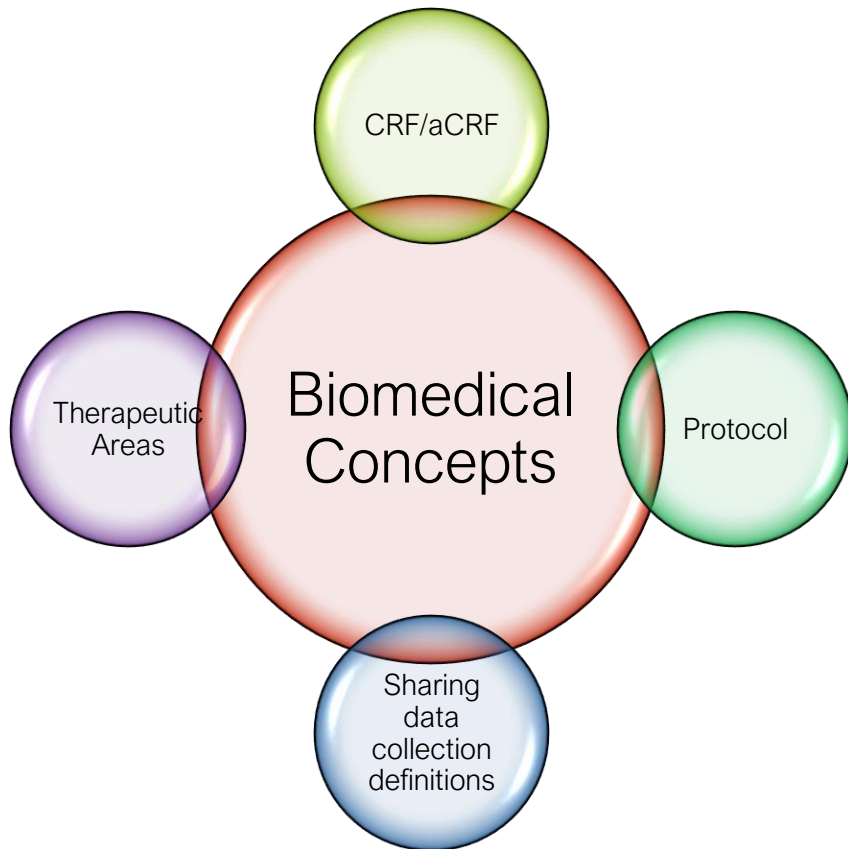


- We use a framework (BRIDG) and templates to ensure consistency of approach

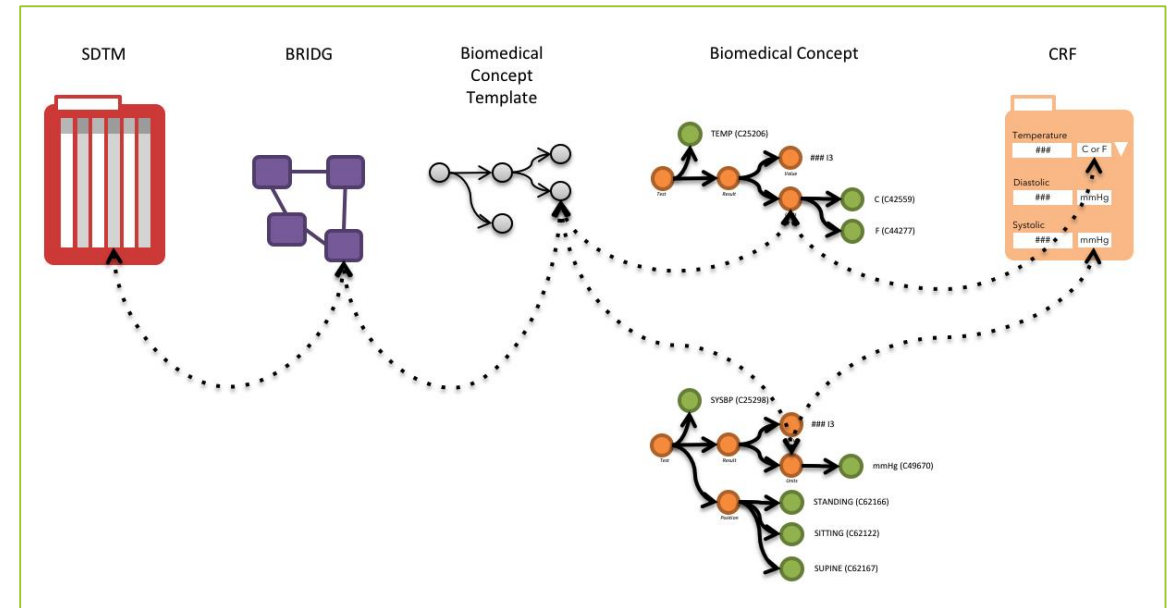


Why bother?

Consistency across the life-cycle



- BC is a standardised definition that can be used for various purpose and facilitates faster and more flexible study setup



Standardisation - From Forms to BCs

Flexible form creation

- Ensures we have compliance with the CDISC standards

Annotated CRF: Vital Signs VS BC 1 (V0.1.0, 1, Incomplete)

Vital Signs		VS=Vital Signs
Vital Signs		
On what date were the measurement performed?	VSDTC where VSTESTCD=DIABP VSDTC where VSTESTCD=SYSBP	<input type="text"/>
In what position was the subject during the measurement?	VSPOS where VSTESTCD=DIABP VSPOS where VSTESTCD=SYSBP	<input type="radio"/> Sitting <input type="radio"/> Standing <input type="radio"/> Supine Position
Which arm?	VSLAT where VSTESTCD=DIABP VSLAT where VSTESTCD=SYSBP	<input type="radio"/> Right <input type="radio"/> Left
Is this a baseline value?		<input type="radio"/> No <input type="radio"/> Yes
Systolic Blood Pressure (BC C25298)		
What was the result of the measurement?	VSORRES where VSTESTCD=SYSBP	<input type="text"/>
The unit of the measurement	VSORRESU where VSTESTCD=SYSBP	<input type="radio"/> Millimeter of Mercury
Diastolic Blood Pressure (BC C25299)		
Result of the measurement	VSORRES where VSTESTCD=DIABP	<input type="text"/>
Result units	VSORRESU where VSTESTCD=DIABP	<input type="radio"/> Millimeter of Mercury

BC for systolic blood pressure

- Date and Time...
- Body Positio...
- Laterality (...)
- Baseline (-...)
- Sitting
- Standing
- Supine Position
- Right
- Left
- Result Value...
- Result Units...
- Millimeter o...
- No
- Yes

BC for diastolic blood pressure

- Date and Time...
- Body Positio...
- Laterality (...)
- Baseline (-...)
- Sitting
- Standing
- Supine Position
- Right
- Left
- Result Value...
- Result Units...
- Millimeter o...
- No
- Yes

- Forms
- Dashboard
- Namespaces
- Registration Authorities
- Managed Items
- Edit Locks
- Audit Trail
- Upload
- Import
- Export
- Background Jobs
- Ad Hoc Reports
- Tags
- Markdown
- Terminology
 - CDISC Terminology
 - Biomedical Concept Templates
 - Biomedical Concepts
- Forms
 - CDISC SDTM Model
 - CDISC SDTM IGs

Index: Forms

Show 15 entries

Search:

Owner	Identifier	Label	
ACME	ADVERSE EVENTS	Adverse Events	History
ACME	VENTOUX	Ventoux Test Form	History
ACME	AE	Adverse Events	History
ACME	ANNO	Annotations One	History
ACME	ANNO 2	Annotations Two	History
ACME	ANNO 3	Annotation Three	History
ACME	ANNO 4	Annotation Four	History
ACME	ANNO 5	Annotation Five	History
ACME	API	API test	History
ACME	BC LINK	BC Link Demonstration	History
ACME	CMED	Concomitant Treatment	History
ACME	DEMO QUESTION	Demo Form Question	History
ACME	DM	Demographics	History
ACME	DM ALL	Demographics Library	History
ACME	DM DEMO	Demographic Simple Demonstration	History

Showing 1 to 15 of 38 entries

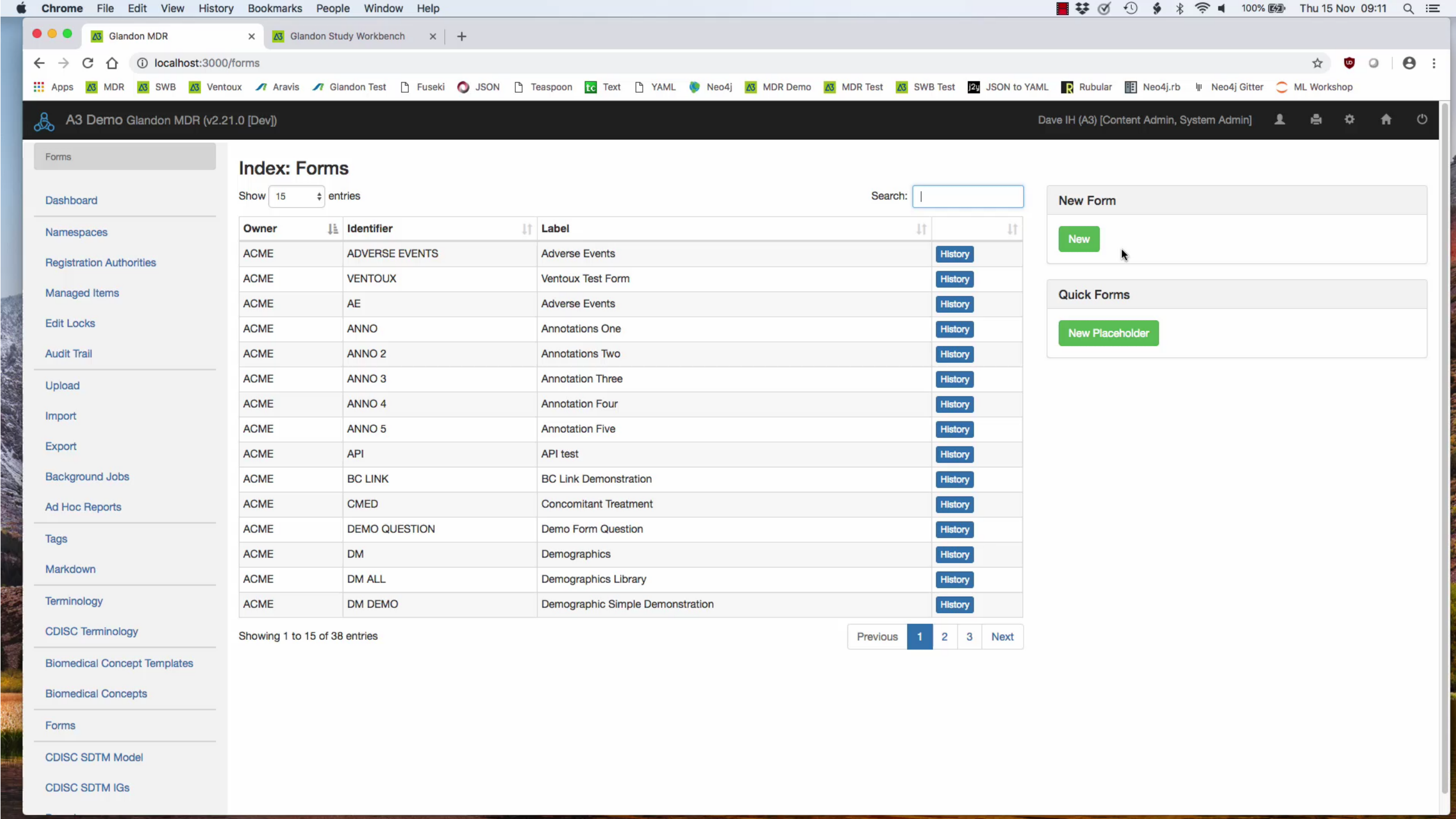
Previous **1** 2 3 Next

New Form

[New](#)

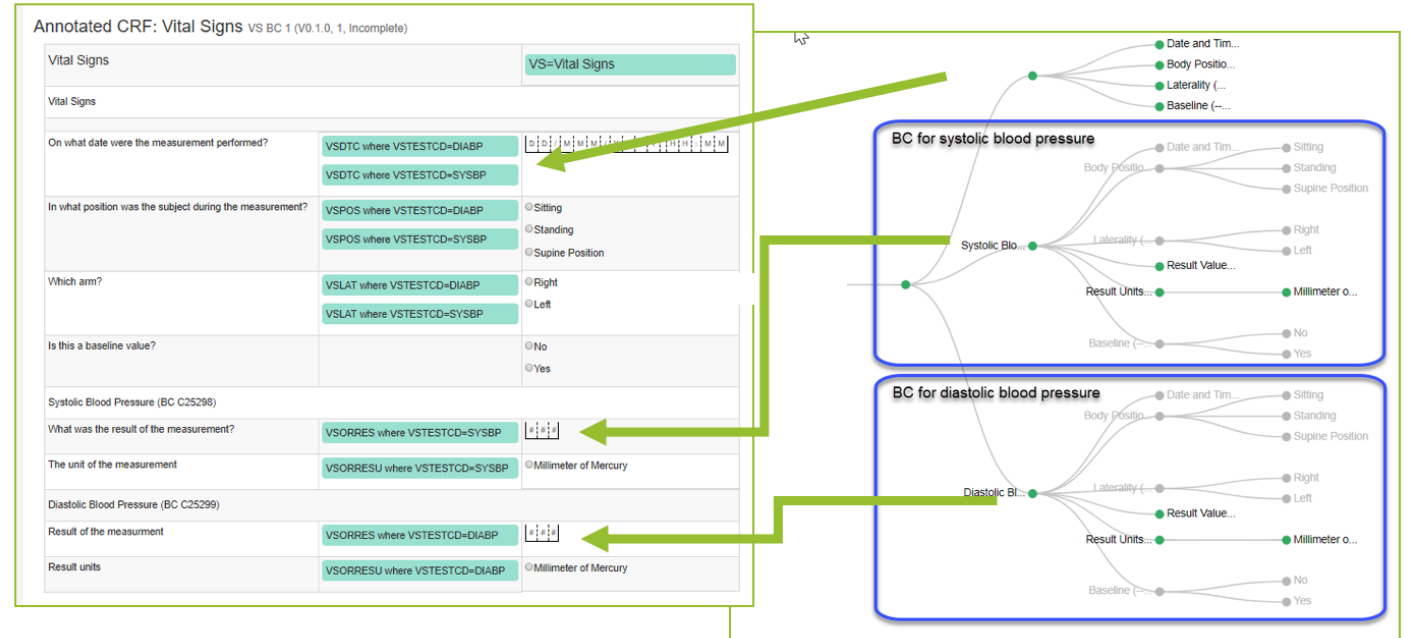
Quick Forms

[New Placeholder](#)



Standardisation - From Forms to BCs

Flexible form creation



The flexibility is achieved on 3 levels:

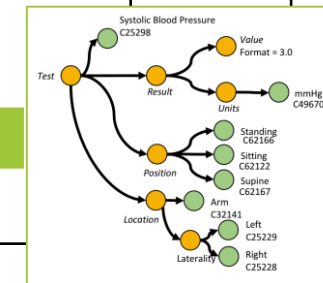
1. The user can decide which BCs to add to a Vital Signs form, i.e. which questions are included in the vital sign page
2. The user can enable/disable data elements in a BC, e.g. decide not to use the baseline flag question if not relevant, i.e. what the level of response is needed for the question
3. The user can decide if questions and/or responses are optional/mandatory

Upstream Standardisation

BCs in Protocols

Assessments	Screening	Baseline	Treatment	EndOfTrial
Demographics	x			
Vital signs	x			
CT Scan		x		
Dosing		x	x	x
EQ-5D	x			x
Lipids	x			x
Haemoglobin	x			x
Adverse Events	x	x	x	x

Assessments	BC	Screening	Baseline	Treatment	EndOfTrial
Demographics	Age Race Date of Birth Sex	x			
Vital signs	Height Weight Heart Rate Temperature Systolic Blood Pressure Diastolic Blood Pressure	x			x
CT Scan	CT scan timing				
Dosing	Number of dosing units		x	x	x
EQ-5D	Mobility	x			x
Lipids	LDL HDL Total Cholesterol	x			x
Haemoglobin	Haemoglobin	x			x
Adverse Events	Adverse Events	x	x	x	x



Upstream Standardisation

BCs in Protocols

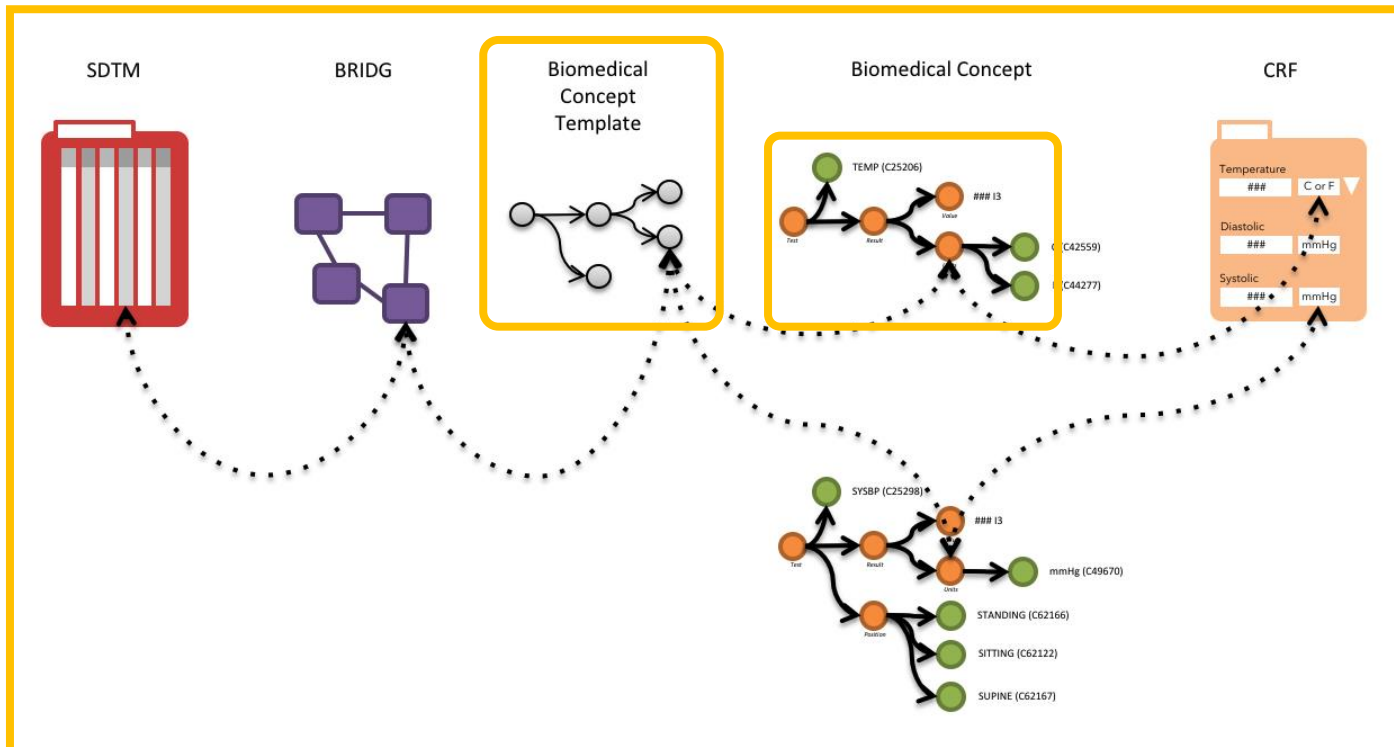
- Forms containing these BCs will then be listed and the CRF designer would then pick the appropriate CRF.
- CRF reviewed early by the study group allowing for adjustments to the protocol if needed.

Assessments	BC	Screening	Baseline	Treatment	EndOfTrial
Demographics	Age Race Date of Birth Sex	X			
Vital signs	Height Weight Heart Rate Temperature Systolic Blood Pressure Diastolic Blood Pressure	X			X
CT Scan	CT scan timing		X		
Dosing	Number of dosing units		X	X	X
EQ-5D	Mobility	X			X
Lipids	LDL HDL Total Cholesterol	X			X
Haemoglobin	Haemoglobin	X			X
Adverse Events	Adverse Events	X	X	X	X

Sharing BCs

Common definitions based on templates

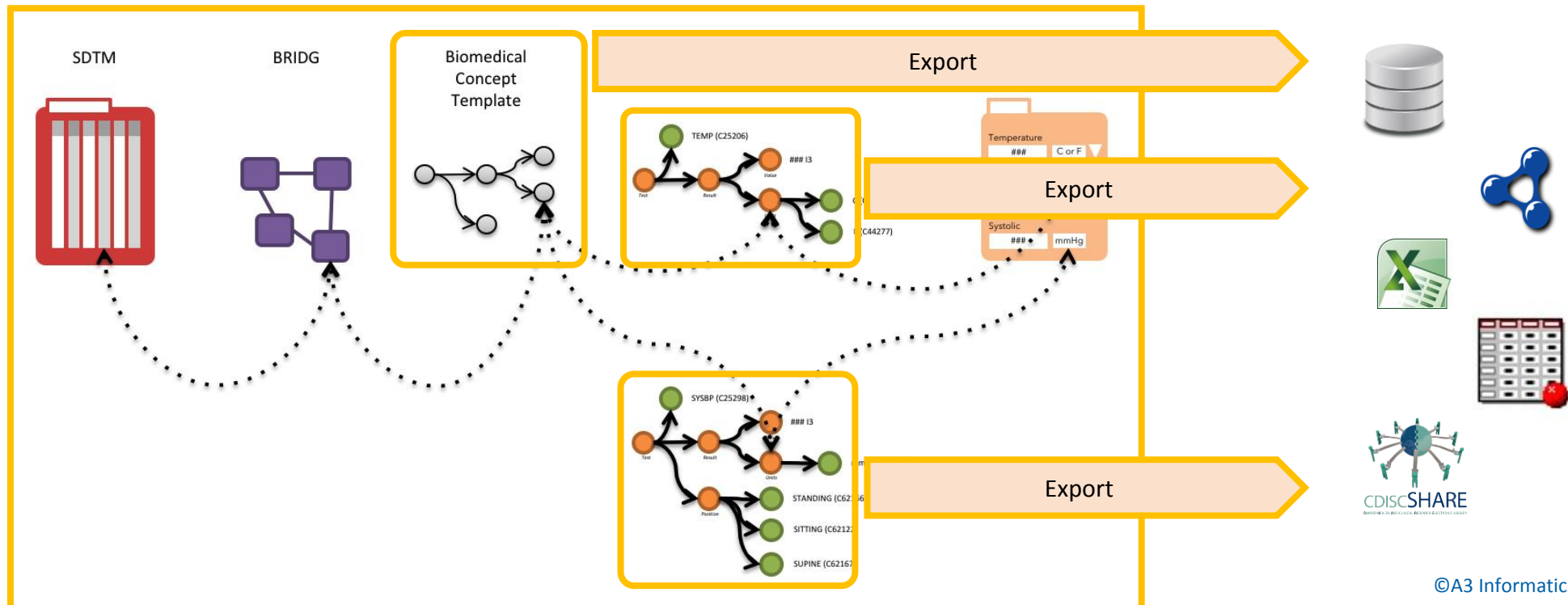
- BCs should be made based on templates to ensure consistency.
- Contributors could be both pharmaceutical companies, CROs as well as regulators.
- Sharing the definition of a BC does not disclose any intellectual property or any sensitive data that needs de-identification



Sharing BCs

Common definitions based on templates

- Distribute the information via SAS tables, linked data, spreadsheets (MS Excel), database loads etc.
- Share with CDISC



BCs For Defining Therapeutic Areas (TAs)

Current metadata for TAs – a BC template

Domain	Question Text	Prompt	SDTM or CDASH Variable Name	BRIDG	Definition	Codelist	CRF Completion Instructions	Core	Data Type
VS	What is the vital sign test name?	<Test>	VSTEST	PerformedActivity.PerformedObservation > PlannedActivity > StudyActivity > DefinedActivity.Define dObservation.nameCode.CD.originalText	Verbatim name of the test or examination used to obtain the measurement or finding. {VSTEST} (See Section 2.2.)	VSTEST	Record the name of the vital sign test if not pre-printed on the CRF.	Highly Recommended	Char
VS	What was the unit of the measurement?	<Units>	VSORRESU	PerformedObservation > PerformedObservationResult.value.ANY=> PQ.translation.PQR.code	Original units in which the data were collected. {VSRESU} (See Section 2.2.)	VSRESU	'Record or select the unit of measure associated with the test, if not pre-printed on the CRF.'	Recommended /Conditional	Char

Doesn't define the possible/required tests for the TA

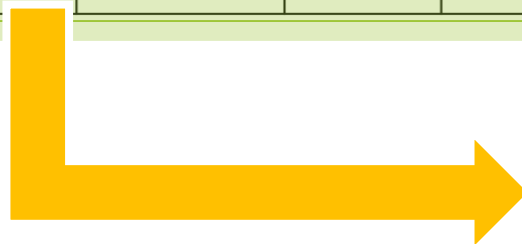
Doesn't define the possible/required units for the test

BCs For Defining Therapeutic Areas (TAs)

TAs as a set of BCs

Domain	Question Text	Prompt	SDTM or CDASH Variable Name	BRIDG	Definition	Codelist	CRF Completion Instructions	Core	Data Type
VS	What is the vital sign test name?	<Test>	VSTEST	PerformedActivity.PerformedObservation > PlannedActivity > StudyActivity > DefinedActivity. DefinedObservation.nameCode.CD.originalText	Verbatim name of the test or examination used to obtain the measurement or finding. {VSTEST} (See Section 2.2.)	VSTEST	Record the name of the vital sign test if not pre-printed on the CRF.	Highly Recommended	Char
VS	What was the unit of the measurement?	<Units>	VSORRESU	PerformedObservation > PerformedObservationResult.value.ANY=>PQ.translation.PQR.code	Original units in which the data were collected. {VSRESU} (See Section 2.2.)	VSRESU	Record or select the unit of measure associated	Recommended /Conditional	Char

- TAs could be defined as a set of BCs
- Also a set of relationships with target domains
- Those domain relationships might change in TAs!

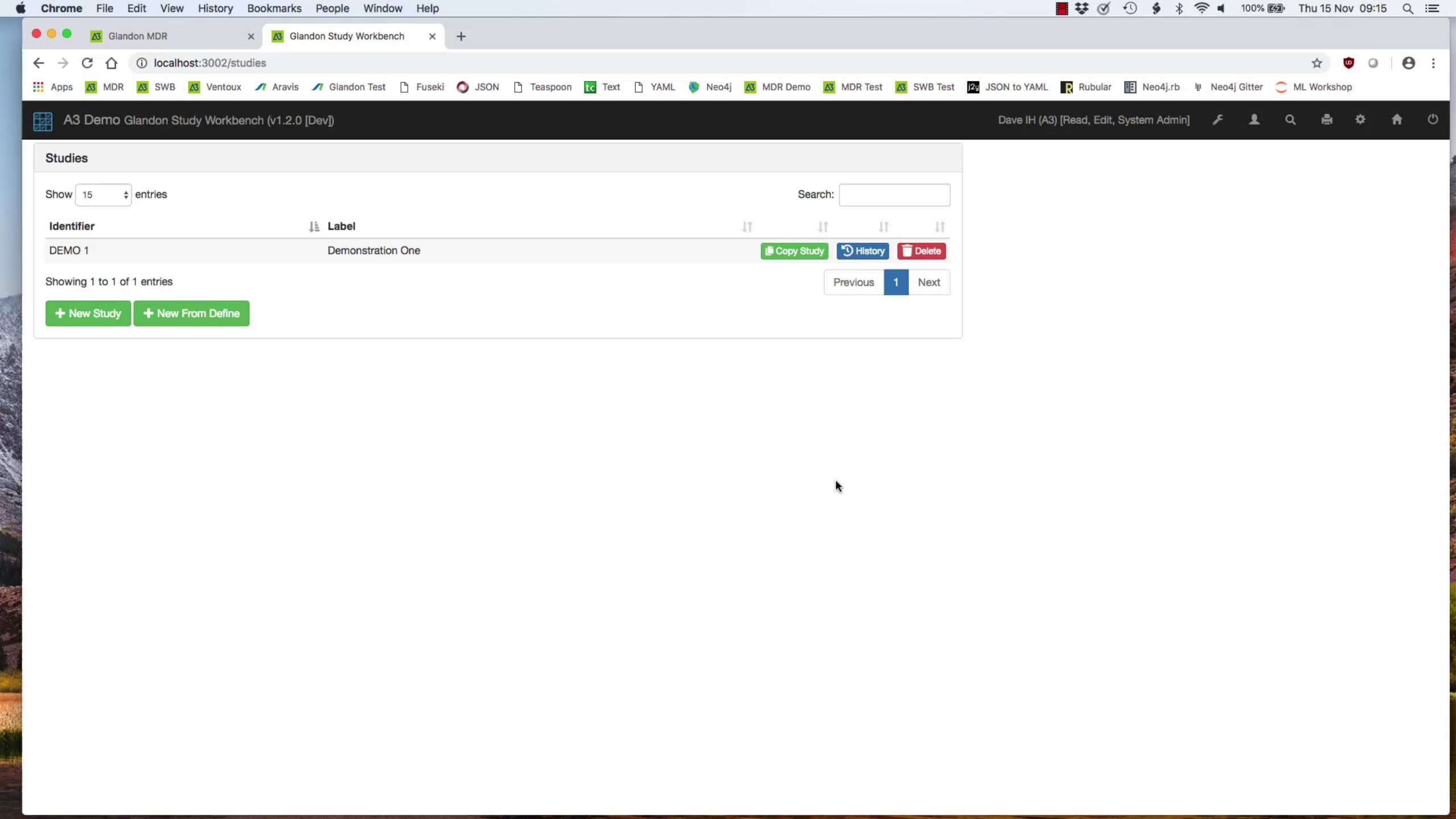


Show: Systolic Blood Pressure (BC C25298) BC C25298 (V3.1.0, 4, Incomplete)

Identifier	Label	Owner	Status	Version	Version Label	Impact
BC C25298	Systolic Blood Pressure (BC C25298)	ACME	Incomplete	3.1.0	0.3	Impact

Items

Alias	Question Text	Prompt Text	Enabled	Collect	Datatype	Format	Terminology
Baseline (-BLFL)	Is this a baseline value?	Baseline	✓	✓	boolean		N (C49487) Y (C49488)
Body Position (-POS)	In what position was the subject during the measurement?	Position	✓	✓	string		SITTING (C62122) STANDING (C62166) SUPINE (C62167)
Date and Time (-DTC)	On what date were the measurement performed?	Date	✓	✓	dateTime		
Laterality (-LAT)	Which arm?	Arm	✓	✓	string		RIGHT (C25228) LEFT (C25229)
Location (-LOC)	The location of the measurement	Location	✓	✗	string		ARM (C32141)
Method Code (-METHOD)			✗	✗	string		
Result Units (-ORRESU)	The unit of the measurement	Units	✓	✓	string		mmHg (C49670)
Result Value (-ORRES)	What was the result of the measurement?	Result	✓	✓	float	3	
Test Code (-TESTCD)			✓	✗	string		SYSBP (C25298)
Test Name (-TEST)			✓	✗	string		Systolic Blood Pressure (C25298)



Studies

Show 15 entries

Search:

Identifier	Label				
DEMO 1	Demonstration One	Copy Study	History	Delete	

Showing 1 to 1 of 1 entries

Previous 1 Next

+ New Study + New From Define

Study Details: Demonstration One (DEMO 1)

Study Name:
Demonstration One

Study Description:
To be set.

Protocol Name:
To be set.

[Submit](#) [History](#)

SDTM IG Version

SDTM IG Version:
3.1.2

[Submit](#) [History](#)

Define.xml Version

Define.xml Version:
2.0.0

[Submit](#) [History](#)

Export Study

File exports: The study version can be exported in a variety of formats.

[Export ALS](#) [Export JSON](#) [Export ODM](#) [Export Define](#)

PDF exports: The study version can be exported as a CRF or Annotated CRF. The full case book format will be used.

[CRF Report](#) [aCRF Report](#)

Define.xml Stylesheets

Define.xml Version:
CDISC

[Submit](#) [History](#)

Conclusion

BCs: Define Once ... Use Many

- Protocol specification – facilitating early data flow decisions.
- CRF build – facilitating flexible and distributed CRF build while still ensuring adherence to SDTM standards.
- Definition of Therapeutic Areas (TAs) – facilitating more precise guidance on the content to the users.
- To ensure consistent definition of BCs a set of templates can be defined.
- BCs should also be shared which would expand the reuse beyond a single company and hereby minimise the variance in SDTM implementations.

Questions & Answers

Email:

dih@A3Informatics.com

More information at:

www.A3Informatics.com

