Easing Your Pain with Biomedical Concepts

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CDISC GUF

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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

Picture by @cyclingalps, www.cycling-challenge.com

Study Setup

Translating study specifications to reality

protocol -> data collection -> reporting

Study Setup

Standards … but not connected


protocol -> data collection -> reporting

Study Setup

Standards ... but not connected

No link to terminology

No link to terminology

No link to annotation

Library of CRFs and aCRFs

Standard Mappings

Silo

Silo

Silo

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

EDC, Labs etc.
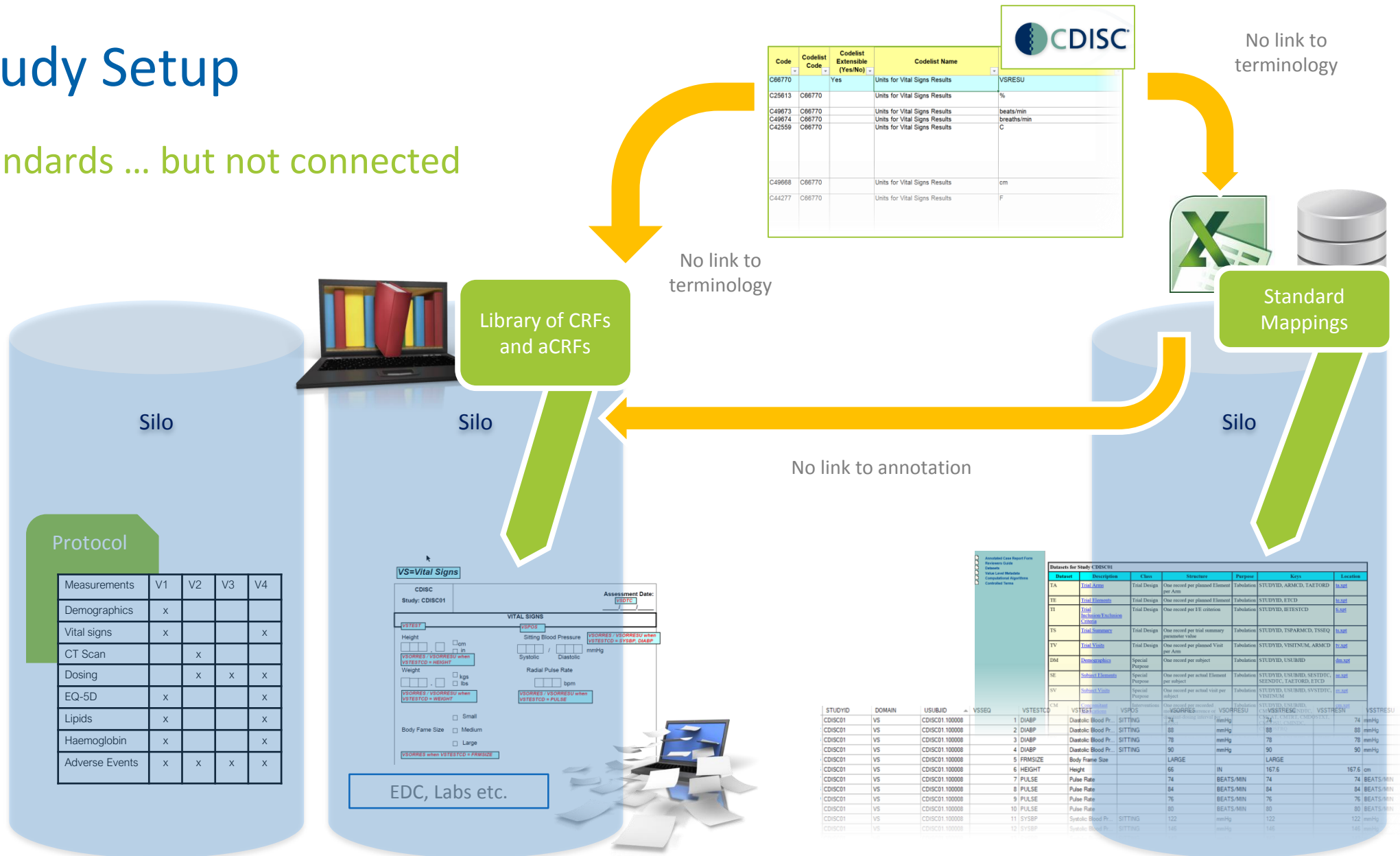
protocol -> data collection -> reporting

Study Setup

## Challenge – maintaining transformations and traceability effectively
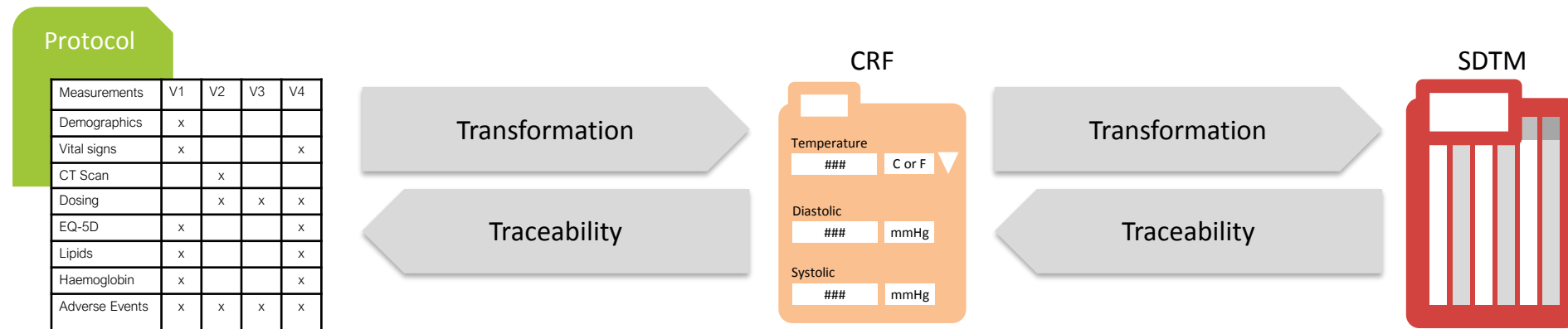
Biomedical Concepts (BCs) break down the "silos" and facilitate a consistent way of collecting the data across studies

What is a Biomedical Concept?

Clinical view
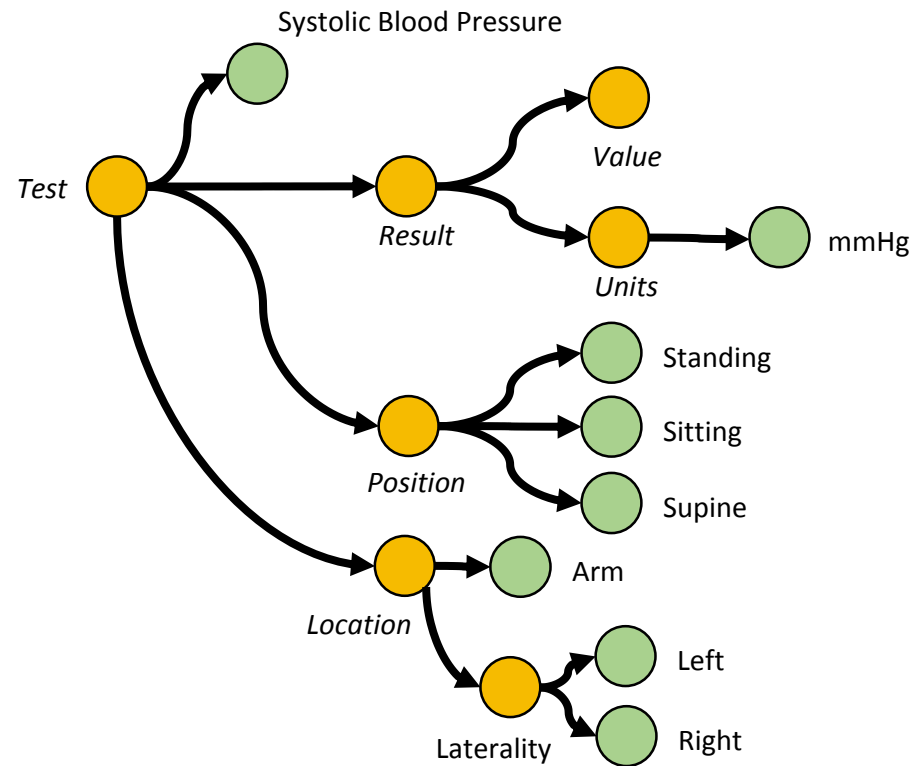
- A collection of variables

- A real-world entity

- Something a physician would recognize

What is a Biomedical Concept?

Data Manager / Programmer view
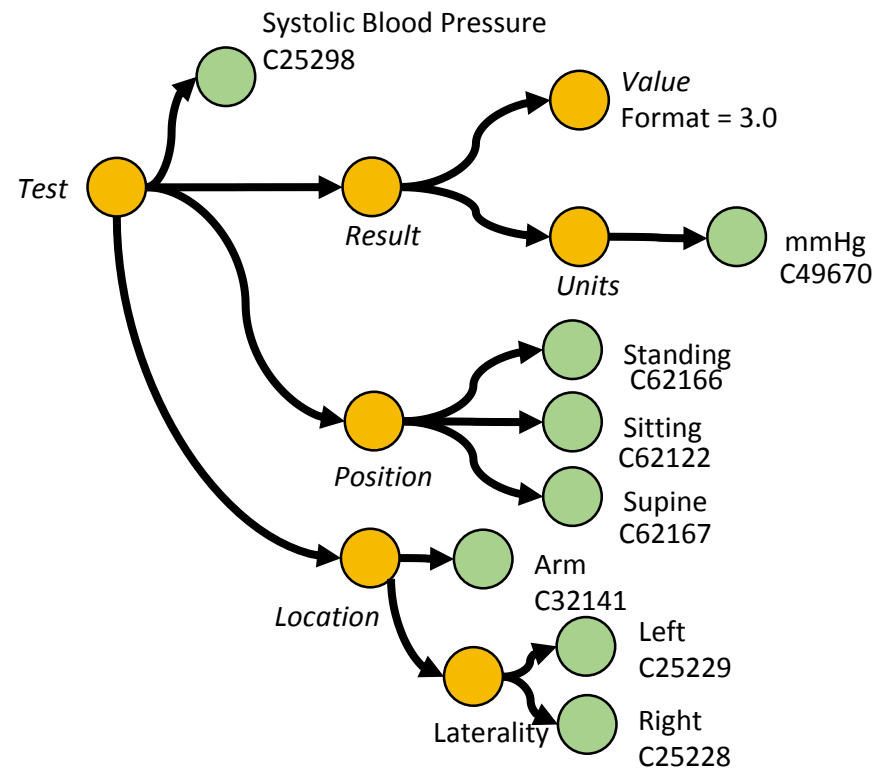
- Some more detail

- 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

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

Items

Show 10 ▼ 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	✔	✔	float	3	
Test Code (--TESTCD)			✔	✖	string		SYSBP (C25298)
Test Name (--TEST)			✔	✖	string		Systolic Blood Pressure (C25298)
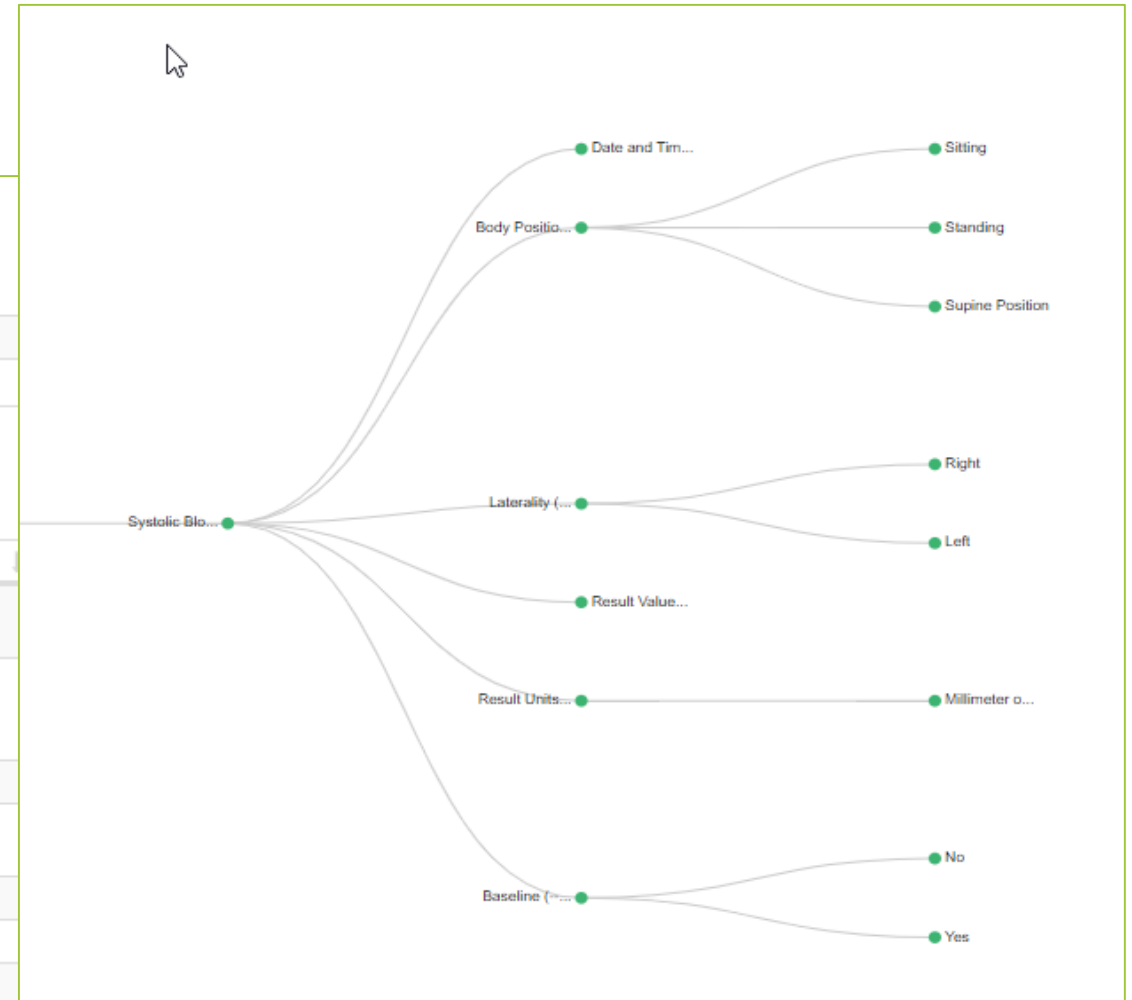
Refer domains to Biomedical Concepts

Where does the collected information belong?

BCs added to the VS domain

- Multiple domains can refer to the same BC.

- The context of the study will then determine which domain is used

- **IMPORTANT:** The domain referrers to the BC. They BC DOES NOT refer to the domain. Can be used with any appropriate SDTM domain of the correct class

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"
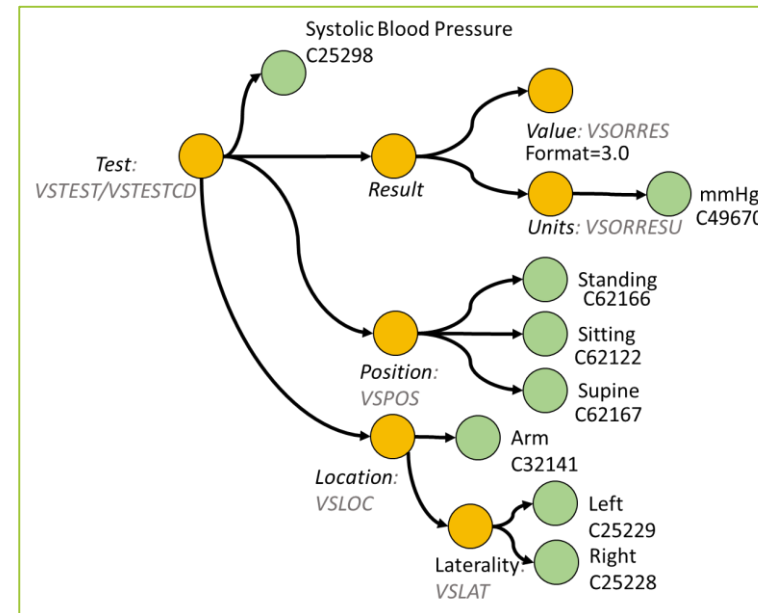
Biomedical Concepts

Domain relationship
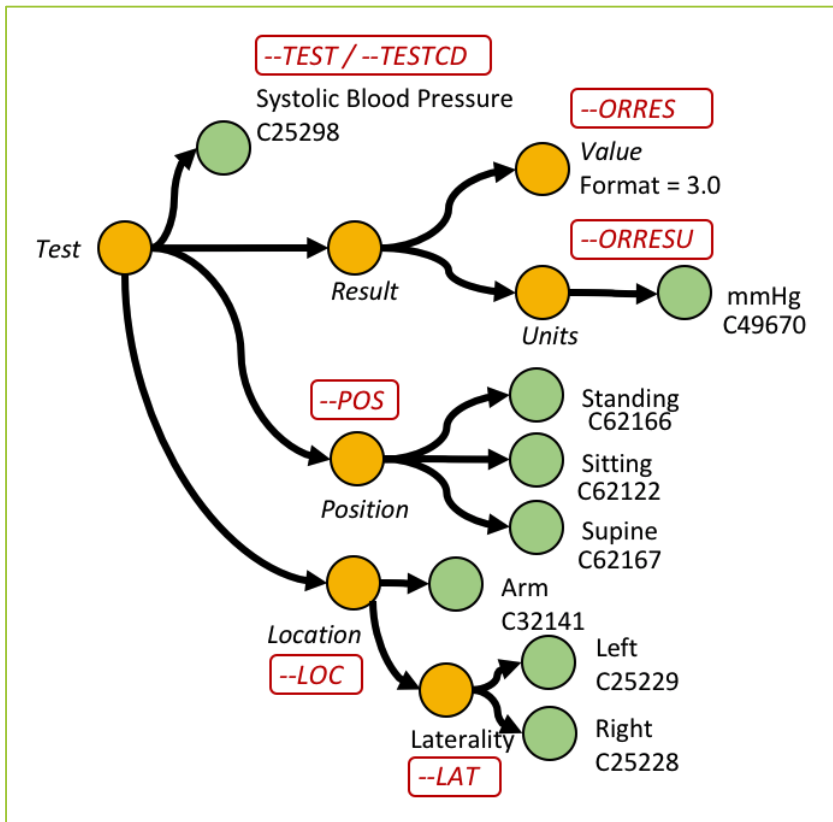
- We use a framework (BRIDG) and templates to ensure consistency of approach
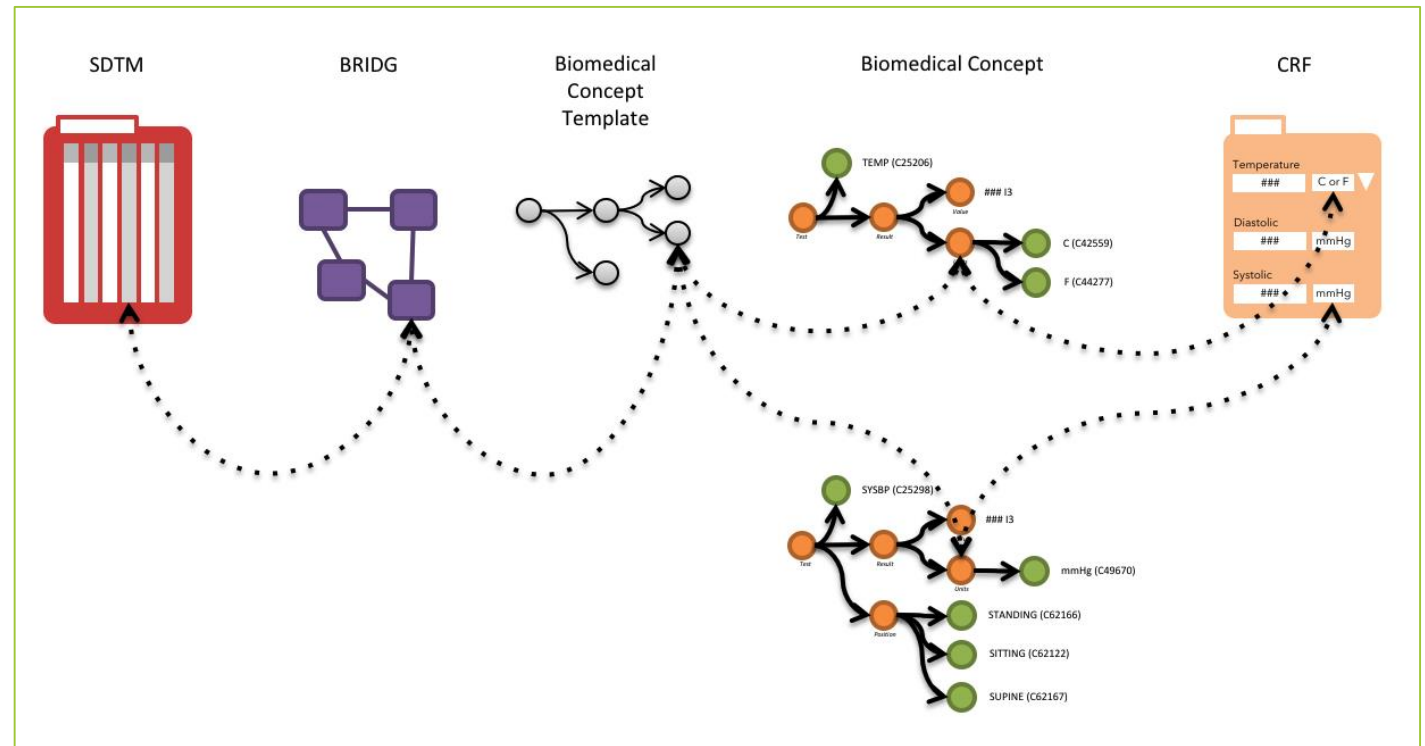
Why bother?

Consistency across the life-cycle
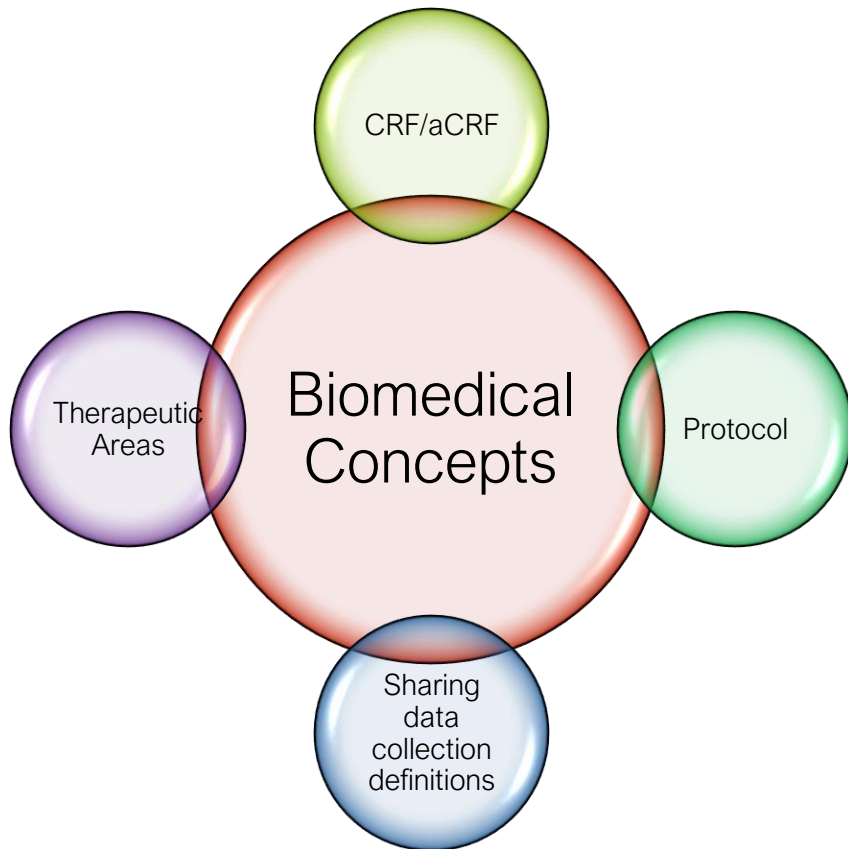
- BC is a standardised definition that can be used for various purpose and facilitates faster and more flexible study setup
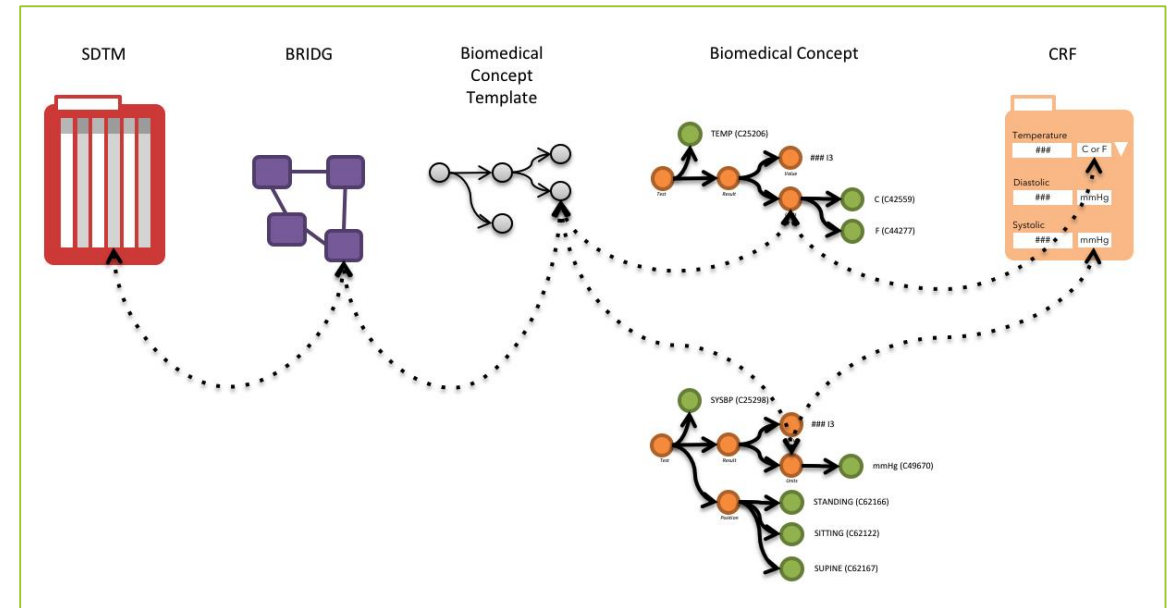
Standardisation - From Forms to BCs

Flexible form creation

- Ensures we have compliance with the CDISC standards

Glandon MDR Glandon Study Workbench

localhost:3000/forms

A3 Demo Glandon MDR (v2.21.0 [Dev])

Dave IH (A3) [Content Admin, System Admin]

Forms			

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

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New Form

New

Quick Forms

New Placeholder

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Registration Authorities

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Background Jobs

Ad Hoc Reports

Tags

Markdown

Terminology

CDISC Terminology

Biomedical Concept Templates

Biomedical Concepts

Forms

CDISC SDTM Model

CDISC SDTM IGs
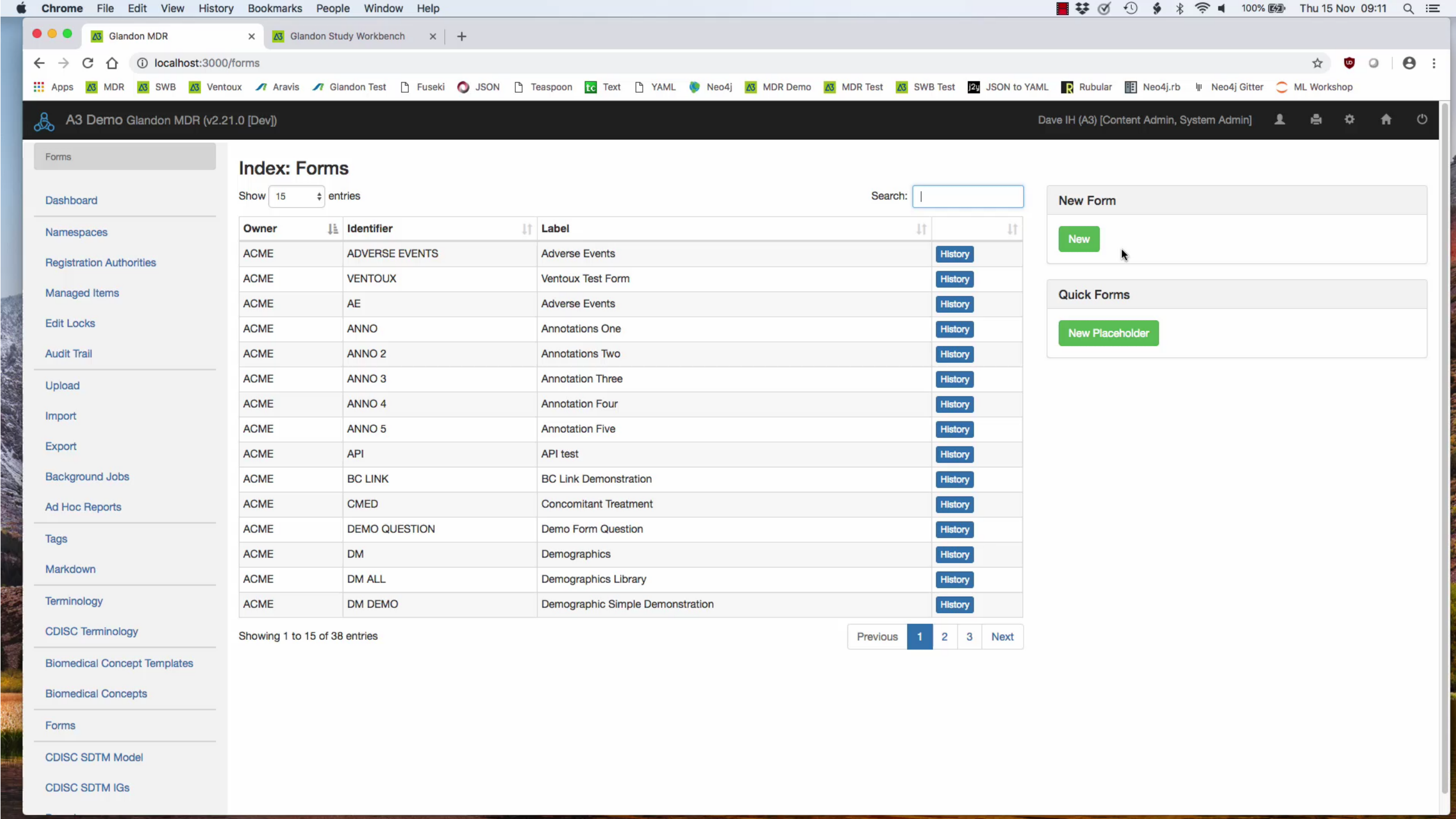
Standardisation - From Forms to BCs

Flexible form creation
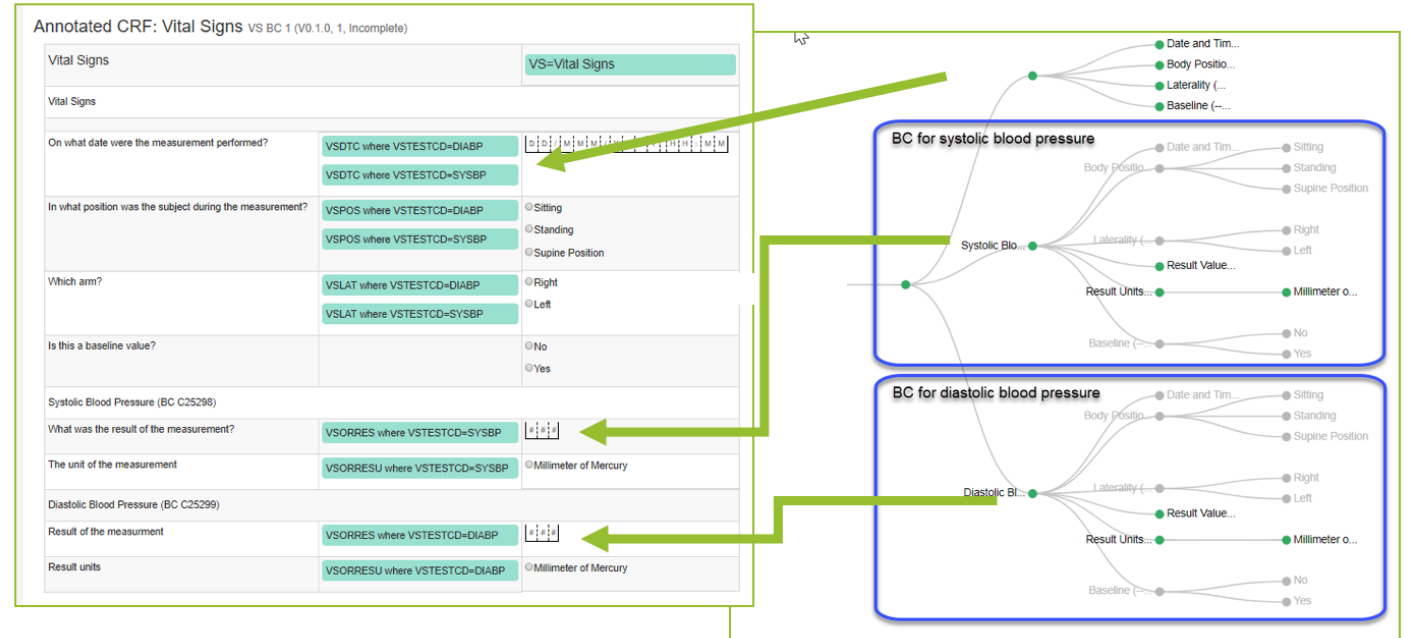
The flexibility is achieved on 3 levels:

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
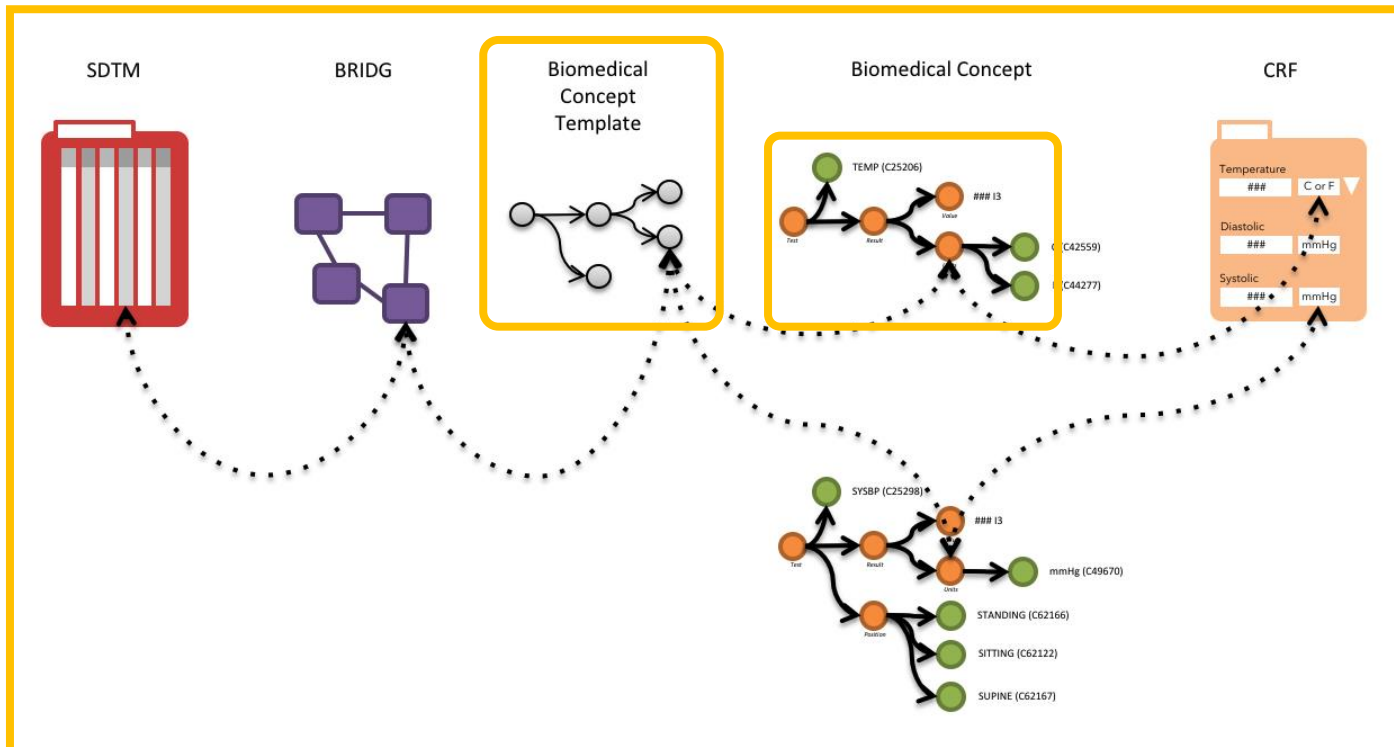
Sharing BCs

Common definitions based on templates

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

- Share with CDISC
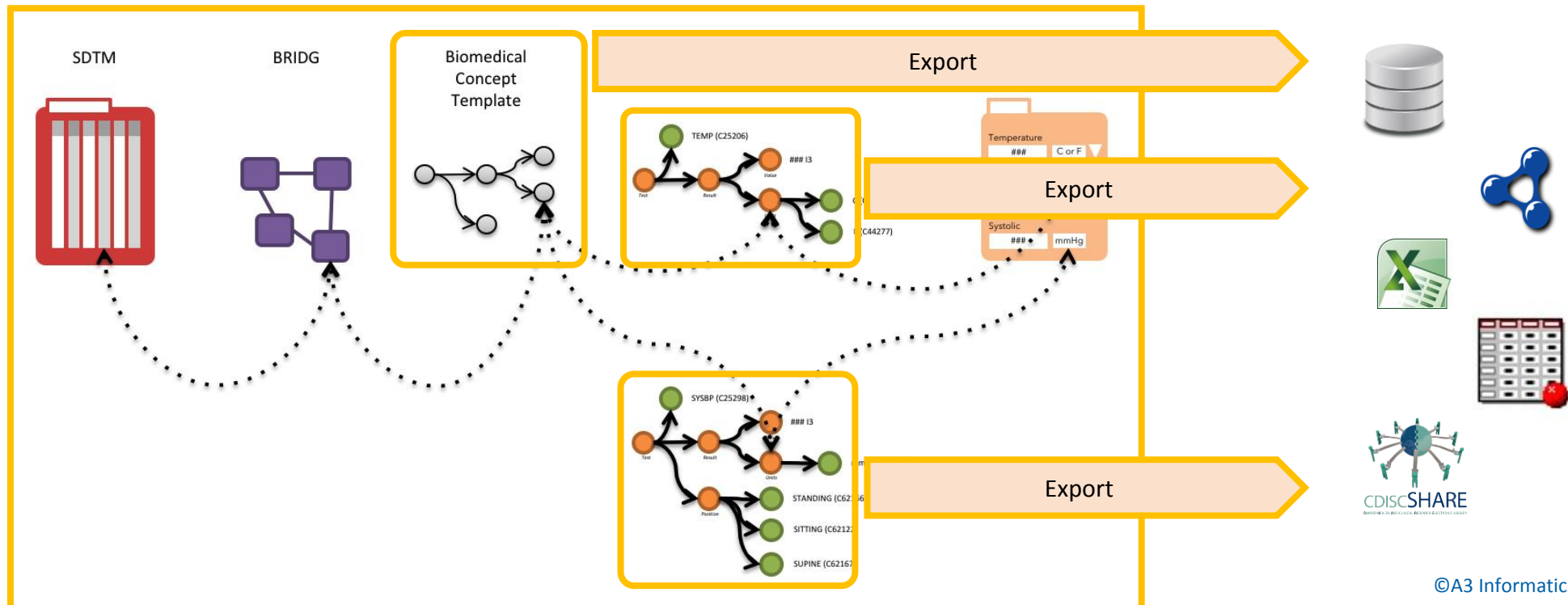
BCs For Defining Therapeutic Areas (TAs)

Current metadata for TAs – a BC template

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

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

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 with the test, if not pre-printed on the CRF.'	Recommended /Conditional	Char

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

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

Details

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

Items

Show 10 ▼ entries   Search:

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)

- TAs could be defined as a set of BCs

- Also a set of relationships with target domains

- Those domain relationships might change in TAs!

localhost:3002/studies

A3 Demo Glandon Study Workbench (v1.2.0 [Dev])

Dave IH (A3) [Read, Edit, System Admin]
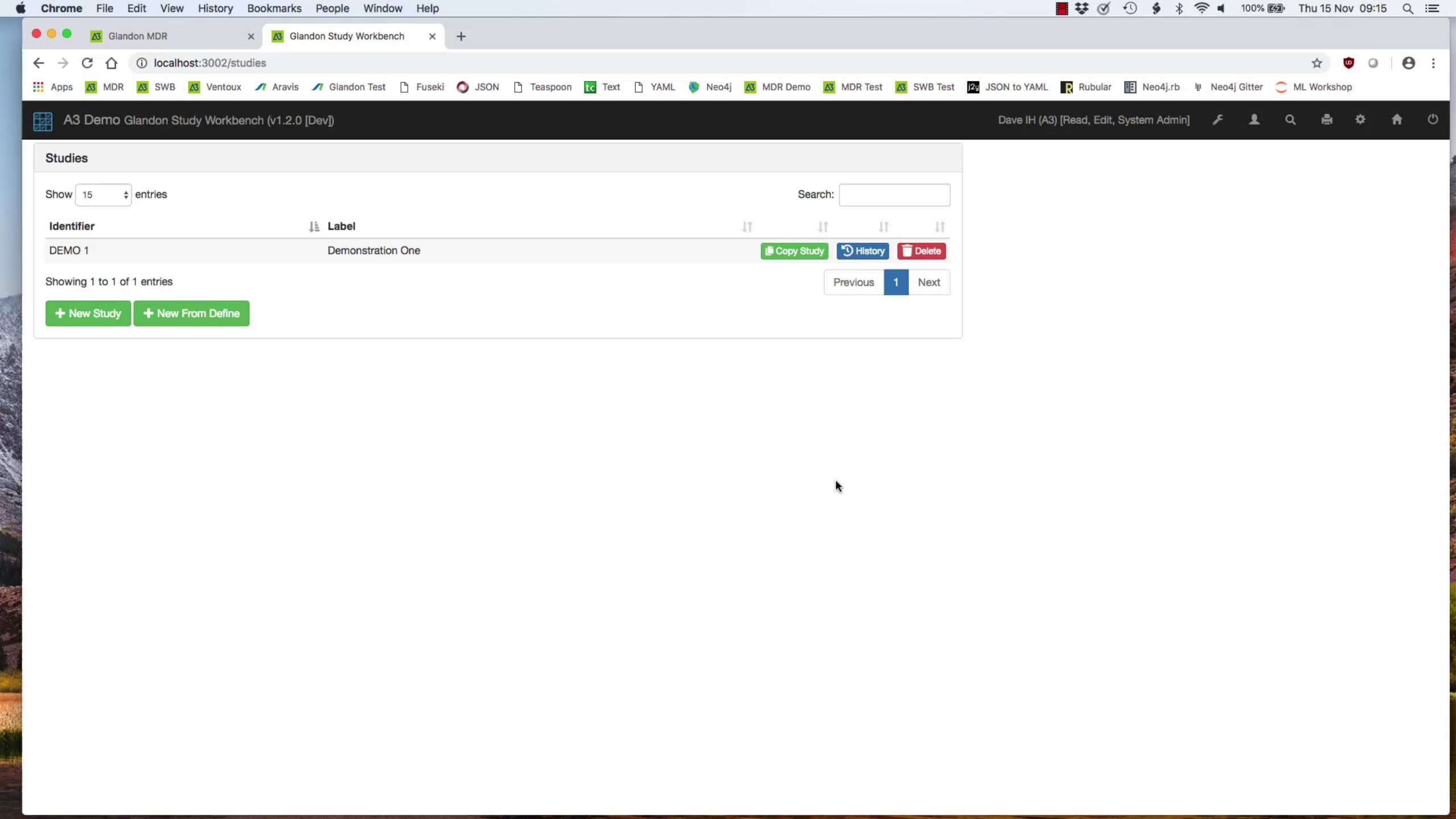
Studies

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

Glandon Study Workbench

localhost:3002/studies/versions/3e085d5e-c744-48a8-9769-9b26d6487bed/edit

Apps   MDR   SWB   Ventoux   Aravis   Glandon Test   Fuseki   JSON   Teaspoon   Text   YAML   Neo4j   MDR Demo   MDR Test   SWB Test   JSON to YAML   Rubular   Neo4j.rb   Neo4j Gitter   ML Workshop

A3 Demo Glandon Study Workbench (v1.2.0 [Dev])

Dave IH (A3) [Read, Edit, System Admin]

Study   SoA   Detail   CRF   aCRF   Domains   Documents   Terminologies

Study Details: Demonstration One (DEMO 1)

Study Name:

Demonstration One

Study Desciption:

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

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www.A3Informatics.com