

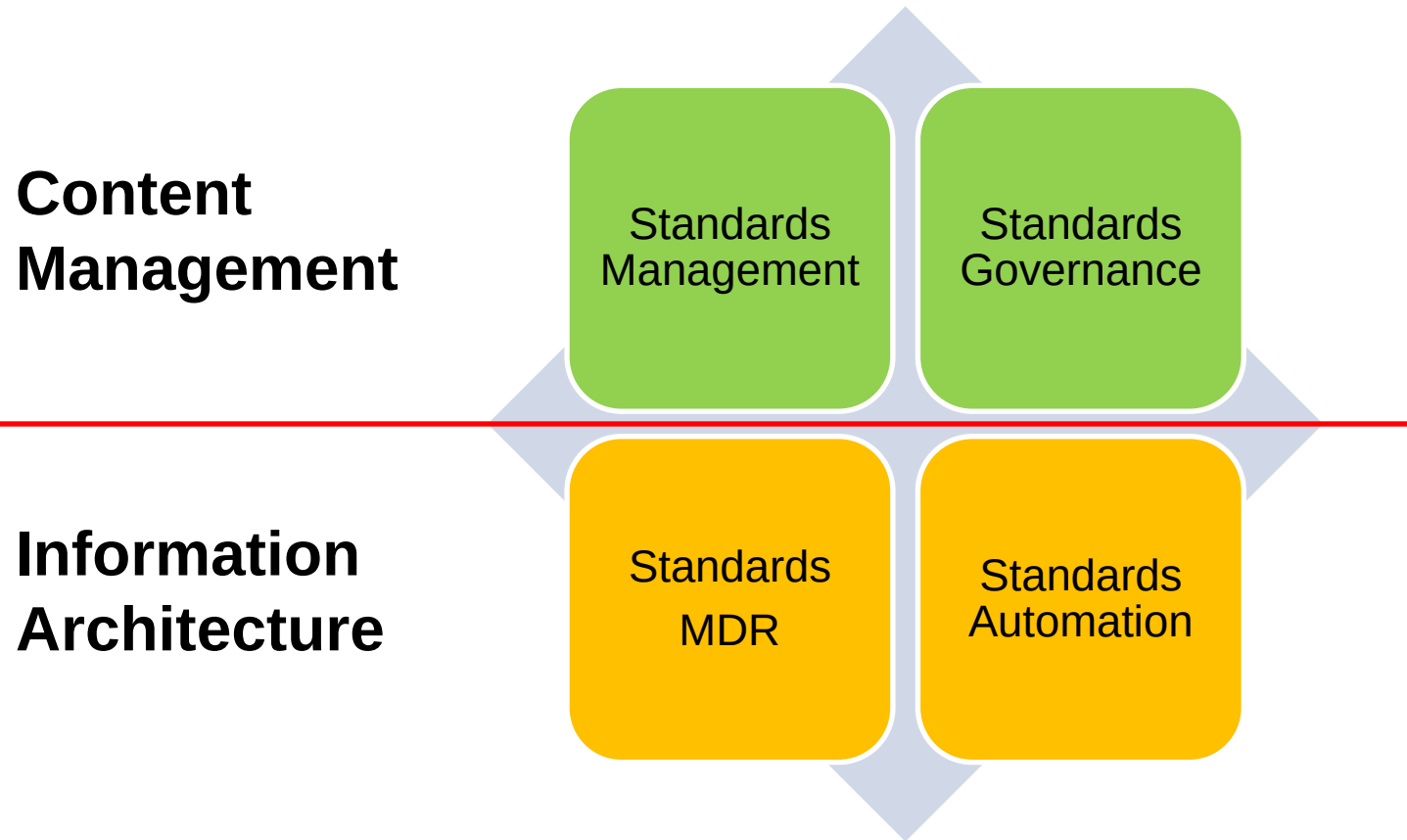
Standards Driven Innovation

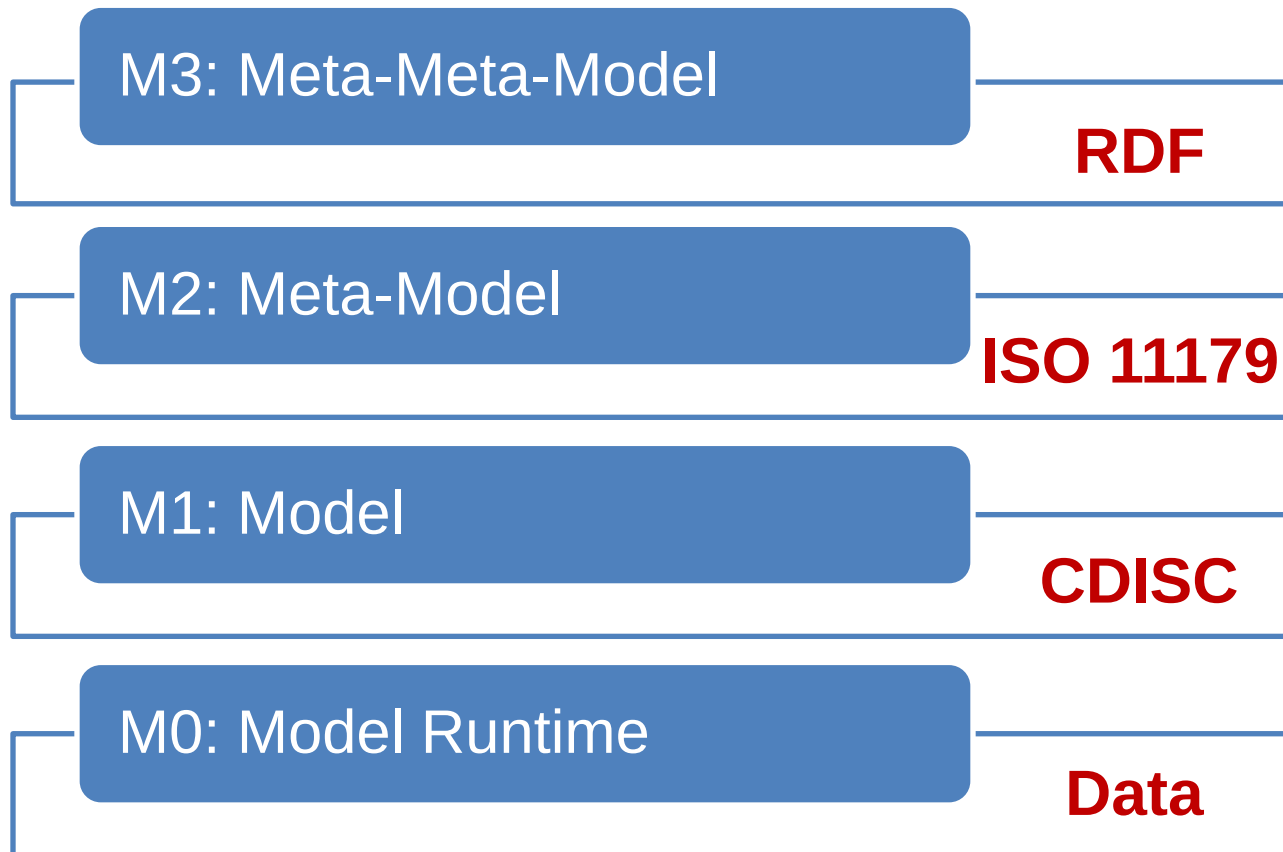
PhUSE Annual Conference 2014

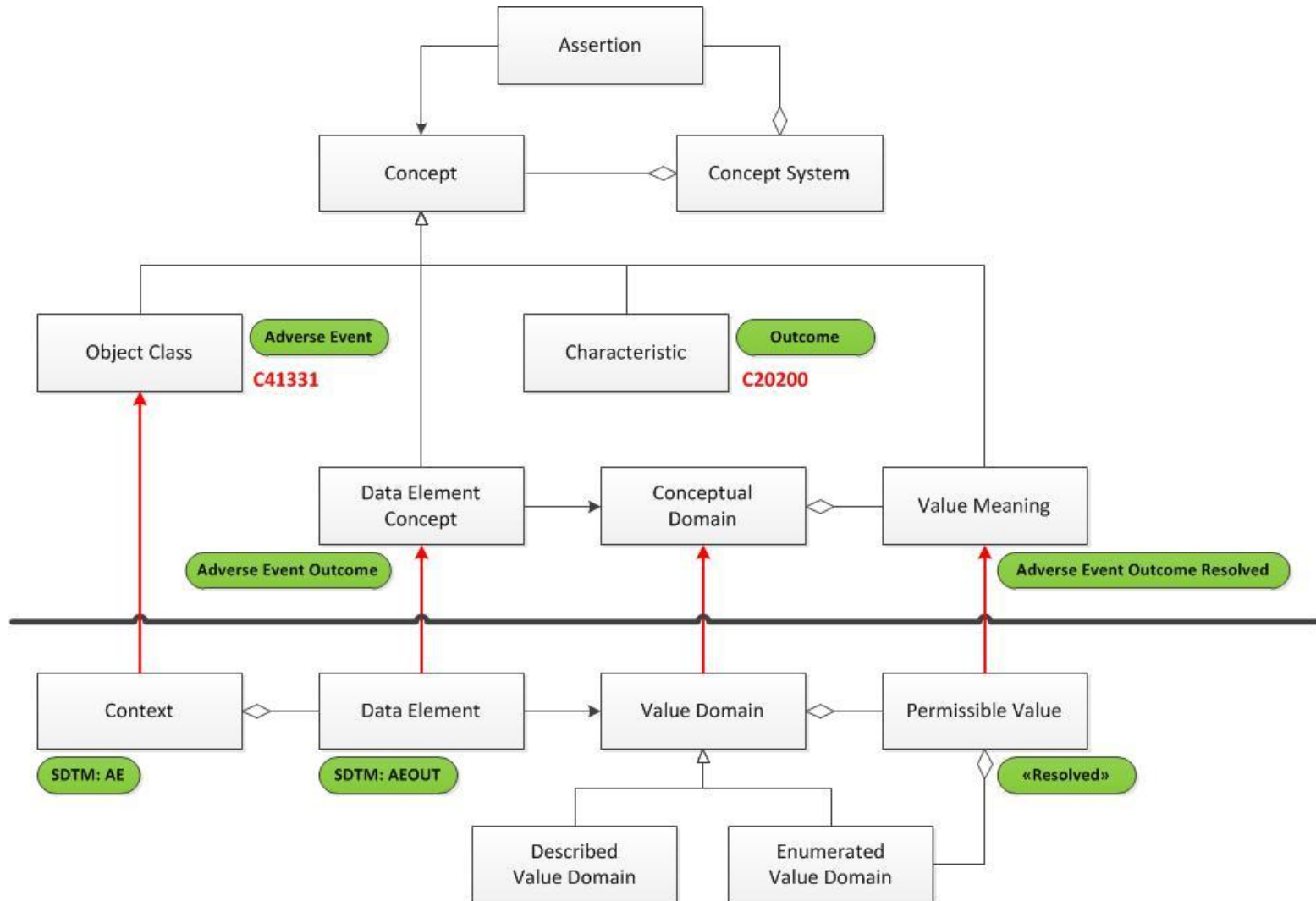
Frederik Malfait
IMOS Consulting GmbH, Hoffmann-La Roche AG

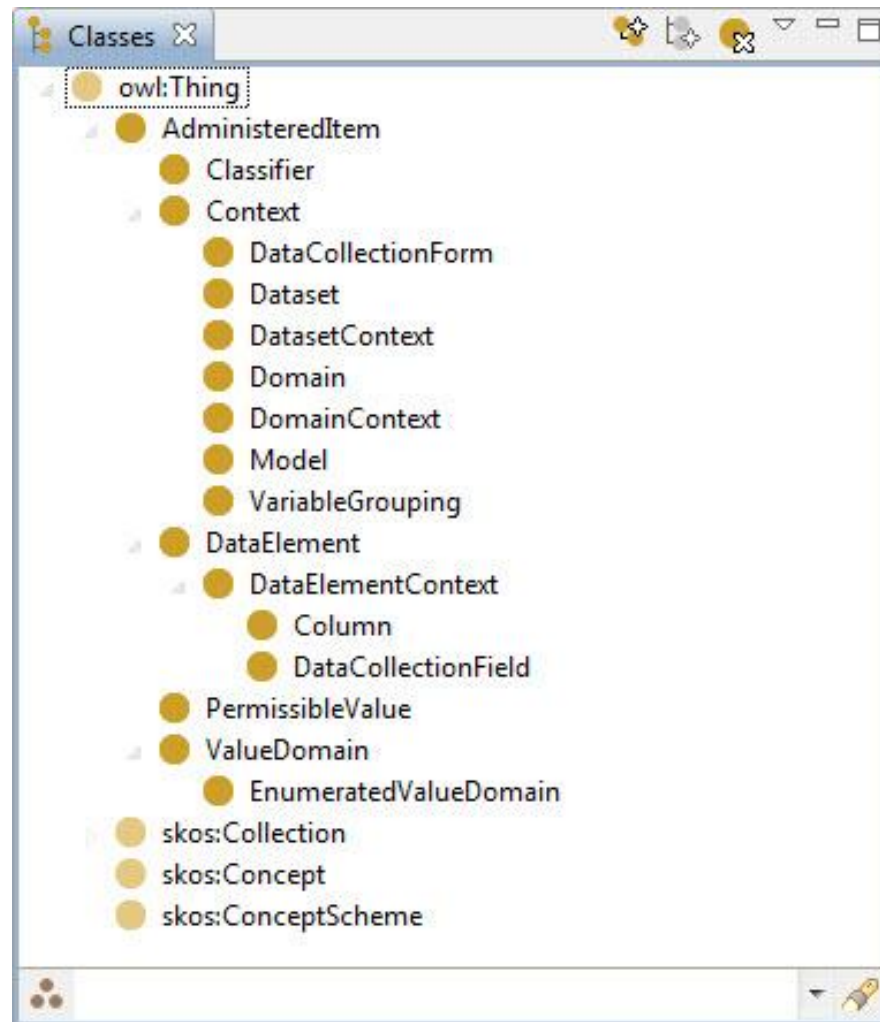
Managing Standards

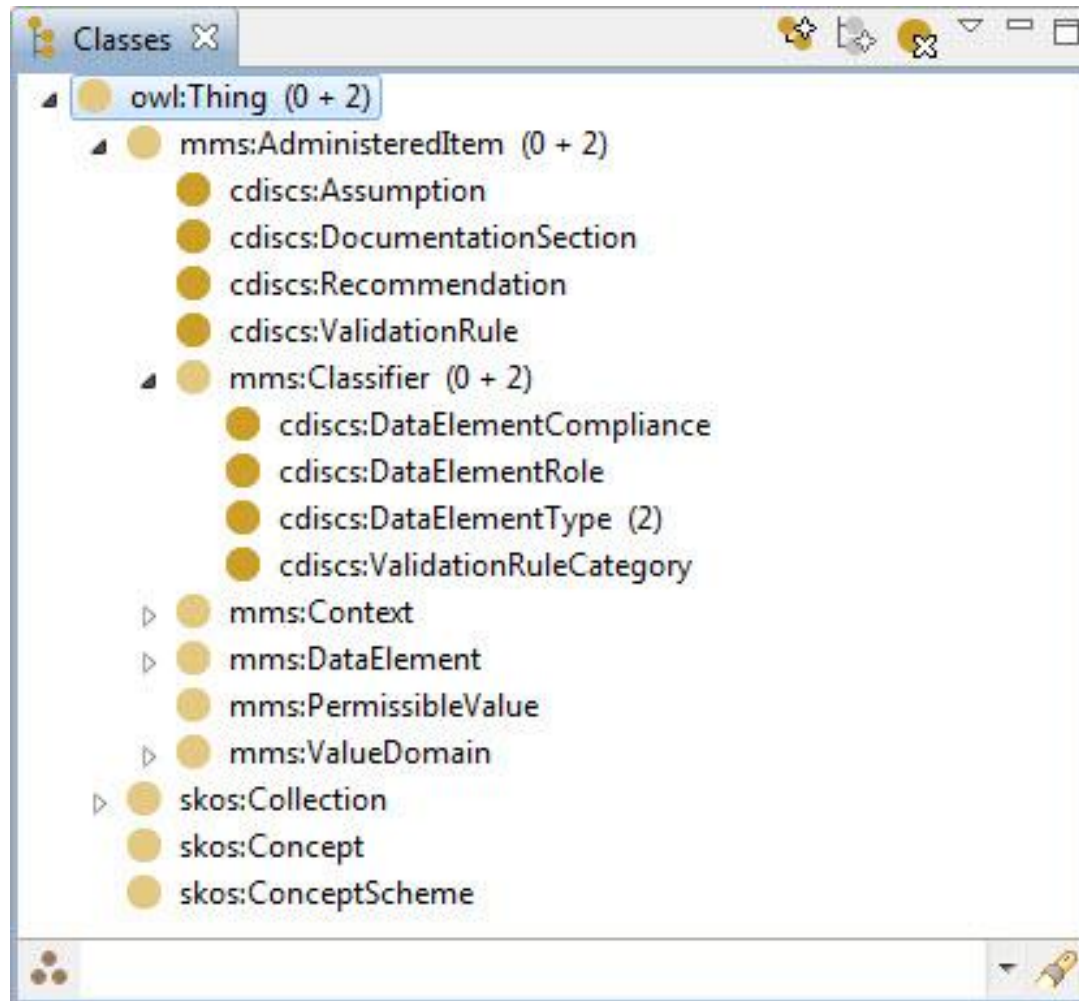
- Standards are increasingly mandated
 - You have to do it anyway
 - You can as well make the best of it
- Define once, use many times
- When submitting data and analysis results, standards can ensure
 - Compliance
 - Consistency
 - Correctness
- Have a repeatable process, do things faster
- Make data semantically meaningful
 - Precisely define models and content
 - Store semantics with the data, so it can be remembered
 - Supports understanding and transparency of the data
 - Semantically align and integrate data from different sources
- Standards based automation
 - Store data standards in a Metadata Registry
 - Workflow automation

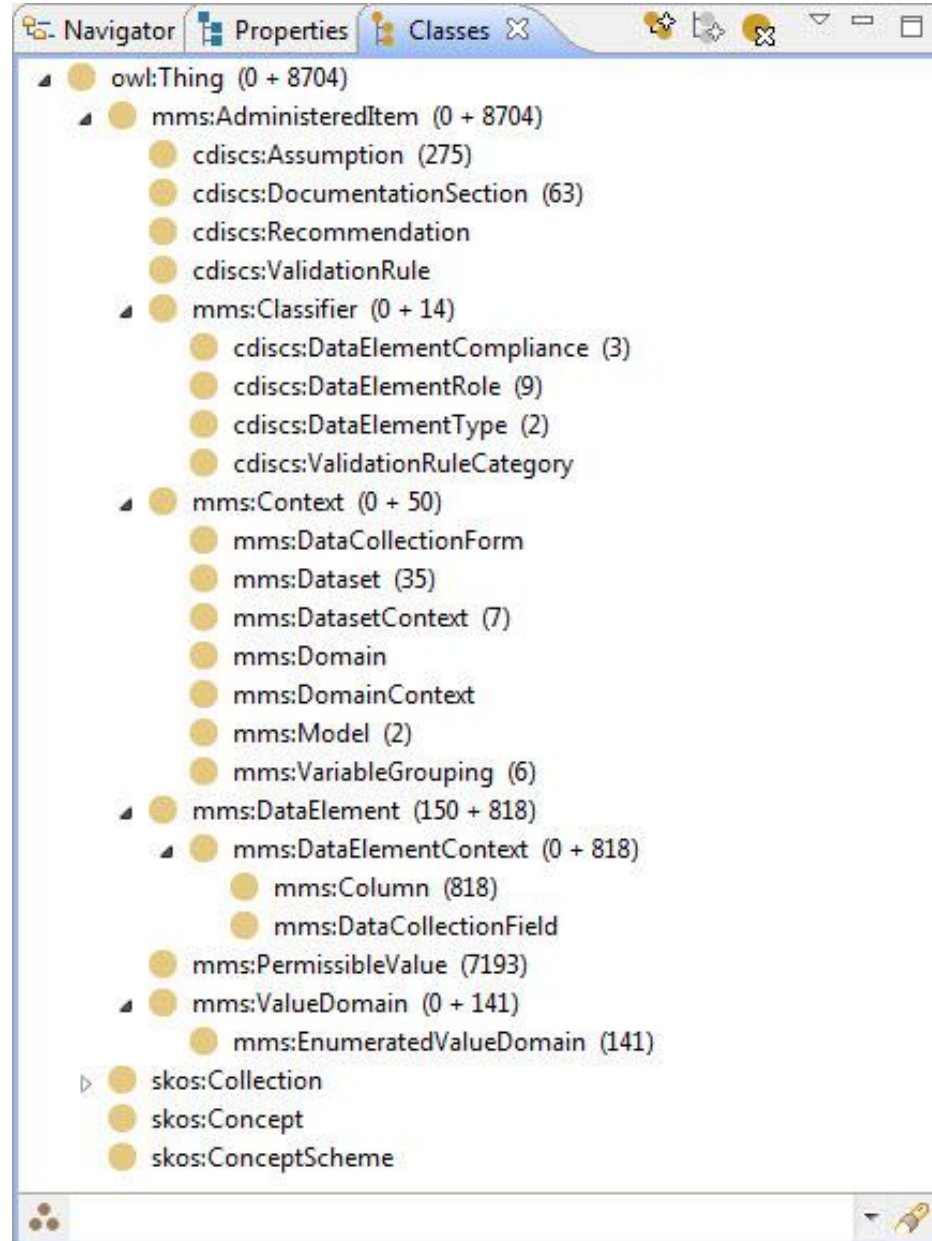


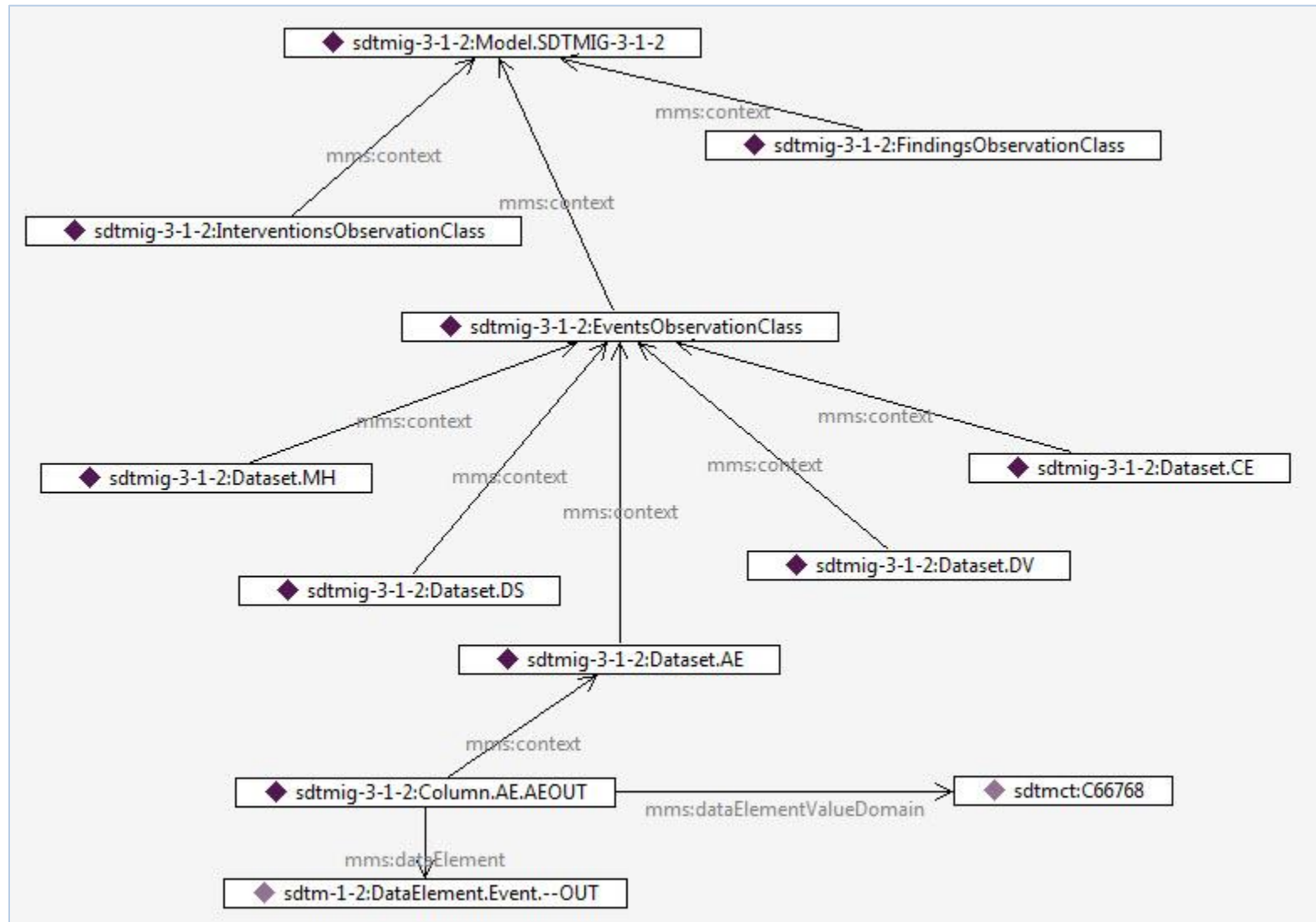












sdtmig-3-1-3.ttl

Resource Form

URI: <http://rdf.cdisc.org/std/sdtmig-3-1-3#Model.SDTMIG-3-1-3>

Annotations

Incoming References

← mms:context

- sdtmig-3-1-3:EventsObservationClass
- sdtmig-3-1-3:FindingsAbout
- sdtmig-3-1-3:FindingsObservationClass
- sdtmig-3-1-3:InterventionsObservationClass
- sdtmig-3-1-3:RelationshipDataset
- sdtmig-3-1-3:SpecialPurposeDomain
- sdtmig-3-1-3:TrialDesignModel

Other Properties

mms:contextDescription

The Study Data Tabulation Model Implementation Guide is a CDISC defined guide for the implementation of SDTM providing a detailed specification of the SDTM domains.

mms:contextLabel

Study Data Tabulation Model Implementation Guide (SDTMIG) Version 3.1.3

mms:contextName

sdtmig-3-1-3

rdf:type

mms:Model

Form | Browser | Graph | Source Code

sdtmig-3-1-3.ttl

Resource Form

URI: <http://rdf.cdisc.org/std/sdtmig-3-1-3#EventsObservationClass>

Annotations

Incoming References

← mms:context

- ◆ sdtmig-3-1-3:Dataset.AE
- ◆ sdtmig-3-1-3:Dataset.CE
- ◆ sdtmig-3-1-3:Dataset.DS
- ◆ sdtmig-3-1-3:Dataset.DV
- ◆ sdtmig-3-1-3:Dataset.MH

Other Properties

mms:context

◆ sdtmig-3-1-3:Model.SDTMIG-3-1-3

mms:contextDescription

S The Events class captures planned protocol milestones such as randomization and study completion, and occurrences, conditions, or incidents independent of planned study evaluations occurring during the trial (e.g., adverse events) or prior to the trial (e.g., medical history).

mms:contextLabel

S Events Observation Class

mms:contextName

S Events

mms:ordinal

3

rdf:type

● mms:DatasetContext

Form | Browser | Graph | Source Code

sdtmig-3-1-3.ttl

Resource Form

URI:

▼ Annotations

▼ Other Properties

mms:context ▼
◆

mms:contextLabel ▼
S

mms:contextName ▼
S

mms:ordinal ▼
■

cdiscs:datasetCode ▼
S

cdiscs:datasetStructure ▼
S

rdf:type ▼
●

► Incoming References

Form | Browser | Graph | Source Code

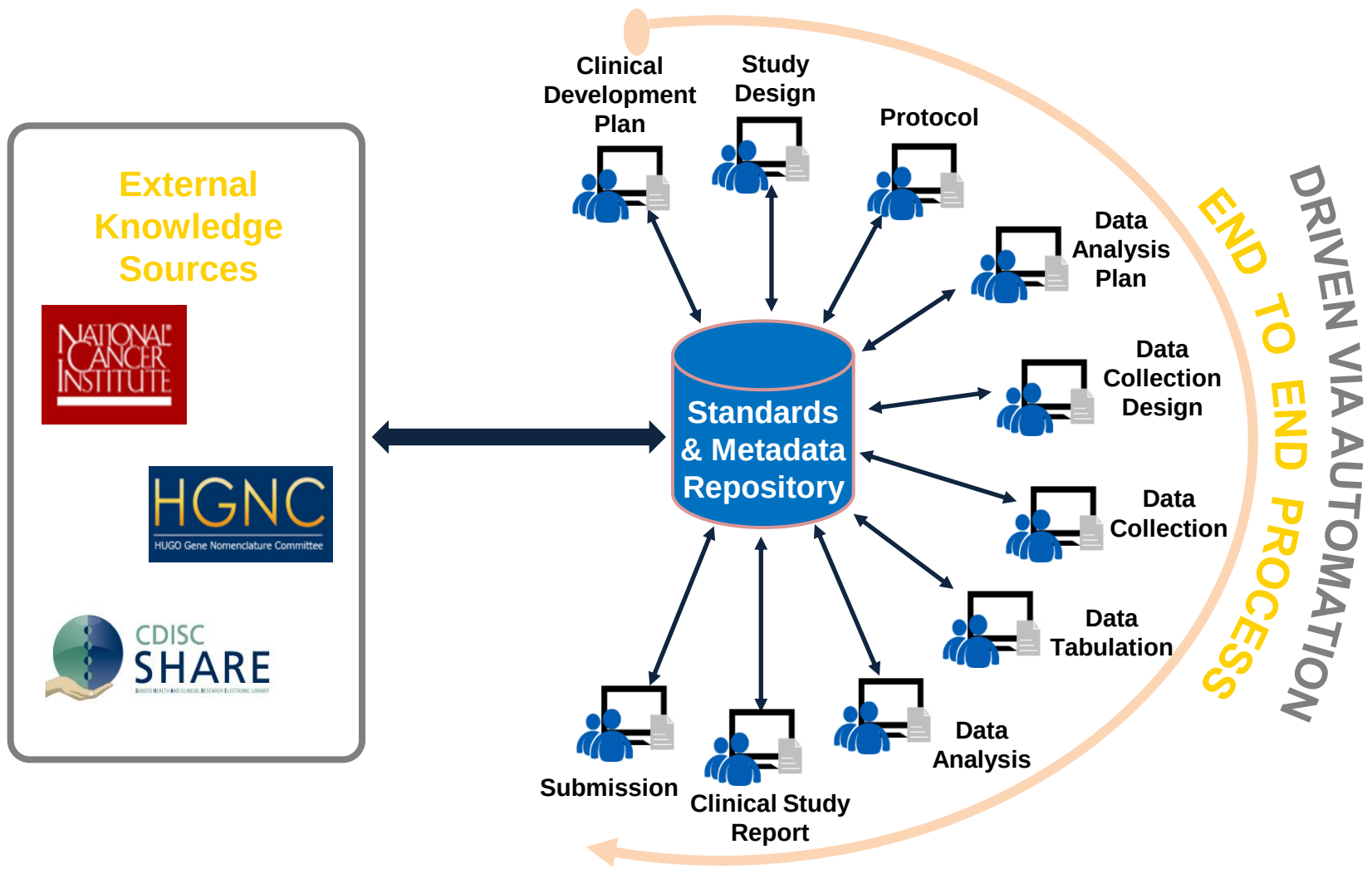
- Integrated data standards Roche and Genentech 2010
- MDR with operational metadata
 - Enterprise level application, fully validated system
 - First production release 2011
- MDR components
 - Browser, web services, search, item level versioning
- MDR concepts
 - Prepared first half of 2013
 - To be integrated in standards development over the next few weeks
- Model driven capabilities (2014-2015): use RDF to specify
 - Model driven read/write web services + XSLT engine
 - Model driven search
 - Model driven validation rules
 - Model driven UI
 - Model driven security
 - MDR used by other parties in Roche
 - Master data management
 - Configuration of integrated document management systems

- Existing CDISC Standards in RDF
 - CDASH
 - SDTM
 - SEND
 - ADaM
 - Controlled Terminology
- Protocol and Schedule of Activities in RDF
- Analysis Results Metadata in RDF
- Link to EHR
 - Co-lead from CDISC
- Regulatory Guidance in RDF
 - Co-lead from FDA

MDR Driven Study Workflow Automation (SWA)

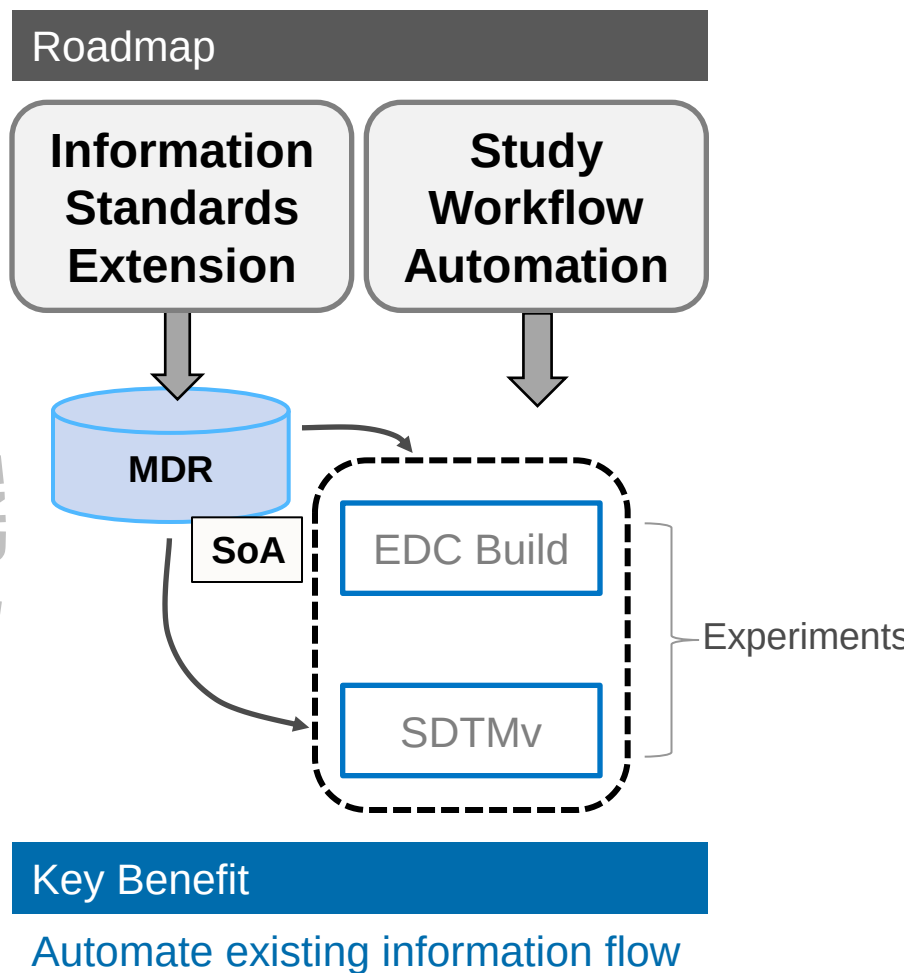
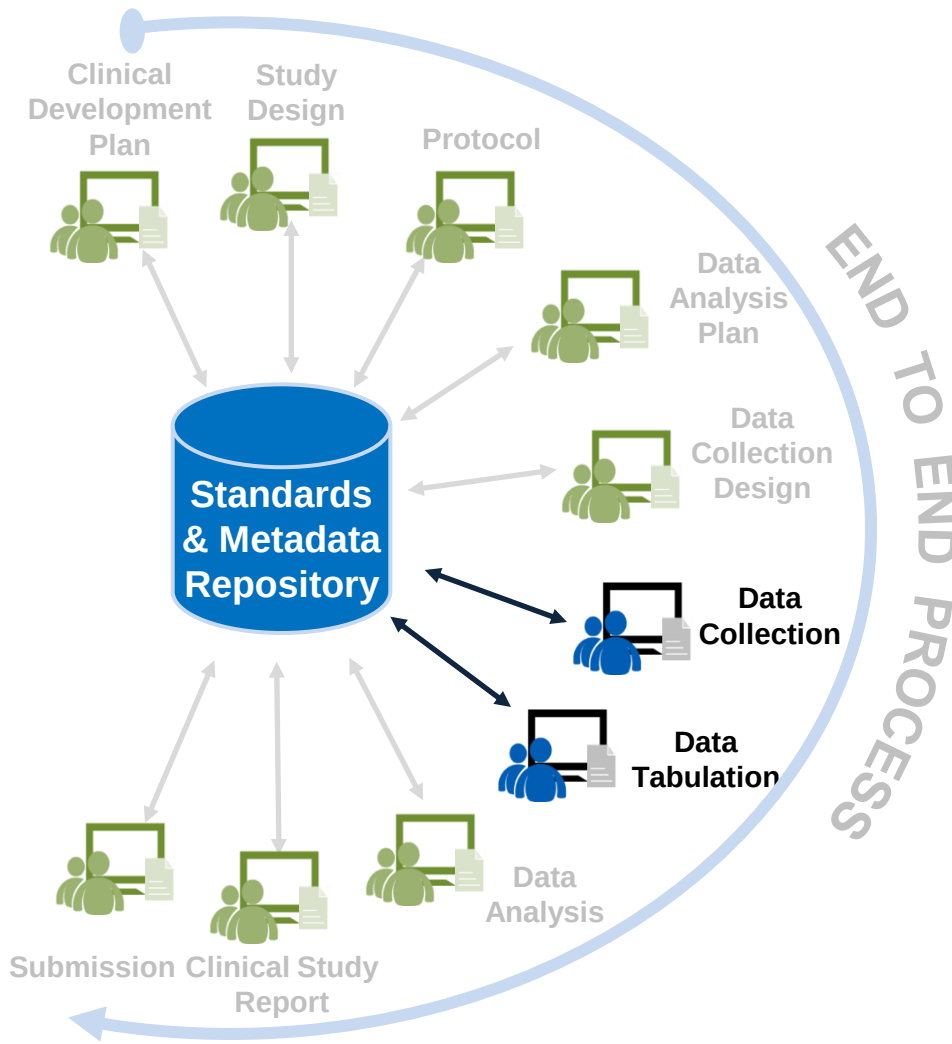
Clinical Data – Future State

Standards & Metadata Repository: Integrated Workflow



Building out the vision, step by step

Standards can help drive automation of key clinical processes...



Experiment Set A: Creating a machine-readable SOA

Experiment	Description	Status
Exp. 1	Create a schema for a machine-readable SOA.	Complete.
Exp. 2	Upload a SOA into the GDSR.	Complete. Includes representation of SOA in Word and HTML.

Experiment Set B: Leveraging Global Data Standards

Exp. 3	Use the GDSR to generate an operational annotated eCRF of the Global Data Standards.	Complete.
Exp. 4	Use the GDSR to generate submission-ready annotated eCRFs of the Global Data Standards.	Complete.
Exp. 5	Use the GDSR to generate ALS templates including edit checks of the Global Data Collection Standards.	Complete (excluding edit checks).
Exp. 6	Develop a tool that will produce a mapping specification and corresponding programming environment-independent SAS program that transforms collected data to SDTMv.	Ongoing. - Code list alignment opportunity identified. - Reuse of data element mappings across forms - Potential to generate SDTMv annotations from mappings. - Platform-independent

Experiment Set C: Expedite the Study Build

Experiment	Description	Status
Exp. 7	Design an interface that will enable the definition eCRFs from Global Data Standards or definition of new eCRFs.	First SME workshop completed. Process analysis ongoing.
Exp. 8	Design an interface that will enable the definition a non-CRF File Format Specification.	First SME workshop completed. Process analysis ongoing.
Exp. 9	Design an interface that will enable the definition of a Visit Form Matrix.	First SME workshop completed. Process analysis ongoing.
Exp. 10	Use the GDSR to generate a study-specific ALS template from study-level metadata.	First SME workshop completed. Process analysis ongoing.
Exp. 11	Use the GDSR to generate a non-CRF File Format Specification from study-level metadata.	First SME workshop completed. Process analysis ongoing.

Schedule of Activities - SDM XML

4	STRUCTURAL ELEMENTS	8
4.1	BACKGROUND CONCEPTS: EPOCHS, ARMS, CELLS, SEGMENTS	8
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4.2.2	<i>Arm</i>	10
4.2.3	<i>CellDef</i>	10
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6.1.3	TIMING TYPES	22

Schedule of Activities

5. SCHEDULE OF ASSESSMENTS AND PROCEDURES

Table 2 Schedule of Assessments and Procedures—Group A (PEG-IFN) and Group C (Advanced Fibrotic PEG-IFN)

Assessment/Procedure	Screen (days)	BL (days)	Treatment Period (weeks)																Initial 24 Weeks of Follow-Up (Weeks Post-End of Treatment)			Extended Long-Term Follow-Up Period (Years Post-End of Treatment Period)				
	-35 to -1	1	2	4	8	12	18	24	30	36	42	48	4 ^a	12 ^a	24 ^a	1 ^a	1.5 ^a	2 ^a	3 ^a	4 ^a	5 ^a					
Informed Consent/Assent ^a	x																									
Complete medical history, including family history of HBV	x																									
Physical examination	x																									
Symptom-directed physical examination		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x									
Vital signs	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x									
Weight ^a	x	x ¹	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x									
Height ^{a,2}	x	x ¹				x ¹	x ¹	x ¹	x ¹				x			x	x									
Parental height ¹		x																								
Ultrasound ^a	x																									
Ophthalmology exam ¹	x																									

^a Or upon and following study treatment withdrawal.

GDSR Browser
Global Data Science Repository Browser

Home | Biomedical Concepts | Data Collection | Data Tabulation | Resources | Search

Schedule of Activities YV25718 C

Test document

Assessment/Procedure	Screen (days)	BL (days)	Treatment Period (weeks)																Initial 24 Weeks of Follow-Up (Week Post- End of Treatment)			Extended Long-Term Follow- Up Period (Year Post-End of Treatment Period)				
	-35 to -1	1	2	4	8	12	18	24	30	36	42	48	4	12	24	1	1.5	2	3	4	5					
Informed Consent/Assent	x																									
Complete medical history, including family history of HBV	x																									
Physical examination	x																									
Symptom-directed physical examination		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x										
Vital signs	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x										
Weight	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x										
Height	x	x				x	x	x	x				x			x										
Parental height		x																								
Ultrasound	x																									
Ophthalmology exam	x																									
Urine or serum HCG pregnancy test (selected subjects)	x																									

- owl:Thing (0 + 509)
 - sdm:StudyDesignElement (0 + 509)
 - sdm:Activity (0 + 455)
 - sdm:DefinedActivity
 - sdm:PlannedActivity (415)
 - sdm:StudyActivity (40)
 - sdm:Arm (2)
 - sdm:Cell (7)
 - sdm:CellReference (10)
 - sdm:Epoch (5)
 - sdm:Protocol
 - sdm:ProtocolVersion
 - sdm:Schedule (1)
 - sdm:Segment (7)
 - sdm:Study
 - sdm:StudyEvent (22)
 - sdm:TimingConstraint
 - sdm:Transition
 - sdm:Trigger
- skos:Collection
- skos:Concept
- skos:ConceptScheme

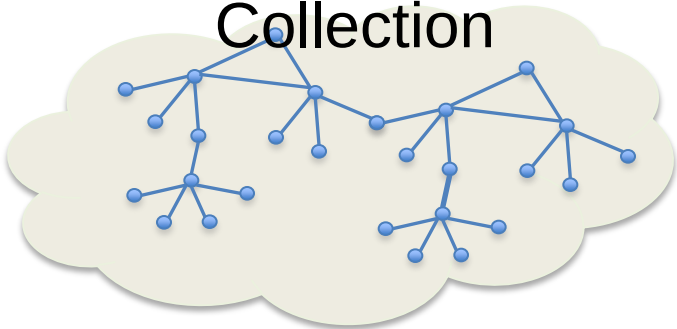
Web
Service

Schedule of Activities

Operational CRF and Submission CRF



Data Collection



Web Service



GDSR

Operational CRF
Modified Hachinski Ischemia Scale

Modified Hachinski Ischemia Scale (MHIS)

Form OID: MHIS
Form Source: Global Data Standards
Domain: Alzheimer
Form Layout: Single Form
Study Build Policy: Study Build Optional Form
SDTM Annotations: ZA = Clinical Findings
ZA.ZACAT = 'MODIFIED HACHINSKI ISCHEMIA SCALE'

	Field Label	Field OID	Format	Dictionary	SDTM Annotation
R	Was the Modified Hachinski Ischemia Scale performed?	MM.HPF	\$3	YES_NO_V1	ZA.ZASTAT, if assessment performed = 'No'
R	☐ Yes				
R	☐ No				
R	Date of assessment	MM.HID	dd-MMM-YYYY		Date part of ZA.ZADTC
R	Rater initials	RA.NIT	\$3		ZA.EVALID in SUPP2A
R	1. Abrupt onset	MM.HAM1	\$11	PRESENT_ABSENT_V1_REVIEW	ZA.ZAORRES ZA.ZATESTCD = 'MHIS01'
R	☐ Absent = 0				
R	☐ Present = 2				
R	2. Stepwise deterioration	MM.HAM2	\$11	PRESENT_ABSENT_V1_REVIEW	ZA.ZAORRES ZA.ZATESTCD = 'MHIS02'
R	☐ Absent = 0				
R	☐ Present = 2				

Download Date: 03.12.2013

Page 5 of 17

Status: Standard as of 03.12.2013

GDSR

Submission CRF
Neurological Exam

Neurological Exam

ZA = Clinical Findings
ZA.ZACAT = 'NEUROLOGICAL EXAMINATION'

At the Screening visit, enter any findings/conditions on the General Medical History and Baseline Conditions form. After the screening visit, enter any new or worsened findings/conditions on the Adverse Event form.

Timepoint

ZA.ZATPT

Was a (neurological) examination performed?

Yes ☐

No ☐

If Yes, date of exam

ddmmYYYY

Date part of ZA.ZADTC

Enter the complete date in dd MM/yyyy format.

Time of exam

hhmm

Time part of ZA.ZADTC

Type of (neurological) examination performed

ZA.ZATESTCD (see Value Level Metadata, Clinical Findings)
ZA.ZATEST (see Value Level Metadata, Clinical Findings)

Exam performed?

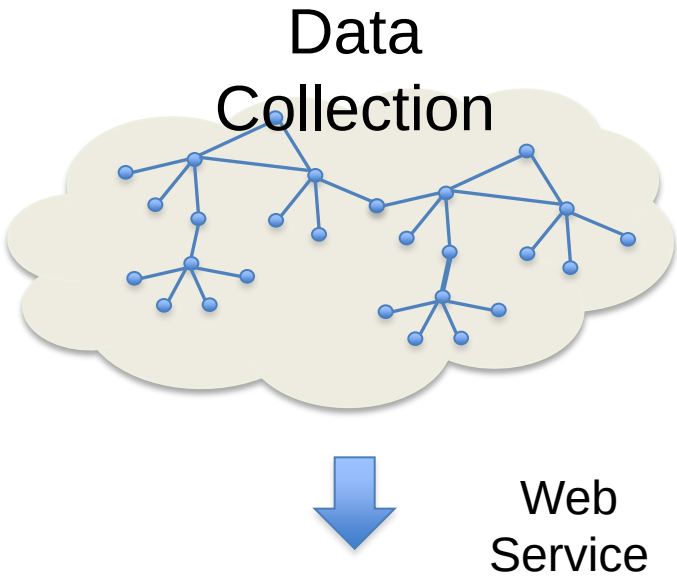
Yes ☐
No ☐

ZA.ZASTAT, if test done = 'No'

Download Date: 03.12.2013

Page 8 of 17

Status: Standard as of 03.12.2013



1	OID	Ordinal	DraftFormName	DraftFormActive	HelpText
2	ALZHX	1	Alzheimer Disease History		
3	MHS	2	Modified Hachinski Ischemia Scale		
4	NE	3	Neurological Exam		
5	SCHZX	4	History of Schizophrenia		
6	CGINFO1	5	Caregiver Information (Screening)		
7	CGINFO2	6	Caregiver Information (Post Screening)		

1	DataDictionaryName	CodedData	Ordinal	UserDataString	Specify
2	CAREGIVER_DATA_V1		1	In person	FALSE
3	CAREGIVER_DATA_V1		2	By phone	FALSE
4	CAREGIVER_DATA_V1		3	Not at all	FALSE
5	CAREGIVER_DATA_V2		1	Family member living with subject	FALSE
6	CAREGIVER_DATA_V2		2	Family member not living with subject	FALSE
7	CAREGIVER_DATA_V2		3	Professional caregiver	FALSE
8	CAREGIVER_DATA_V2		4	Friend/Neighbor	FALSE
9	CAREGIVER_DATA_V2	OTHER	5	Other	FALSE
10	DURATION_V1		1	6 months and < 1 years	FALSE
11	DURATION_V1		2	1 to <= 5 years	FALSE
12	DURATION_V1		3	> 5 years	FALSE
13	NORMAL_ABNORMAL_V4	NORMAL	1	Normal	FALSE
14	NORMAL_ABNORMAL_V4	ABNORMAL	2	Abnormal	FALSE
15	NUMERIC_VALUE_V5		1	0	FALSE
16	NUMERIC_VALUE_V5		2	1	FALSE
17	NUMERIC_VALUE_V5		3	2	FALSE
18	NUMERIC_VALUE_V5		4	3	FALSE
19	NUMERIC_VALUE_V5		5	4	FALSE
20	PRESENT_ABSENT_V1_REVIEW		1	Absent = 0	FALSE

Resource Form

Name:

Annotations

Incoming References

← raves:checkActionOf

- CheckAction.GEA_V1_FORMS.01
- CheckAction.GEA_V1_FORMS.02
- CheckAction.GEA_V1_FORMS.03
- CheckAction.GEA_V1_FORMS.04

← raves:checkStepOf

- CheckStep.GEA_V1_FORMS.01
- CheckStep.GEA_V1_FORMS.02

rdf:type

- raves:Annotation.CheckStep

mdr:administrationRecord

- mdr:AR.GDSII

mdr:context

- mms:Model.PD-Biometrics.Rave

raves:checkStepFunction

- CheckStepFunction.IsNotEmpty

raves:checkStepOf

- Check.GEA_V1_FORMS

raves:checkStepOrdinal

- 2

Other Properties

mdr:administrationRecord

- mdr:AR.GDSII

mdr:context

- mms:Model.PD-Biometrics.Rave

raves:checkActive

- true

raves:checkBypassDuringMigration

- true

raves:checkInfix

- If VISD in Visit Date in Visit 1 with record position 0 IsNotEmpty then... add the "Hypoglycemic Events" form to the current folder, and add the "Home Glucometer Readings (for hypoglycemic events)" form to the current folder, and add the "Allergic Reaction Events" form to the current folder, and add the "Pancreatitis Events" form to the current folder

raves:checkName

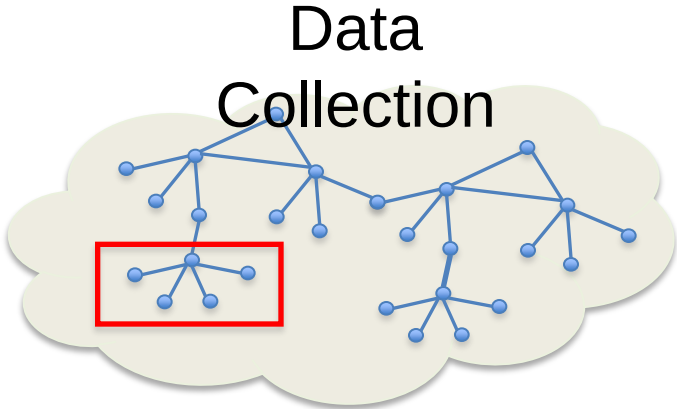
- GEA_V1_FORMS

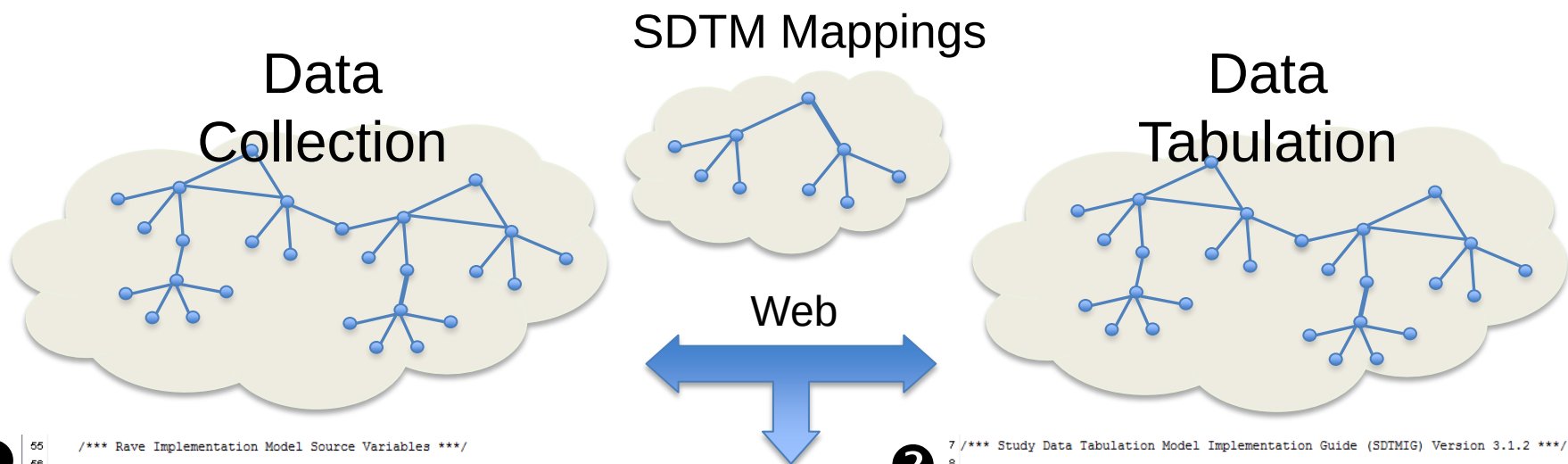
raves:checkNeedsRetesting

- false

rdf:type

- raves:Annotation.Check





1

```
55  /** Rave Implementation Model Source Variables **/  
56  
57  set source.vt1s1 (  
58    keep =  
59      vtlrec  tmptc   vtld   vltm   vltmu   temp   tempu  
60      method pulse  pulseu resp  respu  vspos  bps  
61      bpd    bpu    wt    wtu    ht     bmi  
62      bmiu   bsa    bsau   o2sat  o2satu vsloc  
63  
64    rename = (  
65      vtlrec = rave_vtlrec /* Vital Signs Recorded At This Visit */  
66      tmptc  = rave_tmptc  /* Planned Timepoint */  
67      vtld   = rave_vtld   /* Vital Signs Date */  
68      vltm   = rave_vltm   /* Vital Signs Time */  
69      vltmu  = rave_vltmu  /* Vital Signs Time Unknown */  
70      temp   = rave_temp   /* Temperature */  
71      tempu  = rave_tempu  /* Temperature Unit */  
72      method = rave_method /* Temperature Method */  
73      pulse  = rave_pulse  /* Pulse Rate */  
74      pulseu = rave_pulseu /* Pulse Unit */
```

Source Data

2

```
7  /** Study Data Tabulation Model Implementation Guide (SDTMIG) Version 3.1.2 **/  
8  
9  data work.vs (keep =  
10    studyid domain usubjid vsseq vsgrpid vsspid vstestcd  
11    vstest  vscat  vsscat  vspos vsorres vsorresu vsstresc  
12    vsstresn vsstresu vsstat vsreasnd vsloc vsmethod vsblfl  
13    vsdrvfl visitnum visit visitdy epoch vsdtc vsdy  
14    vstpt vstptnum vseltn vstptref vsrftdc vslat vsdir  
15  );  
16  
17  /** Domain VS Target Variables **/  
18  
19  attrib studyid label="Study Identifier" length=$8;  
20  attrib domain label="Domain Abbreviation" length=$2;  
21  attrib usubjid label="Unique Subject Identifier" length=$50;  
22  attrib vsseq label="Sequence Number" length=$8;  
23  attrib vsgrpid label="Group ID" length=$40;  
24  attrib vsspid label="Sponsor-Defined Identifier" length=$200;  
25  attrib vstestcd label="Vital Signs Test Short Name" length=$8;  
26  attrib vstest label="Vital Signs Test Name" length=$40;
```

Target Data

3

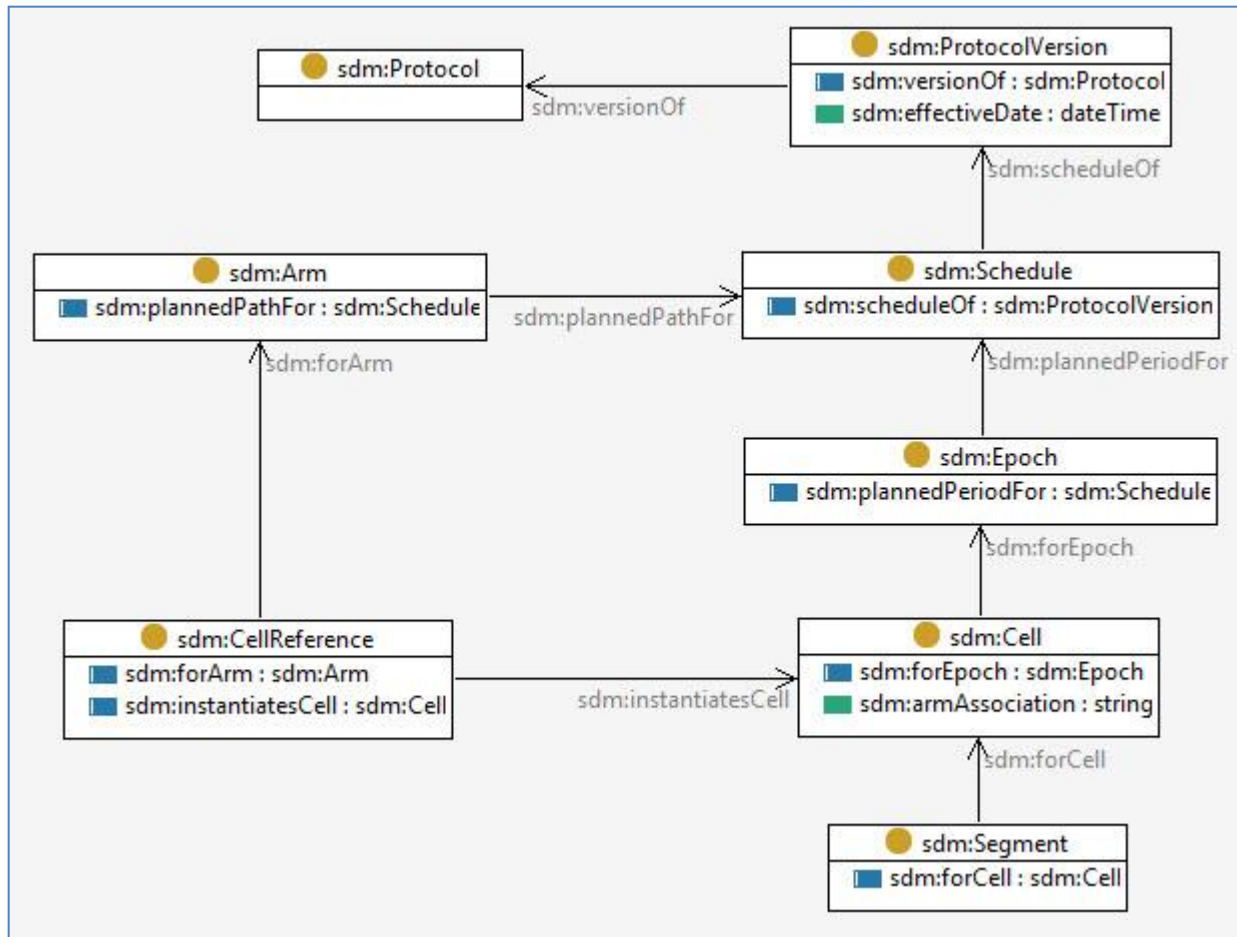
```
94  /** Mappings **/  
95  
96  %rave_to_iso8601(rawdate = rave_vtld, timevar = rave_vltm, isodate = vsdtc);  
97  vstpt = strip(rave_tmptc);  
98  
99  /** Temperature **/  
100  
101  vsorres = strip(rave_temp);  
102  vsorresu = strip(rave_tempu);  
103  output;  
104  
105  /** Pulse **/  
106  
107  vsorres = strip(rave_pulse);  
108  vsorresu = strip(rave_pulseu);  
109  output;
```

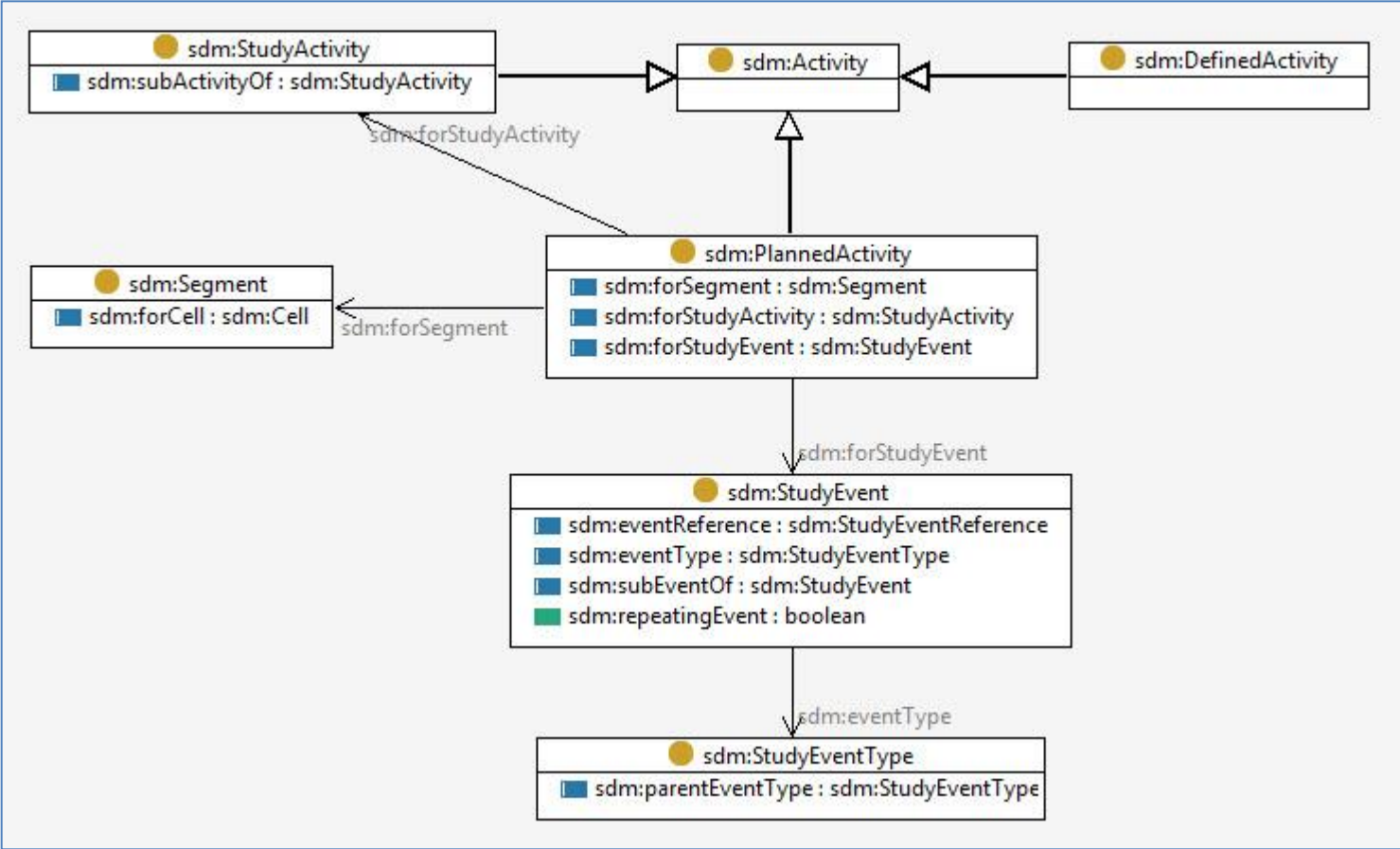
Mappings

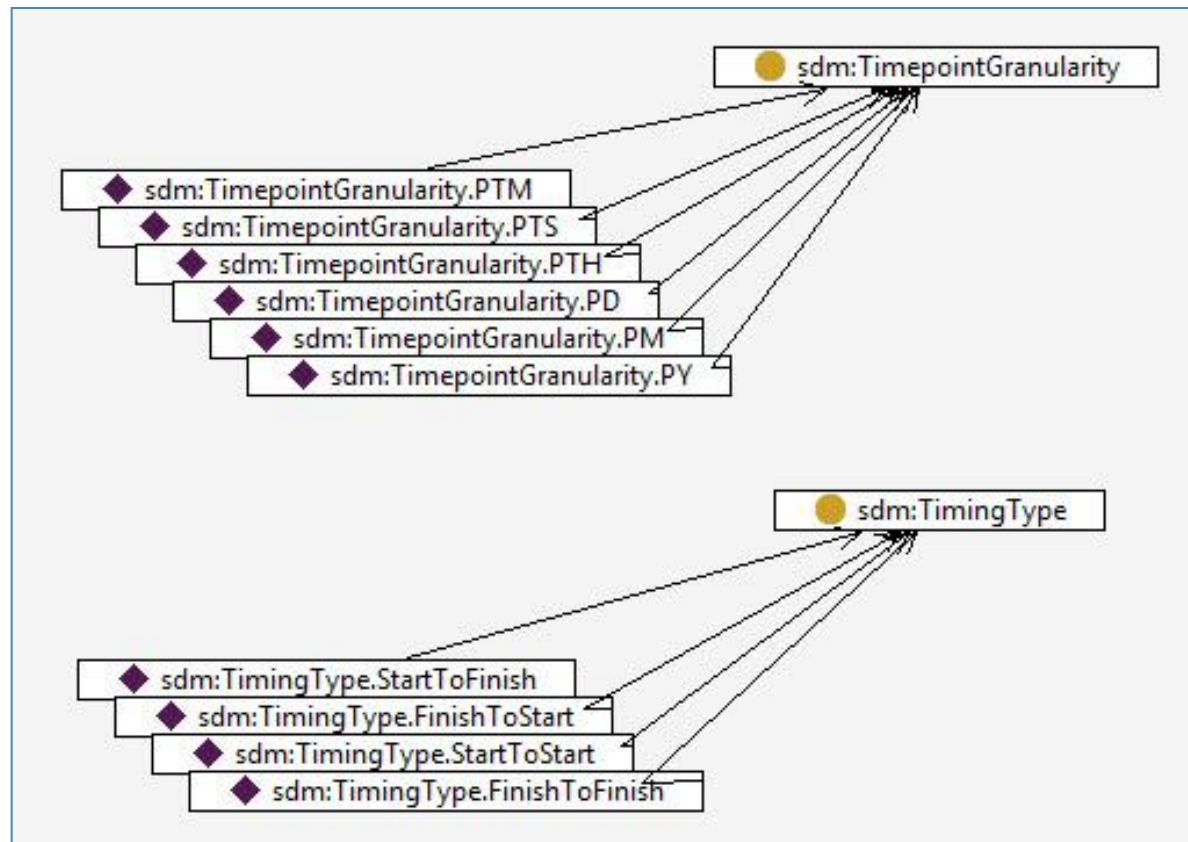
- Reuse of existing data standards
 - Reuse source data elements
 - SDTM target data elements
- Generate easy to understand SAS code
- Maximize platform independent code
- Support multiple target platforms
- Possible extensions
 - Generate mapping specifications
 - Generate conformance checks

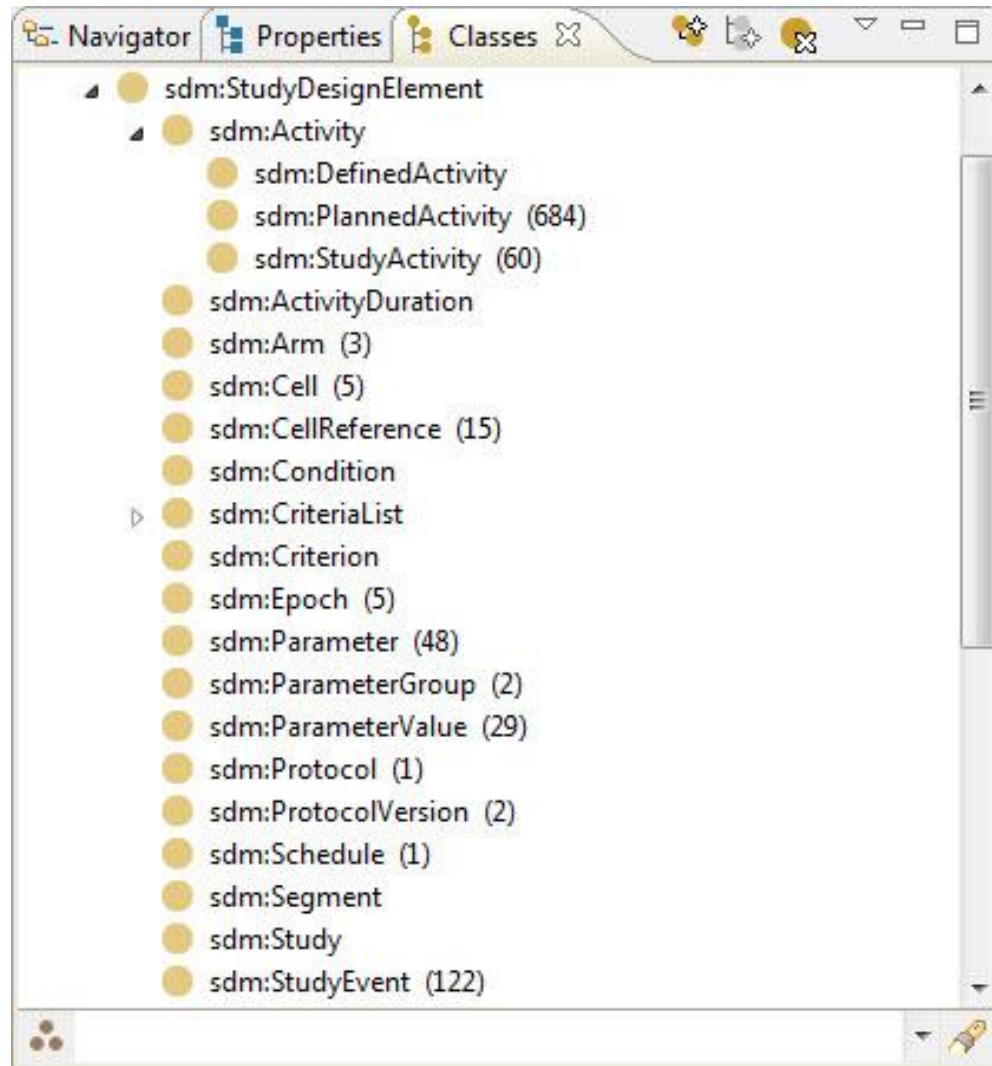
Schedule of Activities

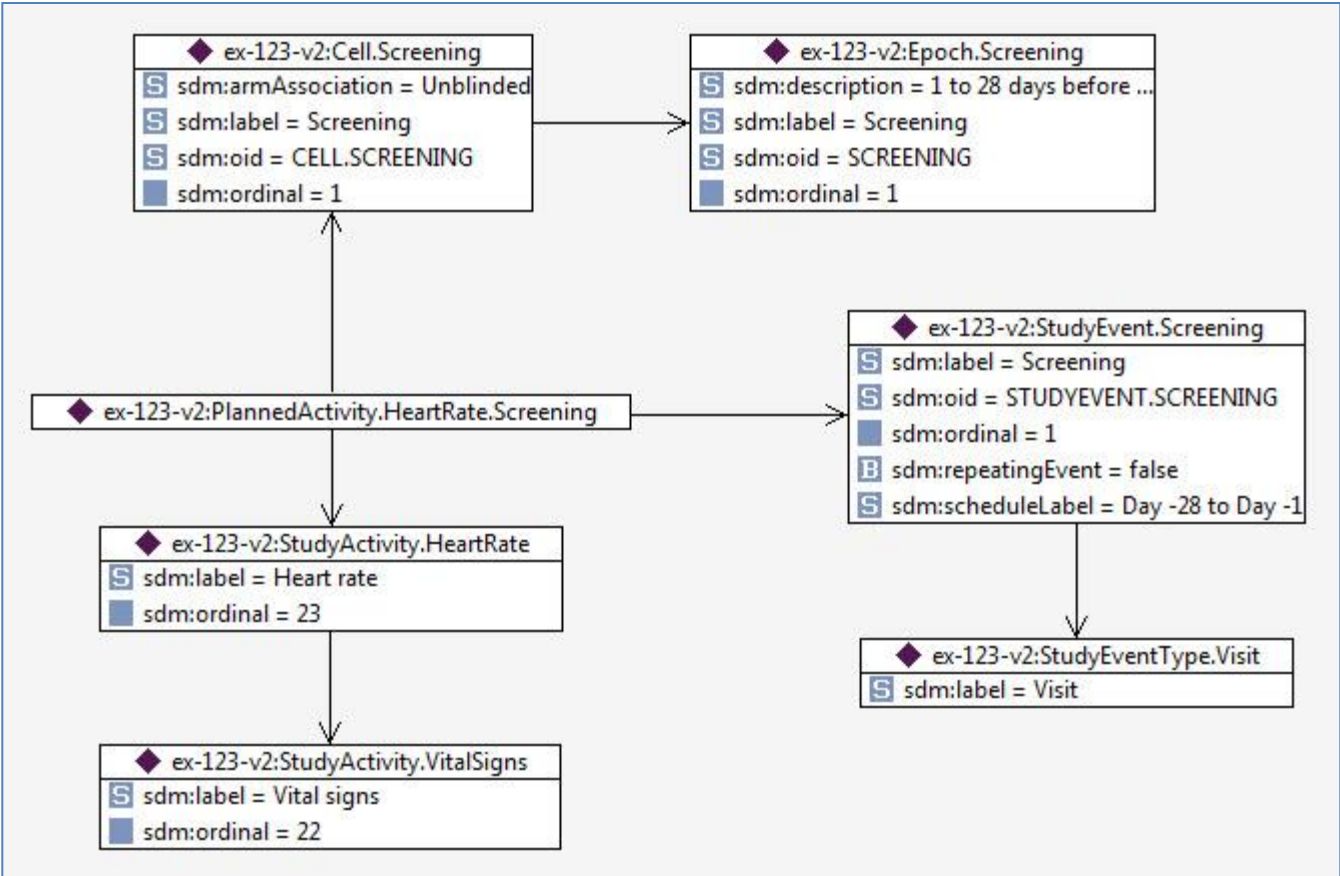
Arms and Epochs











- Full protocol too large to attack at once
- Schedule of Activities key for downstream automation
- Move data collection standards from forms to modules, research concepts, and data elements
- Hard, but necessary for first release
 - Handle protocol amendments
 - Integrate with data standard request process for new items
 - Enterprise integration (App, MDR, EDC, data platform, CTMS etc,)
- Business value
 - Less on the protocol side
 - Massive on automated EDC build
 - Massive on automated SDTM transformations
- Later stages
 - Link SoA to cost information
 - Integrate endpoints and data analysis standards
 - Component based authoring

- TransCelerate Common Protocol Template
 - Human readable protocol
 - Endpoints
 - Technology sub-team
- CDISC Protocol Concept List
 - Excel list, need to accelerate progress
 - Started with concept comparisons in different settings
- PhUSE
 - Prepared first half of 2013
 - Integrated in standards development, second half of 2014
- All these activities complement each other
- Concept Management is a key component to be successful
- End to end standards
 - Create CDISC standards for TA endpoints and activities
 - Link activities to data collection collection standards and metadata
 - Link endpoints to data analysis standards and metadata

Questions ?

