

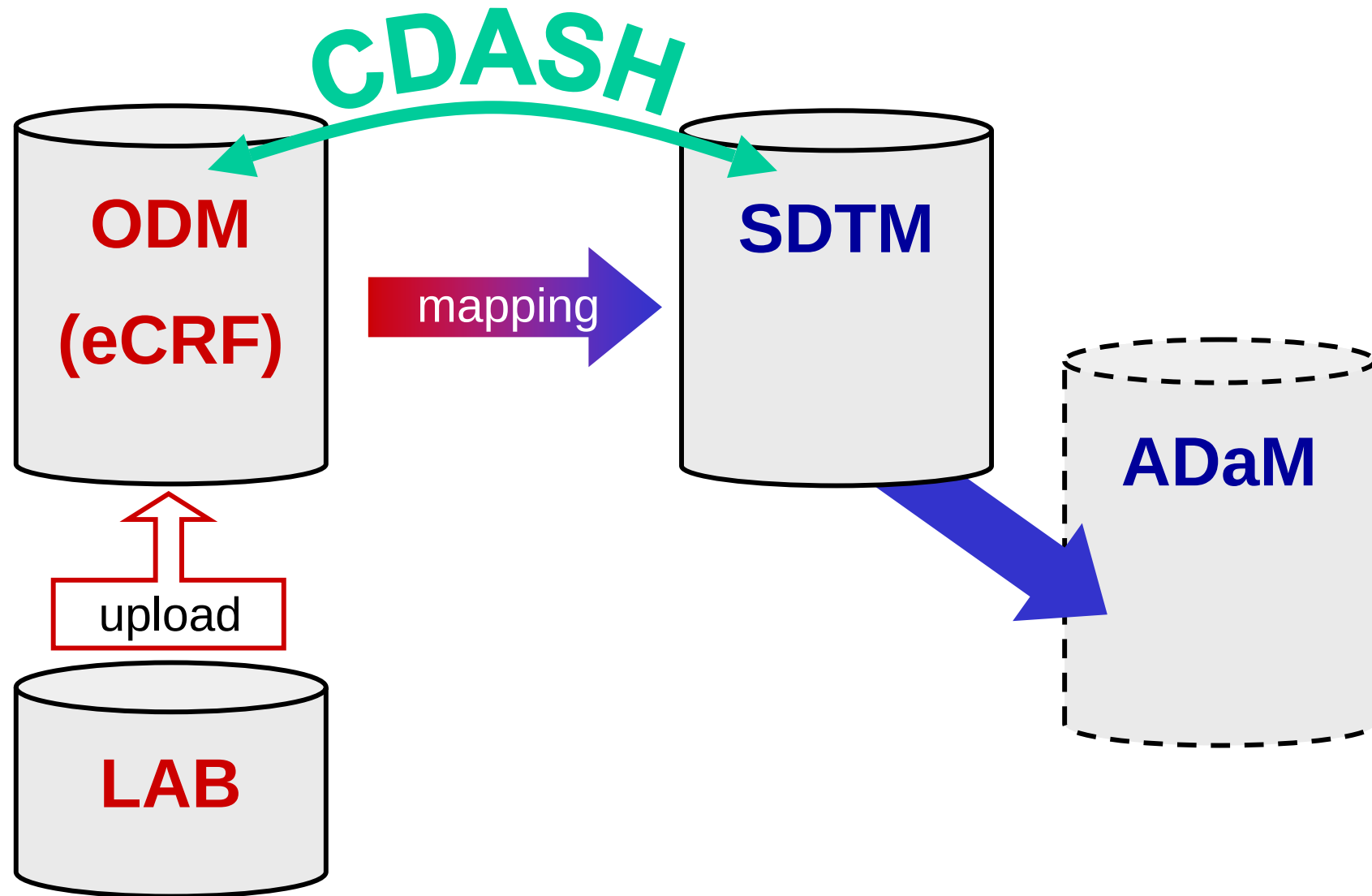
CDISC End-to-End using ODM, LAB and SDTM

PhUSE SDE in Basel

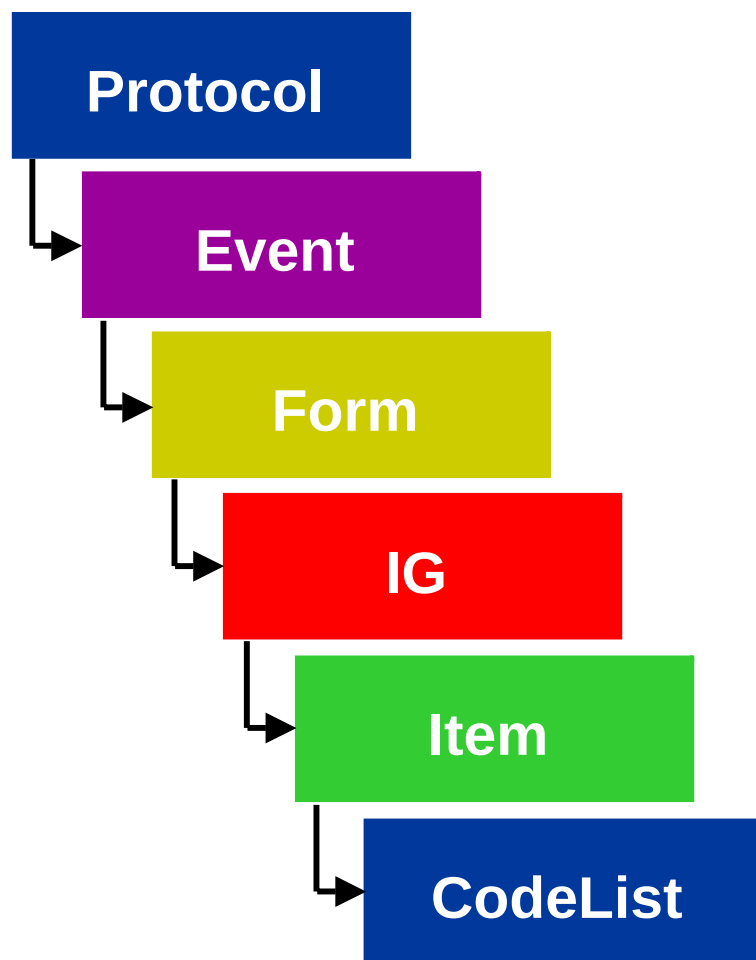
March 18, 2009

Kurt Hellstern

End-to-End?



eCRF based on ODM



ODM in plain XML:

```

1  <?xml version="1.0" encoding="UTF-8"?>
2  <!-- edited with XMLSpy v2006 rel. 3 U (http://www.altova.com) by Kurt Hellstern (Hands-on LLC) -->
3  <!--
4  *****
5  |Written by XClinical ODM Study Composer
6  |Author: Philippe Verplancke <philippe.verplancke@xcclinical.com> XClinical GmbH
7  |Info:  this is the first license
8  |*****
9  -->
10 <ODM xmlns="http://www.cdisc.org/ns/odm/v1.2" xmlns:xc="http://www.xclinical.com/xmlns/odm/xc-
Granularity="Metadata" FileOID="Export.493585239632820445" CreationDateTime="2008-10-28T05:27:
1.2" XClinicalVersion="marvin-2.0" AsOfDateTime="2008-10-28T05:55:48+01:00">
11   <Study OID="SNT-II-003">
12     <GlobalVariables>
13     <BasicDefinitions>
130    <MetaDataVersion OID="MDV.0.3" Name="Version 0.3">
131      <Protocol>
397      <StudyEventDef OID="Event.ENTRY.SCREEN" Name="Demographic Data" Repeating="No"
398      <FormRef FormOID="Form.DEMOG" OrderNumber="1" Mandatory="Yes"/>
399      </StudyEventDef>
400      <FormDef OID="Form.DEMOG" Name="Demographic Data" Repeating="No">
401      <ItemGroupRef ItemGroupOID="IG.BASE" OrderNumber="1" Mandatory="Yes"/>
402      </FormDef>
403      <ItemGroupDef OID="IG.BASE" Name="Demographic Data" Repeating="No">
404      <ItemRef ItemOID="Item.DM.INITIALS" OrderNumber="2" Mandatory="Yes"/>
405      <ItemRef ItemOID="Item.DM.SEX" OrderNumber="3" Mandatory="Yes"/>
406      <ItemRef ItemOID="Item.DM.AGE" OrderNumber="4" Mandatory="Yes"/>
407      <ItemRef ItemOID="Item.DM.RACE" OrderNumber="6" Mandatory="Yes"/>
408      <ItemRef ItemOID="Item.DM.RACEOTH" OrderNumber="7" Mandatory="No"/>
409      </ItemGroupDef>
410      <ItemDef OID="Item.DM.BIRTHDTC" Name="Date of Birth" DataType="date" Length="10">
411      <Question>
412      <TranslatedText xml:lang="en">Date of birth</TranslatedText>
413      </Question>
414      </ItemDef>
415      <CodeList OID="CodeList.RACE" Name="Race" DataType="integer">
416      <CodeListItem CodedValue="1">
417      <Decode>
418      <TranslatedText xml:lang="en">Caucasian/white</TranslatedText>
419      </Decode>
420      </CodeListItem>
421      <CodeListItem CodedValue="2">
422      <Decode>
423      <TranslatedText xml:lang="en">Black</TranslatedText>
424      </Decode>
425      </CodeListItem>
426      <CodeListItem CodedValue="3">
427      <Decode>
428      <TranslatedText xml:lang="en">Oriental</TranslatedText>
429      </Decode>
430      </CodeListItem>
  
```

Schedule of Assessments and ODM

	Screening	Baseline		Visit	Event	Visit	Follow-up
Months			Day 1	1		6	7
Informed consent	X	confirm.					
Inclusion/Exclusion criteria	X	confirm.					
Form	X	confirm.					
Previous medication	X	confirm.					
Vital signs	X	X		X		X	X
Physical examination	X	X		X		X	X
ItemGroup				X		X	X
				X		X	X
				X			
				X	X	X	X
Compliance				X	X	X	X
						X	

Are there any clinically relevant previous and ongoing diseases or procedures?

Yes

Q

ItemGroup

Smoking history

Has the patient ever smoked?

Yes

Q

Clinically Relevant Previous and Ongoing Diseases and Procedures (enter only one condition per box)

Description (precise medical terminology)

Thyreotoxic crisis with following

Q

Ongoing at Screening

Yes

Q

Please enter additional information onto the Concomitant Medications including Vitamins Form.

Is there a treatment related to this disease?

Yes

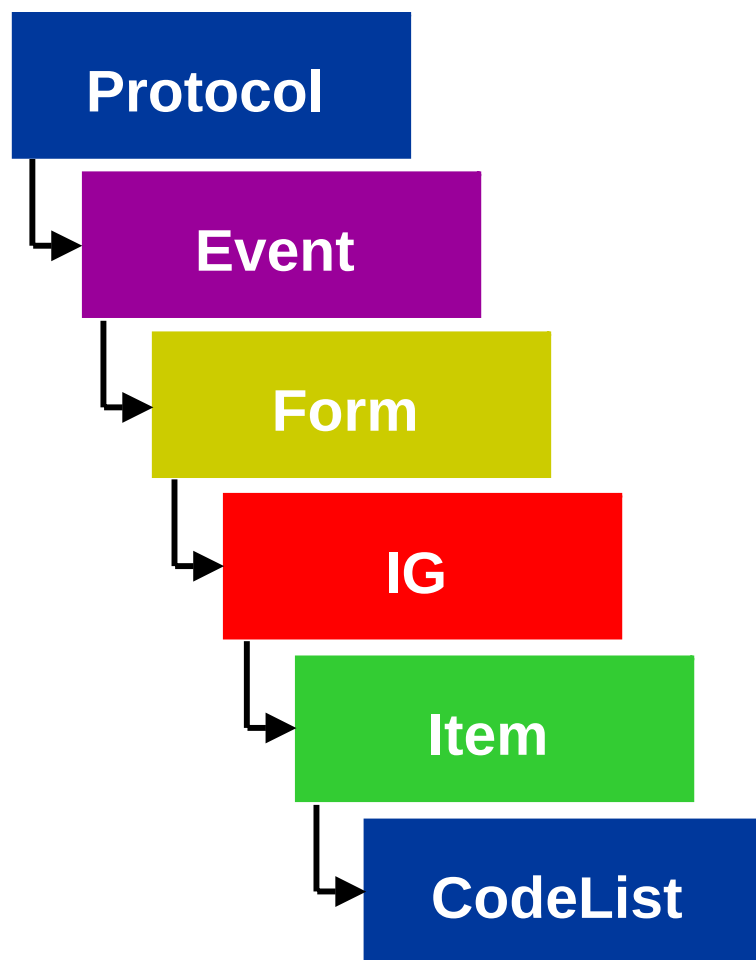
Q

HANDS ON

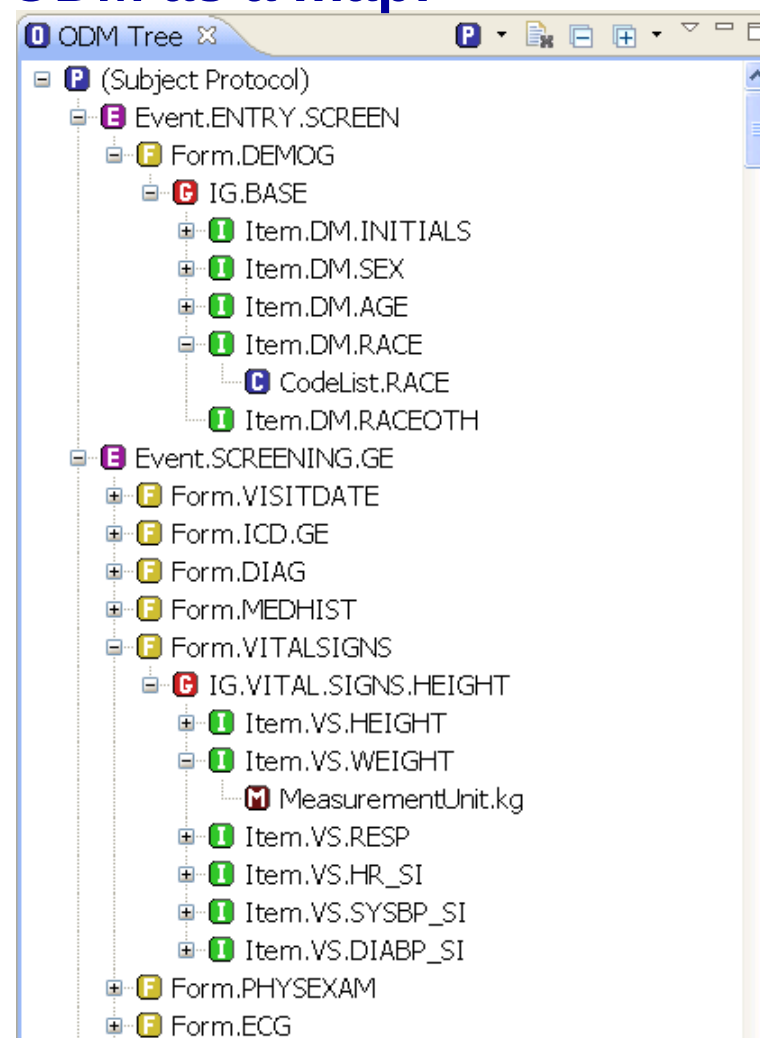
4

Survival Kit: A Ready to Use System

ODM in plain XML:



ODM as a map:



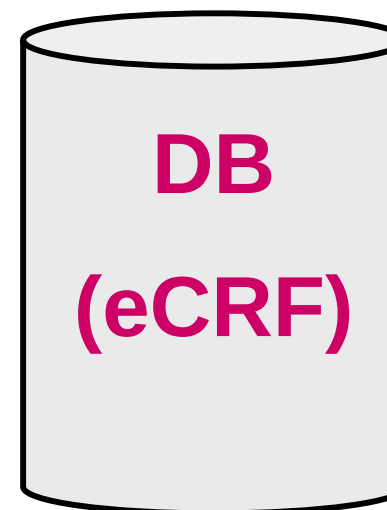
... Validated and CDISC Certified

```
1 <?xml version="1.0" encoding="UTF-8"?>
2 <!-- edited with XMLSpy v2006 rel. 3 U (http://www.altova.com) by Kurt Hellstern (Hands-on LLC) -->
3 <!--
4 *****
5 Written by XClinical ODM Study Composer
6 Author: Philippe Verplancke <philippe.verplancke@xcclinical.com> XClinical GmbH
7 Info: this is the first license
8 *****
9 -->
10 <!-- ODM xmlns="http://www.cdisc.org/odm/v1.2" xmlns:xc="http://www.xclinical.com/xm/odm/xc"
11 Granularity="Metadata" FileOID="Export.493585239632820445" CreationDateTime="2008-10-20T05:21:22"
12 XClinicalVersion="maven-2.0" AsOfDateTime="2008-10-28T05:55:48+01:00" -->
13 <Study OID="SMT-B003">
14 <GlobalVariables>
15 <BasicDefinitions>
16 <MetadataVersion OID="MDV.0.3" Name="Version 0.3">
17 <Protocol>
18 <StudyEventDef OID="Event.ENTRY.SCREEN" Name="Demographic Data" Repeating="No">
19 <FormRef FormOID="Form.DEMOG" OrderNumber="1" Mandatory="Yes"/>
20 </StudyEventDef>
21 </Protocol>
22 </BasicDefinitions>
23 </GlobalVariables>
24 <FormDef OID="Form.DEMOG" Name="Demographic Data" Repeating="No">
25 <FormItem OID="Item.DEMOG.1" Name="Patient ID" DataElement="Text" Length="10" Mandatory="Yes"/>
26 </FormItem>
27 </FormDef>
28 </Study>
29 </Study>
30 </Study>
31 </Study>
32 </Study>
33 </Study>
34 </Study>
35 </Study>
36 </Study>
37 </Study>
38 </Study>
39 </Study>
40 </Study>
41 </Study>
42 </Study>
43 </Study>
44 </Study>
45 </Study>
46 </Study>
47 </Study>
48 </Study>
49 </Study>
50 </Study>
```

ODM

Import

Export



... with a Graphical User Interface

The screenshot displays the Eclipse Platform GUI for the Study - Corellia02/Corellia-02.odm project. The interface is divided into several panels:

- Navigator:** Shows the project structure, including the (Subject Protocol) tree with various events and items.
- Definitions:** Lists the data definitions for the study, including items like SCHED.BG.VAL2, SCHED.TIME1, V5.CONDITION, V5.DIABP, V5.HEIGHT, V5.PULSE, V5.SYSBP, and V5.WEIGHT.
- Data Definition:** Provides a detailed view of the selected item, Item.V5.SYSBP. It includes fields for OID, Name, Binary, DataType, Length, SASFieldName, and SDSVarName. Below this, there are sections for Questions, Description, InformationTexts, CodeList reference, and MeasurementUnit references.

The Data Definition panel for Item.V5.SYSBP shows the following details:

- OID:** Item.V5.SYSBP
- Name:** Systolic blood pressure
- Binary:** No
- DataType:** integer
- Length:** 3
- SASFieldName:** SYSBP
- SDSVarName:**

The Questions section shows a question with the text "Systolic blood pressure".

The Description section shows the text "Systolic blood pressure measured in mmHg".

The InformationTexts section is currently empty.

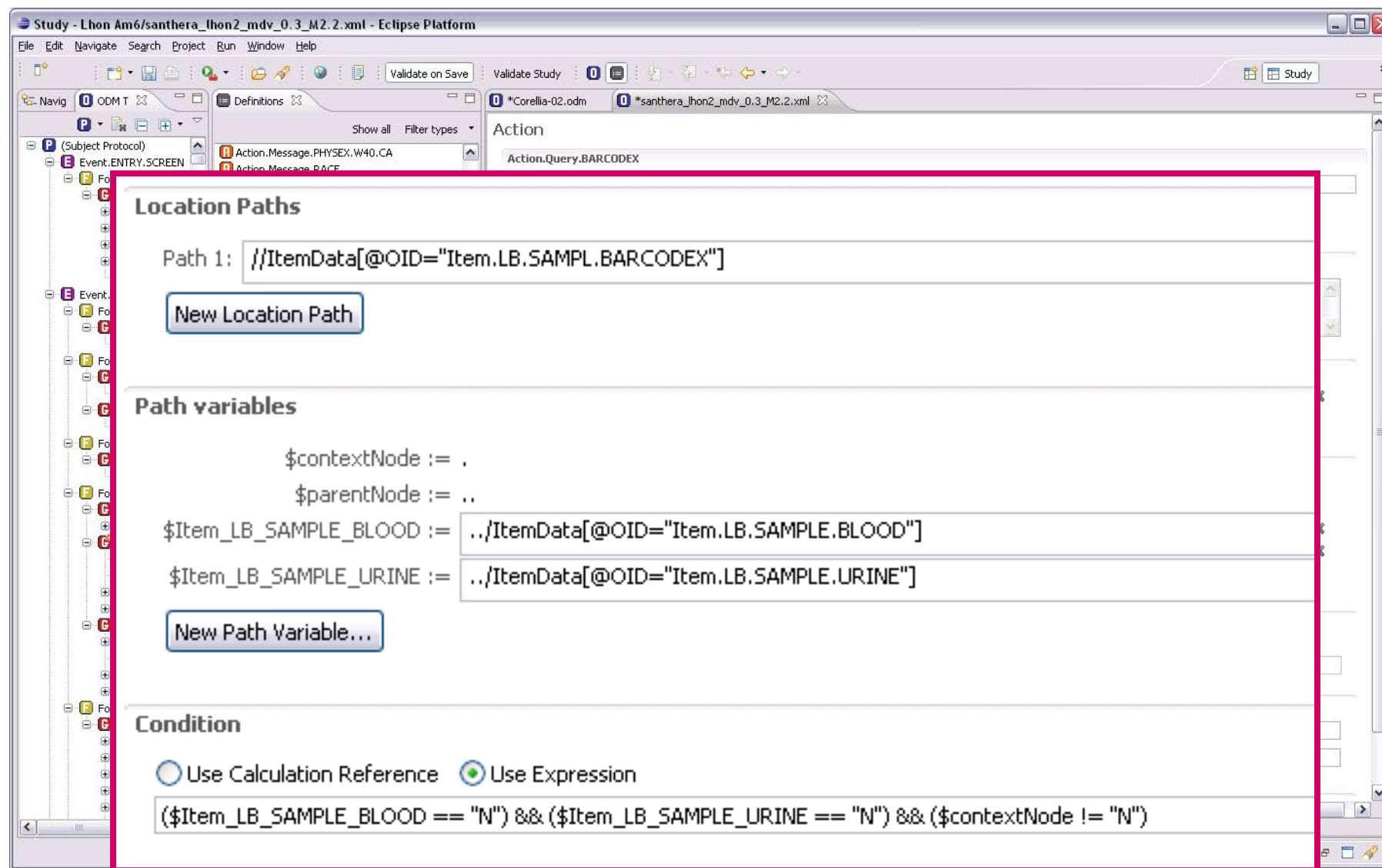
The CodeList reference section shows a table with the following data:

OID	
CodeList.AE_ACTION	
CodeList.AE_DEV	
CodeList.AE_OUTCOME	
CodeList.AE_REL	
CodeList.AE_SEV	
CodeList.ALBUM	
CodeList.BASE_MED_EVENT_TYPE	
CodeList.BGDEVICE	
CodeList.BPSTATE	
CodeList.COLOR	

The MeasurementUnit references section shows a table with the following data:

OID	Name
MeasurementUnit.mmHg	mercury column

... and Integrated Programming



Vendors are Progressing

ODM

The screenshot shows the CDISC website with a focus on ODM Certification. A red arrow points to the 'CDISC ODM CERTIFICATION' link in the right-hand navigation menu. The main content area features a section titled 'CDISC ODM Certification' with a brief description of the program and a table listing certified products.

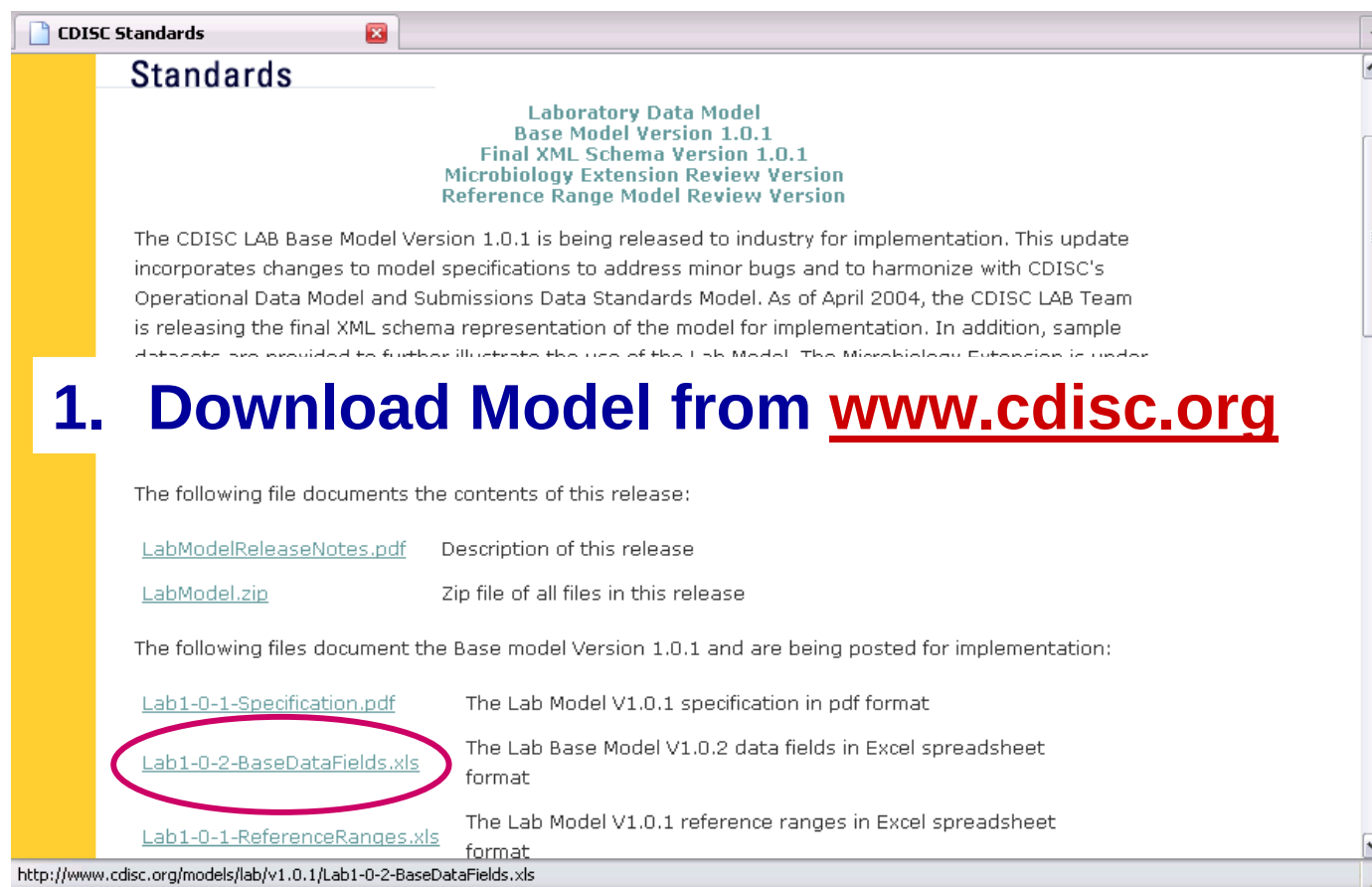
CDISC ODM Certification

The ODM Data Standard is increasingly recognized, as the ideal transport method for data across the entire clinical trial enterprise. In order to ensure consistency across toolsets and interoperability between ODM implementations, the ODM Certification Program has been developed. Click here to read the details and process for the [ODM Certification Program](#).

Following are details of products that have received CDISC ODM Certification:

	ODM Data Import				ODM Data Export			
	Snapshot		Transactional		Snapshot		Transactional	
	Metadata	Data	Metadata	Data	Metadata	Data	Metadata	Data
Company: ClinPhone (DataLabs) URL: www.clinphone.com Product: DataLabs Clinical Version: V4.1.2.1 build 11300 Date of Certification: 12-Jun-07 ODM Version: V1.2 (V1.2.1)				✓	✓	✓	✓	✓
Company: xClinical URL: www.xclinical.com Product: MARVIN Version: V1.7.7 Date of Certification: 12-June-07 ODM Version: V1.2 (V1.2.1)	✓				✓	✓		
Company: Medidata Solutions URL: www.mdsol.com Product: Medidata Designer					✓			

LAB – Take it Easy!



The screenshot shows a web browser window titled "CDISC Standards". The page content includes a list of standards: "Laboratory Data Model", "Base Model Version 1.0.1", "Final XML Schema Version 1.0.1", "Microbiology Extension Review Version", and "Reference Range Model Review Version". A paragraph describes the release of the CDISC LAB Base Model Version 1.0.1. Below this, a large blue number "1." is followed by the text "Download Model from www.cdisc.org". Underneath, it lists files for download: "LabModelReleaseNotes.pdf" (Description of this release) and "LabModel.zip" (Zip file of all files in this release). It then lists files for the Base model Version 1.0.1: "Lab1-0-1-Specification.pdf" (The Lab Model V1.0.1 specification in pdf format), "Lab1-0-2-BaseDataFields.xls" (The Lab Base Model V1.0.2 data fields in Excel spreadsheet format), and "Lab1-0-1-ReferenceRanges.xls" (The Lab Model V1.0.1 reference ranges in Excel spreadsheet format). The URL "http://www.cdisc.org/models/lab/v1.0.1/Lab1-0-2-BaseDataFields.xls" is visible at the bottom of the browser window. The link "Lab1-0-2-BaseDataFields.xls" is circled in red.

1. Download Model from www.cdisc.org

2. Agree details with Sponsor and central lab

3. Run test load / adapt specifications

LAB – the Details

	A	B	C	D	E	F	G	H
	FIELD NAME	REQD	SAS VARIABLE NAME	DEFAULT REPRESENTATION	MAX LEN	DATA TYPE	EXPLANATION	SUGGESTED CODELIST or CONSTANT
1								
27	Base Battery Level							
28	Battery Name	No	BATTRNAM	(none)	40	Text	The name of battery or panel to which the test belongs.	names according to BARC database
29	Base Test Level							
30	Lab Test ID	Yes	LBTESTCD	(none)	0	Text	The ID of the test performed as defined by the data provider.	Terms according CDISC SDTM in Appendix 2, mapped to Test Name
31	Lab Test Name	No	LBTEST	(none)	100	Text	The name of the test performed as defined by the data provider.	names according to BARC database
32	Test Status	Yes	TSTSTAT	(none)	2 (non CDISC standard)	Code	This indicates what the status of the test is. There are three test statuses: D - Done N - Not Performed X - Cancelled	codes as in BARC database, no sponsor mapping
33	Test Level Comments	No	TSTCOM	(none)	2048	Text	Free or standardized texts of all laboratory-generated comments relating to the specific test.	(none)
34	Base Result Level							
35	Reported Text Result	Cond.	RPTRESC	(none)	2048	Text or Coded	Reported text result by laboratory.	(none)
36	Reported Numeric Result	Cond.	RPTRESN	(none)	20	Numeric	Reported numeric result by laboratory.	(none)
37	Reported Numeric Result Precision	Cond.	RPTRESNP	(none)	5	Text	Reported numeric result precision at laboratory. Example: 5,3 - representing the total size of 5 with 3 positions to right of the decimal. (1.345)	(none)
38	Reported Reference Range Low	No	RPTNRLO	(none)	40	Text	Reported lower limit of reference range.	(none)
39	Reported Reference Range High	No	RPTNRHI	(none)	40	Text	Reported upper limit of reference range.	(none)
40	Reported Units	No	RPTU	(none)	20	Text or Coded	Reported result units by laboratory.	HL7 Common ISO derived units and ISO+ extensions
	Reported Result Type	Cond.	RPTRTYP	(none)	1	Code	This indicates what the type of the reported result is if the test was done. There are 6	N, T, G and or L

LAB – Loaded into the eCRF

... and amended by the investigator's evaluation of results outside of the normal range

POTASSIUM						
Reference Range Low	Result	Reference Range High	Alert	Evaluation	BARC Status	
3.1	4.1 mmol/L	5.1	N		D	☐ ▼

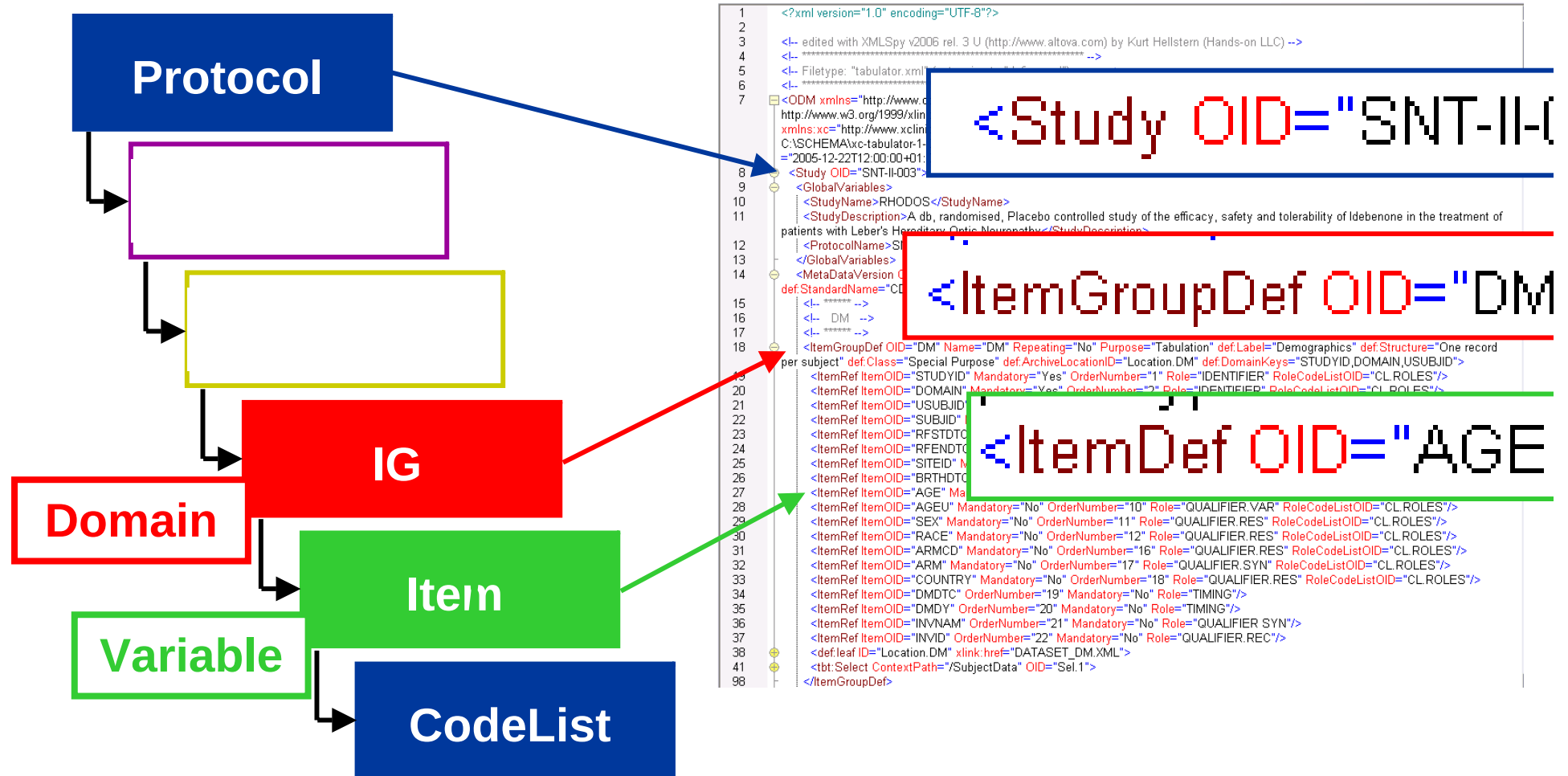
SODIUM						
Reference Range Low	Result	Reference Range High	Alert	Evaluation	BARC Status	
132	146 mmol/L	145	HN	Not clinically significant	D	☐ ▼

ALBUMIN						
Reference Range Low	Result	Reference Range High	Alert	Evaluation	BARC Status	
35	52 g/L	52	N		D	☐ ▼

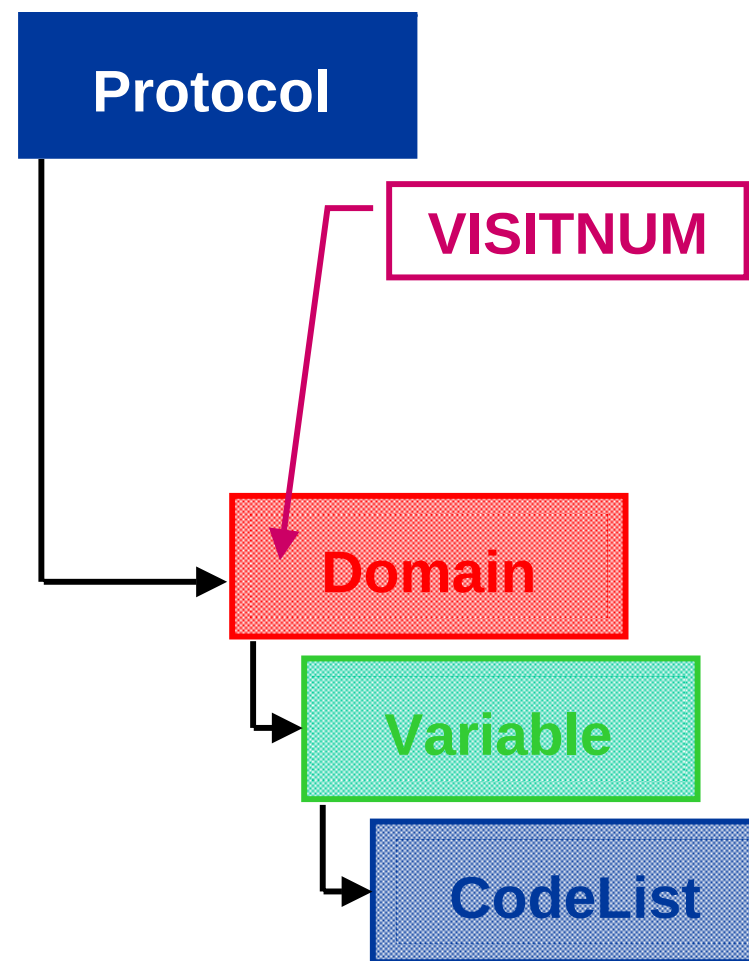
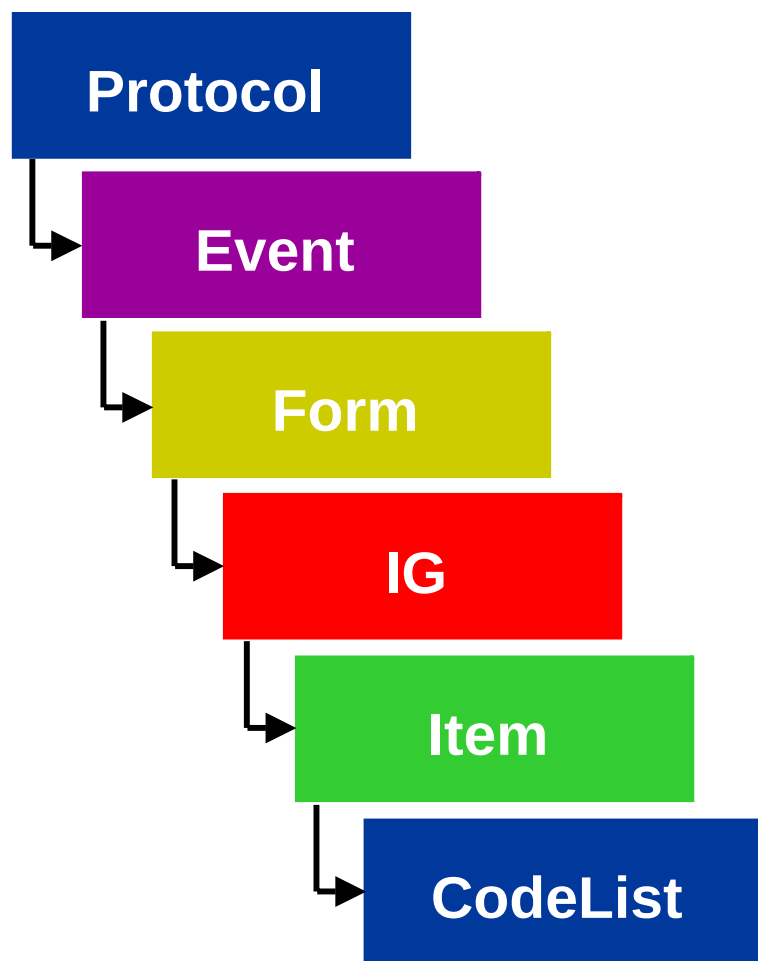
ALKALINE PHOSPHATASES						
Reference Range Low	Result	Reference Range High	Alert	Evaluation	BARC Status	
0	84 U/L	267	N		D	☐ ▼

All entries protected against changes – except
“Evaluation” in case of alerts not equal “N”

SDTM as Presented by CDISC



From ODM to SDTM



Item Names to Variable Names

- No requirements in ODM

Mandatory names in SDTM

- Container for precisely defined items

Specifications by --TESTCD, etc

- In some cases, names are equal, e.g. AETERM

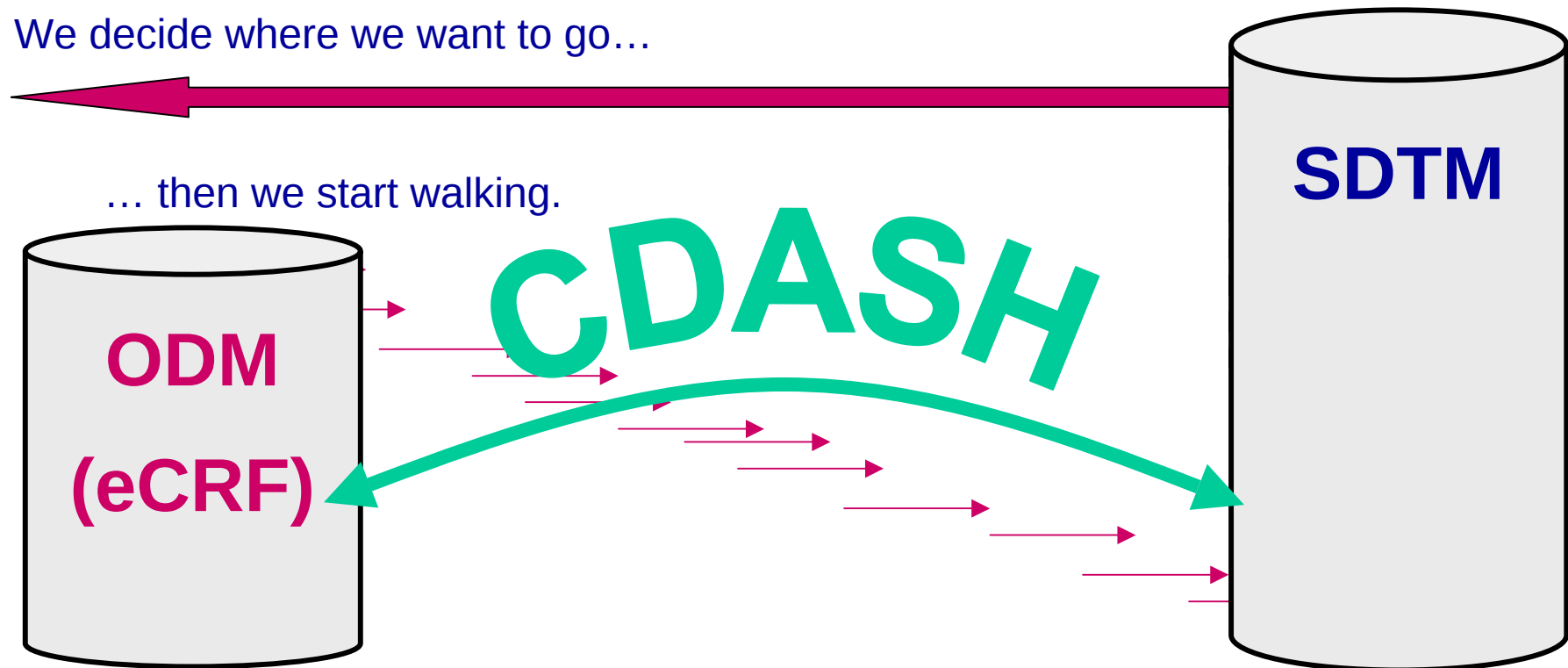


Think backwards – start at the end!

Preparation of eCRF

We believe in „Reverse Development“:

We decide where we want to go...



Why Two Standards?

CDASH (ODM)

- Recommended standard for the collection of data
- ... from a clinical, scientific and regulatory perspective

SDTM

- (Mandatory?) standard for the submission of data
- ...from an analysis and review perspective

overlapping

- Field/variable names and attributes if data are identical, e.g.
RACE, AETERM, EXTRT, EXDOSE, ect.

AE: Apparently a 1:1 Mapping

ODM(CDASH)

SDTM

Item in CRF

Var in AE Domain

Other Source

AEYN

--

AETERM

AETERM

AESTDAT

AESTDTC

AESTTIM

--

AEDY

derived

AESEV

AESEV

AEREL

AEREL

... not at all!

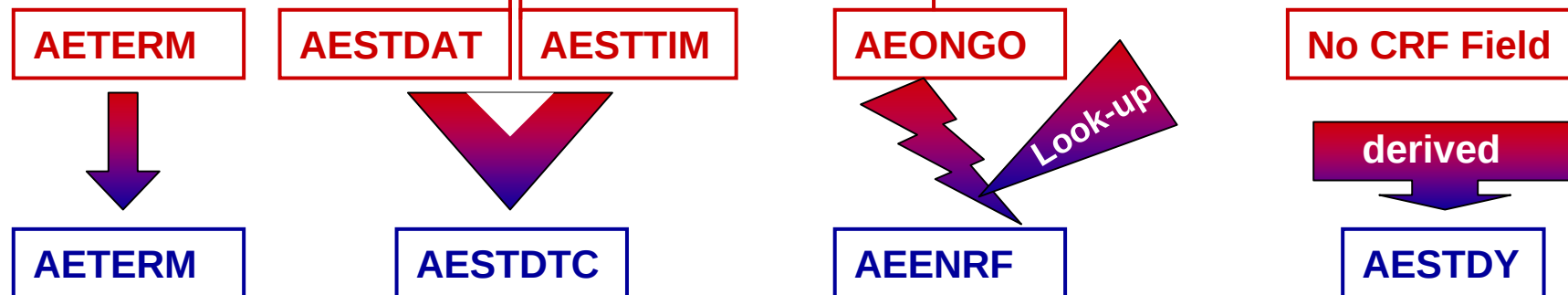
Patient Diary **AEYN**

Were the Adverse Events and Concomitant Medications recorded in the patient diary, transferred to the eCRF? Yes ☒

Was a patient diary handed out to the patient? Yes ☒

No Var in SDTM

Adverse Events								
Adverse event	Is this event serious?	Start Date	Start Time	End Date	End Time	Adverse event ongoing at final visit?	Severity	Causal Relationship
infectious gastroenteritis	No	27/06/2008	10:00	27/06/2008	10:00	No	Mild	Unrelated
headache	No	14/08/2008	14:30	15/08/2008	22:00	No	Mild	
stomach ache right site	No	[Unknown]		[Unknown]		No	Mild	



VS Domain

Item in CRF

DIASBP

Var in VS Domain

VSTESTCD

VSTEST

VSORRES

VSORRESU

VSORNRLO

VSORNOHI

VSDTC

VSDY

Add. Source

metadata

metadata

look-up table

look-up table

visit header: **VISDAT**

derived

--

VS Domain 1: Single Items in ODM

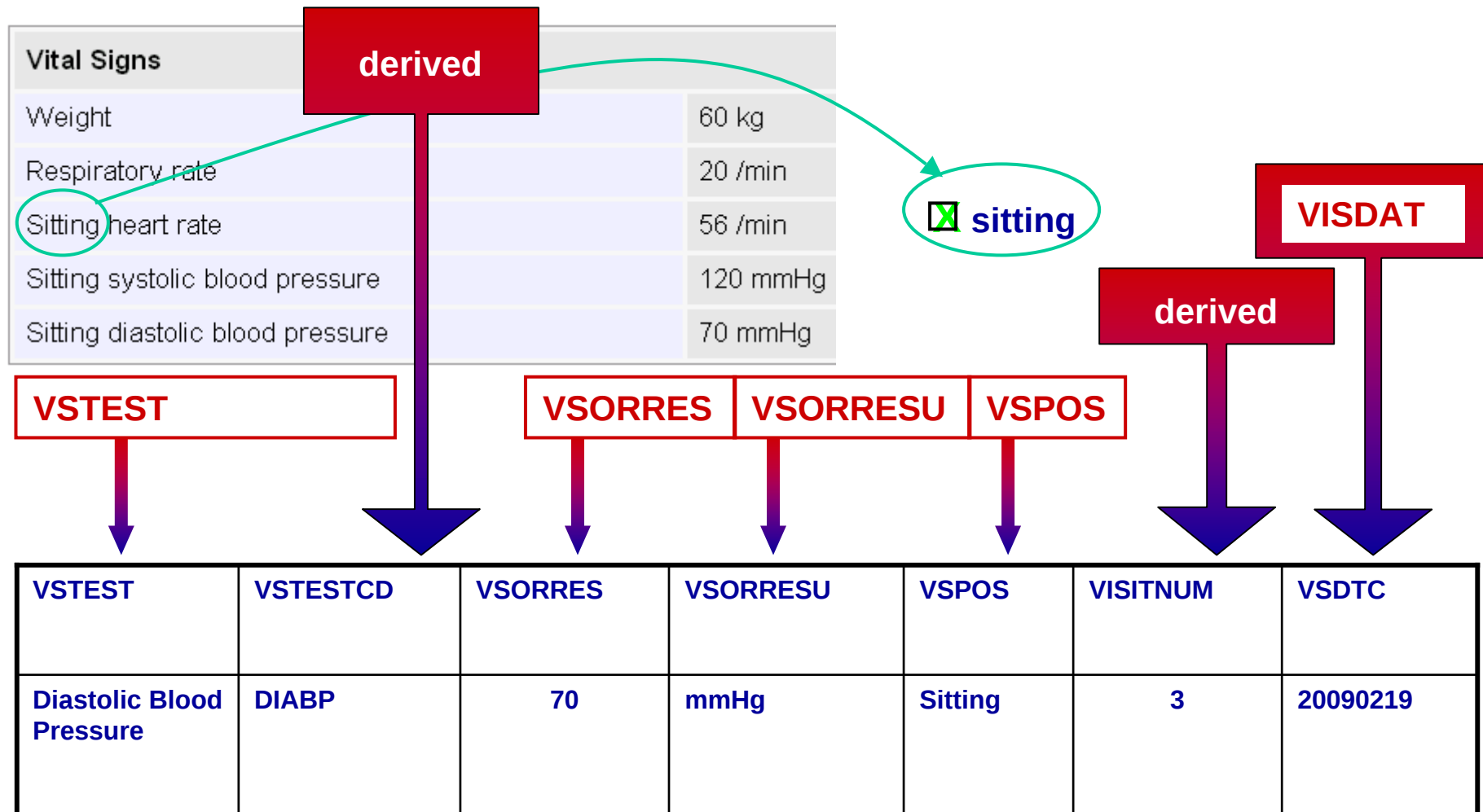
Vital Signs		
Weight	WEIGHT	60 kg
Respiratory rate	RESP	20 /min
Sitting heart rate	HR	56 /min
Sitting systolic blood pressure	SYSBP	120 mmHg
Sitting diastolic blood pressure	DIABP	70 mmHg

VSTEST	VSTESTCD	VSORRES	VSORRESU	VSPOS	VISITNUM	VSDTC
Diastolic Blood Pressure	DIABP	70	mmHg	Sitting	3	20090219

derived

VISDAT

VS Domain 2: Table Items in ODM



VS Domain 1 vs. 2: Discussion

- Do you define items like VSORRES related to VSTESTCD in your Data Management System or do you prefer to define items like SYSBP (Systolic blood pressure, numeric, 3.0, mmHG)?
- In both cases, there is mapping programming to be done.
- How do you build up your (company's) Meta Data Repository?

How to Program the Mapping?

1. SAS – Go the well known way
2. SAS – do it using PROC CDISC
3. Create a mapping using SQL, C, C++, ...
4. Use a ODM-SDTM mapping tool

... validated and CDISC Certified?

An Expl of a Mapping Tool with a GUI

The screenshot displays the Tabulator application interface within the Eclipse Platform. The main window is titled "Tabulator - LHON-SDTM/tabulator.tbt - Eclipse Platform". The interface is divided into several panes:

- Navigator:** Shows a hierarchical tree of data elements. The "Input ODM" pane is highlighted with a red box and labeled "ODM". It contains a tree structure starting with "Event.FUP.CA", "Event.AE", "Form.AE", "IG.AE_CORE1", and "Item.AE.SHORTTERM".
- Domains:** The central pane shows the "Properties" for a selected domain. The "Domain" is set to "CM". The "Domain OID" is "CM", "Domain Name" is "CM", "Label" is "Concomittant Medications", "Class" is "Interventions", "Structure" is "Zero to n records per subject", and "Repeating" is "Yes".
- Domain Columns:** A table at the bottom shows domain columns and their roles. It is highlighted with a blue box and labeled "SDTM".
- Domain Definition:** A table on the right lists domain definitions. It is highlighted with a blue box and labeled "Domain Definition".

The "Domain Columns" table is as follows:

OID	Mandatory	Role
STUDYID	Yes	IDENTIFIER
DOMAIN	Yes	IDENTIFIER
USUBJID	Yes	IDENTIFIER
CMSEQ	Yes	
CMTRT	Yes	
CMDECOD	No	
CMINDC	No	
CMDOSE	No	
CMROUTE	No	
CMSTDTOT	No	
CMROUTE	No	

The "Domain Definition" table is as follows:

OID	Name
CMDECOD	CMDECOD
CMDOSTOT	CMDOSTOT
CMDOSE	CMDOSE
CMENDTC	CMENDTC
CMENRF	CMENRF
CMINDC	CMINDC
CMROUTE	CMROUTE
CMSEQ	CMSEQ
CMSTDTOT	CMSTDTOT
CMTRT	CMTRT
DOMAIN	DOMAIN
STUDYID	STUDYID
USUBJID	USUBJID

The Mapping Program Window

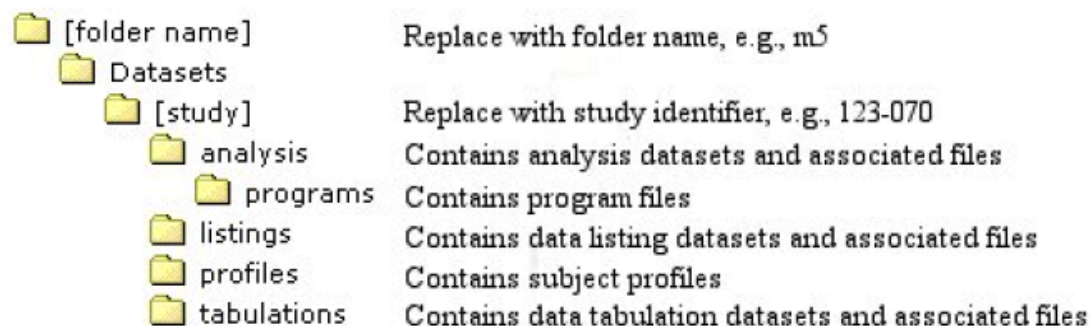
The screenshot displays the Tabulator Mapping Program Window, which is used for mapping ODM (Operational Data Model) data to SDTM (Standard Data Tabular Model) data. The window is divided into several panes:

- Navigator:** Shows the project structure, including ODM data sources like Event.FUP.CA, Event.AE, Form.AE, IG.AE_CORE1, and IG.MEDICATION.SHORT.
- Condition:** A text area for defining mapping conditions.
- Writers:** A list of data elements being mapped, such as STUDYID, DOMAIN, USUBJID, CMSEQ, CMTRT, CMDECOD, CMINDC, CMDOSU, CMDOSTOT, CMROUTE, CMSTDTC, CMENDTC, and CMENRF.
- SDTM:** A table showing the SDTM data elements and their corresponding ODM data sources. The table has columns for OID and Name.
- Mappings:** A table showing the mapping between ODM and SDTM data elements. The table has columns for ODM, SDTM, and Mapping.

Annotations in the image highlight the ODM, SDTM, and Mappings views. A red box labeled "ODM" points to the Navigator pane. A blue box labeled "SDTM" points to the SDTM table. A red box labeled "Mappings" points to the Mappings table. A blue arrow points from the "Mappings" table to the "Writers" list.

Tasks to Be Done:

1. Create analysis datasets (ADaM) → **Statistician**
2. Create the define.xml file
3. Store data and define.xml files in correct location in the eCTD



5. Wait on submission day

push the **submit** button...

Conclusions

- CDISC supporting tools are coming
- Not CDISC is the problem – it's the change
- CDASH – a starting point for a metadata repository
- CDASH – why not? Your names are not better!
- Increasing clarity of our communication
- Only practical experience brings us forwards

The Team:



eCRF & Database Design



**Programming &
Statistics**



MARVIN eCRF

eCRF Composer

SDTM Tabulator

**Please do not hesitate to send your
questions to
kurt.hellstern@hands-on.ch**