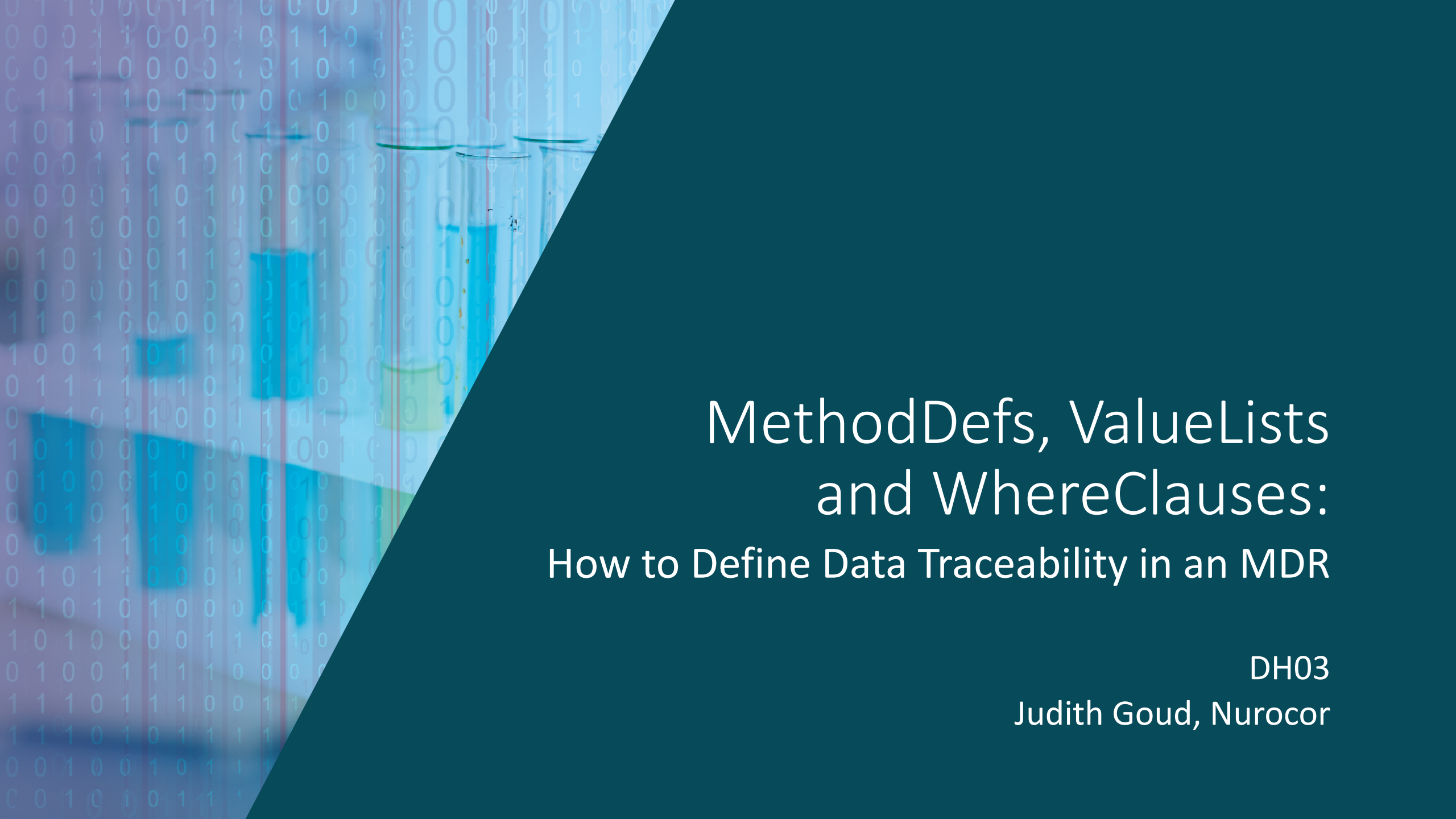




MethodDefs, ValueLists and WhereClauses: How to Define Data Traceability in an MDR

DH03

Judith Goud, Nurocor



Agenda

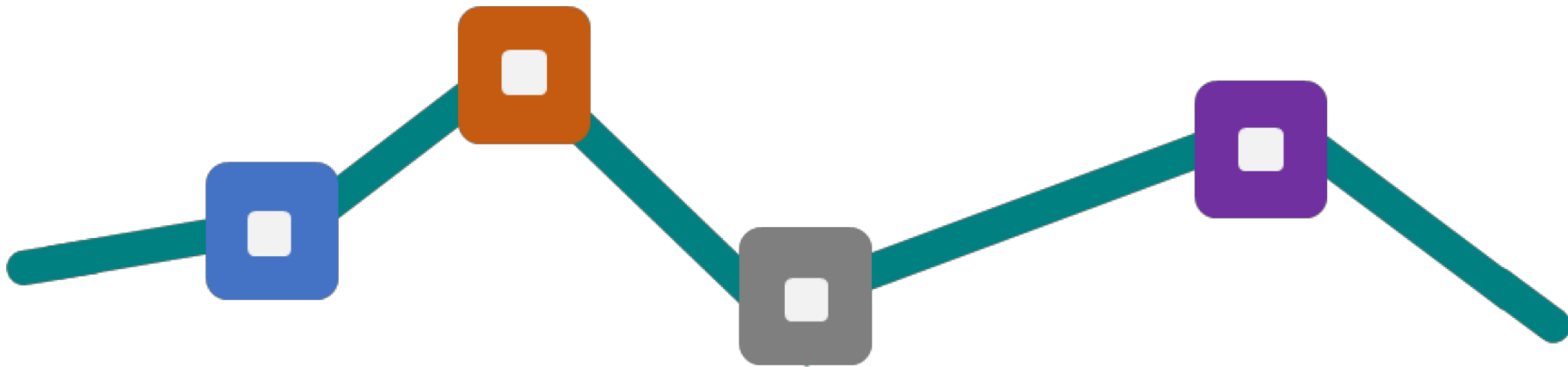
Data Traceability

Standards

Traceability in Clinical Development Systems

Conclusion

Data Traceability



Data Traceability Definition



Data Traceability Drivers

Regulatory requirements

- The US Food & Drug Administration states in their Study Data Technical Conformance Guide section 4.1.3.2.1:



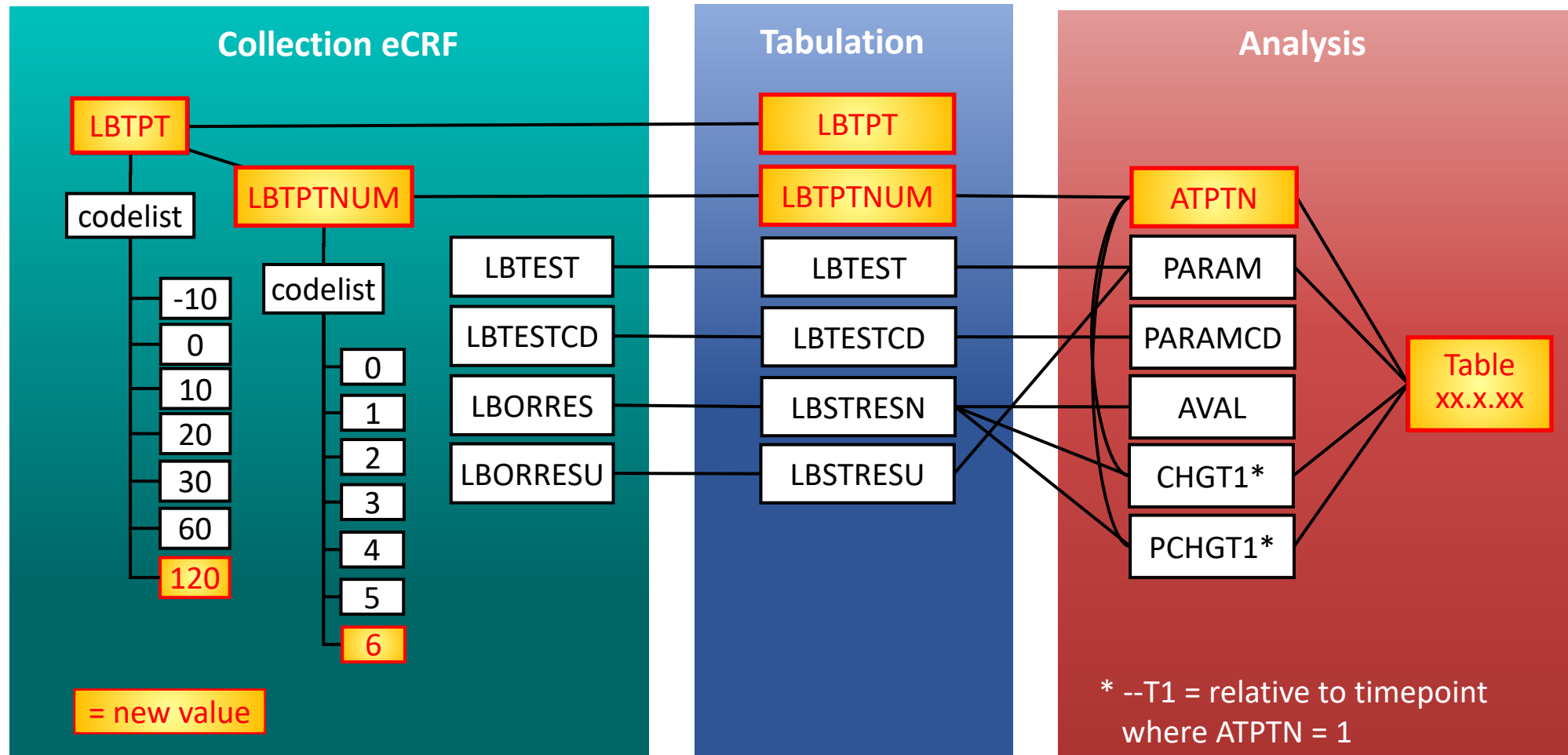
“it is very important that the results presented in the accompanying study report be traceable back to the original data collected”

- The Japanese Pharmaceutical and Medical Devices Agency Notification on Practical Operations of Electronic Study Data Submission asks in section 3(1)a(v) to:



“.. explain the traceability between the submitted data (such as the procedures in which both datasets were prepared, the relationship between the variables ..., and whether there was any information used during the preparation)”

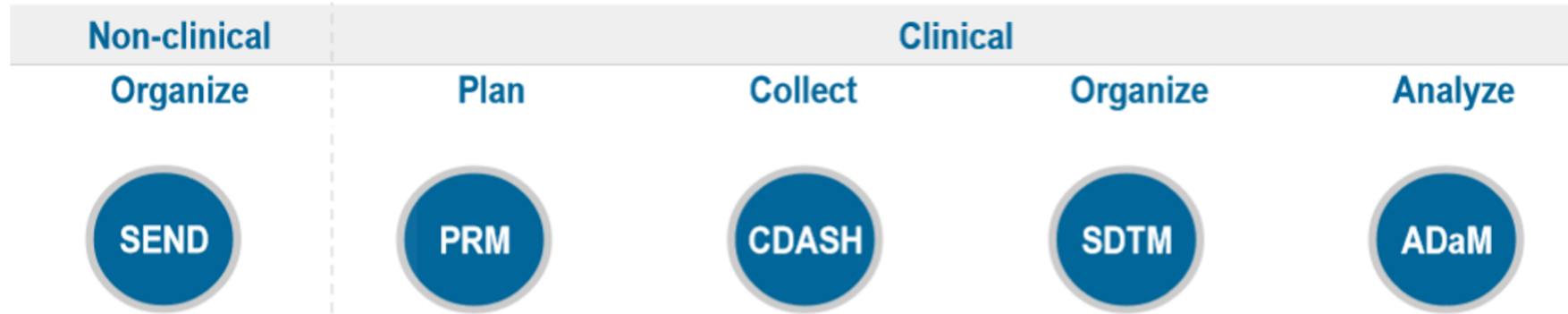
Business Process Efficiency



Standards



CDISC Standards

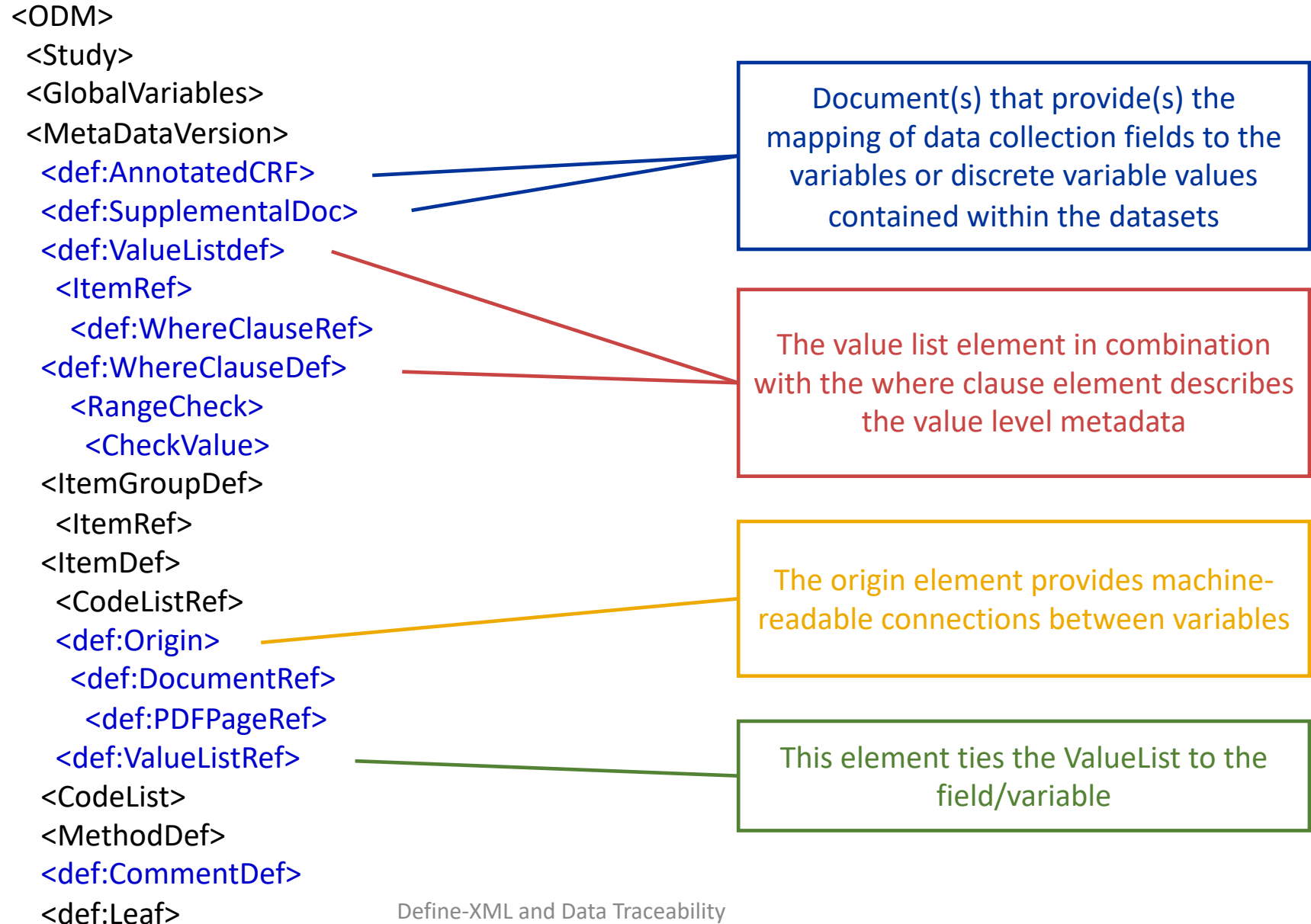


- Foundational standards defined separately for lifecycle stages
- Additional metadata needs to be defined to bridge the gaps between the lifecycle stages



- Define-XML standard is the only CDISC Data Exchange standard designed to describe data traceability

Define-XML Elements for Data Traceability



* elements in blue
are additional
compared to ODM

Derivation Example

Birth Month and Year	BRTHDTC BIRTHMO BRTHYY	__/____
Sex	SEX	☐ Female ☐ Male
Race	RACE	☐ American Indian or Alaska Native ☐ Asian ☐ Black or African American ☐ Native Hawaiian or Other Pacific Islander ☐ White

```

<ItemGroupDef OID="IG.DM" Domain="DM" Name="DM"
  <Description>
    <TranslatedText xml:lang="en">Demography</TranslatedText>
  </Description>
  <ItemRef ItemOID="IT.DM.BRTHDTC" OrderNumber="1" Mandatory="Yes" MethodOID="MT.BRTHDTC"/>
  ...
</ItemGroupDef>
<ItemDef OID="IT.DM.BRTHDTC" Name="BRTHDTC" DataType="date" Length="20" SASFieldName="BRTHDTC">
  <Description>
    <TranslatedText xml:lang="en">Date/Time of Birth</TranslatedText>
  </Description>
  <def:Origin Type="Derived">
</ItemDef>
<MethodDef OID="MT.BRTHDTC" Name="Algorithm to derive BRTHDTC" Type="Computation" >
  <Description>
    <TranslatedText xml:lang="en">Derived from BIRTHMO and BRTHYY, appending '01' for the day
      and concatenated into ISO 8601 format.</TranslatedText>
  </Description>
</MethodDef>

```

VLM Example

```
<ItemGroupDef OID="IG.VS" Domain="VS" Name="VS"
  <Description>
    <TranslatedText xml:lang="en">Vital Signs</TranslatedText>
  </Description>
  <ItemRef ItemOID="IT.VS.VSORRES" OrderNumber="2" Mandatory="Yes"/>
  ...
</ItemGroupDef>
<ItemDef OID="IT.VS.VSORRES" Name="VSORRES" DataType="text" Length="30" SASFieldName="VSORRES">
  <Description>
    <TranslatedText xml:lang="en">Result or Finding in Original Units</TranslatedText>
  </Description>
  <def:Origin Type="CRF">
    <def:DocumentRef leafID="LF.blankcrf">
      <def:PDFPageRef PageRefs="11" Type="PhysicalRef"/>
    </def:DocumentRef>
  </def:Origin>
  <def:ValueListRef ValueListOID="VL.VS.VSORRES"/>
</ItemDef>
```

Date	VSDTC VSDAT	__/__/__
Diastolic Blood Pressure	VSORRES where VSTESTCD = "DIABP" DIABP	__ __ __
Diastolic Blood Pressure Unit	VSORRESU where VSTESTCD = "DIABP" DIABPU	mmHg
Systolic Blood Pressure	VSORRES where VSTESTCD = "SYSBP" SYSBP	__ __ __
Systolic Blood Pressure	VSORRESU where VSTESTCD = "SYSBP" SYSBPU	mmHg

VLM Example (cont.)

```
<def:ValueListDef OID="VL.VS.VSORRES">
  <ItemRef ItemOID="IT.VS.VSORRES.DIABP" OrderNumber="1" Mandatory="Yes">
    <def:WhereClauseRef WhereClauseOID="WC.VS.VSTESTCD.DIABP"/>
  </ItemRef>
  <ItemRef ItemOID="IT.VS.VSORRES.SYSBP" OrderNumber="2" Mandatory="Yes">
    <def:WhereClauseRef WhereClauseOID="WC.VS.VSTESTCD.SYSBP"/>
  </ItemRef>
  ...
</def:ValueListDef>

<def:WhereClauseDef OID="WC.VS.VSTESTCD.DIABP">
  <RangeCheck SoftHard="Soft" def:ItemOID="IT.VS.VSTESTCD" Comparator="EQ">
    <CheckValue>DIABP</CheckValue>
  </RangeCheck>
</def:WhereClauseDef>

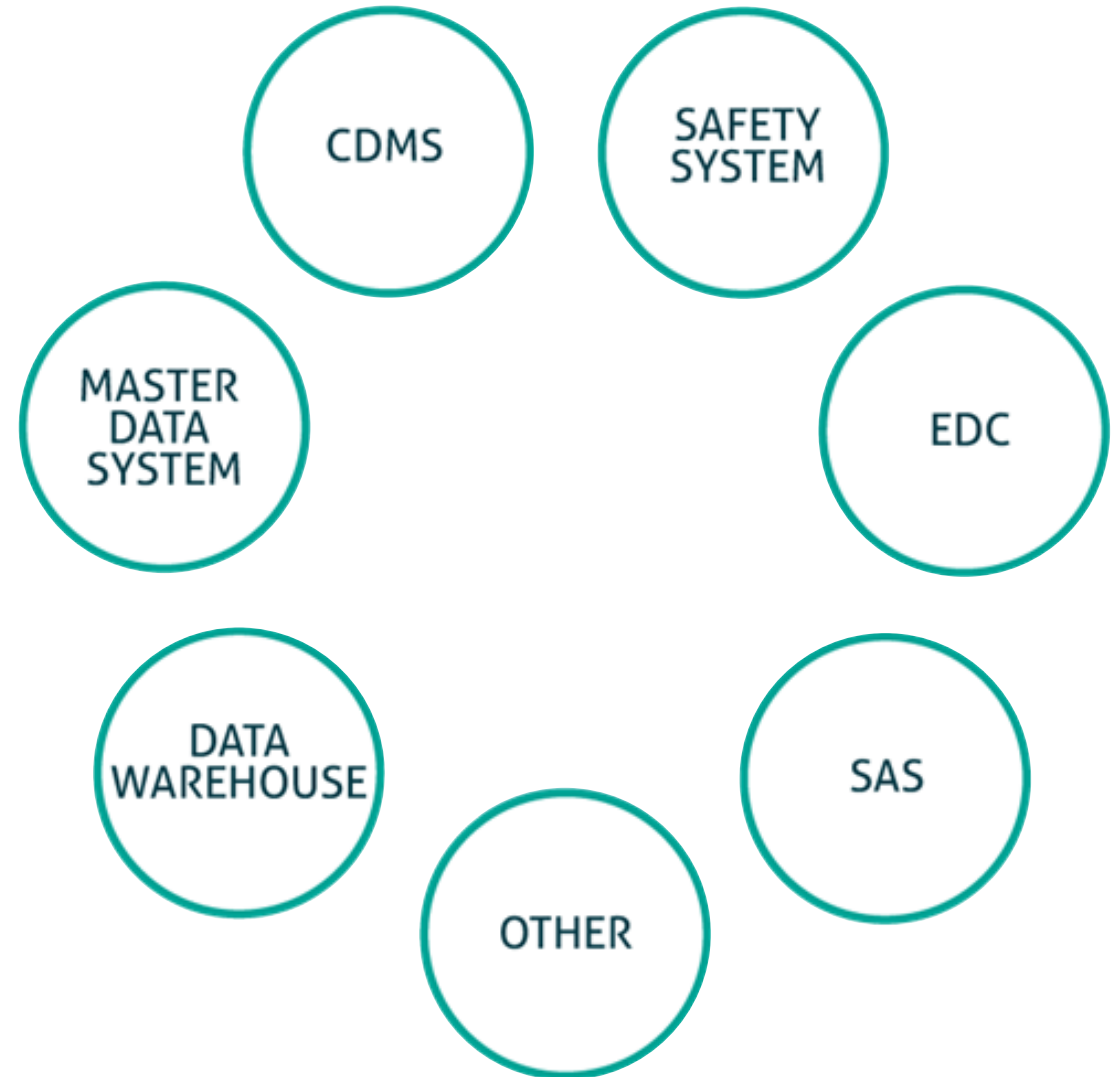
<def:WhereClauseDef OID="WC.VS.VSTESTCD.SYSBP">
  <RangeCheck SoftHard="Soft" def:ItemOID="IT.VS.VSTESTCD" Comparator="EQ">
    <CheckValue>SYSBP</CheckValue>
  </RangeCheck>
</def:WhereClauseDef>
...
```

Data Traceability in Clinical Development Systems



Clinical Development Systems

- Many systems contain data for parts of the clinical data lifecycle
- A metadata repository can manage standards across the data lifecycle and is the primary candidate for defining traceability between stages



Traceability in the MDR: <def:Origin>

- Values: CRF, Derived, Assigned, Protocol, eDT, Predecessor
- Should be defined in context

Published Asset: BRTHDTC ([SDTM DM] MDE 1)

Asset Type: Metadata Element

Classifiers

Name	Value
Business Object Type	Variable
Clinical Lifecycle Stage	Data Tabulations

Relationships

Relationship	Asset Type	Asset Name
Implements Concept	Concept	Birth Date and Time (C83217) (C 1)
Included in Sets	Metadata Element Set	DM ([SDTM] MDES 1)
Included in Sets	Metadata Element Set	DM ([SDTM] MDES 2)
Included in Sets	Metadata Element Set	DM ([SDTM] MDES 3)
Product of Rule	Rule	BRTHDD/MO/YY.BRTHDTC (R 1)
Represented by Data Type and/or Codelist	Value Domain	ISO 8601 (VD 1)

DM ([SDTM] MDES 3)

Relationship Properties

MDES Name (Version): SDTM(MDES 3.2)

Role: Record Qualifier

Label: Date/Time of Birth

Core: SDTM|Perm

Ordinal: 16

Origin: Derived

Traceability in the MDR: <MethodDef>

- Unique Name, Type and Description are required

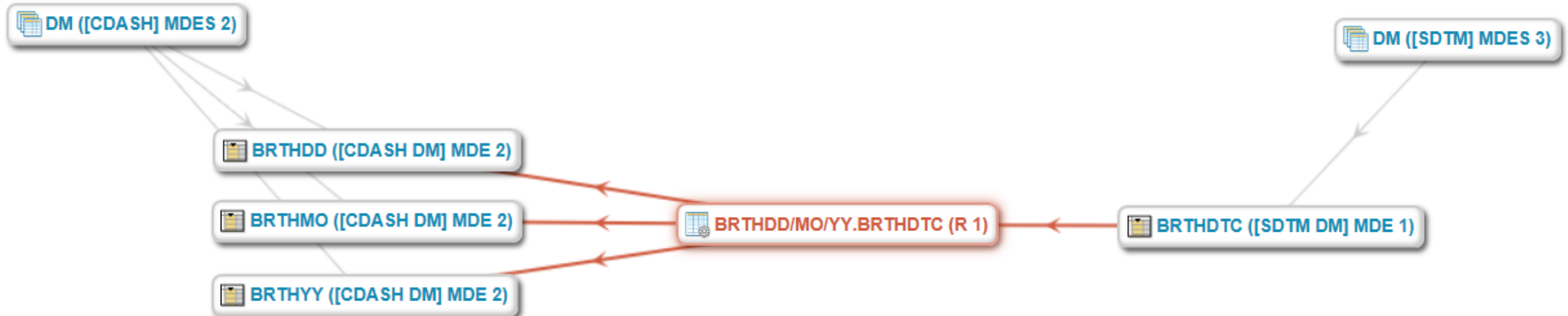
Published Asset: BRTHDD/MO/YY.BRTHDTC (R 1)

Asset Type: Rule

Classifiers

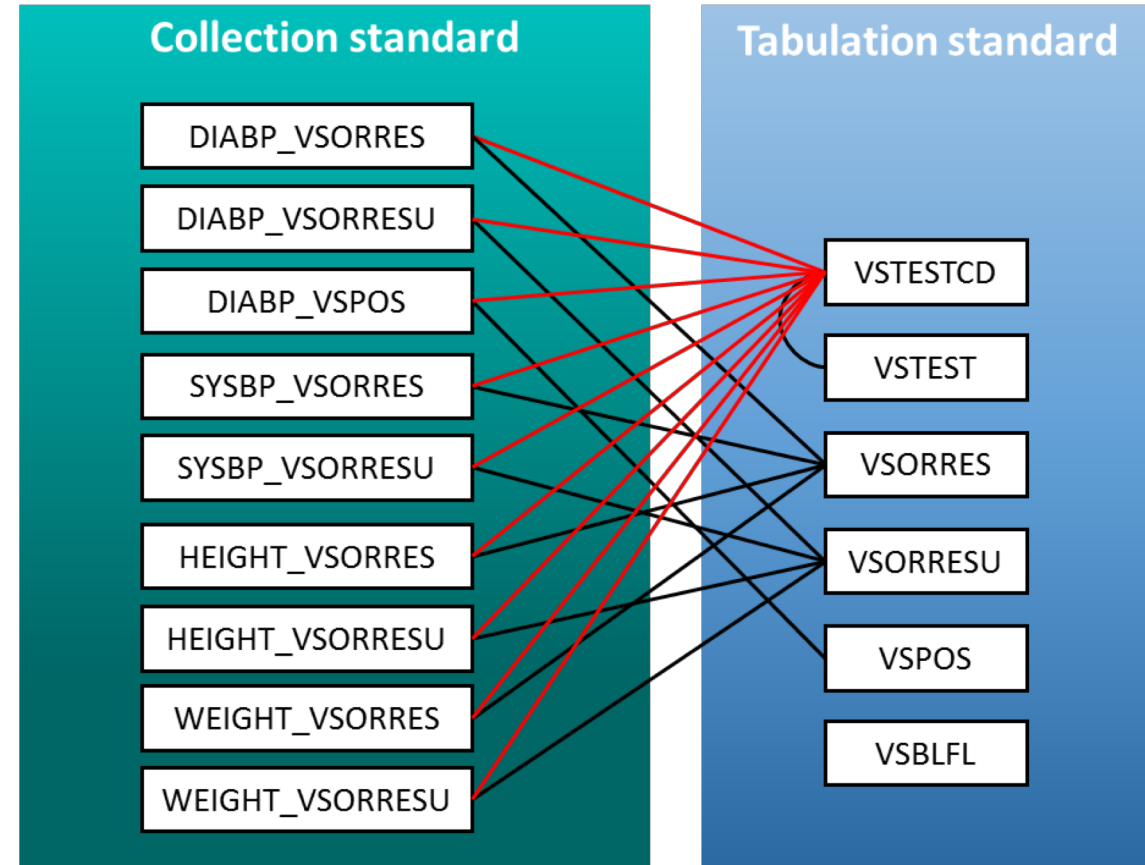
Name	Value
Business Object Type	Transformation
Clinical Lifecycle Stage	Data Tabulations
SAS Derivation	BRTHDTC = input(cat(BRTHYY,'-',BRTHMO,'-',BRTHDD),is8601da.);
Computational Method	Concatenation of 4 digit year, 2 digit month, and 2 digit day with a dash in between each to create an ISO 8601 date format.

Relationships



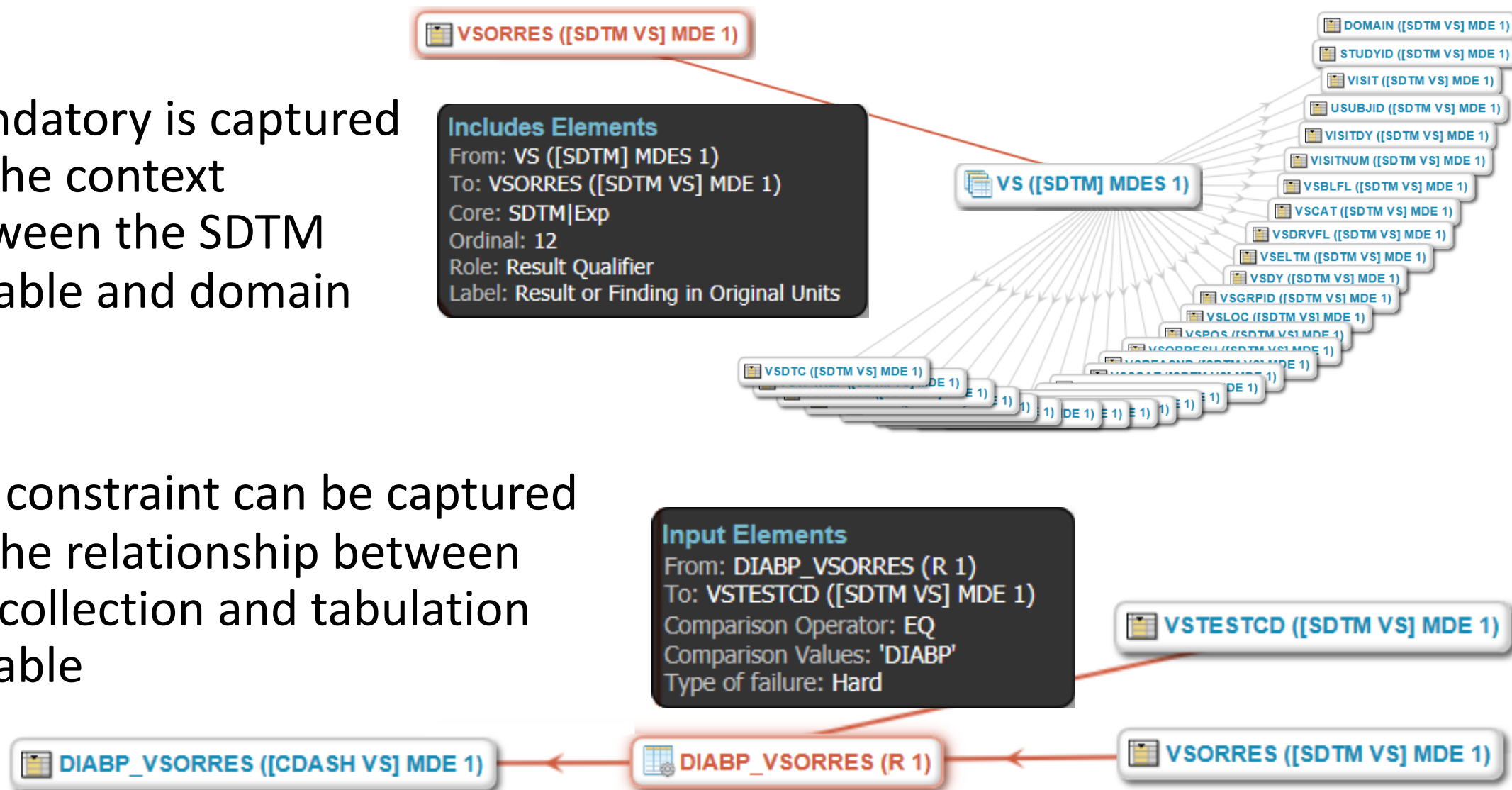
Value Level Metadata

- Most often used in Findings domains
- Providing additional definitions for variables like Result and Unit specific to each value of Test
- References should capture:
 - whether target variable is mandatory
 - the constraint for each of the values, including
 - comparator
 - check value
 - failure type



Traceability in the MDR: VLM

- Mandatory is captured on the context between the SDTM variable and domain
- The constraint can be captured on the relationship between the collection and tabulation variable



<def:CommentDef>

- Comments for Define-XML should be facilitated on any element

Published Asset: QS ([SDTM] MDES 1)

Asset Type: Metadata Element Set
Description: Questionnaires

Classifiers

Name	Value
Business Object Type	Domain
Clinical Lifecycle Stage	Data Tabulations
Structure	One record per questionnaire per question per time point per visit per subject
Comment Documentation for ODM/Define Export	QS is submitted as a split dataset. The split was done based on QSCAT. See additional documentation in the Reviewer's Guide, Split Datasets Section.

Relationships

Relationship	Asset Type	Asset Name
Includes Elements	Metadata Element	DOMAIN ([SDTM QS] MDE 1)
Includes Elements	Metadata Element	QSBFL ([SDTM QS] MDE 1)
Includes Elements	Metadata Element	QSCAT ([SDTM QS] MDE 1)
Includes Elements	Metadata Element	QSDRVFL ([SDTM QS] MDE 1)

MDR Output

- When all standards and transformational metadata is captured in an MDR it can produce:
 - Define-XML for submission
 - Annotated CRF

Screening		
Study Design: Demographics [DM]		DM
Demography		
1.*	Birth date	Birth Year ▼ Birth Month ▼ Birth Day ▼ BRTHDTC For the SDTM-based dataset, the SDTM variable BRTHDTC is derived from the collected date and time components (BRTHDAT or BRTHYR, BRTHMO, BRTHDY, and BRHTIM) concatenating as necessary into the ISO 8601 format.
2.*	Sex	☐ Male ☐ Female SEX
3.*	Ethnicity	☐ HISPANIC OR LATINO ☐ NOT HISPANIC OR LATINO ☐ NOT REPORTED ☐ UNKNOWN ETHNIC

Conclusion



Conclusion

- ✔ A metadata repository is well suited for control and versioning of data traceability and can serve as the single source or truth
- ✔ The repository should hold all information about data elements and all references and transformations the data element was subject to
- ✔ Define-XML provides a good framework of what information should be captured in the MDR to satisfy regulatory reviewers requirements for data traceability
- ✔ The origin, derivation and value level metadata attributes should be managed as context-dependent attributes to facilitate reuse of core data elements

Any questions?





Judith Goud
judith.goud@Nurocor.com