



CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

**It's the semantics stupid!  
The last mile (or kilometer?)  
in interoperability between healthcare, clinical research  
and regulatory agencies**

*The CDISC Vision is to Inform Patient Care & Safety  
Through Higher Quality Medical Research*

*Strength through Collaboration*

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# The long and winding road to Interoperability

- Technical interoperability
  - iPhone versus Android
- Syntactic (exchange format) interoperability
  - CDISC ODM, SAS XPT, HL7-CDA
- Semantic interoperability
  - Codelists

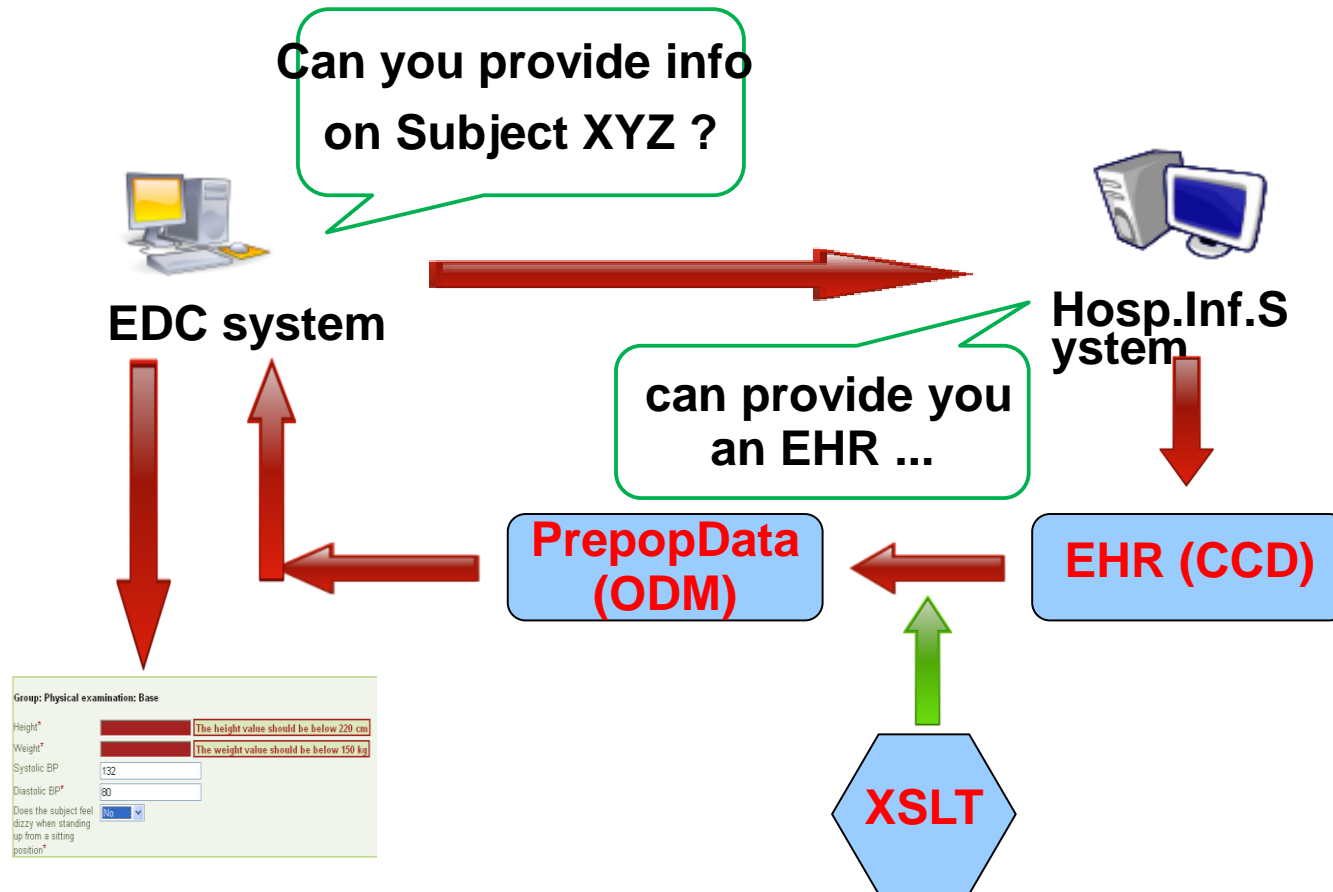
# Interoperability between Healthcare and Clinical Research - a breakthrough

- IHE Profiles **RFD** (Retrieve Form for Data Capture) and **CRD** (Clinical Research Data Capture)
  - Provide a standardized process
  - Provide a method (stylesheet) to transform HL7-CDA (CCD) into CDASH-ODM.



# HL7-CCD to CDASH

- RFD proves we master technical interoperability

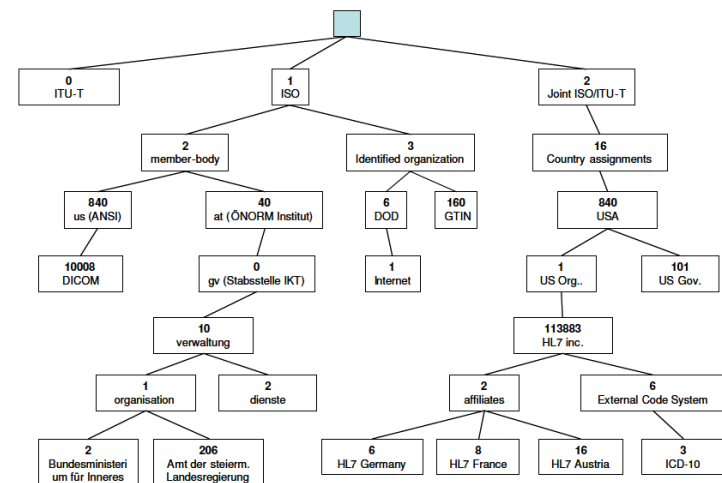


# Coding systems in Healthcare

- Use of OIDs (e.g. HL7 = 2.16.840.1.113883)
  - Does CDISC have/use OIDs?
- Popular coding systems in e-Healthcare
  - SNOMED [2.16.840.1.113883.6.96]
  - LOINC - lab tests [2.16.840.1.113883.6.1]
  - ICD-10 - diagnoses [2.16.840.1.113883.6.90]
  - UCUM - units of measure [2.16.840.1.113883.6.8]

Object Identifier (OID) Konzept  
für das Österreichische Gesundheitswesen

Technikum Wien GmbH



# Use of coding systems in EHRs

- Example: HL7-CDA CCD
  - here: body height: 3137-7 (LOINC)

```
<entry typeCode="DRIV">
  <observation classCode="OBS" moodCode="EVN">
    <templateId root="2.16.840.1.113883.10.20.9.2"/>
    <code code="3137-7" codeSystem="2.16.840.1.113883.6.1"
    codeSystemName="LN" displayName="BODY HEIGHT:"/>
    <effectiveTime value="201207190946"/>
    <value xsi:type="PQ" value="193" unit="cm"/>
  </observation>
</entry>
<entry typeCode="DRIV">
  <observation classCode="OBS" moodCode="EVN">
    <templateId root="2.16.840.1.113883.10.20.9.2"/>
    <code code="11378-7" codeSystem="2.16.840.1.113883.6.1"
    codeSystemName="LN" displayName="SYSTOLIC BLOOD PRESSURE"/>
    <effectiveTime value="201207190952"/>
    <value xsi:type="PQ" value="131" unit="mm[Hg]"/>
  </observation>
</entry>
```

# CDISC Controlled Terminology

## CDISC SDTM Controlled Terminology

CDISC SDTM Controlled Terminology, 2012-12-21

Legend:

CodeList
CodeListItem
NCI attributes

### Codelist Definitions

OID	Name (CDISC Submission Value)	Data Type Extensible	NCI Code	CDISC Synonym	CDISC Definition	Preferred Term
	<b>CDISC Submission Value [ODM:CodedValue]</b>					
CL.C66767.ACN	Action Taken with Study Treatment (ACN)	text Extensible: No	C66767	Action Taken with Study Treatment	Action Taken with Study Treatment	CDISC SDTM Action Taken with Study Treatment Terminology
	DOSE INCREASED		C49503		An indication that a medication schedule was modified by addition; either by changing the frequency, strength or amount. (NCI)	Dose Increased
	DOSE NOT CHANGED		C49504		An indication that a medication schedule was maintained. (NCI)	Dose Not Changed
	DOSE REDUCED		C49505		An indication that a medication schedule was modified by subtrac	

C66767	<a href="#">Action Taken with Study Treatment</a>
C66768	<a href="#">Outcome of Event</a>
C66780	<a href="#">Age Span</a>
C66781	<a href="#">Age Unit</a>
C66797	<a href="#">Category for Inclusion/Exclusion</a>
C66784	<a href="#">Common Terminology Criteria for Adverse Events</a>
C87162	<a href="#">Common Terminology Criteria for Adverse Events V4.0</a>
C66785	<a href="#">Control Type</a>
C66786	<a href="#">Country</a>
C66787	<a href="#">Diagnosis Group</a>
C66788	<a href="#">Dictionary Name</a>
C66789	<a href="#">Not Done</a>
C66790	<a href="#">Ethnic Group</a>
C66726	<a href="#">Pharmaceutical Dosage Form</a>
C66727	<a href="#">Completion/Reason for Non-Completion</a>
C66728	<a href="#">Relation to Reference</a>

# CDISC Controlled Terminology

C66741	<a href="#">Vital Signs Test Code</a>	<a href="#">Back to top</a>				
C67153	<a href="#">Vital Signs Test Name</a>	CL.C71620.UNIT	Unit (UNIT)	text Extensible: Yes	C71620	Unit
C66742	<a href="#">No Yes Response</a>		Gy		C18063	Gray
C65047	<a href="#">Laboratory Test Code</a>		Rad		C18064	Rad
C67154	<a href="#">Laboratory Test Name</a>		DAYS		C25301	Day
C71113	<a href="#">Frequency</a>		HOURS		C25529	Hour,hr
C71148	<a href="#">Position</a>		%		C25613	Percentage
C71150	<a href="#">ECG Result</a>		mm		C28251	Millimeter
C71153	<a href="#">ECG Test Code</a>		kg		C28252	Kilogram
C71152	<a href="#">ECG Test Name</a>					
C71151	<a href="#">ECG Test Method</a>					
C71620	<a href="#">Unit</a>					
C74456	<a href="#">Anatomical Location</a>					



# Are CDISC codes used in Healthcare?

- **No!**
- Healthcare uses:
  - LOINC for VS test codes
  - LOINC for lab test codes
  - UCUM for Units of Measure
- Did CDISC reinvent the wheel?
  - I think so - well, at least partially
  - I will explain so in a moment ...
- Current CDISC-CT seriously hinders integration with healthcare

# LOINC test codes

- Example: Bilirubin

```
- <EnumeratedItem CodedValue="BILI" nciodm:ExtCodeID="C38037">
  <nciodm:CDISCSynonym>Bilirubin</nciodm:CDISCSynonym>
  <nciodm:CDISCSynonym>Total Bilirubin</nciodm:CDISCSynonym>
  <nciodm:CDISCDefinition>A measurement of the total bilirubin in a biological specimen.</nciodm:CDISCDefinition>
  <nciodm:PreferredTerm>Total Bilirubin Measurement</nciodm:PreferredTerm>
  <!-- here an example when there is also a SNOMED-CT code available -->
  <Alias Context="SNOMED-CT" Name="359986008" />
  <!-- here an example of a case where there is more than 1 LOINC Code, as the CDISC term is not specific -->
  <!-- source of the information: CDISCcommonLOINCtests20050214.pdf -->
  <!-- Bilirubin in Serum/Plasma, Substance Concentration -->
  <Alias Context="LOINC" Name="14631-6" />
  <Alias Context="LOINC-Name" Name="BILIRUBIN:SCNC:PT:SER/PLAS:QN" />
  <!-- Bilirubin in Body Fluid, Mass concentration -->
  <Alias Context="LOINC" Name="1974-5" />
  <Alias Context="LOINC-Name" Name="BILIRUBIN:MCNC:PT:FLU:QN" />
  <!-- Bilirubin in Serum/Plasma, Mass Concentration -->
  <Alias Context="LOINC" Name="1975-2" />
  <Alias Context="LOINC-Name" Name="BILIRUBIN:MCNC:PT:SER/PLAS:QN" />
  <!-- Bilirubin in Urine, Arbitrary Concentration, Ordinal -->
  <Alias Context="LOINC" Name="1977-8" />
  <Alias Context="LOINC-Name" Name="BILIRUBIN:ACNC:PT:UR:ORD" />
  <!-- Bilirubin in Body Fluid Substance Concentration -->
  <Alias Context="LOINC" Name="29767-1" />
  <Alias Context="LOINC-Name" Name="BILIRUBIN:SCNC:PT:FLU:QN" />
```

# LOINC test codes

## **BILIRUBIN:MCNC:PT:SER/PLAS:QN**

- Bilirubin example explained:
  - 1974-5: test code + check digit
  - BILIRUBIN: substance analysed or tested
  - MCNC: mass concentration
  - PT: single point in time
  - SER/PLAS: in Serum/Plasma
  - QN: quantitative measurement
- Each LOINC code uniquely identifies a test

# Can we map LOINC to CDISC-CT?

- Topic of one of our students Master thesis
- Result: N LOINC codes map to 1 CDISC code
  - E.g. >8 different Glucose tests
- LOINC codes are much more fine grained
- LOINC codes are used by
  - Every hospital lab
  - EHRs

```

- <EnumeratedItem CodedValue="BILI" nciidm:ExtCodeID="C38037">
  <nciidm:CDISCSynonym>Bilirubin</nciidm:CDISCSynonym>
  <nciidm:CDISCSynonym>Total Bilirubin</nciidm:CDISCSynonym>
  <nciidm:CDISCDefinition>A measurement of the total bilirubin in a biological specimen.</nciidm:CDISCDefinition>
  <nciidm:PreferredTerm>Total Bilirubin Measurement</nciidm:PreferredTerm>
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  <Alias Context="LOINC-Name" Name="BILIRUBIN:MCNC:PT:FLU:QN" />
  <!-- Bilirubin in Serum/Plasma, Mass Concentration) -->
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  <!-- Bilirubin in Body Fluid Substance Concentration -->
  <Alias Context="LOINC" Name="29767-1" />
  <Alias Context="LOINC-Name" Name="BILIRUBIN:SCNC:PT:FLU:QN" />

```

# OK - but we have LBCAT, LBMETHOD,

...

- LBCAT, LBSCAT, LBMETHOD, LBSPEC do not have controlled terminology!
- Example glucose test

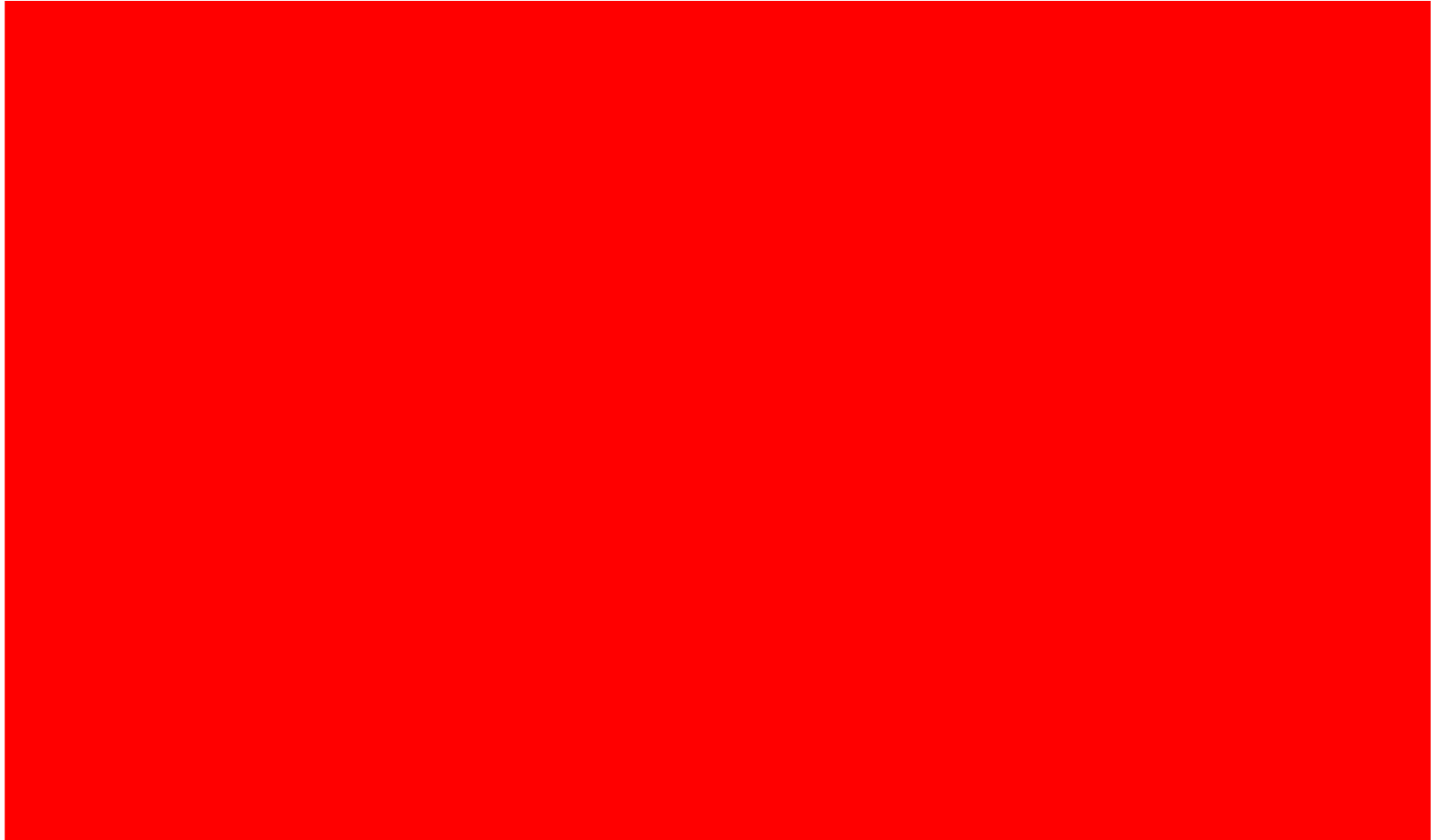
	LBTESTCD	LBCAT	LBSPEC	LBMETHOD	LBLOINC
Sponsor 1	GLUC	CHEMISTRY	BLD	QUANT	2339-0
Sponsor 2	GLUC	CHEM	WHOLE BLOOD	ENZYMATIC	15074-8
Sponsor 3	GLUC	CHEMI	BLOOD	HEXOKINASE	2339-0

Where these the same test?

# Why CDISC does not use LOINC codes

- Labs don't use them
- SEND test codes not covered
- Sponsors don't know LOINC
- =MYTH: Labs do not provide them when we don't ask
- Sufficient reason to redefine those covered by LOINC?
- But they can learn ... (the labs can provide them anyway)

# Why CDISC does not use LOINC codes (and created it own ones ...)



# Units of measure in healthcare

- Healthcare uses UCUM (Unified Code for Units of Measure)
- Consist of prefix (e.g. "m" for "milli"), base unit (e.g. "m" for meter) and in some cases a further designation
  - Examples:
    - mm = millimeter
    - mm[Hg]: millimeter mercury column (pressure)  
or ... m[H2O]: meter water column
- Mandatory use in HL7-CDA, ISO-21090



# UCUM units are easily interconvertible

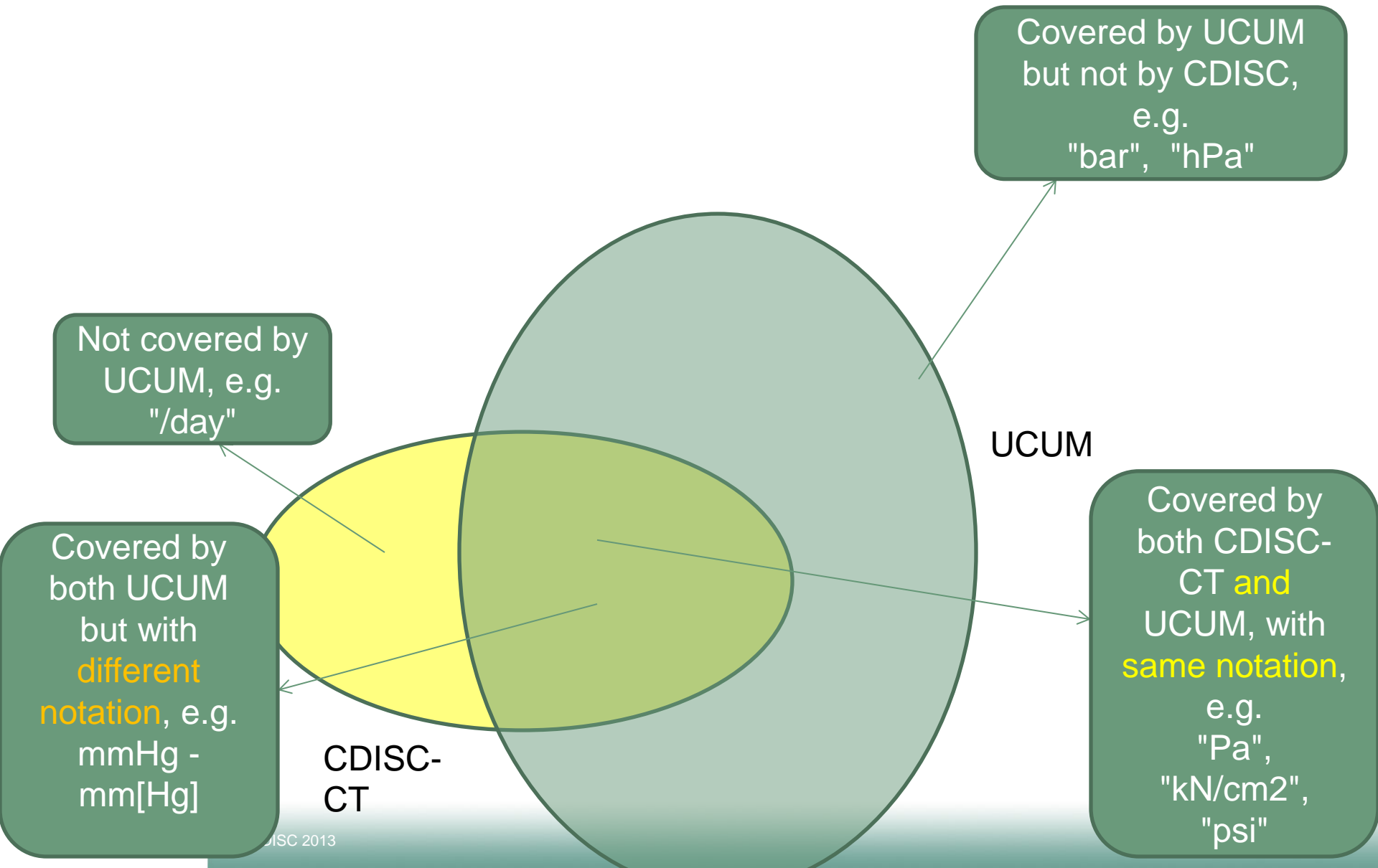
- Exam question:
  - Calculate (using ucum-essence.xml) how many millibar (mbar) 80 mm Mercury column is (mm[Hg])

ucum-essence.xml:

```
<unit Code="m[Hg]" CODE="M[HG]" isMetric="yes" class="clinical">  
  <name>meter of mercury column</name>  
  <printSymbol>m Hg</printSymbol>  
  <property>pressure</property>  
  <value Unit="kPa" UNIT="KPAL" value="133.3220">133.3220</value>  
</unit>
```

```
<unit Code="bar" CODE="BAR" isMetric="yes" class="iso1000">  
  <name>bar</name>  
  <printSymbol>bar</printSymbol>  
  <property>pressure</property>  
  - <value Unit="Pa" UNIT="PAL" value="1e5">  
    1 × 10  
    <sup>5</sup>  
  </value>  
</unit>
```

# CDISC-CT claims to use a subset of UCUM



# CDISC-CT claims to use a subset of UCUM

- But some terrible collisions: units covered by both but with different notations
  - **mmHg** versus **mm[Hg]**
  - **ft** versus **[ft\_i]**
  - **Joule** versus **J**
  - **Years** versus **a**
  - ...

CDISC-CT  
UCUM

# Advantages and disadvantages CDISCT-CT for Units

- Advantages:
  - Covers (un)common units used in clinical research
  - Covers units used in preclinical research (SEND)
- Disadvantages
  - Not a system - just a list
  - Can (and will) grow to infinite size
  - Not the flexibility of UCUM
  - No interconversion possible
  - Refuses to use some UCUM codes, and provides a different notation for them

# What the FDA says about this - some e-mails to me ...

- *I believe that Jozef makes an excellent point. Precoordinating UCUM values and then obtaining NCI codes for the combination can be labor and time intensive, and is probably unnecessary. SPL's use of UCUM without such precoordination has gone amazingly well*
- *I have been following this discussion with interest and I would like to say that I personally support your position. FDA already supports UCUM for submissions of product labeling information using SPL so it makes sense to support it also for submissions of study data. I'm trying to raise awareness of this issue internally at FDA.*

mails from FDA representatives

# CDISC-end-to-end Integration with healthcare

- Scenario: lab test values and units are extracted from EHRs or HIS
- EHRs (HL7-CDA, ISO-21090) are **mandated** to use LOINC (for lab tests) and UCUM (for units)
- Currently, these need to be mapped manually to CDISC-CT + --CAT, --SCAT, --METHOD, --SPEC
- This must lead to errors and incomparable results

# What we can do

- CDISC-ODM:
  - Allow **UCUMUnit** attribute in MeasurementUnit
  - Allow **code/codeSystem** like in HL7-CDA
  - Encourage usage of ICD-10, LOINC, and other coding systems used in healthcare
- CDISC-CT / SDTM
  - Strongly encourage use of --LOINC in LB,VS,MB
    - The FDA should make it "required"
    - Otherwise it can't compare between studies and sponsors
  - Allow each UCUM-unit as a valid value for --ORRESU, and (maybe a subset) for --STRESU
    - And take some duplicate codes for granted

## Our Projects

- Continue LOINC - CDISC-CT mapping
- Write a few whitepapers ...
- Encourage integration with healthcare (semantics!)
- Start working on future ODM 1.4
  - Some work needed for healthcare integration

Thank you for your  
attention!