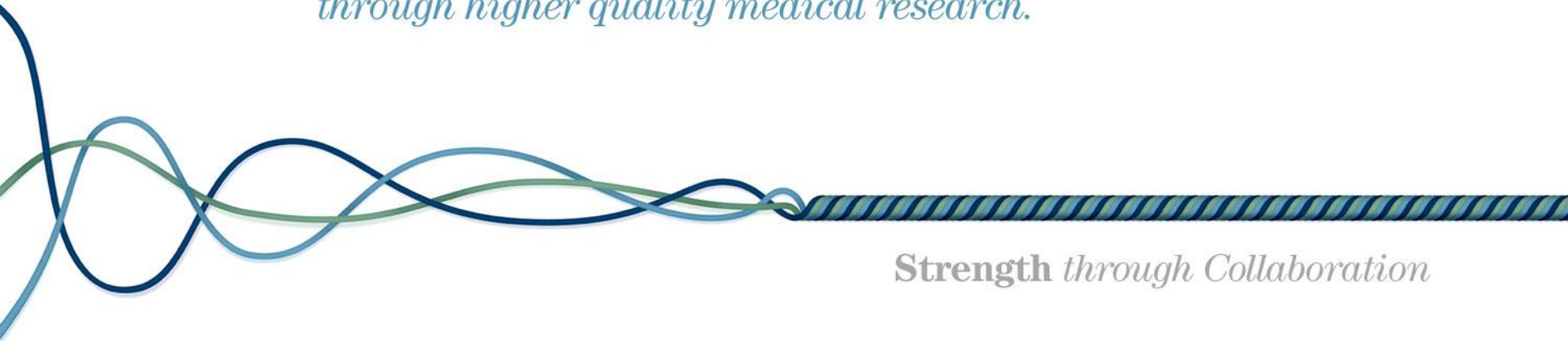




CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

*The CDISC vision is to inform patient care & safety
through higher quality medical research.*

A decorative graphic consisting of several overlapping wavy lines in dark blue, light blue, and teal, extending horizontally across the lower portion of the slide. The lines eventually merge into a solid horizontal band with a diagonal hatched pattern.

Strength *through Collaboration*

CDISC Standards May Harm Your Health - Unless You SHARE Them (CDISC 2~~0~~0) 2017?

Presented by FH-Prof.Dr. Jozef Aerts
University of Applied Sciences FH Joanneum
Graz, Austria

FH | JOANNEUM
University of Applied Sciences

XMI
4Pharma

Strength through Collaboration

A valid VS SDTM Dataset?

STUDYID	DOMAIN	USUBJID	...	VSTESTCD	VSTEST	VSPOS	VSORRES	VSORRESU	VSSTRESC	VSSTRESN	VSSTRESU
CDISCPIL...	VS	01-701-1015	1	DIABP	Diastolic Blood Pressure	SUPINE	64	mmHg	64	64	mmHg
CDISCPIL...	VS	01-701-1015	2	DIABP	Diastolic Blood Pressure	STANDING	83	mmHg	83	83	cm
CDISCPIL...	VS	01-701-1015	3	DIABP	Diastolic Blood Pressure	STANDING	57	mmHg	57	57	mmHg
CDISCPIL...	VS	01-701-1015	4	DIABP	Diastolic Blood Pressure	SITTING	68	mmHg	68	68	mmHg
CDISCPIL...	VS	01-701-1015	5	DIABP	Diastolic Blood Pressure	STANDING	59	mmHg	59	59	mmHg
CDISCPIL...	VS	01-701-1015	...	HEIGHT	Height	SITTING	58.0	mmHg	147.32	147.32	cm
CDISCPIL...	VS	01-701-1015	...	PULSE	Pulse Rate	SUPINE	57	BEATS/MIN	57	57	BEATS/MIN
CDISCPIL...	VS	01-701-1015	...	PULSE	Pulse Rate	STANDING	62	BEATS/MIN	62	62	BEATS/MIN
CDISCPIL...	VS	01-701-1015	...	PULSE	Pulse Rate	STANDING	65	BEATS/MIN	65	65	BEATS/MIN
CDISCPIL...	VS	01-701-1015	...	SYSBP	Systolic Blood Pressure	SUPINE	131	mmHg	131	131	mmHg
CDISCPIL...	VS	01-701-1015	...	SYSBP	Systolic Blood Pressure	STANDING	129	mmHg	129	129	mmHg
CDISCPIL...	VS	01-701-1015	...	SYSBP	Systolic Blood Pressure	STANDING	147	cm	147	147	mmHg
CDISCPIL...	VS	01-701-1015	...	SYSBP	Systolic Blood Pressure	SUPINE	138	mmHg	138	138	mmHg
CDISCPIL...	VS	01-701-1015	...	SYSBP	Diastolic Blood Pressure	STANDING	137	mmHg	137	137	mmHg
CDISCPIL...	VS	01-701-1015	...	TEMP	Temperature		96.9	F	36.06	36.06	C
CDISCPIL...	VS	01-701-1015	...	TEMP	Temperature	SITTING	97.0	F	36.11	36.11	C
CDISCPIL...	VS	01-701-1015	...	TEMP	Temperature		97.2	F	36.22	36.22	C

Validates in OpenCDISC without errors or warnings

Using a web service

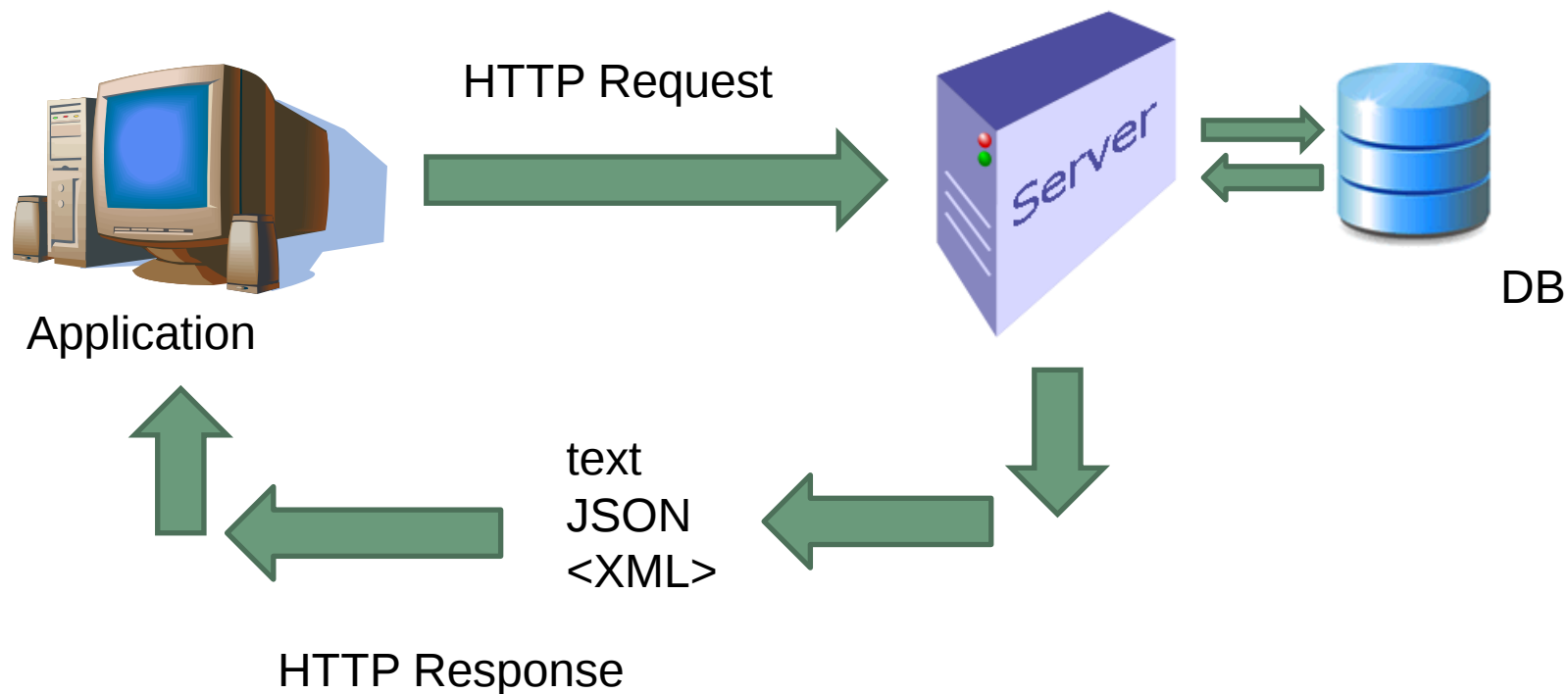
- The web service is asked 2 questions:
 - is the unit (VSORRESU, VSSTRESU) applicable to the VSTESTCD?
 - is the VSPOS applicable to VSTESTCD?

STUDYID	DOMAIN	USUBJID	...	VSTESTCD	VSTEST	VSPOS	VSORRES	VSORRESU	VSSTRESC	VSSTRESN	VSSTRESU	VSSTAT
CDISCPIL...	VS	01-701-1015	1	DIABP	Diastolic Blood Pressure	SUPINE	64	mmHg	64	64	mmHg	
CDISCPIL...	VS	01-701-1015	2	DIABP	Diastolic Blood Pressure	STANDING	83	mmHg	83	83	cm	
CDISCPIL...	VS	01-701-1015	3	DIABP	Diastolic Blood Pressure	STANDING	57	mmHg	57	57	mmHg	
CDISCPIL...	VS	01-701-1015	4	DIABP	Diastolic Blood Pressure	SITTING	68	mmHg	68	68	mmHg	
CDISCPIL...	VS	01-701-1015	5	DIABP	Diastolic Blood Pressure	STANDING	59	mmHg	59	59	mmHg	
CDISCPIL...	VS	01-701-1015	...	HEIGHT	Height	SITTING	58.0	mmHg	147.32	147.32	cm	
CDISCPIL...	VS	01-701-1015	...	PULSE	Pulse Rate	SUPINE	57	BEATS/MIN	57	57	BEATS/MIN	
CDISCPIL...	VS	01-701-1015	...	PULSE	Pulse Rate	STANDING	WARNING: VSPOS 'SITTING' is not valid VSPOS value for Test Code 'HEIGHT (VSPOS)					
CDISCPIL...	VS	01-701-1015	...	PULSE	Pulse Rate	STANDING	65	BEATS/MIN	65	65	BEATS/MIN	
CDISCPIL...	VS	01-701-1015	...	SYSBP	Systolic Blood Pressure	SUPINE	131	mmHg	131	131	mmHg	
CDISCPIL...	VS	01-701-1015	...	SYSBP	Systolic Blood Pressure	STANDING	129	mmHg	129	129	mmHg	
CDISCPIL...	VS	01-701-1015	...	SYSBP	Systolic Blood Pressure	STANDING	147	cm	147	147	mmHg	
CDISCPIL...	VS	01-701-1015	...	SYSBP	Systolic Blood Pressure	SUPINE	138	mmHg	138	138	mmHg	
CDISCPIL...	VS	01-701-1015	...	SYSBP	Diastolic Blood Pressure	STANDING	137	mmHg	137	137	mmHg	
CDISCPIL...	VS	01-701-1015	...	TEMP	Temperature		96.9	F	36.06	36.06	C	O
CDISCPIL...	VS	01-701-1015	...	TEMP	Temperature	SITTING	97.0	F	36.11	36.11	C	O
CDISCPIL...	VS	01-701-1015	...	TEMP	Temperature		97.2	F	36.22	36.22	C	O

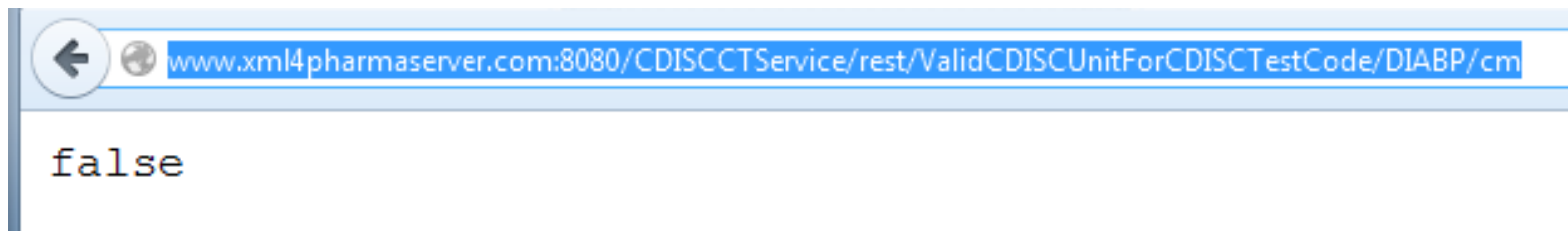
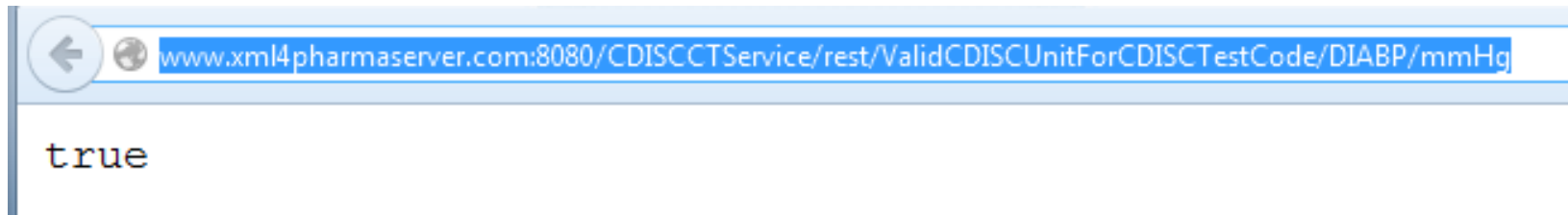
Using a web service

- The **rules** have NOT been programmed in the tool – they are on a **public** server which can be queried using a **RESTful web service**

RESTful Web Services Simplified



RESTful web services for CDISC testing in a browser



Request:

- a) Is unit mmHg a valid unit for test DIABP?
- b) Is unit cm a valid unit for test DIABP?

`/CDISCCTService/rest/ValidCDISCUnitForCDISCTestCode/DIABP/mmHg`
`/CDISCCTService/rest/ValidCDISCUnitForCDISCTestCode/DIABP/cm`

Current Validation Tools

Rules are:

- are hardcoded in software
- are **intransparent** (you can't see how exactly the rule has been implemented)
- are own interpretations by a few people only
- are not owned by CDISC
- are sometimes just damned wrong
- **are only updated when a new release becomes available**

A typical question on a forum

- "Hi, ... we found following false positive ..."
- "Thanks for reporting this, we will fix it in the next release which will be available within the next few weeks"

**We don't want to wait
until the next
release!**

with web services, updates within a few hours or less are possible

Currently implement Web Services

- Get CDISC Test Name from CDISC Test Code
- Get NCI Code from CDISC Test Code
- Get CDISC Definition from CDISC Test Code
- Get whether a coded value is a valid value for the given codelist
 - e.g. "COMPLETED" in CodeList "NCOMPLT" (DS)
- Get CDISC Definition from NCI code
- Get UCUM notation of CDISC unit
- Get whether a unit is a correct CDISC unit
- Get whether a CDISC unit is a correct unit for a given (VS) test code

Currently implement Web Services (cont.)

- Get whether a Vital signs "position" (VSPOS) is a correct "position" for a given (VS) test code
- Get whether a Character Result/Finding in Standard Format text value (EGSTRESC) for a given ECG Test code (EGTESTCD) is a valid value
- Get whether an SDTM variable is "required", "expected" or "permissible"
 - for a given SDTM Version
- Get the Label for a given SDTM variable
- Get the "CDISC Notes" for a given SDTM variable
 - for a given SDTM Version

Currently implement Web Services (cont.)

- Get name of standard (and version) in which a given domain is used/valid
- Get the list of domain names for a specific version and class of a given standard
- Get domain label from domain name and standard and version
 - SDTM labels have changed between versions!

Currently implement Web Services

LOINC and UCUM Web Services

- Get LOINC Name from LOINC code
- Get LOINC long name from LOINC code
- Get example UCUM units for LOINC code
- UCUM unit conversion service
- UCUM unit validation service

DM		LB										
D	LBSEQ	LBTESTCD	LBLOINC	LBORRES	LBORRESU	...	...	LBORNRL	LBORNRLH	LBSTRESC	LBSTRESN	LBS
15	259	ALB	1751-7	3.8	g/dL	...	...	3.3	4.9	38	38	g/L
15	294	ALB	1751-7	3.8	g/dL	...	...	3.3	4.9	38	38	g/L
15	2	ALP	6768-6	34	U/L	...	...	35	115	34	34	U/L
15	40	ALP	6768-6	50	U/L	...	...	35	115	50	50	U/L
15	75	ALP	6768-6	41	U/L	...	...	35	115	41	41	U/L
15	105	ALP	6768-6	6768-6 (LBLOINC)								/L
15	135	ALP	6768-6	LOINC Name: Alkaline phosphatase:CCnc:Pt:Ser/Plas:Qn								/L
15	165	ALP	6768-6	LOINC Common Name: Alkaline phosphatase [Enzymatic activity/volume] in Serum or Plasma								/L
15	200	ALP	6768-6	Example UCUM Units: U/L								/L

But also many other public Web Services can be used

DM	LB				
D	LBSEQ	LBTESTCD	LBLOINC	LBORRES	LBO
15	259	ALB	1751-7	3.8	g/dL
15	294	ALB	1751-7	3.8	g/dL
15	2	ALP	6768-6	34	U/L
15	40	ALP	6768-6	50	U/L
15	75	ALP	6768-6	41	U/L
15	105	ALP	6768-6	6768-6 (LBLOINC) LOINC Name: Alkaline LOINC Common Name Example UCUM Units:	
15	135	ALP	6768-6		
15	165	ALP	6768-6		
15	200	ALP	6768-6		



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ALP - blood test

Alkaline phosphatase (ALP) is a protein found in all body tissues. Tissues with higher amounts of ALP include the liver, [bile](#) ducts, and bone.

A blood test can be done to measure the level of ALP.

A related test is the [ALP isoenzyme test](#)

- MedLinePlus (National Library of Medicine)
- RxNav (National Library of Medicine)
- UNII / SPL / ... (DailyMed NLM)
- ...

Other uses of the web services

- Why do we need to submit --TEST (test name)?
 - there is a 1:1 relationship with --TESTCD anyway

DOMAIN	USUBJID	LBSEQ	LBTESTCD	...	LBCAT	LBORRES	LBORRES
LB	01-716-1024	1	ALB	...	CHEMISTRY	4.1	g/dL
LB	01-716-1024	2	ALP	...	CHEMISTRY	68	U/L
LB	01-716-1024	3	ALT	...	CHEMISTRY	17	U/L
LB	01-716-1024	4	AST	...	CHEMISTRY	26	U/L
LB	01-716-1024	5	BASO		HEMATOI	0.03	THOU/uL
LB	01-716-1024	6	BILI	AST (LBTESTCD) Aspartate Aminotransferase NCI: C64467			mg/dL
LB	01-716-1024	7	BUN				mg/dL
LB	01-716-1024	8	CA				mg/dL
LB	01-716-1024	9	CHOL	...	CHEMISTRY	206	mg/dL

Let the service do the work,
not the dataset !

Currently implement Web Services

No panic!

- You can find an overview, detailed explanations and instructions at:

www.xml4pharmaserver.com/WebServices/

- free use for everyone and every application

SDTM & FDA validation rules in XQuery

The "OpenRules" Project

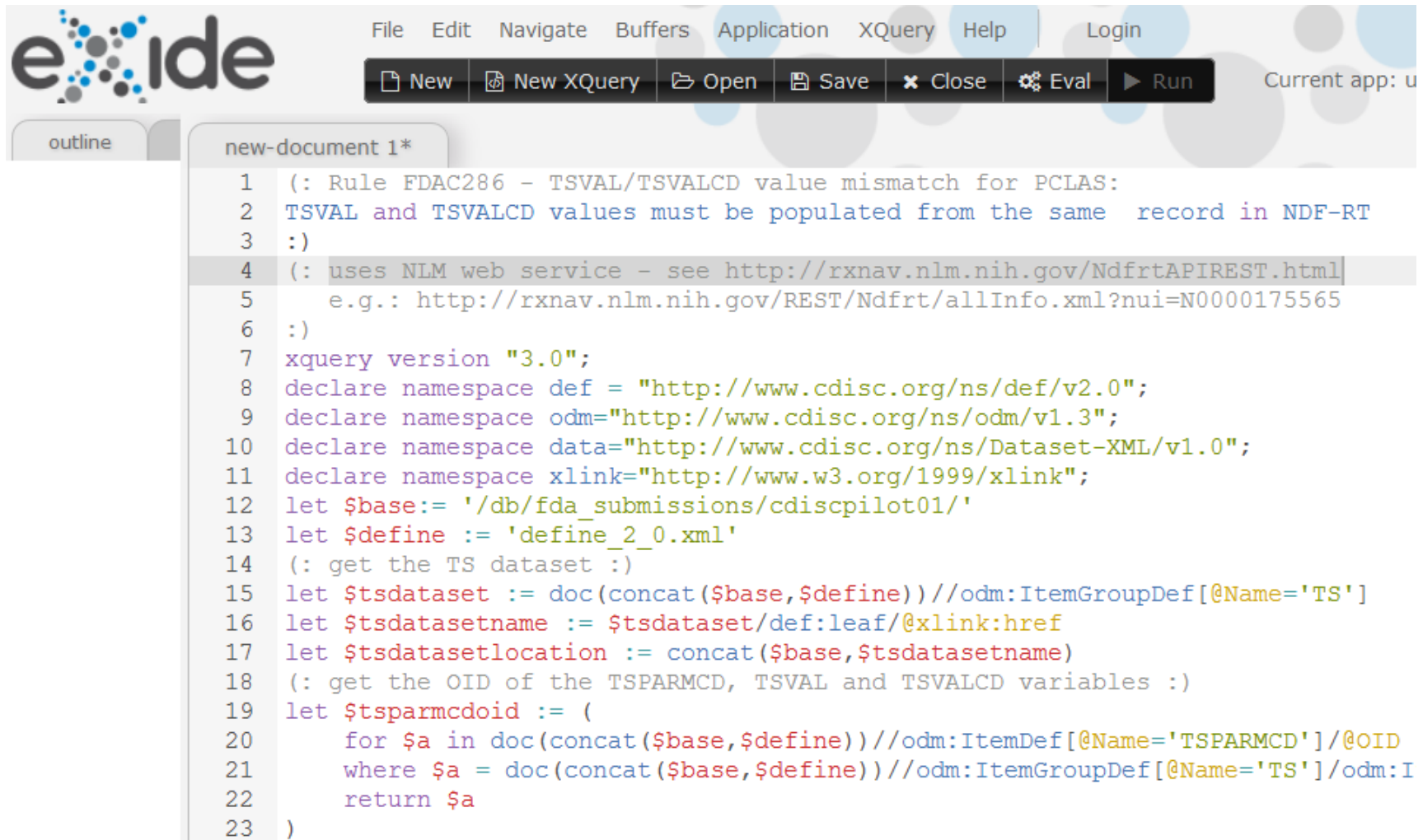
- SDTM and FDA rules are currently implemented as "black box" in validation tools
 - failing transparency
- Are sometimes incorrectly implemented or "just damned wrong"

146	FDAC154	Missing value for --ORRESU, when --ORRES is provided	Original Units (--ORRESU) should not be NULL, when Result or Finding in Original Units (--ORRES) is provided	EG, LB, VS, DA, MB, MS, PC, PP, FA
-----	---------	--	--	------------------------------------

- When wrongly implemented => next release
- Do not take ValueLevel into account

OpenRules

SDTM & FDA validation rules in XQuery



The screenshot shows the eXide IDE interface. The menu bar includes File, Edit, Navigate, Buffers, Application, XQuery, Help, and Login. The toolbar contains buttons for New, New XQuery, Open, Save, Close, Eval, and Run. The current application is 'new-document 1*'. The main editor displays an XQuery rule with the following content:

```
1 (: Rule FDAC286 - TSVAL/TSVALCD value mismatch for PCLAS:
2 TSVAL and TSVALCD values must be populated from the same record in NDF-RT
3 :)
4 (: uses NLM web service - see http://rxnav.nlm.nih.gov/NdfrtAPIREST.html
5 e.g.: http://rxnav.nlm.nih.gov/REST/Ndfrt/allInfo.xml?nui=N0000175565
6 :)
7 xquery version "3.0";
8 declare namespace def = "http://www.cdisc.org/ns/def/v2.0";
9 declare namespace odm="http://www.cdisc.org/ns/odm/v1.3";
10 declare namespace data="http://www.cdisc.org/ns/Dataset-XML/v1.0";
11 declare namespace xlink="http://www.w3.org/1999/xlink";
12 let $base:= '/db/fda_submissions/cdiscpilot01/'
13 let $define := 'define_2_0.xml'
14 (: get the TS dataset :)
15 let $tsdataset := doc(concat($base,$define))//odm:ItemGroupDef[@Name='TS']
16 let $tsdatasetname := $tsdataset/def:leaf/@xlink:href
17 let $tsdatasetlocation := concat($base,$tsdatasetname)
18 (: get the OID of the TSPARMCD, TSVAL and TSVALCD variables :)
19 let $tsparmcdoid := (
20   for $a in doc(concat($base,$define))//odm:ItemDef[@Name='TSPARMCD']/@OID
21   where $a = doc(concat($base,$define))//odm:ItemGroupDef[@Name='TS']/odm:I
22   return $a
23 )
```

The rule uses an NLM web service itself!

OpenRules

"OpenRules" Project - Status

- Created XQuery rules for 80% of the "FDA SDTM rules"
 - 10% just "damned wrong"
 - 10% not a rule / unclear rule / an expectation instead of a rule
- Student is working on SDTM rules from CDISC Team
- Expected to be made public early next year
- Retrievable using a web service
 - so you always get the latest version
 - or the version of a specific date / period / release

Validation rules in XQuery

A paradigm shift

OpenRules

- machine- and human-readable rules
 - you can easily inspect each rule
- public (transparency)
- not open for different interpretations (precise description and implementation)
- everybody plays by the same rules
- everyone can make his own validation software
 - effort: 1-2 days
- retrievable from a server (e.g. using a web service)
 - if error in the rule, it can be updated within a few hours and the update is immediately available
- output is XML, easily transformable (PDF, HTML, ...)

Validation rules in XQuery

Disadvantages

- Only for Dataset-XML
(hopeless for SAS-XPT, forget about it)
- slower as when hardcoded in (compiled) software
(but you can e.g. run it as a scheduled batch job)

OpenRules

What has this all got to do with SHARE?

- **Everything**
- SDTM/SEND/ADaM validation rules are shared, they are transparent
- functionality: these web services is exactly what users expect from SHARE, i.e.
it answers their questions (like "*when xxTESTCD=A, what are the allowed values for xxSTRESU*")
- **OpenRules** for SDTM will be made available through SHARE
- We are talking to the SHARE team about formal implementations
- **OpenRules** for FDA will be donated to the FDA
 - hopefully they will do something with it

What has this all got to do with SHARE?

- Recent RFI ("Request for Information") of CDISC for SHARE:

Among the features that the API should eventually support are:

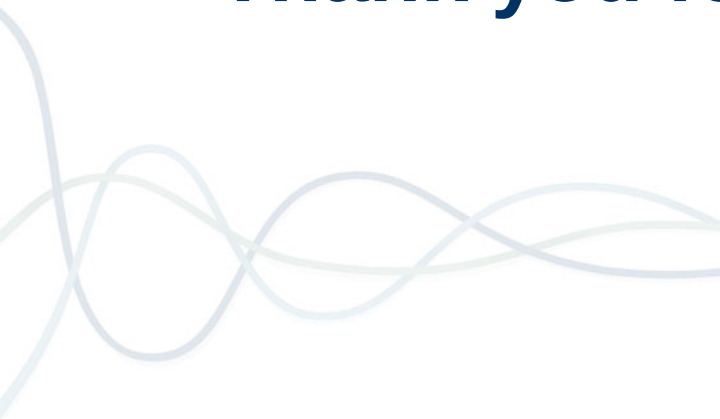
- Retrieval of sets of standard metadata or specified components (such as a domain) in various formats
- Retrieval of changes between versions of standards and update packages
- Lookup capabilities from codes, such as Test names associated with Test codes, available supplemental qualifiers, or alternative representations such as UCUM notations associated with CDISC controlled terms for units
- Ability to look up rules, such as validation rules, associated with standards, domains or variables
- Ability to access mapping data associated with variables (such as from CDASH to SDTM).
- Ability to retrieve research concept or value-level metadata (sets of metadata variables bound with relevant terminology).

<http://www.cdisc.org/cdisc-share>

One can share information between **people** using websites

One can SHARE information between **applications** using **web services**

Thank you for your attention



CDISC
SHARE