

# Next Generation LIS: Part II



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# Who Will Build It?

- We will.
  - Although there is tension between vendor-sourced and user-community-sourced functionality, the pendulum is swinging back towards a user-driven model
  - Development will be in partnership with the LIS vendor community

# What will it look like?

- Agile software development - deep partnership with domain expertise
- Reverse federation in support of personalized medicine
- Intrinsic support for customized workflow
  - “Workflow Engines”
- Support for High Dimensional Data
- Cloud-based Information Exchange
- Cloud-based data orchestration and transformation
- LIS interoperability
- Examples of advanced LIS functionality:
  - Generation of Results from Encoded Data
    - Thiopurine Metabolite Calculation
  - Automated orchestration of structured data in addition to narrative text
    - AJCC Breast Cancer Reporting

# Some Building Blocks:

*enabling technologies and methods*

- eXtensible Markup Language (XML)
- Federated architectures (Peer LIS, Cloud Network)
- Properly adjudicated namespaces and strongly typed concepts and data elements (ISO-11179)
- Service-oriented Architectures (SOAs) and normalized data models
- Grid Computing
- Cloud-based Service Architectures

Our present manner of construction of conventional LIS interfaces differs from the above list in essentially every aspect.

# Concept: Reverse Federation

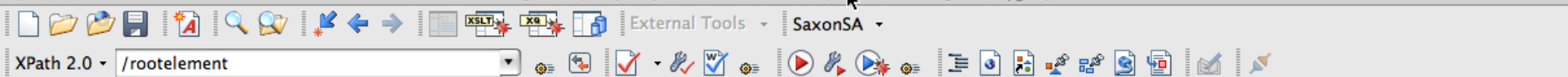
- Not only does the LIS serve the greater EHR connectivity ecosystem, so to *should* the greater plurality of EHR repositories serve the LIS and its emerging workflow needs, in the capacity of *decision support* data feeds assisting in report generation.
  - Increasingly essential for:
    - Molecular reporting
    - Personalized medicine
    - Synoptic cancer checklist reporting of correlation of histopathology staging in concert with clinical stage and longitudinal reporting (AJCC Cancer Staging Manual, 7<sup>th</sup> edition and later...)

# Web Portals

- Rapidly becoming Commoditized
- Multiple deployment strategies:
  - “Home-grown”
  - LIS-provided
  - Third-party best of breed solutions
- Can be either locally hosted, remotely hosted (SAAS), or both
- Multiple potential users:
  - Clinicians
  - Outside RHIO institutions and entities, in the setting of Meaningful Use Phases II & III
  - Patients themselves

# Web Services

- A logical extension of Web Portals
- The only logical interoperability strategy for true LIS-LIS connectivity
- Heavy utilization of XML



XPath 2.0 /rootelement

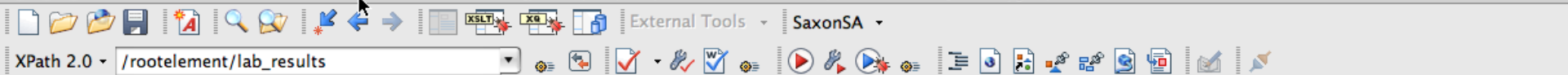
• build.xml x • Untitled1.xml\* x

```

1 <?xml version="1.0" standalone="yes"?>
2 <rootelement>
3   <lab_results>
4     <InterOp_Site_Key>6864</InterOp_Site_Key>
5     <InterOp_Site_Name>UM Reference Node</InterOp_Site_Name>
6     <lab_result Flag="" Location="University of Michigan" Resulted_Date="2020-09-07">
7       <lab_test LOINC_Code="2571-8" High_Test_Reference_Range="0"
8         Low_Test_Reference_Range="150" Unit_of_Measure="mg/dL "
9         Test_Method="Enzymatic Colorimetric"/>
10      <Numeric_Test_Result>
11        <valueModifier>=</valueModifier>
12        <actualValue>104</actualValue>
13      </Numeric_Test_Result>
14    </lab_result>
15    <lab_result Flag="" Location="University of Michigan" Resulted_Date="2020-09-07">
16      <lab_test LOINC_Code="2777-1" High_Test_Reference_Range="2.7"
17        Low_Test_Reference_Range="4.6" Unit_of_Measure="mg/dL"
18        Test_Method="Phosphomolybdate"/>
19      <Numeric_Test_Result>
20        <valueModifier>=</valueModifier>
21        <actualValue>3</actualValue>
22      </Numeric_Test_Result>
23    </lab_result>
24    <lab_result Flag="L" Location="University of Michigan" Resulted_Date="2009-07-26">
25      <lab_test LOINC_Code="3094-0" High_Test_Reference_Range="8"
26        Low_Test_Reference_Range="20" Unit_of_Measure="mg/dL " Test_Method="Urease"/>
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```

Text Grid Author



XPath 2.0 > /rootelement/lab\_results

Project

Archive Browser

Outline

- rootelement
  - lab\_results
    - InterOp\_Site\_Key 6864
    - InterOp\_Site\_Name UM Referenc
    - lab\_result
    - lab\_result
    - lab\_result "L"
    - lab\_result
      - lab\_test "19123-9"
        - Numeric\_Test\_Result
          - valueModifier =
          - actualValue 2
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_result
      - lab\_results "http://www.w3.org/199
        - InterOp\_Site\_Key 9862005
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16   <lab_test LOINC_Code="2777-1" High_Test_Reference_Range="2.7"
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18     Test_Method="Phosphomolybdate"/>
19   <Numeric_Test_Result>
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25   <lab_test LOINC_Code="3094-0" High_Test_Reference_Range="8"
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27   <Numeric_Test_Result>
28     <valueModifier>=</valueModifier>
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30   </Numeric_Test_Result>
31 </lab_result>
32 <lab_result Flag="" Location="University of Michigan" Resulted_Date="2020-09-07">
33   <lab_test LOINC_Code="19123-9" High_Test_Reference_Range="1.5"
34     Low_Test_Reference_Range="2.4" Unit_of_Measure="mg/dL " Test_Method="Formazan Dye"/>
35   <Numeric_Test_Result>
36     <valueModifier>=</valueModifier>
37     <actualValue>2</actualValue>
38   </Numeric_Test_Result>
39 </lab_result>
40 <lab_result Flag="" Location="University of Michigan" Resulted_Date="2009-07-13">
41   <lab_test LOINC_Code="19123-9" High_Test_Reference_Range="1.5"
42     Low_Test_Reference_Range="2.4" Unit_of_Measure="mg/dL " Test_Method="Formazan Dye"/>
43   <Numeric_Test_Result>
44     <valueModifier>=</valueModifier>
45     <actualValue>2</actualValue>
46   </Numeric_Test_Result>
47 </lab_result>
48 <lab_result Flag="" Location="University of Michigan" Resulted_Date="2020-09-07">
49   <lab_test LOINC_Code="2571-8" High_Test_Reference_Range="0"
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51     Test_Method="Enzymatic Colorimetric"/>
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56 </lab_result>
57 <lab_result Flag="" Location="University of Michigan" Resulted_Date="2009-07-26">

```

Model

Elements

Entities

XSLT/XQuery Input

Schema Components

Text Grid Author

# Cloud-based Data Transformation and Orchestration

- Anticipating the availability of tests that are too complex to deploy in every LIS, these techniques will allow for simplified provisioning of such functionality to essentially any LIS
- Simplified support model

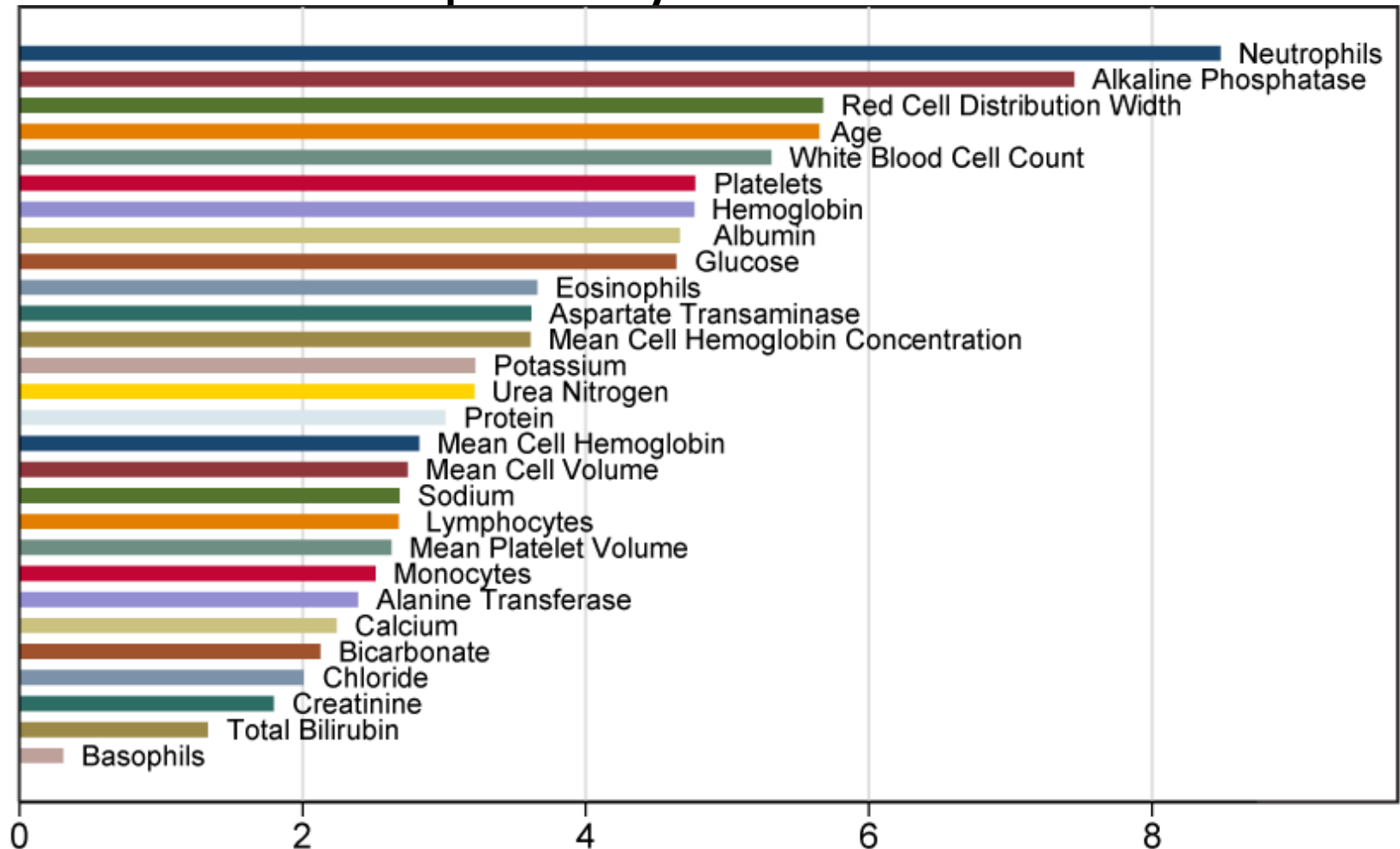
# Cloud-based Data Orchestration and Transformation

- One step beyond use of the cloud as merely an aggregation and distribution solution
- Instantiation of complex algorithms and rules in a centrally-curated location, simplifying both validation and maintenance
- Two Examples:
  - Thiopurine Metabolite Testing
  - Breast Cancer Checklist structured reporting validation, *pre-signout*

# Disruptive Potential of use of Orchestration and Transformation:

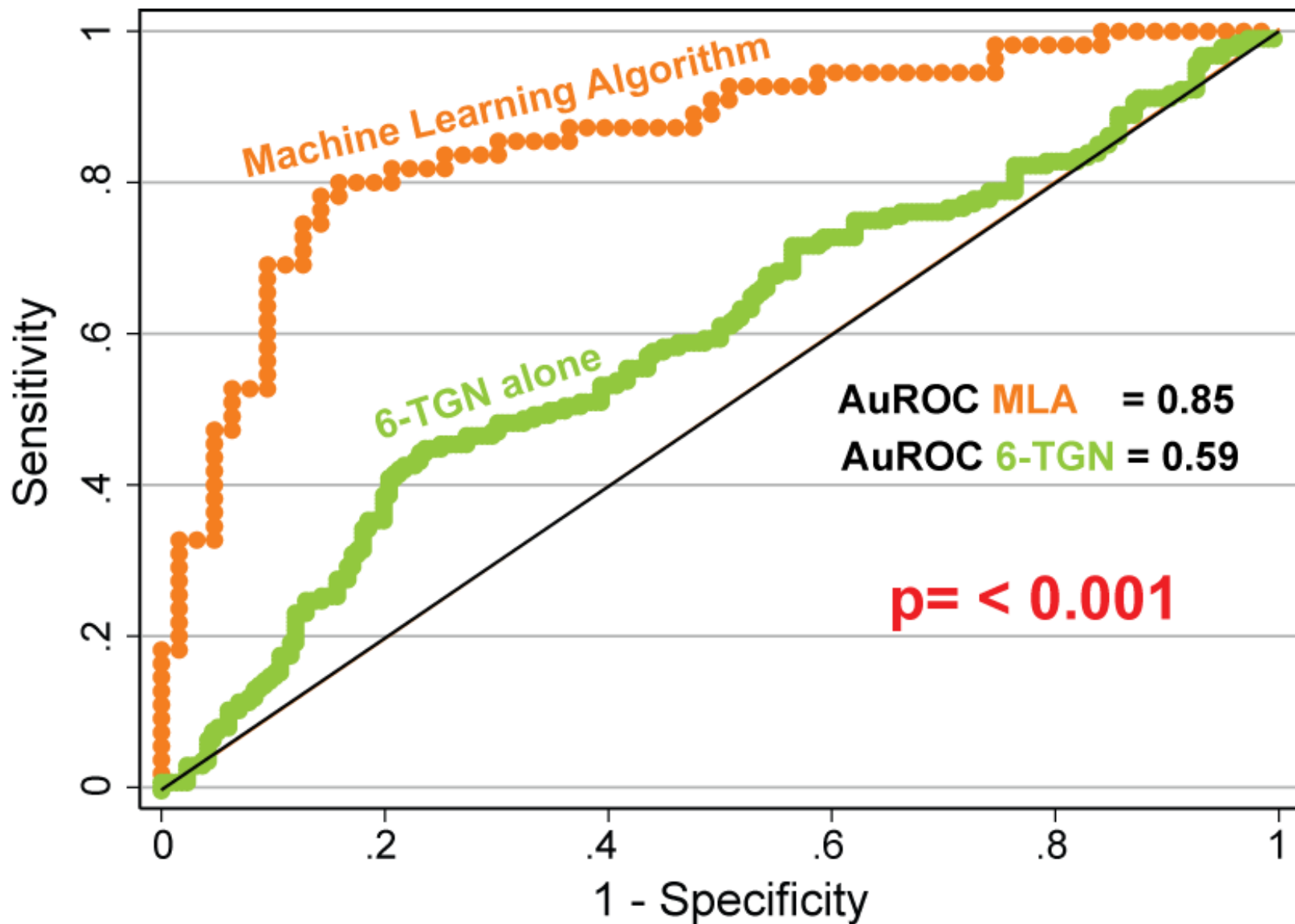
- Using the centrally placed rules engine to carry out non-trivial data transformation tasks:
  - Generation of calculated results from ultra-high complexity, rules-based indexed assays, such as the thiopurine metabolites test (which are extremely difficult to implement in conventional LIS architectures)
  - Pre-signout adjudication of surgical pathology breast cancer reporting, for compatibility with AJCC published guidelines, allowing for corrective action prior to signout.
- Implementing such solutions on a plurality (or multitude) of LIS locales would be intractable, owing to initial deployment and maintenance burden
- Central curation is the only feasible manner in which to surface such emerging testing and reporting complexity

# Thiopurine Metabolite testing: The emergence of **Encoded Data** from primary lab test data



% Importance of Clinical Predictors

# Comparing MLA to 6-TGN

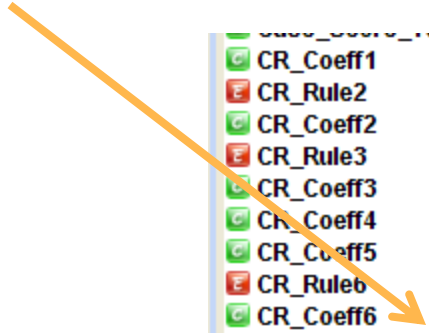


# Data Elements received from the LiddEx Cloud

Case View	
718	
	22 Apr 10 05:00
CollectTime	5:00:00
CollectDate	22/04/2010
Patient	718
age	25.941
sod	139
pot	4.7
chlor	107
co2	28
un	15
creat	0.8
gluc	84
cal	8.8
prot	7.2
ast	34
alb	3.9
alt	28
alk	387
tbil	0.3
wbc	3.6
hgb	10.1
hct	31.1
plt	162
mcv	75.4
mch	24.5
mchc	32.4
rdw	14.9
mpv	8.5
neut	1.6
lymph	0.9
mono	0.4
eos	0.7
baso	0
CR_Probability	0.6778



# Rules-Derived Data elements



CR_Coeff1	0
CR_Rule2	true
CR_Coeff2	0.2415
CR_Rule3	true
CR_Coeff3	0.2136
CR_Coeff4	0
CR_Coeff5	0
CR_Rule6	true
CR_Coeff6	0.2428
CR_Coeff7	0
CR_Rule8	true
CR_Coeff8	0.1838
CR_Rule9	true
CR_Coeff9	0.1976
CR_Coeff10	0
CR_Rule11	true
CR_Coeff11	0.1793
CR_Rule12	true
CR_Coeff12	0.1681
CR_Coeff13	0
CR_Coeff14	0
CR_Coeff15	0
CR_Coeff16	0
CR_Rule17	true
CR_Coeff17	-0.700704
CR_Coeff18	0
CR_Coeff19	0

CR_Coeff1	0
CR_Rule2	true
CR_Coeff2	0.2415
CR_Rule3	true
CR_Coeff3	0.2136
CR_Coeff4	0
CR_Coeff5	0
CR_Rule6	true
CR_Coeff6	0.2428
CR_Coeff7	0
CR_Rule8	true
CR_Coeff8	0.1838
CR_Rule9	true
CR_Coeff9	0.1976
CR_Coeff10	0
CR_Rule11	true
CR_Coeff11	0.1793
CR_Rule12	true
CR_Coeff12	0.1681
CR_Coeff13	0
CR_Coeff14	0
CR_Coeff15	0
CR_Coeff16	0
CR_Rule17	true
CR_Coeff17	-0.700704
CR_Coeff18	0
CR_Coeff19	0

**Edit episode attribute - CR\_Rule2**

Conditions

- eos > 0.05
- rdw ≤ 18.55
- un > 6.5

Add  
Edit  
Remove

CR\_Rule 2 is true when the episode values in the current case satisfy all of these conditions.

AND

**Edit: CR\_Coeff2**

Expression

0.2415 whenever CR\_Rule2 is true otherwise 0

Evaluates to: <0.2415>

Show

Attributes

CollectTime  
CollectDate  
Patient  
age  
sod  
pot  
chlor  
co2  
un

OK Cancel Help

The value of CR\_Coeff2 is dependent on the outcome of CR\_Rule2.

Case View

721

	16 Apr 10				
	08:00				
<b>Patient</b>					
<b>ClinicalResponse</b>					
<b>Clin_High</b>					
<b>Clin_Mod</b>					
<b>Clin_Low</b>					
<b>Shunting</b>					
<b>Shunt_High</b>					
<b>Shunt_Mod</b>					
<b>Shunt_Low</b>					
<b>Non_Adherence</b>					
<b>NonComp_High</b>					
<b>NonComp_Med</b>					
<b>NonComp_Low</b>					
<b>CollectDate</b>					
<b>CollectTime</b>					
<b>Age</b>					

Preview

Clinical Response:      Probability = 21.6 %  
 Shunting to 6-MMP:      Probability = 14.4 %  
 Non-compliance:        Probability = 4.6 %

Assuming this patient has been on the same dose of thiopurine medication for at least 4 weeks and is at steady state:

LML

This patient has had very little hematologic and chemistry response to thiopurines, has low probability of shunting and a low probability of non-adherence.

Consider increasing the thiopurine dose to increase the probability of clinical response.

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This new report is not yet allowed to be autovalidated.

# University of Michigan

Date:

# Rippledown® – Thiopurine Clinical Interpretation

Preview  
Clinical Response Interpretation  
Assuming this patient has been on the same dose of thiopurine medication for at least 4 weeks and is at steady state:  
Studies on this patient show a probability for Clinical response of 14.616923% which indicates that they had very little hematologic and chemistry response to thiopurines,

Preview  
Clinical Response Interpretation  
Assuming this patient has been on the same dose of thiopurine medication for at least 4 weeks and is at steady state:  
Studies on this patient show a probability for Clinical Response of 43.36358% which indicates that they have had a moderate hematologic and chemistry response to thiopurines,

This  
Preview  
Clinical Response Interpretation  
Assuming this patient has been on the same dose of thiopurine medication for at least 4 weeks and is at steady state:  
Studies on this patient show a probability for Clinical Response of 67.77725% which indicates that they have had a good hematologic and chemistry response to thiopurines,

This new report is not yet allowed to be autovalidated. Allow Settings

Comments Preview Approval Autovalidation Queues Notes

Case View

706

23 Mar 10  
05:00

<b>Patient</b>	706
<b>ClinicalResponse</b>	70.2
<input checked="" type="checkbox"/> Clin_High	False
<input checked="" type="checkbox"/> Clin_Mod	True
<input checked="" type="checkbox"/> Clin_Low	False
<b>Shunting</b>	29.4
<input checked="" type="checkbox"/> Shunt_High	True
<input checked="" type="checkbox"/> Shunt_Mod	False
<input checked="" type="checkbox"/> Shunt_Low	False
<b>Non_Adherence</b>	2.6
<input checked="" type="checkbox"/> NonComp_High	False
<input checked="" type="checkbox"/> NonComp_Med	False
<input checked="" type="checkbox"/> NonComp_Low	True
CollectDate	23/03/2010
CollectTime	5:00:00
age	47.088

Preview

Clinical Response:      Probability = 70.2 %  
 Shunting to 6-MMP:    Probability = 29.4 %  
 Non-compliance:        Probability = 2.6 %

Assuming this patient has been on the same dose of thiopurine medication for at least 4 weeks and is at steady state:

MHL  
 This patient has had a moderate hematologic and chemistry response to thiopurines, has a high probability of shunting and a low probability of non-adherence.

Consider testing for shunting to 6-MMP in this patient and/or increasing the thiopurine dose to increase the probability of clinical response.

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# University of Michigan

Date:

Case View

702

	24 Jun 10
	01:00

<b>Patient</b>	702
<b>ClinicalResponse</b>	80.0
<input checked="" type="checkbox"/> Clin_High	True
<input checked="" type="checkbox"/> Clin_Mod	False
<input checked="" type="checkbox"/> Clin_Low	False
<b>Shunting</b>	7.0
<input checked="" type="checkbox"/> Shunt_High	False
<input checked="" type="checkbox"/> Shunt_Mod	False
<input checked="" type="checkbox"/> Shunt_Low	True
<b>Non_Adherence</b>	2.2
<input checked="" type="checkbox"/> NonComp_High	False
<input checked="" type="checkbox"/> NonComp_Med	False
<input checked="" type="checkbox"/> NonComp_Low	True
CollectDate	24/06/2010
CollectTime	1:00:00
age	20.378

Preview

```

Clinical Response:      Probability = 80.0 %
Shunting to 6-MMP:     Probability = 7.0 %
Non-compliance:       Probability = 2.2 %

Assuming this patient has been on the same dose of thiopurine medication for at least 4 weeks and is at steady state:

HLL
This patient has had a good hematologic and chemistry response to thiopurines, has a very low probability of shunting and a low probability of non-adherence.

If this patient has not obtained a good response, they may have a non-inflammatory cause of symptoms, or if inflamed, may need a different form of therapy, as increases in dose are unlikely to produce large therapeutic gains.

Interpretations derived from Version 1.01 of Algorithm.  Copyright U Michigan - all rights reserved.
                
```

This new report is not yet allowed to be autovalidated.

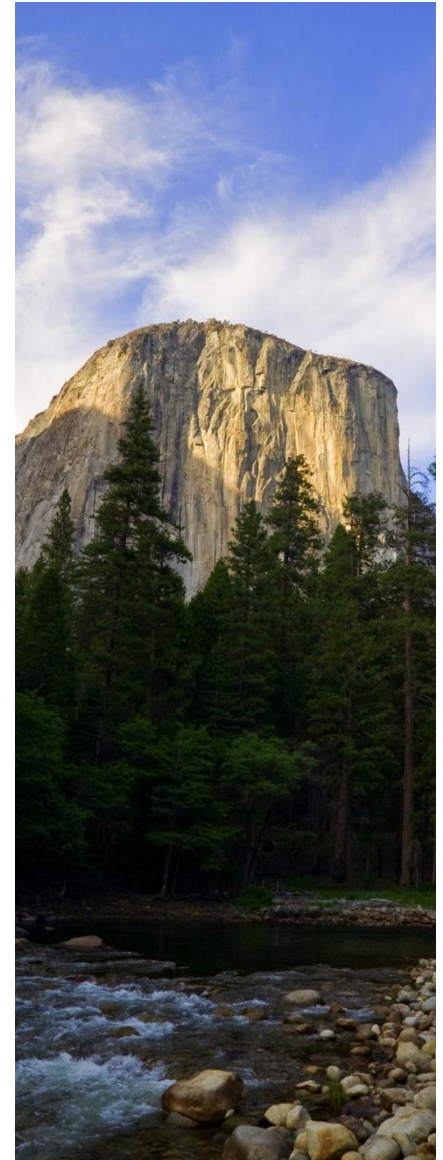
Pdf Preview	Allow	Settings
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# University of Michigan

Date:

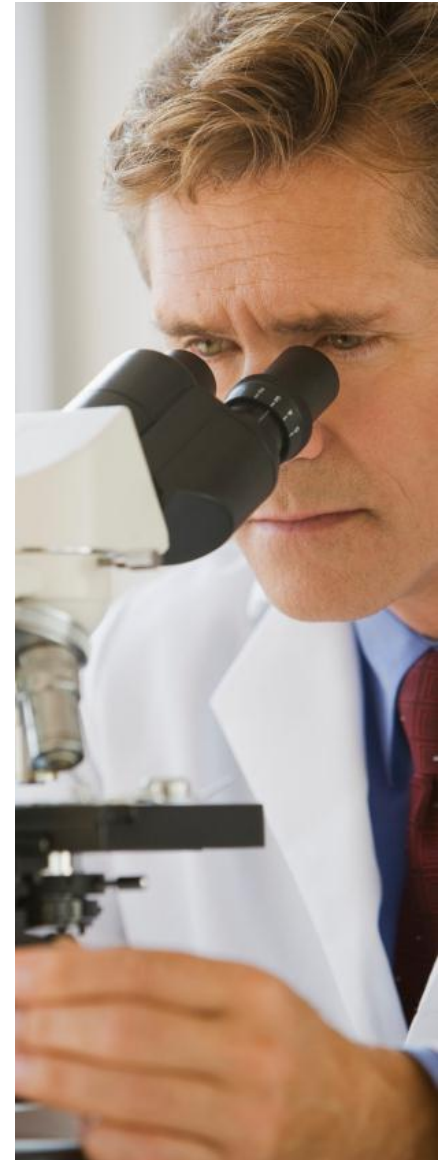
# Use of Web services for pre-signout validation of pathology reports

- John F. Madden, MD, PhD (Duke University)
- Shane Brown, PhD (PKS, Inc.)
- John Hamilton (University of Michigan)
- Fede Lopez (PKS, Inc.)
- Rob Manser, MSc (PKS, Inc.)
- Jeffrey Sica (University of Michigan)
- Ulysses Balis, MD (University of Michigan)



# Problem statement

- Cancer pathology report validation is complex, consensus driven, evolves quickly
- Pathologists need feedback *prior* to signout
- Some LIS systems support structured input, but flatten results to text
  - → no easy validation possible



# Solution

- ▶ Report validation as a real-time web service
- ▶ Accept and parse text reports using rules
- ▶ Convert to standardized data format
- ▶ Validate content using centrally-curated rules
- ▶ Return error/warnings as response

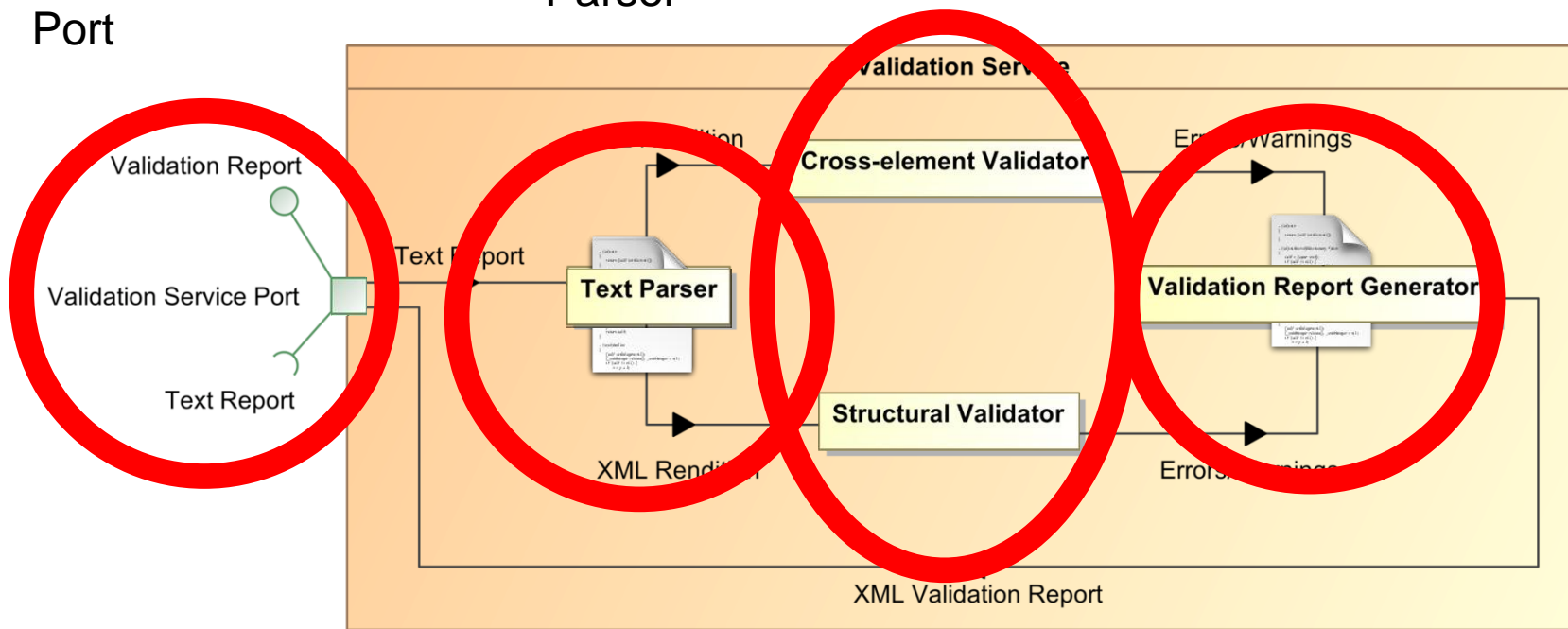


Webservice Port

Text Parser

Validator

Orchestration



# LIDDEx/PKS Realization

# Implementation

	Service	Orchestration	Parser	Validation
This Pilot	SOAP/WSDL	PKS- Rippledwn + Ant + XProc	PKS- Rippledwn Rules Engine	PKS/ Relax NG/Schemat ron
Other Options	REST	Various	PKS- Rippledwn Rules Engine	PKS- Rippledwn

# Service implementation

- ▶ Web Services Description Language (WSDL)
- ▶ Service calls are publicly-defined, included in LIDDEx service standard
- ▶ Payload is in SOAP Wrapper
  - ▶ Incoming: Pathology report as semi-structured text
  - ▶ Outgoing: XML report of warnings and errors, using publicly-defined LIDDEx validation vocabulary



# Summary

- The future LIS will leverage:
  - Strong Development partnership with the vendor.
  - Development and use of true interoperability standards
    - XML
    - ISO-11179
  - Development of standardized Web services
  - Development of cloud-based rules that run, centrally, within cloud services
  - Instantiation of all the above as core functionality within all commercial LIS solutions
- The pathway there:
  - User driven

Questions

