

Methods Database moves beyond PoC

Allotrope Foundation
Connect workshop October 8th, 2019
Genentech, San Francisco

Gerhard Noelken
Project Manager Lab of the Future
Pistoia Alliance





- **Pistoia Alliance and precompetitive collaboration**
- **Methods Database PoC**
- **Methods Database Phase 2 RFP**
- **Community Methods Database >>> Marketplace**

Pistoia Alliance Member Companies

METHODS
DATABASE



Pistoia Alliance Strategic Themes

Building momentum and ideas



**METHODS
DATABASE**

FY'18/19
Themes

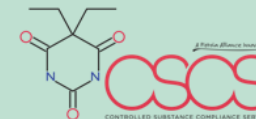
Lab of the
Future

AI/Machine
Learning

RWD

Active

ONTOLOGIES
MAPPING



UDM

AbVance

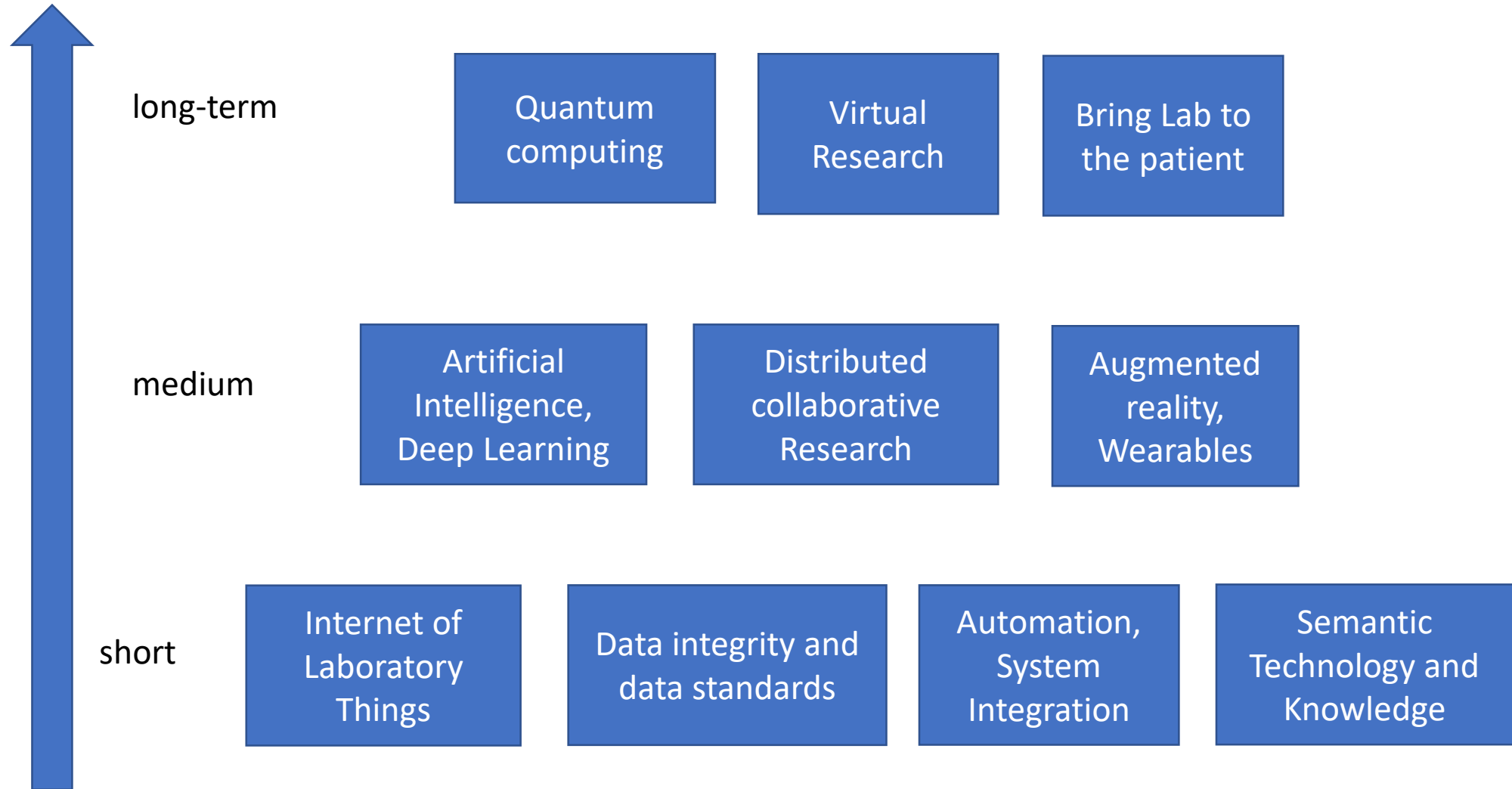
PISTOIA ALLIANCE
USER EXPERIENCE
FOR LIFE SCIENCES

METHODS
DATABASE
PISTOIA ALLIANCE & ALLOTROPE FOUNDATION

Data Sharing, Best Practice and Standards/Tools

Communities of Interest: LotF, AI, UX, RWD and Non-Clinical Development

Lab of the Future horizons



Methods Database

A Joint Pistoia Alliance-Allotrope Foundation Initiative

What happened so far ?

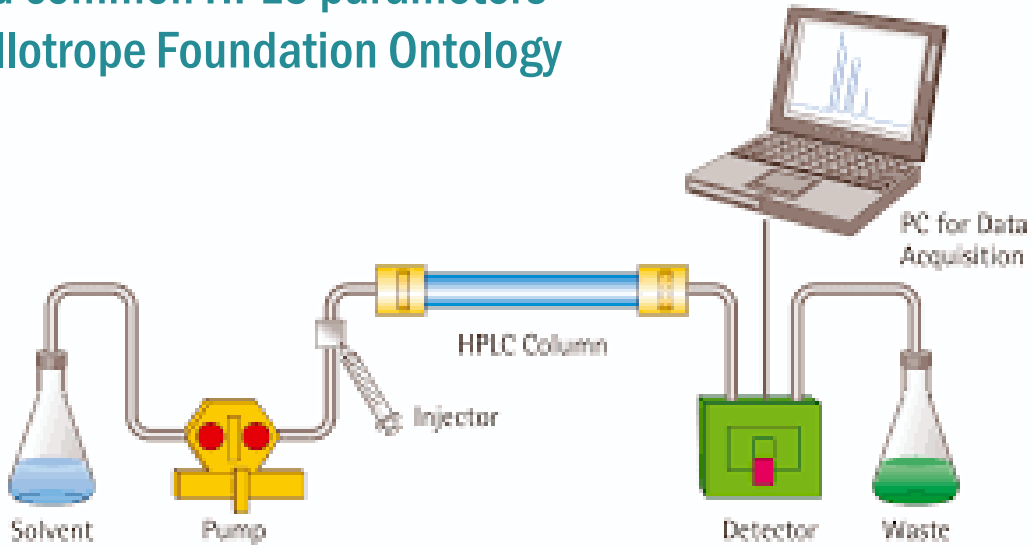


Why are we doing it?

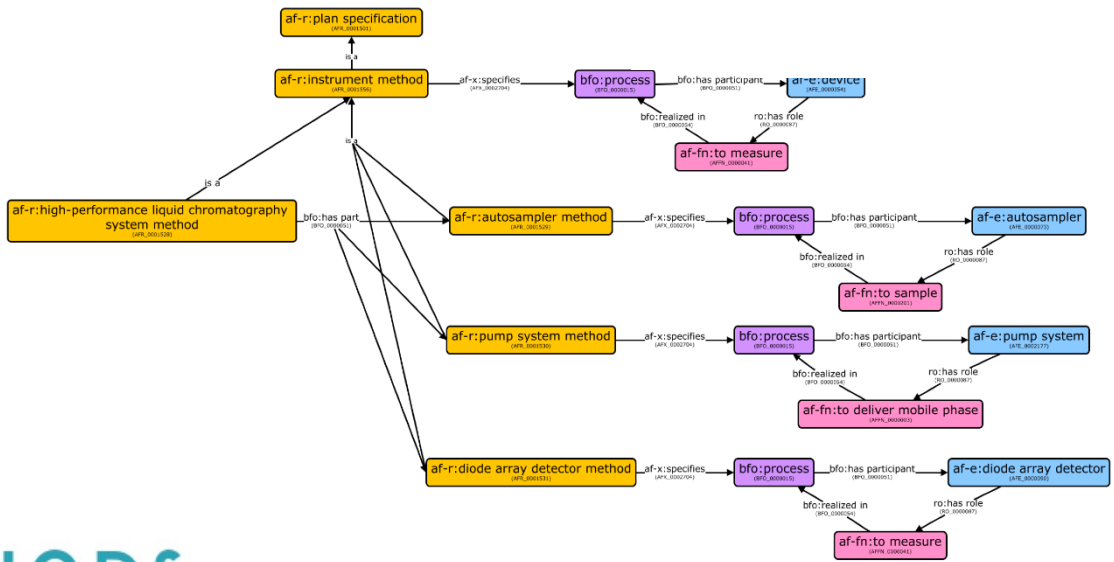


- Method descriptions are still mainly text-based documents
- Reproducibility of Methods limited by interpretation of free text
- Descriptions use different terminology and levels of detail
- Version control often difficult because of number of copies
- Storage often in local PC's with limited cyber resiliency ...

1 Feed common HPLC parameters into Allotrope Foundation Ontology

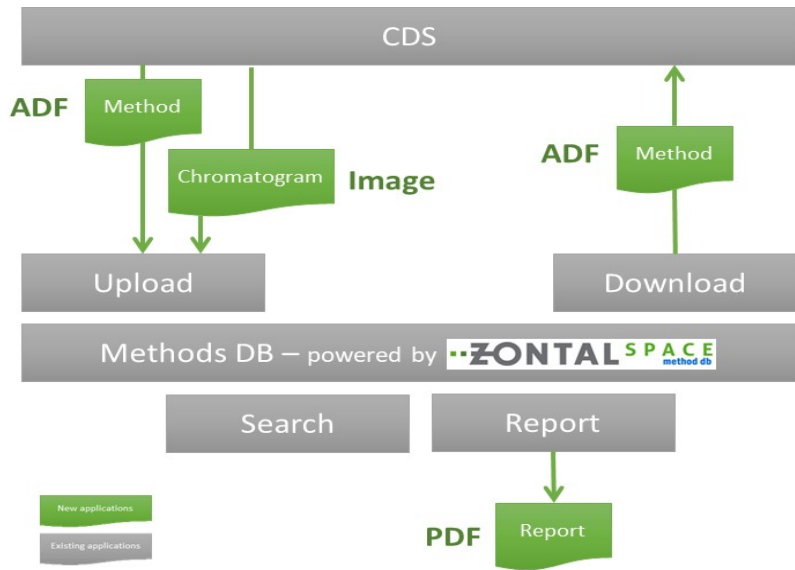


2 Build the RDF Data Model

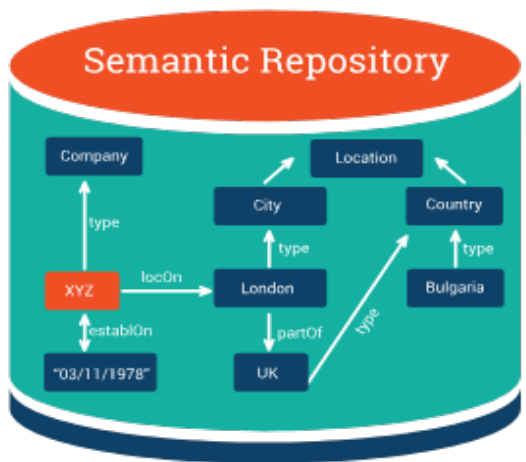


METHODS DATABASE

3 Create the CDS adapters



4 Provide the Methods Database



It allows you to:

- Change the data schema "on the fly" without interfering with the data;
- Automatically discover new facts and build new data based on semantic rules (data inference or reasoning);
- Seamlessly integrate data from distributed data sets and data sources (data federation);
- See your data as flexible, interconnected, interlinked graph data models.

Different personas, different expectations



Analytical Scientist (R&D and QC)

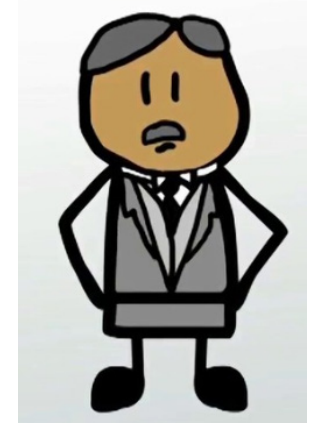
CRO Scientist



Common Success Criteria

- Standardized Instruction sets
- Method Transferability
- Secure location of experimental details
- Improved Reproducibility
- Introduced Searchability
- Report Generation

All success criteria met for Phase 1 PoC!



CRO Manager

Research Manager



Methods Database

A Joint Pistoia-Allotrope Initiative

What is happening now in phase 2?

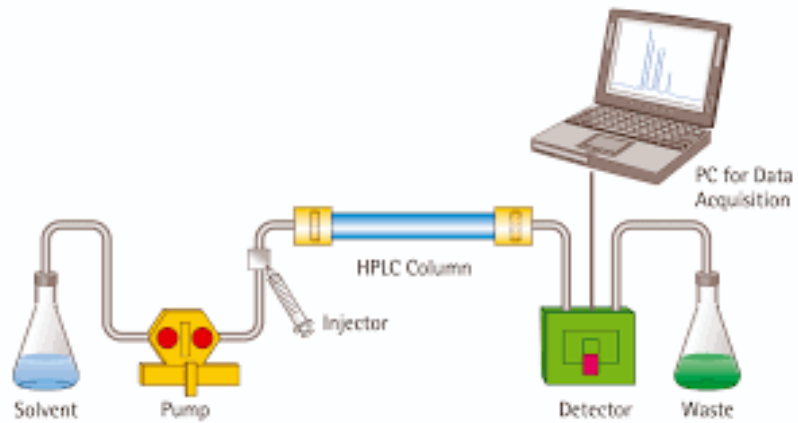


RFP process for Methods Database Phase 2



- Gathering of user stories and functional requirements
- F2F meeting at TetraScience in Boston for prioritization of functional requirements
- Vivenics (Petrik Cuijpers) support for writing Request for Proposal document
- Distribution of RFP and two rounds of RFP open questions review
- Received RFP proposals by September 22, 2019
- Currently in last steps of decision process

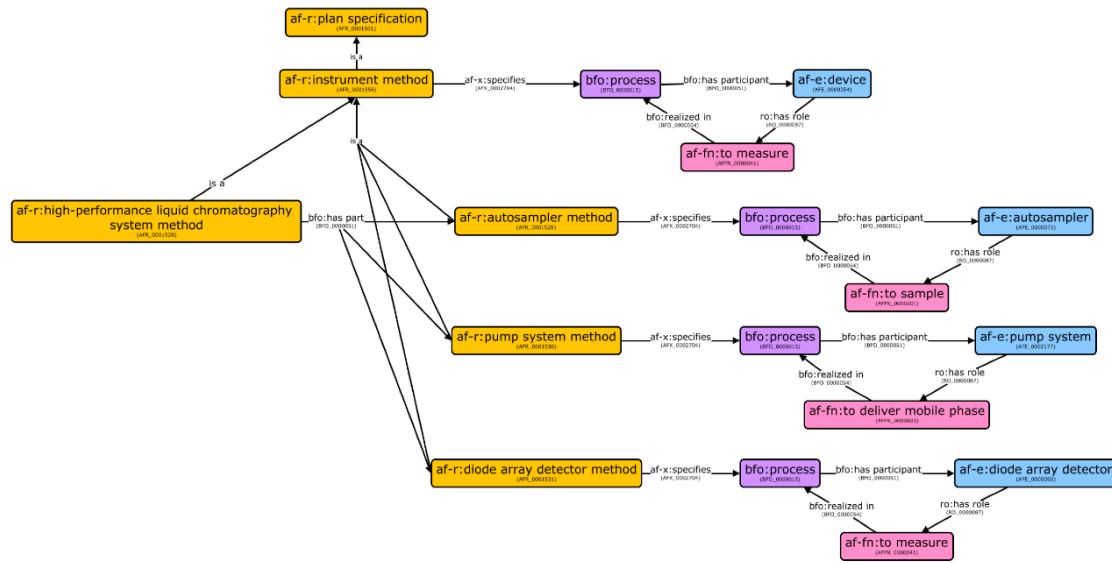
1 Feed common HPLC parameters into AFO



More Metadata

- Area of Usage
- Project context
- Maturity
- Limitations

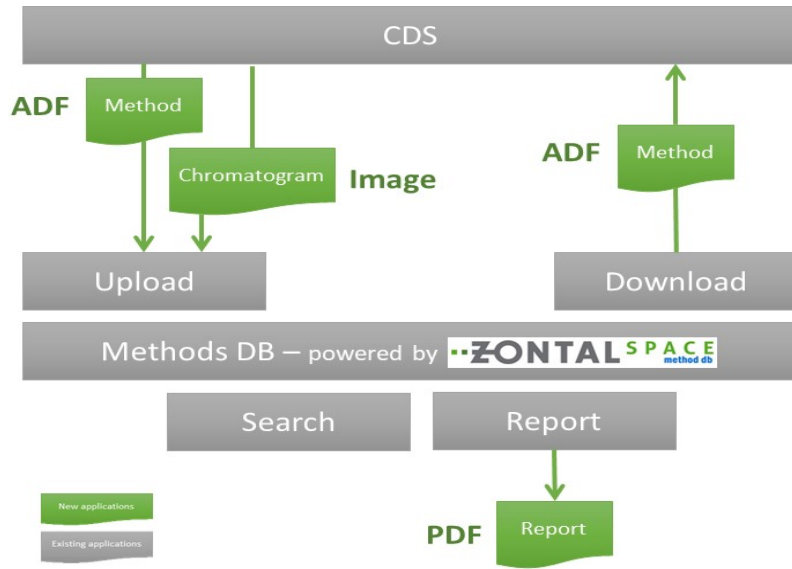
2 Build the RDF Data Model



Multitier Data-model

1. Default value tier
2. HPLC common parameters tier
3. Vendor specific parameter tier

3 Create the CDS adapters



More CDS's supported

- Vendor specific functionality
- Data upload through API
- Audit trail

Methods Db phase 2 components and process



Methods Database standard

Multitier Data-model

1. Default value tier
2. HPLC common parameters tier
3. Vendor specific parameter tier

API specification
Allotrope Ontology

Methods Database application

- Search, sort, compare
- Storage of ADF containers
- Visualization (Human readable report)

CDS adapter	<ul style="list-style-type: none"> • Up to 4 CDS systems • Audit trail
LIMS/ELN adapter	API connectivity for Lab Informatics Systems



RESTful based interface
 A RESTful based interface for the Methods Database version that can serve as a central point with an API to connect together with other systems for the exchange and specification of Analytical Methods information that will allow software vendors to easily serve Analytical Methods information to their informatics systems (ELN, LIMS, CDS)

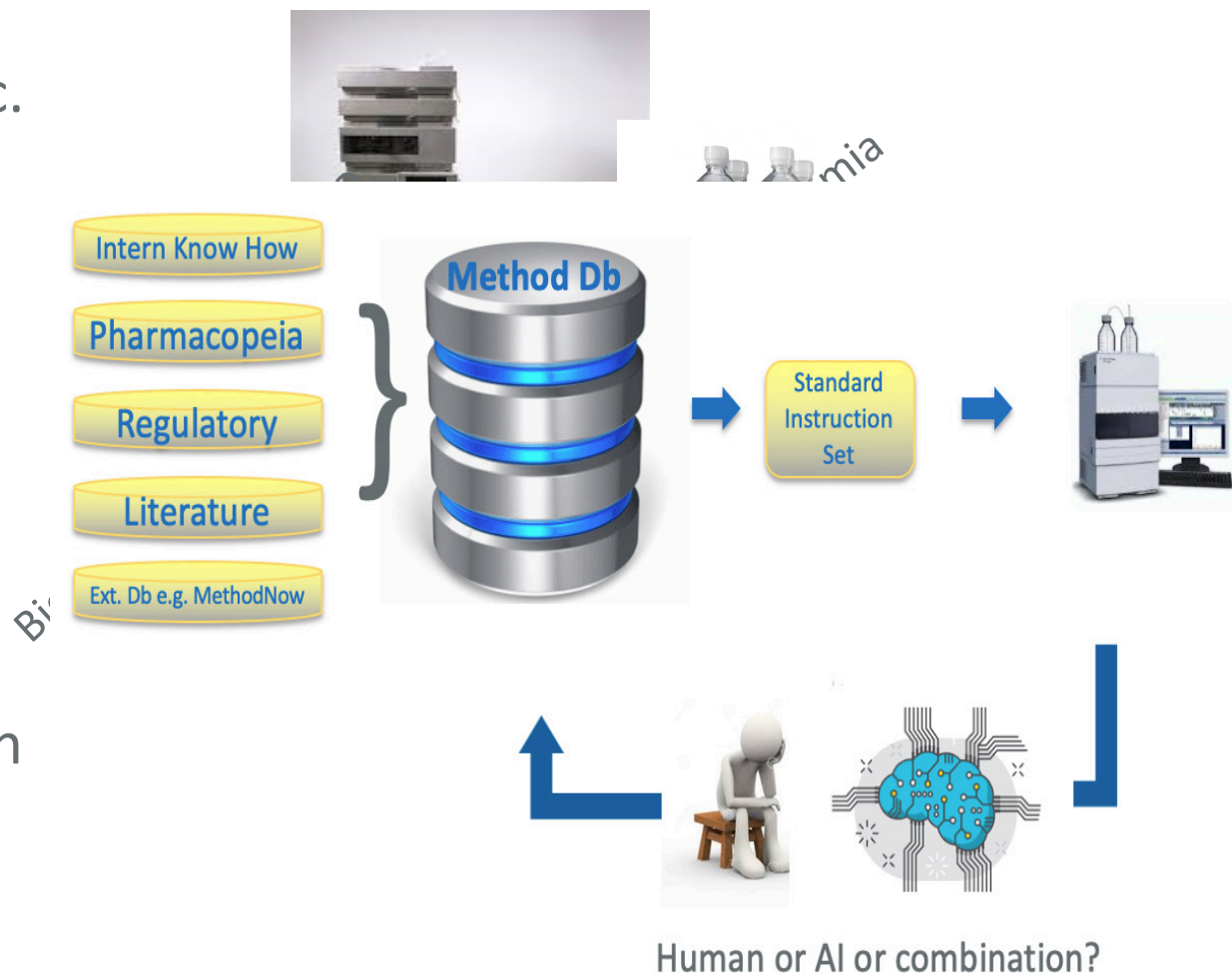
Goals for phase 2



- Big Learning in RFP process that Methods Db standard and application should be looked at separately
- Deliver the new version ready for use for targeted usage in H2 2020
- Promote the Methods Db standard for broader usage across CDS's and multiple Lab informatics platforms
- Build support for a Community version of the Method Db that invites sharing of Analytical Method Information

Vision for the Methods Database

1. Bring more analytical technics into the Methods Database concept e.g. MS, NMR etc.
2. Encourage Method Information exchange between Biopharma, CRO's, Academia, Regulators ...
3. Make Method information available for Artificial Intelligence and Machine Learning
 - Amount of consistent data
4. Increase consistency of information between different sources on a Method Marketplace
 1. Scientific Literature, Publishers
 2. Pharmacopeia USP
 3. Commercial Method Information sources



The Community Methods Database >>> Marketplace



**METHODS
DATABASE**

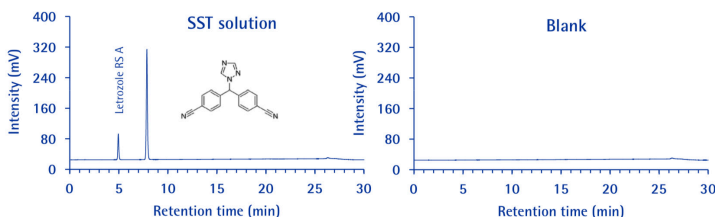
Letrozole and Related Substances (USP)

Purospher® STAR RP-18 endcapped

Chromatographic Conditions

Column:	Purospher® STAR RP-18 endcapped (5µm) Hibar® RT 125x4.6	1.51914.0001
Injection:	20 µL	
Detection:	UV 230 nm	
Cell:	10 µL	
Flow Rate:	1.0 mL/min	
Mobile Phase:	A: Water B: Acetonitrile	
Gradient:	See table	
Temperature:	25 °C	
Diluent:	Acetonitrile and water; 3:7 (v/v)	
SST solution:	2 µg/mL of Letrozole Related Compound A and 10 µg/mL of Letrozole in Diluent	
Standard solution:	1 µg/mL of USP Letrozole in Diluent.	
Sample solution:	Transfer 25 mg of Letrozole to a 250-mL volumetric flask. Dissolve in 75 mL of acetonitrile, and dilute with water to volume.	
Pressure Drop:	72 - 28 Bar (1044 - 410 psi)	

Time (min)	A (%)	B (%)
0.01	70	30
25.0	30	70
26.0	70	20
30.0	70	30



Chromatographic Data :

No	Compound	Retention Time (min)	RRT	Resolution	Theoretical Plate	Assymetry
1	Letrozole related compound A	4.9	0.62		11641	1.10
2	Letrozole	7.9	1.0	14.3	20133	1.07

HPLC analysis

1. Perform HPLC analysis using a (Merck Hitachi, Germany) equipped with an auto sampler (Merck Hitachi L 7200); Pump Merck Hitachi L 7100; Merck L 7614; Diode Array Detector L 7455; Peltier sample cooler Merck for L 7200; Interface System Merck Hitachi D7000.
2. Carry out chromatography on 10 mm, 5 µm ODS2 metal free guard column, 100 x 4.6 mm, 5 µm ODS2 metal free column (Alltech Ass.) con analytical column 250 x 4.6 mm Grace Vydac 201 TP 54 modified with bio-compatible frits.
3. Inject 20 µL of the sample on to the column at a flow rate of 1.5 mL/min maintained at 20 °C.
4. Employ mobile phase of acetonitrile/methanol/dichlorom ethane (75:21:4 v/v/v) and 0.1% BHT + 0.05% triethylamine (MeOH + 0.05 M amm acetate).
5. Detect the sample on UV - VISIBLE Spectrophotometer Equipment (Jasco V-630, Japan).
6. Perform data control and acquisition by Software Merck Hitachi HSM 1999.

Experimental

Chromatographic conditions

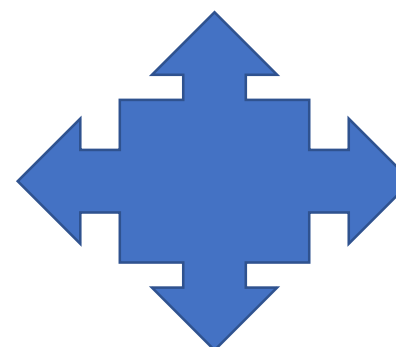
A Jasco HPLC system equipped with a supelcosil C18 column (250 mm x 4.6 mm; 5µ), a pump (PU 2080), a sample injector (Rheodyne 7125) with a 20 µL loop and a UV detector (UV-2075) connected to a model 720 Data Module integrator was employed for the analysis.

A mobile phase consisting of a mixture of 0.01 M ammonium acetate buffer (pH 6.8) and acetonitrile in the ratio of 35:65 v/v was prepared, filtered through a 0.45 µm membrane filter and degassed prior to use. All the reagents used were of analytical grade. Acetonitrile of HPLC grade (Merck), ammonium acetate (Aldrich) and water purified by Milli-Q system (Millipore) were used for the preparation of the mobile phase.

**Scientific
Literature**

**Pharmacopeia
e.g. USP**

**In-house
Experience**



**Commercial
Services**

CAS MethodNow



Conclusions for Methods Database



- PoC has been a success and motivated everybody to progress
- The Methods Db Phase 2 should be ready for targeted use H2 2020
- The Communication of the Business benefit of a Methods standard has to be sharpened and explained efficiently
- The FAIR approach has to be extended beyond just data, to methods, interfaces and laboratory workflows.

It takes a village to raise a child



**Maybe the Methods Db
is not that different**

Thank You for your
attention !