

CAPITAL MARKETS DAY

JUNE 14-15, 2018 | PARIS CAMPUS, FRANCE



3DEXPERIENCE®

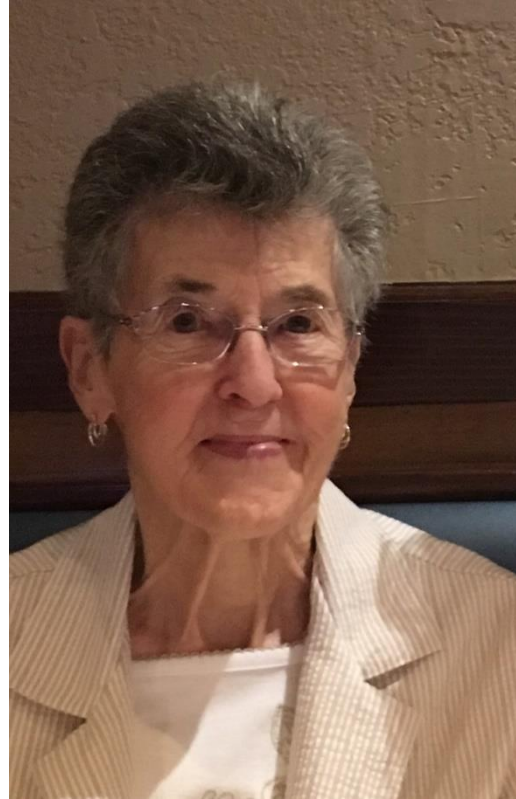
Janet CHEETHAM

Executive Director Process Development, Amgen

Leif PEDERSEN

BIOVIA CEO

Why we are here!



CAPITAL MARKETS DAY

JUNE 14-15, 2018 | PARIS CAMPUS, FRANCE



3DEXPERIENCE Value | Life Sciences: Amgen

3DEXPERIENCE®



ACHIEVING A DIGITAL TRANSFORMATION OF THE LABS ECOSYSTEM – INDUSTRY 4.0

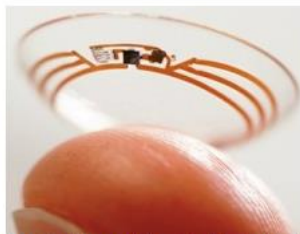
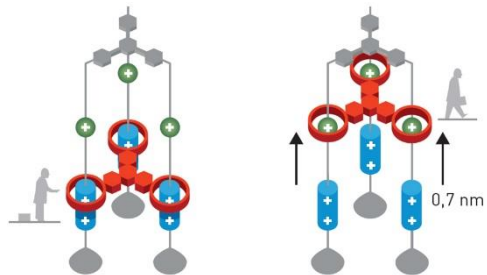
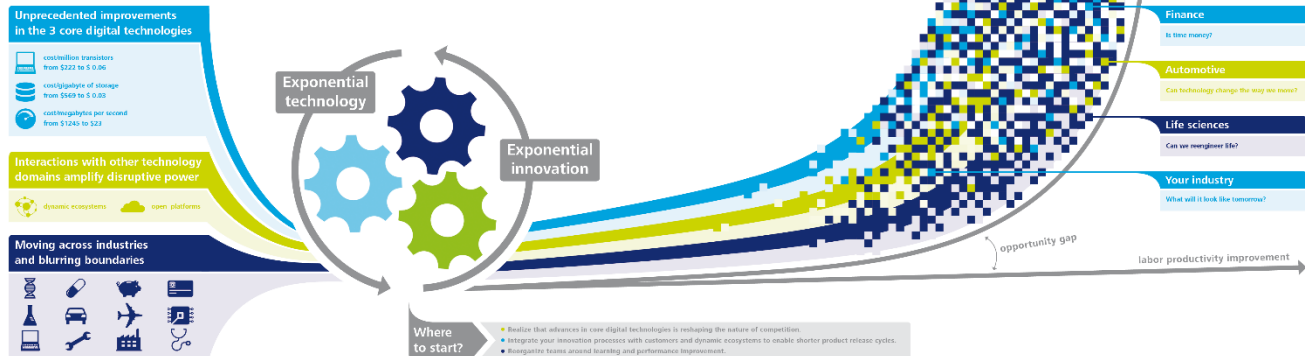
JANET CHEETHAM

DASSAULT JUNE 2018, VELIZY

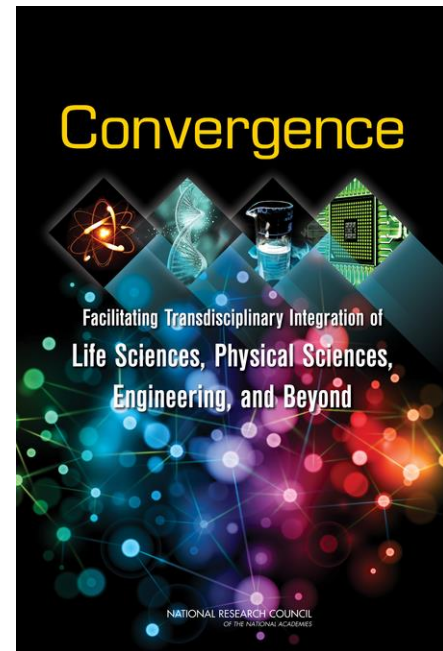
AMGEN[®]

EARLY 21ST CENTURY....A CONVERGENCE OF SCIENTIFIC DISCIPLINES COUPLED WITH AN EXPONENTIAL GROWTH IN TECHNOLOGIES ...AND DATA

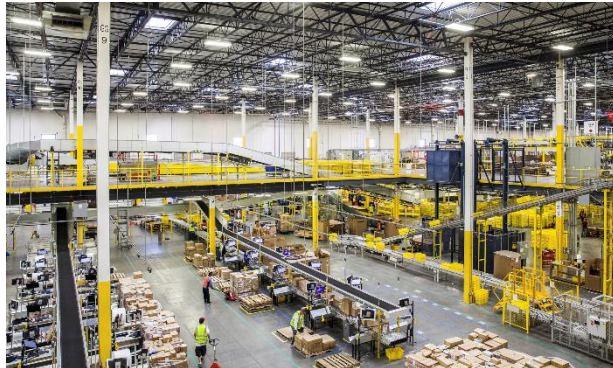
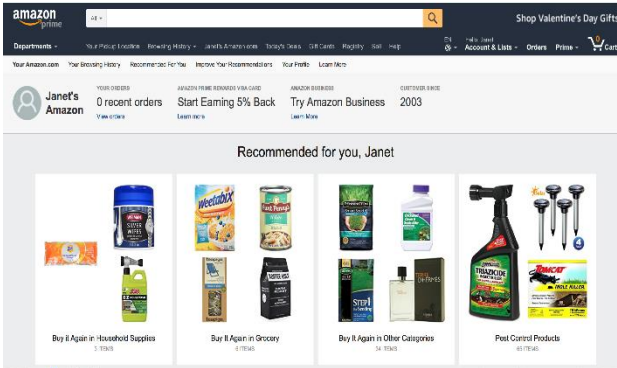
Exponential technologies are driving wave after wave of exponential innovation



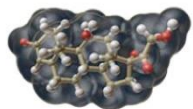
A contact lens with embedded circuitry monitor blood glucose levels (Source: Google)



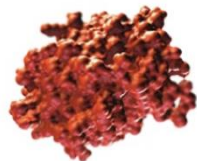
TRANSFORMATION IN OTHER INDUSTRIES VIA DATA CENTRICITY AND DIGITAL



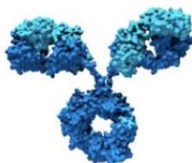
GROWING MOLECULAR VARIETY, INCREASING MANUFACTURING COMPLEXITY OF OUR THERAPEUTIC PIPELINE AND EMPHASIS ON SPEED CATALYSTS FOR TRANSFORMATION



Small Molecules



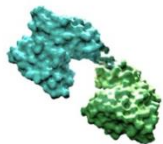
Therapeutic Proteins



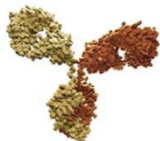
Monoclonal Antibodies



Fusion Proteins



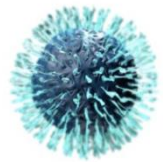
Bite



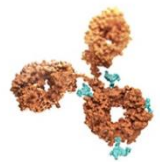
Peptides



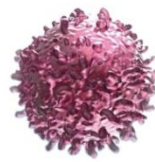
Peptibodies



Oncolytic Immunotherapy Viruses



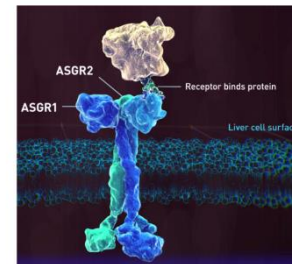
Antibody Drug Conjugates



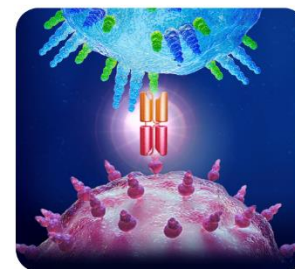
Cart Cells



a **MUTATION**
in **95%** of
PANCREATIC
CANCER



a **GENE LINKED TO**
LOWER RISK
of **HEART ATTACKS**



a **MODALITY** for the
IMMUNE SYSTEM
to **FIGHT CANCER**

A Biology First Approach

A FOCUS ON PATIENT CENTRICITY IS DRAMATICALLY CHANGING HOW WE MUST APPROACH DEVELOPING AND DELIVERING OUR PRODUCTS TO PATIENTS



Process is the Product

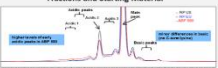


Patient Needs Define the Product

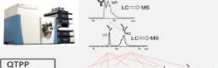
LINKING ATTRIBUTES TO BIOLOGICAL PERFORMANCE

MAM Platform

Distribution of Identified CQA Modifications in CEX Fractions and Starting Material



Sample	Mod 1	Mod 2	Mod 3	Mod 4	Mod 5	Mod 6	Mod 7	Mod 8	Mod 9	Mod 10
Sample 1	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
Sample 2	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.1
Sample 3	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2
Sample 4	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3
Sample 5	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4
Sample 6	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.5
Sample 7	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.5	1.6
Sample 8	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.5	1.6	1.7
Sample 9	0.9	1.0	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8
Sample 10	1.0	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9



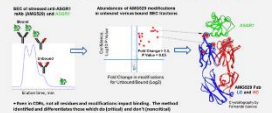
Biological relevance

Cell Line PBMC (iVCA) Xeno-het Mouse



Inflammation PRR response* Mechanistic studies
Inflammation T-cell response
Inflammation T-cell response Anti-drug antibodies

NEW METHOD: DIRECT EXPERIMENTAL CRITICALITY ASSESSMENT BY SEC AFFINITY BINDING FOLLOWED BY LC-MS CHARACTERIZATION - MAB / ASSESS



Molecule Differentiation



DIFFERENTIATING THE PATIENT EXPERIENCE

Patient Centric Manufacturing

- Vein to vein, on demand, just in time manufacturing
- Limited understanding from molecular design and cell phenotype to patient outcomes
- Point of Use vs. centralized manufacturing strategy
- Linking Attributes to pathways



Beyond The Molecule

A PARADIGM SHIFT IN THE MANUFACTURING NETWORK, INTEGRATED END TO END PLATFORMS AND DEMATERIALIZATION

MODALITY DIVERSITY DRIVES MANUFACTURE INNOVATION TO DELIVER QTTP

Conventional



750K sq ft | Sits on 80 acres across 3 buildings | Cost to build over \$1 billion over 4 years

Cost and footprint make geographic expansion difficult

Key Enabling Technologies

- High titer processes
- Single-use systems
- Modular design and construction
- Connected processing
- Online / At-line analytics
- Real-time remote monitoring
- Raw material variation control

Flexible

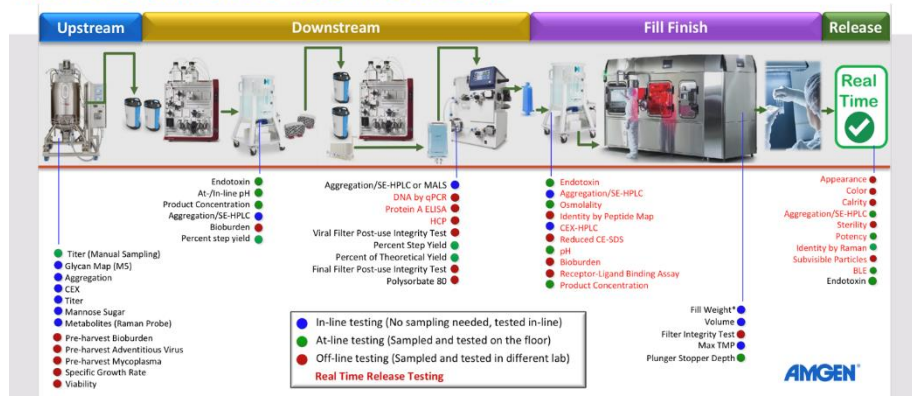


120k sq ft | Will sit on 5 acres | 1/5 of the cost and can be built in 2 years

New facility allows expansion almost anywhere in the world to support local market needs

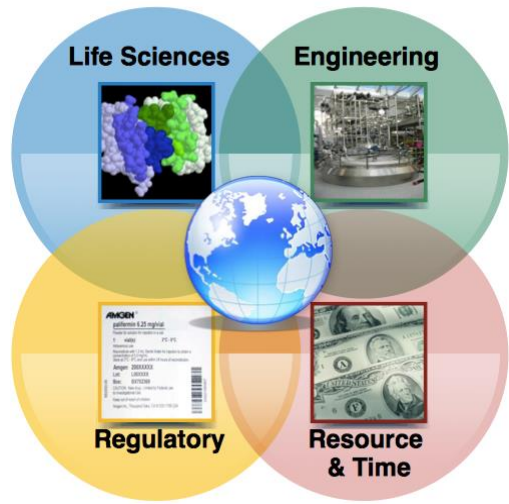
PATIENT BASED, MODULAR AND DISTRIBUTED MANUFACTURING MAY REPRESENT OUR NEXT PARADIGM SHIFT

BATCH MANUFACTURING AND BATCH RELEASE TO INTEGRATED CONTINUOUS MANUFACTURING AND REAL TIME RELEASE

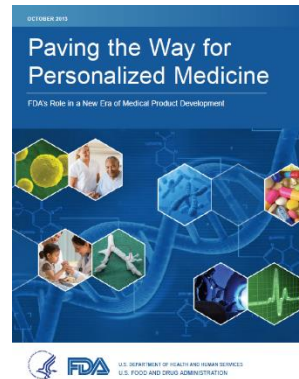
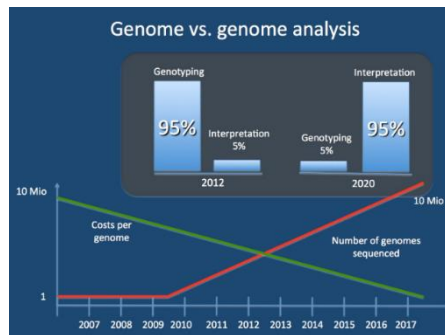


~41% Reduction in # of In-Process and Release Tests
~77% Reduction in Release Testing TAT for Material Disposition

OUR “LABORATORIES” LANDSCAPE IS PRIMED TO REALIZE ENORMOUS BENEFIT FROM THE DATA CENTRIC PARADIGM AND DIGITAL TECHNOLOGIES



- Manufacturing Flexibility
- Shorter Cycle Time and Lower Costs
- Supply Chain Complexity
- Evolving Regulatory Environment



Advancement of Emerging Technology Applications to Modernize the Pharmaceutical Manufacturing Base Guidance for Industry

DRAFT GUIDANCE

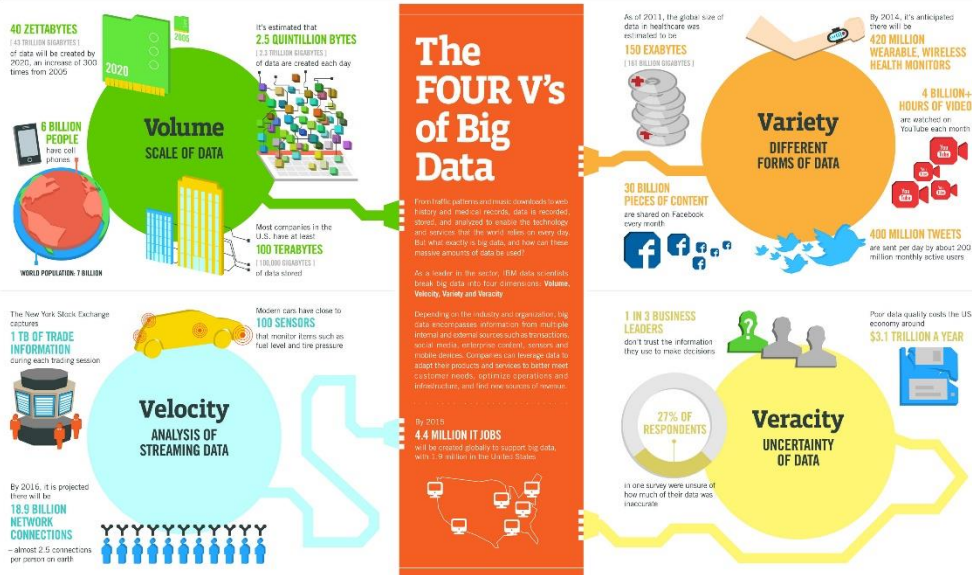
This guidance document is being distributed for comment purposes only.
Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <http://www.fda.gov/oc/ohrt>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 560 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.
For questions regarding this draft document contact (CDER) Sai L. Lee 240-594-6134.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

December 2015
Pharmaceutical Quality/CMC



THE BIG DATA REVOLUTION HAS DRIVEN A MAJOR TRANSFORMATION OF IT ARCHITECTURES AND SYSTEMS ACROSS MULTIPLE INDUSTRIES AND DOMAINS



IBM.

BIG DATA TO SMART DATA – THE INTELLIGENCE IS IN UNDERSTANDING THE RELATIONSHIPS AND PATTERNS



Smart Data



Reason,

And then ... Infer

Contextualize,

De-complexify,



Big Data

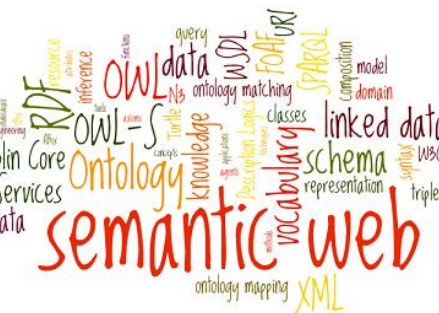
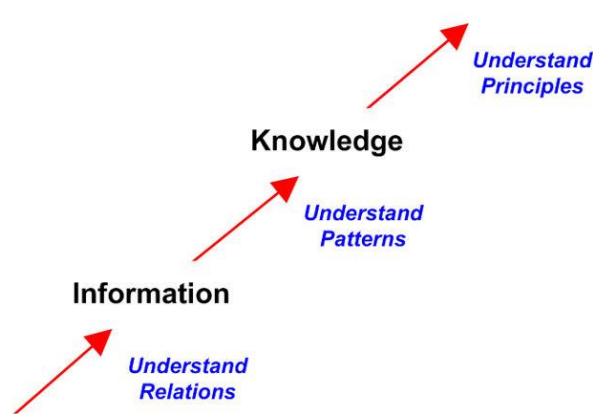
Waypoints From Big Data to Smart Data

Connectedness

Wisdom

Data

Understanding



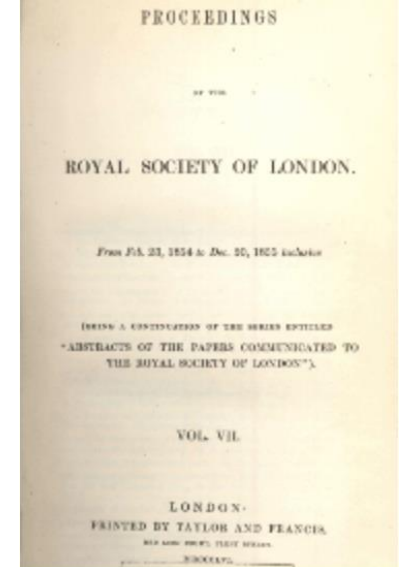
SCIENTIFIC COLLABORATION AND DATA SHARING IN THE 1800S.....



Public Lectures – Michael Faraday, Royal Institution London 1855

Manual documentation of experiments

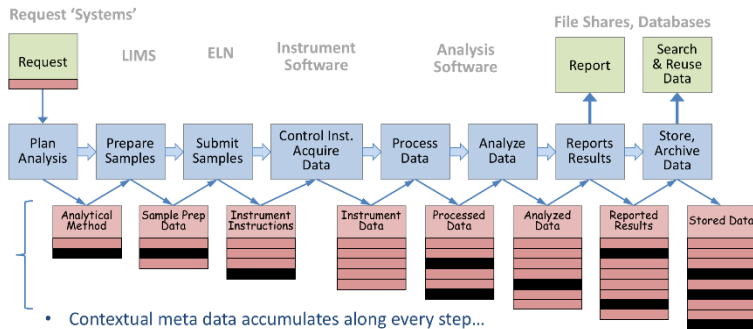
103 The mutual relation of electrical magnetism of motion may be represented by three lines at right angles to each other any one of which may represent any one of these points and the other two lines the other points. Then if electricity be determined in one line of motion in the other magnetism will be developed in the third or if electricity be determined in one line of magnetism in another motion will occur in the third. Or if magnetism be determined first then motion will produce electrical or electricity motion. Or if motion be the first point determined Magnetism will induce electrical or electrical magnetism



Peer Reviewed Scientific Journals

AND THE STATUS QUO IN MANY LABORATORIES IN 2018

Fundamentals of a measurement workflow

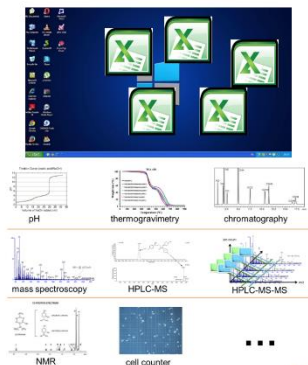


- Contextual meta data accumulates along every step...
- Distributed across multiple systems and records

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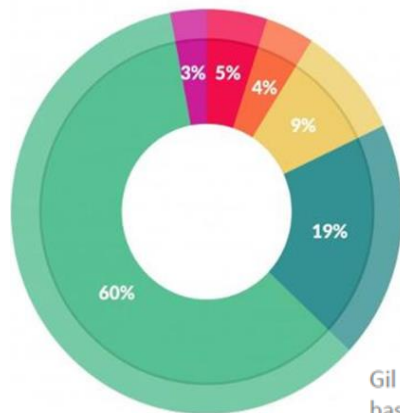


- Manual transcription of methods
- Incompatible instruments & software systems
- Manual data handling that challenges data integrity
- Legacy architectures are brittle & rigid
- Knowledge & context resides in people's heads
- Silos of data, context and meaning



From Eric Little, Osthus

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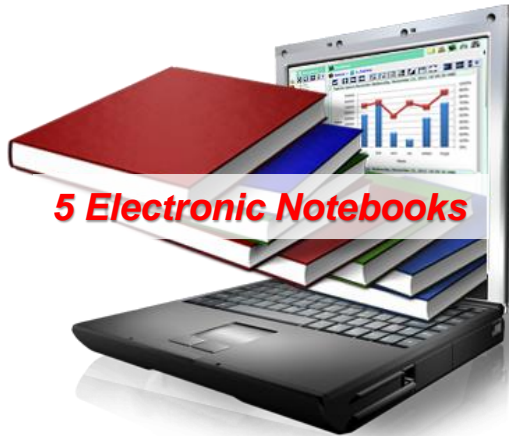
What data scientists spend the most time doing

- Building training sets: 3%
- Cleaning and organizing data: 60%
- Collecting data sets; 19%
- Mining data for patterns: 9%
- Refining algorithms: 4%
- Other: 5%



Gil Press, www.forbes.com, March 23, 2016;
based on CloudFlower survey of data scientists

THE HOLISTIC LAB PROJECT – AMGEN PROCESS DEVELOPMENT CIRCA 2015



- *Disparate Workflows (SM vs. LM)*
- *Incompatible Lab Systems*
- *Resource-Intensive & Error-Prone Processes*
- *Manual Transcription & Verification*
- *Limited Integration of Instrument Data*



COMMUNICATING A COMPELLING VISION AT START OF THE PROJECT

AMGEN

Holistic Lab | Connected Execution Environment

IS4PD

What It Is

An open & connected ecosystem of platforms, workflows & instruments that create an environment for more intuitively generating, retrieving & sharing data.

An Example

Drug substance & attribute scientists are able to design & execute an experiment in a single end-to-end interface.

CHALLENGE

Multiple, incompatible systems

- Multiple electronic lab notebook platforms
- Disparate workflows (small vs. large molecule)
- Resource-intensive & error-prone processes
- Incompatible lab systems
- Manual transcription & verification
- Limited integration of instrument data

4,000+ Instruments



Electronic Lab Notebooks

Siloed by site, function or modality



Integrates
& Enriches Data
Across PD Sites

Holistic Lab

OUTCOME

Powerful and connected tools across PD that create an environment for scientists to spend less time searching for data and more time using data

- Single electronic notebook platform
- Design interfaces that allow cross-lab execution
- Streamlined data retrieval
- Automated data collection across equipment & instruments
- Simple sample management
- More contextually rich data & metadata



SCIENTISTS WILL BE ABLE TO ADVANCE PD SCIENCE IN A DATA-DRIVEN, CONNECTED ENVIRONMENT

What It Is

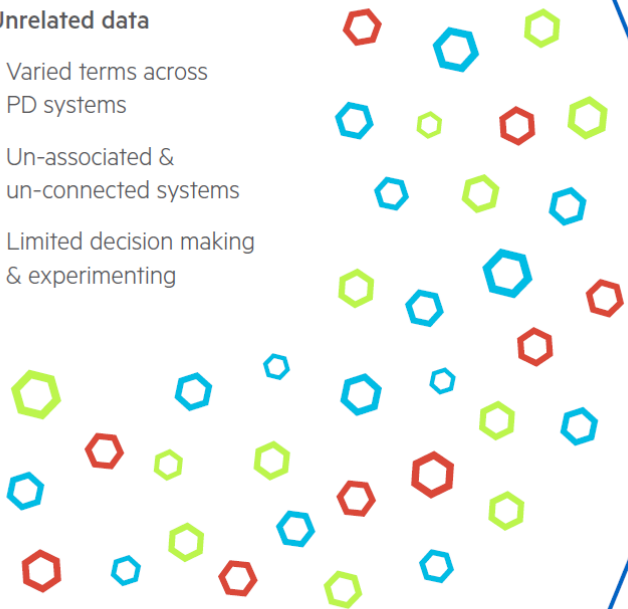
The initiative for the standardization of Amgen terminology to create a common language.

Why Now?

The foundation of what we build rests upon data information relating to one another.

CHALLENGE**Unrelated data**

- Varied terms across PD systems
- Un-associated & un-connected systems
- Limited decision making & experimenting



Standardizes
units of measure,
chemical properties,
nomenclature &
metadata

Reference Data**OUTCOME****Rapid localization and disambiguation of data with a common language**

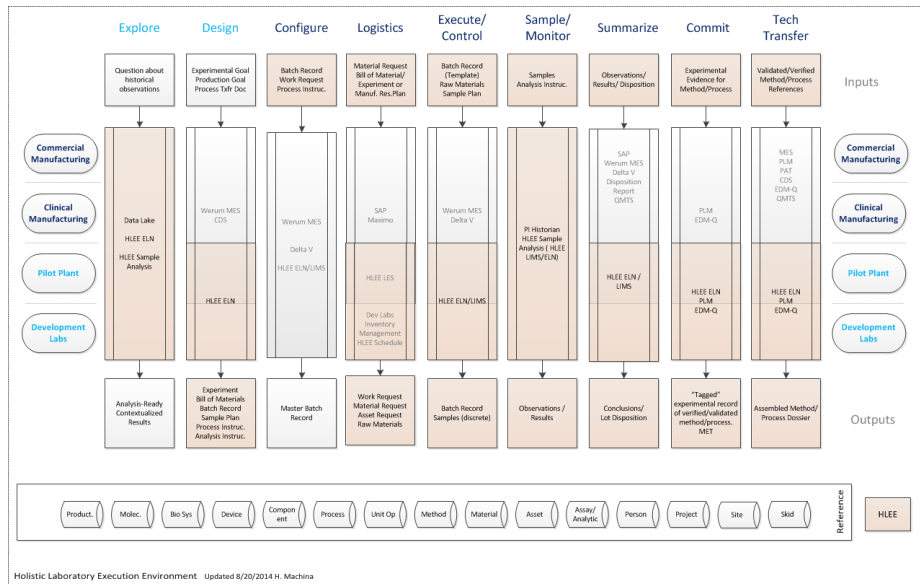
- Visibility & rich insight across PD systems
- Better data integrity
- Broader analytic & predictive capabilities
- More robust pattern detection
- Standardized workflow templates
- Less time spent searching for data
- Quicker question answering

**Bigger
Picture for
Amgen**

The opportunity to collaborate with industry peers in the standardization of terminologies beyond our own organization.

LESS TIME FINDING & TRANSLATING DATA WITH A COMMON DATA LANGUAGE

BUSINESS DRIVEN ALIGNMENT - CROSS DISCIPLINARY CAPABILITIES



Request for
Study / Lab Work



Samples/Materials
Inventory



Recipe/Method
Development



Review &
Confirm



Personnel



Recipe/Method
Adaption



Plan, Assign &
Schedule



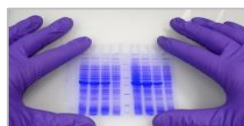
Instrument
Inventory



Recipe/Method
Management



Generate & Submit
Reports



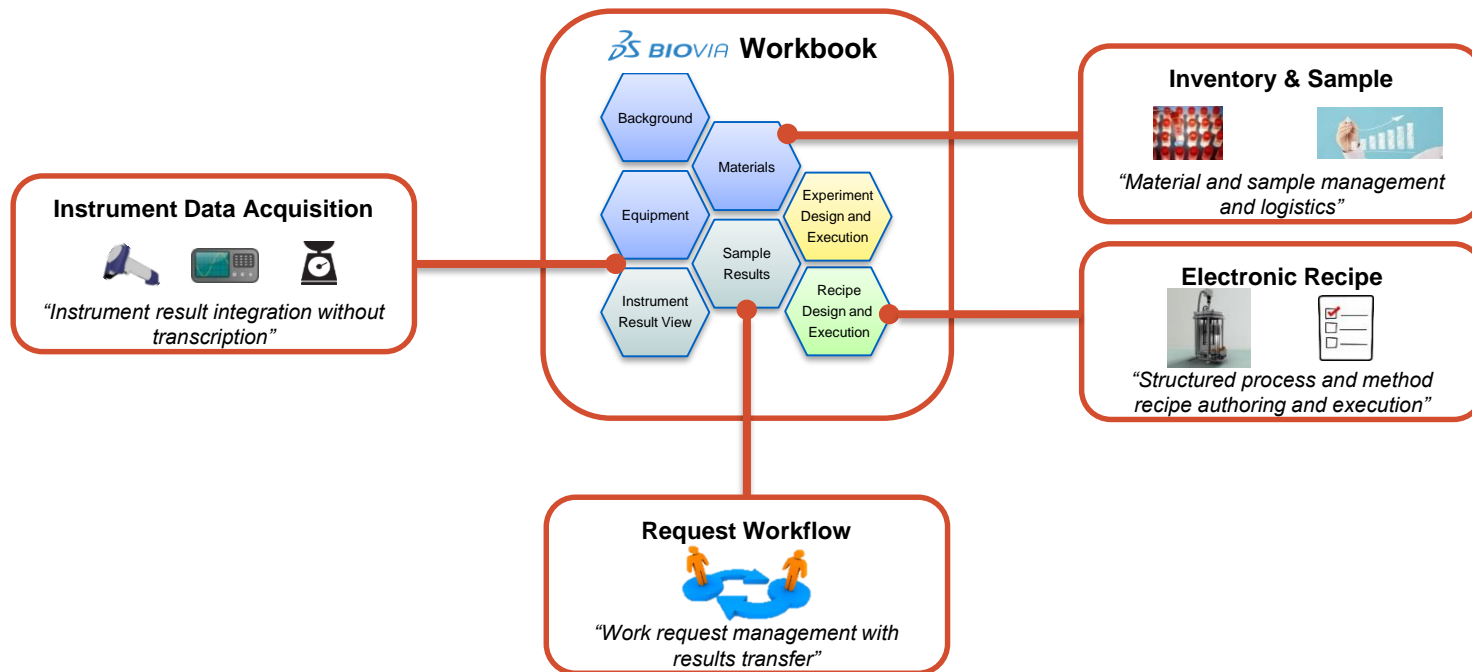
Compile & Interpret
Data/Results



Lab Work,
Test Samples

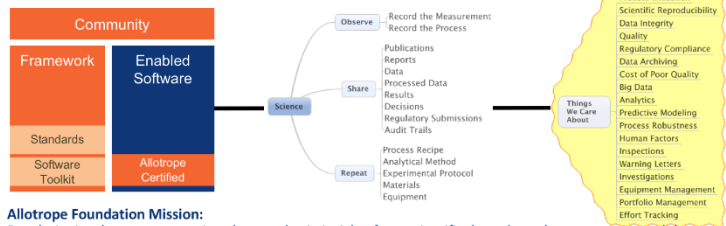
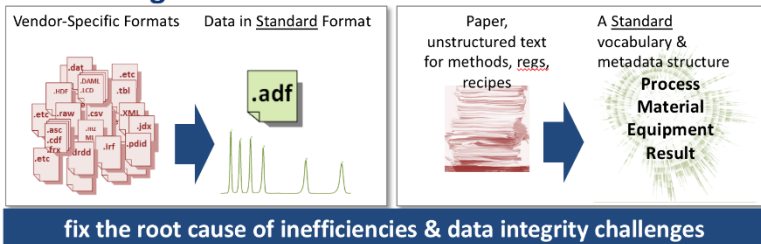
THE HOLISTIC LAB “ECOSYSTEM” – A SINGLE PD SOLUTION

MODULAR ARCHITECTURE WITH DATA INTEGRITY BY DESIGN



SOLUTIONS TO COMMON PROBLEMS IN PRE-COMPETITIVE AREAS - COLLABORATING TO INNOVATE AND ACCELERATE DELIVERY – THE ALLOTROPE CONNECTION

Rethinking Scientific Data



Allotrope Foundation Mission:

Revolutionize the way we acquire, share and gain insights from scientific data, through a community and the framework for standardization and linked data.

The Allotrope Community

Allotrope Foundation

abbvie, Baxter, Genentech, AMGEN, Biogen, Boehringer Ingelheim, MERCK, gsk, Bristol-Myers Squibb, Pfizer, Lilly, novo nordisk

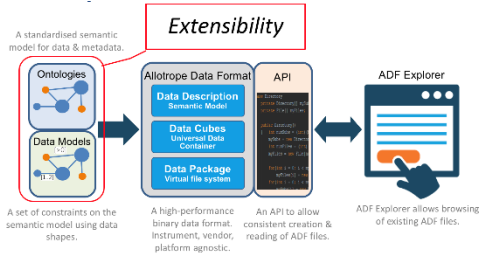
Allotrope Framework Architect (OSTHUS), **Allotrope Foundation Secretariat** (DrinkerBiddle)

Allotrope Partner Network

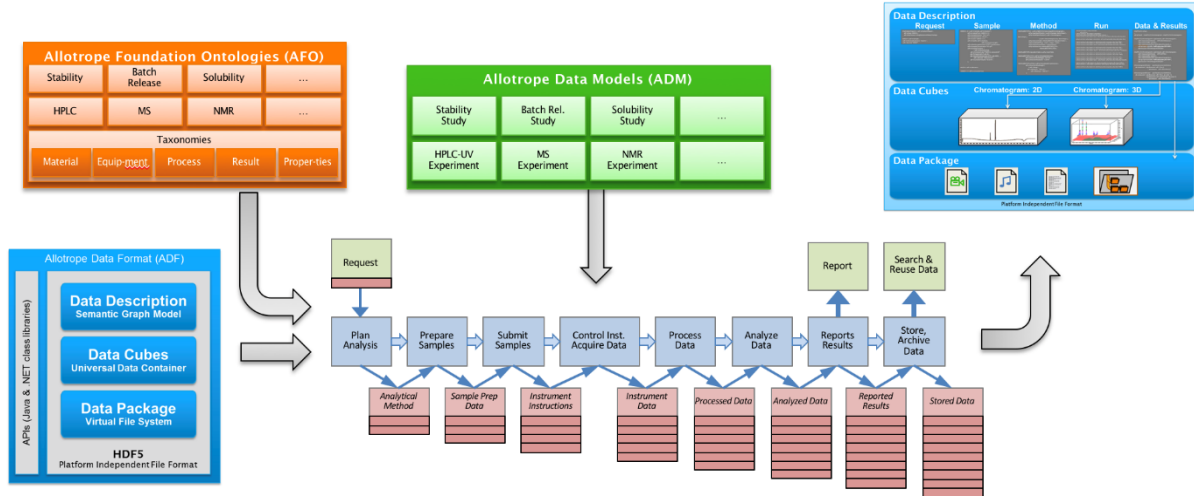
LEAP TECHNOLOGIES, HCL, epam, SCIENCE, UNCHAINED LABS, TETRASCIENCE, Agilent Technologies, SHIMADZU, BIOVIA, BIO-RAD, Cytobank, Waters, ZIFU, LABWARE, PERKINELMER, MESTRELAB RESEARCH, RONDAXE, ZONTAL, HALO DIGITAL, Sartorius, idbs, Riffyn, paradigm4, ThermoFisher Scientific, Cognizant, Mestrelab Research, Science & Technology Facilities Council, Broker, University of Strathclyde Glasgow, ACD/Labs, The HDF Group

Astrix Technology Group • BSSN Software • DEXSTR • Elemental Machines • Erasmus MC • Fraunhofer IPA • LabAnswer • Mettler Toledo • NIST • SciBite • Stanford University • University of Illinois at Chicago • University of Southampton

THE ALLOTROPE FRAMEWORK: THREE PRODUCTS, ONE HOLISTIC SOLUTION



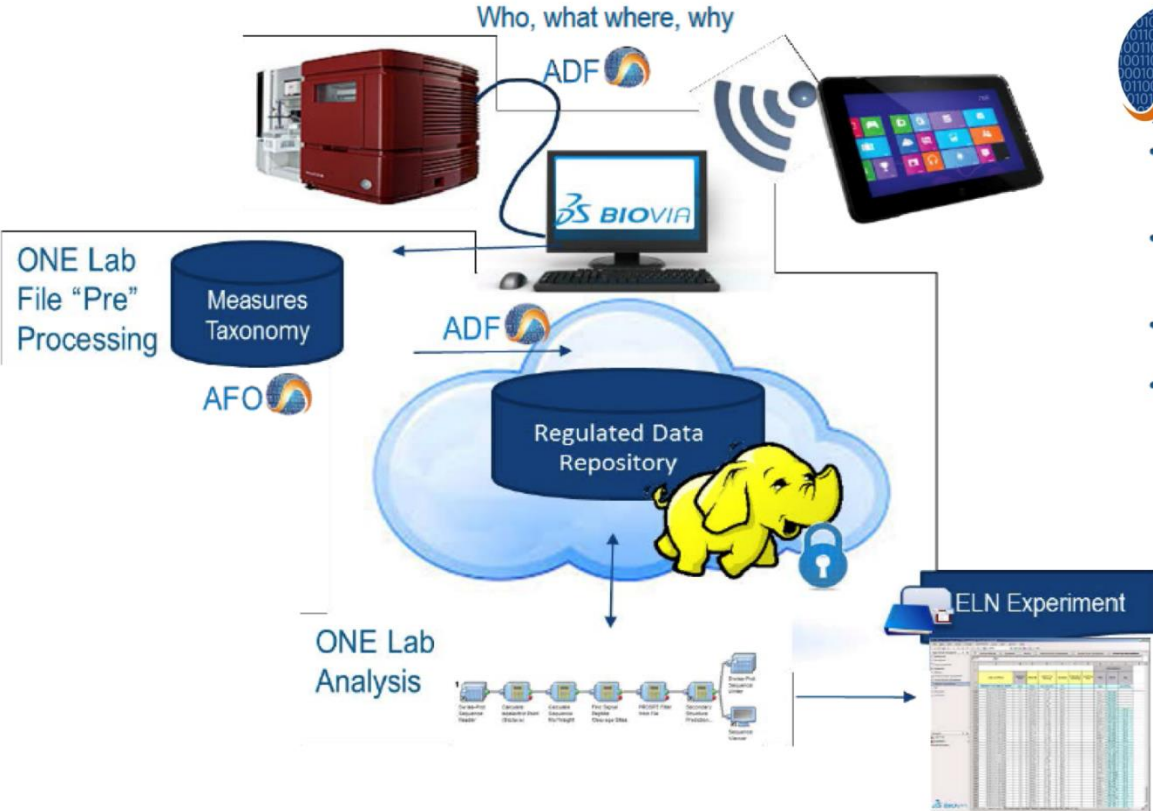
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AGILE APPROACH TO THE INTEGRATION OF ALLOTROPE FRAMEWORK IN HOLISTIC LAB

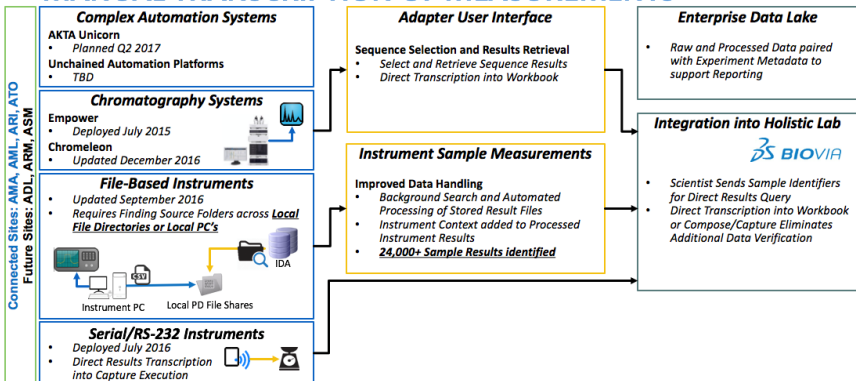


- BIOVIA foundational management of Allotrope Ontologies & Vocabularies
- BIOVIA foundational connection to laboratory instruments using Allotrope ADF format
- BIOVIA Recipe and Methods in S88 format
- Customer focused proof of concept projects in process and in the works



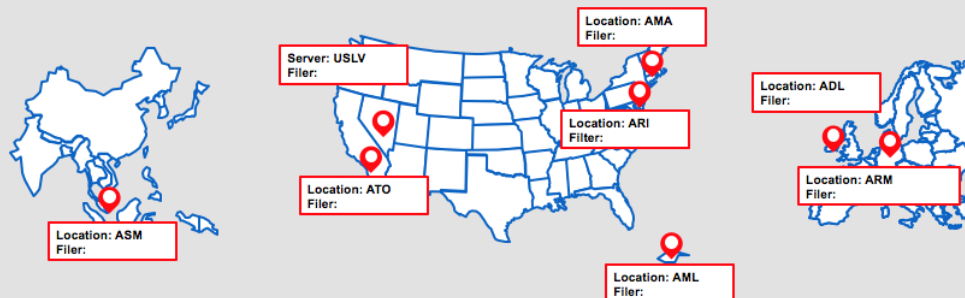
CAPTURE OF CONTEXTUALIZED EXPERIMENTAL DATA ACROSS A GLOBAL FOOTPRINT

INSTRUMENT DATA ACQUISITION INTERFACE IS REDUCING MANUAL TRANSCRIPTION OF MEASUREMENTS

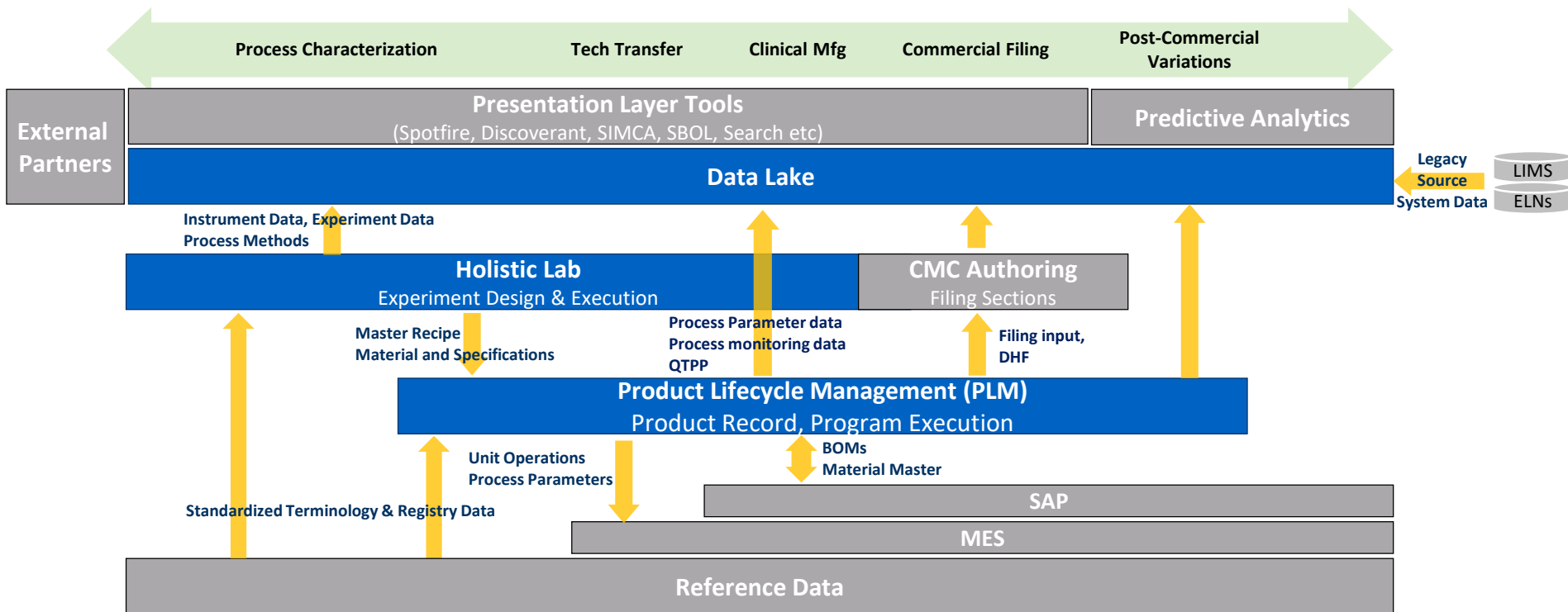


ENABLING SCIENTISTS TO FIND GLOBAL PD DATA

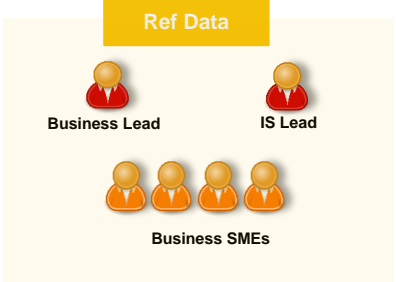
Application servers at each PD site are constantly crawling local filesystems making instrument results readily available & searchable by experiment



DRIVING DATA FLOW ACROSS THE PROCESS DEVELOPMENT LIFECYCLE LEVERAGING AN INTEGRATED IS SYSTEMS LANDSCAPE



HIGHLY MATRIXED CROSS FUNCTIONAL TEAM, SENIOR EXECUTIVE SPONSORSHIP, STRATEGIC LEVEL VENDOR PARTNERSHIPS



REALIZING THE BENEFITS TODAY OF A DATA CENTRIC “SMART” LAB POWERED BY THE ALLOTROPE FRAMEWORK AND DIGITAL PLATFORMS

Reduced Manual Effort &



Better Scientific Reproducibility



Increased Data Integrity,
Context, Quality



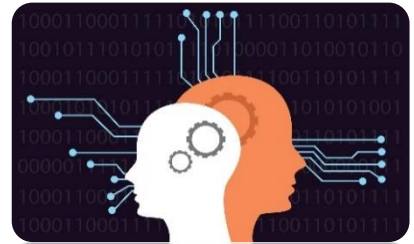
Streamlined
Access, Sharing,



Consolidated Requirements
Lower Innovation Barrier

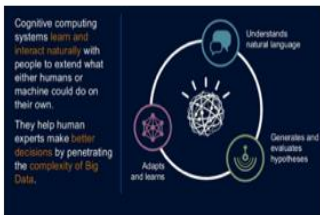
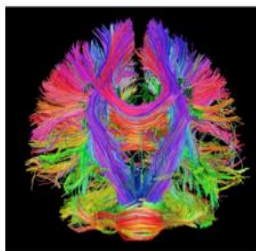


Foundation for Data
Science



A CONNECTED DATA ECOSYSTEM POWERING DIGITAL PROCESS DEVELOPMENT, DIFFERENTIATED PATIENT CENTRIC INNOVATION

Cognitive Computing Capabilities Will Increase Our Innovation Capacity and Capabilities



Powering Life Science Innovation Through A Connected Ecosystem Science and Medicine



26+ BILLION devices will be connected by 2020

\$4-11 Trillion Economic Impact

54% of top performer companies will invest more in sensors this yr

