Life Sciences PI User Group (PUG)

Join to discuss best practices, white papers, share news, and exchange ideas.

Board Members	Company
Craig Taylor - Chair	BioMarin
Cassandra Murillo	Regeneron
Colm Bambury	Amgen
Jeff Denz	Eli Lilly
Myles Sumlin	Genentech
Sarosh Guzder	Shire

Objectives:

- Identify Best Practices
- Share knowledge and ideas across our industry
- Foster communication with OSIsoft regarding our industry needs

Want to opt in?
https://pisquare.osisoft.com/groups/life-sciences

Or contact jsirois@osisoft.com

Have questions?

- Craig.taylor@bmrn.com
- pmoree@osisoft.com
- Visit the PI Square Booth

Recap from PUG meeting yesterday

When: Tuesday 9/27/2016 5:30 PM to 7:30 PM CEST (Central European Summer Time)

Agenda:

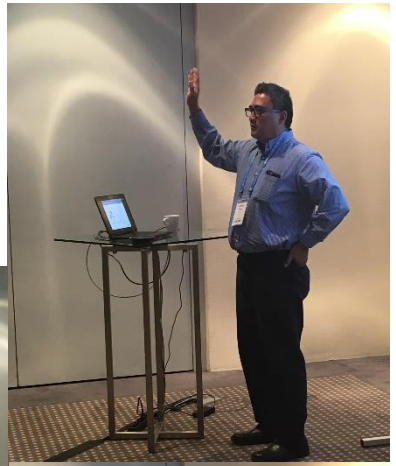
5:30 p.m. – PUG Meeting Start / Icebreaker (Craig/Petter/Jarita)

5:45 p.m. – Charter Review (Craig)

6:15 p.m. – Craig Taylor **“Regional PI System Implementation at BioMarin”**

6:30 p.m. – Anthony Narag **“Shire’s Global PI Implementation”**

6:45 p.m. – Workshop Item #1 **“PI Batch to Event Frames Risks, Concerns and Opportunities”**



Day at glance

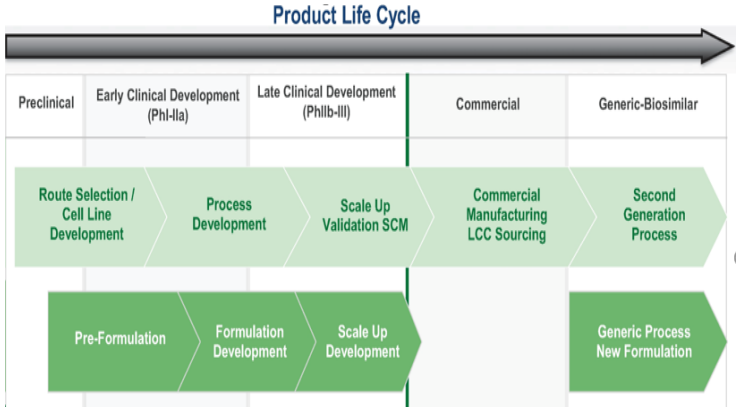
Time	Title	Presenter(s)
9:00 – 9:30	Enabling Decisions and improving Quality	Petter Moree - OSIsoft
9:30 – 10:00	Using Data Analytics to drive Process Optimization in Whiskey Manufacturing	Dagmara Dabrowska - Irish Distillers Pernod-Ricard
10:00 – 10:15	**Transfer Time**	
10:15 – 10:45	Monitoring Environmental Conditions on the Manufacturing Floor with PI Coresight	Arsenio Sanchez - Janssen
10:45 – 11:00	**BREAK - Potsdam Foyer**	
11:00 – 11:30	Productivity and Quality Improvements Through Continuous Contextualization of PI System Data	James Li, Shamus Cunningham - Abbott Nutrition & Seeq
11:30 – 11:45	**Transfer Time**	
11:45 – 12:15	Transitioning to a Modern PI System in a Validated Environment	Julio López, Marc Olive - Abbott Labs & AG Solution
12:15 – 14:15	**LUNCH - Pavillon**	
14:15 – 14:45	The PI System - Enabling a Digital Factory	Michael Pelz - Clariant
14:45 – 15:00	**Transfer Time**	
15:00 – 15:45	GxP Compliant Alarm Handling with Event Frames and AF	Gerd Fromm, Christian Wirth, Philipp Sutter - Roche
15:45 – 16:15	Wrap-up and Next steps	Petter Moree, David Casazza - OSIsoft
18:00 -	Dinner Party	Berlin U3

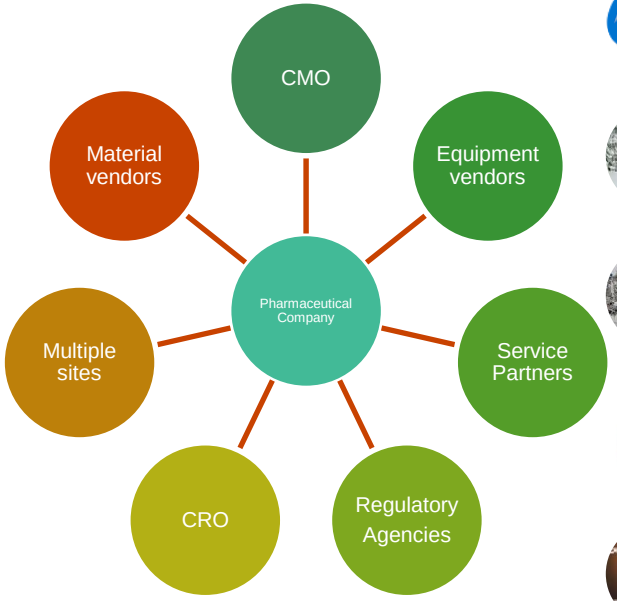
Enabling Decisions and Improving Quality

Presented by **Petter Moree, Industry Principal –**
Food & Beverage, Life Sciences, Specialty Chemicals

Current Trends

The phases of product and process
The Ecosystem
The levels of operation






Communities


Enterprise


Plants

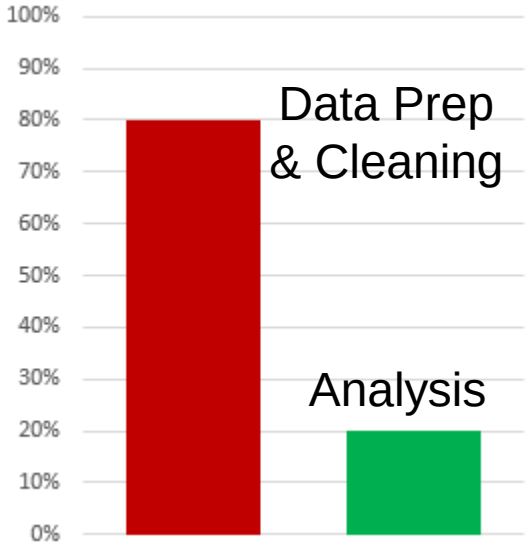

Units


Assets


Sensors

Data Integration and Analytics

Time

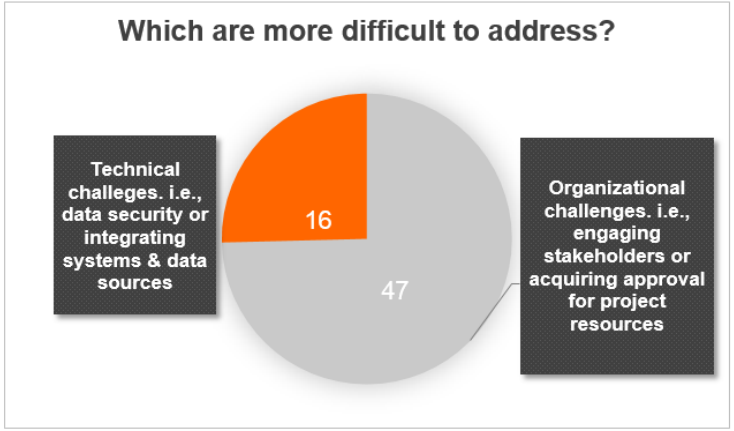


Warning: Currently, data analysts spend 50-80% of their time merely collecting and preparing data[1]

Expense

Warning: data integration often requires ongoing upkeep

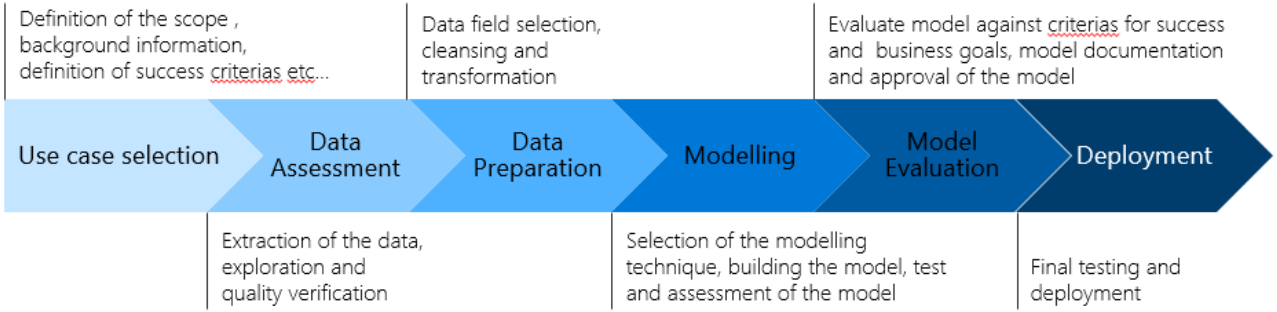
Risk



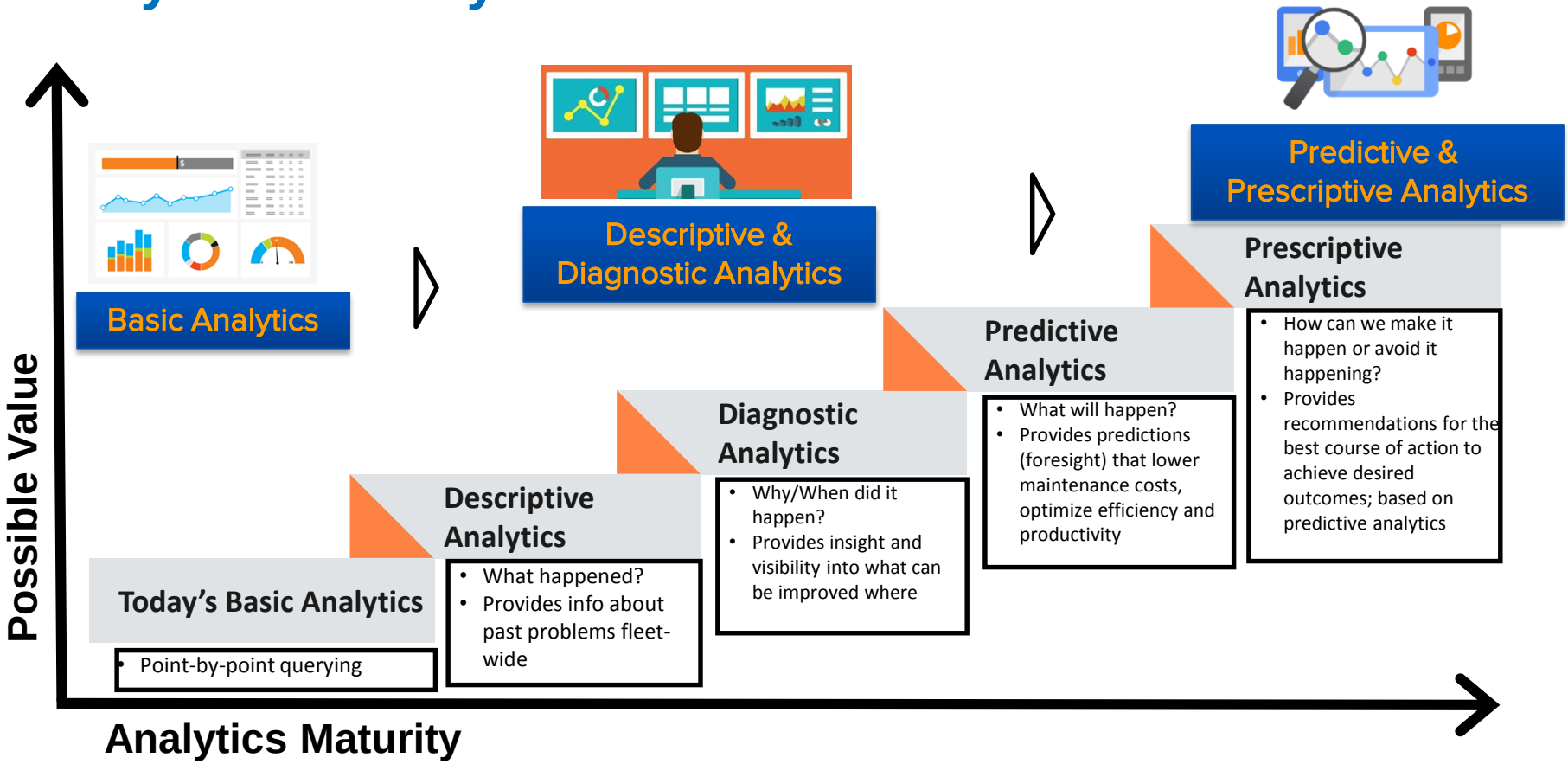
Warning: If “why?” for the project is not clearly communicated, business barriers will delay and risk the project

[1] *https://hbr.org/2014/04/the-sexiest-job-of-the-21st-century-is-tedious-and-that-needs-to-change/*

Typical Planning for Data Science Experiments



Analytics Journey



Analytics in Life Sciences, F&B and Chemicals

Process Understanding
Scale up/down
Tech transfer
Material influence
Risk Assessment
CPP, CMA, CQA
Golden batch analysis
Time-to-market

Site to site comparison
CAPA
De-bottlenecking
Predict Quality attributes
Capacity
Calibration
Real-time control (APC)
Golden Batch analysis
Scale up/down
Supply Chain Management

Trouble Shooting
Trending
Out of Specification Investigation
Real-time monitoring/SPC
End process
prediction/determination
Optimization
Process Analytical Technology
Early Fault detection
Asset Health

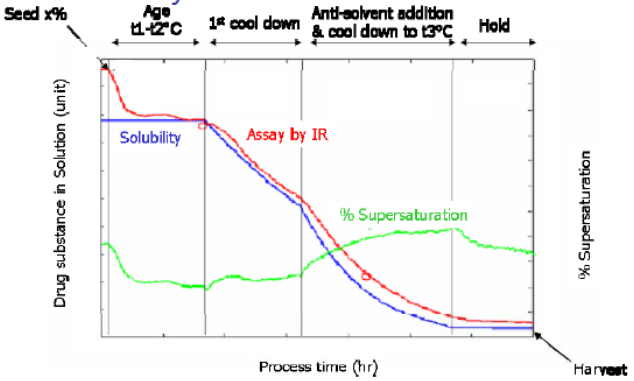
Real time release testing (RTRt)
Batch release
CPV/OPV (Continued Process Verification)
Annual Product and Quality Reviews
Reporting & RBE
Quality be Design

Analytical Applications in different phases

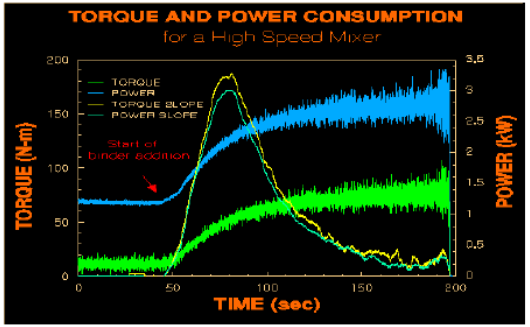
Process Data brings value to process & product

Process Signatures

Crystallization



Wet Granulation



http://www.mcc-online.com/granulation.htm

- Many batch processes are path dependent
  - Arriving at the same endpoint does not assure the same quality product
  - Often important physical or chemical attributes are not measured routinely but can affect downstream product performance

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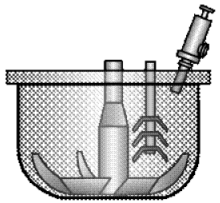
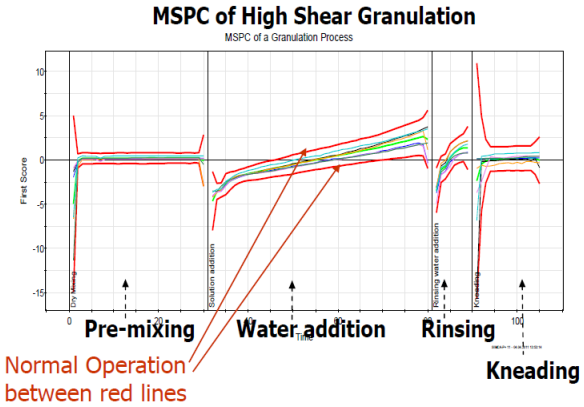
FDA References on analytics

U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.gov

Multivariate Statistical Process Control Example



High Shear
Wet Granulator



- MSPC flags atypical or previously unseen operation
- Outliers do not mean a failed batch but trigger investigation
- Growing examples of "saved" batches due to MSPC

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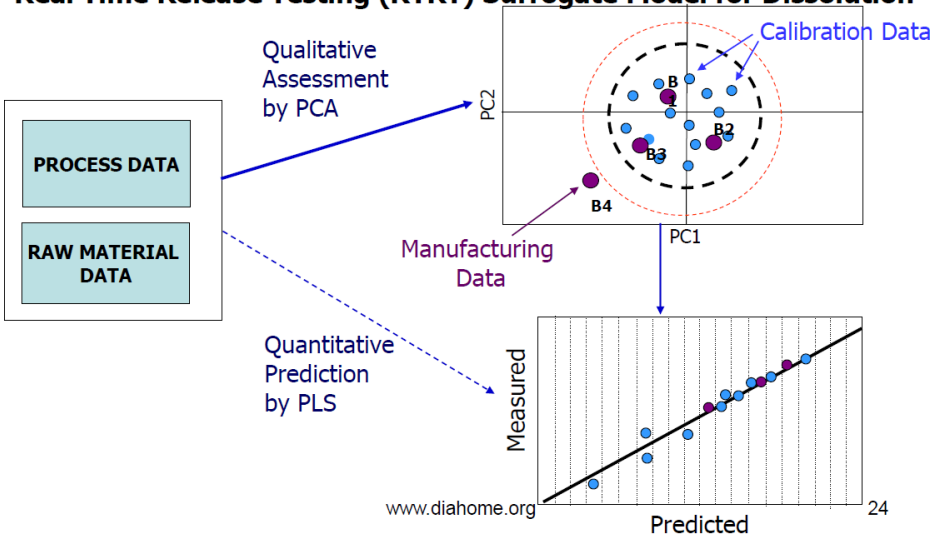
U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.gov

Multivariate Model for Predicting Dissolution

Real Time Release Testing (RTRT) Surrogate Model for Dissolution



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FDA view: Model impact and validation

Considerations for Submission of Models

- **Level of detail in submission should depend on the importance of the model to the overall control strategy**

- **Low Impact Model** (e.g., Models for development)
  - General discussion of how model was used to make decisions during process development
- **Medium Impact Model** (e.g., Design space models)
  - More detailed information about model building, summary of results and statistical analysis
  - Discussion of how the model fits into the control strategy
- **High Impact Model** (e.g., RTRT models)
  - Full description of data collection, pretreatment and analysis
  - Justification of model building approach
  - Statistical summary of results
  - Verification using data external to calibration set
  - Discussion of approaches for model maintenance and update

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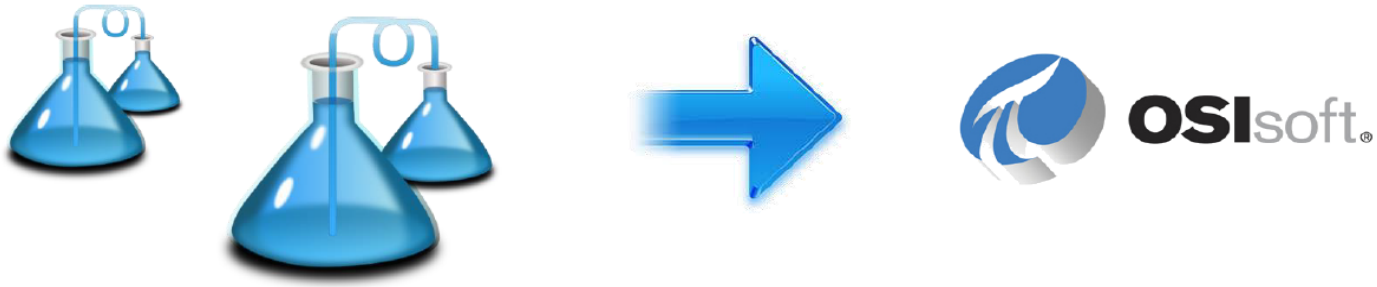
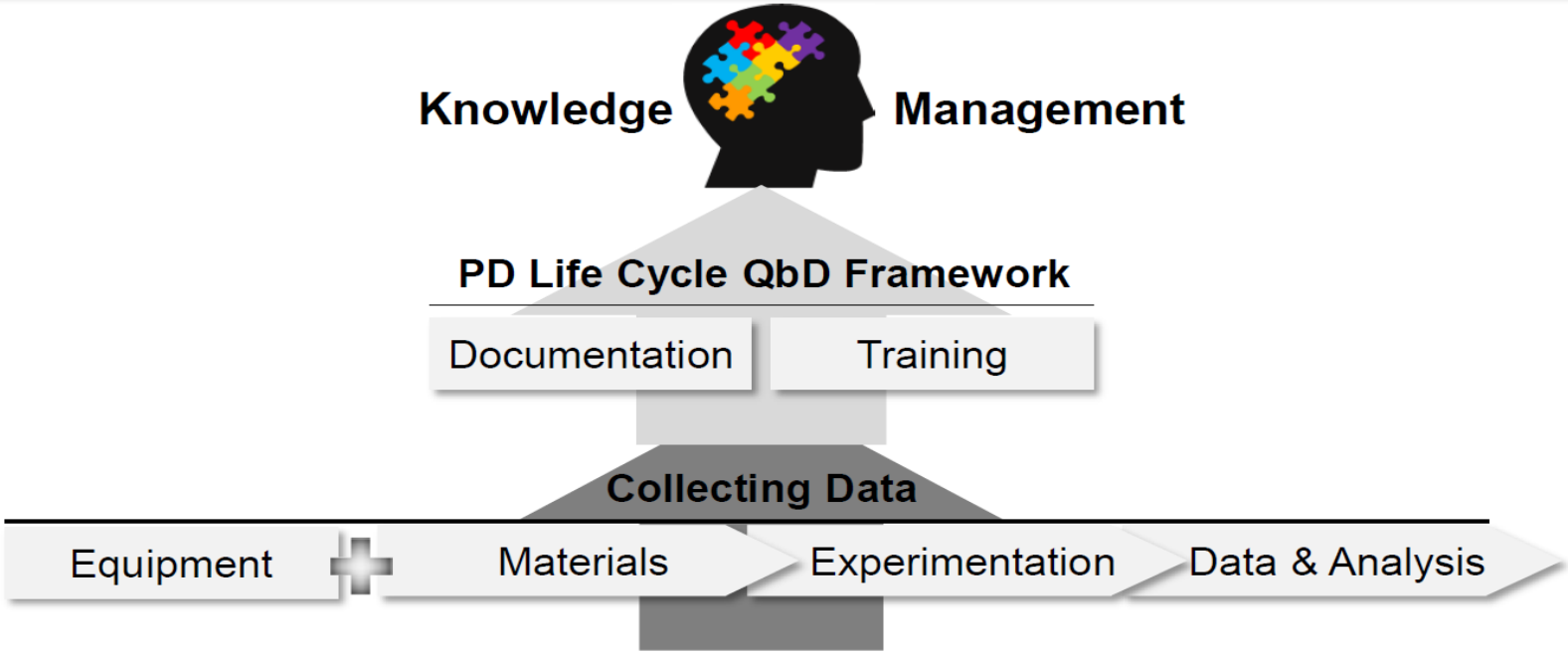
R&D Program Vision

- Ensure a single-source-of-truth for all master data in PD
- Guarantee access to accurate, verified data
- Enable any scientist to analyze an experiment in under **10 minutes**
- **Consolidate tribal knowledge** and redundant spreadsheets in favor of scalable enterprise solutions
- Shift the paradigm from single data points to **streaming-data visualization**

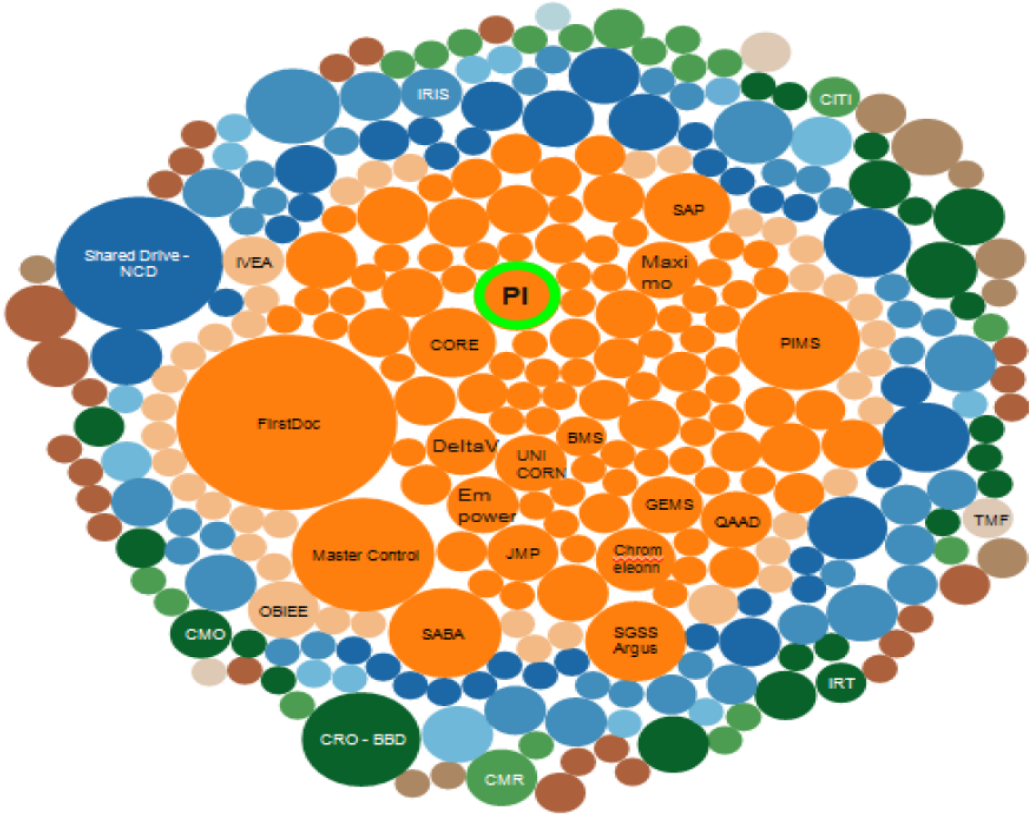


Assimilation of Data into Knowledge



"In Pharmaceutical Development, knowledge not only defines our product - it is our product."

323 sources of information were identified across R&D



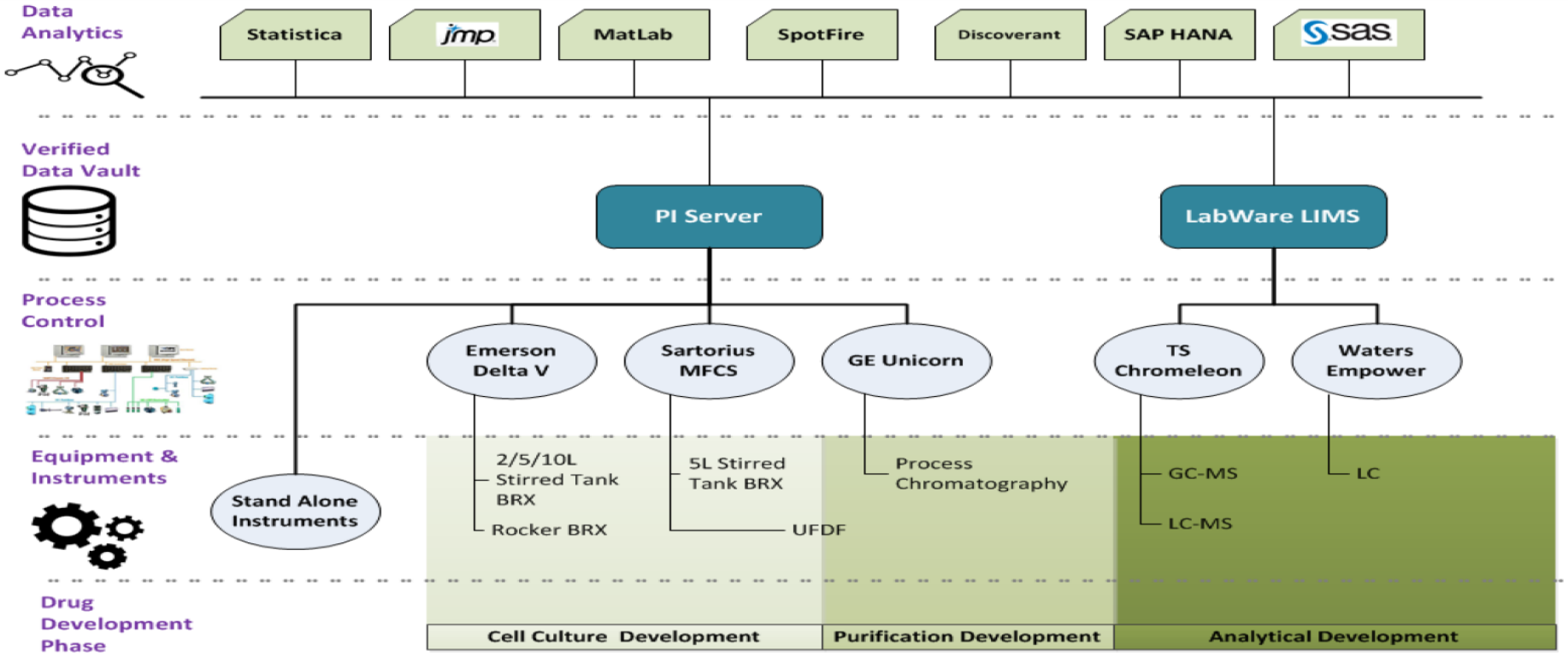
Type1

- Application
- Analysis Tool
- Shared Drive
- SharePoint Site
- Access DB
- Excel Worksheet
- Partner
- External Source
- Instrument
- Local drives
- Paper
- Other

- 34% of the sources are applications
- 29% of the sources are shared storage
- 24% of the sources are Instruments, paper or other
- 13% of the information sources are external

The size of the bubble indicates the complexity of information within that source; not the volume of data

Informatics Architecture (Major Systems)



Justifying an Expansion Project

PI SYSTEM EXPANSION ROI Assessment

Assumptions

Annual FTE Cost	X $ / Yr
Hours/Yr	2000
Working Days/Yr	255
FTE Cost/Hr	X $/Hr
Consultant Cost/Hr	X $/Hr
Discount Rate	8.5%

Savings Cash Flows

1. NEW SYSTEMS INTEGRATION

1.1 Justification — Reduction of manual data entry for wave BRX & UFDF (37 Units)

Data collection (min/1 wk wave expt)	Data transcription (min/1 wk wave expt)	Data verification (min/1 wk wave expt)	Total waves & UFDF units	Total Time savings (Hr/wk)	**Total Savings/yr**
5	5	5	37	**9.25**	**X $/yr**

2. DATA INTEGRITY IMPROVEMENT

2.1 Justification — If data integrity is breached (data filed is not valid), could result in loss of Shire reputation, delay of filing, FDA 483 or additional post marketing commitments (PMC). Previous experience incurred 30 man months of work to verify all PD data in one product filing during internal audit. **We assume this improvement will eliminate one data integrity issue per 2 year period.**

Total FTE Audit Support (Hr)	Total Consult Audit Support (Hr)	FTE Cost	Consultant Cost	**Total Savings/ 2yr**
2400	2400	$ 100,000	$ 300,000	**X $/yr**

ROI Calculation (5 Year)

CashFlow Series	**Year 0**	**Year 1**	**Year 2**	**Year 3**	**Year 4**
Costs	**$ (500,000)**	$ -	$ -	$ -	$ -
Savings	$ 10,221	$ 20,443	$ 410,443	$ 20,443	$ 410,443
Net	$ (489,779)	$ 20,443	$ 410,443	$ 20,443	$ 410,443

NPV5	**$175K**
IRR	**21.9%**

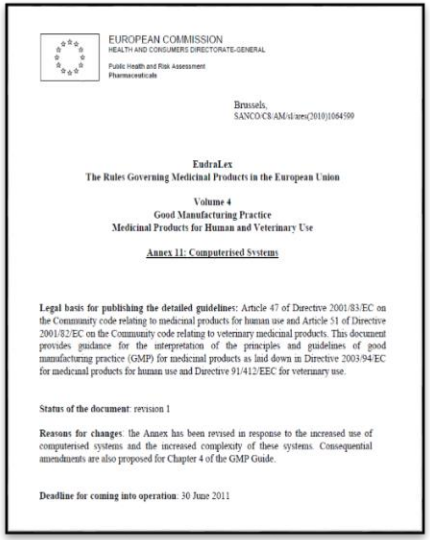
Data Integrity

"Data integrity is fundamental in a pharmaceutical quality system which ensures that medicines are of the required quality…Data integrity requirements apply equally to manual (paper) and electronic data." (MHRA,2014)

What is Data Integrity?

- Refers to maintaining and assuring the accuracy and consistency of data over its entire life cycle and is a critical aspect to the design, implementation and usage of any system which stores, processes or retrieves data
- Data is recorded exactly as intended, and upon later retrieval, the data is the same as it was when it was originally recorded
- Data is complete, consistent & accurate

ALCOA
A – attributable to the person generating the data
L – legible and permanent
C – contemporaneous
O – original record or true copy
A – accurate


EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Public Health and Risk Assessment
Pharmaceuticals

Brussels,
SANCO/C8/AM/sl/ares(2010)1064590

EudraLex
The Rules Governing Medicinal Products in the European Union

Volume 4
Good Manufacturing Practice
Medicinal Products for Human and Veterinary Use

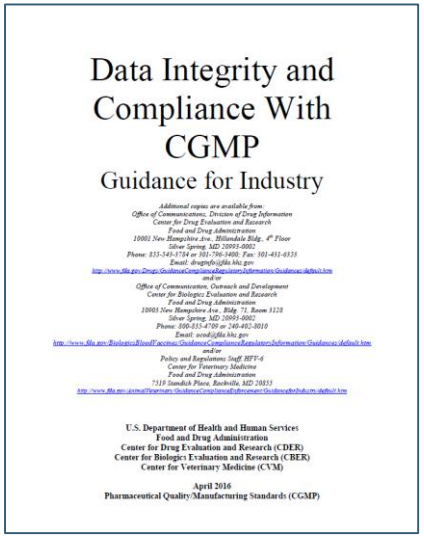
Annex 11: Computerised Systems

Legal basis for publishing the detailed guidelines: Article 47 of Directive 2001/83/EC on the Community code relating to medicinal products for human use and Article 51 of Directive 2001/82/EC on the Community code relating to veterinary medicinal products. This document provides guidance for the interpretation of the principles and guidelines of good manufacturing practice (GMP) for medicinal products as laid down in Directive 2003/94/EC for medicinal products for human use and Directive 91/412/EEC for veterinary use.

Status of the document: revision 1

Reasons for changes: the Annex has been revised in response to the increased use of computerised systems and the increased complexity of these systems. Consequential amendments are also proposed for Chapter 4 of the GMP Guide.

Deadline for coming into operation: 30 June 2011


Data Integrity and Compliance With CGMP

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)

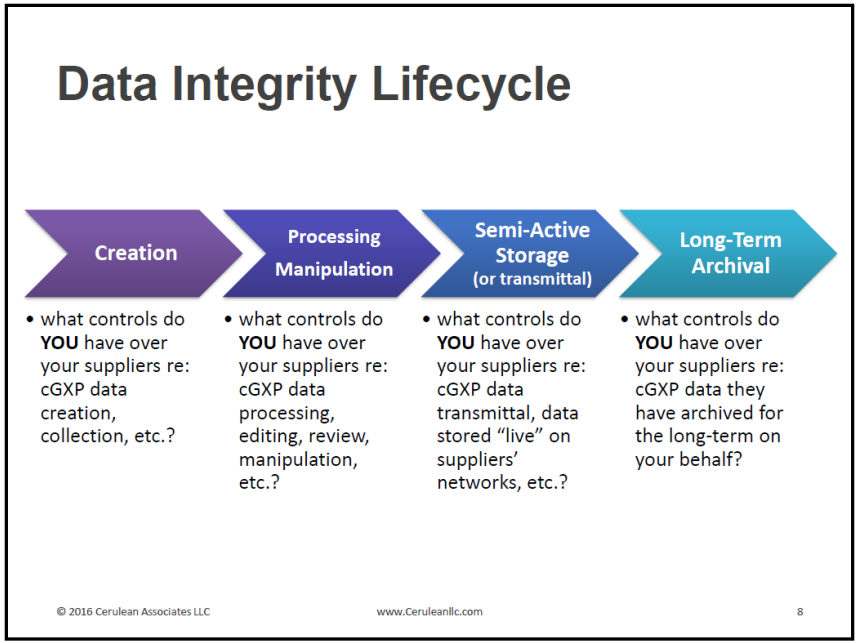
April 2016
Pharmaceutical Quality/Manufacturing Standards (CGMP)

Data Integrity

- Data Integrity are those elements that give the data its trustworthiness
- Reliability: Completeness and Accuracy
- Authenticity: It is what it claims to be
- Reviewability: It can be reviewed, analyzed and interpreted with its full meaning and context

Data Integrity and Contract Organizations (CMO/CDMO)

- Carmelo Rosa, Director of FDA OMPQ's (Office of Manufacturing & Product Quality), recently acknowledged that "*Data integrity issues have always existed!",* but now FDA is doing more to uncover the evidence of such problems.
- Drug makers should not look to contract manufacturers to reduce their responsibility for data accuracy and reliability, Some biopharma companies regard contract testing and production operations as one way to alleviate their involvement in inspections and dealings with regulatory authorities.
- Rosa emphasized that the licensed manufacturer remains responsible for products meeting all quality standards and noted that FDA and other authorities are looking closely at all facilities, including CMOs.
- Although a Global issue, many of the most egregious data integrity transgressions have surfaced at Indian API & finished product manufacturing facilities. **Data Integrity issues are a Global problem**



Source: **John Avellanet – CMO Conference 2016, New Brunswick, www.ceruleanllc.com**

Metadata – Data about Data

- Metadata is structured information that describes, explains or makes it easier to retrieve, use and manage data.

- *Examples:*
  - *Time/date, Data source, Type (Clinical trial batch, validation batch manufacturing, OOS, …), person ID, unit of measure (UOM), asset, version/producer of sensor/equipment, in operation since, last calibration/maintenance, next planned maintenance, Batch ID, sub-batch, lot, material(s), recipe, customer, previous batch, performance, risk/FMEA/RPN, CPP, CQA, CMA, detection limit, NOR, PAR, …*

Fundament for Electronic data

Paper

1. Legible
2. Contemporaneous
3. Permanent (no white out)
4. Attributable
5. Traceable
6. Changes

Electronic

1. Legible
2. Time date stamp
3. Annotation tools
4. User ID & password
5. Meta data
6. Audit trails, meta data

Data Integrity includes several parts

- Breach of Data Integrity is a violation of the integrity of Data. Which means, the actions performed and the documents/records written do not reflect the truth and the reality which has taken place. *It is not about Lab Data alone* “Data Integrity is not only about the QC, it applies to compliance with GMPs and Relates to:

1. **Research & Development**
2. **Clinical Trials**
3. **Manufacturing & Testing**
   i. **Including CMO and CMA**
4. **Inspection - Post Inspection Activities**

Data Integrity in your ecosystem

What controls do **YOU** have over your data at or from your suppliers so that **FDA can rely on your data?**

Wrap Up

Our Ask?
Your requests?

What would you like to see?

What do you like to share?

Business critical applications/analytics

QbD

This article presents the results of a survey conducted by the ISPE United Kingdom/Ireland PAT COP.

The Business Benefits of Quality by Design (QbD)

by Theodora Kourti and Bruce Davis

Pharmaceutical Engineering, July/Aug 2012, 32(4), 1-10

Introduction

The business case for Quality by Design (QbD) was a hot discussion topic during a meeting of the Process Analytical Technology Community of Practice of United Kingdom/Ireland (PAT COP UK/IR). The discussion concluded with a plan to conduct a survey that would aim to gather actual experiences, examples and candid industry opinions on the business benefits of QbD. The questions one questionnaire. Written answers also were produced for the telephone interviews and these were approved by the interviewees. Interviewees were from development, manufacturing and regulatory while the companies range from large and small, both small molecule and biotech.

In total, we received 15 completed questionnaires from 12 companies. The responses were received between November 2010 and September 2011. The companies agreed to have their

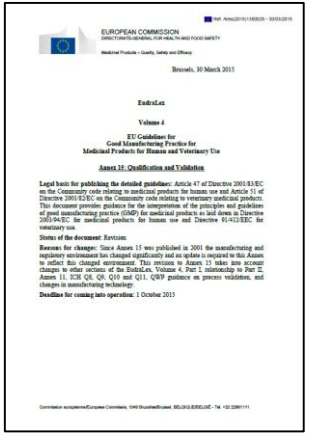
CPV and OPV

- Ongoing Process Verification – OPV

  Manufacturers should monitor product quality to ensure that a state of control is maintained...

  Annex 15

- Continued Process Verification – CPV
  - *Phase 3 of Validation Process* of FDA Guideline


EUROPEAN COMMISSION

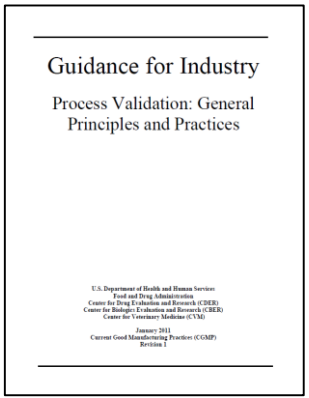
Brussels, 30 March 2015

EudraLex

Volume 4

EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use

Annex 15: Qualification and Validation


Guidance for Industry

Process Validation: General Principles and Practices

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)

January 2011
Current Good Manufacturing Practices (CGMP)
Revision 1

Data collection





Starting Mtrl CMA

Unit Operation 1 CPP

IPC

Unit Operation 2 CPP

IPC

Unit Operation n CPP

IPC

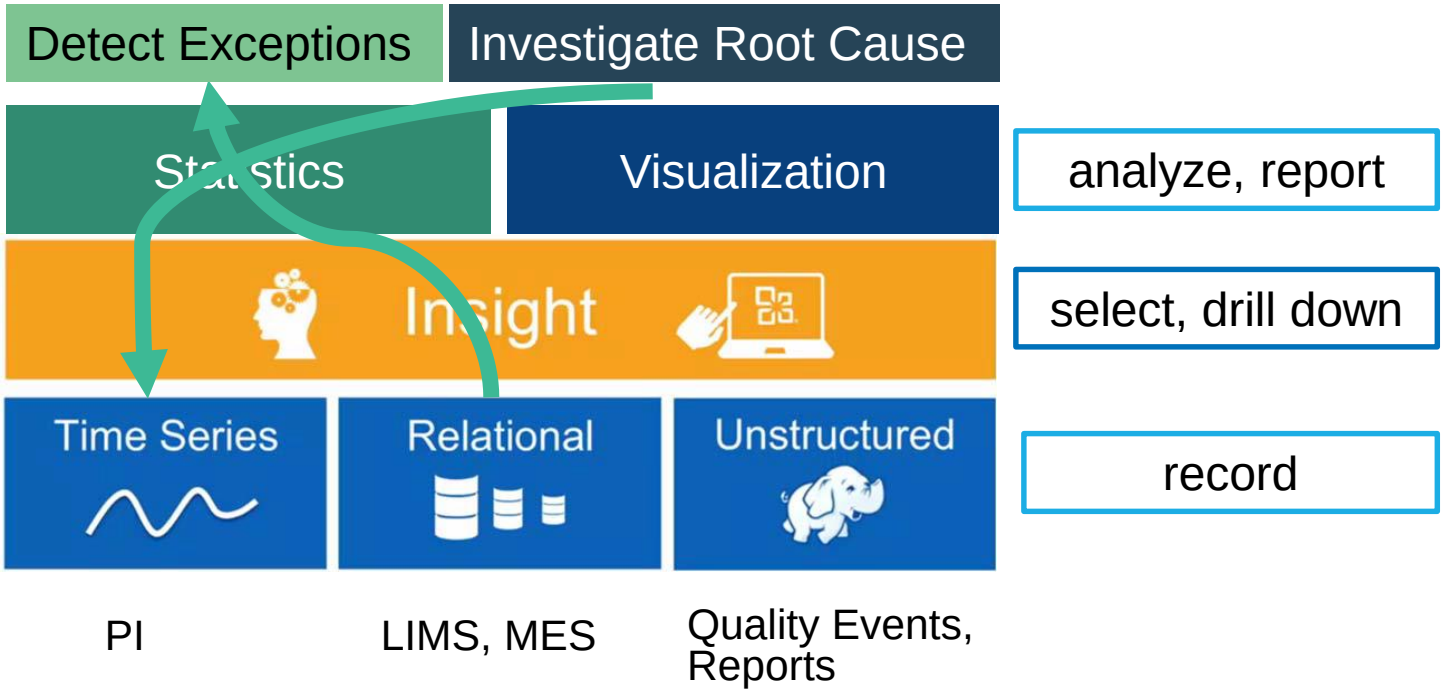
Final Product CQA

Input data - X

Output data - Y

Challenge 1: IT-related task to establish a platform where all data coming from different sources are compiled
Challenge 2: Data analysis approach for trending CQA and CPP/CMA

CPV possible workflow



How is real-time data Used in Life Science, F&B and Chemicals?

Process Engineer

- Analyze Process Behavior
- Monitor Equipment Performance
- Energy management

Operator

- Analyze Process Behavior
- Monitor Equipment Performance
- Bridge DCS Gaps

R&D

- Product Development
- Process scale up/down
- Analytical Development
- Experimentation
- Design Space

MS&T and PAT Teams

- Model building
- Predictive analytics
- Review Batch Report
- Trouble shooting
- CPV enablement

Quality Assurance

- Review Batch Report by Exception
- Analyze Batch Quality
- Verify Room Conditions
- Release or RTRt

Management

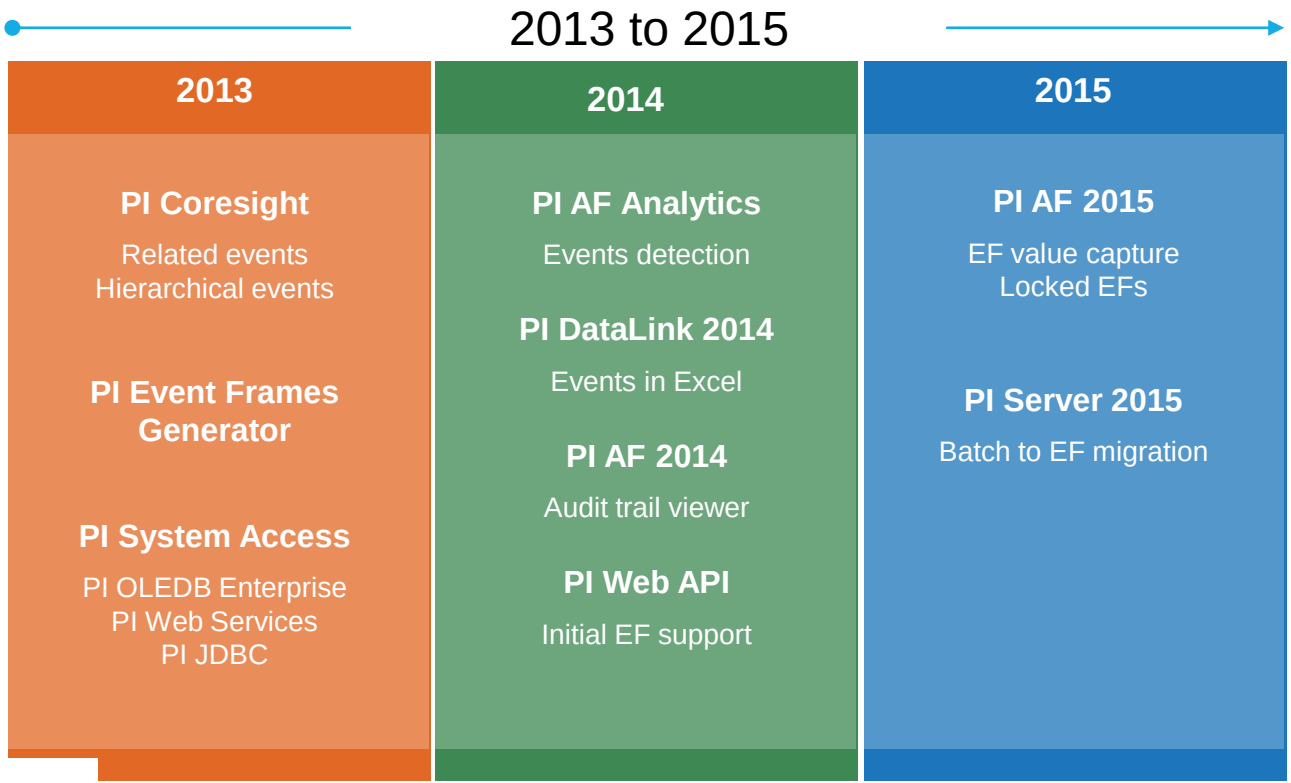
- Review KPIs
- Establishment of regulatory initiatives
- See Multiple Sites

Our commitment

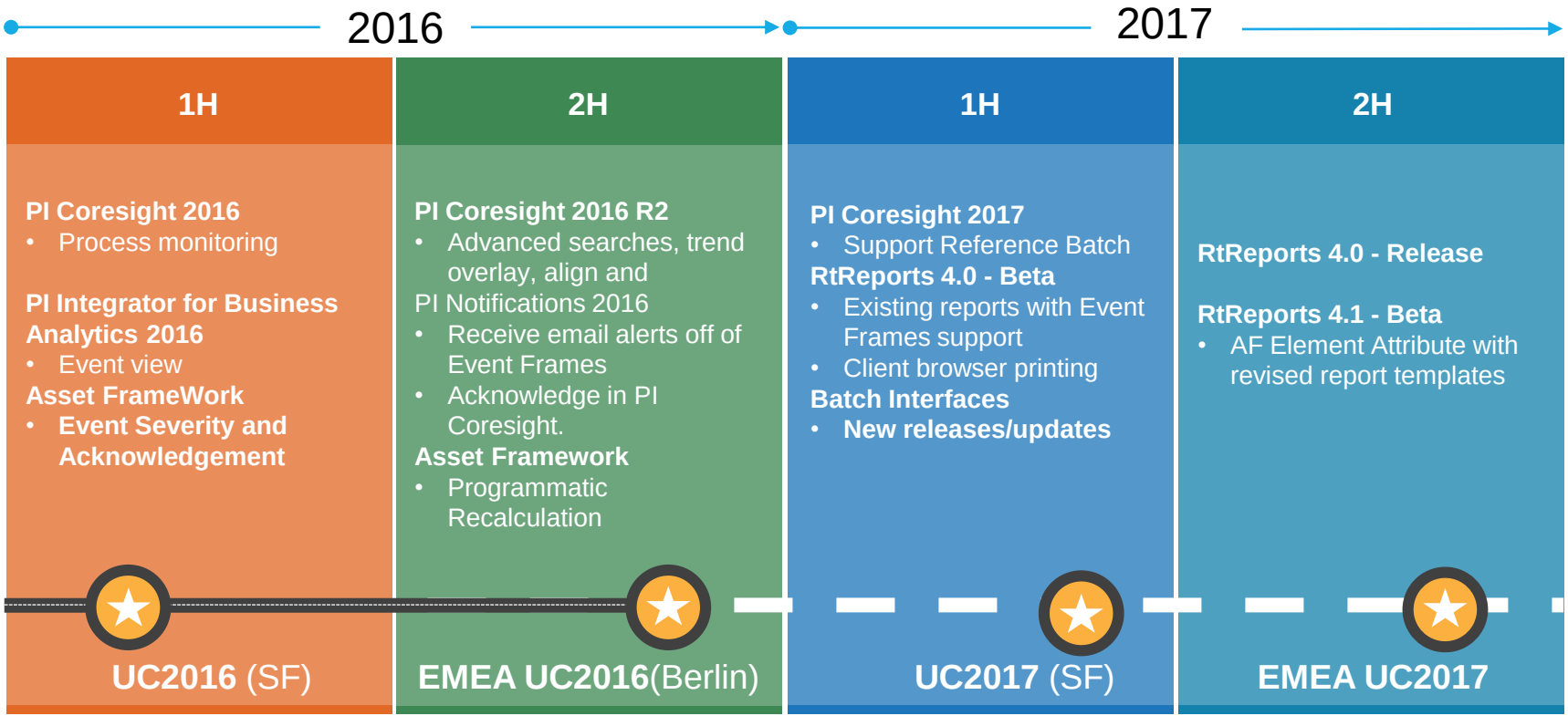
PI Event Frames Initiative Roadmap

Presented by **Chris Nelson, David Casazza**
Dan Fishman, Tom LeBay

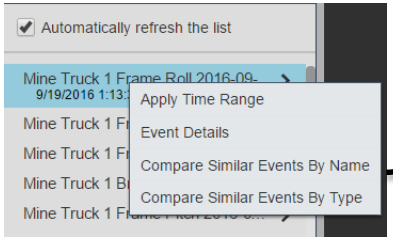
Event Frames Roadmap – The story until now



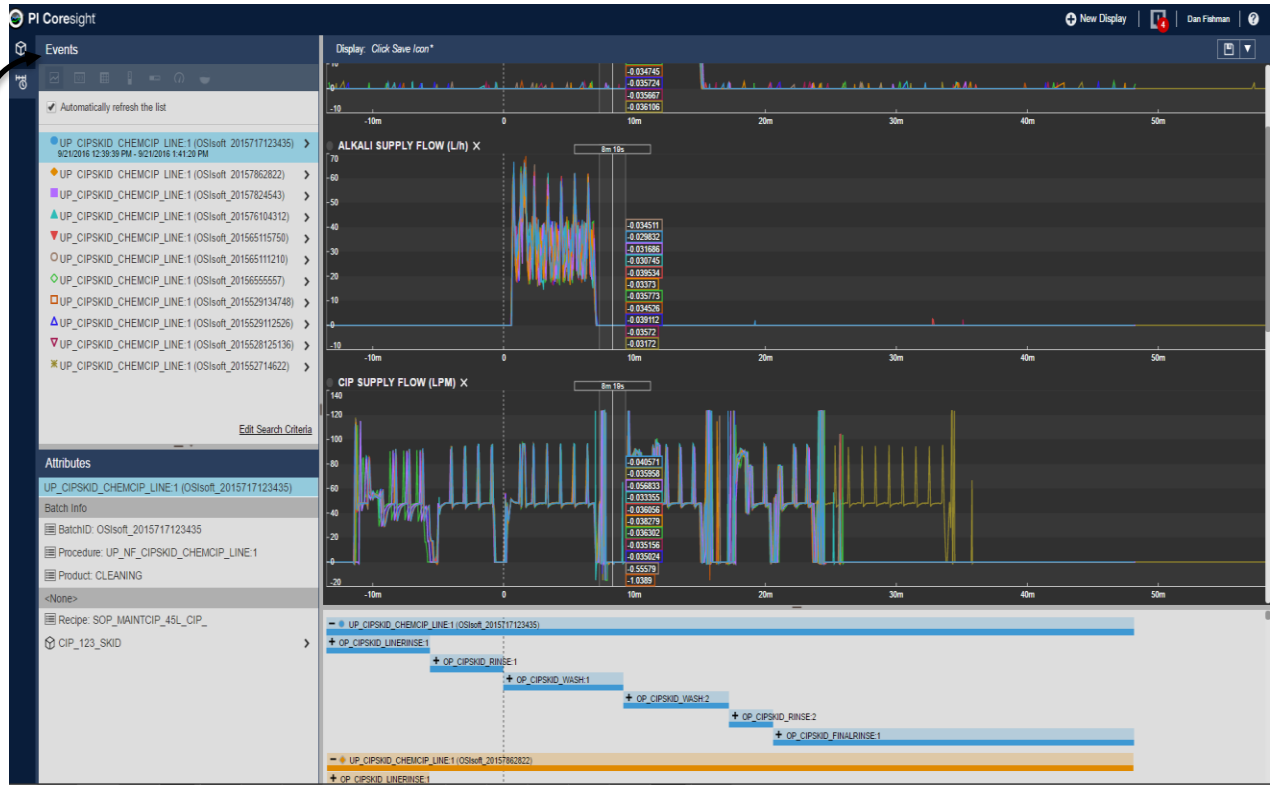
Event Frames Roadmap – The story continues



Event Comparison lets you easily compare and analyze similar events

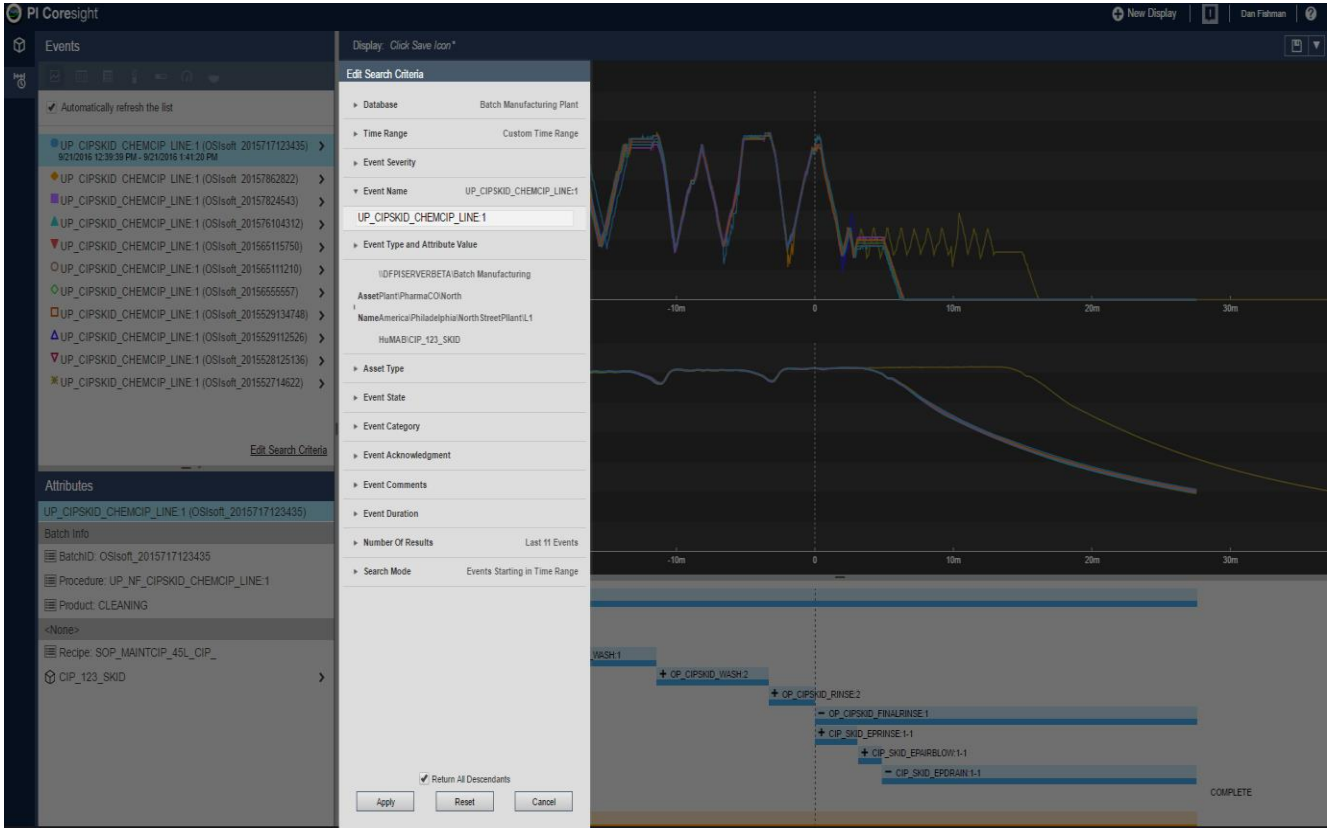


- Automatically compare last 10 similar events with a single click
- Overlay trend & Gantt chart
- Root cause time period
- Explore/align/zoom Child events
- Save analysis



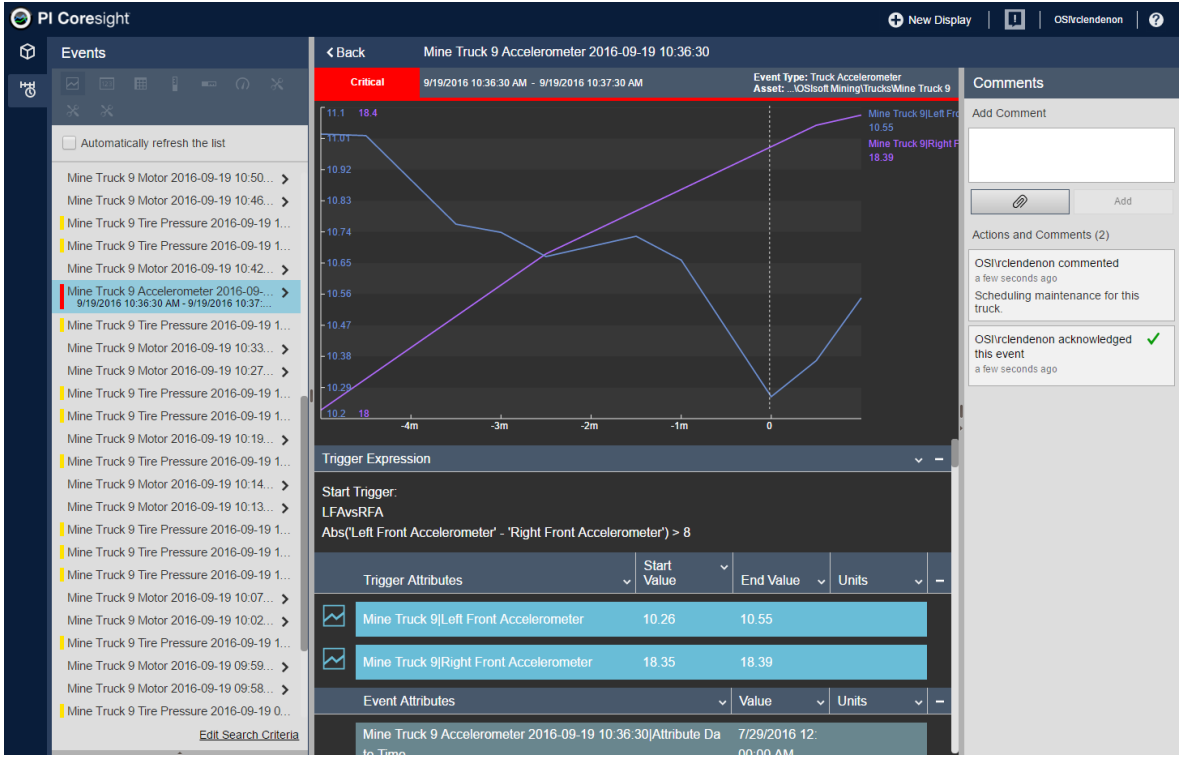
Events Palette gives you a complete picture

- Automatically view events related to assets & time range on display.
- View/trend event attribute values
- Trend Related Element Attributes
- Advanced searching features



Event Details

- Integrated with Notifications so events are delivered to you email
- Acknowledge an Event
- Event Annotations with Attachments
- Start Trigger Information
- Mobile friendly



Call to Action – Customer Success Stories

- Migrate Batch data to Event Frames
- Adopt PI Coresight 2016 R2
- We are looking for customers who want to verify the Event Comparison capability!

Time	Title	Presenter(s)
9:00 – 9:30	Enabling Decisions and improving Quality	Petter Moree - OSIsoft
9:30 – 10:00	Using Data Analytics to drive Process Optimization in Whiskey Manufacturing	Dagmara Dabrowska - Irish Distillers Pernod-Ricard
10:00 – 10:15	**Transfer Time**	
10:15 – 10:45	Monitoring Environmental Conditions on the Manufacturing Floor with PI Coresight	Arsenio Sanchez - Janssen
10:45 – 11:00	**BREAK - Potsdam Foyer**	
11:00 – 11:30	Productivity and Quality Improvements Through Continuous Contextualization of PI System Data	James Li, Shamus Cunningham - Abbott Nutrition & Seeq
11:30 – 11:45	**Transfer Time**	
11:45 – 12:15	Transitioning to a Modern PI System in a Validated Environment	Julio López, Marc Olive - Abbott Labs & AG Solution
12:15 – 14:15	**LUNCH - Pavillon**	
14:15 – 14:45	The PI System - Enabling a Digital Factory	Michael Pelz - Clariant
14:45 – 15:00	**Transfer Time**	
15:00 – 15:45	GxP Compliant Alarm Handling with Event Frames and AF	Gerd Fromm, Christian Wirth, Philipp Sutter - Roche
15:45 – 16:15	Wrap-up and Next steps	Petter Moree, David Casazza - OSIsoft
18:00 -	Dinner Party	Berlin U3

Contact Information

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Questions

Please wait for the **microphone** before asking your questions

State your **name & company**

Please remember to…

Complete the Online Survey for this session

http://ddut.ch/osisoft

감사합니다

谢谢

Danke

Gracias

Merci

Thank You

ありがとう

Спасибо

Obrigado