Data Infrastructure and Analytics in Life Sciences

Presented by

Petter Moree
Industry Principal
Life Sciences, Food & Beverage and Specialty Chemicals

Time	Title	Presenter(s)
9:00 – 9:30	Data Infrastructure and Analytics	Petter Moree – OSIsoft
9:30 – 9:45	**Transfer Time**	
9:45 – 10:15	Monitoring bioreactor cell culture data in real-time with the PI System	Cassandra Murillo, Anthony DeBiase – Regeneron
10:15 – 10:45	**Break**	
10:45 – 11:15	Data Sharing in an OEM Environment	Brian Goldinger, Abel Padilla, Christian Jaeger – Eli Lilly & Process Automation
11:15 – 11:30	**Transfer Time**	
11:30 – 12:15	Data Sharing in a Contract Manufacturing Environment	Brian Goldinger, Abel Padilla, Christian Jaeger – Eli Lilly & Process Automation
12:15 – 2:15	**LUNCH – Grand Ballroom**	
2:15 – 2:45	Pharmaceutical Manufacturing Improvement through leverage of PI Data and Analytical Tools	Robert Forest, Daniel Wasser – Bristol Myers Squibb & Seeq
2:45 – 3:00	**Transfer Time**	
3:00 – 3:30	The Value of the Novartis EA for the San Carlos Site and Novartis Achievements/Goals of the PI System strategy	Serge De Grandpre – Novartis
3:30 – 4:00	**Break**	
4:00 – 4:45	Leveraging the PI System to Build a Biologics Analytics Tool for Laboratory-Scale Bioreactor Data	Sohan Patel – Bristol Myers Squibb
4:45 – 5:15	Wrap-Up	Petter Moree – OSIsoft

Life Sciences PI User Group

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

263 Members

Customer run, customer led, OSIsoft assisted

Objectives:

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

This is NOT an avenue for sales presentations or marketing

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

Or contact jsirois@osisoft.com

Have questions?

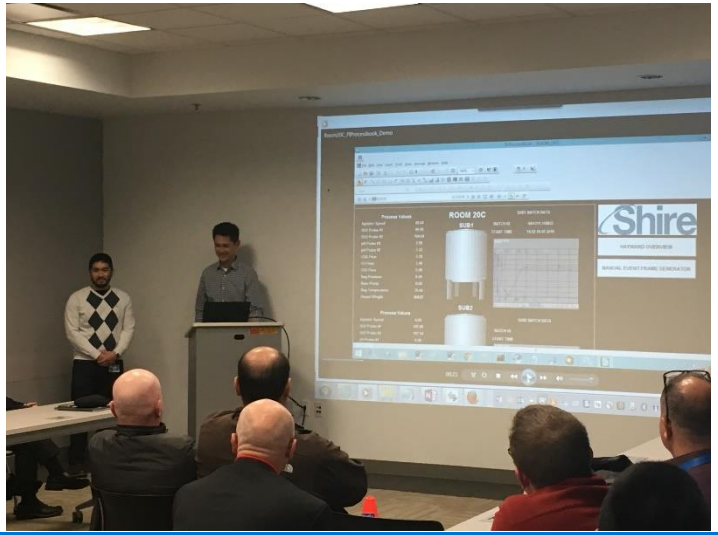
- jsirois@osisoft.com
- pmoree@osisoft.com
- Visit the PI Square Booth

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

Recap from PUG meeting Monday

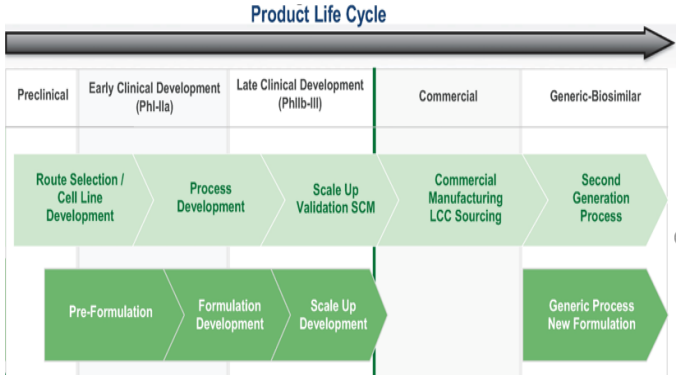
Pharma PUG team has 260+ members

- Monday site visit Shire Hayward, CA
- Presentation regarding MVDA from Hugo Guerra, Shire
- PUG meeting and workshops related to
  - EF visualization
- PUG dinner at Ideale
- New Chairperson

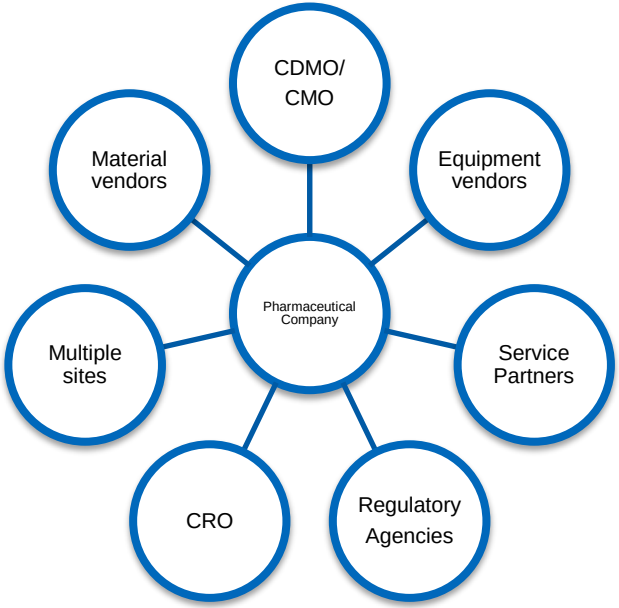


Multi-Dimensional

Time



Ecosystem



Corp.


Communities


Enterprise


Plants


Units


Assets

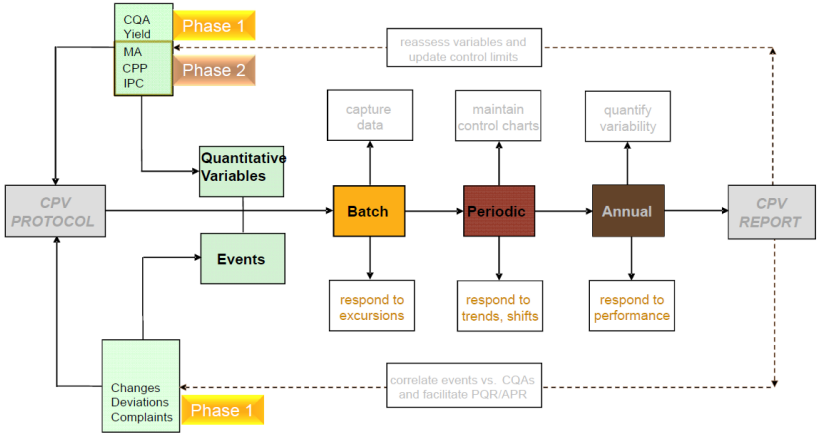

Sensors

Pharmaceutical Trends

Regulatory Trends from a data perspective
CPV and Data Integrity

Roadmap for Continued Process Verification

[3]

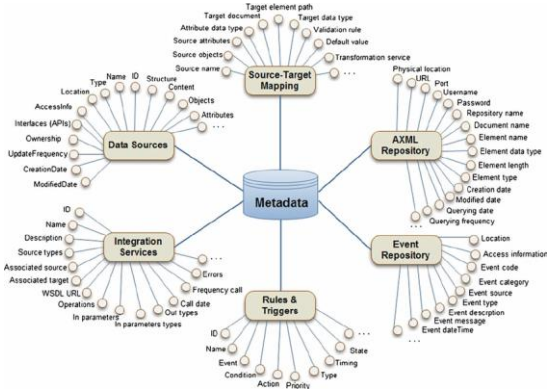


14 | IFPAC 2015 | A. Zilian | 28 Jan 2015 | Continued Process Verification program © 2015 Novartis Pharma AG | Public

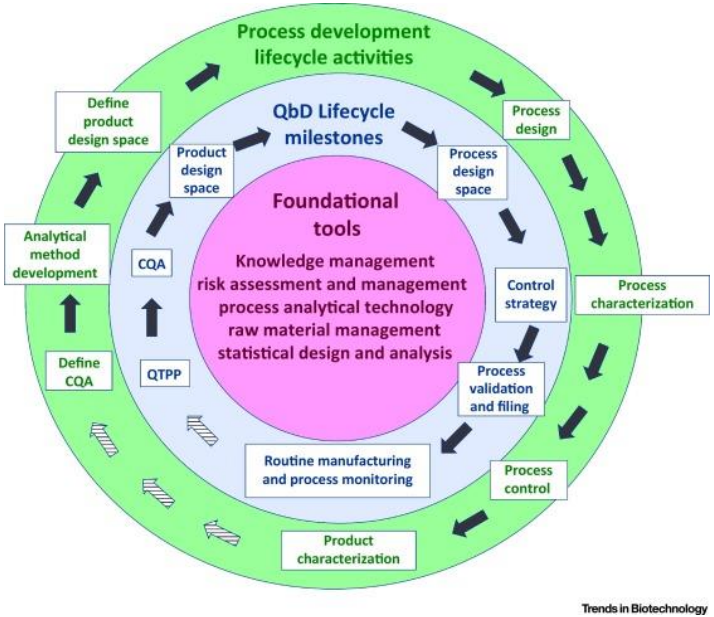
NOVARTIS PHARMACEUTICALS

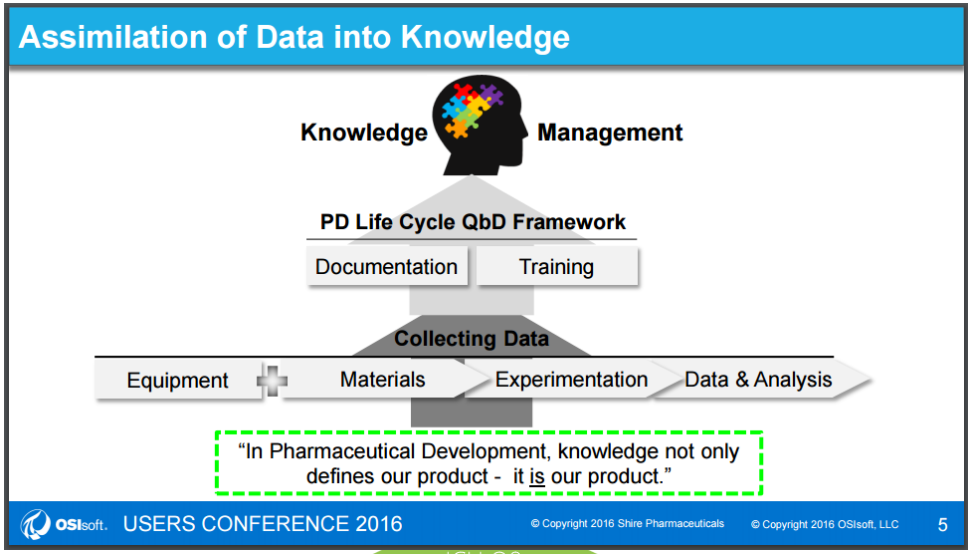
Data Integrity and Compliance With CGMP

Guidance for Industry

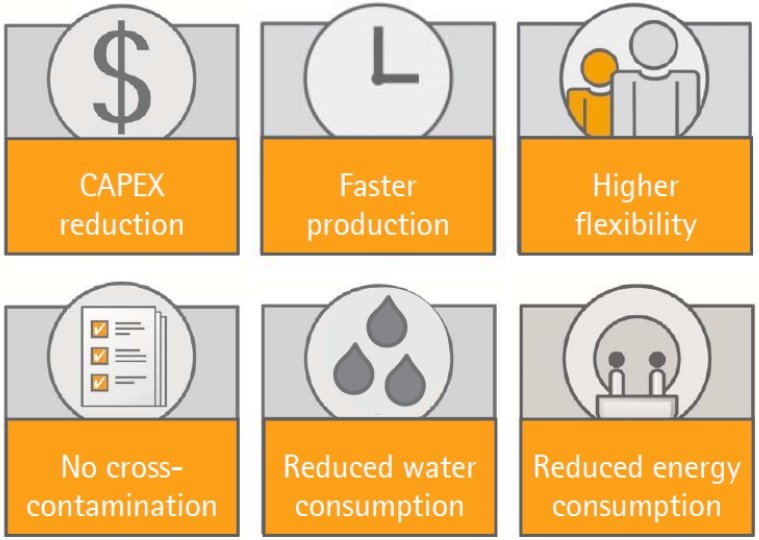


Process and Product Development

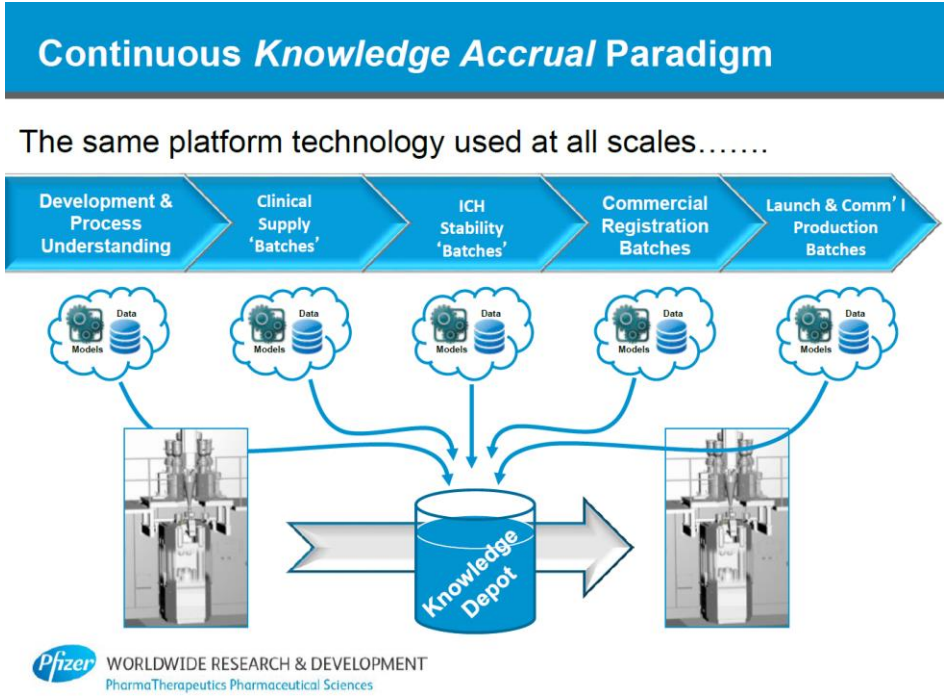


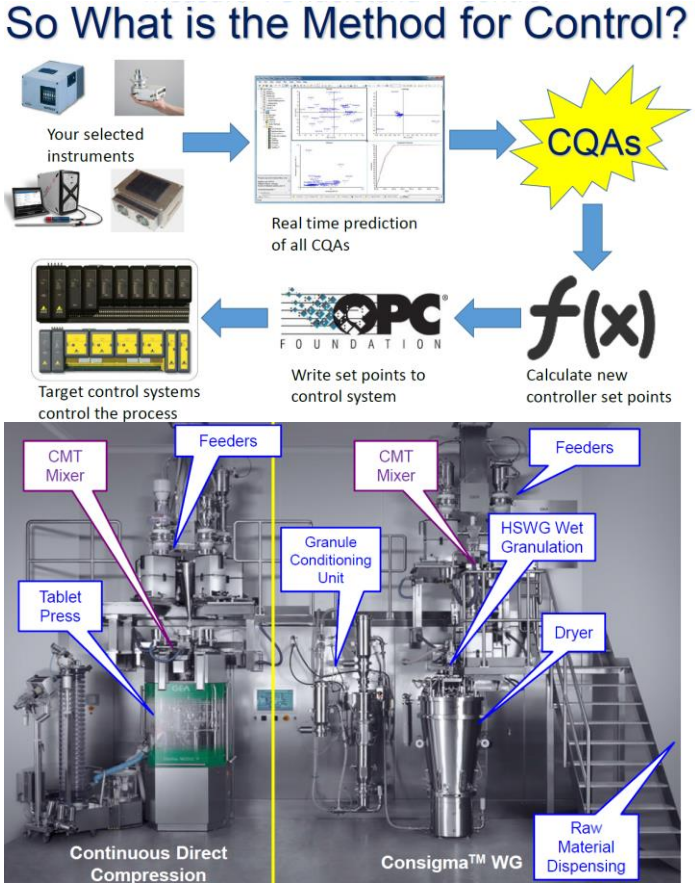


New Technology
Single Use



Technology
Continuous Manufacturing





Advanced Control
Data Driven control using MPC

Abstract

Predictive monitoring is a key feature of biopharmaceutical manufacturing; making predictions about the key process end points such as process performance indicators or quality attributes using a process model offers the unique advantages of process improvement and optimisation, and helps give insights into variability. However, whilst model-predictive monitoring is advantageous, it is also desirable to apply model predictions for closed loop control of biologics manufacturing using various process analytical technology (PAT) tools. We summarise some of our experiences with predictive monitoring, closed loop control using in situ Raman spectroscopy and state-space methods for model predictive control of cell culture bioreactors.

Engineering Conferences International
ECI Digital Archives

Cell Culture Engineering XV — Proceedings

Spring 5-10-2016

Agent-based model predictive framework to control cell culture bioreactors

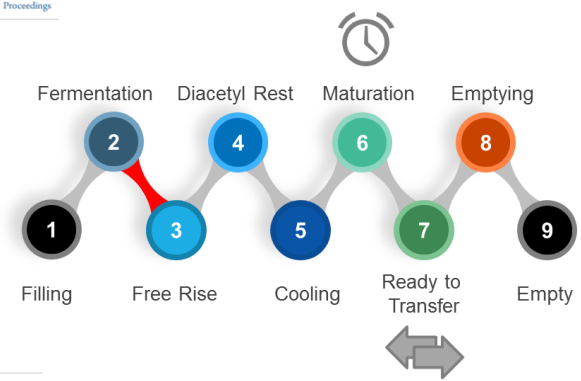
Elif Bayrak
Amgen, ebayrak@amgen.com

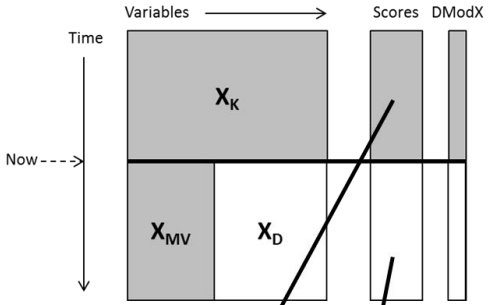
Tony Wang
Amgen

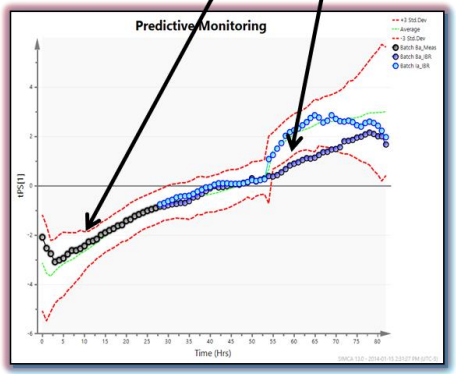
Myra Coufai
Amgen

Ali Cinar
Illinois Institute of Technology

Cenk Undey
Amgen

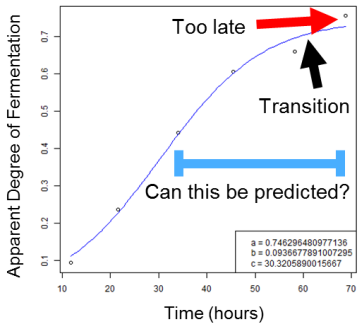






Challenge

Transition occurs between infrequent manual measurements



Outsourcing
CMO/CDMO and critical materials

The Numbers Game

➢ > 200	**Individual Product Families**
➢ > 2000	**SKUs**
➢ >18000	**Raw Material SKUs**
➢ 29	**Internal Sites**
➢ 130	**External Sites**
➢ 0	**Products Made all Internally**

	External Mfg	Procurement	Total
# of Partners	108	480	588
# of Sites	130	614	744
# of SKUs	2000	18,000	20,000

janssen

Data Integrity Lifecycle

- what controls do **YOU** have over your suppliers re: cGXP data creation, collection, etc.?
- what controls do **YOU** have over your suppliers re: cGXP data processing, editing, review, manipulation, etc.?
- what controls do **YOU** have over your suppliers re: cGXP data transmittal, data stored "live" on suppliers' networks, etc.?
- what controls do **YOU** have over your suppliers re: cGXP data they have archived for the long-term on your behalf?

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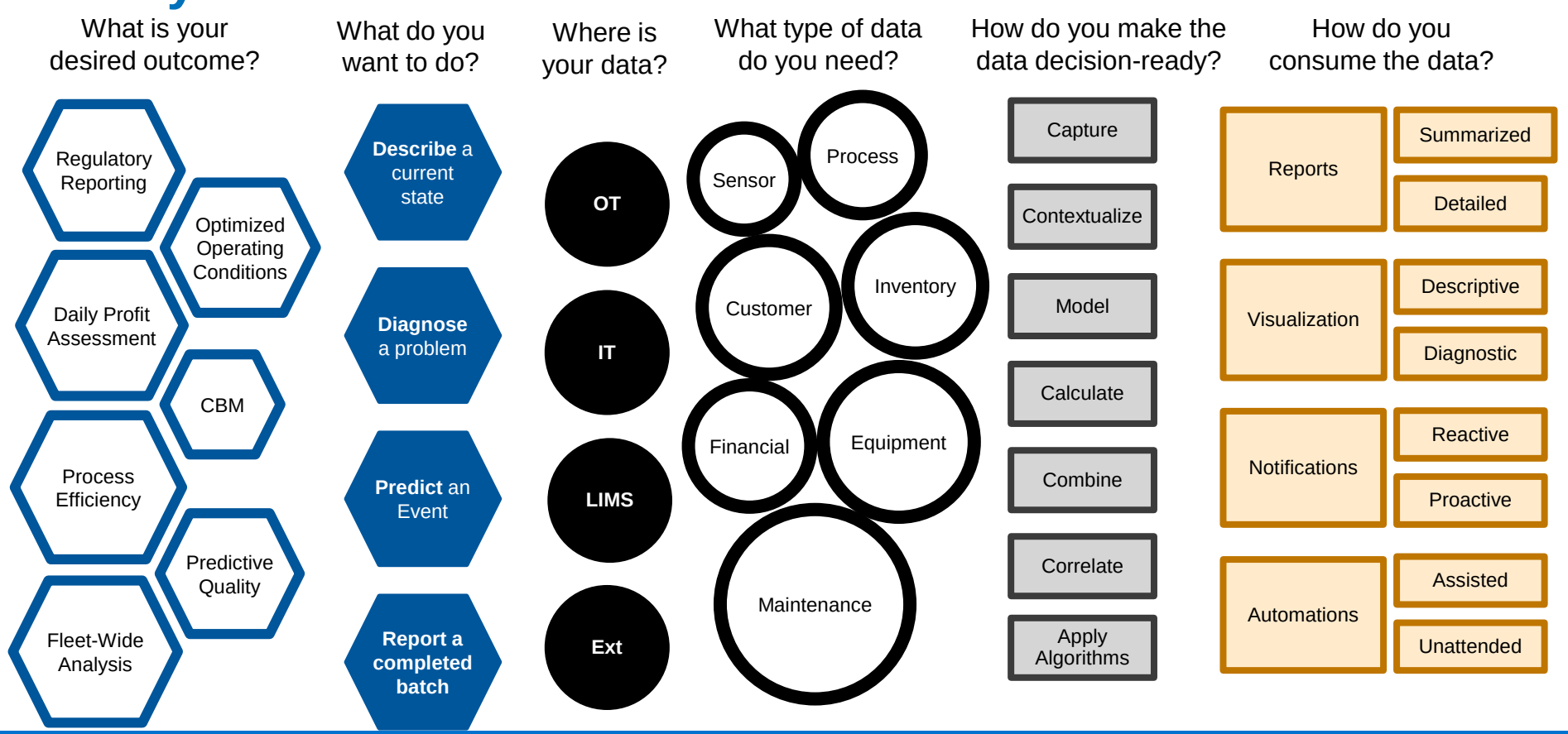
8

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

Analytics



Data supported business

Knowledge

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

Analytics

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

Operational Exc.

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

Compliance

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

Pharma becomes data and analytics driven

Analytics in the Life Sciences market

Process Engineer

- Analyze Process Behavior
- Monitor Equipment Performance
- Material characteristics

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
- Parametrical Release

Management

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

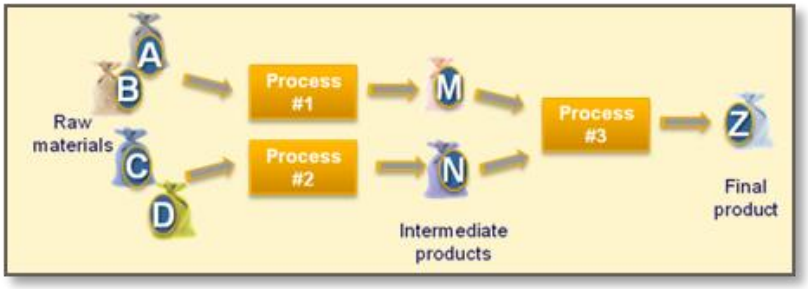
Story

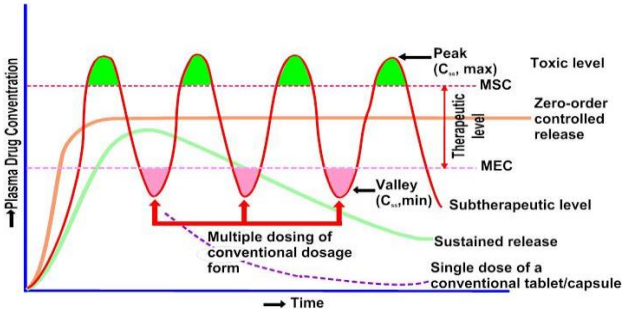
Challenge

All batches are not meeting release criteria – use test
Release criteria known after 30 days!
Number of non conforming batches increases in time

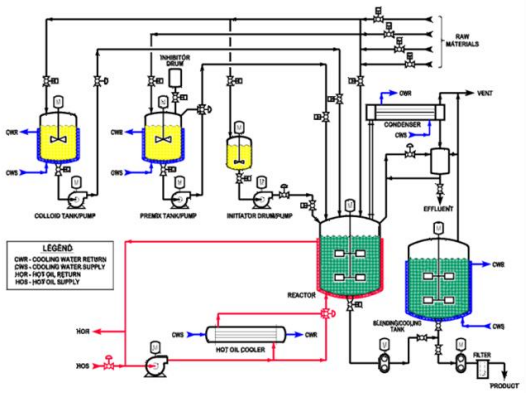
Product

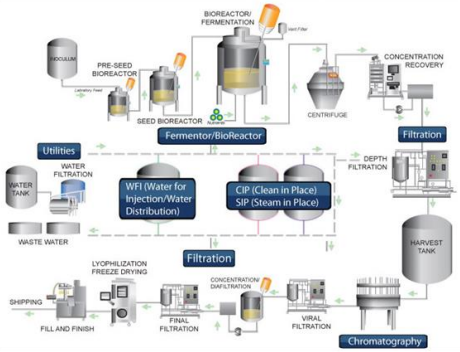
High Revenue Product
Extended release, drug given every XXth day
Global Market
Extended therapeutically application





The processes





Country 1

Country 2

Country 3

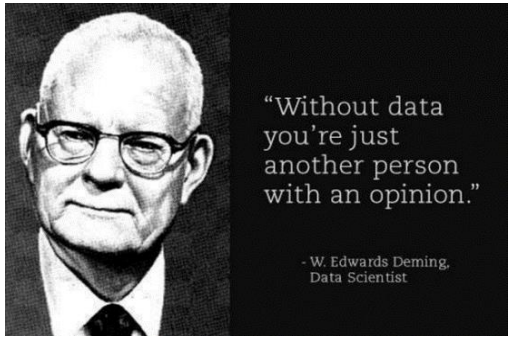
Process
- Biotech
- Chemical
- Pharmaceutical

Poor infrastructure
- Paper driven records
- iFix
- historians

Analytics

Stakeholders, managers, experts

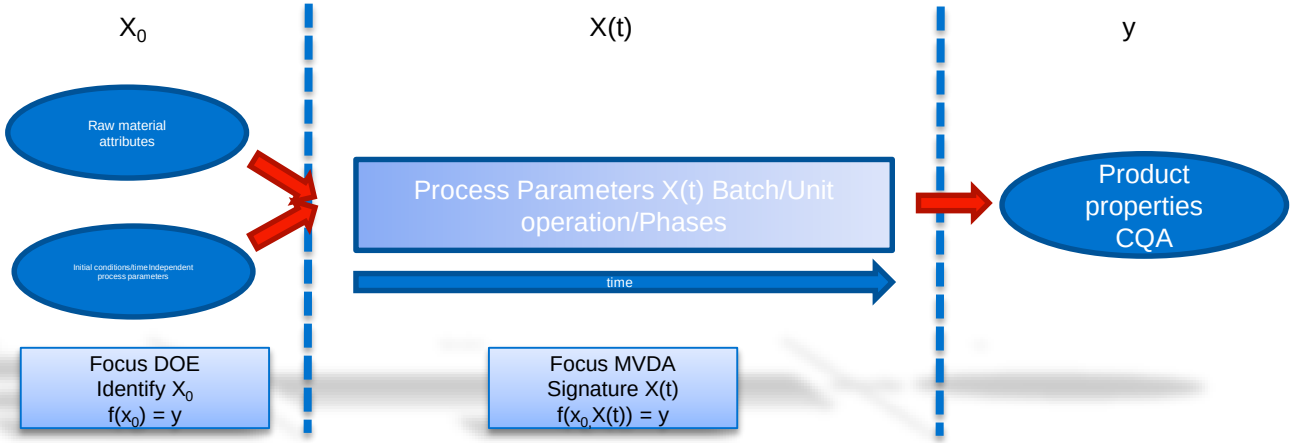
"it is due to hygroscopic material"
"particle size distribution"
"impurities"
"molecular weight"
"Reaction time"
"Starting materials



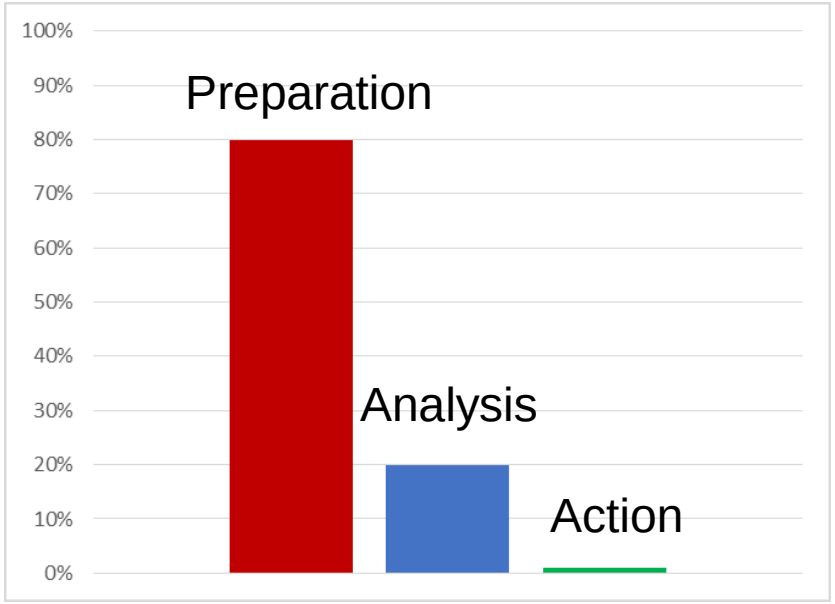
Hierarchical Batch PLS models with time resolved process data as X and QC/CQA test as Y

Investment

Paper to digital – 2 month, 3 persons
Historian alignment – 2 month 1 PhD.
Data preparation almost took 10 month
Modelling took 1-2 days!



Data Wrangling



Data cleansing and preparation tasks can take 50-80% of the development time and cost

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

Analytics

Hierarchical Batch modelling (PLS) combining all process trajectories, IPC and initial conditions as X, CQA as Y

SIMCA mks

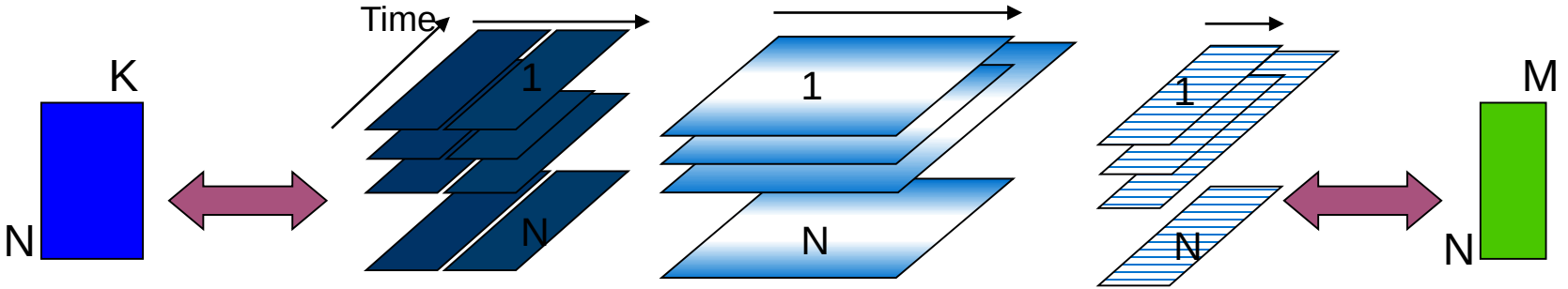
Batch conditions (X0)

Process data Chemical (X1)

Process data Biotech (X2)

IPC data (X3)

CQA (Y)

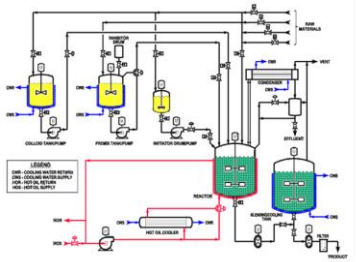


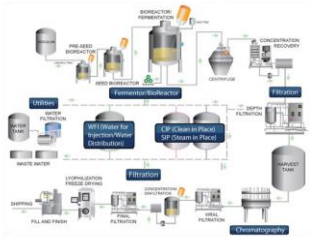
Both actuators, mesurments and setpoints

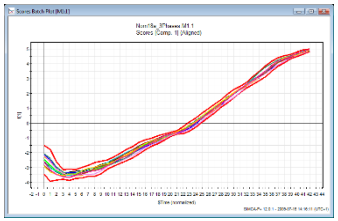
Multiple phases
Variating batch length
Calculated parameters

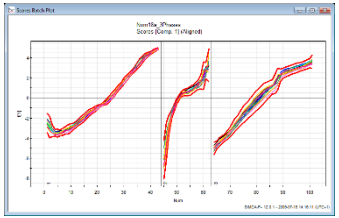
Long inhomogenious sampling interval

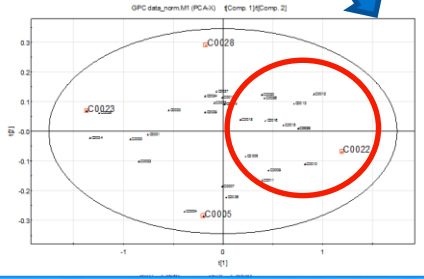
Result – Data driven decision for release

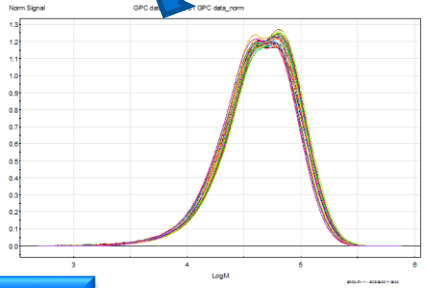




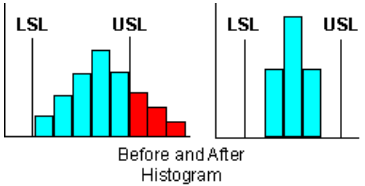




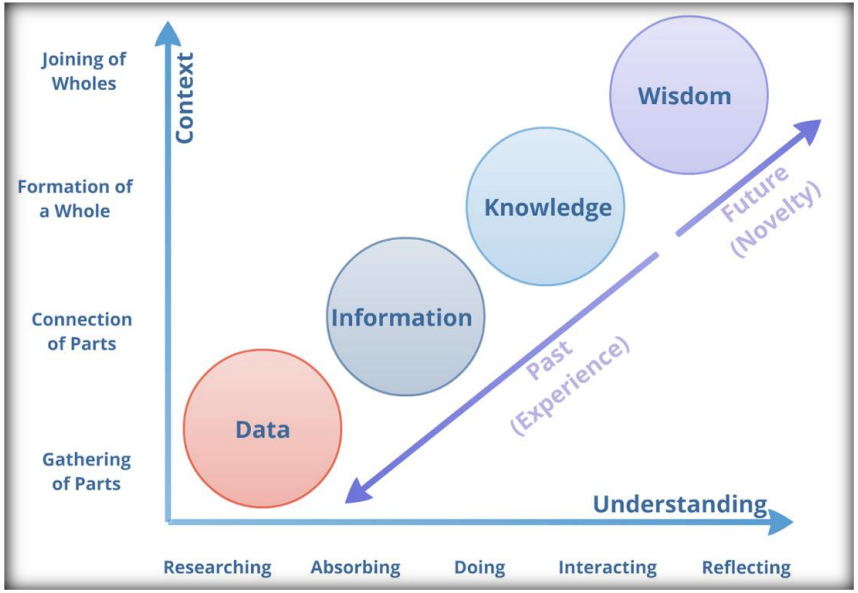




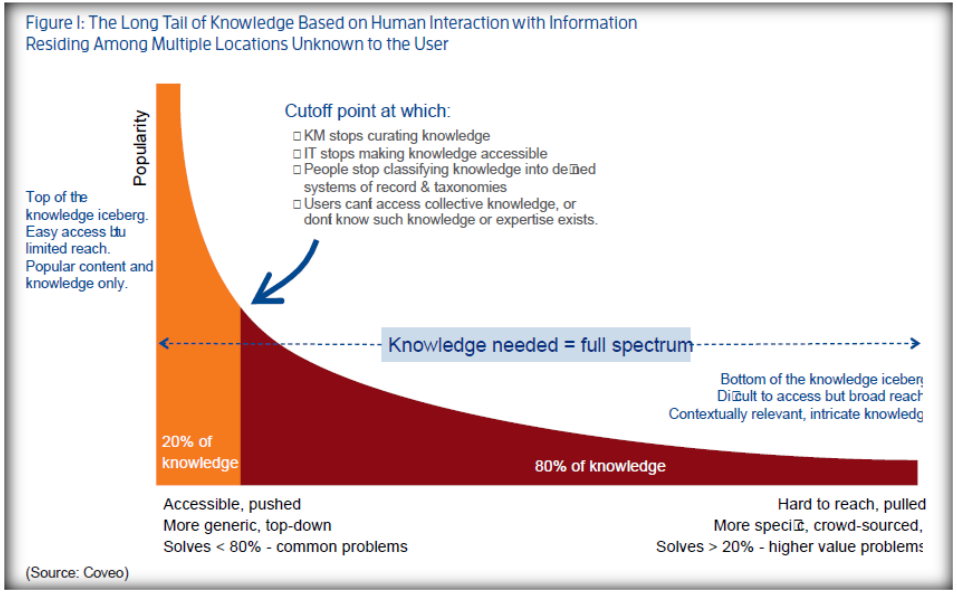
- ✓ CQA variation correlated to chemical process
- ✓ Better control using batch **trajectories** enabled less variation in CQA
- ✓ New control strategy developed based on Design Space
- ✓ Distributed islands of operations, centralized analytics

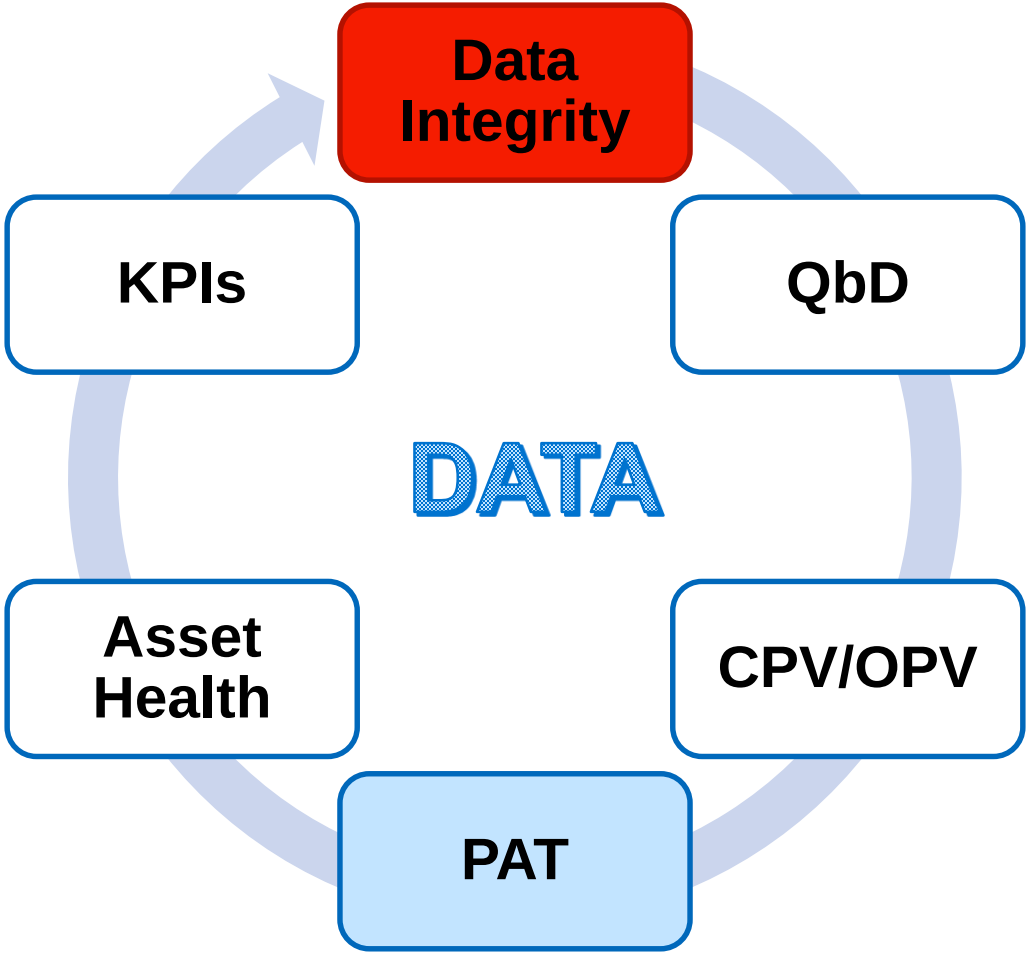


Knowledge Management



Source: Russ Ackoff “From Data to Wisdom”, Journal of Applied Systems Analysis, Volume 16, 1989 p 3-9.





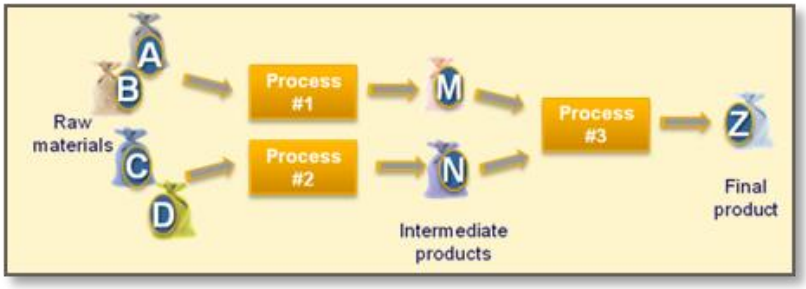
Story

Challenge

All batches are not meeting release criteria

Release criteria known after 30 days

Number of non confirming batches increases in time

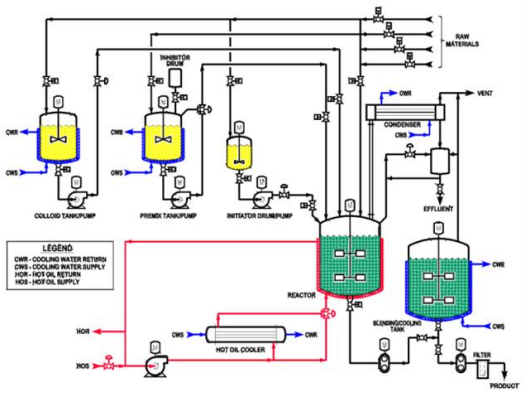


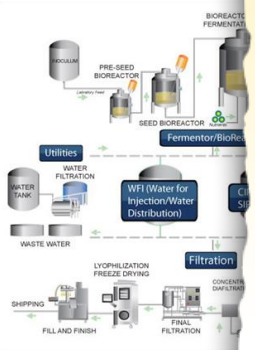
QbD

Risk assessment to identify the CQAs and how these are related to CPPs and CMAs would lead to:

- ✓ Design Space – a relationship between process and material to quality
- ✓ Enables a control strategy to meet specs and economical benefits

The processes





Country 1

Countr

Country

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

Applicable for

1. Research & Development
   - Including CDMO
2. Clinical Trials
3. Manufacturing & Testing
   - Including CMO and CMA

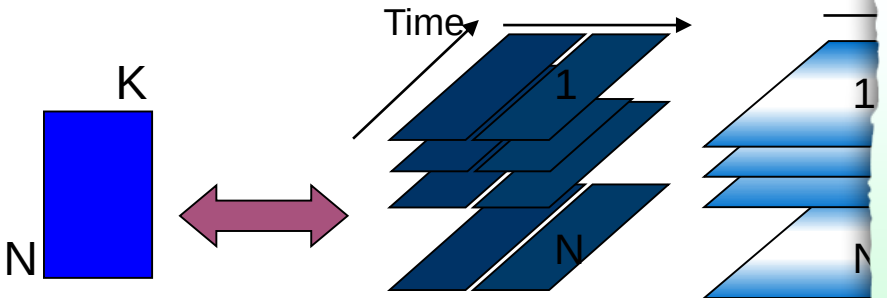
Analytics

Hierarchical Batch modelling (PLS) comb
trajectories, IPC and initial conditions as

Batch conditions (X0)

Process data Chemical (X1)

Pro Biot



Both actuators, mesurments and setpoints

Multiple pi
Variating batch length
Calculated parameters

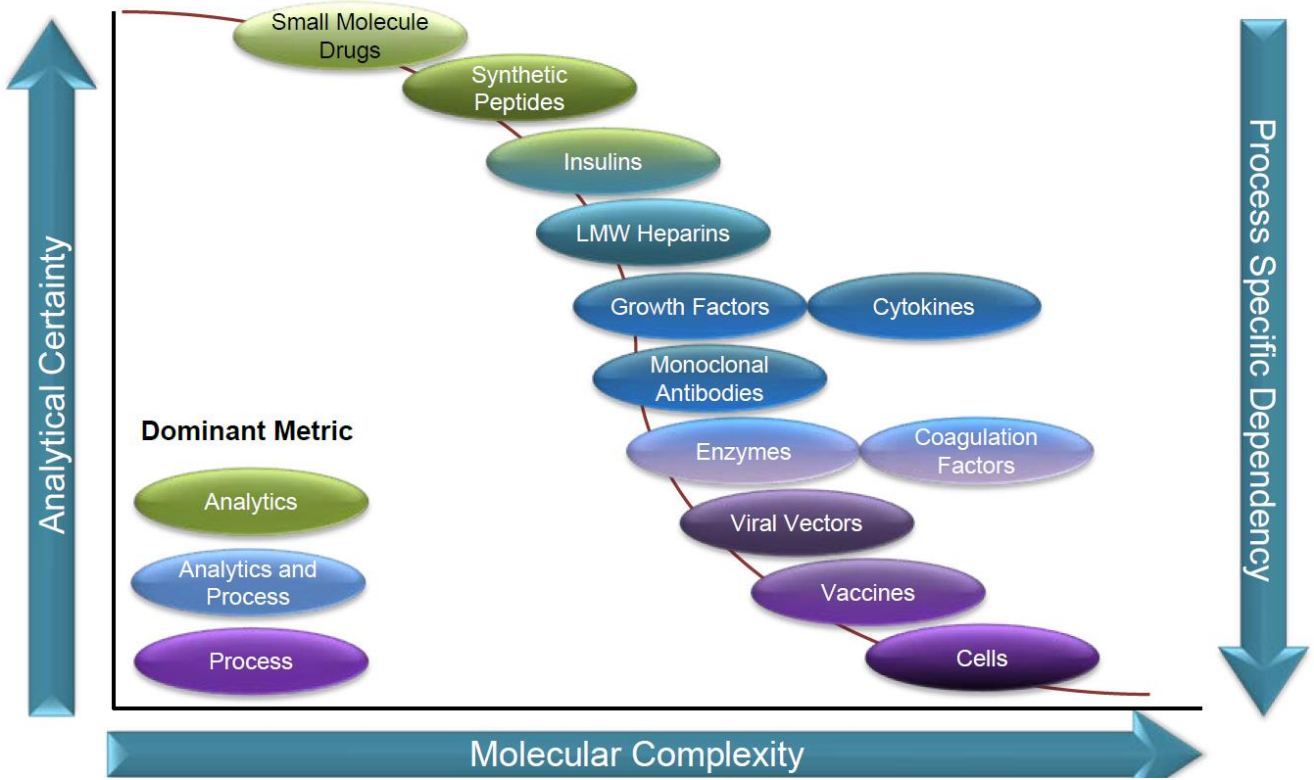
sampling interval

PAT

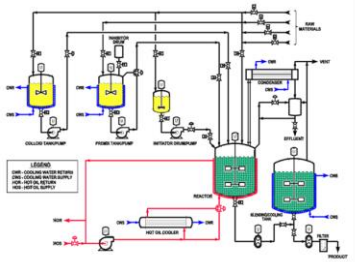
Benefits & Business Drivers

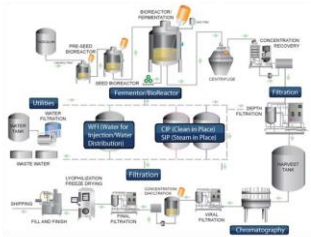
- Better process control / Lower process variability
  - Reduce number of OOS and batch failures
- Process improvement
  - Increase of yield, throughput & quality
- Efficient and lean QC testing
  - Replacement by faster analytical technologies (on-line PAT tools)
  - Real time release (RTRt)
- Prerequisite for continuous manufacturing

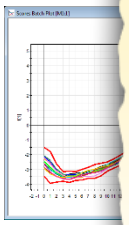
Importance of process data in biopharmaceutical

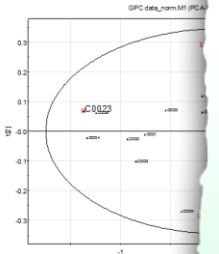


Result – Data driven decision fo release









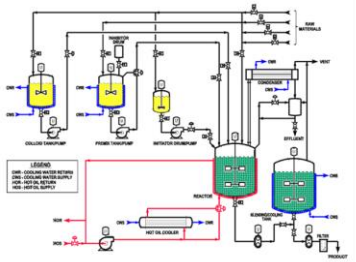
- ✓ CQA variation correlated to chemical process
- ✓ Better control using batch **trajectories** enabled less
- ✓ New control strategy developed based on Design Sp
- ✓ Distributed islands of operations, centralized analytic

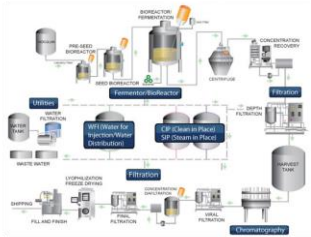
CPV/OPV

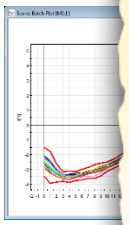
An ongoing program for collecting and analyzing product and process data that relate to product quality

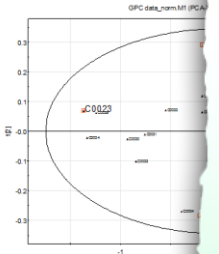
- Procedures for data collection and trending
- Data collected should verify that the quality attributes meet specs
- Intra-batch and inter-batch variation
- Data should be collected to evaluate process stability and capability
- Data should be statistically trended

Result – Data driven decision fo release









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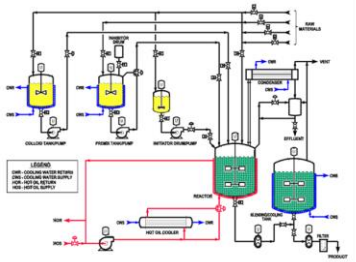
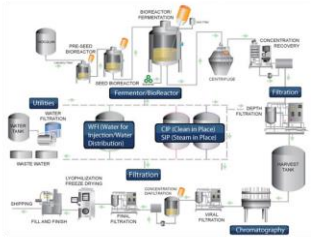
Asset Health

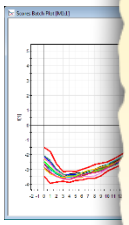
Optimizing asset health, minimizing asset failures and understanding optimal maintenance programs are critical to reducing operation costs. Going from calendar based to situation based to condition based maintenance is becoming common in the process industry. Several companies also adopt Predictive or Prescriptive Maintenance.

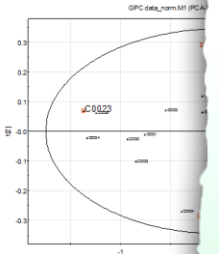
E.g. When do we need to change the packaging material in the chromatography column?

Result – Data driven decision fo release









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KPI

Key Performance Indicators are common tools to track success and status of an organization, process or system.

Common KPI's in Pharma Manufacturing are:

- OEE, generated of Productivity, Availability and Quality
- Cycle Time
- NC or OOS – Non Conformity or Out Of Specification batches/lots
- Yield

Trending of KPIs gives insight in performance and can highlight problems. It is often valuable to be able to drill down into the elements building a KPI to allow corrective actions

CPV is about understanding variation and the ability to demonstrate and use that knowledge

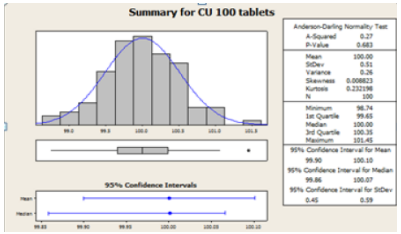
A successful validation program depends upon information and knowledge from product and process development. This knowledge and understanding is the basis for establishing an approach to control that is appropriate for the manufacturing process.

Manufacturers should:

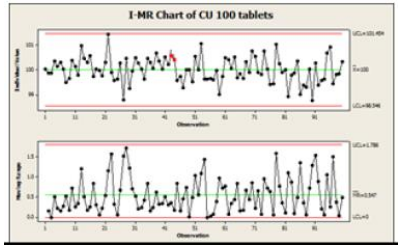
1. **detect the presence and degree of variation**
2. **understand the sources of variation**
3. **understand the impact of variation on the process and ultimately on product attributes**
4. **control the variation in a manner commensurate with the risk it represents to the process and product**

Common CPV requirements

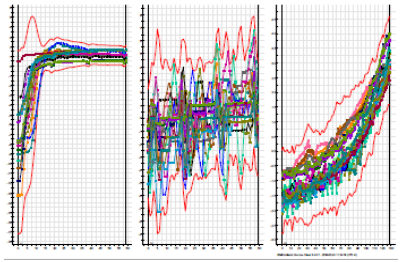
- **Data Management**
  - Data Integrity and Data Quality
  - Fast and Secure access to data on demand
  - Data search and analytics capabilities
  - CMO data access
- **Statistical and analytical**
  - Contextualization of batch data
  - Flexibility of statistical tools
  - Interactivity of visualizations and plots
- **Processes improvements**
  - Storing data assessments and investigations
  - CAPA and continuous improvements
  - Non conformity documentations and follow ups



CQA Data with CpK

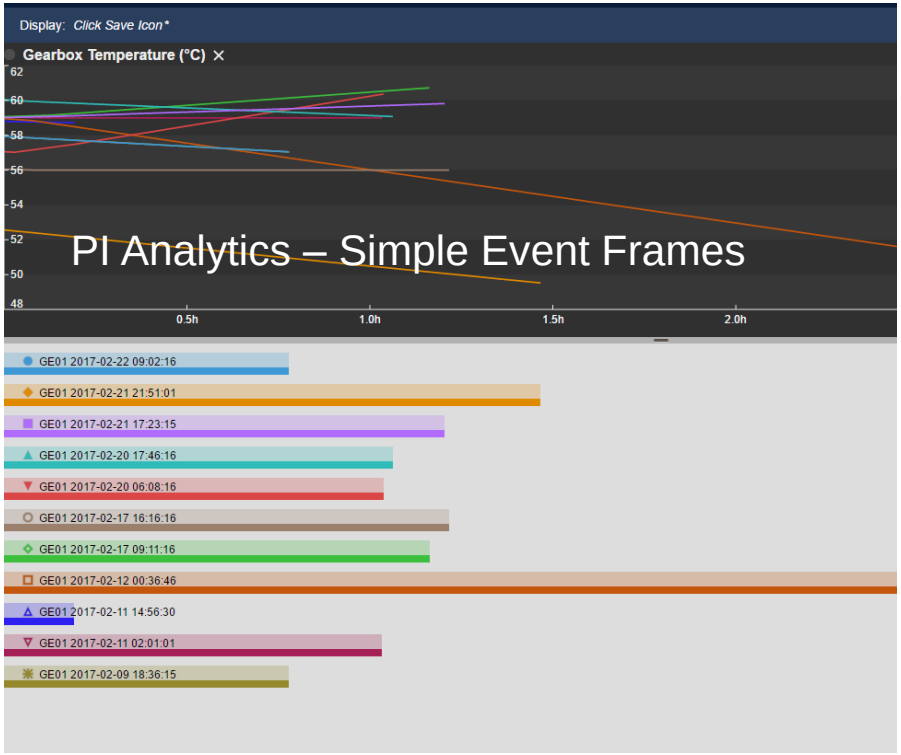


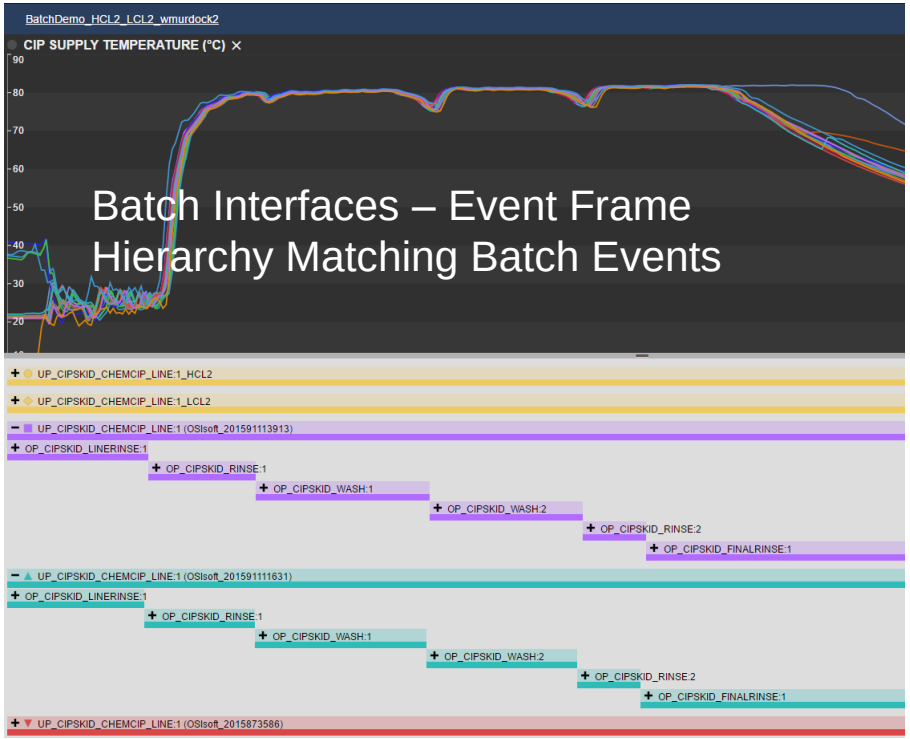
Trending of CQA



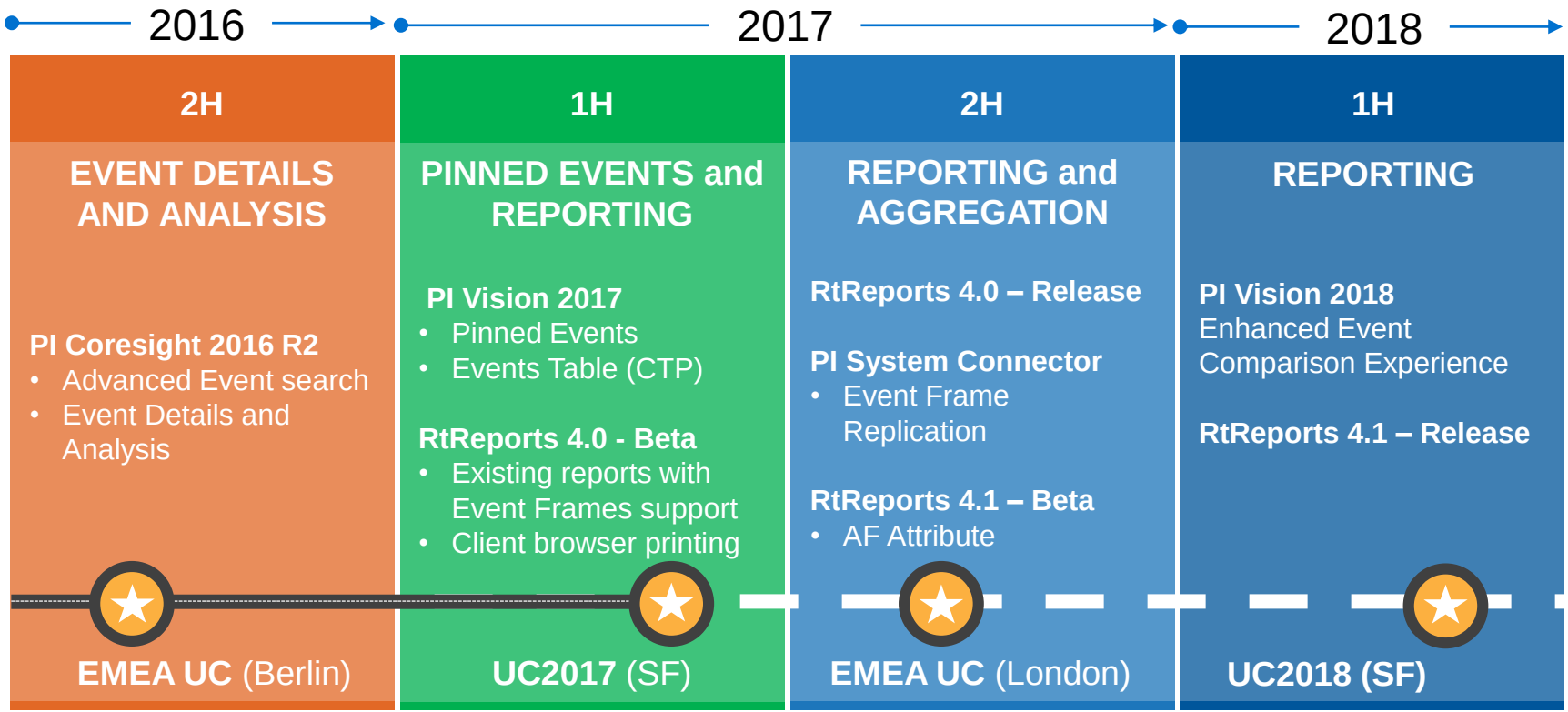
CPP Data using MVDA

PI Analytics vs. Batch Interfaces





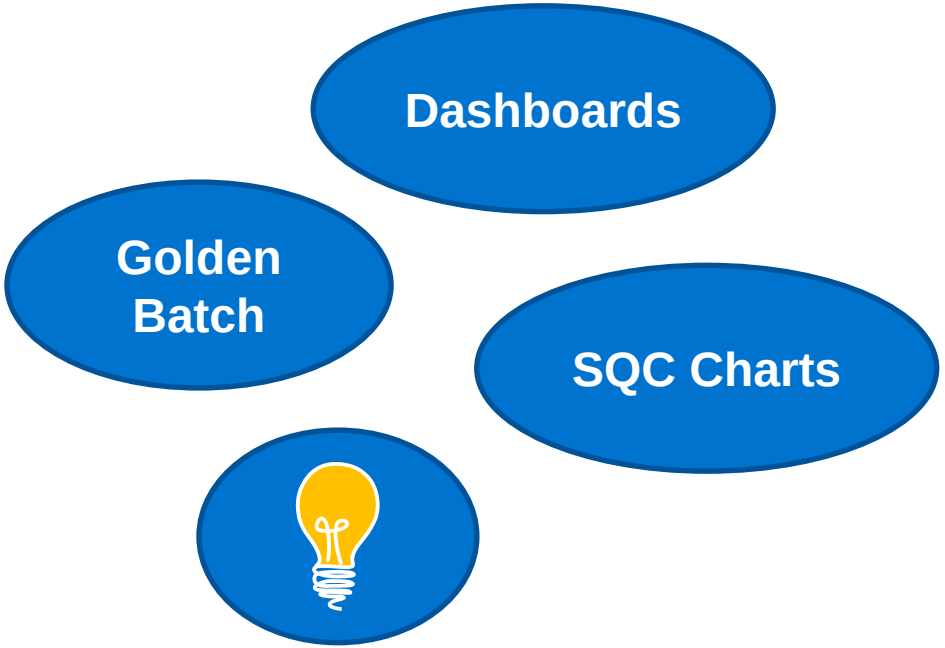
Event Frames Roadmap – moving forward to 2017-2018



We want to hear from you!

Chris Nelson
CNelson@osisoft.com
Director, Visualization Products
OSIsoft

Alicia Coppock
acoppock@osisoft.com
Product Manager, Visualization Products
OSIsoft



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Contact Information

Petter Moree
pmoree@osisoft.com
+46736997999
Industry Principal
OSIsoft, LLC

Questions

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State your **name & company**

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Complete the Online Survey for this session

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감사합니다

谢谢

Danke

Merci

Gracias

Thank You

ありがとう

Спасибо

Obrigado