Leveraging Data Analytics to Support Merck's Journey in Continuous Manufacturing

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Leveraging Data Analytics to Support Merck's Journey in Continuous Manufacturing

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About Our Company - Merck

VISION

To make a difference in the lives of people globally through our innovative medicines, vaccines, and animal health products. We are committed to being the premier, research-intensive biopharmaceutical company and are dedicated to providing leading innovations and solutions for today and the future.

BUSINESSES	Pharmaceuticals, Vaccines, Animal Health
HEADQUARTERS	Kenilworth, New Jersey
EMPLOYEES	Approximately 69,000 worldwide
CORE PRODUCT CATEGORIES	Diabetes, cancer, vaccines, hospital acute care

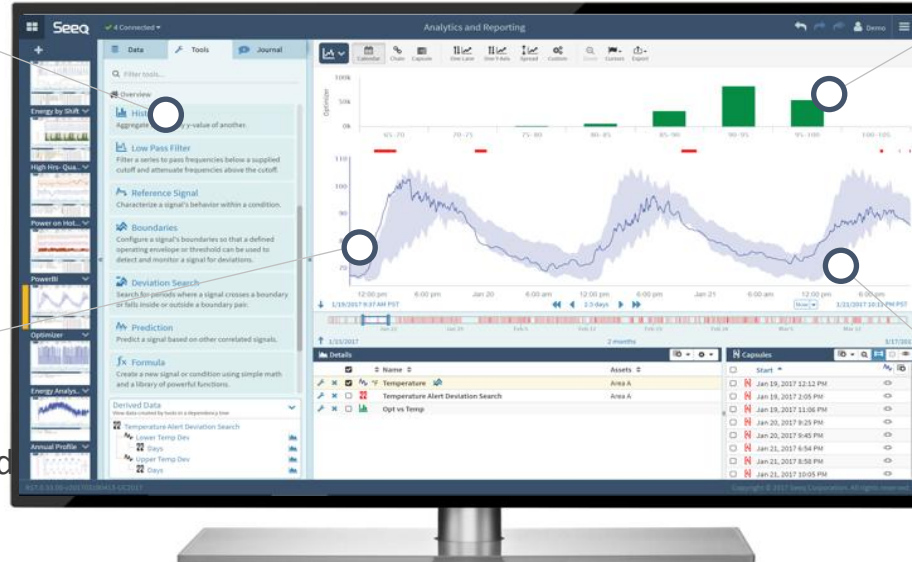# About Our Company - Seeq

Application

Subject Matter Experts
Teams and colleagues
Managers

Value from PI Data

Rapid install on PI
Keep PI as system of record
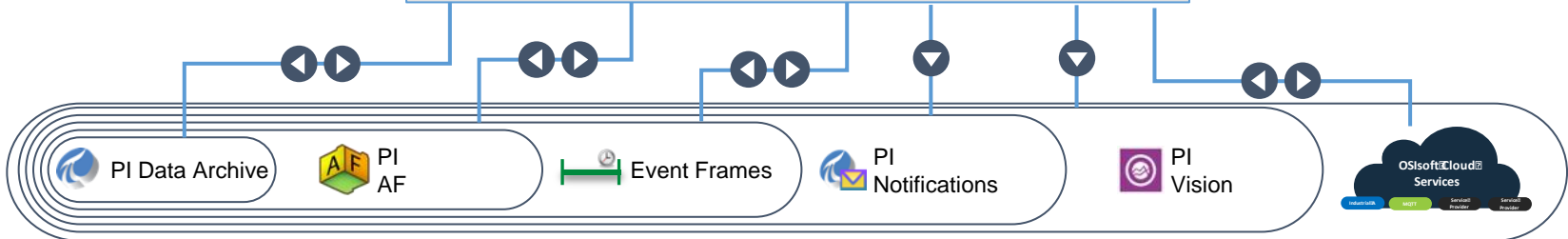Extensive integration

Impact

Faster insights
Knowledge capture
Dynamic reports

Advanced Analytics

Big data
Machine learning
Cloud or on-premise

Advanced Analytics for OSIsoft PI System

Agenda

- Welcome & Introductions
- The Challenge – Big Data in Continuous Manufacturing
- The Solution – Use Case Examples in PI & Seeq
  - Diagnostics and Root Cause Analysis
  - Monitoring for Early Detection
  - Predictive Strategies for Ensuring Operational Robustness
- The Results – Supporting CM & Knowledge Management
- Looking Forward & Acknowledgements

Continuous Manufacturing

"A process in which the input material(s) are **continuously fed and transformed** within the process, and the processed output materials are continuously removed from the system… An integrated process that consists of a series of two or more unit operations."
— FDA Draft Guidance (Feb 2019)

Flexibility to meet changing demand
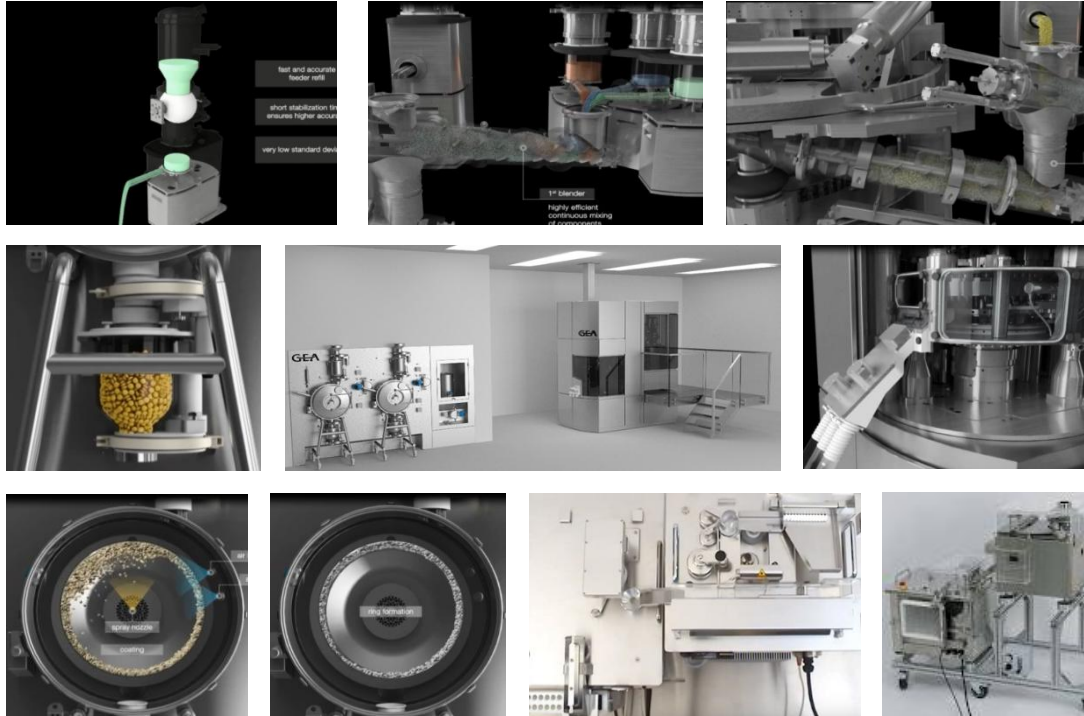
High assurance of product quality

Lower cost, no "scale-up" to commercial

Smaller equipment footprint

Merck's Continuous Manufacturing Process: GEA CDC-50, ConsiGma Coater, Bruker TANDEM

Link to GEA ConsiGma™ DC Video

Equipment & Manufacturing Layout Overview

Raw Material Charging

Docked IBCs

Transfer and Docking

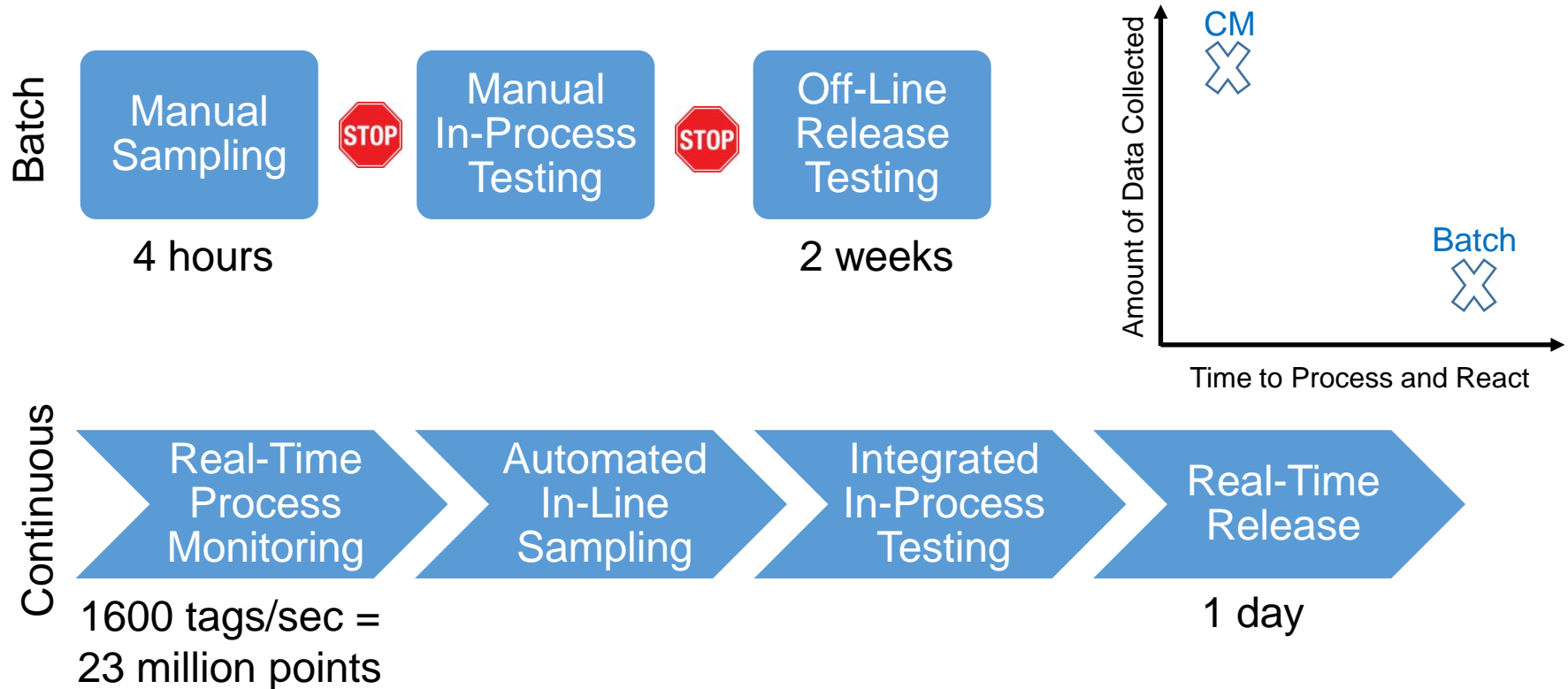**Second Floor**

First Floor

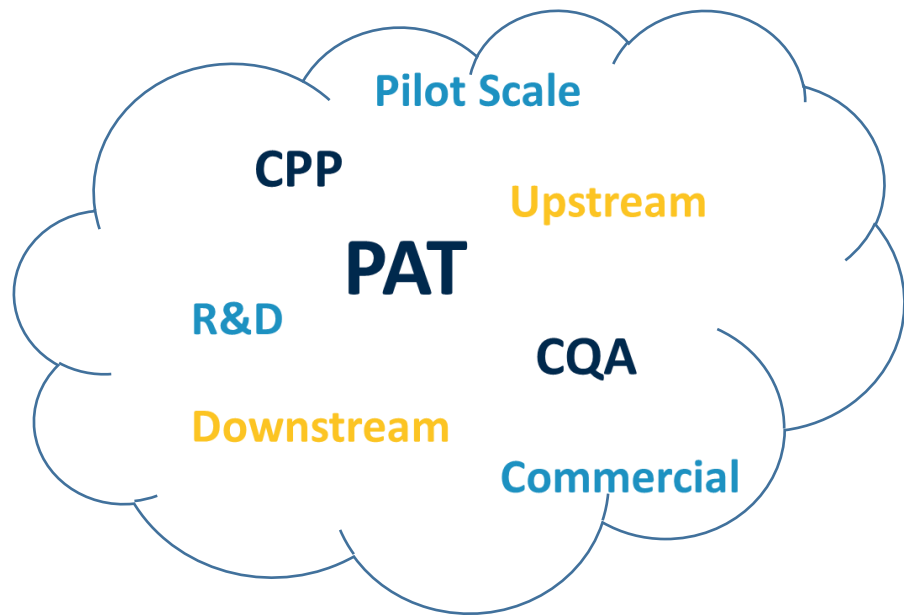CDC-50

Bruker Tandem

Coaters

Distribution Arm

The Challenge
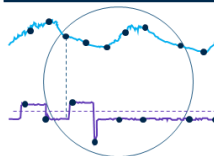
Batch and Continuous Manufacturing

Batch

Manual Sampling	STOP	Manual In-Process Testing	STOP	Off-Line Release Testing

4 hours   2 weeks

Continuous

Real-Time Process Monitoring → Automated In-Line Sampling → Integrated In-Process Testing → Real-Time Release

1600 tags/sec = 23 million points   1 day

CM

Batch

Amount of Data Collected

Time to Process and React

The Process Data Reality

Disparate Data Sets

- Pilot Scale
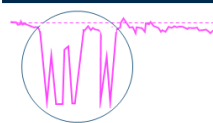- CPP
- Upstream
- PAT
- R&D
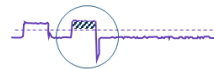- CQA
- Downstream
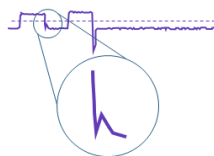- Commercial

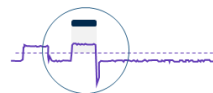**Analytical Challenges**

- Data Alignment
- Noisy Signals
- Calculations
- Trending
- Contextualization

The Solution

The Solution

Connect the Subject Matter Expert to Interactive, Intuitive Applications

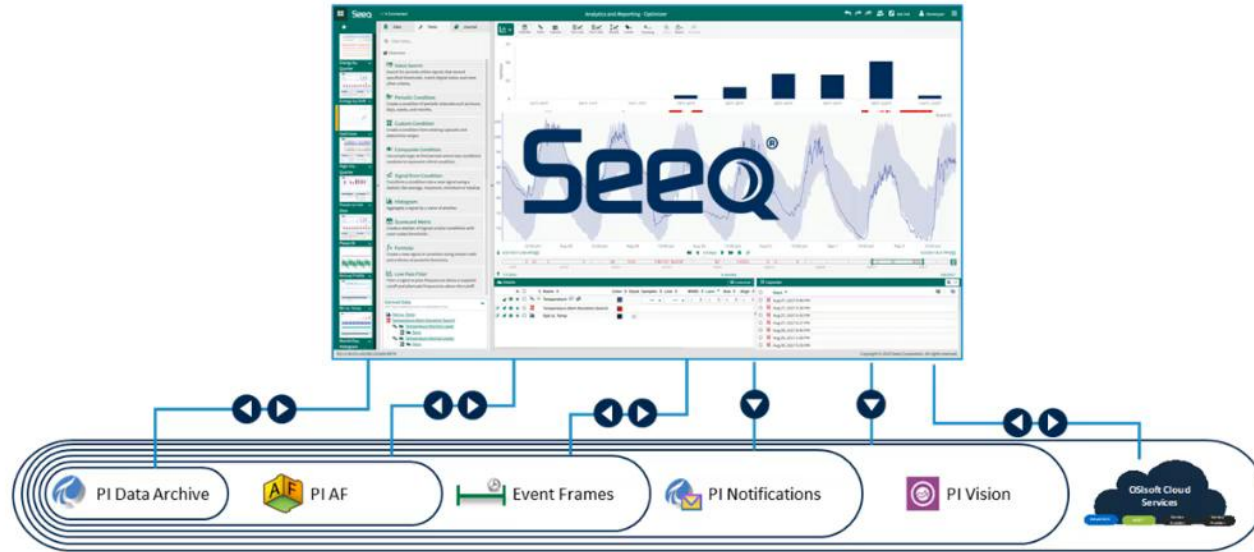## Connect the Team to the Insights

- Enable collaboration
- Highlight key insights
- Document analysis steps
- Update in near real time

Solution Demo

Advanced Analytics Examples

Bristol-Myers Squibb	Abbott Nutrition	devon	Taswater	AVANGRID	ERCOT
UC 2017	**UC 2018**	**ARC 2018**	**UC 2018**	**ARC 2016**	**T&D 2016**

Investigate

CIP Analytics
Determine CIP requirements and then monitor for adherence to plan
Benefit: Increase Uptime

Recover revenue
Find value of curtailments across 6,000 windmills over last year
Benefit: Increase Revenue

Optimize

Truck Haul Planning
Calculate optimized plan for oil pick up across oil pumps and track volume
Benefit: Improve Efficiency

Crystallization stage
Identify time of state transition in batch process to improve yield
Benefit: Increase Yields

Predict

Sewage Overflow
Detect sewage pump issues 12 hours in advance of overflow
Benefit: Prevent Contamination

Price Elasticity in Grid
Create model to define expected power use based on price
Benefit: Improve Resource Planning

Leverage knowledge from other industry verticals to the benefit of pharma

The Solution

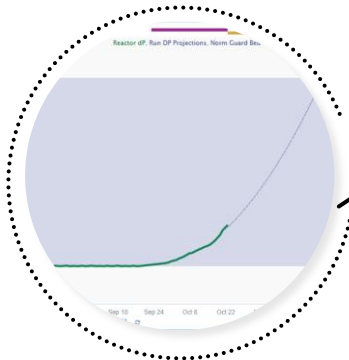## Diagnostic
Why did it happen?

Benefits
Avoid downtime and affiliated losses of through root cause analysis
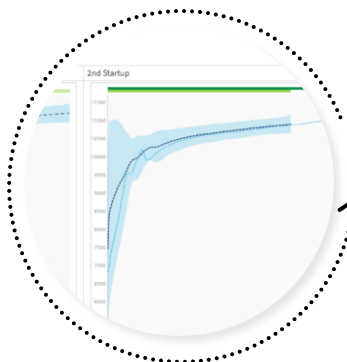
Predictive
What will happen?

Benefits
Increase revenue by maintaining nearly 100% uptime at lower cost

Monitoring
What is happening?

Benefits
Advisory real-time and prediction view of process and asset status

Prescriptive
What should happen?

Benefits
Evaluate options to make decisions that optimize outcomes

Descriptive
What happened?

Benefits
Near real-time distribution of insights share and inform plant-wide decisions

Seeq Architecture

Seeq Workbench

Seeq Organizer
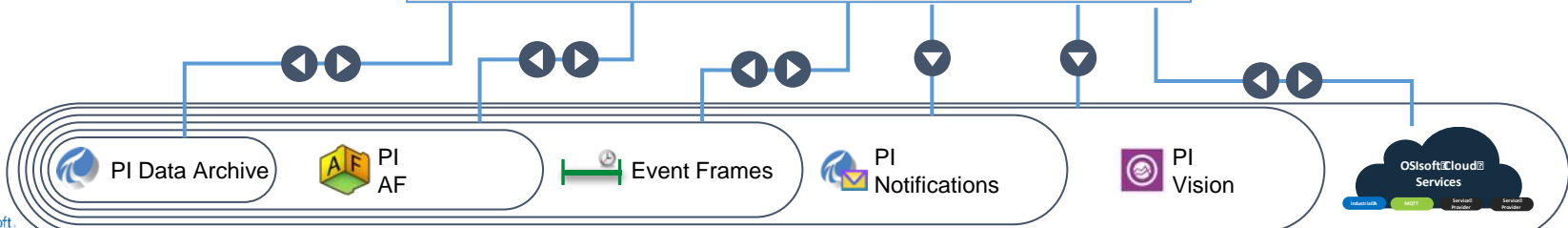

Seeq Server
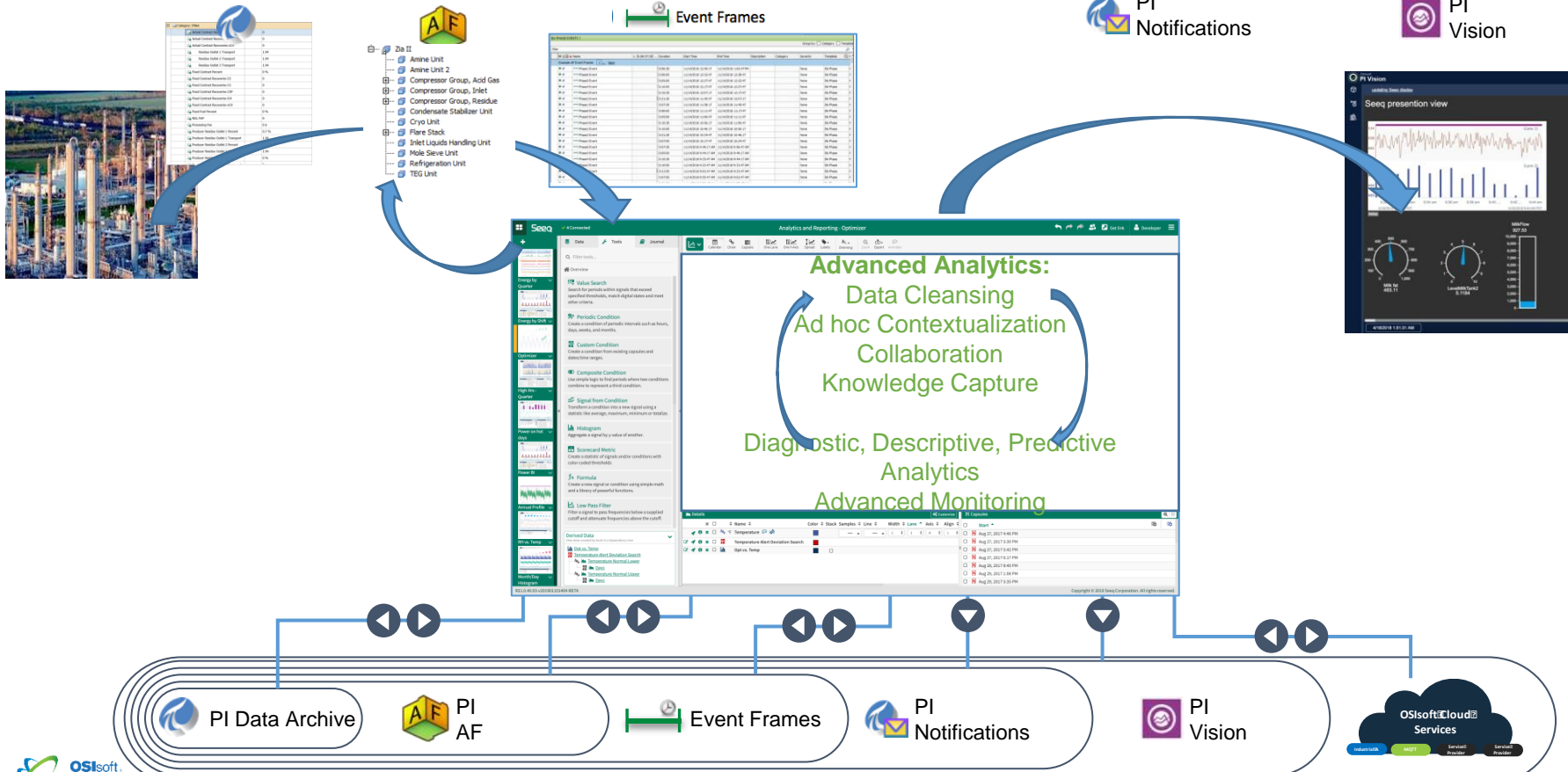
On-Premise or Cloud

SaaS Option on Azure

1 or many sources

Time series AND context

Data not moved/copied

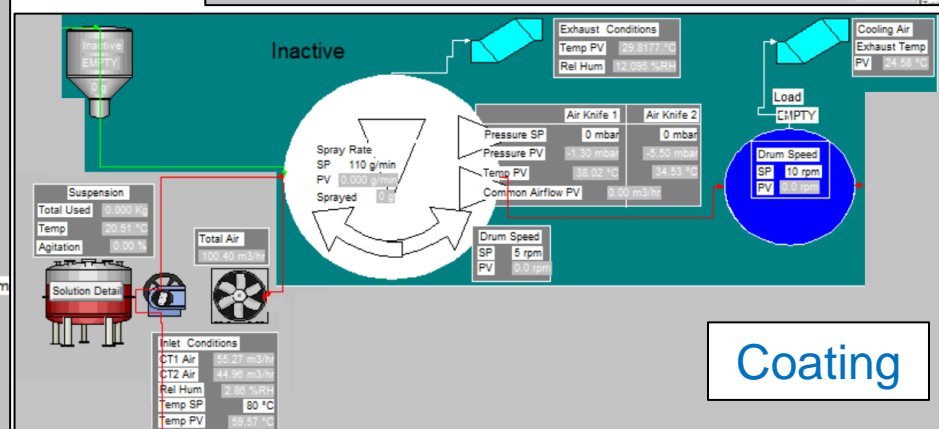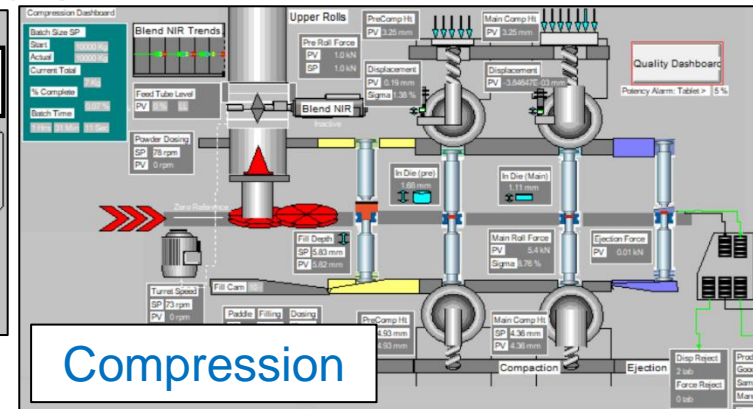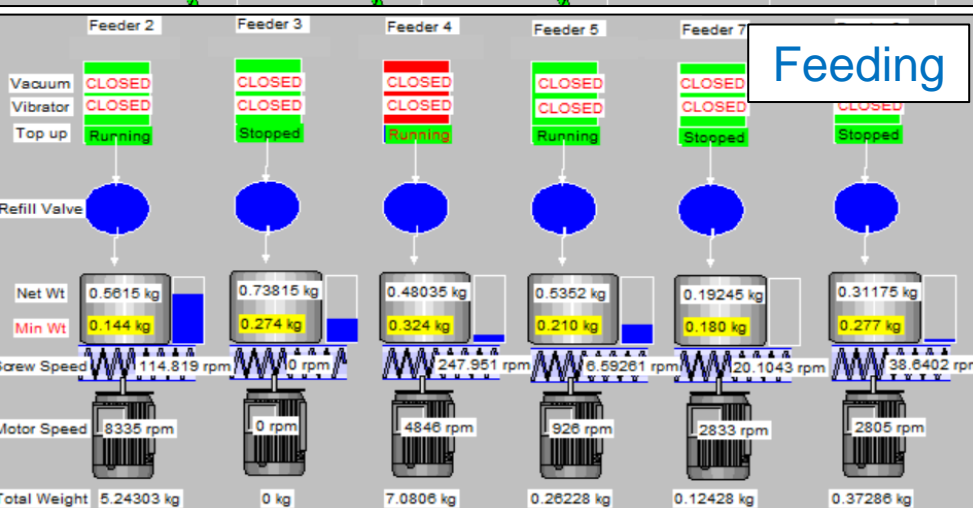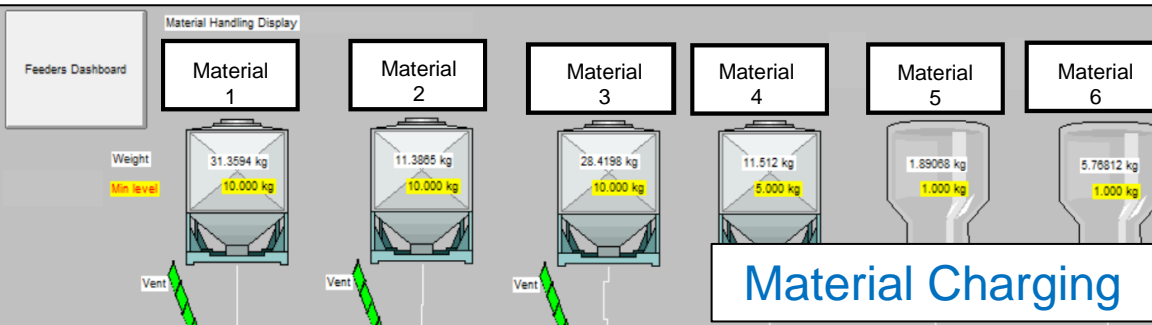# Advanced Analytics for OSIsoft PI System

Advanced Analytics for OSIsoft PI System

PI ProcessBook Dashboards

Material Charging

Compression

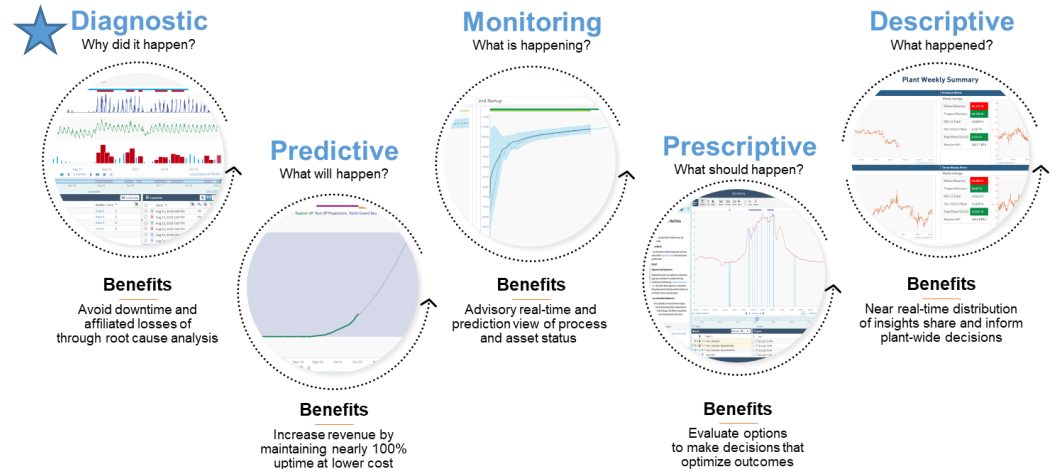Feeding

Coating

OSIsoft.
PI World SAN FRANCISCO 2019

The Results

Diagnostics – Insight into Performance

e.g., Nozzle Fouling

Identifying Opportunities for Avoiding Downtime and Enabling Preventative Maintenance

Diagnostic
Why did it happen?

Monitoring
What is happening?

Descriptive
What happened?

Predictive
What will happen?

Prescriptive
What should happen?

Benefits
Avoid downtime and affiliated losses of through root cause analysis

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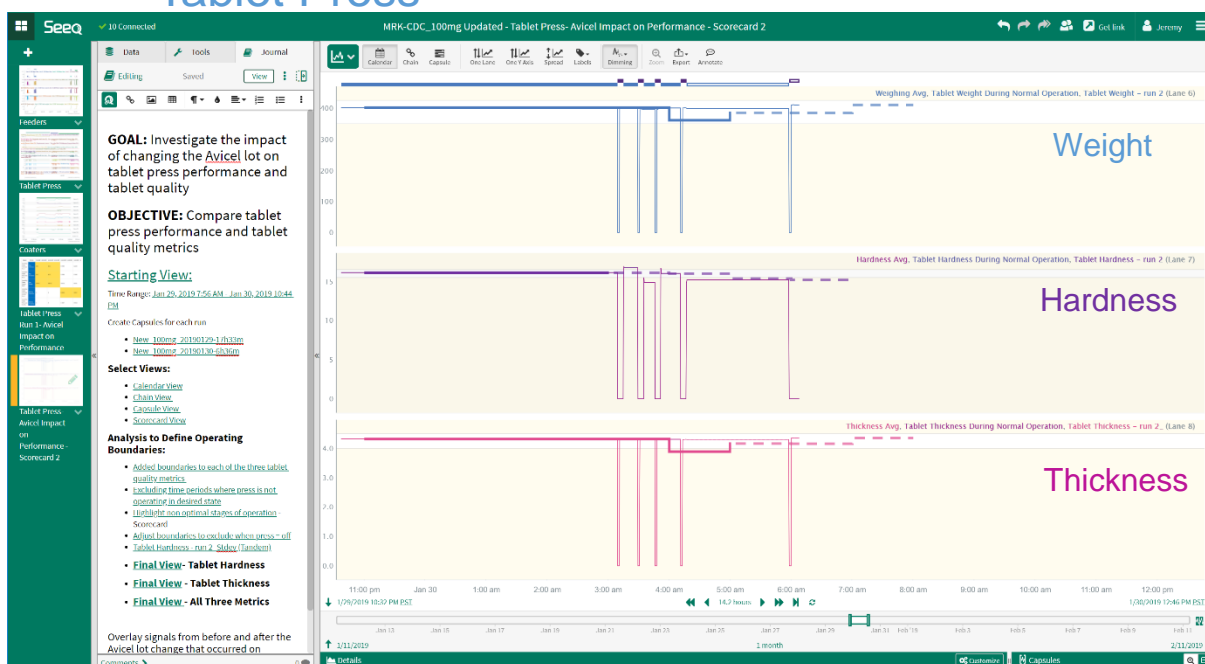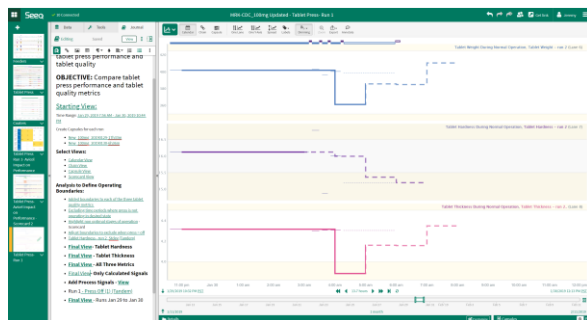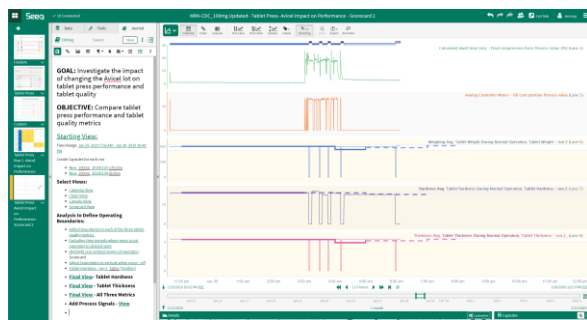
Confirmation of Process Robustness:
Impact of Raw Material Variability on Tablet Press Performance and Tablet Metrics

CDC-50

- Tablet Press
  - Final Compression Force
  - Calculated Dwell Time (ms) – Final Comp. Force
  - Calculate Dwell Time (ms) – Pre-Comp. Displacement
  - Displacement Sensor- Top Roller Compression

- Tablet Metrics
  - Hardness
  - Weight
  - Thickness

Enabling CM Robustness with Seeq and PI:
Selection of Process States and Modeling Within a Single Run

Tablet Press

Correlating Tablet Metrics with Process

Enabling CM Robustness with Seeq and PI:
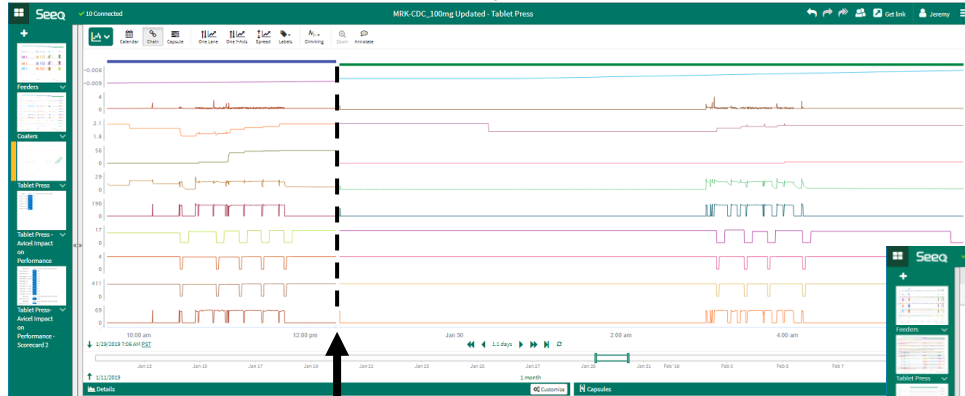## *Connectivity of Sequential Unit Operations*

Confirmation of Process Robustness:
Impact of Raw Material Variability on Tablet Press Performance and Tablet Metrics

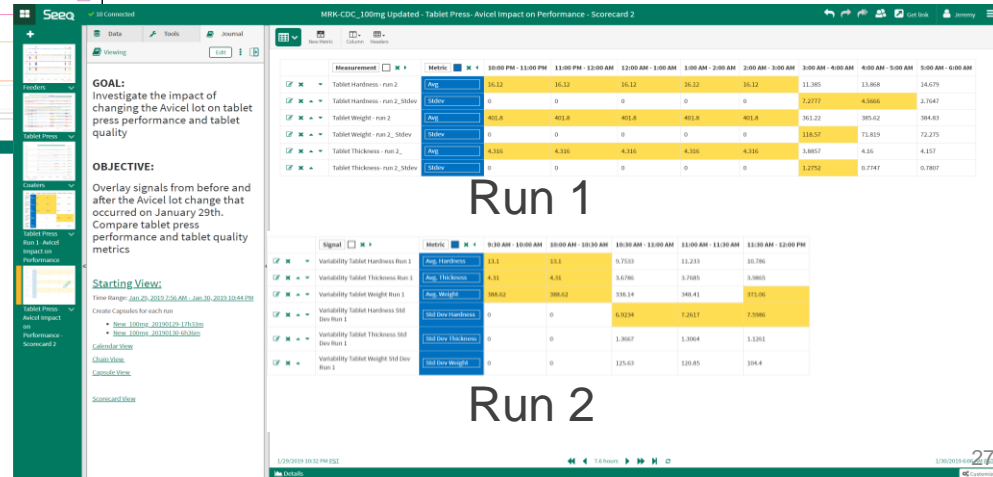Process and Quality Measurements

Run 1   Run 2

Avicel raw
material lot
changed

Tablet Metrics (Tandem):

Leverage Statistics to Compare
Pre- and Post- Outputs
→
Add Boundaries

Run 1

Run 2

Confirmation of Process Robustness:
Impact of Raw Material Variability on Tablet Press Performance and Tablet Metrics
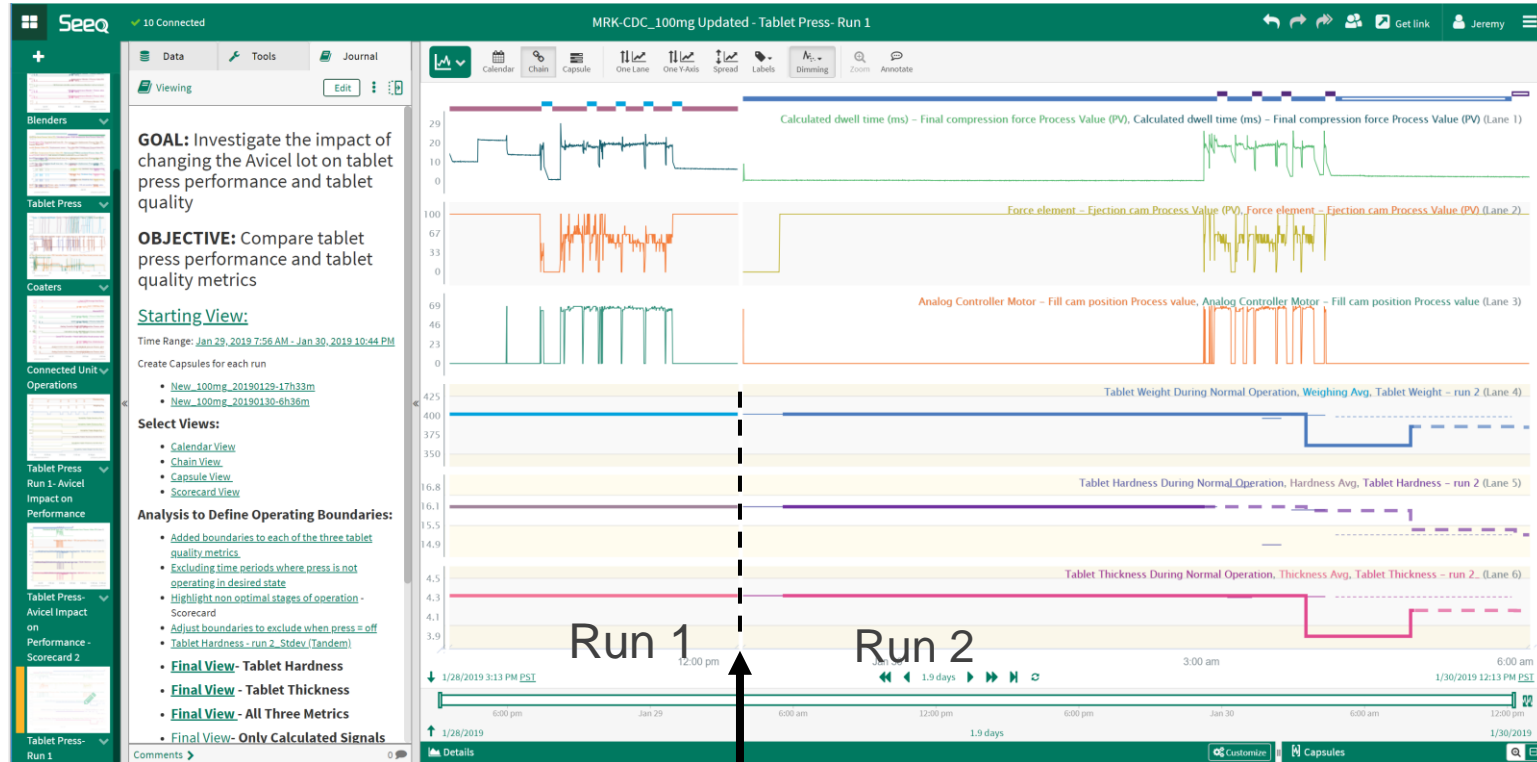
Avicel raw material lot changed;
Tablet quality metrics remain within specs

Knowledge Management

Analytics Process
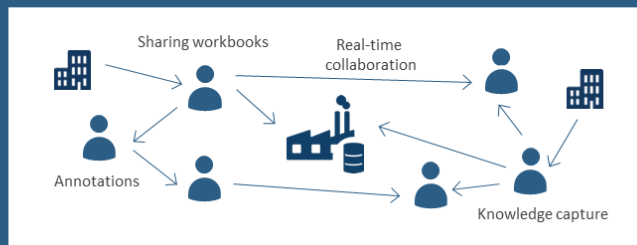
Application Requirements:

- Enable collaboration
- Highlight key insights
- Document analysis steps
- Update in near real time
- Providing lab to pilot to commercial connection of results
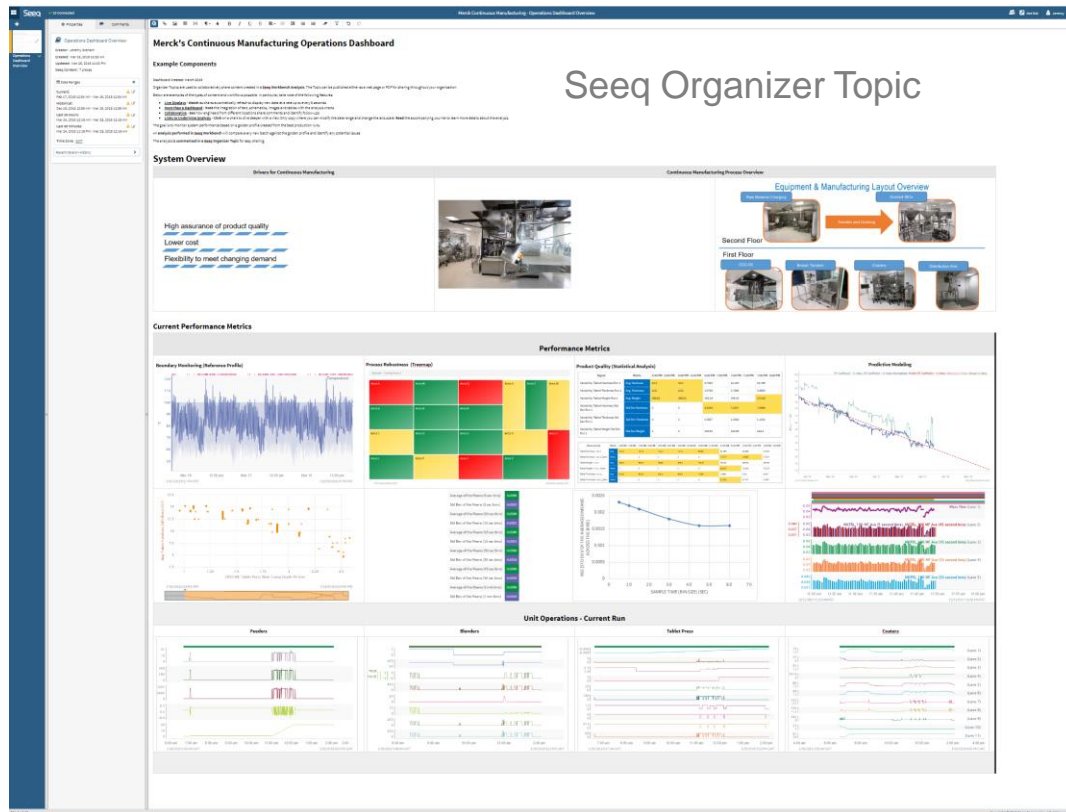
Seeq Organizer Topic

Looking Forward:
Knowledge Management From Lab to Pilot to Commercial
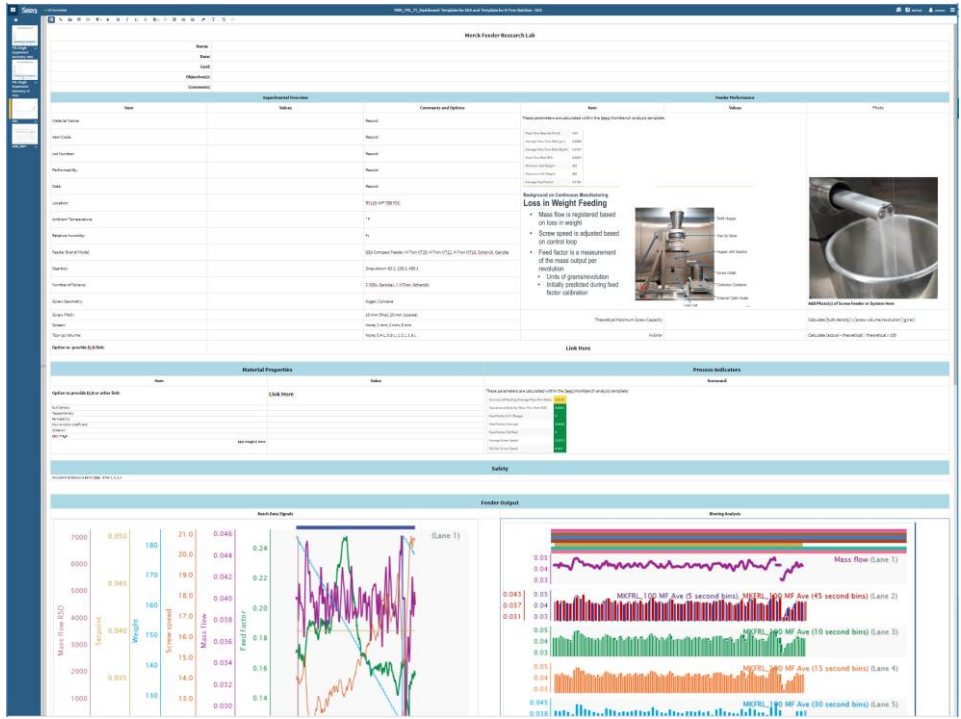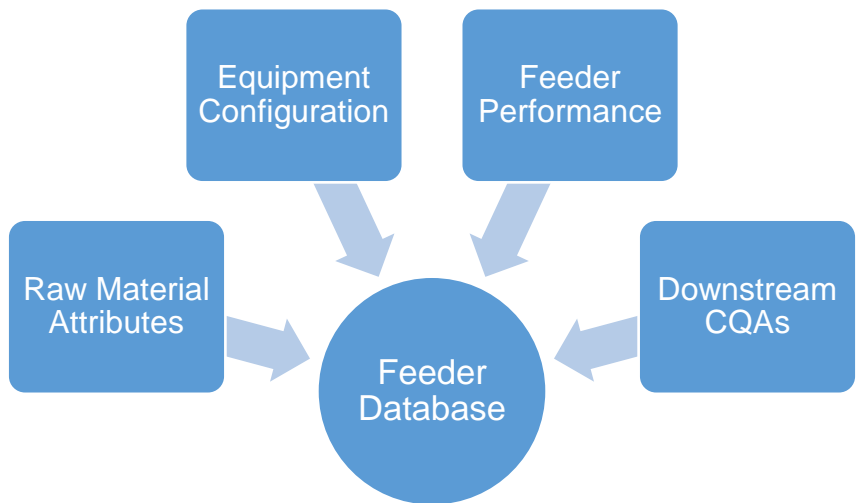
Seeq Organizer Topic: Feeder Research Lab

Future Work

- Unified analysis and knowledge management across sites and functions

- Integrated PAT and automated spectral analysis

- Automated RTD analysis

- Preventative maintenance plans supported by data

- Real-time process monitoring beyond product launch

Summary of Merck's CM Journey

CHALLENGE

Collect, analyze, interpret, and act on 1600 process and analytical tags collected each second

- Representing production areas and QC labs
- Significantly more data, less time, but more opportunity to respond

SOLUTION

Utilize PI DataLink, PI ProcessBook, and Seeq for trends, analysis, visualization, and knowledge management

- Application across development and commercial manufacturing
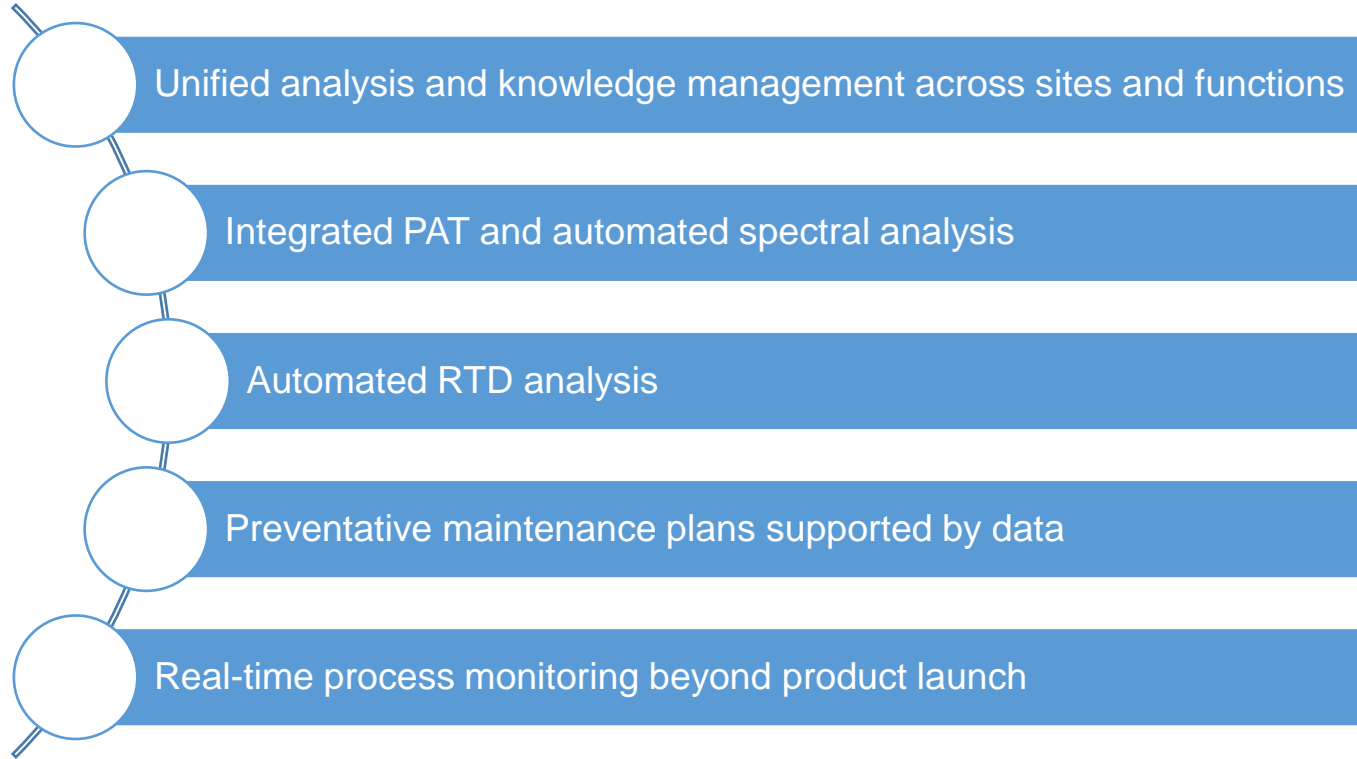- Cross-functional (operations, analytical, PAT, etc.)
- Useful over the product lifetime

RESULTS

Ability to support real-time process monitoring and performance diagnostics

- Complements CM – highly automated and integrated processing
- Long-term knowledge capture strategy supporting continuous improvement
- Provides an agile, flexible foundation for CM to grow

Seeq

Questions?

Please wait for
the **microphone**

State your
name & company

Please remember

TO DOWNLOAD
APP, SEARCH
OSISOFT

OSIsoft
PIWorld

Download on the App Store

GET IT ON Google Play

Additional Follow Up:

- **Seeq** #Y23
- **Alkemy Innovation** #Y17
- **OSIsoft Booths**

Acknowledgements:
- Bob Meyer
- Frank Witulski
- Anthony Tantuccio
- Jeremy Graham
- Many, many others…

謝謝 KEA LEBOHA

DZIĘKUJĘ CI TAPADH LEIBH 고맙습니다

NGIYABONGA БАЯРЛАЛАА MISAOTRA ANAO

TEŞEKKÜR EDERIM GRÀCIES OBRIGADO شكرا

DANKIE TERIMA KASIH DANKON TANK TAPADH LEAT

СПАСИБО MULȚUMESC

KÖSZÖNÖM PAKMET CI3ГE HVALA FAAFETAI

GO RAIBH MAITH AGAT ESKERRIK ASKO

БЛАГОДАРЯ GRACIAS HVALA ХВАЛА ВАМ

ТИ БЛАГОДАРАМ DANK JE ЕΥΧΑΡΙΣΤΩ GRATIAS TIBI TEŞEKKÜR EDERIM

TAK DANKE AČIŪ SALAMAT MAHALO IĀ 'OE TAKK SKAL DU HA ДЗЯКУЙ GRAZIE DI OU MÈSI

RAHMAT MERCI GRAZZI PAKKA PÉR ありがとうございました ĎAKUJEM

HATUR NUHUN PAXMAT CAΓA SIPAS JI WERE TERIMA KASIH MATUR NUWUN

CẢM ƠN BẠN UA TSAUG RAU KOJ

WAZVIITA ТИ БЛАГОДАРАМ

СИПОС

OSIsoft PIWorld THANK YOU

MAHADSANID FALEMINDERIT

Thank You!