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.

<table>
<thead>
<tr>
<th>BUSINESSES</th>
<th>Pharmaceuticals, Vaccines, Animal Health</th>
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<tbody>
<tr>
<td>HEADQUARTERS</td>
<td>Kenilworth, New Jersey</td>
</tr>
<tr>
<td>EMPLOYEES</td>
<td>Approximately 69,000 worldwide</td>
</tr>
<tr>
<td>CORE PRODUCT CATEGORIES</td>
<td>Diabetes, cancer, vaccines, hospital acute care</td>
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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– FDA Draft Guidance (Feb 2019)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

Second Floor
- Raw Material Charging
- Docked IBCs
- Transfer and Docking

First Floor
- CDC-50
- Bruker Tandem
- Coaters
- Distribution Arm
The Challenge
Batch and Continuous Manufacturing

**Batch**

- Manual Sampling: 4 hours
- Manual In-Process Testing
- Off-Line Release Testing: 2 weeks

**Continuous**

- Real-Time Process Monitoring
- Automated In-Line Sampling
- Integrated In-Process Testing
- Real-Time Release: 1 day

- 1600 tags/sec = 23 million points

- CM
  - Batch

Time to Process and React

Amount of Data Collected
The Process Data Reality

Disparate Data Sets

- Pilot Scale
- CPP
- PAT
- R&D
- Upstream
- 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

- Cleanse
- Analyze
- Contextualize
- Compute
- Investigate

Connect the Team to the Insights

- Enable collaboration
- Highlight key insights
- Document analysis steps
- Update in near real time
Solution Demo
## Advanced Analytics Examples

<table>
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<tr>
<th>Investigate</th>
<th>Optimize</th>
<th>Predict</th>
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<tbody>
<tr>
<td><strong>CIP Analytics</strong>&lt;br&gt;Determine CIP requirements and then monitor for adherence to plan&lt;br&gt;<strong>Benefit: Increase Uptime</strong>&lt;br&gt;<strong>Recovery revenue</strong>&lt;br&gt;Find value of curtailments across 6,000 windmills over last year&lt;br&gt;<strong>Benefit: Increase Revenue</strong></td>
<td><strong>Truck Haul Planning</strong>&lt;br&gt;Calculate optimized plan for oil pick up across oil pumps and track volume&lt;br&gt;<strong>Benefit: Improve Efficiency</strong>&lt;br&gt;<strong>Crystallization stage</strong>&lt;br&gt;Identify time of state transition in batch process to improve yield&lt;br&gt;<strong>Benefit: Increase Yields</strong></td>
<td><strong>Sewage Overflow</strong>&lt;br&gt;Detect sewage pump issues 12 hours in advance of overflow&lt;br&gt;<strong>Benefit: Prevent Contamination</strong>&lt;br&gt;<strong>Price Elasticity in Grid</strong>&lt;br&gt;Create model to define expected power use based on price&lt;br&gt;<strong>Benefit: Improve Resource Planning</strong></td>
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Leverage knowledge from other industry verticals to the benefit of pharma
The Solution

**Diagnostic**
Why did it happen?

**Predictive**
What will happen?

**Monitoring**
What is happening?

**Prescriptive**
What should happen?

**Descriptive**
What happened?

**Benefits**
Avoid downtime and affiliated losses of through root cause analysis

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

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

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

Benefits
Evaluate options to make decisions that optimize outcomes
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

Advanced Analytics:
- Data Cleansing
- Ad hoc Contextualization
- Collaboration
- Knowledge Capture

Diagnostic, Descriptive, Predictive Analytics
Advanced Monitoring

PI Data Archive
PI AF
Event Frames
PI Notifications
PI Vision

OSIsoft Cloud Services

PI AF
Event Frames
PI Notifications
PI Vision
The Results
Identifying Opportunities for Avoiding Downtime and Enabling Preventative Maintenance

e.g., Nozzle Fouling
Confirmation of Process Robustness:
Impact of Raw Material Variability on Tablet Press Performance and Tablet Metrics

- **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

Feeders

Blenders

Press

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

Process and Quality Measurements

Tablet Metrics (Tandem):
Leverage Statistics to Compare Pre- and Post- Outputs
→ Add Boundaries

Avicel raw material lot changed
Run 1
Run 2
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

Application Requirements:

• Enable collaboration
• Highlight key insights
• Document analysis steps
• Update in near real time
• Providing lab to pilot to commercial connection of results
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
Questions?

Please wait for the microphone

State your name & company

Please remember

TO DOWNLOAD APP, SEARCH OSIsoft

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Acknowledgements:

- Bob Meyer
- Frank Witulski
- Anthony Tantuccio
- Jeremy Graham
- Many, many others…
Thank You!