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Advantages of Deploying PI for the Collection of Discreet Data from an Automated Bioreactor Sampling System

Presented by Kristin O'Neill

ERCK



Agenda

- About Merck
- Background on Merck and OSIsoft.
- Business Challenges
- Solution
- Results and Benefits
- Conclusion and Future Plans



INVENTING FOR LIFE

A CALLING TO CURE

FOR MORE THAN A CENTURY, MERCK HAS **BEEN INVENTING** TO SOLVE SOME OF THE **GREATEST CHALLENGES** TO PEOPLE'S HEALTH AND WELL-BEING AROUND THE WORLD.

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BUSINESSES

Prescription medicines Vaccines, Biologic therapies, Animal Health products



sales come from outside the United States 2017 R&D EXPENSE

\$9.98 billion; 20+ product pipeline programs in late-stage development



MRK Merck & Co., Inc. is our legal name and is listed on the New York Stock Exchange under the symbol "MRK."



EMPLOYEES approximately 69,000 worldwide (as of 12/31/17)



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, researchintensive biopharmaceutical company and are dedicated to providing leading innovations and solutions for today and the future.

MISSION

To discover, develop and provide innovative products and services that save and improve lives around the world.

WE ARE INSPIRED BY A SHARED VISION AND A MISSION TO SAVE AND IMPROVE LIVES.

MERCK

We believe it is our responsibility to address the health needs of patients and society through transformational science: delivering vaccines, medicines and animal health products that can help millions around the world.

CORE AREAS OF FOCUS

Diabetes Hospital Acute Care Oncology Vaccines

ANIMAL HEALTH

Swine

Companion Animal

Aquaculture Poultry

Equine



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Background - OSIsoft and Merck

- First OSIsoft PI implementation was 1993 (26 years ago)
- PI is at ~ 18 sites around the world
- Manufacturing, Research, and Utilities
- >700,000 tags
- >400 interfaces
- >200 servers
- 24x7x365 availability
- >1000 users

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PI Common Use Cases



Excel Datalink

Web (PI Vision)

Proactive analysis of processes & optimization

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- Process investigations
- Batch reporting

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ProcessBook

- Multivariate data analysis (SBOL)
- Shop floor displays
- Remote alerting

RtReports

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- Environmental monitoring and reporting
- Utilities cost reduction
- Annual product reports



Mobile (PI Vision)



SBOL (multivariate analysis)

Background - OSIsoft and Merck Biologics Process Development

- · Historically used primarily for continuous time series data
 - Bioreactor controllers
 - Clean utilities
 - Chromatography
- Initial implementation for pilot scale and now includes bench scale and mini automated bioreactors
 - Stainless Steel 650L reactors (Delta V control)
 - Xcellerex 500L SUBs
 - Thermo-Finesse 200L SUBs
 - Sartorius Biostat B-DCU 3L reactors
 - Sartorius ambr250
- Biologics PRD server:
- >25,000 tags
- >23 interfaces
- 24x7x365 availability

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Biologics PRD Use Cases and Displays



Excel Datalink

- Remote monitoring •
- Process investigations •



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- Batch comparison
- Multivariate data analysis (SBOL)



PI Vision with AF - Collections orld







ProcessBook

Lab floor displays

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Utilities monitoring



SBOL (multivariate analysis)

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Overview of Manual 3L Reactor Operations



- Bioreactor controllers generate a lot of process data:
 - Temperature
 - DO
 - pH
 - Agitation
 - Air flow
 - O2 flow
 - CO2 flow
 - Etc.
- Already available in PI system
- <u>BUT</u> this is only part of the picture....

Overview of Manual 3L Reactor Operations



1. Sample -clear dead leg -collect sample





2. At-Line Analysis -blood gas -cell count -nutrients/byproducts -osmolality



3. Retain -cell removal -supernatant at 2-8C



4. Feed

-fixed or calculated volume -multiple feed solutions per tank



Overview of Manual 3L Reactor Operations



1. Sample -clear dead leg -collect sample



- 2. At-Line Analysis
- -blood gas -cell count -nutrients/byproducts -osmolality

- Sample analysis and feed data export/import or manually transcribed to notebook
- Manual data aggregation for visualization purposes
- Challenge:
 - Rapid remote monitoring or batch to batch comparison of discreet data <u>combined</u> with reactor control parameters
 - Some sample analysis instrumentation challenging to integrate directly to PI due to limitations in native instrument communication protocols



3. Retain -cell removal -supernatant at 2-8C







Automated Sampling and Feedback Control



Automated Sampling and Feedback Control



- Complex system installed and expanded in multiple phases with hardware and software updates over time
- Weekend coverage to ensure system is operational
- Challenge
 - System health remotely assess if automated system is running as expected, especially after system updates



Business Challenges

• Rapid remote monitoring and batch to batch comparison of full bioreactor process: continuous controller data AND discrete sample and feed data

• Auto-sampler system health: remotely assess if automated system is functioning as expected



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Solution: Autosampler Integration with PI





SegFlow Autosampler Lends Itself to PI Integration

• Flownamics utilized a variety of protocols to integrate the target bundle of devices to the SegFlow

Device	Communication Protocol
Cedex HiRes	TCP/IP
Cedex Bio HT	Serial
Bioprofile Flex	OPC
Fraction collector	Serial
32x Feed pumps	Analog
8x Reactor scales	TCP/IP
16x SegMods (32 fluid sensors)	Analog

- OPC used for an instrument integration provided the FlowWeb server which could be leveraged for PI
- · SegFlow aggregates data by vessel number and can contextualize further with user defined Batch ID
- FlowWeb[™] OPC software can create OPC tags from data tables populated with information collected via all protocols

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Architecture: SegFlow and PI System



Implementation Challenge

- Issue:
- Both Cogent DataHub and PI Interface need to launch FlowWeb
- One launches as local and one as service
- · Didn't play well together
- Solution
 - Critical setting in Component Services forFlowWeb OPC Server Properties
 - For Identity: Set the user account to run application to "Interactive User"

	FlowNetOPCServer Properties	8 23
D 🖀	General Location Security Endpoints	Identity
Þ 🖀	Which user account do you want to use to	orun this application?
Þ 🖀		Critical
Þ 🖀	The interactive user.	Ontiour
D 🖀	The launching user.	Setting
▷ 🖀	0.71	Ŭ
▷ 🎬	This user.	
▷ 🛗	User:	Browse
	Password:	
	Confirm password:	
P 🗃	The sector sector is a set of	1.5
P 🚞	The system account (services only).	
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PI Tools Utilized in Solution

Current:

- PI OPC DA Interface couple with FlowWeb OPC server from auto-sampler to bring discreet data into PI
- PI Data Archive
- PI Vision clear displays to enable remote monitoring and assess system health, including control plus sample data
- PI AF hierarchy enables quick building of displays, also allowed to solve urgent problems first with ability to easily add new functions
- AF Analytics some simple calculations created for averaging vessel scale data, additional calculations planned
- AF Event Frames quick comparison of historical batches

Future:

• Notifications



PI Integration: Remote Monitoring and Fast Data Visualization



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Use Case: Batch to Batch Comparison of Full Process Data Enabled by Event Frames

- Recent system upgrade to autosampler, lower than expected cell count
- Understand if automated cell counts were real or system issue
- Quickly looked at some parameters alongside cell count using Event Frames
 - Temperature and pH from reactor controllers
 - Another sample measurement that should trend with cell count



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Results Obtained and Business Impact

- Discreet data, including feed volumes and sample analysis results, brought into PI system providing a true full process view for bioreactor operations
 - Enabled remote monitoring of control data along with sample/feed data
 - Event frames provided time saving approach to comparison with historical batches
- Visualization built to enable system function check remotely
 - Eliminated the need for weekend trips to the lab!



Conclusions and Future Work

- Information silos created by storing different data types in different repositories required inefficient manual aggregation steps prior to visualization
- SegFlow automated sample system with FlowWeb OPC Server provided an avenue to aggregate data from multiple devices, create OPC tags, and enabled PI integration
- New pre-built displays in PI Vision and the simplicity of ad-hoc displays empowered by PI AF provided time savings on multiple fronts:
 - Quick visualization of current process performance
 - Easy comparison to historical batches with Event Frames
 - Enabling remote monitoring of the system health of the autosampler
- Future work will include:
 - Leveraging AF Analytics for additional calculations
 - Notifications for autosampler system health

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CHALLENGE

Remote monitoring of all aspects of cell culture process

Information silos:

- Bioreactor controller data in PI
- Sample results and feed additions in notebook
- Automated sample and feed system without remote monitoring

SOLUTION

Bring discrete data into PI utilizing an Autosampler which aggregates data and creates OPC tags

- SegFlow withFlowWeb OPC server
- PI OPC DA Interface
- PI Vision
- PI AF

RESULTS

Time saving visualization of discrete bioreactor process data alongside continuous control data without any manual aggregation steps.

- Quick visualization of current process
 performance
- Easy comparison to historical batches with Event Frames
- Eliminating weekend trips to the lab with remote monitoring of the system health of the autosampler

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Questions?

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State your name & company





