Reversing the Paradigm: Being Strategic About Data Management

Presented by Stacy Price, Bruce Sohmer

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√ Reverse the Paradigm

Reverse the Paradigm: Be Strategic About Data Management by Starting In Process Development

- **The work product of Process Development is process knowledge in the form of data - the foundation of the technology transfer to Manufacturing.**
- **Manufacturing data strategies include the implementation of the PI System to monitor data and better regulate & control the process.**

But why wait until Manufacturing has begun?

- **We will outline the value and the rationale for implementing the PI System first in Process Development. Topics will include:**
- **Why implementing in Process Development first is strategic and forward thinking**
- **How to assess what the tipping point is to invest in Process Development**
- **How tech transfer becomes more efficient and effective with the PI System**
- **How PI System data can be strategically used in PD to make faster & more confident data analysis**

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Today Shire is a Fully-Integrated Specialty Pharma Co

- Founded in UK in 1986
- Offices in 30+ countries
- Key sites: US, UK & Switzerland
- Continued international expansion, including Japan, China & Brazil

- ~5,000 employees, including >1K engaged in Research & Development
- Committed to a BRAVE culture and being patient focused

- Now sell products in more than 50 countries
- ~$6 billion in revenues 2014 and a current market capitalization of $46B
- Historical compounded revenue growth of ~15.7% since 2003
- Listed on London Stock Exchange and NASDAQ (SHPG)

Wall Street Journal. (2015). Market capitalization for SHPG as of 11MAR15 from http://quotes.wsj.com/SHPG?mod=DNH_S_cq

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Shire Process Development Organization

Process Development is Focused on Biotherapeutics for rare diseases:

- ~175 scientists/engineers
- ~15 programs in development at any given time
- >3000 pieces of equipment
- Standard unit operations
  - Bioreactors
  - Clarification
  - UFDF (Utra-Filtration, Dia-Filtration)
  - Protein Chromatography
  - Lyophilization
- The Department develops and scales up processes for tech-transfer to Manufacturing

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Reversing the Paradigm

Shire implemented the OSIsoft PI System First in Process Development
(Manufacturing was not first!)

Why is this significant?

1. Process Development is recognized as a key generator of data - a place to invest in infrastructure
2. Data monitored in Manufacturing is only a subset of the data generated in Process Development
3. Efficiency in Process Development translates to efficiency and robustness for technology transfers to Manufacturing
4. Process Development is a controlled environment but not a GxP environment, so implementation can be agile, and test protocols can be readily vetted.

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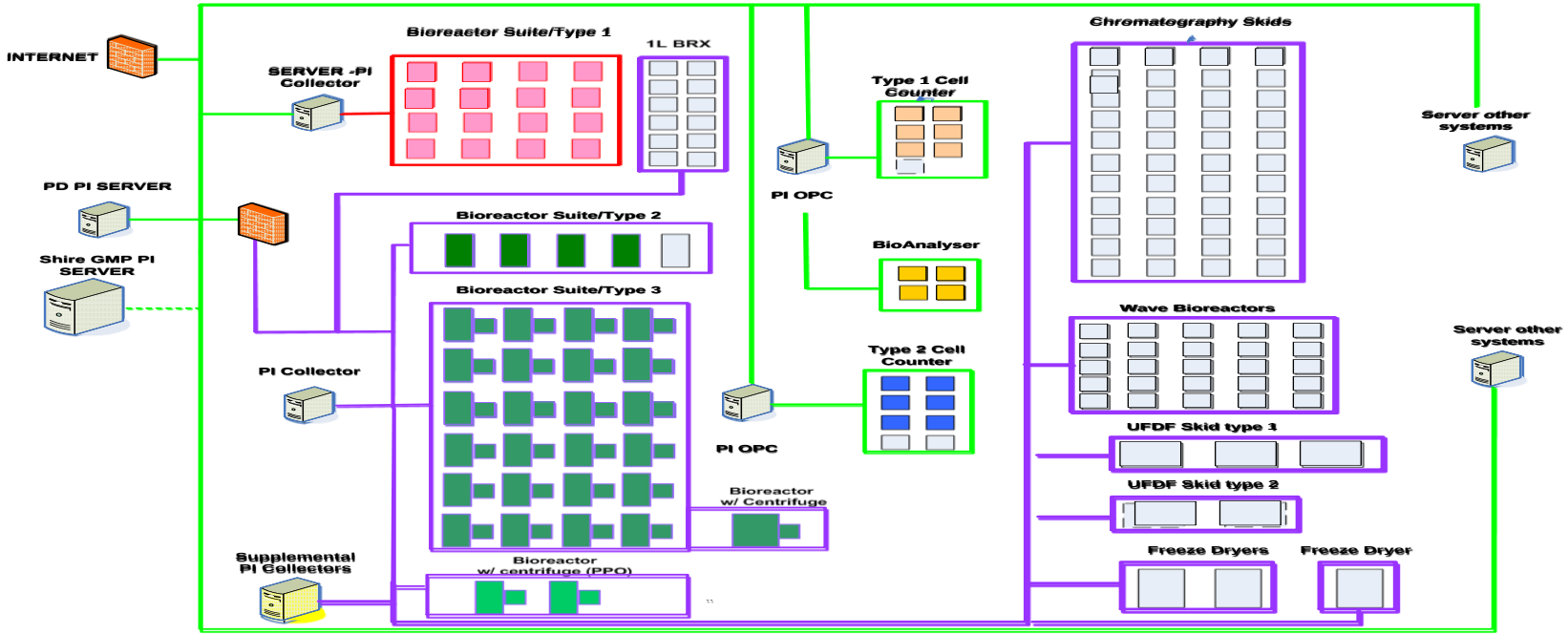
Comparison of PD and Manufacturing Infrastructure

Process Development systems



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Data Management is like the Chemistry of Distillation

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Distilling large volumes

The result of distillation of large volumes
of Malts in vats…Produces these Fine Spirits.

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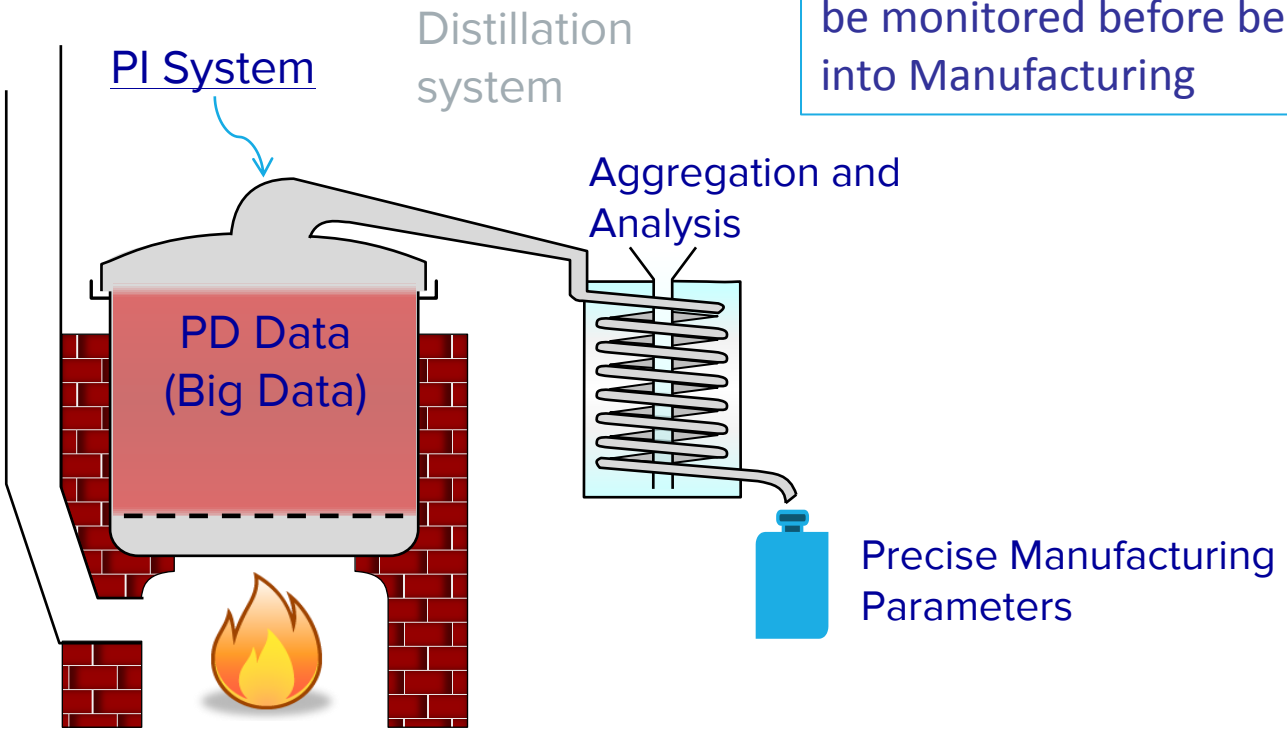
Distilling Big Data

Volumes of data are generated in PD and distilled to the exact parameters to be monitored before being transferred into Manufacturing



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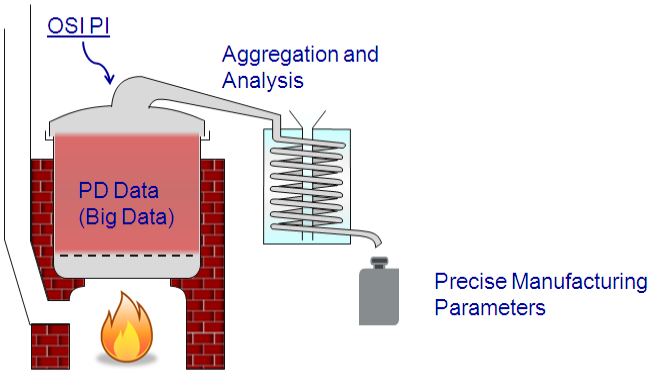
One Platform

PI System Provides the Perfect Platform for:

- Managing Big Data
- Technology Transfer Data Management
- Process Development Efficiency
- Data Integrity



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The PI System Advantage to Technology Transfer

- If you build the templates, definitions and trends in the PI System for a process in PD, these items are ready to go for Manufacturing when its time for Technology Transfer
- Comparison between PD and MFG become simple and fast, enabling real time data analysis

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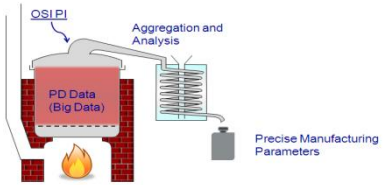
The PI System Advantage to Process Development Efficiencies

- The volume of systems and the number of simultaneous experiments makes Data Management in Process Development challenging



A Panacea:

The PI System provides a platform that enables scientists to maintain their independence for their studies while providing a means to easily aggregate data for analysis (distillation)

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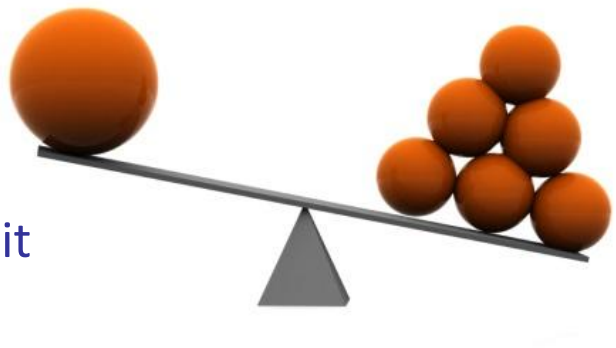
Tipping Point for Implementing PI System in Process Development

Factors to consider:

- Quantity of systems
- Quantity of scientists/engineers
- Data integrity – where is the data stored now? Is it accessible & useful once retrieved?
- How are data driven decisions made now? How much time does it take to aggregate and analyze the data?
- How does the current collective cost compare with implementation of a PI System?



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Case Study: PD Challenges for Cell Culture Bioreactor Labs

- **Integrity**: Data was not always backed up. Finite storage space means data can eventually get overwritten – resolved at Shire with OSIsoft PI System
- **Storage**: Large volumes of data from multiple platforms was not always stored centrally. Downloading & aggregating data from multiple sources for analysis is time consuming – resolved at Shire with OSIsoft PI System
- **Utilization**: Data was not always utilized fully. Decisions made from the analysis of a partial data set (offline data). – resolved at Shire with the PI System
- **Tech Transfer**: Data package for technology transfer and production support was not always as robust as desired – resolved at Shire with OSIsoft PI System

How?…

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Set the Vision & Scope

1. PD Vision for Data Management:
   - To enable PD scientists/engineers to retrieve, compare and contrast any data within 10 minutes of conceiving the idea.

2. PD current state & gaps
   - data integrity concerns, data storage shortage, data accessibility – hours to aggregate data for a simple analysis

3. Prioritization
   - Immediate needs: bioreactor streaming data was in greatest risk of potential loss and was most labor intensive to aggregate
   - Mid Term needs: to have all bioreactor supportive data in one location for batch analysis and batch comparison
   - Long Term needs: to have product development data retrievable from one location for batch analysis and comparison

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Identified the Stakeholders

Project stakeholders are those that have an interest in the outcome of the Implementation. They may be inside or outside an organization and:

- Sponsor the OSIsoft Implementation
- Have an interest or a gain upon a successful Implementation.
- Exert influence over the project's objectives and outcomes.

To mitigate risk on our project and ensure its success, we identified the stakeholders, determined their requirements and expectations, and managed their influence in relation to the requirements.

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Stakeholders

Examples of Shire PD OSIsoft PI System stakeholders:

- **Sponsors/Primary Leadership Supporter**
  - ✓ SVP Process Development
- **Resource/Line Managers**
  - ✓ Lab Managers & department heads in Pilot Plant & Development groups
- **Subject Matter Experts**
  - ✓ Experiment Leads in Pilot Plant & Development groups, System Integrator
- **User Group**
  - ✓ General Lab personnel in Pilot Plan & Development groups
- **Groups impacted by the project as it progresses**
  - ✓ IT, Engineering Technical Support
- **Groups impacted by the project when it is completed**
  - ✓ Manufacturing, Manufacturing Technical Support

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Business Case Showed Value to Secure Funding and Project Approval

- Identified Business Drivers
  - Data integrity – Measure the cost of inaccurate data
  - Data security – Estimate the cost and impact if IP is lost
  - Data accessibility – Calculate cost of resource time (effectiveness, efficiency) when trying to retrieve the correct data
- Linked Business drivers to corporate goals
  - Shire: improve the quality and speed of technology transfers, commercial investigations, and regulatory responses
- Outlined high level plan
- Quantified Savings

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Business Case Study: PI System for Process Development Department

Bioreactor Data Management Project

Date: 9May11 | Owner: | Approval Date: | Manager Approval:

PD-IT TEAM

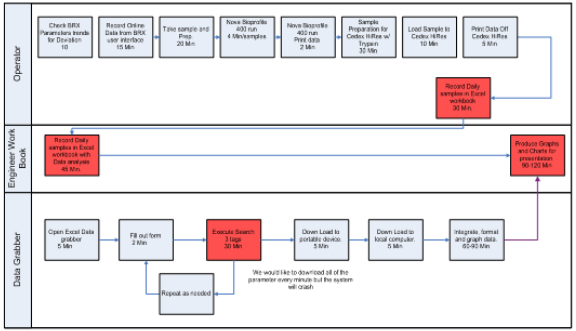
Shire

BACKGROUND

- Large Scale Development Lab (LSDL) and the Bioengineering labs currently have three independent bioreactor systems, running a total of 36 bioreactors of various sizes.
- There are 18 lab scale bioreactors in Bioengineering, 16 lab scale bioreactors in Bioengineering on the control system and 2 pilot scale bioreactors on the control system in LSDL.

CURRENT STATE

Data from the three independent bioreactor systems is not stored in a central location; it is not backed up and can be overwritten due to finite storage space. An increased amount of time and effort is required to access the data since it is not stored centrally and it is necessary to utilize portable storage devices to download data from each bioreactor system and then upload it onto desktop computers. Due to this increased effort online data is rarely analyzed and therefore process decisions are made from the analysis of a partial data set (offline data).



Bioengineering & LSDL are unable to.....	Business Impact: Data Integrity	Decision Making	Resource Time
Perform batch reporting – download tags by batch externally with real time and historical context		X	X
Access bioreactor data/process data remotely	X	X	X
Easily retrieve system data for analysis without significant resource commitment/time	X (transcription)	X	X
Store data globally (it is not backed up) – it is only stored locally	X	X	X
Compare/trend real-time data to historical data electronically – only historical data can be downloaded		X	
Easily access data from Finesse backup files, Sartorius backup is very laborious, therefore, not done	X	X	X
Collate offline data with batch data – it's treated as a separate entity	X	X	X
Gain desktop access for real time and historical data		X	X

ANALYSIS

Bioreactor Sampling (Per Experience of 4 reactors)

	Current state Time (min)	Current state NVA Time (min)	Phase 1 Time (min)	Phase 1 NVAT time (min)	Phase 2 Time (min)	Phase 2 NVAT time (min)	Cumulative Time (min)	Cumulative NVAT time (min)
Bioreactor Daily Data collection	15	15	0		0			
Sampling and sample Prep	30		30		30		30	
Data collection	10	10	10	10	0			
Data Transcription to excel sheet	30	30	0		0			
Data Transcription (Eng)	45	45	45		0			
Charts and Analysis	15		15		15		15	
Cycle time	146	100	100	55	45	0	45	0
Cycle time reduced by :			46	45	55	55	100	100
Cycle time %reduction			31%	55%	55%	100%	69%	100%

Back Up Data per System (Per Month)

	Current state Time (min)	Current state NVA Time (min)	Phase 1 Time (min)	Phase 1 NVAT time (min)	Phase 2 Time (min)	Phase 2 NVAT time (min)	Cumulative Time (min)	Cumulative NVAT time (min)
B.Braun	20	20	0					
Finesse	60	60	0					
Cedex (Machine)	20	20	20	20	0			
Nova	10	10	10	10	0			
Nova Flex (Machine)	20	20	20	20	0			
Cycle time	130	130	60	60	0	0	0	0
Cycle time reduced:			80	80	60	0	130	130
Cycle time %reduction			62%	62%	100%	100%	100%	100%

Tag info collation per run 12 tags

	Current state Time (min)	Current state NVA Time (min)	Phase 1 Time (min)	Phase 1 NVAT time (min)	Phase 2 Time (min)	Phase 2 NVAT time (min)	Cumulative Time (min)	Cumulative NVAT time (min)
B.Braun (20 min * units)	150	150	0					
Finesse (210 min x units)	5880	5880	0					
Cycle time	6030	6030	0	0			6030	6030
Cycle time reduced:			6030	6030			6030	6030
Cycle time %reduction			100%	100%			100%	100%

GOAL (Business Value)

This project will increase decision making integrity for bioreactor process development work by providing:

1. **Data Integrity:**
   - Capture – Collect data from multiple bioreactor sources and sites and associated analytical equipment in a central location
     Result: Reduce Transcription Errors– Eliminate the current data transcription process which includes recording from bioreactor to lab notebook and then lab notebook into excel spreadsheet
   - Backup/Disaster Recovery – To have data backed up on a predefined frequency with a disaster recovery plan in place
     Result: Be able to recover data after adverse events
2. **Data Accessibility:**
   - Centralized Data Storage – To have data from multiple bioreactor sources and sites and associated analytical equipment accessible in a central location
   - Local vs. Remote Access – Accessible for multiple users at multiple locations (e.g. personal workstation, offsite, SharePoint)
     Result: Reduce time and resources required to access the data
3. **Data Usability:**
   - Search – Be able to search data by batch identification
   - Trending – Have data available for real time and historical trending, comparisons, data analysis by searchable batch identification
   - Analysis – Be able to perform batch analysis with continuous data instead of single point analysis as is currently done
     Result: Reduce rework and increase decision quality
4. **Future Expandability:**
   - A requirement for the system is that it be based on a universal platform to enable it to communicate with other Shire systems, other Shire sites, and other enterprise systems for future growth.
     Result: Be able to meet immediate data needs through a capital purchase that will provide a solid foundation for future growth.

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Phased Approach for Execution

- PD Bioreactors provided a solid business case to justify implementation of PI System into the PD data and Data Management Strategy
- Phased approach included just starting with the PD Bioreactors with the plan to expand use of PI System to other PD systems in the future
- The approach was manageable, cost effective, & an efficient use of resources

Visit our Webex presentation to understand our 'Road Map' for this phased approach!

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Created a Project Charter to Facilitate Implementation

- Outlines a Governance structure – who makes the decisions, what is the escalation process
- Outlines project goals and deliverables
- Outline team members, their roles & responsibilities

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Case Study Project Charter: PI System for Process Dev.

Project Charter example…

OSIsoft PI System Data Aggregation Team Charter

Team Purpose	**Governance**
The purpose of this team is to implement the data Aggregation of legacy data from various systems and devices, into the Process Development instance of OSI PI	PD Senior Staff

Role	Team Members	Key Responsibilities
Project Sponsors	Head of PD-Ops : Director IT Director IT	– Provide resources and budget for the project. – Provide strategic guidance and decision making. – Ensure project scope fits in with business objectives. – Endorse plans and action proposals. – Provide guidance and support for conflict resolution. – Reviews and approves the Project Charter, along with other senior managers.
Team Members	**Program Management:**	– Coordinate business resources. – Main contact for project. – Develop and manage schedule. – Report project progress. – Issue agendas and minutes. – Facilitate working sessions and meetings.
	OSI Integration:	– Support schedule development and management. – Support project progress reporting. – Lead OSI Aggregation tasks – Create and execute testing – Main OSI contact for project and support.
	User representation:	– Review schedule development. – Guide integration resources in mapping data. – Support OSI Aggregation tasks – Support and execute testing
	Lab Ops	– Lead business administration for OSI PI. – Manage support resources upon project completion.

Team Objectives	**Expectations**
1. Aggregate data from various systems 2. Define plan to test migration effort 3. Establish and maintain the process for project execution. 4. Ensure accuracy and confidence in migrated data	1. Weekly one hour meetings. 2. Review of test approach 3. Execution of testing 4. Training of Shire Resources

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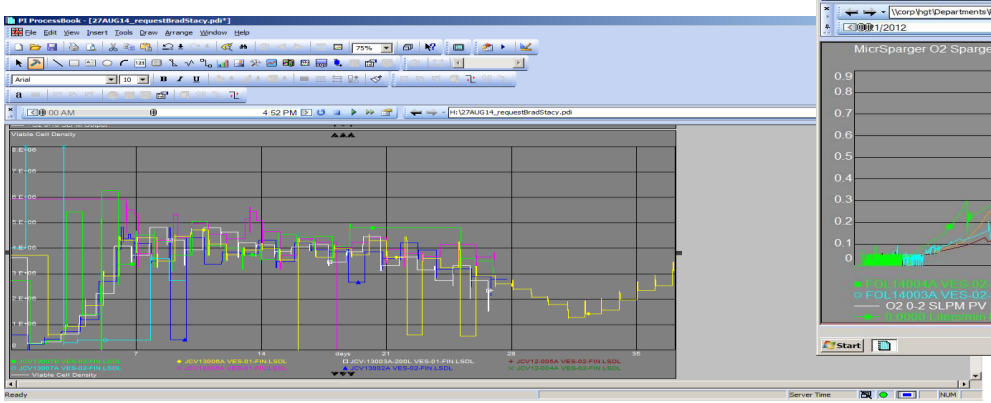
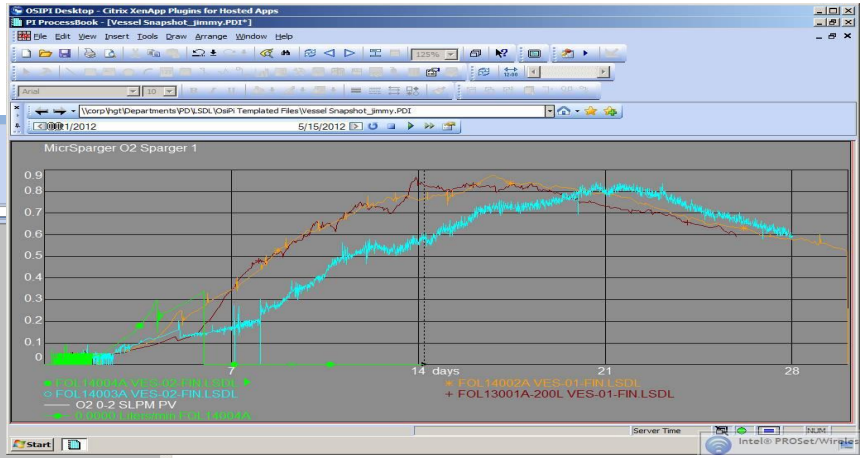
Results of Project Execution: Fast &Confident Data Analysis

- Understanding data makes the difference between success and failure in today's environments.
- You need to visualize your data, you need to be able to understand what it means to you. Shire uses OSIsoft specifically to make analytics easier and to drive faster insights to Processes.





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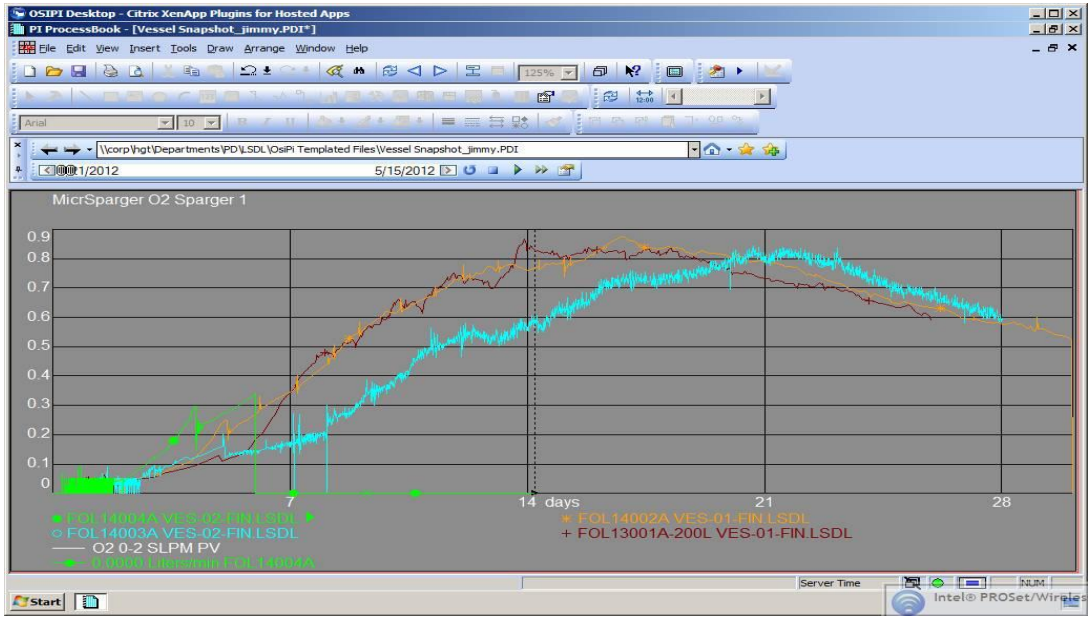
Fast and Confident Data Analysis

- With a few clicks of the mouse, batch comparison & troubleshooting is possible.
- In this example, the scientist was able to quickly draw conclusions about whether oxygen usage lag was a result of the bioreactor inoculation density



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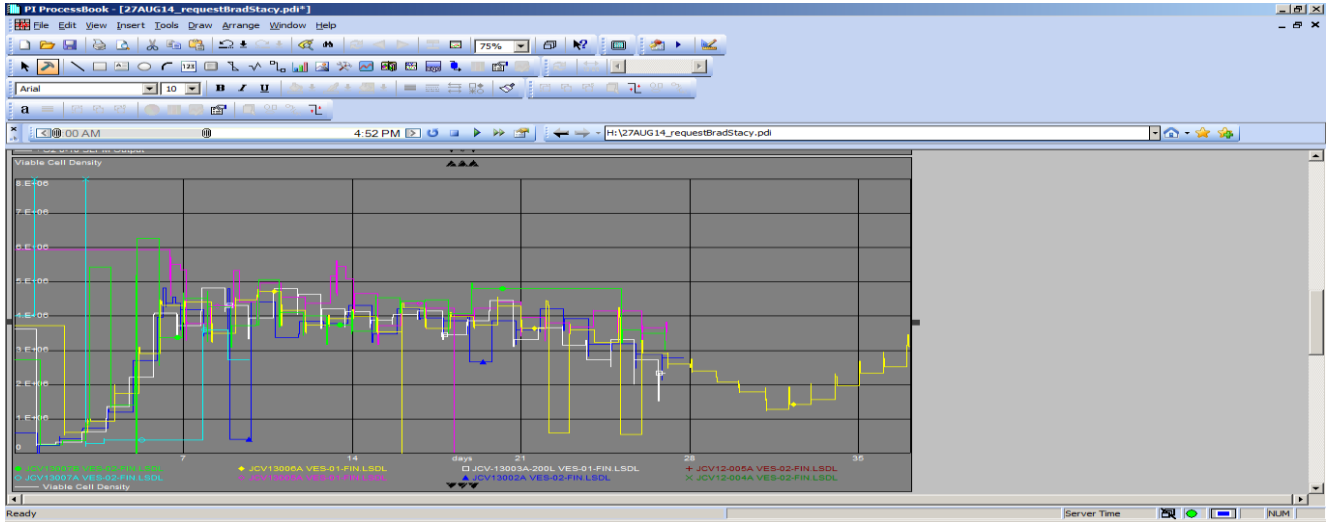
Fast and Confident Data Analysis

- Scientists spend their time analyzing data instead of aggregating data manually. They log into the system to assess how the current run compares with historical experience. (No transcription or copy/paste necessary)



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Benefit of Integrating Discrete and Streaming Data into the PI System

Streaming bioreactor data from the control systems:

- Dissolved Oxygen
- On line pH
- Temperature

Coupled with discrete offline data

- Cell count
- Metabolites
- Off line pH

Tell the complete ‘Story’ of the bioreactor performance first in Process Development, later as comparison in MFG.

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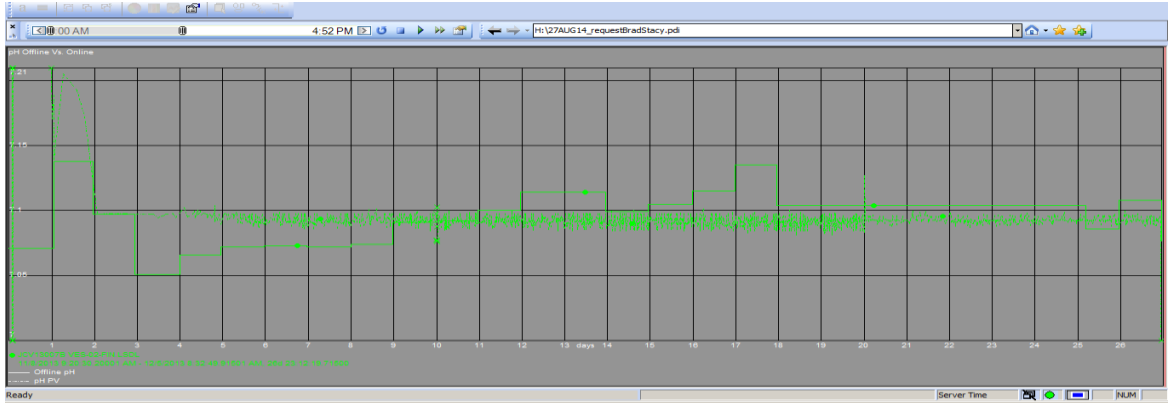
Benefit of Integrating Discrete Data with Streaming Data in the PI System

- Scientists are able to look at the whole picture of the bioreactor performance by comparing streaming and discrete data on the same graph without spending time aggregating it manually.
- This graphs shows a comparison of the online pH data (streaming) with the offline pH data (discrete).



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Summary - Value of the PI System in Process Development

- Data Integrity: Data is expensive - keep it reliable
- Data Accessibility: The data is automatically there, when you need it.
  No expensive transcription time or copy/paste effort required
- Provide scientists time to focus on the science - for more comprehensive data analysis
- Timely decisions based on complete data set

And importantly:

- Robust Technology Transfer Package
- Pre-configured data in Process Development yields templates for the distilled data to be transferred to Manufacturing

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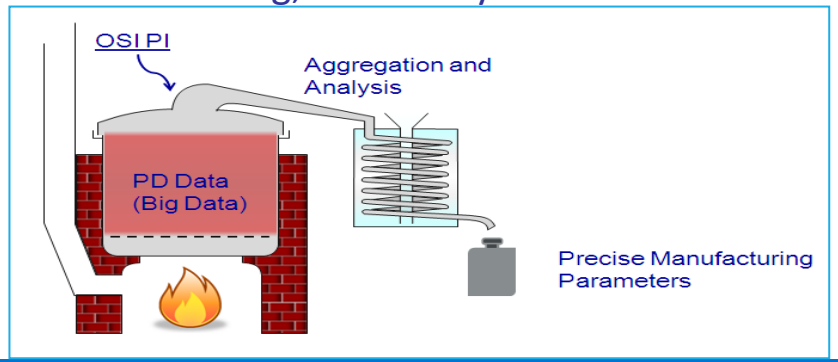
Summary - Value of Implementing the PI System in Process Development

Reverse the Paradigm! BIG Data starts in Process Development

(Manufacturing monitors only a subset of the data generated in PD)

- Data is valuable: Leverage development work by utilizing the PI System.
- With the PI System Your Technology Transfer to Manufacturing will be more robust and seamless
- Use the PI System to distill your Process Development data in order to get your Precise Manufacturing Parameters
- Phase your implementation to ensure quick wins and funding; establish your foundation



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Questions

Please wait for the microphone
before asking your questions

State your
name & company

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THANK YOU

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