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A Knowledge Management Model for Pharmaceutical Development

Presented by

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Agenda

- Knowledge Management Vision
- The Diverse Data Sources in R&D
- Infrastructure & Architecture
- Project Considerations
- Visualization Showcase
 - Batch Context (Event Frames)
 - PI Coresight
 - Notifications
- Q&A

R&D Program Vision

- Ensure a single-source-of-truth for all master data in PD
- Guarantee access to accurate, verified data
- Enable any scientist to analyze an experiment in under **10 minutes**
- Consolidate tribal knowledge and redundant spreadsheets in favor of scalable enterprise solutions
- Shift the paradigm from single data points to **streaming-data visualization**



Assimilation of Data into Knowledge



323 sources of information were identified across R&D



- 34% of the sources are applications
 20% of the sources
- 29% of the sources are shared storage
- 24% of the sources are Instruments, paper or other
- 13% of the information sources are external

The size of the bubble indicates the complexity of information within that source; not the volume of data

Infrastructure

Defining the foundation to enable the vision

Informatics ArchitectureRole of Virtualization



Informatics Architecture (Major Systems)



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The Role of Virtualization: Infrastructure Consolidation

- Virtual cluster based on 3 High Availability physical servers and a Storage Area Network managed as one asset via vmware ESXi
- Consolidated 6 Physical Servers & 5 stand alone systems



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9

Project Considerations

Building the foundation via Incremental improvements

System Expansion
 Flexible Integration Approaches
 Project Justification



PI Expansion Projects 2015-2017

Current System Scope

- (47) Chrome Skids
- (36) 10L Bioreactors
- (12) 5L Bioreactors
- (2) 250L Bioreactors
- (8) Bio-analyzers





Equipment Completion

Class	Iteration	Units	Comp	%Comp	% Start	%EV
AKTA	Class A Pri/A	47	0	0%	100%	51%
Analyzer	Class B	6	0	0%	67%	3%
Autoclave	Class B	3	0	0%	0%	0%
Cedex	Class A Pri	5	0	0%	100%	85%
Clarification Skid	Class B	2	0	0%	100%	5%
DeltaV	Class A Pri	3	3	100%	0%	100%
LYO	Class B	3	0	0%	100%	5%
Nova Flex	Class A Pri	5	0	0%	100%	85%
Sartorius Qplus	Class B	1	0	0%	100%	1%
UF Skid	Class B	3	0	0%	0%	0%
Washer	Class B	2	0	0%	0%	0%
Class	Iteration	Units	Comp	%Comp	% Start	%EV
All Classes	All	80	3	0%	84%	44.2%

Diverse Equipment-Flexible Integration Approaches





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Justifying an Expansion Project

PI SYSTEM EXPANSION ROI Assessment

Assumptions	
Annual FTE Cost	X \$ / Yr
Hours/Yr	2000
Working Days/Yr	255
FTE Cost/Hr	X \$/Hr
Consultant Cost/Hr	X \$/Hr
Discount Rate	8.5%

Savings Cash Flows

1. NEW SYSTEMS INTEGRATION

1.1 Justification	Reduction of manual data entry for wave BRX & UFDF (37 Units)							
	Data transcription (min/1 wk wave	Data verification (min/1 wk wave		Total Time savings				
Data collection (min/1 wk wave expt)	expt)	expt)	Total waves & UFDF units	(Hr/wk)	Total Savings/yr			
5	5	5	37	9.25	X \$/yr			

2. DATA INTEGRITY IMPROVEMENT

If data integrity is breached (data filed is not valid), could result in loss of Shire reputation, delay of filing, FDA 483 or additional post marketing commitments (PMC). Previous experience incurred 30 man months of work to verify all PD data in one product filing during internal audit. We assume this improvement will eliminate one data integrity issue per 2 year period.

Total FTE Audit Support (Hr)	Total Consult Audit Support (Hr)	FTE Cost		Consultant Cost		Total Savings/ 2yr
2400	2400	\$	100,000	\$	300,000	X \$/yr

ROI Calculation (5 Year)

2.1 Justification

CashFlow Series	Year 0		Year 1		Year 2		Year 3	Year 4
Costs	\$	(500,000)	\$	-	\$	-	\$ -	\$ -
Savings	\$	10,221	\$	20,443	\$	410,443	\$ 20,443	\$ 410,443
Net	\$	(489,779)	\$	20,443	\$	410,443	\$ 20,443	\$ 410,443

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IRR								21.	.9%

Visualization Showcase

Brad Ebel – Pilot Plant Operations

Transforming data into accessible process knowledge

Batch Context (Event Frames)
 PI Coresight
 Notifications



Value of Process Visualization

Batch Context

- Define your process
 - Structure
 - Hierarchy
 - Relevance
- Event definition
- Enable batch-tobatch comparisons
 - Reduce Process variability



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Asset Framework Event Frames

PI Coresight

- Visually appealing
- Mobile devices
 - Anywhere, Anytime
- Ease of access
 - Enterprise-wide
- User-friendly
 - Intuitive, click-anddrag interface



PI Notifications

- R&D not staffed 24x7
- Remote monitoring
- Event escalation
- Excursion analysis
- Peace of mind

Batch Context Strategies



1) 2008 - No Batch Context

- Difficult to correlate streaming data with stages of a batch
- No batch-to-batch comparisons
- Paper batch records

2) 2012 - Manual Model: Operators manually input stages of a batch

- Simplicity, lower up front costs
- Flexibility

3) 2015 - Inferred Model: Based on manual Set Point changes

- Can now make batch-to-batch comparisons
- Golden Trends
- Remains operator dependent

4) 2016 - S88 Model: Recipe sequentially coordinates batch

- Batch context defined by design
- Reduced human error ↔ Reduced Flexibility
- Automation Investment ↔ Operator Labor
- EBR

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2015: Batch Context in Pilot Plant Operations

Manual Entry of Operations



- 1. Operator enters "Batch ID" tag
- 2. Operator enters "Operation" Tag
- 3. Operator selects "Batch Start"



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Current state depends on operators rigorously selecting "Batch Start"

- This directly effects data from being correctly overlapped
- Example Below: operator likely selected "batch start" for two runs **one day** late on the Red and Orange runs



2016 Batch Context: Inferred via PI System Triggers

Run Start	Batch Triggers							
Run Start		Trigger 1		Trigger 2		Trigger 3	Trigger 4	
+	Active	Batch ID con	tains HCV	TIC-VSL_SP = 36		SIC-AGIT_SP = 80	FIC-1_SP = 2.5	
Add Media	Sub-Batch Trig	gers (Ope	erations)					
	Т	rigger 1		Trigger 2		Trigger 3	Trigger 4	
Inoculate	Media Addition ^B	atchID contains H0	CV	TIC-VSL_SP = 36		SIC-AGIT_SP = 80	FIC-1_SP=2.5	
+	Inoculation ^B	ase Pump Mode T	arget=Cascade	CO2 Air Flow Mode Target=Cascade		pH Mode Target=Auto		
Growth	Growth F	FIC-5_SP=0.5 OR 1 OR 1.5		AIC-PH_SP = 7.2 OR 7.1 OR 7.0				
	Transition F	IC-5_SP=2		AIC-PH_SP = 6.9				
Production	Production ^T	ransition +48h						
+			Trigger 1		Trigg	jer 2	Trigger 3	
Run Complete	Inactive		SIC-AGIT_SP =	= 0 FIC-1_		_SP = 0	FIC-5_SP = 0	

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PI Coresight Showcase Landing Page

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PI Coresight				<table-cell-rows> New Display 🛛 🚺 ?</table-cell-rows>
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	MFC 02 Flow 2 SHIRE-PD-DV/SHIRE_PD_PI	MFC 02 Flow 1 SHIRE-PD-DV\SHIRE_PD_PI	MFC Air Flow 3 SHIRE-PD-DV\SHIRE_PD_PI	MFC Air Flow 2 SHIRE-PD-DV\SHIRE_PD_PI

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20

Bioreactor Information Screen



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PI Coresight Advanced Trend with Operating Limits (Control Chart)





22

PI Coresight on iPhone 5S

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Any tag in the PI System can be accessed remotely instantly with a simple search.

Two Types:

1.) Single Tag

i.e. Harvest Rate, Pump RPM, Cent RPM.

2.) Operation Group Tag

i.e. PV, High and Low limit, SP, and Output all displayed on same screen.

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Alarm Strategy

- R&D is <u>not</u> staffed 24X7!
- Began with Plant Messenger in 2008
 - Product reached End-Of-Life
 - Migrated to Notifications 2012
- Implemented an escalation framework

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- Alarm notifications are sent immediately to the first contact on the list
- Notifications sent sequentially to escalation team until alarm acknowledgement

Advantages

- Alerts can go to a single recipient, a group of contacts or an escalation team
- Every notification and alarm event is chronicled



24

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- Stacy Price, Shire
- Bruce Sohmer, Shire
- Chloe Laffan, TQS
- Chris Beaupre, New England Controls
- Greg Fisher, ICQ

Shire Enabling people with life threatening conditions to lead better lives.

Questions

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谢谢 감사합니다 Danke Gracias Merci **Thank You** ありがとう Спасибо Obrigado

"In Pharmaceutical Development, knowledge not only defines our product - it is our product."

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