Towards a Recipe Driven Organization

Presented by **Terry Murphy, Strategic Operations**
Pharmaceutical Development & Manufacturing Sciences

janssen
PHARMACEUTICAL COMPANIES
OF Johnson&Johnson

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Overview

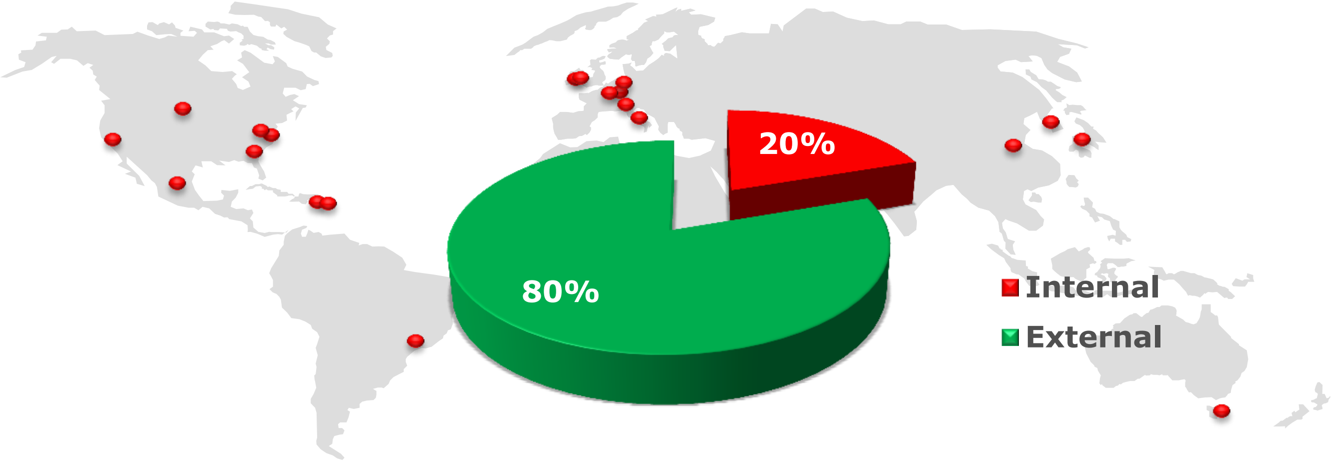
- Introduction to Janssen and our challenges
- Defining the recipe based knowledge management strategy
- How the OSIsoft PI System enables that strategy
- Closing remarks

Janssen

Johnson & Johnson

Janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

- Cardiovascular & Metabolism
- Immunology
- Infectious Diseases & Vaccines
- Neuroscience
- Oncology



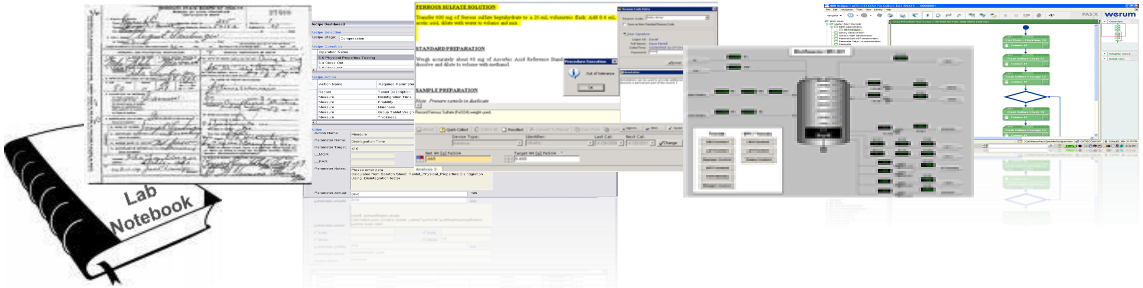
Current State

REACTIVE ANALYSIS

- More time spent on aggregation than analysis
- Lack of knowledge management strategy

- Mix of paper/electronic
- Unstructured data
- Few standards
- Little built-in context
- Efforts mainly focused internally

Lab/Clinical/Commercial



Future State

PROACTIVE ANALYSIS

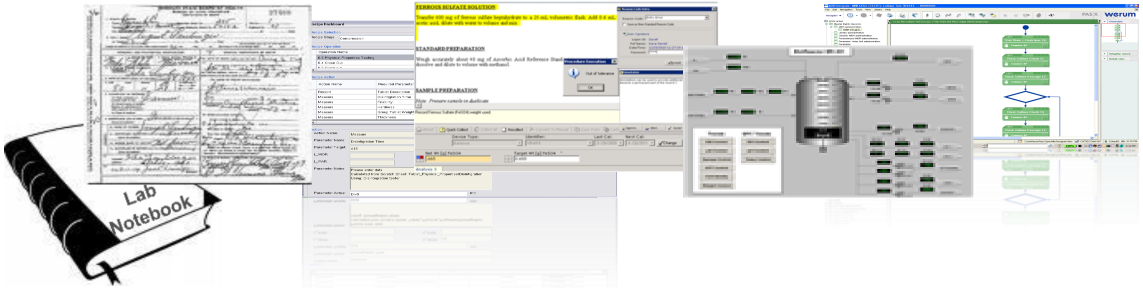
- Automated data aggregation
- More time spent on analysis than aggregation
- Common knowledge management strategy

- Electronic data capture
- Structured data
- Common standards
- Internal/external focus

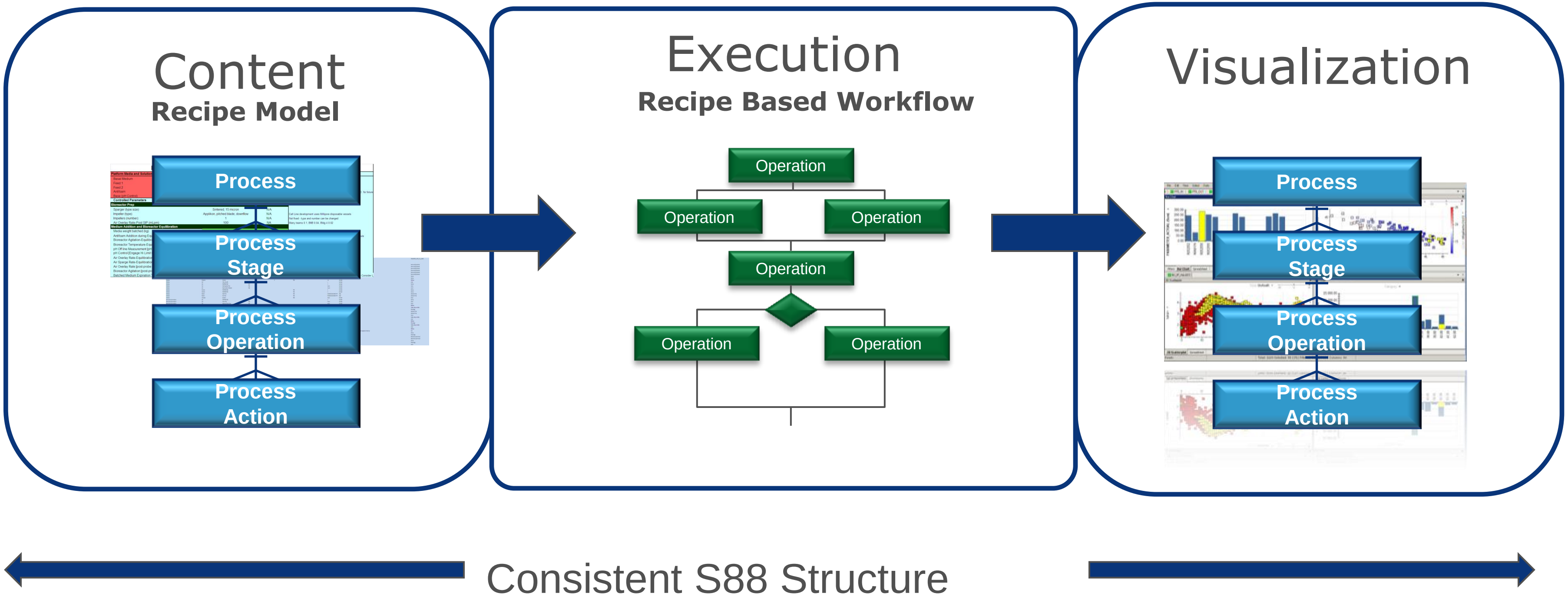
Pressure (bar)
STEP_MATERIAL_INSTANCE
Batch day
Average_Day

Recipe Based Knowledge Management

Lab/Clinical/Commercial


Lab Notebook
FERROUS SULFATE SOLUTION
STANDARD PREPARATION
SAMPLE PREPARATION

S88 Recipe Based Knowledge Management Strategy



Content

Recipe Model

Process
Process Stage
Process Operation
Process Action

Execution

Recipe Based Workflow

Operation
Operation
Operation
Operation
Operation
Operation

Visualization

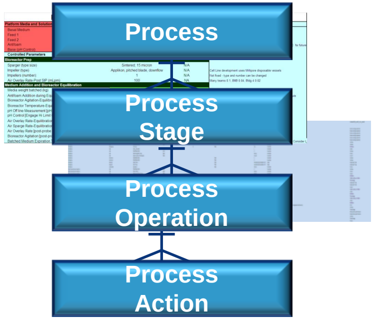
Process
Process Stage
Process Operation
Process Action

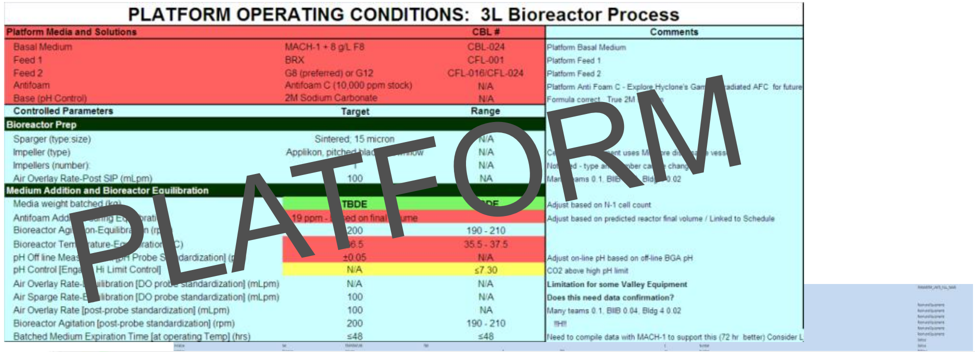
Consistent S88 Structure

S88 Recipe KM Strategy: Content

Content

Recipe Model

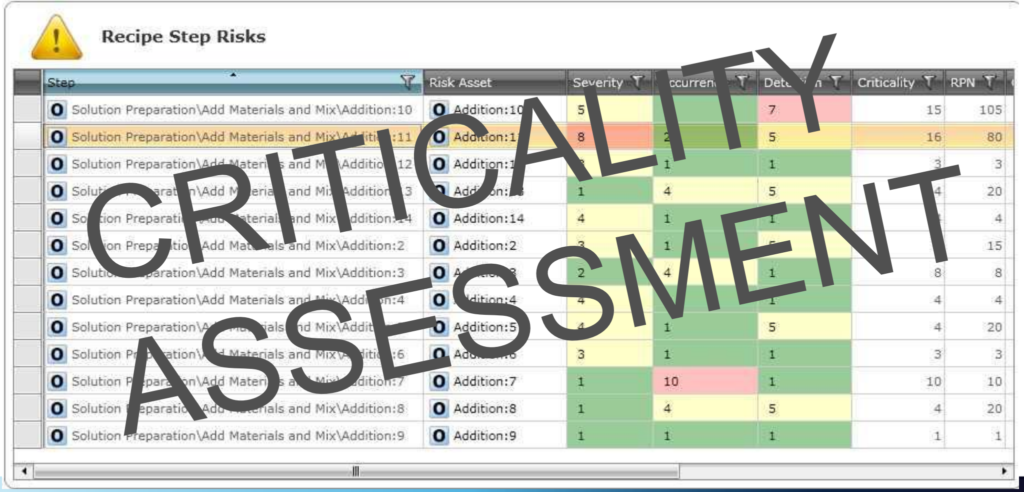




PLATFORM

PLATFORM OPERATING CONDITIONS: 3L Bioreactor Process

Platform Media and Solutions		CBL #	Comments
Basal Medium	MACH-1 + 8 g/L F8	CBL-024	Platform Basal Medium
Feed 1	BRX	CFL-001	Platform Feed 1
Feed 2	G8 (preferred) or G12	CFL-016/CFL-024	Platform Feed 2
Antifoam	Antifoam C (10,000 ppm stock)	N/A	Platform Anti Foam C - Explore Hyclone's Gam[illegible]radiated AFC for future
Base (pH Control)	2M Sodium Carbonate	N/A	Formula correct. True 2M [illegible]
Controlled Parameters	**Target**	**Range**	
Bioreactor Prep			
Sparger (type:size)	Sintered; 15 micron	N/A	
Impeller (type)	Applikon, pitched blad[illegible]nflow	N/A	Ce[illegible]ent uses Mi[illegible]ore di[illegible]sa[illegible] vess
Impellers (number):	1	N/A	No[illegible]ed - type a[illegible]ber ca[illegible] chang
Air Overlay Rate-Post SIP (mLpm)	100	NA	Ma[illegible]ams 0.1, BIIB [illegible] Bld[illegible] 0.02
Medium Addition and Bioreactor Equilibration			
Media weight batched (kg)	TBDE	[illegible]DE	Adjust based on N-1 cell count
Antifoam Add[illegible]uring Eq[illegible]brati[illegible]	19 ppm - [illegible]sed on final [illegible]ume		Adjust based on predicted reactor final volume / Linked to Schedule
Bioreactor Agi[illegible]on-Equilibra[illegible]n (rp[illegible]	200	190 - 210	
Bioreactor Tem[illegible]rature-Eq[illegible]ration [illegible]C)	[illegible]6.5	35.5 - 37.5	
pH Off line Meas[illegible]pH Probe S[illegible]dardization] (p[illegible]	±0.05	N/A	Adjust on-line pH based on off-line BGA pH
pH Control [Enga[illegible] Hi Limit Control]	N/A	≤7.30	CO2 above high pH limit
Air Overlay Rate-[illegible]uilibration [DO probe standardization] (mLpm)	N/A	N/A	**Limitation for some Valley Equipment**
Air Sparge Rate-E[illegible]ilibration [DO probe standardization] (mLpm)	100	N/A	**Does this need data confirmation?**
Air Overlay Rate [post-probe standardization] (mLpm)	100	NA	Many teams 0.1, BIIB 0.04, Bldg 4 0.02
Bioreactor Agitation [post-probe standardization] (rpm)	200	190 - 210	!!H!!
Batched Medium Expiration Time [at operating Temp] (hrs)	≤48	≤48	Need to compile data with MACH-1 to support this (72 hr better) Consider L

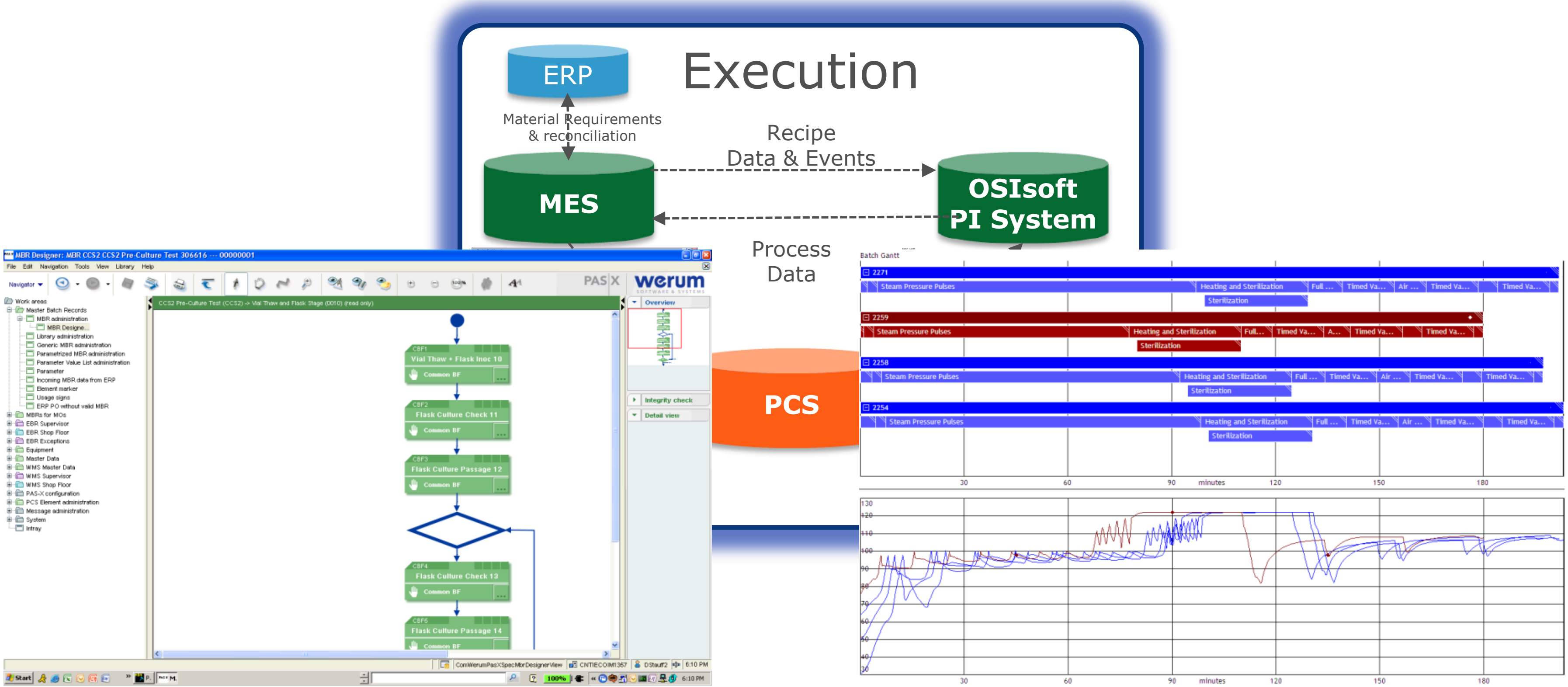


CRITICALITY ASSESSMENT

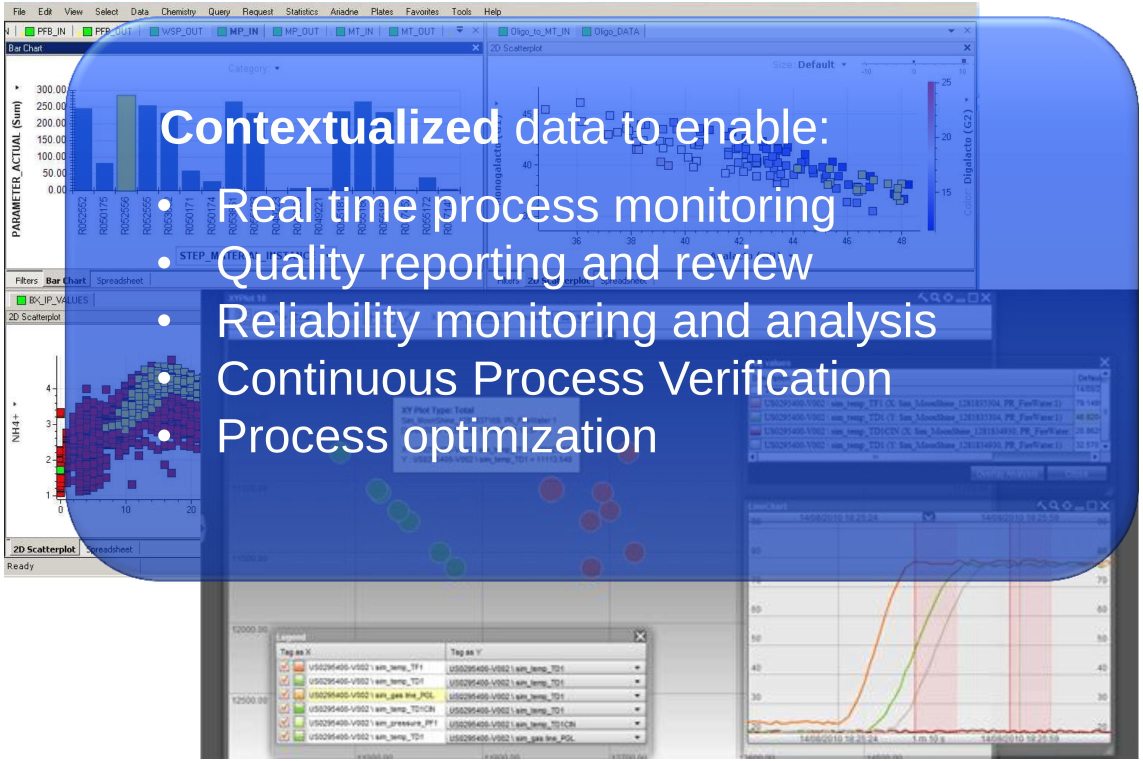
Recipe Step Risks

Step	Risk Asset	Severity	Occurrence	Detection	Criticality	RPN
Solution Preparation\Add Materials and Mix\Addition:10	Addition:10	5	[illegible]	7	15	105
Solution Preparation\Add Materials and Mix\Additi[illegible]:11	Addition:1[illegible]	8	2	5	16	80
Solution Preparation\Add Materi[illegible]s and M[illegible]\Additio[illegible]12	Addition:1[illegible]	[illegible]	1	1	3	3
Solu[illegible]arat[illegible]n\Add M[illegible]teria[illegible] and Mi[illegible]Addition[illegible]3	Add[illegible]on:[illegible]	1	4	5	4	20
So[illegible]tion Preparati[illegible]aterial[illegible]and Mix[illegible]ddition:14	Addition:14	4	1	1	[illegible]	4
Sol[illegible]ion Prepa[illegible]tio[illegible]Add Mat[illegible]als and Mix\Addition:2	Addition:2	[illegible]	1	[illegible]	[illegible]	15
Soluti[illegible]paration\Add Materials and Mix\Addition:3	A[illegible]	2	4	1	8	8
Solution Preparation\Add Materials and [illegible]Add[illegible]n:4	[illegible]dition:4	[illegible]	[illegible]	[illegible]	4	4
Solution Preparation\A[illegible]als[illegible]nd Mix\Addit[illegible]	Addition:5	[illegible]	1	5	4	20
Solution Pr[illegible]ation\[illegible] Materials and Mix\[illegible]iti[illegible]:6	Ad[illegible]	3	1	1	3	3
Solution P[illegible]para[illegible]on\Add Materi[illegible]s a[illegible] Mix[illegible]ddition:7	Addition:7	1	10	1	10	10
Solution [illegible]eparatio[illegible]Add [illegible]erials and Mix\Addition:8	Addition:8	1	4	5	4	20
Solution Preparation\Add Materials and Mix\Addition:9	Addition:9	1	1	1	1	1

S88 Recipe KM Strategy: Execution


Execution
ERP
Material Requirements & reconciliation
MES
Recipe Data & Events
OSIsoft PI System
Process Data
PCS
MBR Designer: MBR CCS2 CCS2 Pre-Culture Test 306616 --- 00000001
File
Edit
Navigation
Tools
View
Library
Help
Navigator
PAS X
werum SOFTWARE & SYSTEMS
Work areas
Master Batch Records
MBR administration
MBR Designe...
Library administration
Generic MBR administration
Parametrized MBR administration
Parameter Value List administration
Parameter
Incoming MBR data from ERP
Element marker
Usage signs
ERP PO without valid MBR
MBRs for MOs
EBR Supervisor
EBR Shop Floor
EBR Exceptions
Equipment
Master Data
WMS Master Data
WMS Supervisor
WMS Shop Floor
PAS-X configuration
PCS Element administration
Message administration
System
Intray
CCS2 Pre-Culture Test (CCS2) -> Vial Thaw and Flask Stage (0010) (read only)
CBF1
Vial Thaw + Flask Inoc 10
Common BF
CBF2
Flask Culture Check 11
Common BF
CBF3
Flask Culture Passage 12
Common BF
CBF4
Flask Culture Check 13
Common BF
CBF6
Flask Culture Passage 14
Common BF
Overview
Integrity check
Detail view
ComWerumPasXSpecMbrDesignerView
CNTIECOIM1357
DStauff2
6:10 PM
Start
100%
Batch Gantt
2271
Steam Pressure Pulses
Heating and Sterilization
Full ...
Timed Va...
Air ...
Sterilization
2259
A...
2258
2254
30
60
90
minutes
120
150
180
130
120
110
100
90
80
70
60
50
40
30

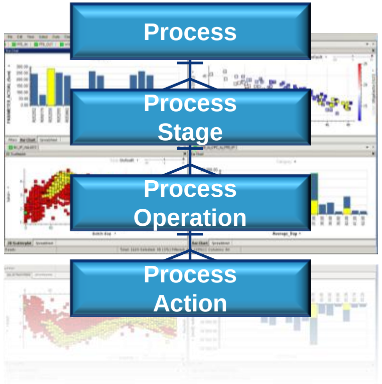
S88 Recipe KM Strategy: Visualization



Contextualized data to enable:

- Real time process monitoring
- Quality reporting and review
- Reliability monitoring and analysis
- Continuous Process Verification
- Process optimization

Visualization



Process

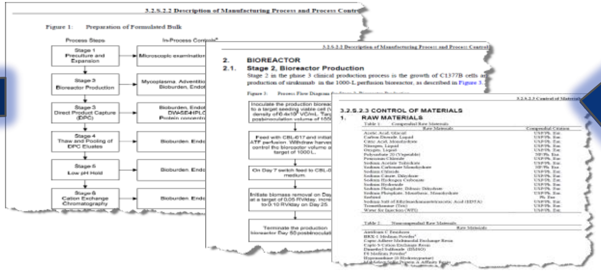
Process Stage

Process Operation

Process Action

S88 Recipe KM Strategy: Link to the Regulatory Filing

Regulatory Filing = General Recipe



3.2.S.2.2 Description of Manufacturing Process and Process Contr

Figure 1: Preparation of Formulated Bulk

Process Steps	In-Process Controls
Stage 1 Preculture and Expansion	Microscopic examination
Stage 3 Bioreactor Production	Mycoplasma, Adventitio Bioburden, Endo
Stage 3 Direct Product Capture (DPC)	Bioburden, Endo DWASE4HPLC Protein concentr
Stage 4 Thaw and Pooling of DPC Eluates	Bioburden, Endo
Stage 5 Low pH Hold	Bioburden, Endo
Stage 6 Cation Exchange Chromatography	Bioburden, Endo

3.2.S.2.2 Description of Manufacturing Process and Process Controls

2. BIOREACTOR

2.1. Stage 2, Bioreactor Production

Stage 2 in the phase 3 clinical production process is the growth of C1377B cells an production of sirukumab in the 1000-L perfusion bioreactor, as described in Figure 3.

Figure 3: Process Flow Diagram

- Inoculate the production bioreac to a target seeding viable cell (V density of 0.4x10⁶ VC/mL. Targ postinoculation volume of 100
- Feed with CBL-017 and initiat ATF perfusion. Withdraw harves control the bioreactor volume a target of 1000 L.
- On Day 7 switch feed to CBL-0 medium.
- Initiate biomass removal on Day at a target of 0.05 RV/day, incre to 0.10 RV/day on Day 25.
- Terminate the production bioreactor Day 50 postinoculati

3.2.S.2.3 Control of Materials

3.2.S.2.3 CONTROL OF MATERIALS

1. RAW MATERIALS

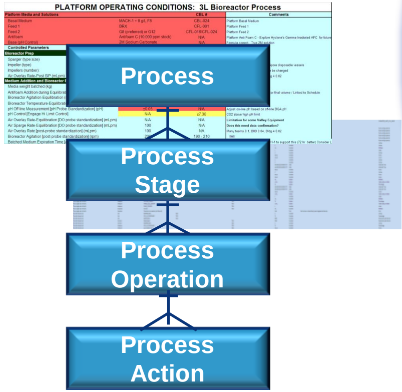
Table 1: Compendial Raw Materials

Raw Materials	Compendial Citation
Acetic Acid, Glacial	USP/Ph. Eur.
Carbon Dioxide, Liquid	USP/Ph. Eur.
Citric Acid, Monohydrate	USP/Ph. Eur.
Nitrogen, Liquid	USP/Ph. Eur.
Oxygen, Liquid	USP/Ph. Eur.
Polysorbate 20 (Vegetable)	NF/Ph. Eur.
Potassium Chloride	USP/Ph. Eur.
Sodium Acetate Trihydrate	USP/Ph. Eur.
Sodium Carbonate Monohydrate	NF/Ph. Eur.
Sodium Chloride	USP/Ph. Eur.
Sodium Citrate, Dihydrate	USP/Ph. Eur.
Sodium Hydrogen Carbonate	USP/Ph. Eur.
Sodium Hydroxide	USP/Ph. Eur.
Sodium Phosphate, Dibasic Dihydrate	USP/Ph. Eur.
Sodium Phosphate, Monobasic, Monohydrate	USP/Ph. Eur.
Sorbitol	Ph. Eur.
Sodium Salt of Ethylenediaminetetraacetic Acid (EDTA)	USP/Ph. Eur.
Tromethamine (Tris)	USP/Ph. Eur.
Water for Injection (WFI)	USP/Ph. Eur.

Table 2: Noncompendial Raw Materials

Raw Materials
Antifoam C Emulsion
BRX-1 Medium Powder
Capto Adhere Multimodal Exchange Resin
Capto S Cation Exchange Resin
Dimethyl Sulfoxide (DMSO)
F8 Medium Powder
Hypoxanthine (6-Hydroxypurine)
MabSelect SuRe Protein A Affinity Resin

CONTENT
Critical Parameters and Steps
Structured in S88 Format



PLATFORM OPERATING CONDITIONS: 3L Bioreactor Process

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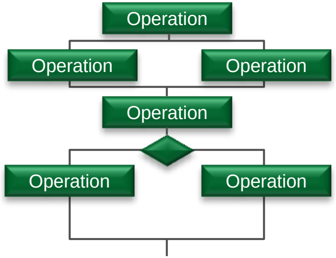
Feed 2	G8 (preferred) or G12	CFL-016/CFL-024	Platform Feed 2
Antifoam	Antifoam C (10,000 ppm stock)	N/A	Platform Anti Foam C - Explore Hyclone's Gamma Irradiated AFC for future
Base (pH Control)	2M Sodium Carbonate	N/A	Formula correct. True 2M solution
Controlled Parameters			
Bioreactor Prep			
Sparger (type size)			
Impeller (type)			pore disposable vessels
Impellers (number):			be changed
Air Overlay Rate-Post SIP (mLpm)			g 4 0.02
Medium Addition and Bioreactor E			
Media weight batched (kg)			
Antifoam Addition during Equilibrat			or final volume / Linked to Schedule
Bioreactor Agitation-Equilibration (			
Bioreactor Temperature-Equilibrati			
pH Off line Measurement [pH Probe Standardization] (pH)	±0.05	N/A	Adjust on-line pH based on off-line BGA pH
pH Control [Engage Hi Limit Control]	N/A	≤7.30	CO2 above high pH limit
Air Overlay Rate-Equilibration [DO probe standardization] (mLpm)	N/A	N/A	**Limitation for some Valley Equipment**
Air Sparge Rate-Equilibration [DO probe standardization] (mLpm)	100	N/A	**Does this need data confirmation?**
Air Overlay Rate [post-probe standardization] (mLpm)	100	NA	Many teams 0.1. BIIB 0.04. Bldg 4 0.02
Bioreactor Agitation [post-probe standardization] (rpm)	20	190 - 210	!!!!!
Batched Medium Expiration Time [			H-1 to support this (72 hr better) Consider L

Process

Process Stage

Process Operation

Process Action



Site Executable Recipe

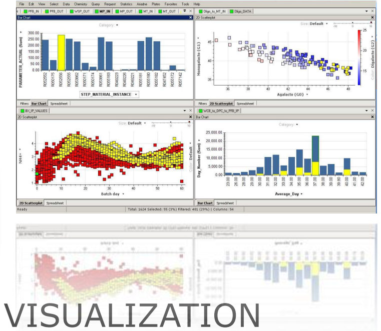
Operation

Operation Operation

Operation

Operation Operation

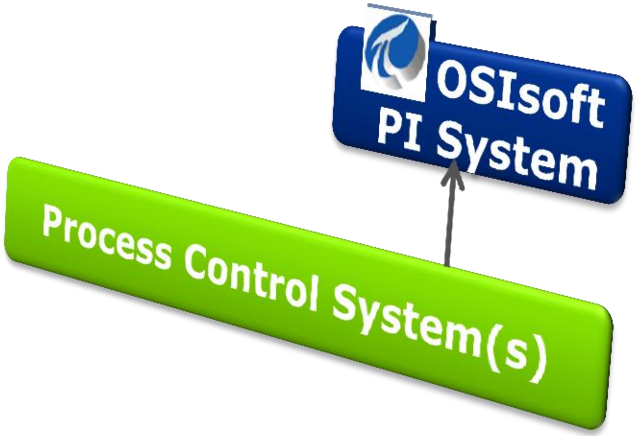
EXECUTION
Data generated in S88 Format
Contains additional site details

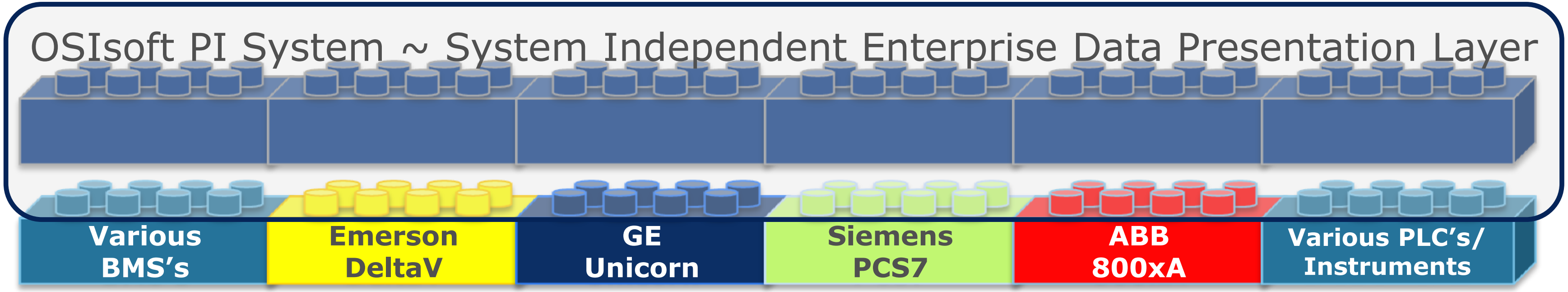


VISUALIZATION
Critical Parameters and Steps
Context rich data

Value of the OSIsoft PI System

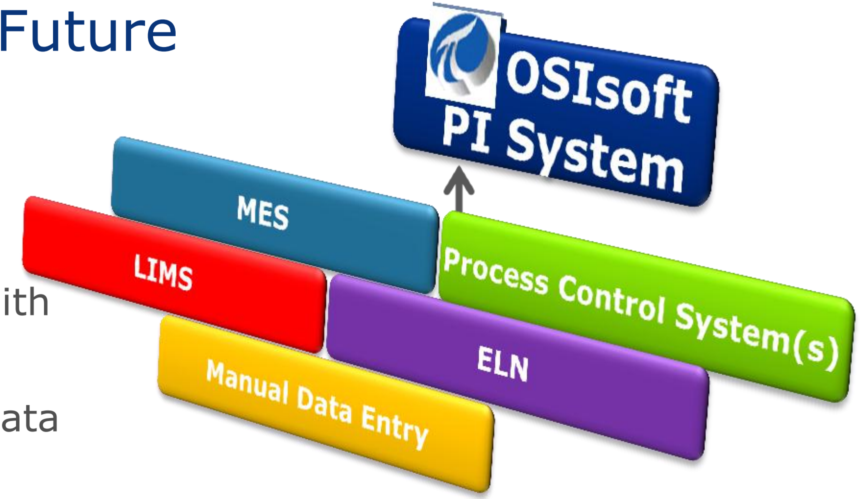
- Very disparate systems landscape
  - ranging from distributed process control systems with inherent historian capability to stand-alone instruments with paper printouts
- Require capability to capture and aggregate data for visualisation, reporting & analysis


OSIsoft
PI System
Process Control System(s)


OSIsoft PI System ~ System Independent Enterprise Data Presentation Layer
Various BMS's
Emerson DeltaV
GE Unicorn
Siemens PCS7
ABB 800xA
Various PLC's/ Instruments

Value of the OSIsoft PI System: Future

- Very disparate systems landscape – now including MES, ELN, Manual Data Entry…
- Ability to share contextualized process data with external partners is critical
- Require capability to capture and aggregate data for visualisation, reporting & analysis



OSIsoft PI System

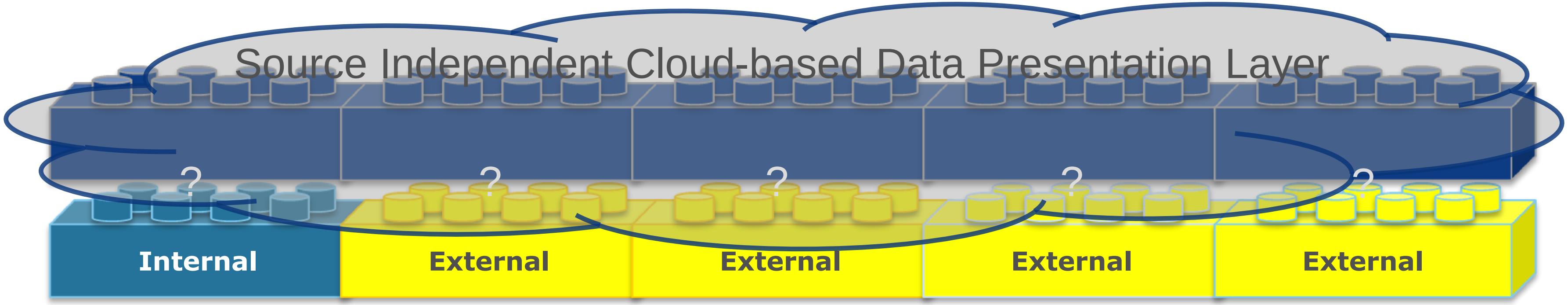
MES

LIMS

Process Control System(s)

ELN

Manual Data Entry



Source Independent Cloud-based Data Presentation Layer

?

?

?

?

?

Internal

External

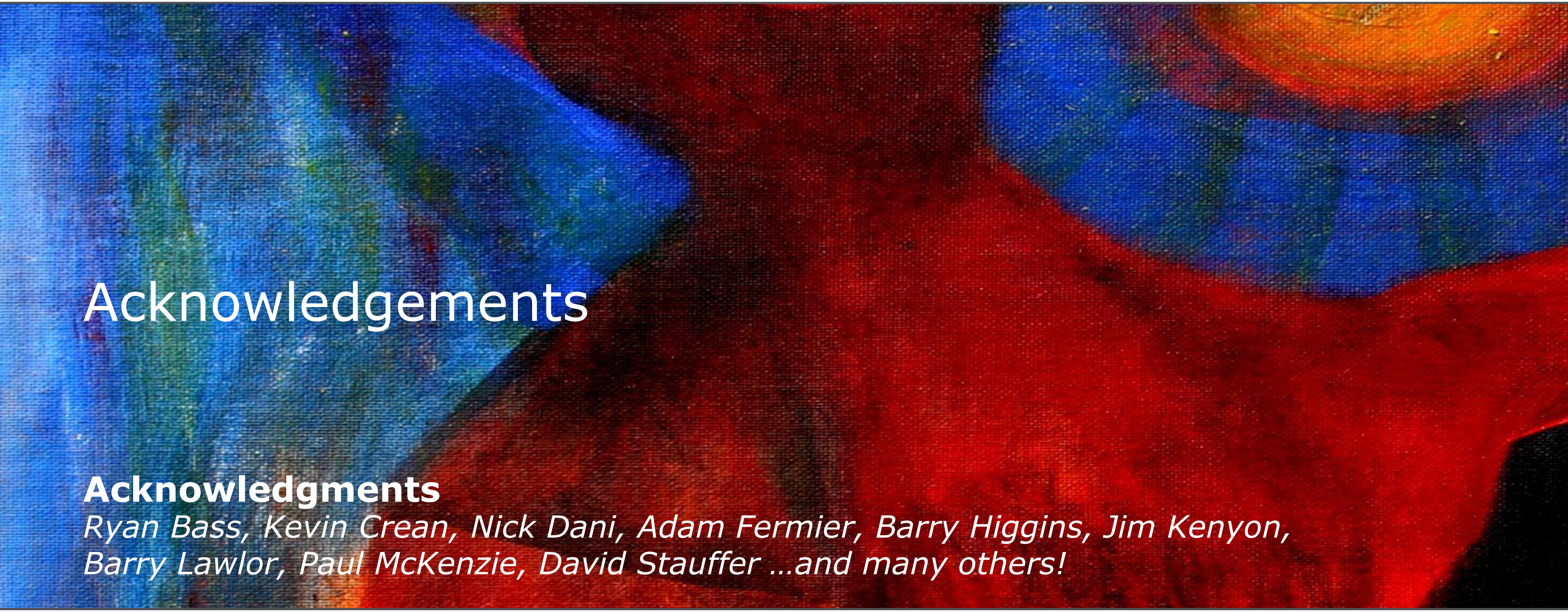
External

External

External

Conclusions

- Janssen is actively driving forward on S88 KM Strategy:
  - Content: Defining platform recipes
  - Execution: Aligning systems to S88 Platform definitions
  - Visualization: Building advanced analytical and modeling tools to help scientists and engineers gain advanced understanding of our processes
- A solution is required for a source independent data aggregation layer to include contextualized data from multiple enterprises.
- Collaboration with other companies would help drive this solution.



Acknowledgements

Acknowledgments
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Pharmaceutical Development & Manufacturing Sciences

Janssen R&D

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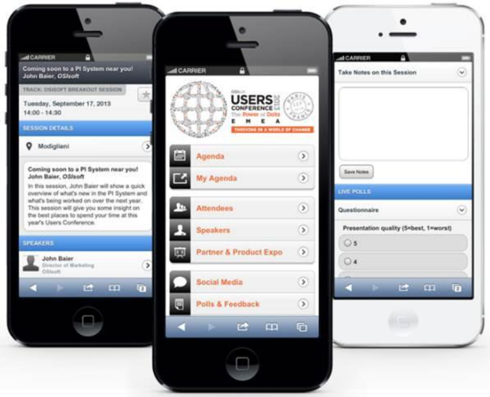
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The Power of Data
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THRIVING IN A WORLD OF CHANGE
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FRANCE
TRACK: OSISOFT BREAKOUT SESSION
SESSION DETAILS
SPEAKERS

Coming soon to a PI System near you!
John Baier, *OSIsoft*

Tuesday, September 17, 2013
14:00 - 14:30

Modigliani

In this session, John Baier will show a quick overview of what's new in the PI System and what's being worked on over the next year. This session will give you some insight on the best places to spend your time at this year's Users Conference.

John Baier
Director of Marketing
OSIsoft

Presentation quality (5=best, 1=worst)
○ 5
○ 4

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