Leveraging Innovation to Achieve Manufacturing Excellence Across Mammalian and Microbial Biologics Processes

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Cytovance Biologics

Our Facilities

Manufacturing Facility

- 50,000 sq. ft. Greenfield facility
- Designed and Constructed as a Biologics Contract Manufacturing Facility
- Dedicated Process Development Laboratories
- Mammalian and Microbial manufacturing

Upcoming Additional Facilities

- 1000L Microbial w/ 10,000 L refold - early 2015
- 20,000 sq. ft. cGMP Warehouse
  - Climate Controlled & Monitored
  - Incoming and Outgoing Supply Chain
  - Full Segregation between Incoming, Quarantine & Released Materials
  - Ambient and Cold Chain Storage

cGMP Manufacturing

Bioreactor Cell Culture

- Single Use Systems (25L – 1000L Systems)

25/50 and 100L WAVEs | 50L and 200L Sartorius SUB's | 250L and 1000L Hyclone SUB's

- Traditional Stainless Systems (100L and above)

100L & 500L Sartorius D-Stat Bioreactor Suites | 1000L SS Dakota Bioreactor Suite | 5000L SS Dakota Bioreactor Suite (Q3 2015)

Microbial Fermentation

- Fermentation Equipment
  - 200L B. Braun / Sartorius Fermenter
  - 1000L B. Braun Fermenter Expansion (Q1 2015)

- Cell Processing
  - Disk Stack Centrifugation
    Also have traditional bucket centrifuge options
  - Homogenization
  - Micro-fluidizer

Automated Fill/Finish

- Up to 45 Vials per minute
- 2mL to 20mL Vials
- Typically up to 10,000 Vials per run (larger volume runs also available)

Semi-Automated Fill/Finish

- Capable of 2mL to 100mL fills
- Ideal for smaller fills or non-standard configurations

Innovation In Biopharmaceutical Manufacture

Is Innovation Valuable in MFG…?[Ref]

- Is innovation still required in biopharmaceutical manufacturing, and if so, what kind?
- Is new technology R&D investment directed toward the most pressing issues?
- How do you balance risk and benefits when implementing new technologies?

YES!!!

- What are some practical approaches for introducing new technologies and processes into one's company ?
- Multiple stakeholders' sponsorship to achieve goals:
  - Customers
  - R&D
  - Project Management
  - Manufacturing
  - Finance
  - Board of directors
  - Quality Assurance
  - Legal
- How to drive good ideas?

KYTOS – The Idea Box

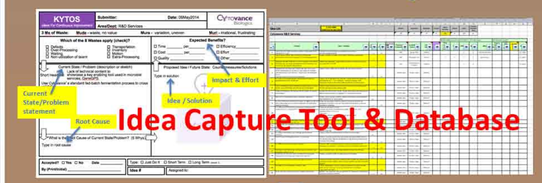
What's in the Box ?

- Idea capture tool and database
- Steering workflow
- Prioritization tools
- Project charters with budgets
- A way to link to SMART goals for individuals

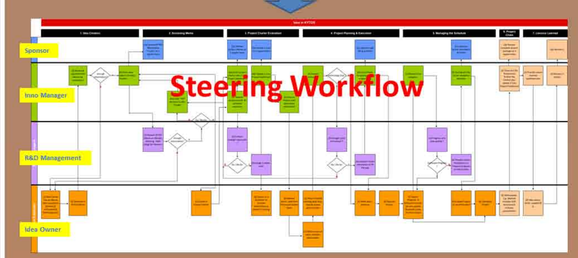
A Practical Idea Management System

What's in the Box ?

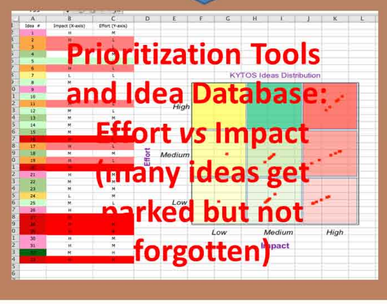
- Leader Standard Work for managing progress
- Close-out presentation deliverables
- Recognition tools
- Patentability Questionnaire



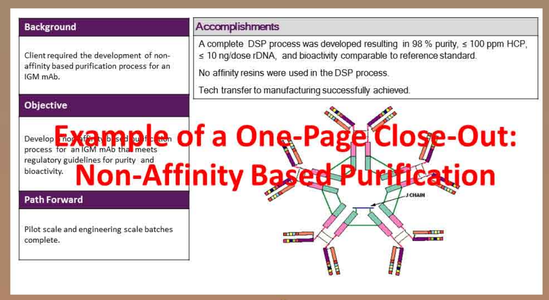
Idea Capture Tool & Database



Steering Workflow



Prioritization Tools and Idea Database: Effort *vs* Impact (many ideas get parked but not forgotten)



Example of a One-Page Close-Out: Non-Affinity Based Purification

Leader Standard Work e.g., Weekly Resource Planning

Project Charters: Approved by Sponsor Goals Created for Individuals

KYTOS Offers a Framework for Achieving Goals

- Enables the capture of employees' ideas for new technologies, problem solving, bioprocessing and business process solutions
- Stimulates innovative thinking and employee engagement
- Enables a structured approach for idea evaluation, ranking and prioritization in the context of IMPACT vs. EFFORT
- Enables routine updates for course correction, resources planning and other decisions

Types of Ideas

- Tools for driving process excellence
- At-scale processing improvements
- New PAT methods
- Creating microbial technologies
- Testing new efficient DoE to enable QbD
- Business process improvement tools

Types of Ideas

Tools for Driving Process Excellence

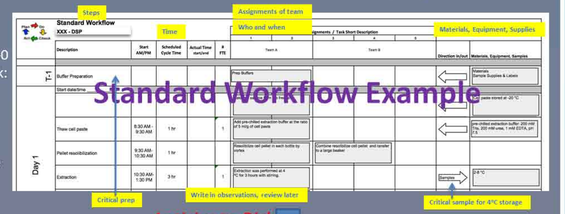
- Standard Workflow (Process Map)
- GAP-Risk Assessment
- First time right
- Standard root cause investigation
- Rolling risk log
- Lessons learned

Tools are more powerful when used as part of a system

ASK: *What is needed to ensure a successful process run?*

Standard Workflow

- Countdown to start work at T-0
- Milestones to check if on track: T-60, T-30, T-14, T-7, T-2
- Visual Management
  - Take out of computer: post on wall, mark up
- Ownership by those doing the work = Confidence
  - Let them see the full plan – to challenge it – to improve it

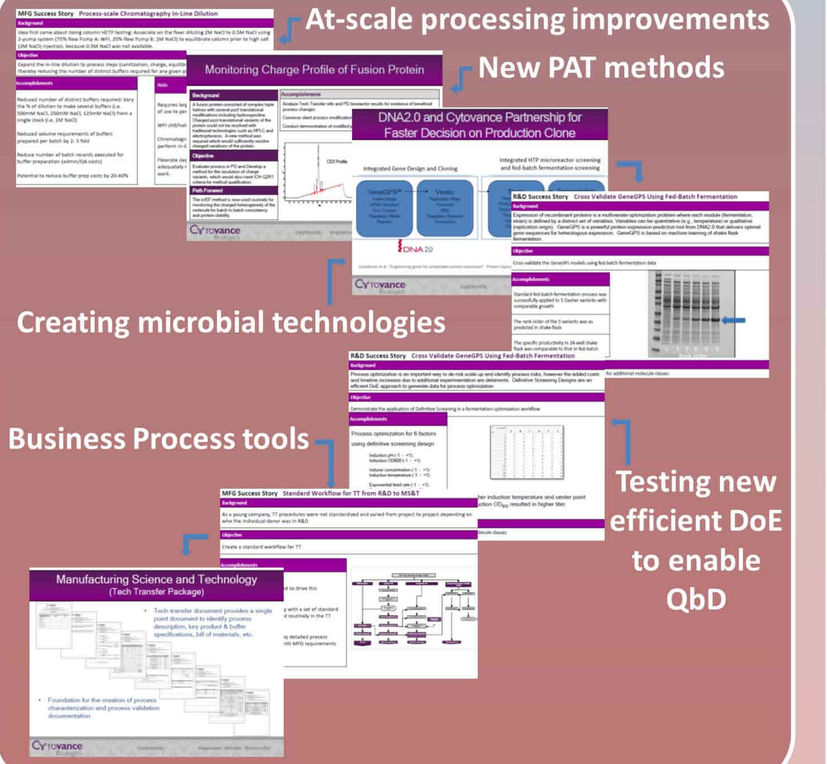


Standard Workflow Example

Anticipate Risk

At-scale processing improvements

New PAT methods



Creating microbial technologies

Business Process tools

Testing new efficient DoE to enable QbD

Reference

This poster is a summary of slides presented at Manu BIO Leaders Innovation Summit in Boston, MA (June 10, 2014).

A. Davidson and S.S. Farid, "Innovation in Biopharmaceutical Manufacture", BioProcess International, 12(1) January 2014, Pages 12-19.