The role of PAT in Lean Manufacturing

Steve Hammond Alan Rhoden Pfizer Global Manufacturing

Presentation Outline

- How does PAT contribute to a Lean supply?
 - Flexible manufacturing
- API crystalization
 - Predictable outcomes!
- RTR testing of a Pfizer product
 - Future RTR measurement strategy
 - Potential for feed frame measurements
- What about the packaging?
 - Potential for PAT to smooth the supply chain.

Technology Development Focus within Pfizer Global Supply

Quality / Compliance

Supply Reliability

Cost / Value Delivery

by Chain Objective – Take a \$ billion out of PGS inventory

Design future analytics to support a transformed supply chain

Context -Three fundamentals for a modern lean and agile supply chain

Synchronize production to demand
 – Pull not push supply chain

Utterly reliable production

 PAT applied to the API-DP interface
 Condition monitoring and advanced control

Flexibility

- Product to product
- Capacity utilization
- Across the Network

Simon Chalk, BioPhorum Operations Group

Context - Where and how to build flexibility API & DP Plants Technologies

- Small batch sizes
 - Reduce inventory and space investment
 - Reduce overall lead time
 - Increase complexity in the site (more orders to manage an approve)
- Quick changeovers
 - Reduce lead time
 - Increase equipment utilization (OEE)
- Reliable and predictable processes
 - Improve process robustness
 - Reduce defect rates increase reliability
 - Improve planning process
 - Improve overall service
- Quick approval (release) times
 - Reduce Lead Time

Juan Fernando Forero, Pfizer Supply Chain

Automated Crystalliser

stir

FBR

Stirrer

Temperature

•PAT Calibration Models & dosing solubility/nucleation curves generated as part of an automated sequend

using a concentrated solution that is sequentially diluted, equilibrated & measured using the PAT devices

 FBRM data with mathematical and heuristic rules to define solubility & nucleation thresholds

Advanced Control Cooling Crystallisation Example

Traditional Process Control

Advanced Process Control

solution

(stable)



Chantix Real Time Release and PAT



Identity Testing

- Replacement of regulatory release test for API in tablet matrix proposed during dispensing
 - Closed manufacturing facility with single API



NIR Mounted on a rotating blender





NIR interfaced with Press

Process Analyzers

• Measure condition of the process material in real time

Collect more information about the batch



Results from 18,000 tablets for a 5mg dose in a 200mg tablet



Standard platform for RTR

- RTR has significant benefits to Pfizer
- To supply chain management
- Reduced testing in a laboratory
- Increased process understanding
- Whilst also increasing the level of Quality
 Assurance of the product
 - Require an easy to implement, low cost, standard platform for the application of PAT

Schematic of Feed Frame PAT Installation



Example Probe Installations

Manesty Unipress Diamond (USA) and Fette 2090 (Germany)



The design and engineering of the probe interface is completed

Intelligent Compression and QbD



SIMCA-P+ 12 - 2010-05-02 19:02:36 (UTC-5)

Reduction in Tablet Tensile Strength vs Time

Potential Benefits

- Increased process understanding of blending and compression processes.
- Understand and monitor feed-frame function
- Ability to detect segregation during powder transfer from IBC to the tablet press
- Applicable to both Batch and Continuous Processes
- Integration of PAT signal and tablet press weight control signal into compression machine logic.
 - Advanced Process Control
 - Opportunity to implement as part of RTRt paradigm

Packaging and supply chain

- Packaging can be a significant pinch-points in pharmaceutical supply chain
- Production errors are generally costly, as product in near the end of manufacturing cycle – added value of previous work
- Almost entirely relies on conventional visible wavelength light for inspection systems

Thermal Imaging can see through most packaging materials

Basis of significantly enhanced packaging inspection systems



Blister Integrity Testing

Blister Sealing and product present count monitoring





Open end of blister

Bottle content inspection Through plastic bottles!!!! Opaque Bottle Content Monitoring



Testing in Pfizer facility



Typical Bottle Failure Modes



Untorqued Cap

Harmed Cap border

Crooked Cap

Bottle miss position

Bottle defects under the cap



Summary

- PAT is making a significant contribution to a Lean supply chain
- Predictable processes advanced control
- RTR as a concept is now well established. New strategies for using sensors on-line provides bigger supply chain benefits
- Thermal imaging is opening the door to better sensors, condition monitoring and optimization of packaging operations
- PAT has an important role to play as an enabler of a modern supply chain

Acknowledgement of the whole army



Acknowledgements

Many, many people have contributed to this presentation:

Pfizer World Wide R&D: Groton Pharm Sciences **Pfizer Global Supply:** Process Analytical Support Group **Pfizer Global Supply: Technology, Science and Operation Group** Pfizer Global Supply: Caguas Site, Illertissen, Freiburg, Vega Baja **Pfizer Global Supply: Product and Process Development, Freiburg**