Platform technologies for manufacturing process optimization through integration of PAT and control system

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Advanced Manufacturing Technology, Pfizer Global Supply

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Overview

• What is a platform technology and how it works?
  ▪ Turnkey solution
  ▪ Integration of multiple technology components

• Business benefits

• Implementations/Case studies
  ▪ Use of advanced software platforms for
    ◆ Integrating PAT/PLC/SCADA
    ◆ Performing data collection/alignment/modeling and advanced process control
  ▪ Throughput optimization
  ▪ Dryer optimization
  ▪ Effluent Treatment
  ▪ Optimization of production planning & scheduling
Platform Technology refers to a class of process solutions that are not tied to a single application, have generic applicability to a class of processes rather than proprietary equipment, are specifically designed for explicability and ease of implementation, and are based on integration of more than one technical component, often in a turnkey or near-turnkey manner.

Source: IbM in Pfizer, Mojgan Moshgbar, IFPAC 2014

Not all platform technologies have all the elements.
Business Benefits

- Improved overall agility and predictability
- Reduced production/inventory cost
- Increased yield, throughput
- Reduced variation and increased process capability
- De-risking processes
## Application Areas - Platform Technologies

<table>
<thead>
<tr>
<th>Application Area</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Solid Dosage Manufacturing</strong></td>
<td>• Multi-step Process Optimization for Solid Dosage Manufacturing using PAT and Advanced Process Control&lt;br&gt;• Granulation, drying, blending, compression and coating</td>
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<tr>
<td><strong>API</strong></td>
<td>• Monitoring and control of API production&lt;br&gt;• Crystallization, reaction, drying, solvent recovery and waste treatment</td>
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<td><strong>Bio Manufacturing</strong></td>
<td>• Real-time monitoring and control of nutrients and metabolites in cell cultures</td>
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<td><strong>Continuous Manufacturing</strong></td>
<td>• Advanced measurement and control for both API and DP continuous manufacturing, CQV and RTR</td>
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<tr>
<td><strong>Production Planning &amp; Scheduling</strong></td>
<td>• Production planning and scheduling platform for minimizing changeover and inventory, and OEE maximization</td>
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Key Objectives of Multi-Step Optimization

- **Improve blend flow and compressibility**
  - Faster cycle time
  - Higher throughput and yield

- **Reduce tablet weight variation and improve tablet press weight control process capability**

- **Achieve desired tablet potency/CU, appearance, hardness and dissolution**
Multi-Step Optimization Scheme

Desired Attributes / Outcomes

Raw Material Attributes

Process Economics / Constraints

Up/Down Stream Process Knowledge

Optimization System

Unit Operation 1
Intelligent Monitoring / Control
Sensors/soft sensors
PATs
Actuators

Unit Operation 2
Intelligent Monitoring / Control
Sensors/soft sensors
PATs
Actuators

Unit Operation 3...
Intelligent Monitoring / Control
Sensors/soft sensors
PATs
Actuators

Data Management / SCADA Systems
Data Collection/Alignment/Modeling

Data Sources
- JCAMP-DX File
- SPC File
- CSV Data

Spectral and Process Data
- Spectral Data
- Spectral Device(s)
- Spectral Range(s)
- Calibration Block(s)
- Prediction

Process Data

PharmaMV Project

PAT1:
- Spectral File Polling
- OPC Spectral Arrays
- Individual OPC or Modbus Items

PAT2:
- OPC Process Data
- To Simca QP DLL

PAT3:
- DCS/PLC Interface

courtesy of Perceptive Engineering
Control batch evolution/trajectories?

Real-time optimization of process conditions to achieve desired output quality attributes (to setpoint or within constraints), e.g., tablet finish and yield?
Case Study: APC for Throughput Optimization

Maximizing throughput using PAT-based Advanced Process Control and Optimization

Improve flow/compressibility
APC for Throughput Optimization

Granulation and drying APC modules

APC Software (PharmaMV)

PLC  Torque/NIR  PLC  NIR

Granulation
Process Inputs  Process Outputs

Drying
Process Inputs  Process Outputs

Desired tablet properties, and increased throughput

Granulation and drying APC modules

Process Inputs
Process Outputs

Other unit operations

Final Mix

Compression

HSWG  FBD
Granulation Control Strategies

Model Predictive Control

- Trajectory tracking
- Endpoint controller
- Pseudo Endpoint

Dynamic Control Chart

Run 04
Run 06
Run 11
Average
UCL
LCL

Dry mix
Water addition
Kneading

Prediction Horizon
Control Horizon
Control Moves, u1

Control Variable y1
Past
Future

Past
global/local
Future
Trajectory
Time point
Torque (N-M)

Run 04
Run 06
Run 11
Average
UCL
LCL

Control Horizon
Control Moves, u1
Control Variable y1
Wet Granulation APC trial

- Score 1 trajectory from NIR spectral PCA model
- Score 2 trajectory from NIR spectral PCA model
- Score 3 trajectory from NIR spectral PCA model

Impeller speed (RPM)
Binder flow (ml/m)

MV1
MV2

CV1
CV2
CV3
Case Study - Drying APC
- An Example

Project Justification

- Yield increase
- Drying efficiency (capacity) increase
- Reduction in variability
- Energy saving and increased productivity
Interfacing of NIR with a Dryer

- NIR as primary analyzer for measuring powder moisture
- Soft sensor as back up analyzer for powder moisture
Dryer APC Solution

- Real time optimization of the yield and drying rate
- Full Integration with the APC, NIR, PLC and SCADA system
- MVA routines, both in the NIR as well as the APC system
- NIR and Soft Sensor prediction of powder moisture
Case Study - Effluent Treatment

Corporate KPI's

Customer Satisfaction
Corporate Profitability

ROCE, OEE, ROA

Business Unit 1 KPI's

Business Unit 2 KPI's

Production

Maintenance

Quality

Environmental

Control System KPI's

Throughput

Yield

Outages

Consent Limits

Control System Set-points
(for WWTP)

\[ \text{g NH}_4\text{-N removed per kWh (aeration energy)} \]

\[ \text{g SS in effluent per hydraulic load (m³/day)} \]

\[ \text{Organic Loading} \]

\[ \% \text{ BOD Removal/Unit Energy} \]

\[ \% \text{ COD Removal} \]

\[ \% \text{ Ammonia Removal} \]

\[ \% \text{ Solids Removal} \]

\[ \text{DO SP} \]

\[ \text{MLSS SP} \]

\[ \text{Ammonia SP} \]
Case Study - Effluent Treatment

Benchmarking

- Final Water Quality
- Dissolved Oxygen control
- Energy Consumption
- Chemical consumption

Opportunities

- Soft sensors for validating DO
- Multivariable model predictive control for stabilizing blower control
Case Study: Production Planning & Scheduling

- Minimize changeover and inventory
- Maximize overall equipment effectiveness (OEE)

Non-optimal production scheduling
# Changeovers: 263 (conflicts in schedule)

16% improvement in efficiency!

Optimal production scheduling
# Changeovers: 226 (No more conflicts in schedule)
• Intellicentic Collaboration

• Interview with American Pharmaceutical Review

• www.intellicentic.com

• Visit Intellicentic booths for more information
Q &A