The future state of Pharma 4.0 Automation

Thomas Jacobsen, NNE
About me

• Thomas Jacobsen, MS, E.I.T

• M. Ch. Eng., Biomanufacturing from North Carolina State University (2014) and B.S., Biological Engineering & Process Controls from North Carolina State University (2011)

• Automation Manager at NNE

• Special competences with Industrial Networking, VMware Infrastructure, Rockwell Programming, System Architecture Design, DataFlow Design/management
Focused pharma engineering

An international company specialised in pharma engineering

We bring best practices to our customers

3,000 projects globally / year

30% pharma consulting

30% restructuring and facility upgrades

2,000 professionals

40% new production facilities

15 Office locations worldwide

We are supporting our customers globally and on local sites

We enable pharma companies to deliver on demand

AGILE AND FLEXIBLE OPERATIONS
SEAMLESS GMP COMPLIANCE
FUTURE PROOF SOLUTIONS

We are supporting our customers globally and on local sites

We enable pharma companies to deliver on demand

AGILE AND FLEXIBLE OPERATIONS
SEAMLESS GMP COMPLIANCE
FUTURE PROOF SOLUTIONS
INDUSTRY 4.0 IN PHARMACEUTICALS AND PHARMA 4.0
Industry 4.0 – ‘The fourth industrial revolution’

The four design principles in Industry 4.0

Interoperability
• Machines, devices, sensors and people to connect and communicate with each other via the Internet of Things (IoT)

Information transparency
• Information systems to create a virtual copy of the physical world by enriching digital plant models with sensor data. Aggregation of raw sensor data to higher-value context information

Technical assistance
• Systems to support humans by aggregating and visualising information for making informed decisions and solving urgent problems on short notice.
• Cyber physical systems to physically support humans by conducting a range of tasks that are unsafe to the product or the co-workers, unpleasant or too exhausting

Decentralised decisions
• Cyber physical systems to make decisions on their own and to perform their tasks as autonomous as possible. Only in case of exceptions, interferences or conflicting goals, tasks are delegated to a higher level
Pharma 4.0

Automation

End to end, vertical & horizontal integration

Quality Predictive Control

Workforce 4.0
Knowledge Management

Concept: ISPE Pharma 4.0 Special Interest Group
Pharma 4.0 - The Pharma take on Industry 4.0

- Pioneered by the ISPE DACH group (Germany/Austria/Switzerland). NNE is also engaged.
- Enabler for modern innovative technology founded, highly automated, predictive and safe pharmaceutical manufacturing, based on life cycle management principles.

**Pharma 4.0 Key Elements covered by the four components**

- Workforce 4.0
- Data Integrity, Process Maps, Process Data Maps, Critical Thinking
- Integrated Planning & Training & Preventative & Predictive Maintenance
- Environmental Monitoring & Energy Management
- Process Automation, Continuous Process Verification and Continued Process verification (CPV)
- Real Time Release Testing & Batch Release
- Serialization & Track & Trace
Pharma 4.0 - Transformation from Data to Knowledge, Understanding & Wisdom

Available data

Data Transfer

Data Prioritization

Data Analytics

Data Mining & Intelligence

Patterns

Transformed data

Prioritized data

Evaluation, Visualization

Continual Improvement

Controls & Dashboards

Decisions & Actions

Developed further from the ISPE Pharma 4.0 material
Quality Predictive Control

- Big Data - 3 dimensional data collection and analysis, combination of data from many different sources
  - Integrated enterprise production data (across processes, sites and CMOs)
  - Analyse and correlate data for predictive quality control (know the quality of the finished product based on input quality). Data from ERP, LIMS, MES, CAPA, SCADA, Deviation management systems, etc
  - Production data life cycle management (analyse big data across the product life cycle)

Developed further from the ISPE Pharma 4.0 material
Workforce 4.0

- New colleagues – Robots & Cobots
- Operation of Smart Devices
- Flexible operations monitoring & control
- A decentral smart device enables monitoring and operating from distance by operators and supervisors
- It simplifies changeover, setup, maintenance and life cycle management (being able to fast implement changes)
- Cross functional work (integration of several disciplines)
- Computer AI Robotics and Macros

Developed further from the ISPE Pharma 4.0 material
End to End, Vertical & Horizontal Integration
Big Data: Overall Data Collection

PHARMA 4.0

ERP systems
MES systems
LIMS systems
HPLC systems
Logistics
Maintenance
DMS Files
Paper

Across the product lifecycle

Pharmaceutical Development → Technology Transfer → Commercial Manufacturing → Product Discontinuation

SCADA
PLC
Sensors
Equipment Data
Historian Building Mgmt
CAPA systems

Developed further from the ISPE Pharma 4.0 material
Automation

- Automation standards are based on Industry 4.0
- Links to the NNE Automation Manufacturing IT Architecture
- Enables the implementation of the Manufacturing Control Strategy

Manufacturing Control Strategy

- GxP Requirements
  ICH Q10, Pharmaceutical Quality System
  ICH Q8,9,Q11 Control Strategy
  Data Integrity by Design

Developed further from the ISPE Pharma 4.0 material
Data integrity impact on IT

Increasing requirements to:
- System governance
- IT operations maturity

Risk:
- Is basic system governance established?
- Is basic IT operations maturity established?

Source: Figure 4.5, GAMP 5: A Risk-Based Approach to Compliant GxP Computerized Systems. © Copyright ISPE 2008. All rights reserved. www.ISPE.org

Major Information flow between operational activities
Data integrity impact on IT and New Regulatory Impacts

“When legacy systems can no longer be supported, consideration should be given to maintaining the software for data accessibility purposes (for as long possible depending upon the specific retention requirements). This may be achieved by maintaining software in a virtual environment.”

Source MHRA Medicines & Healthcare products Regulatory Agency (MHRA) “GXP' Data Integrity Guidance and Definitions” March 2018

“a copy/copies is/are made of the original electronic data set, preserving the original record format, the dynamic format, as required (e.g. archival copy of the entire set of electronic data and metadata made using a validated back-up process)”

Source WHO TRS 996 Annex 5 “Guidance on good data and record management practices”
Changing the Manufacturing World through new and better connections - Example from Cisco

• Today, the Internet of Everything (IoE) brings them all together by combining machine-to-machine, person-to-machine, and person-to-person connections
• Cisco predicts that between now and 2022, US$19 trillion in value is at stake for organizations willing to take advantage of the immense IoE opportunity
• To realize the potential of IoE, one must act quickly, powered by an efficient infrastructure
• Technology architectures need to be streamlined — to create the agility to keep pace with rapid change
• The infrastructure must help to gain useful intelligence from IoE
• Increased connectivity requires that security threats must be managed in a comprehensive and proactive manner
Cyber Security

• Control System Infrastructure is now becoming a hacker target
• Automation Connectivity including Mobility and wireless - business needs are driving Integration
• Control System Technology (CST), definitely no longer proprietary
• Many Mfg. sites stop dead in their tracks without control systems on-line

- Segmentation of networks separated by firewalls
- Black/white listing of software
- Encryption of data traffic
- Intrusion Prevention/Detection
- Strong Access Control
- Strict Password Management
- Two-factor Authentication
End-to-end Integration

• Vertical integration enables holistic, data driven decisions in real-time supporting supervised data-driven models using machine learning
• Horizontal integration across the entire manufacturing process allowing for backward controls
• Data flow maps
• Design for Data Integrity
Logical Infrastructure Design
DataFlow Modeling

Vendor Supplied Detail Data Flow

Time Synchronization Description

audit Communication Description

Software Management Communication Description

Alarm and Events Communication Description

PCS to PLC

Time Series Communication Description

Delta V

Rockwell Software

Redundancy

OSI PI Software

Interface Appliance

Controllers
From the traditional to the Pharma 4.0 facility

<table>
<thead>
<tr>
<th>Traditional</th>
<th>Pharma 4.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monolithic</td>
<td>Modular</td>
</tr>
<tr>
<td>Fixed locations</td>
<td>Changing locations</td>
</tr>
<tr>
<td>Unknown locations</td>
<td>Location sensing</td>
</tr>
<tr>
<td>Wired</td>
<td>Wireless</td>
</tr>
<tr>
<td>PLC</td>
<td>Power controllers</td>
</tr>
<tr>
<td>SCADA</td>
<td>Cloud based applications</td>
</tr>
<tr>
<td>Paper based SOPs</td>
<td>Holo lenses</td>
</tr>
</tbody>
</table>
Conclusion on Pharma 4.0

Patient & Industry benefits

- Smarter data driven production execution
- High level of process understanding, science and risk based approach, critical thinking, transparent controls and activities
- Processes are designed for life cycle management
- Data Integrity by Design is ensured by the manufacturing control strategy, based on process and data maps, harmonized across the organization
- Data used to control, improve and optimize processes in real time both from a patient and a business perspective
- The holistic manufacturing control strategy enables repeatable and robust processes as well as continued process verification
- Secure safe material and people flow with a secure manufacturing supply chain
- New work force - reduced human interventions
- Needs cross disciplinary work, IT and integrated engineering
- Greater Leverage of new IT concepts and delivery models for reducing effort to project testing and commissioning.
Discover expert insight
Join our Newsletter: TechTalk Updates

On-Demand webinars within Robotics, Personalized Medicine, Tech Transfer, etc.
Thank you

Thomas Jacobsen
Automation Manager, East Coast
+1 919-612-3822
tojb@nne.com

Acknowledgement
Line Lundsberg-Nielsen, Global Technology Partner, NNE, llun@nne.com
Agenda

- SA - International Society of Automation, 67 TW Alexander Dr., Research Triangle Park, NC 27709
- Registration 12:30-1:00pm
- Automation Presentations: 1:00-2:20pm
- Networking/ISA Tour and Refreshments: 2:20-3:00pm
- Automation Presentations: 3:00-5:00pm
- Followed by continuing networking at Therapeutic Thursday at Rookies Sports Bar, sponsored by LB Bohle