Thomas Jacobsen, NNE

The future state of Pharma 4.0 Automation

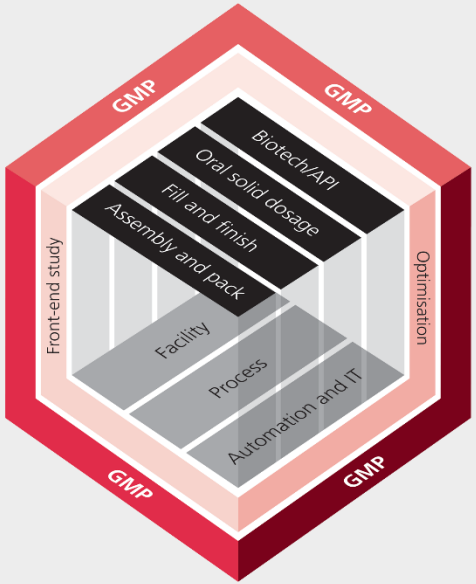
nne®
Focused pharma engineering

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

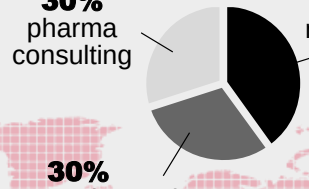


We bring best practices
to our customers

3,000
projects globally / year

We are supporting
our customers globally
and on local sites

We enable pharma companies
to deliver on demand



2,000
professionals

15
Office locations
worldwide

AGILE AND FLEXIBLE OPERATIONS

SEAMLESS GMP COMPLIANCE

FUTURE PROOF SOLUTIONS

INDUSTRY 4.0 IN PHARMACEUTICALS AND PHARMA 4.0

nne®

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

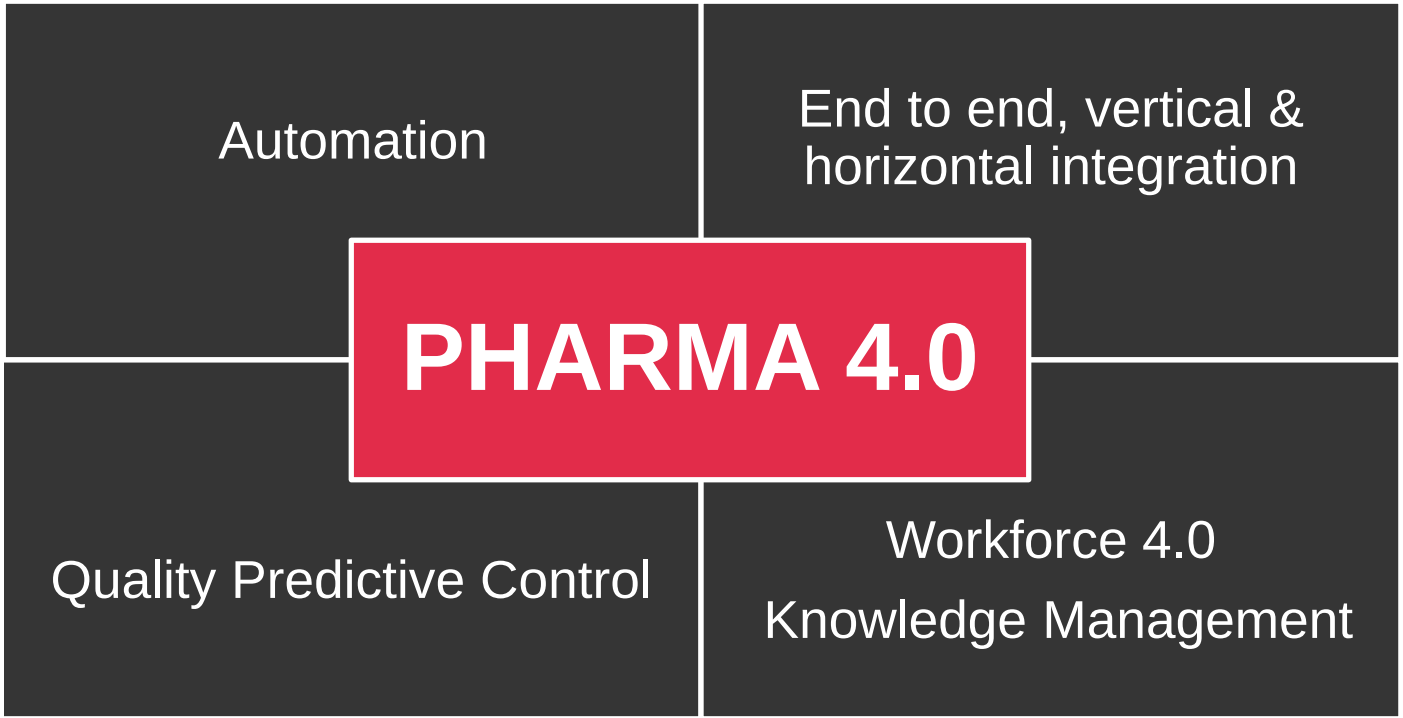
Technical assistance

- 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

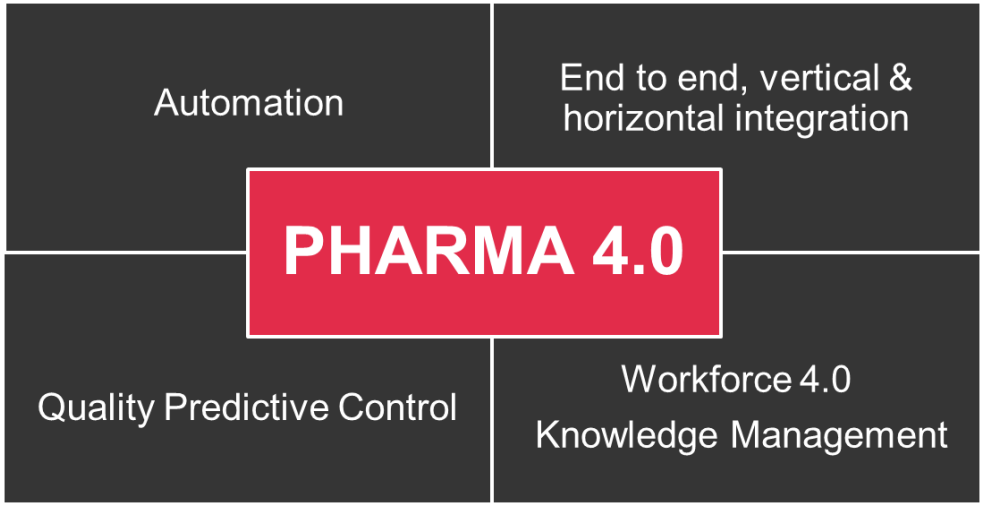
- Cyber physical systems to make decisions on their own and to perform their tasks as autonomous as possible. Only in case of exceptions, interferences or conflicting goals, tasks are delegated to a higher level

Pharma 4.0



Concept: ISPE Pharma 4.0 Special Interest Group

Pharma 4.0 - The Pharma take on Industry 4.0

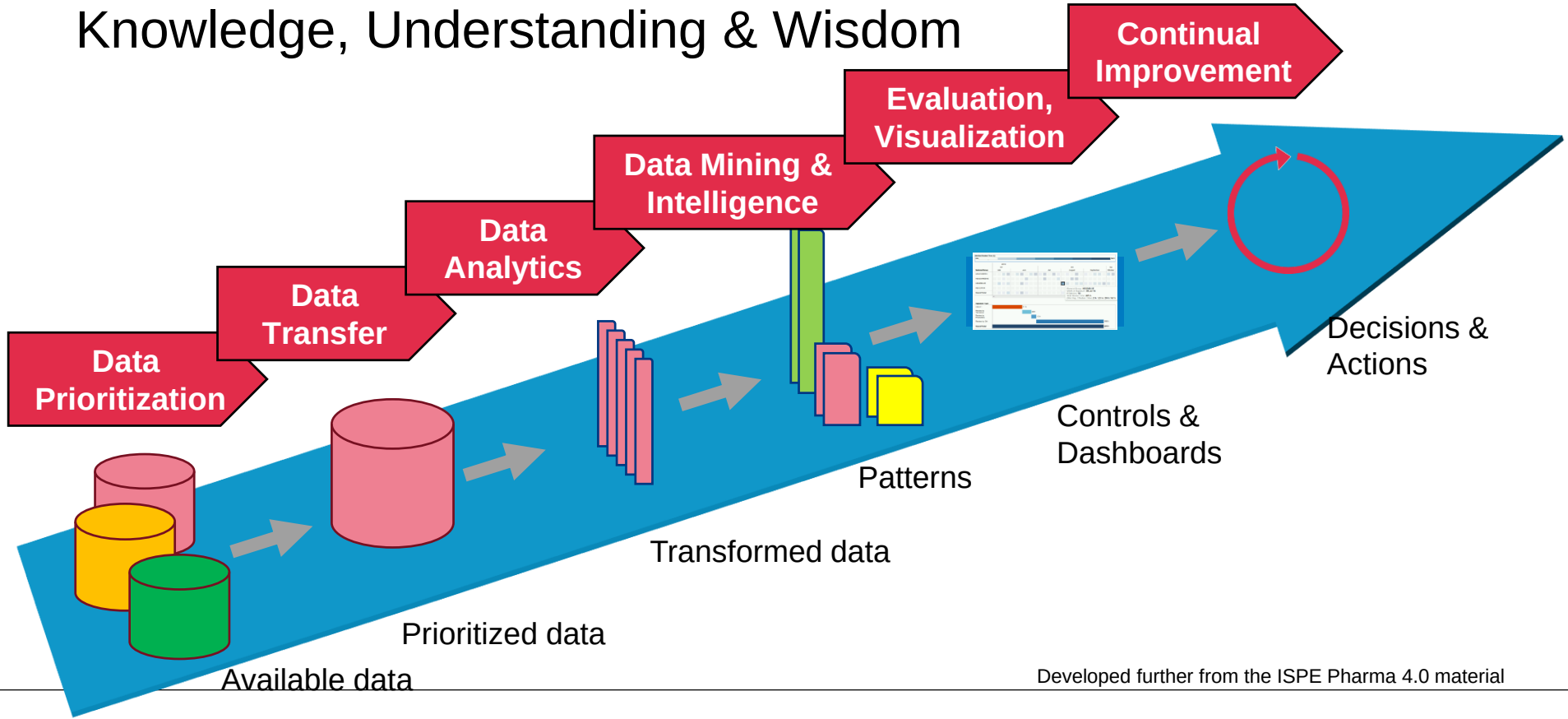


Pharma 4.0 Key Elements covered by the four components

- 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

- 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

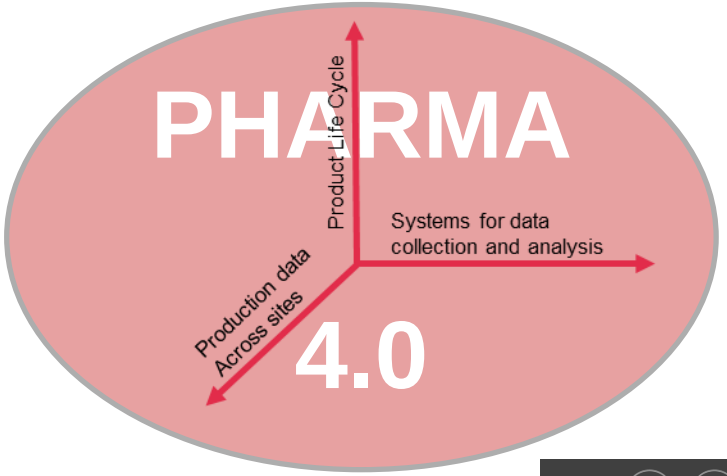
Pharma 4.0 - Transformation from Data to Knowledge, Understanding & Wisdom



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)



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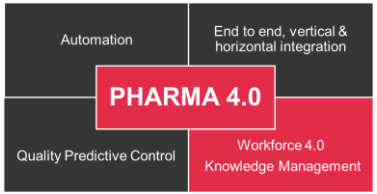
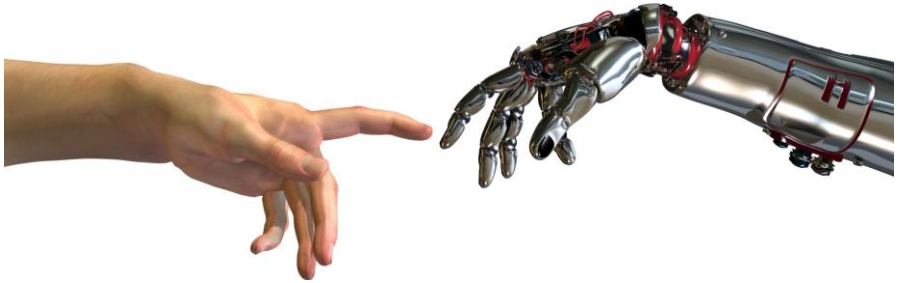
Workforce 4.0



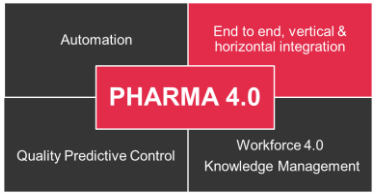
- New colleagues – Robots & Cobots
- Operation of Smart Devices
- Flexible operations monitoring & control
- A decentral smart device enables monitoring and operating from distance by operators and supervisors
- It simplifies changeover, setup, maintenance and life cycle management (being able to fast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

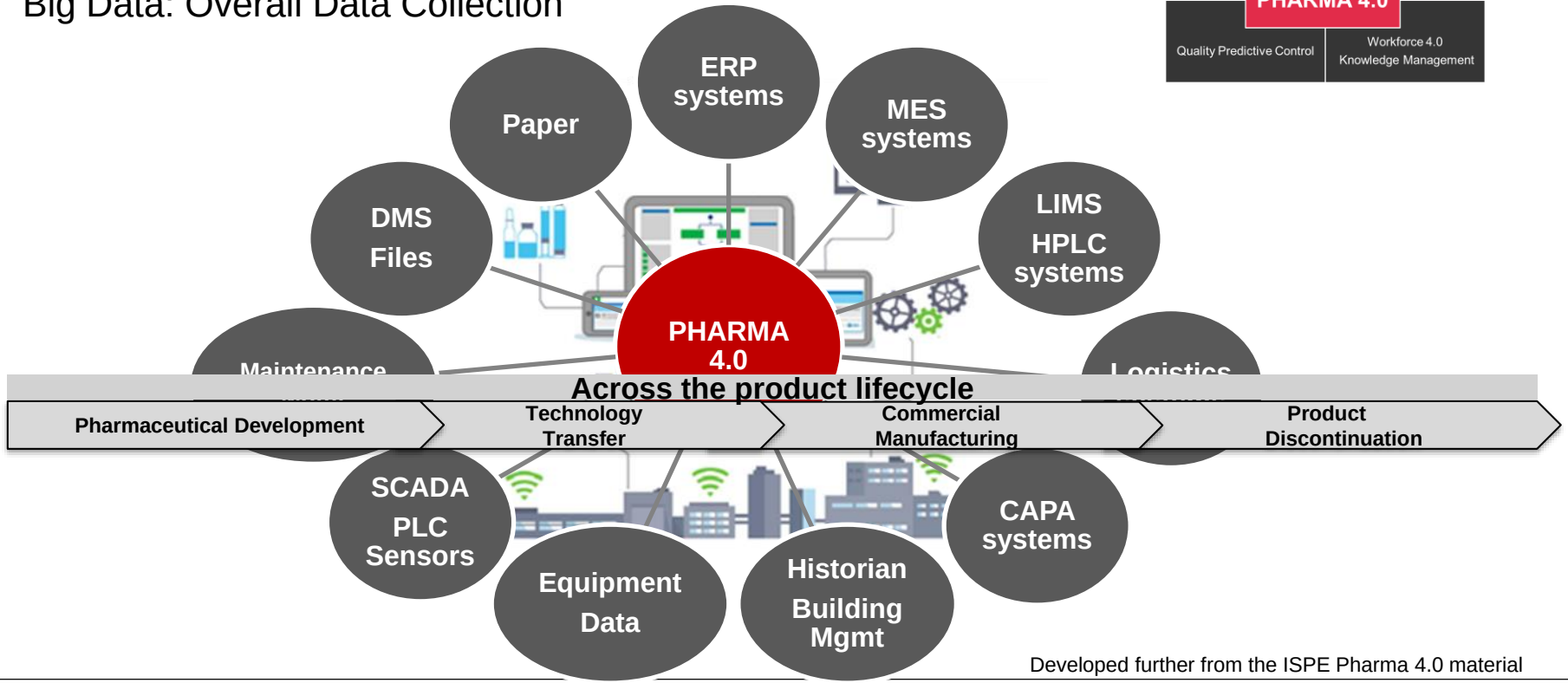


Developed further from the ISPE Pharma 4.0 material

End to End, Vertical & Horizontal Integration

Big Data: Overall Data Collection



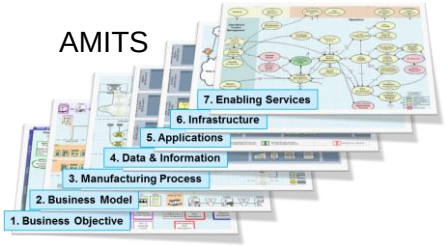


Developed further from the ISPE Pharma 4.0 material

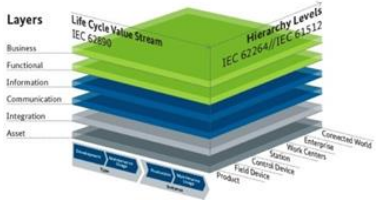
Automation

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

AMITS

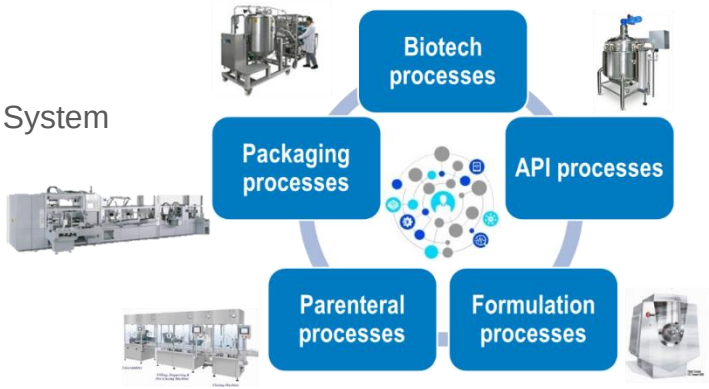


Industrie 4.0 Reference Model,
Smart Factory, IIoT



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

Manufacturing Control Strategy



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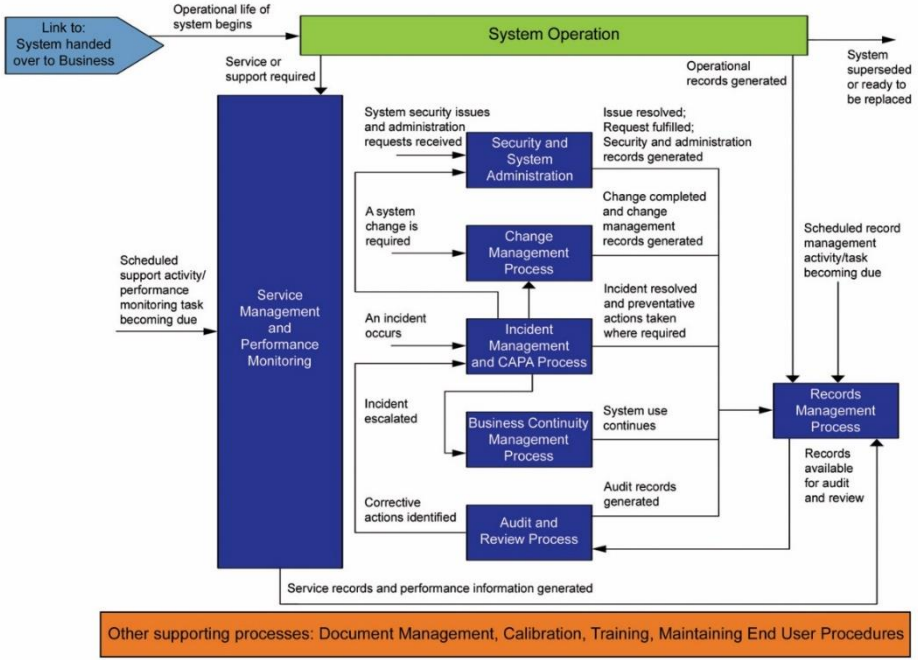
Data integrity impact on IT

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.”

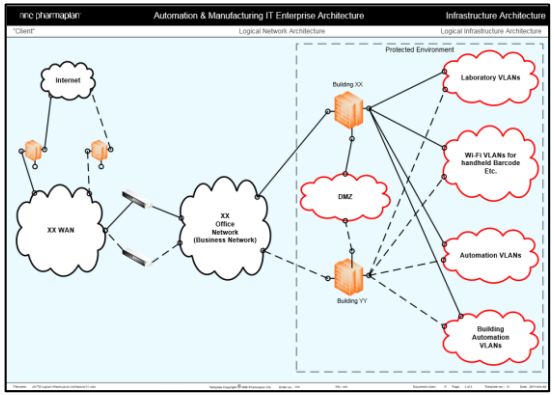
Source MHRA Medicines & Healthcare products Regulatory Agency (MHRA) “‘GXP’ Data Integrity Guidance and Definitions” March 2018

“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”

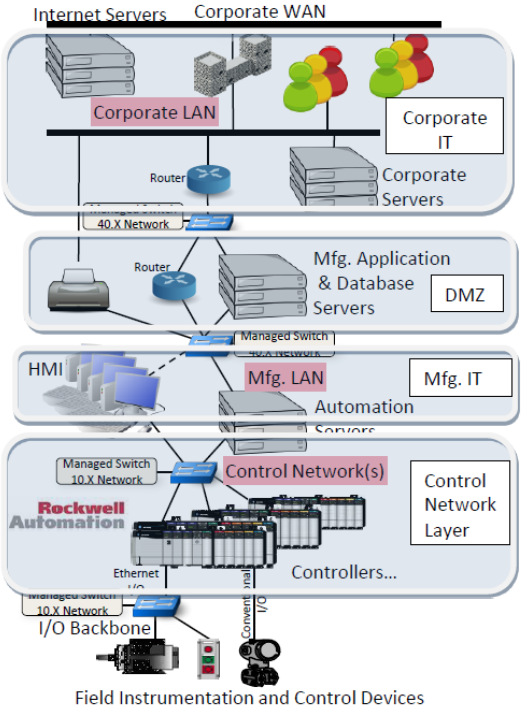
Changing the Manufacturing World through new and better connections - Example from Cisco

- People. Process. Data. Things. Yesterday, they functioned independently
- 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

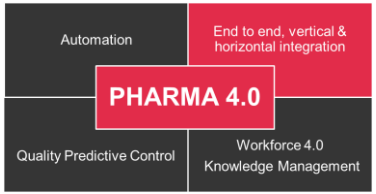


Cyber Security

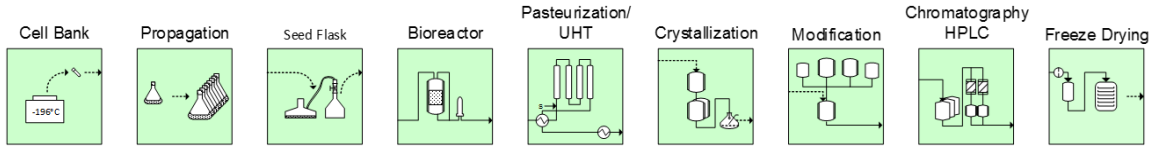
- Control System Infrastructure is now becoming a hacker target
- Automation Connectivity including Mobility and wireless - business needs are driving Integration
- Control System Technology (CST), definitely no longer proprietary
- Many Mfg. sites stop dead in their tracks without control systems on-line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



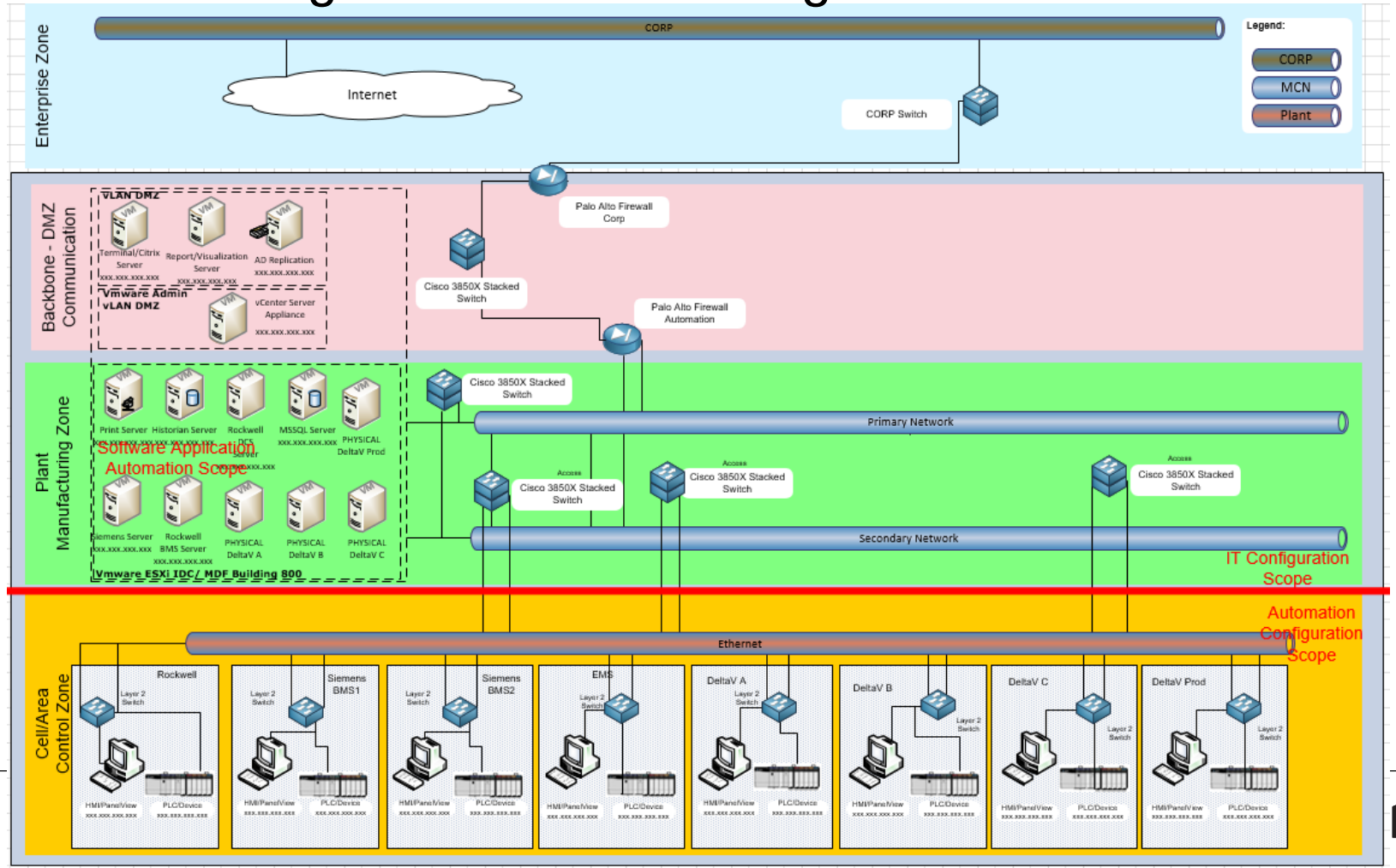
End-to-end Integration



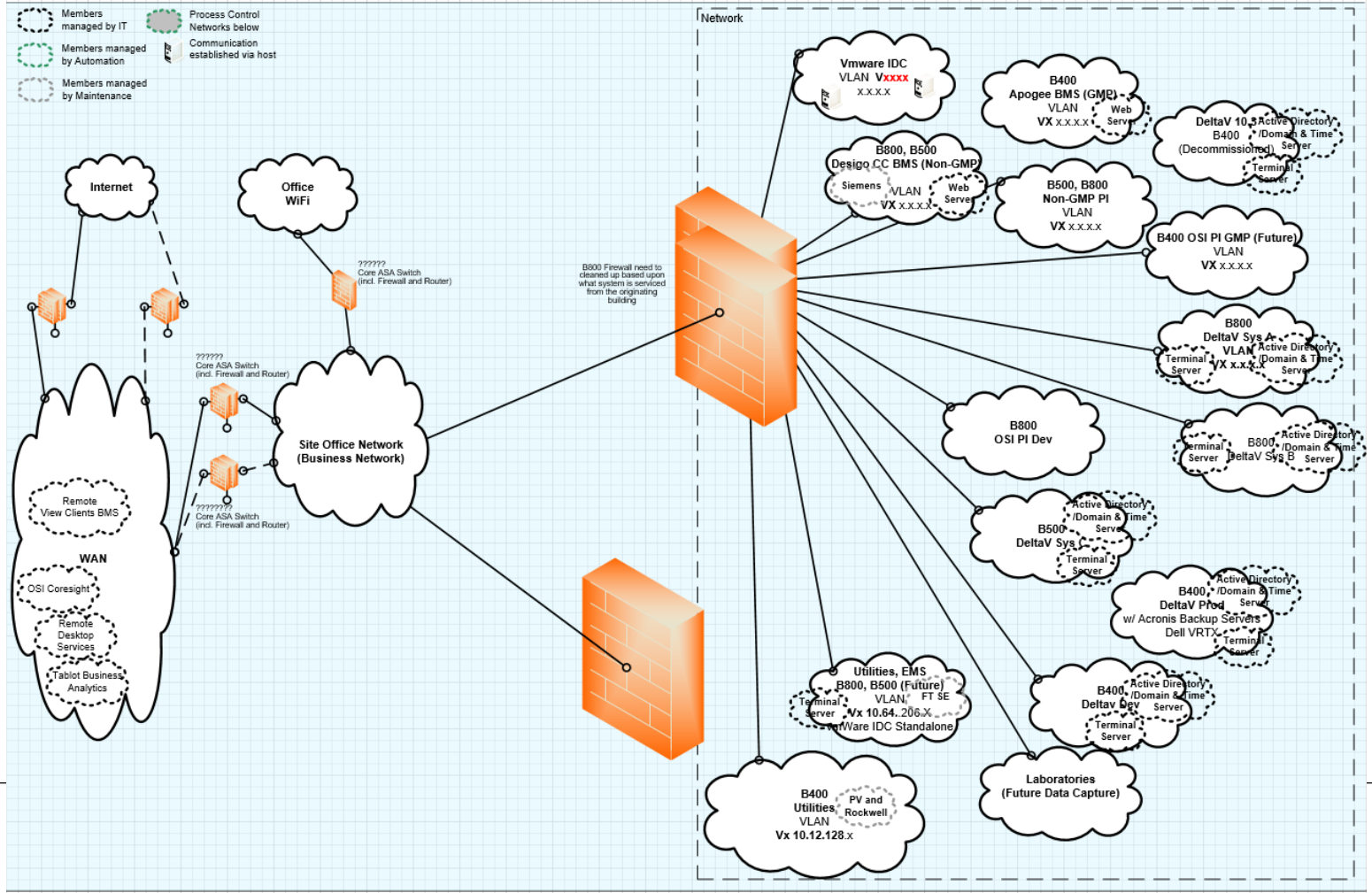
- Vertical integration enables holistic, data driven decisions in real-time supporting supervised data-driven models using machine learning
- Horizontal integration across the entire manufacturing process allowing for backward controls
- Data flow maps
- Design for Data Integrity



Manufacturing Infrastructure Design



Logical Infrastructure Design

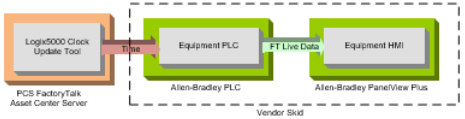


DataFlow Modeling

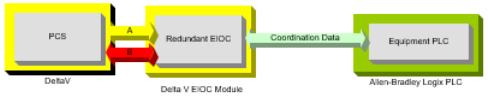
Vendor Supplied Detail Data Flow

VSC Data Flow

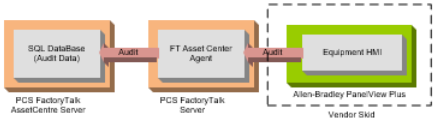
Time Synchronization Description



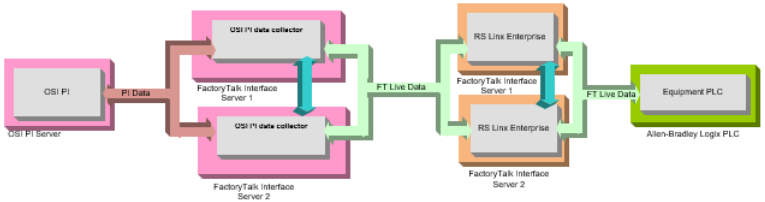
PCS to PLC



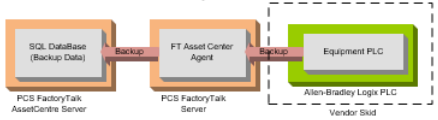
Audit Communication Description



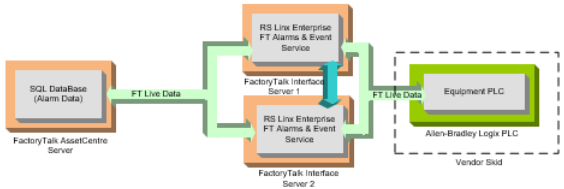
Time Series Communication Description

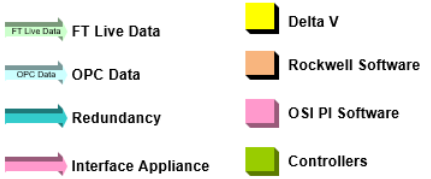


Software Management Communication Description



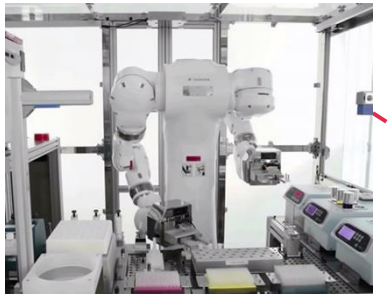
Alarm and Events Communication Description

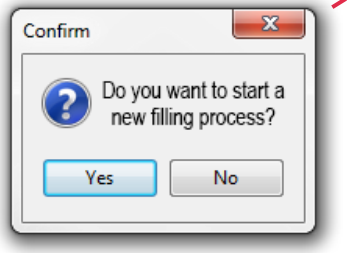




From the traditional to the Pharma 4.0 facility

Traditional		Pharma 4.0
Monolithic	→	Modular
Fixed locations	→	Changing locations
Unknown locations	→	Location sensing
Wired	→	Wireless
PLC	→	Power controllers
SCADA	→	Cloud based applications
Paper based SOPs	→	Holo lenses





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.

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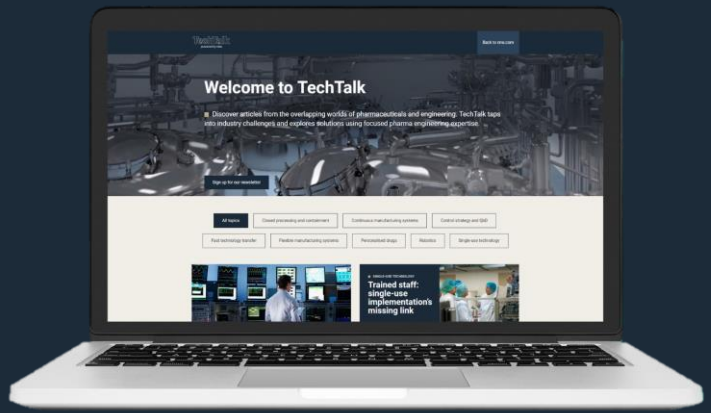

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Thank you

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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