FROM INDUSTRY 4.0 TO PHARMA 4.0

Pharma 4.0 Special Interest Group (SIG)
“Plug & Produce” Workgroup

Wolfgang Dedden, Wolfgang Winter

ALLOTROPE CONNECT WORKSHOP
WALDBRONN, 25-APR-2018
Executive Summary Pharma 4.0 "Plug & Produce"

**Initiative Summary**
- Work group initiated by ISPE DACH Special Interest Group "Pharma 4.0" (approx. 40 active participants)
- Define how "Industrie 4.0" approach, technology and benefits realized in industrial manufacturing can be applied to Pharma → "Pharma 4.0"

**Problem Statement**
- System integrations in pharma manufacturing (ISA 95 levels 2-3) are struggling with the lack of cross-vendor integration standards, resulting in high complexity and engineering effort for definition, implementation/deployment and validation.

**Opportunity Statement**
- Enable Quality & Data Integrity by Design by applying current, new and emerging technologies (connectivity and analytics) under a global "Plug & Produce" Standard
- Simplify, increase usability, reduce engineering effort for implementation and integration & enable end-to-end equipment integration, across Manufacturing, Laboratory / Analytical Devices, LIMS, Process Control Systems from the Sensor up to the long term data archive

**Next Steps and Focus Areas**
- Further assess existing standards and standardization initiatives (NAMUR, MESA, ZVEI, OPC-UA, Allotrope, etc.)
- Foster communication of Plug & Produce concept and status throughout 2018
- Plug & Produce Guidance Document (first white paper planned later in 2018)
- Define and execute Pilot Projects at Pharma organizations to prove the concept and feasibility
OUR VISION
New equipment to expand the production plant! How to connect this to the existing environment?
Why not like connecting a printer to a computer network? 👇 Plug and Produce → a future solution!
PLUG & PRODUCE WORKING GROUP
## Pharma 4.0 – Plug & Produce Workgroup

### Co-Chair

<table>
<thead>
<tr>
<th>Name</th>
<th>Vorname</th>
<th>Firma</th>
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<tbody>
<tr>
<td>Dedden</td>
<td>Wolfgang</td>
<td>Bayer AG</td>
</tr>
<tr>
<td>Sauermann</td>
<td>Klaus</td>
<td>Werum IT Solutions GmbH</td>
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### Core-Team

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<tr>
<th>Name</th>
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<tbody>
<tr>
<td>Buendia</td>
<td>Antonio</td>
<td>Novartis Pharma AG</td>
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<td>Eichmann</td>
<td>Thomas</td>
<td>Bioengineering</td>
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<td>Herta</td>
<td>Karol</td>
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<td>Krauß</td>
<td>Stefan</td>
<td>Siemens AG</td>
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<td>Kritzler</td>
<td>Uwe</td>
<td>F.Hoffmann-La Roche AG</td>
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<td>Maurer</td>
<td>Frank</td>
<td>Boehringer Ingelheim Pharma GmbH &amp; Co.KG</td>
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<td>Mayer</td>
<td>Martin</td>
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<td>Tapscott</td>
<td>Derrick</td>
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<td>Trapi</td>
<td>Josef</td>
<td>Takeda Pharmaceutical International AG</td>
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<td>Winter</td>
<td>Wolfgang</td>
<td>Agilent Technologies</td>
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<td>Wöbeling</td>
<td>Christian</td>
<td>Werum IT Solutions GmbH</td>
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### Extended Team

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<tr>
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<tr>
<td>Bahne</td>
<td>Andreas</td>
<td>Boehringer Ingelheim Pharma GmbH &amp; Co.KG</td>
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<td>Böhle</td>
<td>Thorsten</td>
<td>F. Hoffmann – La Roche AG</td>
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<td>Christmann</td>
<td>Ulrich</td>
<td>Bayer AG</td>
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<td>Fossler</td>
<td>Michael</td>
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<td>Geiger</td>
<td>Robert</td>
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<td>Günther</td>
<td>Kathrin</td>
<td>Uhlmann Pac-Systeme GmbH &amp; Co. KG</td>
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<td>Halfmann</td>
<td>Thomas</td>
<td>HGP</td>
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<td>Hanisch</td>
<td>Christian</td>
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<td>Hensel</td>
<td>Hartmut</td>
<td>Hochschule Harz</td>
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<td>Imisch</td>
<td>Martin</td>
<td>Rockwell Automation</td>
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<td>Kleinpeter</td>
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<td>Mediseal GmbH</td>
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<td>Messmer</td>
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<td>Moree</td>
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<td>Nagler</td>
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<td>Zimmer</td>
<td>Thomas</td>
<td>ISPE</td>
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<td>Zobel</td>
<td>Joachim</td>
<td>Novartis Pharma AG</td>
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Close to 40 active participants (and growing)
ISPE PHARMA 4.0 SIG Workgroups

Holistic Manufacturing Control Strategy

Focused on Product/Quality System with strong relationship to

Plug & Produce

Focused on system/equipment integration with strong relationship to

Allotrope
Pharma 4.0 Plug & Produce Workgroup Goals

Business Case
> Minimize equipment integration costs and total lifecycle cost through global Plug & Produce standard (focus on ISA-95 Levels 2-3)

Holistic Solution
> Create global, vendor-independent vertical & horizontal integration standard for ISA-95 L2 to Level 3, based on established standards & proven concepts (e.g. NAMUR, ZVEI, VDI, OPC-UA, MTP, MESA, Allotrope)

> Enable End-to-End Integration from sensor up to long term data archive: Incl equipment from manufacturing, lab devices, LIMS, Process Control (DCS, SCADA, Historians)

> Contribute Pharma & GMP specific requirements and use-cases - Quality & Data Integrity by Design

Plug & Play
> Module certification approach: Suppliers can easily certify new products
Lack of “Plug & Produce” integration scenarios for existing Pharma specific integration standards

Opportunity:
Simplify, increase usability, reduce engineering & validation efforts through “Plug & Produce”
Status Quo in Pharma Manufacturing: IT/OT Application-Focus

- Driver of shop floor execution related functionalities
- Allotrope for IPC / Offline Lab Analysis Results

Driver of supply chain & planning related functionalities

APO / PP-DS
ERP / PP-PI
Proposed PnP Approach for Pharma Production 4.0: Focus on Functions, not Applications!

**Preparation**
- ERP
  - Order Management
  - Rough Scheduling
  - Detailed Scheduling
  - Resource Management
  - Master Data Management
  - Information Management

**Execution**
- MES
  - Control Recipe Execution
  - [Trend] Data Management
  - Electronic Log Book
  - Alarm & Event Management
  - Visualization
  - Logic & Closed Loop Control

- DCS
  - What to make
    - Priority and/or dates
    - What materials to use
    - What equipment to use
    - What personnel to use
    - Production parameters (e.g., Color, Options,...)

**Reporting**
- ERP
  - MBR
  - EBR
  - BRR

  - Data Analytics
  - Manufacturing Intelligence
  - Reporting/Production Tracing

- User Management
  - CFR 21 Part 11
  - Data Integrity
  - Audit Trail

- [enhanced, predictive] Maintenance
- Equipment Management
- Reporting/Production Tracing

- What was made
  - What material was actually produced
  - What materials were actually consumed
  - Equipment used
  - Personnel used
  - Production data (e.g., Purity, density,...)
Interfacing the Functions Is Key for Quality by Design in Pharma 4.0

**Preparation**
- Order Management
- Rough Scheduling
- Detailed Scheduling
- Resource Management
- Master Data Management (including MBR)
- Information Management

**Execution**
- Equipment Management
- Control Recipe Execution
- [Trend] Data Management
- Electronic Log Book
- Alarm Management
- Visualization
- Logic & Closed Loop Control

**Orchestration**
- Reporting/Production Tracing
- Data Analytics
- Manufacturing Intelligence
  - [enhanced, predictive]
- Maintenance

**Quality Aspects**
- Reporting
- Production Tracing
- Data Integrity
- Audit Trail

**Reporting**
- User Management
- CFR 21 Part 11
- Data Integrity
- Audit Trail
End-to-End Integration for Digitalized Manufacturing Execution

Orchestration Layer (Functional Layer including Levels 2-4)

Data Presentation Layer

- ERP
- LIMS
- MES
- DCS
- SCADA

- Smart Equipment (Machines / PU's)
- Smart Devices (Actors / Sensors)
- HMI
- Report (e.g: EBR)
- Cockpit

Data Repository

- Material
- Recipe (MBR)
- Equipment
- ASSETS
-OBJECTS

Contextualization

- Engineer
- Scientist
Possible Plug and Produce Concept: From Data Generation to Report Rendering
Use Case Example: EBR execution on a Package Unit
## Collaboration with Other Initiatives

<table>
<thead>
<tr>
<th>Organization</th>
<th>Initiative</th>
<th>Description</th>
<th>ISPE Contribution</th>
<th>More Information</th>
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<tbody>
<tr>
<td>NAMUR</td>
<td>Namur Open Architecture (NOA)</td>
<td>Unlock Industry 4.0 potential for process industry</td>
<td>Pharma &amp; GxP specific definitions, requirements and use cases</td>
<td>Namur-WG 2.8 Automation Networks and Services</td>
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<td>ZVEI and NAMUR</td>
<td>Modular Automation (MA) Workgroup</td>
<td>MODULE TYPE PACKAGE (MTP) Service oriented interface for process control</td>
<td>Pharma &amp; GxP specific definitions, requirements and use cases</td>
<td>MTP Whitepaper From ZVEI, Automation Division <a href="mailto:seibl@zvei.org">seibl@zvei.org</a></td>
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<tr>
<td>The Open Group</td>
<td>Open Process Automation (OPA)</td>
<td>Develop standards-based, open, secure, interoperable process control architecture</td>
<td>Alignment</td>
<td><a href="http://www.opengroup.org/">http://www.opengroup.org/</a></td>
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<td>Allotrope Foundation</td>
<td>Allotrope Framework, Allotrope Partner Network</td>
<td>Standardized format, taxonomies, ontologies, data models, API for scientific data</td>
<td>Alignment – extend concept to include analytical device data in EBR</td>
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<td>BPOG</td>
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Leverage and Synergy on technical layer integration
Leverage and Synergy on functional layer integration

Fundamentals of a measurement workflow

Addressing the root causes

EBR relevant data interface requirements needed
SUMMARY
## Executive Summary Pharma 4.0 „Plug & Produce“

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Next Steps: Best Practice Guide to Enable Pharma 4.0 based on existing standards

**Opportunity:** Simplify, increase usability, reduce engineering & validation efforts through “Plug & Produce”
**ISPE Pharma 4.0 Plug and Produce Workgroup**

**Motivation:**
The application of Industry 4.0 in the pharma context will enable the vision of “A maximally efficient, agile, flexible pharmaceutical sector that reliably produces high quality products and services by a digitized, integrated & connected end to end supply chain.” This is what we call “Pharma 4.0.” The mission of “Pharma 4.0” is to “manufacture pharmaceutical products with maximum product & process understanding, data integrity by design, efficiency and optimal resource allocation on the basis of full digital data transparency - to the benefit of the patient.”

**Next Steps**
- Win further subject matter experts from industry, suppliers and consulting firms to volunteer for the working group
- Liaise with and assess existing standardization initiatives (NAMUR, MESA, ZVEI, OPC-UA, Allotrope, etc.)
- Socialize ideas and concepts for Plug and Produce with broader audience
- Presentations at industry conferences (ISPE, Allotrope Connect)
- Publish a first Plug & Produce Guidance Document in 2018
- Pilot Project at Pharma organizations to prove the concept and feasibility

**Plug and Produce Chair:**
Klaus Sauermann, Werum IT Solutions GmbH
Wolfgang Dedden, Bayer AG

**What Is Plug and Produce About?**
Plug and Produce contributes pharma-specific requirements to Industry 4.0-related initiatives in order to define the necessary enablements for end-to-end integration, QbD and Data Integrity by Design → Pharma 4.0

**Key Considerations**
- System and access security
- Data integrity by design
- Traceability from the raw data up to the approved batch specific released data
- Meeting regulatory expectations to provide batch record reports and performing annual product reviews

**Synergies and Collaborations**
The Plug and Produce workgroup is planning to create a global, supplier independent vertical & horizontal integration standard for ISA-95 Level 2-3, based on already established standards & proven technologies & concepts such as NAMUR, MESA, OPC-UA, leveraging activities already undertaken or underway by NAMUR, VDE, VDI, OPC Foundation and the Allotrope Foundation.

**Summary**
The intent is to simplify and increase usability significantly, while reducing engineering effort for implementation and integration & enable end-to-end equipment integration, across Manufacturing, Laboratory / Analytical Devices, LIMS, Process Control Systems. The vision is to achieve horizontal and vertical integration from the sensor/device up to the long-term data archive to realize the full potential of “Pharma 4.0”.

**Plug and Produce Core Team**
Antonio Buendia, Novartis Pharma AG / Thomas Eichmann, Bioengineering / Karol Herta, Merck KGaA / Stefan Knauß, Siemens AG / Uwe Kritzler, F.Hoffmann-La Roche AG / Frank Maurer, Boehringer Ingelheim Pharma GmbH & Co.KG / Martin Meyer, evon GmbH / Derrick Tapscott, Rockwell Automation UK / Josef Traut, Takeda Pharmaceutical International AG / Wolfgang Winter, Agilent Technologies / Christian Wölbeling, Werum IT Solutions GmbH
Questions?
Thank you for your attention!

ISPE Special Interest Group
“PHARMA 4.0”

Working Group:
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