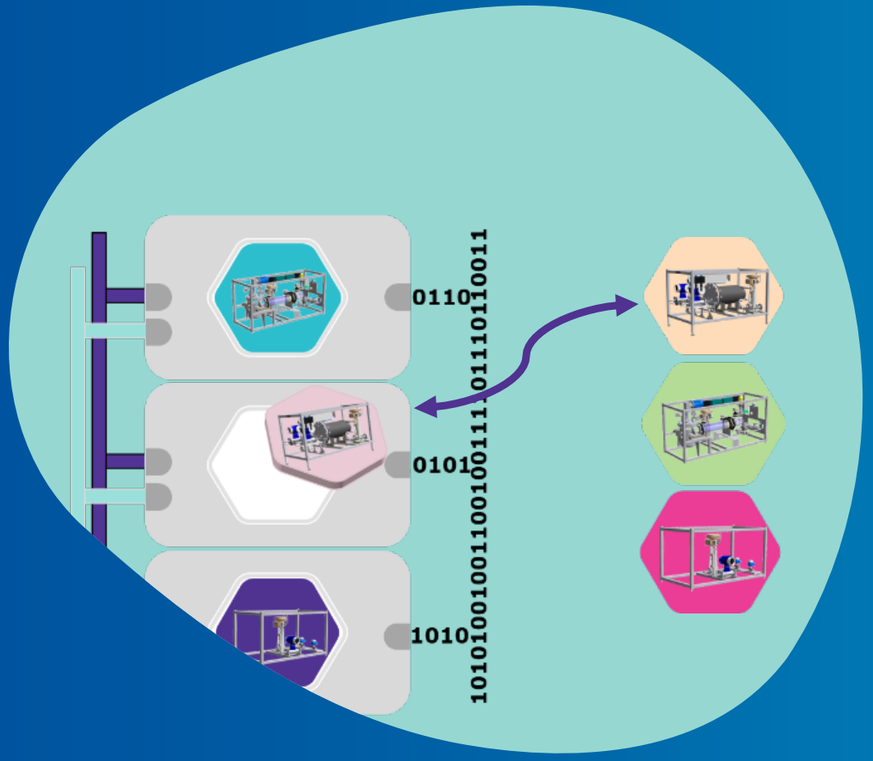


Unlocking Efficiency & Flexibility

The Power of Modular Automation in Process Development Labs

ISPE Boston Product Show 2024

October 2nd , 2024

Giuseppe Menin
Director Life Sciences & Process Industry

ISPE Pharma 4.0 CoP – Plug&Produce Working Group
GAMP Italy CoP - Steering Committee

COPADATA

ISPE® | Boston Area Chapter

PRODUCT SHOW

MERCK

A vibrant science and technology company

Every day, our more than **66,000 employees** work in **66 countries** to make a positive difference to millions of people's lives by creating more joyful and sustainable ways to live.

We are known as **Merck** internationally except for the United States and Canada, where we operate as **EMD Serono** in the biopharmaceutical business, **MilliporeSigma** in the life science business and **EMD Electronics** in the high-tech materials business.

Healthcare

- Pioneer in cancer treatment
- Advancing care in immunology
- Global market leader in **fertility treatments**
- Robust R&D pipeline
- We deliver **personalized treatments** for serious diseases

Life Science

- Trusted supplier and partner for the scientific community
- From research to large scale production with **>300,000 products**
- Novel technologies and world-class solutions driving discoveries

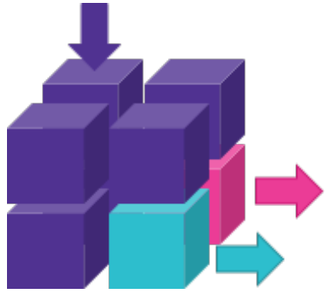
Electronics

- Innovations to change the way we access, store, process and display data
- Enabler of **new generation** electronic products for our everyday lives
- Suppler of innovative, functional and decorative pigments

Different Dimensions of Flexibility

Flexibly Adapt Operations to Changing Demands

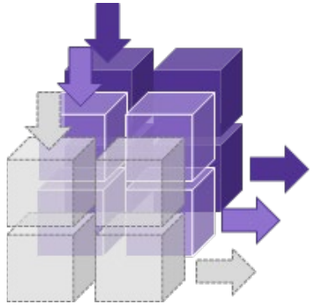
Product Flexibility



- Ability to **adapt the production system** to switch from one product to the another

Flexible Product Portfolio

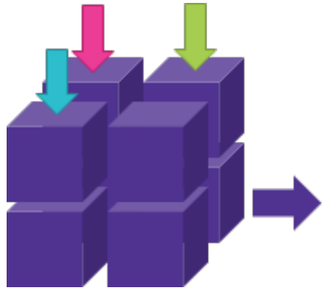
Capacity Flexibility



- Ability to **scale up/out and down in production volume** based on actual and forecasted market demand

Flexible Output

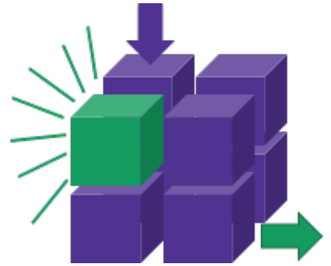
Parameter Flexibility



- Ability to **assure stable and robust operation** of the facility through broad parameter space as well as **rapid and precise adaptation of the parameters**

Flexible Operating Points

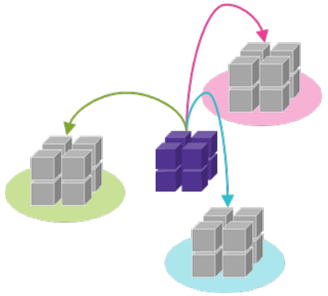
Innovation Flexibility



- Ability to easily adapt small-scale plants in R&D to pilot setting to **rapidly try out innovative products and processes**

Agile Process Development

Location Flexibility



- Ability to **move a production plant from one place to another** because of market conditions, proximity to customers or resources

Flexible Supply Network

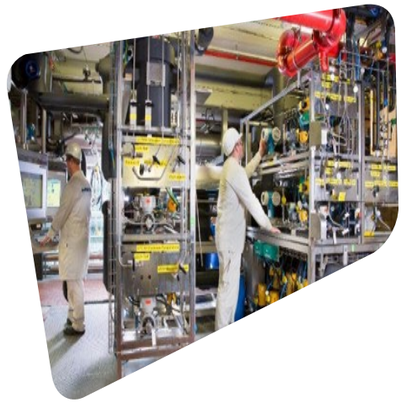
Source: TNO 2015 R10756: Small-scale flexible plants – Towards a more agile and competitive EU chemical industry, 08. June 2015

How to fulfill flexibility demands from labs to production?

Early development: Route Scouting

Lab Scale: Proof of Concept

Pilot Scale: Proof of Process



Production Scale: Standard Production

Classical Automation solutions are inadequate:

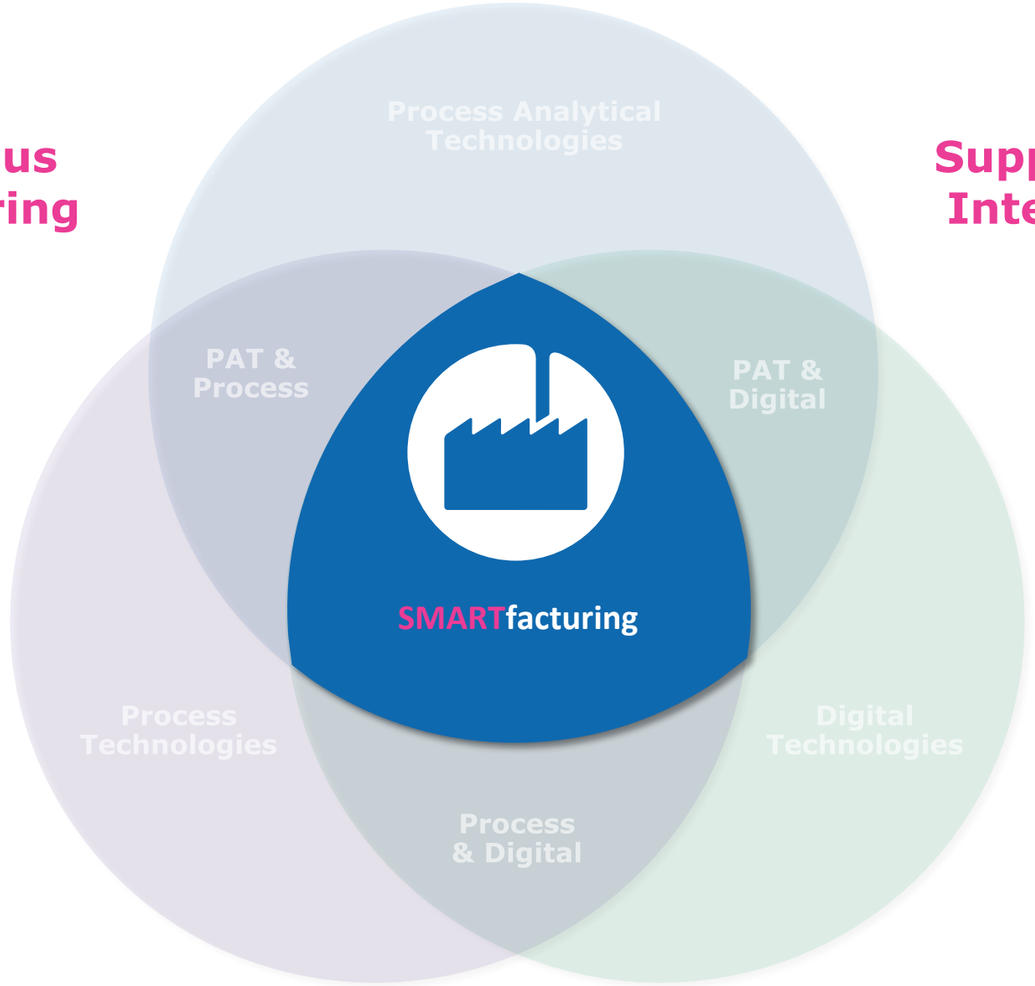
- Customized integrations / Vendors locks / low interoperability
- Requires high automation skills
- Complex scale-up: lab → pilot → production
- Qualification/Validation cost

Evolution from MANUfacturing to SMARTfacturing

1. Foundation **2. Convergence**

Autonomous Manufacturing

Supply Chain Intelligence



Quality by Design

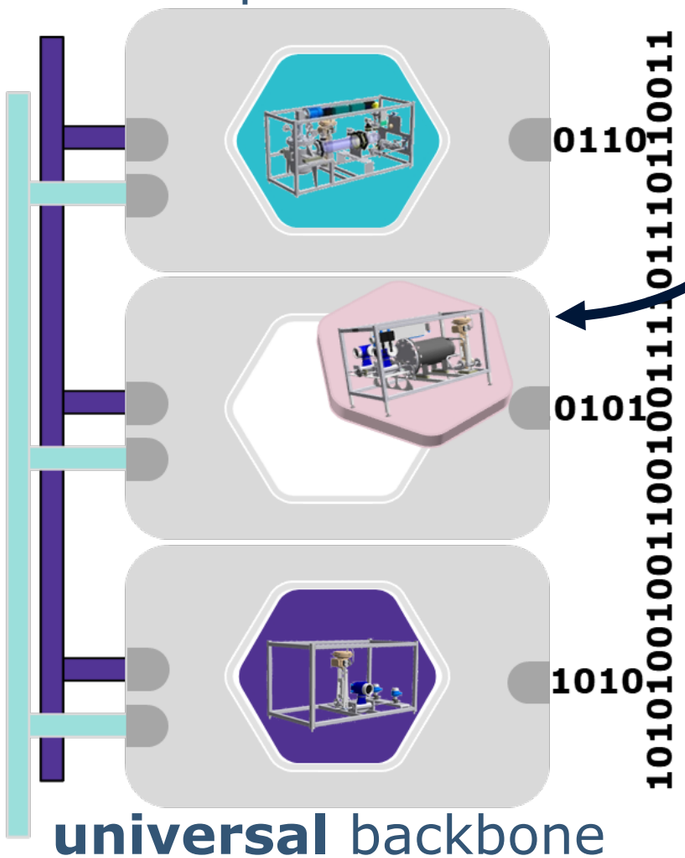
Modular Plant

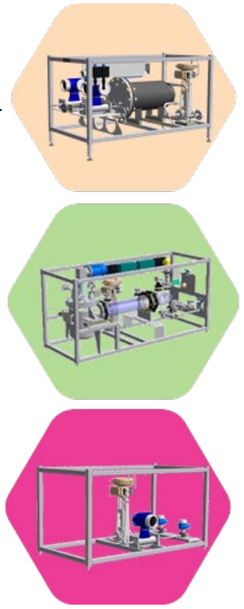
Modular Plant concept

Over 100 modules built

Highly automated platform

Pool of **specifically optimized** modules





- **Low Conversion cost**
- **Flexibility**

Break the paradox

between **flexibility** and **efficiency**.

pre-qualified modules are hooked into the production eco system

Darmstadt Technology Center goes digital

60 hoods equipped with Modular Automation MTP in process development

- Modular approach enables the necessary flexibility and diversity in the laboratory environment
- Automation software platform enables more efficient interaction between R&D and production in pilot plant
  - **Vendor independent** software for modules and process orchestration
- Market launches of new products accelerated by up to 50%

Key project figures

Number of sites	3
Users involved	Process Development & IT (overall for 3 sites: 50-70 users)
Installed Modules types	Over 100
Number of connected Devices	Pilot project: 10, Final Deployment: 150
Overall realization time	Pilot: 6 Months Final deployment after 1 ½ years Schedule timeline: 2019 .. 2021

https://www.merckgroup.com/en/news/introduction-of-modular-automation-for-laboratories-14-07-2002.html

Advantages of modularization

Modularization combines the flexibility of production with high efficiency and low cost

FASTER TIME-TO-MARKET

ENGINEERING EFFORT

INCREASED FLEXIBILITY

CARBON FOOTPRINT REDUCTION

Source: NAMUR, ZVEI, Merck

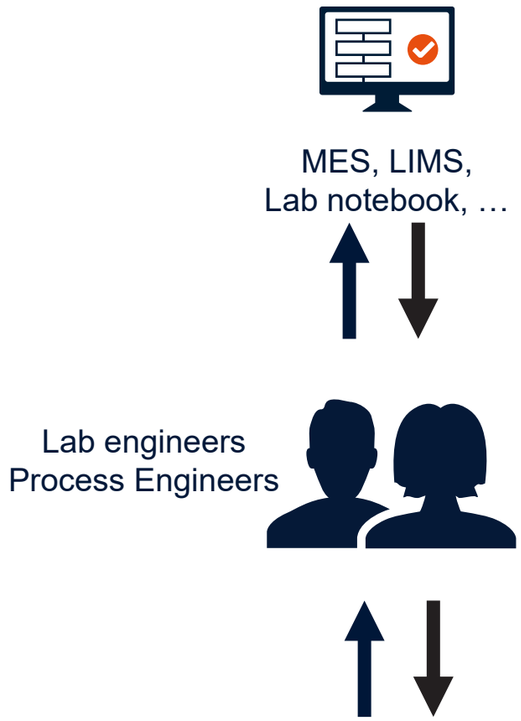
Modular Automation
With MTP (Module Type Package)

At Merck Darmstadt.

Challenges integrating lab devices.

- Lab engineers, follow work instructions:
  - must manually set instrument configuration
  - read the result
  - copy the values on paper or on PC application.
  - A "**Paper on Glass**" approach that could generate Data Integrity issues.

- Instruments can be used for different test / experiments: frequent reconfiguration of instrument setup.



Instrument, process modules

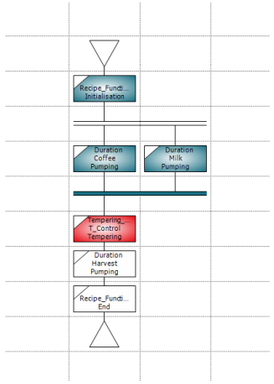
General requirements digitalizing a laboratory or a pilot plant

Sequential execution of modules operation

2

Common HMI

3



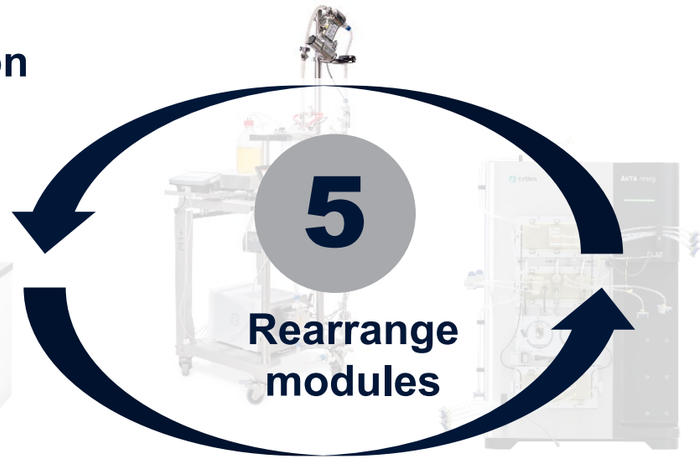
4

Archive Lot information:

- **Process values**
- **Alarms**
- **Audit Trails**

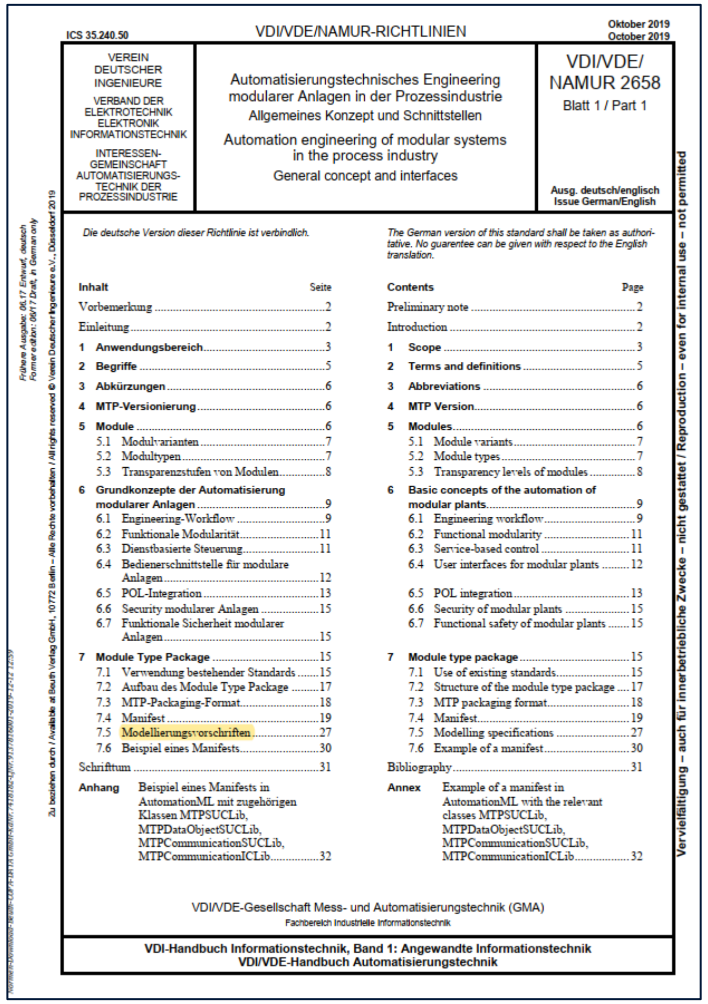
1

Bidirectional communication



What is MTP (Module Type Package)?

- MTP is a vendor independent description of production modules.
- It is the foundation for modular plant engineering by a «Plug & Produce» approach.
- Concept defined and promoted by NAMUR, an international association of companies active in process industry.
- Ref: VDI/VDE/NAMUR 2658 - IEC 63280



ICS 35.240.50

VDI/VDE/NAMUR-RICHTLINIEN

Oktober 2019
October 2019

VEREIN DEUTSCHER INGENIEURE
VERBAND DER ELEKTROTECHNIK ELEKTRONIK INFORMATIONSTECHNIK
INTERESSEN-GEMEINSCHAFT AUTOMATISIERUNGS-TECHNIK DER PROZESSINDUSTRIE

Automatisierungstechnisches Engineering modularer Anlagen in der Prozessindustrie
Allgemeines Konzept und Schnittstellen

Automation engineering of modular systems in the process industry
General concept and interfaces

VDI/VDE/ NAMUR 2658
Blatt 1 / Part 1

Ausg. deutsch/englisch
Issue German/English

Die deutsche Version dieser Richtlinie ist verbindlich.

The German version of this standard shall be taken as authoritative. No guarentee can be given with respect to the English translation.

Inhalt Seite

Contents Page

VDI/VDE-Gesellschaft Mess- und Automatisierungstechnik (GMA)
Fachbereich Industrielle Informationstechnik

VDI-Handbuch Informationstechnik, Band 1: Angewandte Informationstechnik
VDI/VDE-Handbuch Automatisierungstechnik

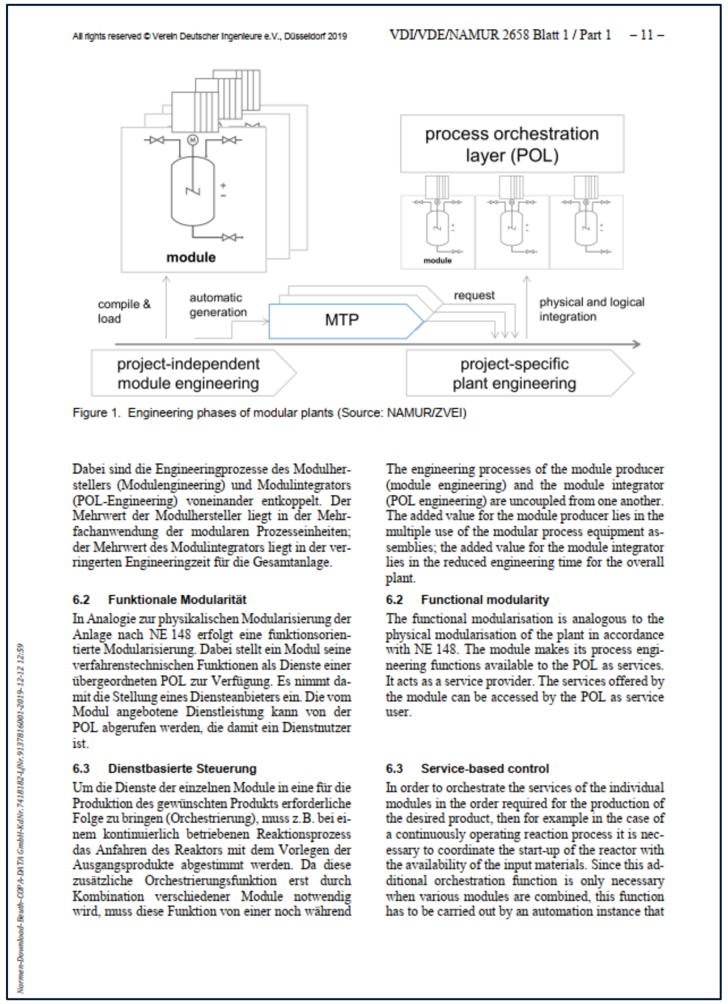


Figure 1. Engineering phases of modular plants (Source: NAMUR/ZVEI)

Dabei sind die Engineeringprozesse des Modulherstellers (Modulengineering) und Modulintegrators (POL-Engineering) voneinander entkoppelt. Der Mehrwert der Modulhersteller liegt in der Mehrfachanwendung der modularen Prozesseinheiten; der Mehrwert des Modulintegrators liegt in der verringerten Engineeringzeit für die Gesamtanlage.

The engineering processes of the module producer (module engineering) and the module integrator (POL engineering) are uncoupled from one another. The added value for the module producer lies in the multiple use of the modular process equipment assemblies; the added value for the module integrator lies in the reduced engineering time for the overall plant.

6.2 Funktionale Modularität

In Analogie zur physikalischen Modularisierung der Anlage nach NE 148 erfolgt eine funktionsorientierte Modularisierung. Dabei stellt ein Modul seine verfahrenstechnischen Funktionen als Dienste einer übergeordneten POL zur Verfügung. Es nimmt damit die Stellung eines Diensteanbieters ein. Die vom Modul angebotene Dienstleistung kann von der POL abgerufen werden, die damit ein Dienstnutzer ist.

6.2 Functional modularity

The functional modularisation is analogous to the physical modularisation of the plant in accordance with NE 148. The module makes its process engineering functions available to the POL as services. It acts as a service provider. The services offered by the module can be accessed by the POL as service user.

6.3 Dienstbasierte Steuerung

Um die Dienste der einzelnen Module in eine für die Produktion des gewünschten Produkts erforderliche Folge zu bringen (Orchestrierung), muss z.B. bei einem kontinuierlich betriebenen Reaktionsprozess das Anfahren des Reaktors mit dem Vorlegen der Ausgangsprodukte abgestimmt werden. Da diese zusätzliche Orchestrierungsfunktion erst durch Kombination verschiedener Module notwendig wird, muss diese Funktion von einer noch während

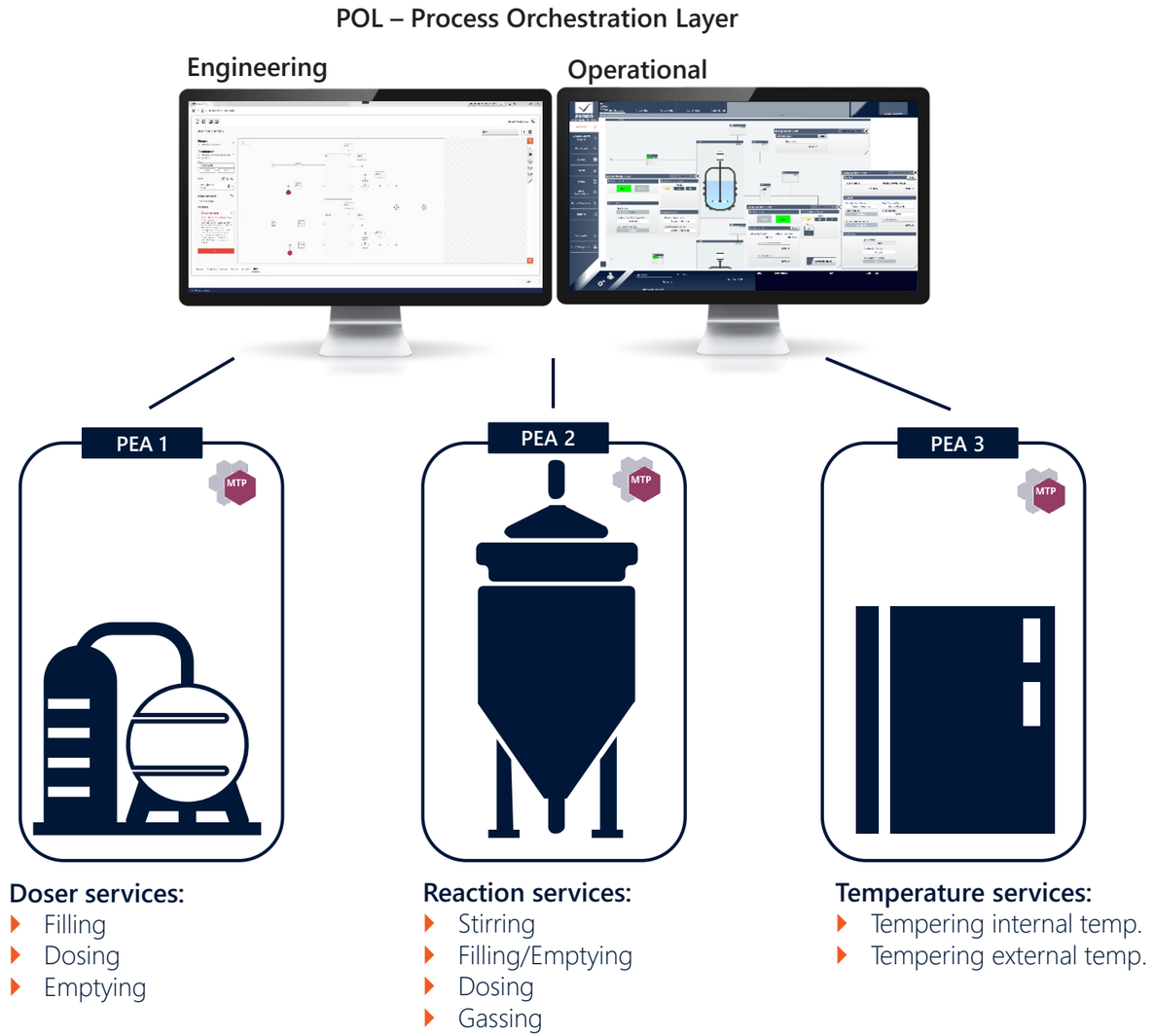
6.3 Service-based control

In order to orchestrate the services of the individual modules in the order required for the production of the desired product, then for example in the case of a continuously operating reaction process it is necessary to coordinate the start-up of the reactor with the availability of the input materials. Since this additional orchestration function is only necessary when various modules are combined, this function has to be carried out by an automation instance that

Module Type Package: The components

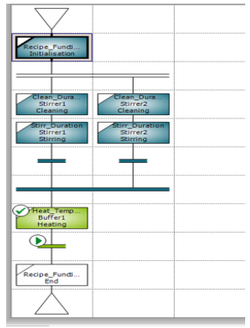
POL
Process Orchestration Layer

PEA
Process Equipment Assembly

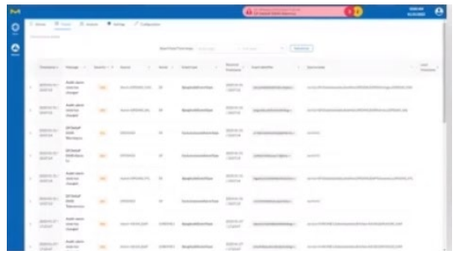


MTP Manifest: the “passport” of the PEA module

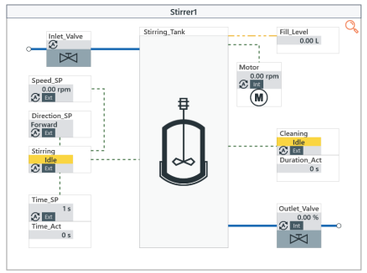
MTP file describes the module characteristics in a standard form.



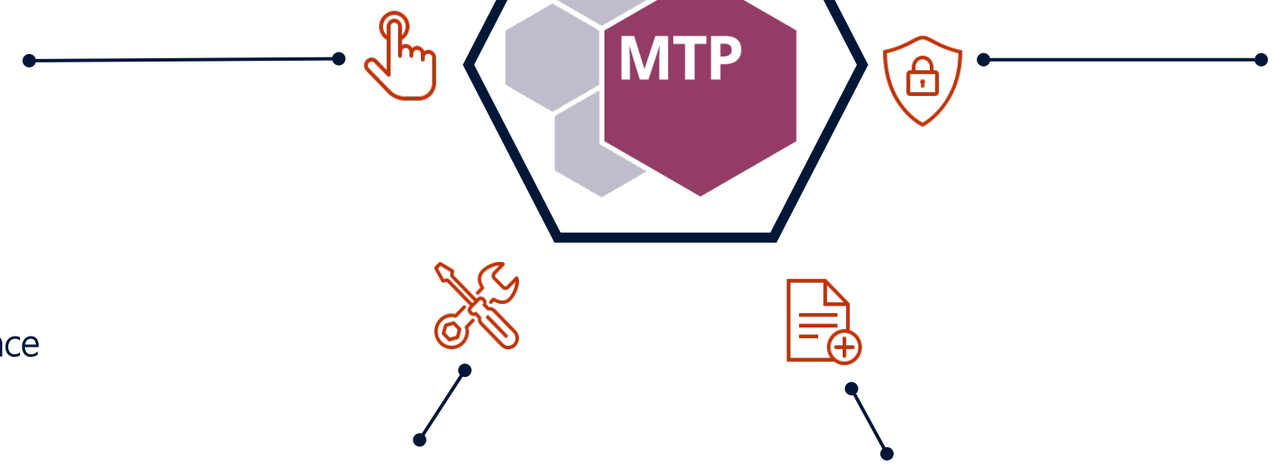
PEA Services & Control parameters
(e.g. for Recipes)



PEA Alarms & Events



PEA Human Machine Interface
(e.g. Description of P&IDs)



PEA Safety & Security Information
(NAMUR standard in progress)

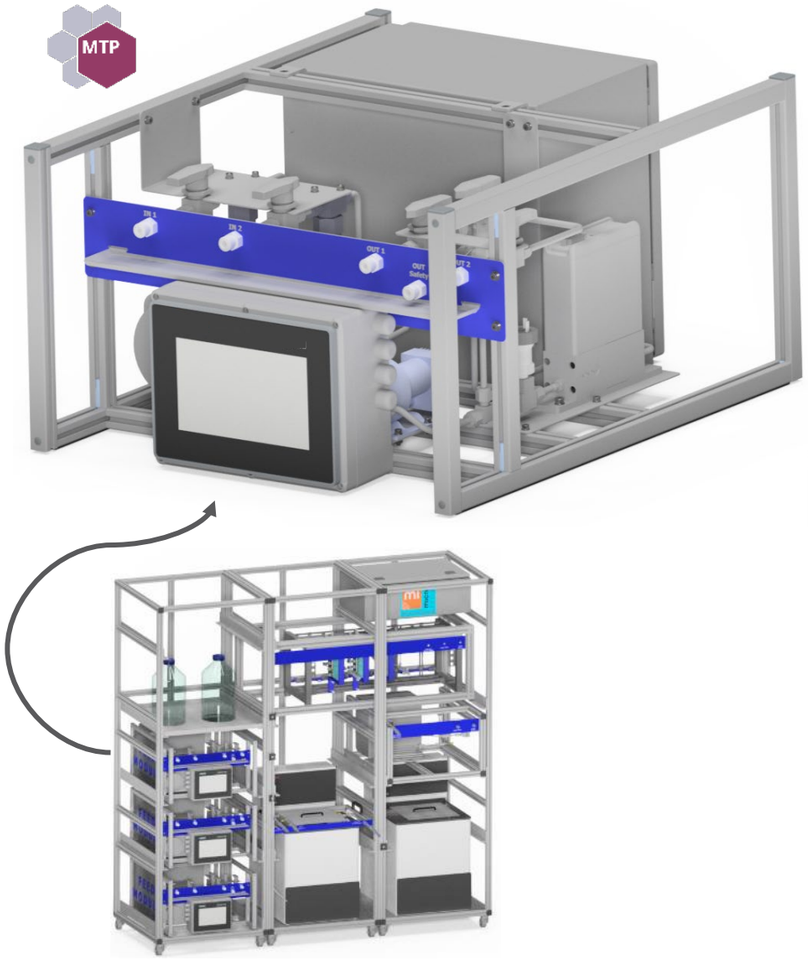
PEA Diagnosis & Maintenance
information
(NAMUR standard in progress)

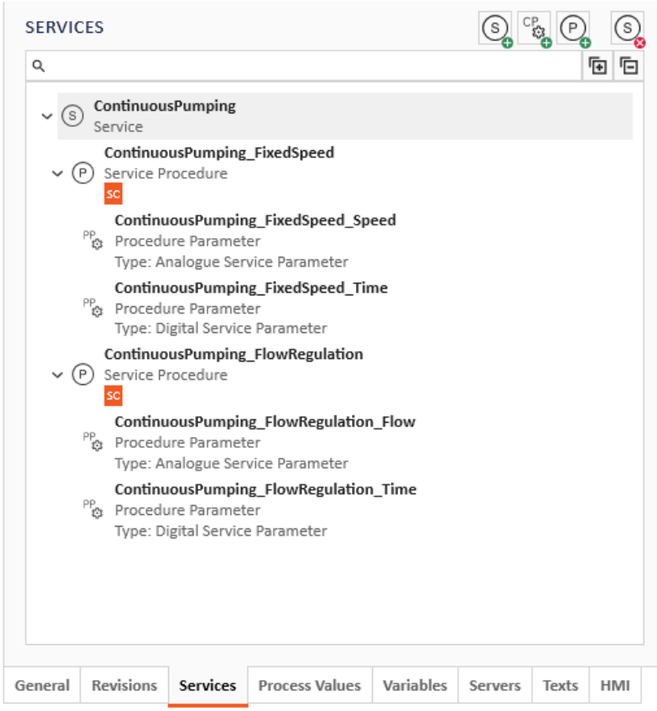
Further aspects for
standardization

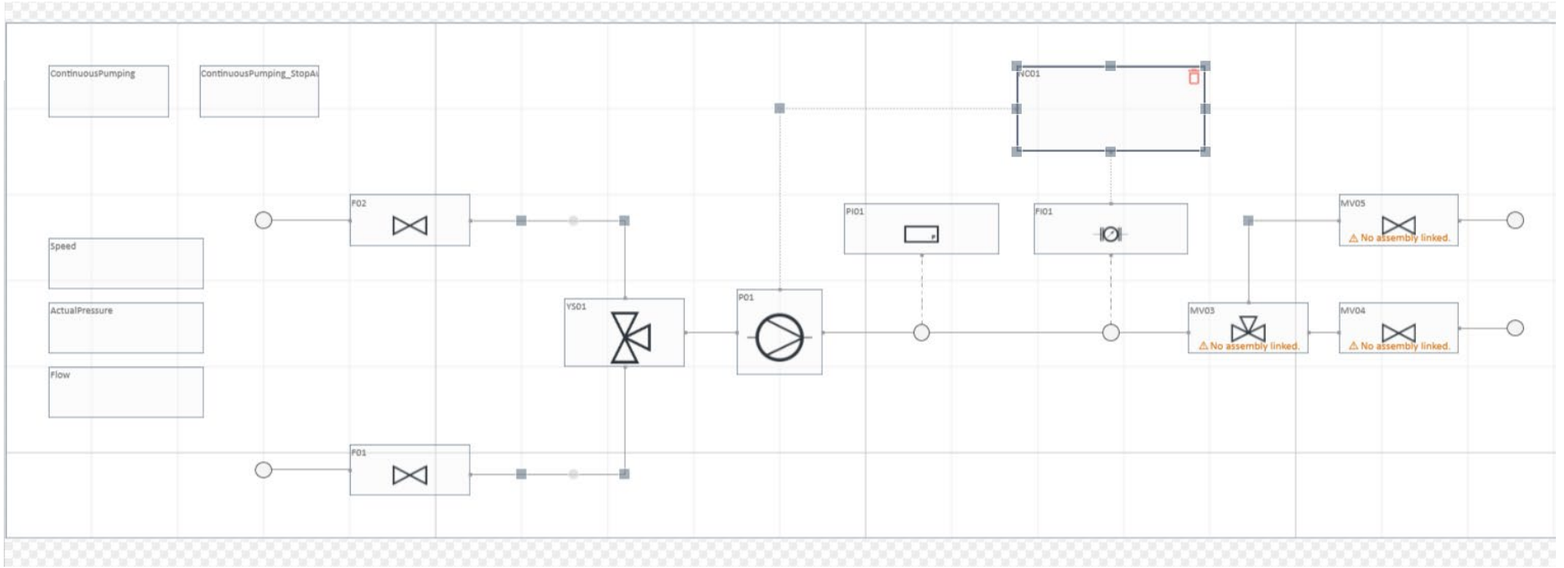
Source: VDI/VDE/NAMUR 2658

PEA example: Microinnova FlowKiloLab

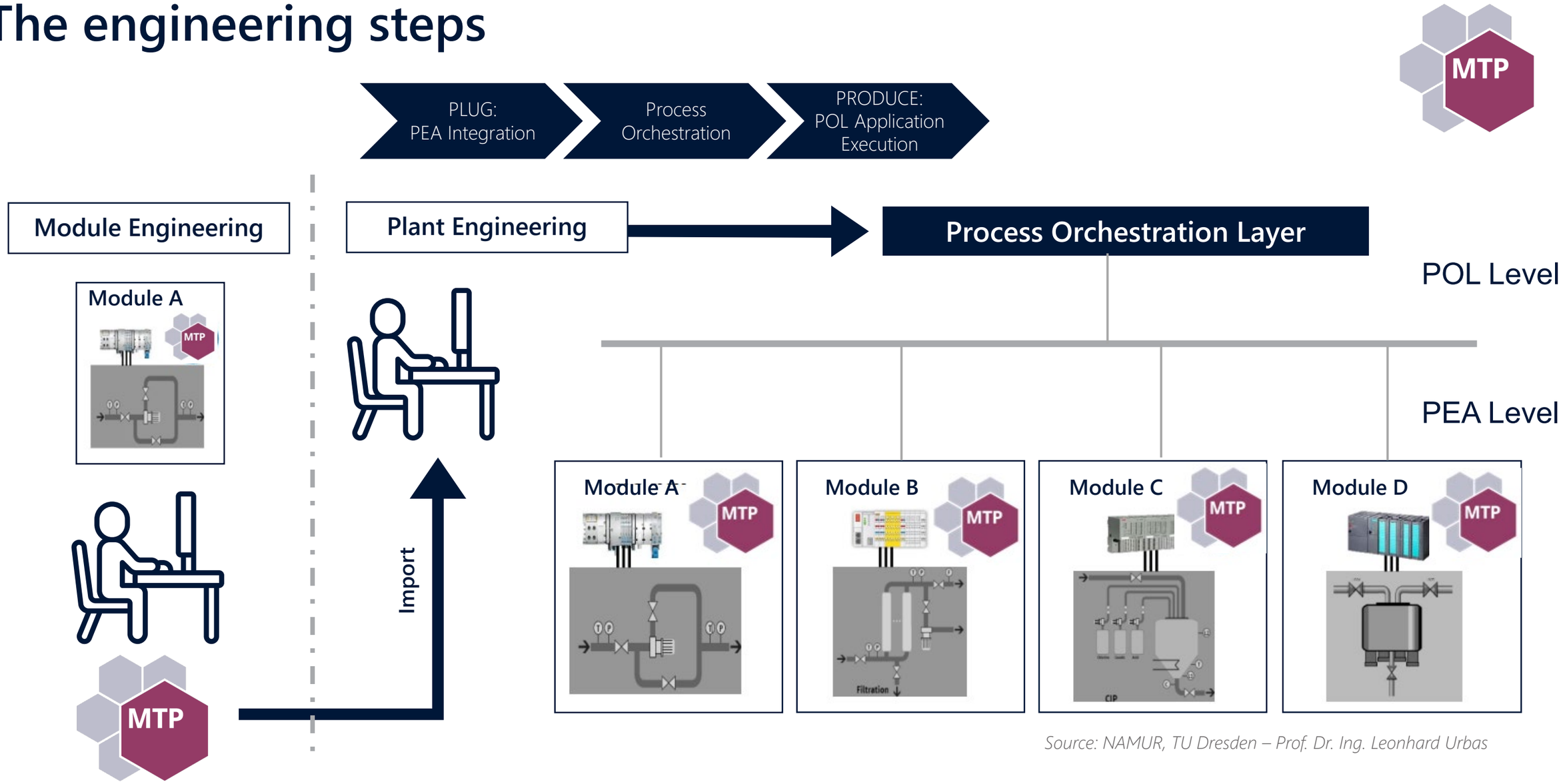
Information defined in the MTP Manifest file.







The engineering steps



Source: NAMUR, TU Dresden – Prof. Dr. Ing. Leonhard Urbas


POL
PEA

API Production - Modular Plant 30l/h

PEA1
2 Dosing Unit

PEA2
2 Dosing Unit

PEA3
Reaction Module

PEA4
Product Module
Temp. / Press. ctrl

How to generate a Process Orchestration Application?

MTP POL application generation in 3 steps

Plug & Produce

Mixer

Pump

pH meter

T Control

MTP

MTP

MTP

MTP

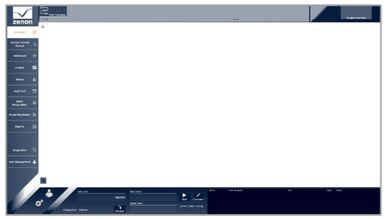
1

Import PEA MTP files
PEA instances configuration

Variable to be shared with POL
Variables for historian configuration
OPC UA server setting
…

2

Process Orchestration
Connect PEAs



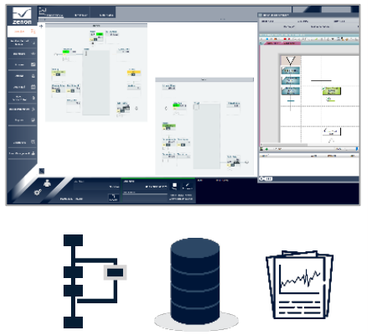
POL Template Project
zenon prj including
basic settings, functions
and common configuration.

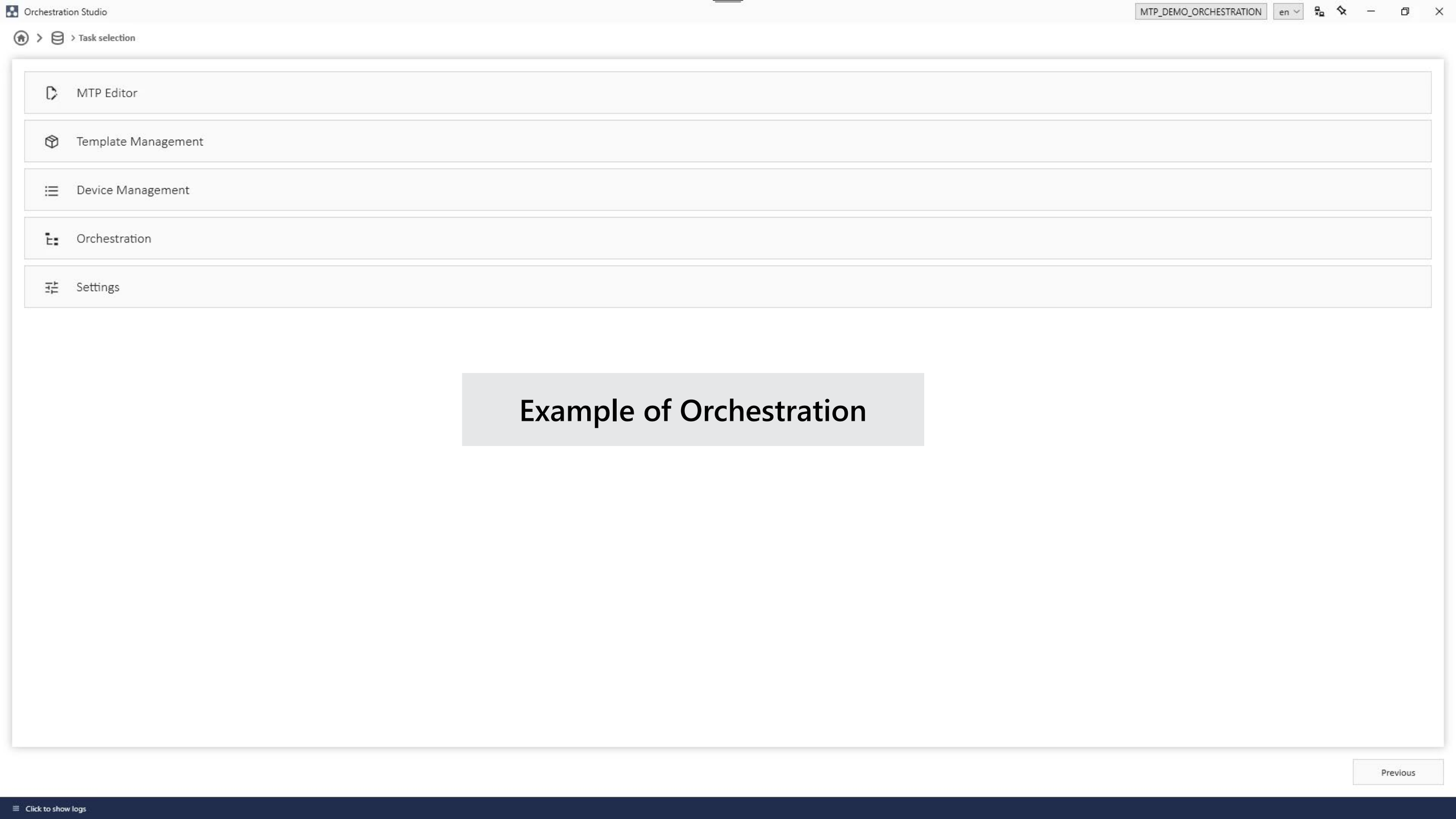
POL Application Generation

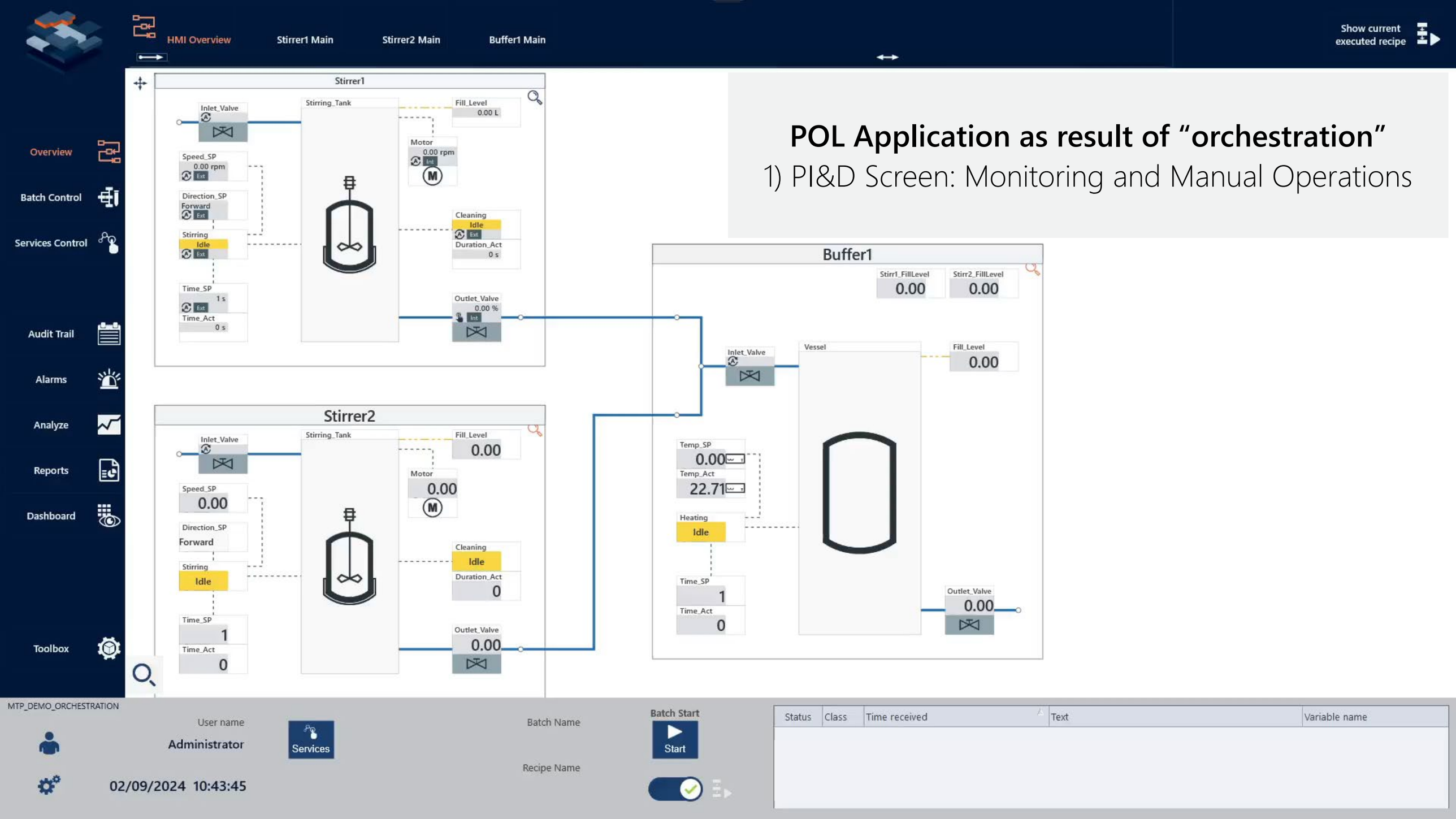
Smart Objects integration & config.
PI&D screens
PEA Manual control faceplates
ISA88 phases generation
ISA88 batch engine
Historian Configuration
Alarm
Audit Trail
Reporting

3

Generated POL Application

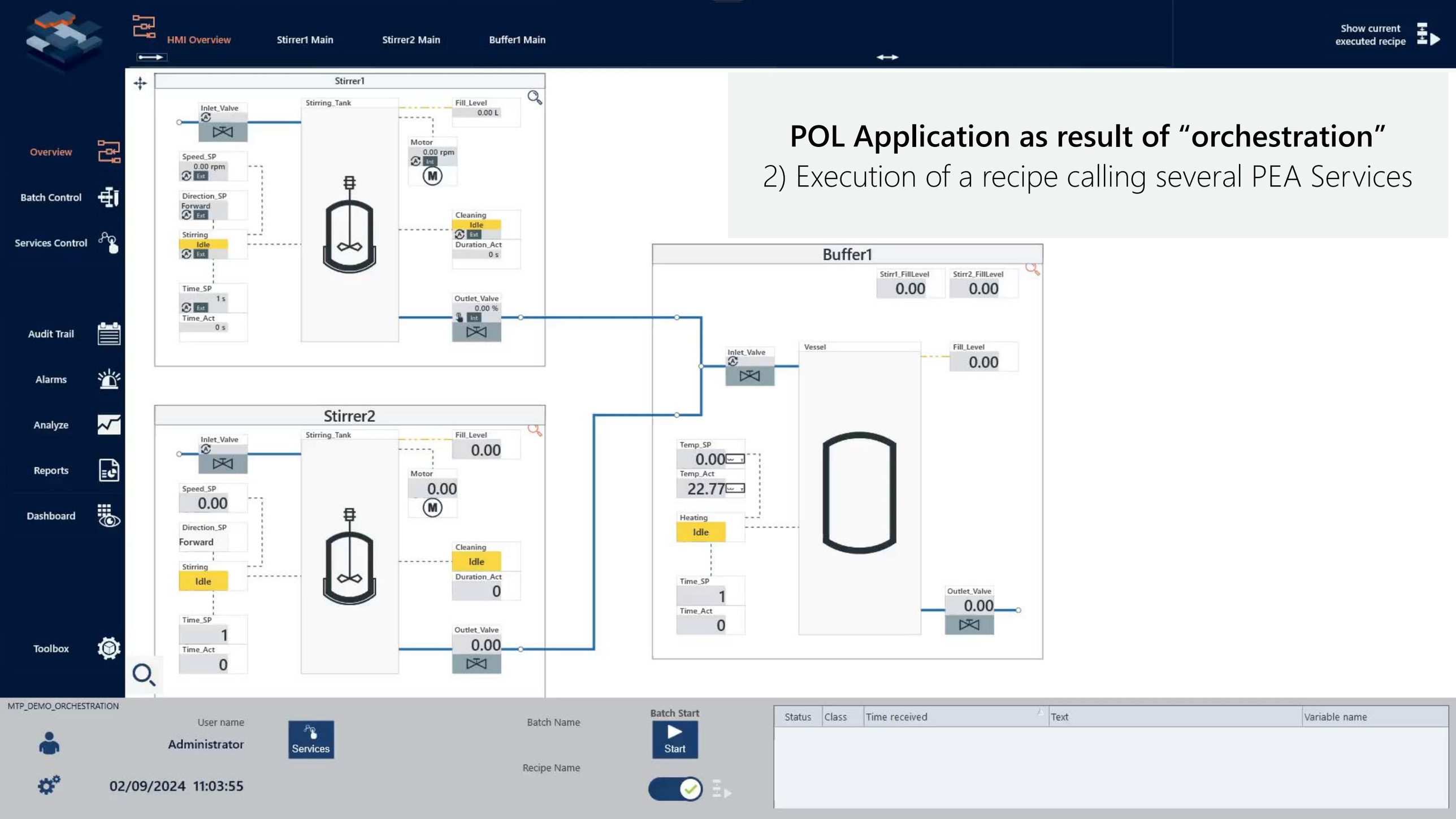



Orchestration Studio
MTP_DEMO_ORCHESTRATION
en
Task selection
MTP Editor
Template Management
Device Management
Orchestration
Settings
Example of Orchestration
Previous
Click to show logs



POL Application as result of "orchestration"

1) PI&D Screen: Monitoring and Manual Operations



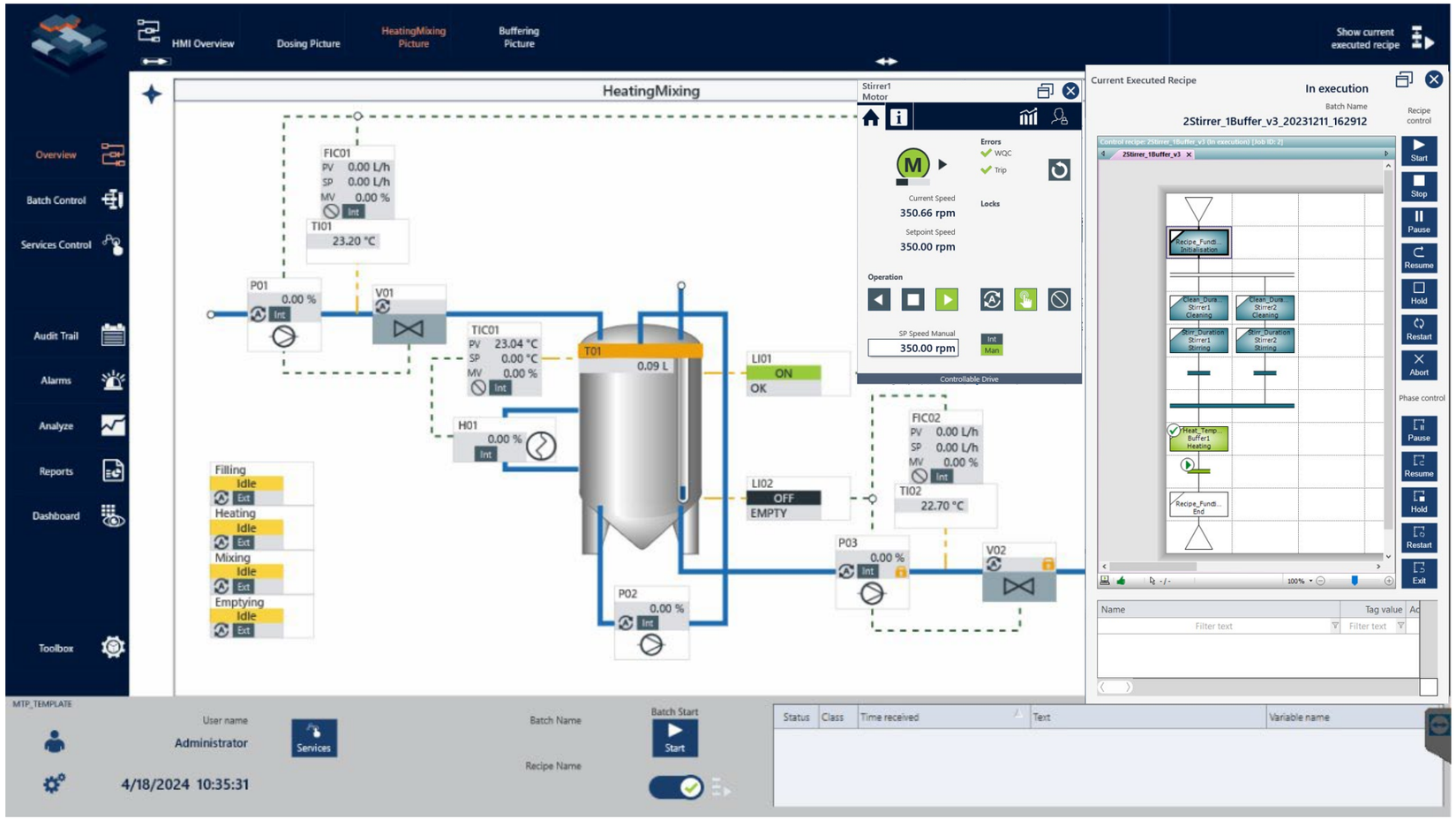
POL Application as result of "orchestration"

2) Execution of a recipe calling several PEA Services

Process Orchestration Layer

Example of automated generated „Modular Plant“: Overall process screen + ISA88 Batch Recipe

- Automatic generation of the "Modular Plant" application:
  - PI&D / Process pictures
  - Services for Batch ISA S88
  - Dashboards
  - Alarm management
  - Audit trail
  - Historian / Trending
  - Reporting
  - …



What if my devices are not ready for MTP?

How to integrate legacy equipment?
Process Development lab -> Pilot Plant -> Industrial scale

Scale

Vacuum controller

Mixer

Ph meters

Peristaltic pumps

Temperature Controller

chromatography system
for small-scale manufacturing

Pilot size crystallizers

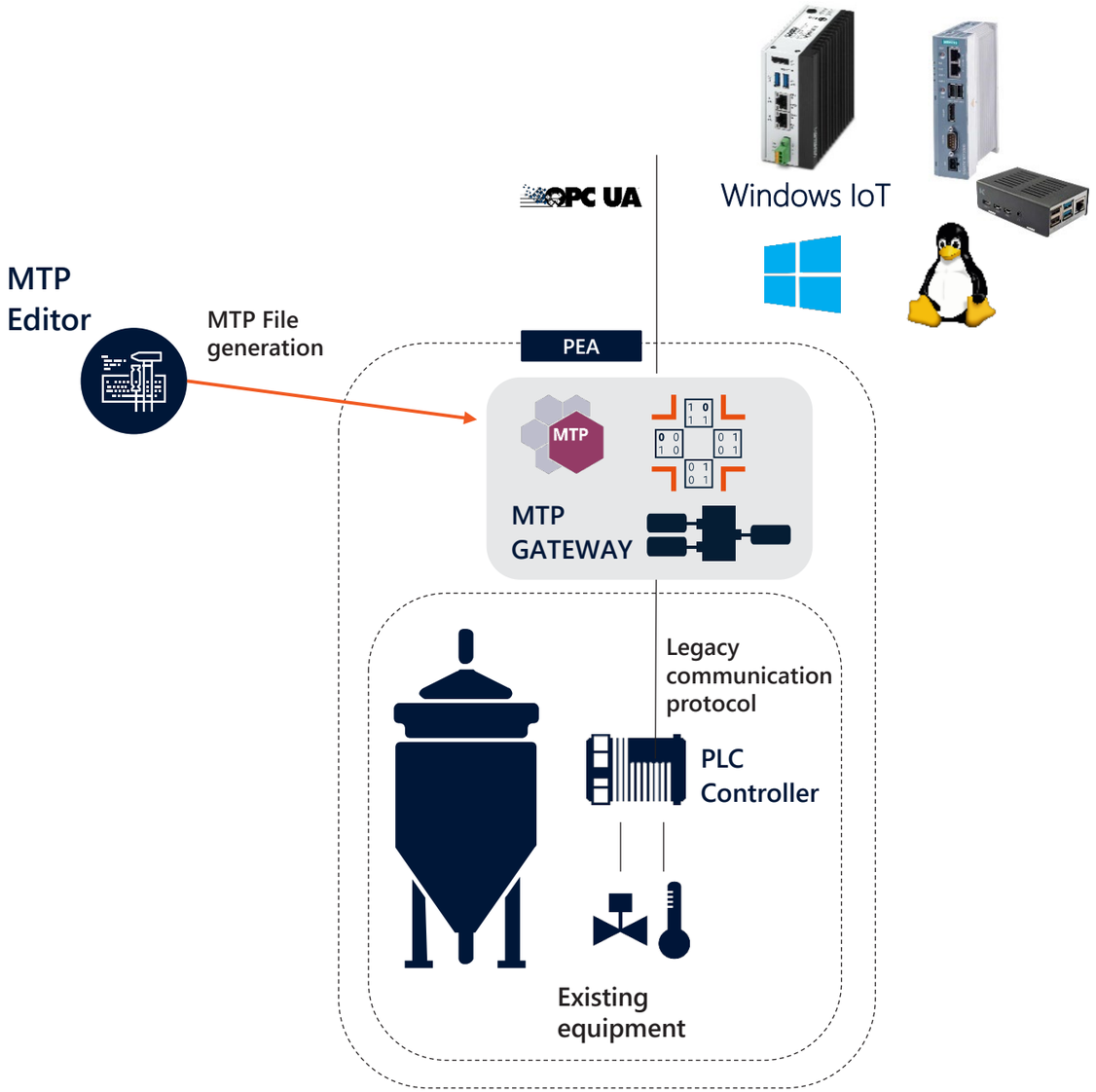
Pilot size Bioreactor

How to integrate existing modules?

MTP Gateway

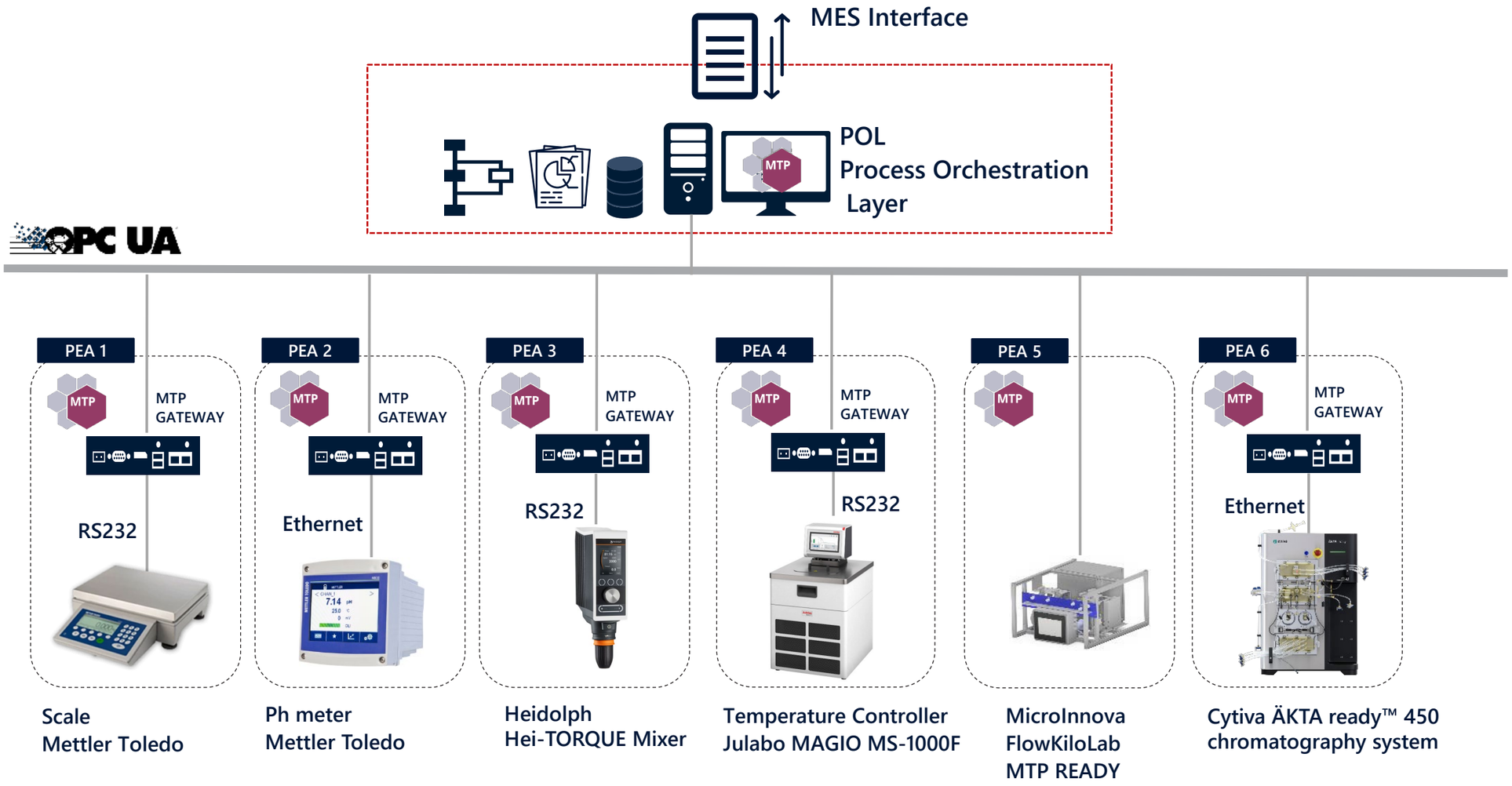
- The MTP Gateway supports you integrating existing production modules and get them MTP ready

- Functions:
  - Connection to existing PLC or controller
  - Communication towards POL as OPC UA server
  - PLC Logic IEC 61131-3:
    - Data aggregation, context.
    - Mapping module variables in OPC UA Variables
    - MTP State Model / MTP services
  - MTP file generation by using the MTP Editor

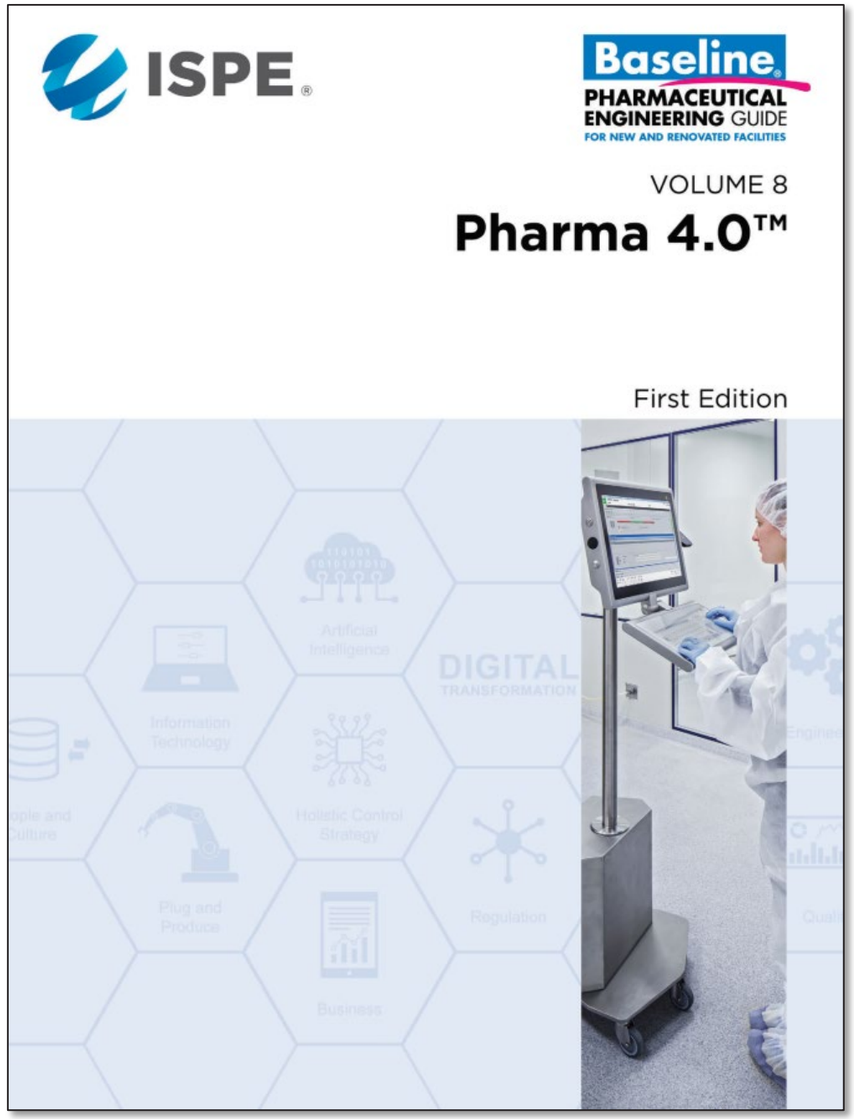


Architecture example

Simple configuration. Integration of existing devices by MTP Gateway.



Merck Case Study in ISPE Pharma 4.0 Baseline Guide



11.22 Case Study Number 308: Modular Automation for R&D Laboratories

11.22.1 Short Description

- **Problem:** R&D laboratory facility typically contains numerous fume hoods equipped with laboratory equipment such as pumps, stirrers, and dosing modules. Experiments with the different modules are carried out either manually or using a conventional laboratory management system. The frequent reconfiguration of the laboratory setup to support the needs of different product process development requests including FAIR (Findable Accessible Interoperable Repeatable) data collection is crucial. In contrast to production, everyday work in a research laboratory uses systems that regularly must be reconfigured and working steps continually changed. This makes the laboratory an environment that, at first glance, appears to have little automation potential.

- **Solution:** The company has found the key to success in modular production and is relying on an industry standard called MTP – Module Type Package (VDI/VDE/NAMUR 2658 [137]). MTP is a solution approach that enables all equipment within a central control system to communicate independently of the typically fragmented hardware and software landscape in use. Individual work steps are saved in completed modules and researchers can repeatedly and quickly combine them into new applications and processes using graphical tools without the need for programming knowledge.

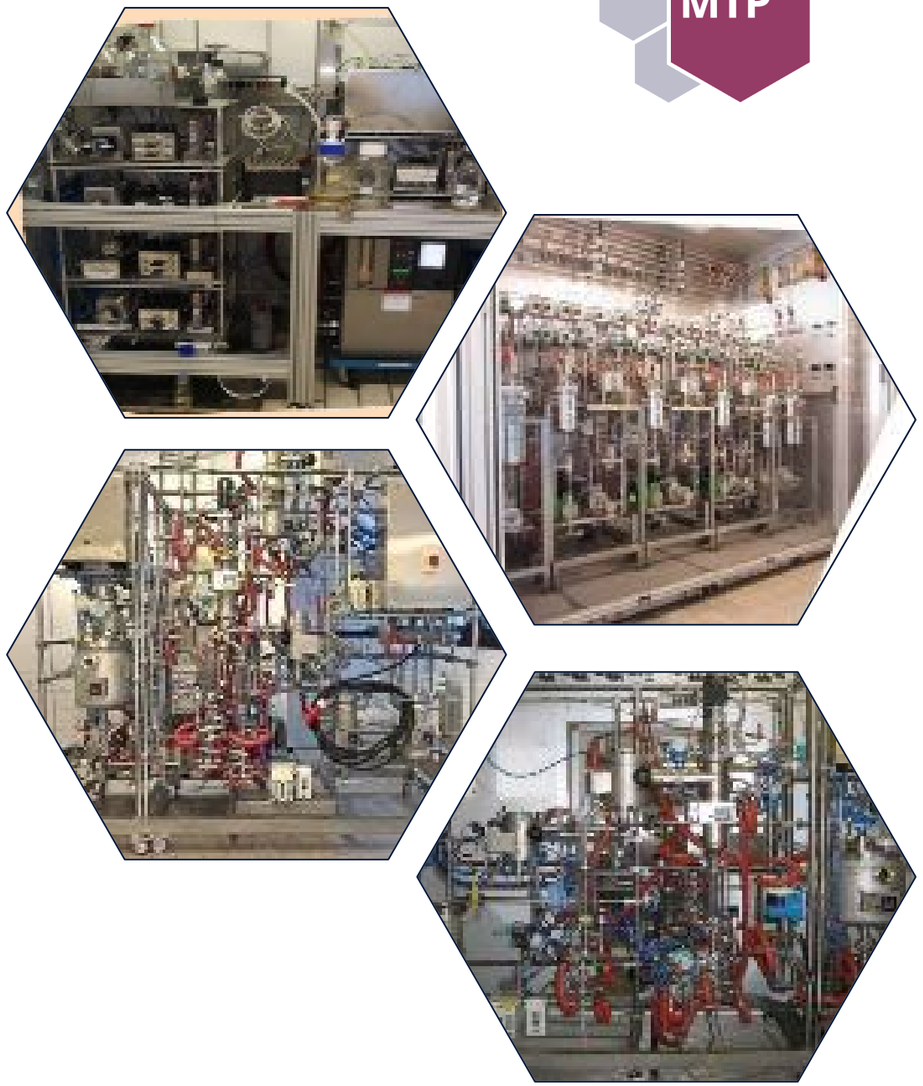
- Benefits:
  - Plug & Produce: By introducing a central system, all instrument functions can be integrated automatically as MTP modules (PEA – Process Equipment Assembly). Central system is a software platform called POL – Process Orchestration Layer: is able to monitor and control PEA from different vendors.
  - Focus on experiment thanks to laboratory operations automation: The core competence of a laboratory technician, namely the planning and execution of experiments, is thus once again in the foreground and not the manual integration of devices or the transfer of written experiment data into Excel tables.
  - Paperless operations: Process values, measurement, deviations and execution log are automatically stored in an electronic format, no longer written in notebooks or excel files improving data integrity. These points apply especially to laboratories in the process and pharmaceutical industries, where processes (upstream as well as downstream) are tested, and data collected for implementation later on a large scale.
  - Fast reconfiguration: Thanks to modular approach and MTP orchestration, laboratory engineers can quickly reconfigure modules, process flow, and execution steps using graphical tools without programming knowledge.
  - Tech Transfer: From the point of view of plant operators in the process industry, it is very important that upscaling from the laboratory to production plants can be done quickly and efficiently without manual adjustments. This can be simplified when the same automation concept is used in the laboratory as well as in the pilot plant and finally in production. If the POL used complies with the MTP standard, manufacturer independence is also achieved.
  - Time to market: Standardization of modules following the two important guidelines (VDI/VDE/NAMUR 2658 [137]) (VDI/VDE/NAMUR 2776 [138]) enables a fast and resilient product supply as a worldwide network of production capabilities can easily exchange equipment and recipes.
  - GxP compliance: Prequalified modules (PEA) can transfer these benefits into the Pharma 4.0 environment

Benefits of Modular Production:

- Requires less automation competence for equipment integration & process setup
- Interoperability: use same integration concept across different module suppliers
- Easy scale-up: Labs → Pilot Plants → Large scale
- Process Orchestrator (POL) fulfills Pharma 4.0 requirements:
  - Plug & Produce
  - Digital Recipe execution
  - Data acquisition, Electronic records, IT integration
  - Simpler validation
- Supported by an international standard:
  MTP - VDI/VDE/NAMUR 2658 - IEC 63280

How can I get started with Modular Automation MTP ?

A digital journey



- Identify the potential use case in your organization.
- Separate process in modules (PEA)
- Define functionalities in modules (PEA Services)
- Adapt existing module to be MTP ready
  Automation job: MTP gateway + MTP File
- Train the people:
  - How to generate a Process Orchestration application: PLUG
  - How to use Process Orchestration Layer: PRODUCE
- Select a technology partner supporting your MTP Digital Journey

Thank you!

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