OPC DAY
FINLAND 2024
21.11.2024

MTP and Modular Automation in the Biopharmaceutical Industry

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Automation – From the Past …

Custom purpose-built static installations

https://www.gea.com/en/products/bioreactors.jsp

To the Future …

Single-use flexible manufacturing systems

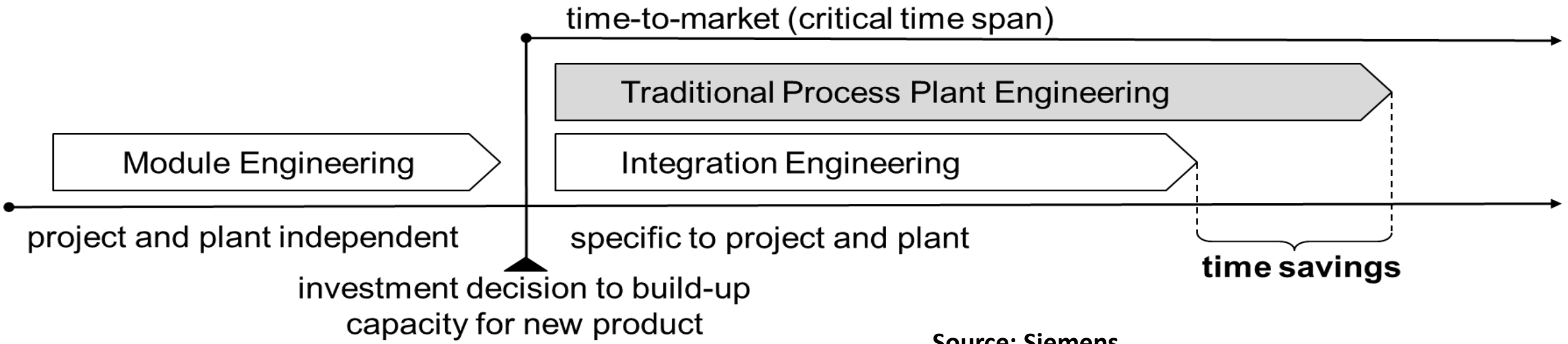
https://www.biotech2019.ch/process-intensification-and-continuous-bioprocessing-single-use-devices

Advantages of Modular Plant Design

Transform our Business

40% Less, 80% Offsite – Capital Effectiveness

MSD VP of Engineering on constructing new facilities



Source: Siemens

Advantages of Modular Plant Design

- Flexible manufacturing (fast change over)
- Cost savings due to compact, pre-fabricated design
- Modular equipment can be reused for new products
- Faster to market
- Reduction of investment risk through market entry with small production capacities
- Faster process understanding and optimization
- Scale-Out instead of Scale-Up
- Easy capacity expansion by adding individual modules to the production line

Problem Statement

The lack of standardization for process equipment and automation in single-use equipment leads to:

- Reduced Flexibility
- Longer Schedules
- High Cost of Integration
- High Cost of Maintenance

Problem Statement

Flexible facilities need flexible automation to fully enable flexible manufacturing in the Facility of the Future.

https://drug-dev.com/pharma-4-0-a-new-initiative-to-help-design-the-pharma-facility-of-the-future/

Vaccine Manufacturing – Drug Substance

Multi-Use Production Space

Bioreactors

Bioreactors

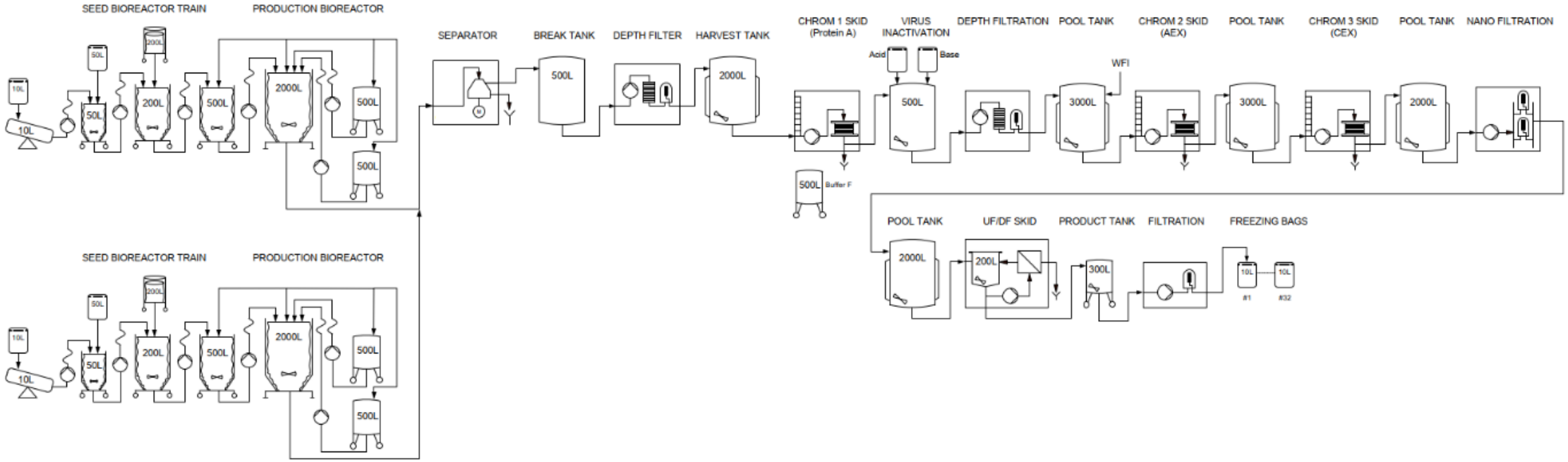
Virus Inactivation

Down Stream Purification

Use of Platform Processes Enables Speed of Commercialization

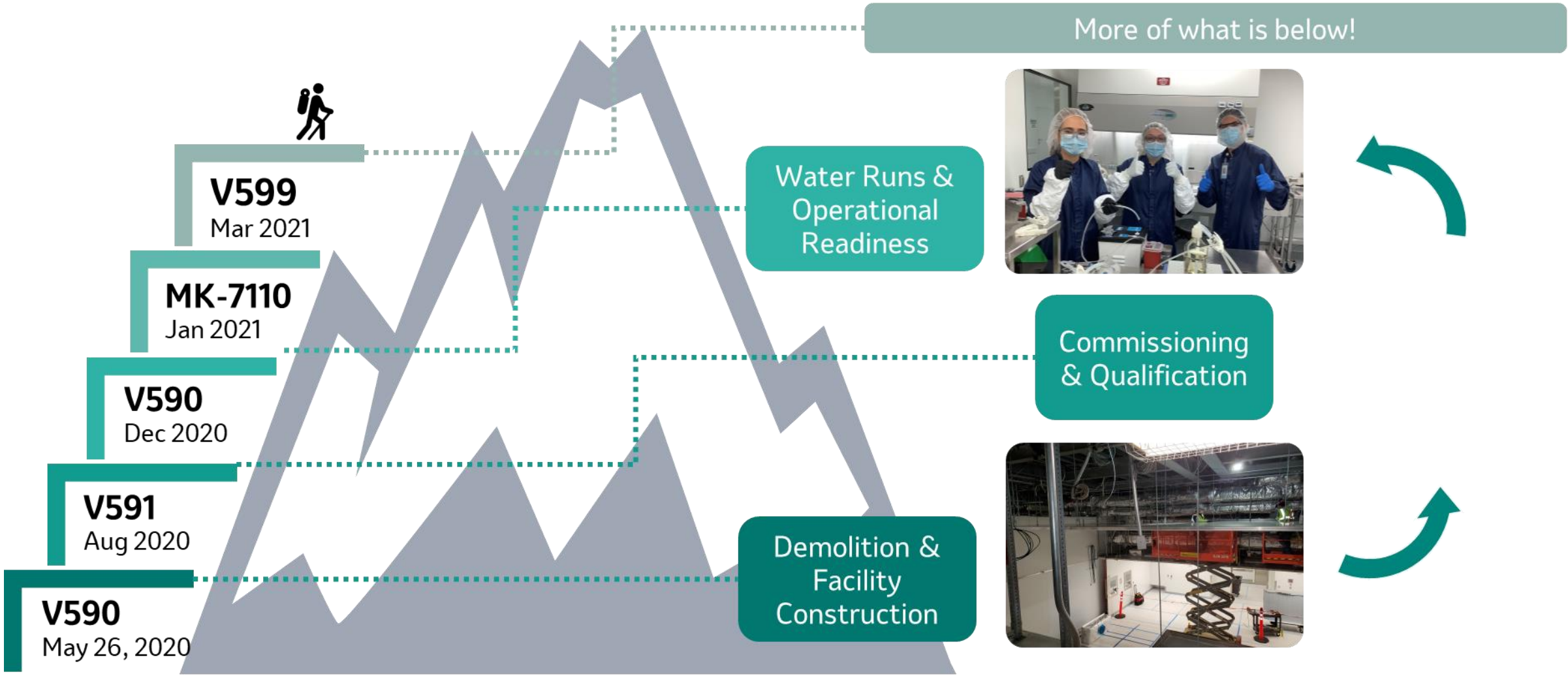
Modularization of Process Equipment in BioPharma

Typical PFD



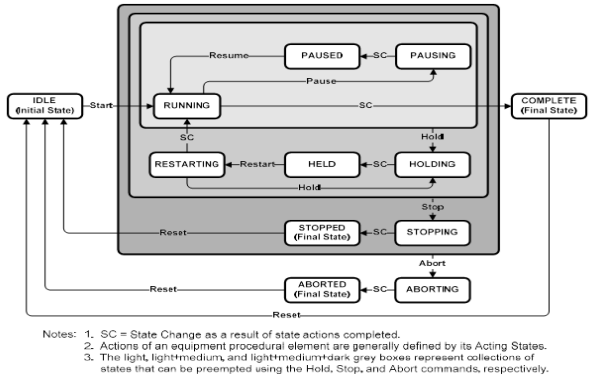
In single-use biopharma plants, the unit operations are off-the-shelf, pre-engineered equipment that are provided with local intelligence by an OEM vendor

Our Drug Substance Facility Journey

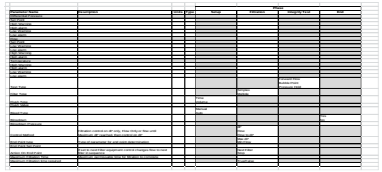


Principles of Plug and Play

- Autonomous Skids
- Supervisory Control System



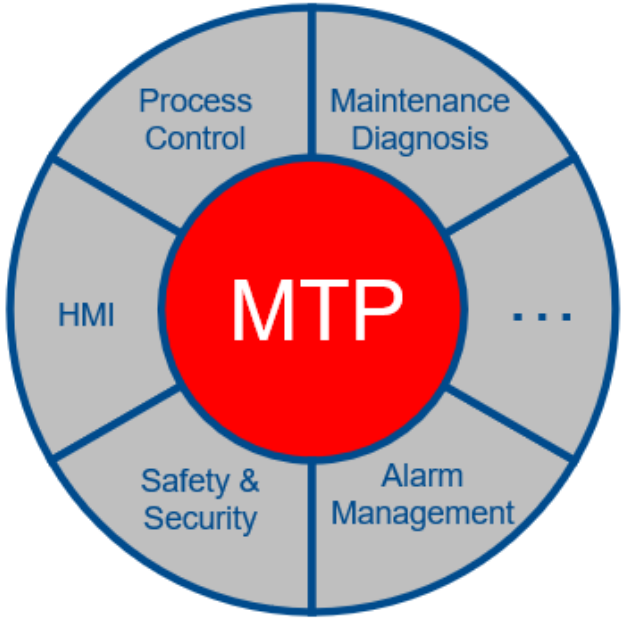
Notes: 1. SC = State Change as a result of state actions completed.
2. Actions of an equipment procedural element are generally defined by its Acting States.
3. The light, light+medium, and light+medium+dark grey boxes represent collections of states that can be preempted using the Hold, Stop, and Abort commands, respectively.



Exchange of Standard data models via OPC UA

Plug and Play: NAMUR 148 MTP – VDI/VDE/NAMUR 2658

- Specification and development of a vendor neutral description language :
  - Called MTP: **M**odule **T**ype **P**ackage
  - Covers the Data Integration into the POL (**P**rocess **O**rchestration **L**ayer)
- Development of MTP Export and Import Engineering-Tools
- Demonstration of first Results started in 2018



Assumptions

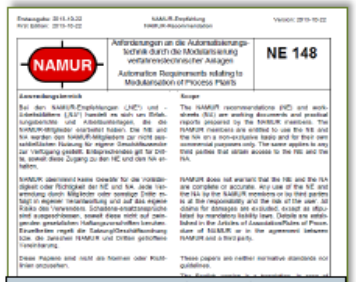
- The Automation concept is based on decentralized Intelligence residing in the Modules (Package Units)
- The Module itself is operating in an intrinsically safe way (totally self-controlled)
- Will not be a 100% working solution when introduced
- This will drive automation from an white Box approach towards an black Box approach

Source: Namur / ZVEI

Evolution of the MTP Standard

In 2022, **PI** has been selected by **NAMUR and ZVEI as additional partner** to drive technology development and market adoption

2013
NAMUR recommendation

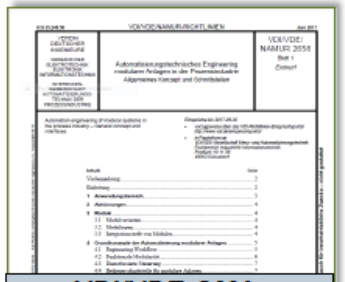


NAMUR: International „User Association of Automation Technology in Process Industries" with about 150 member companies

2015
ZVEI white paper

ZVEI: Industrial association representing interests of about 1600 companies of the electrical industry.

2018-2023
VDI/VDE/NAMUR guideline 2658



VDI/VDE GMA: Association of german engineers in automation is driving standardization projects

2022-20xx
MTP in PI

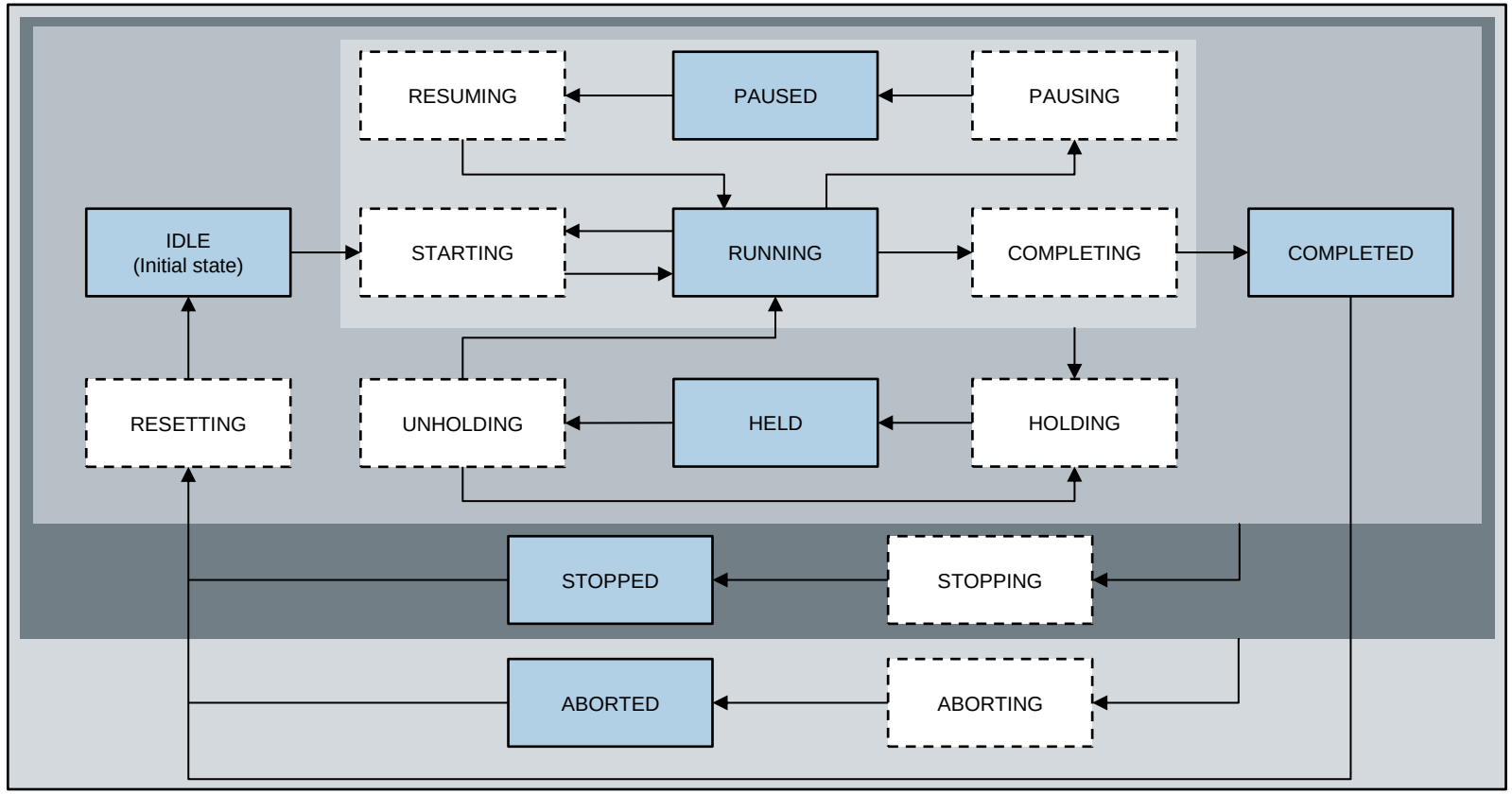
Standardization Activities

- NAMUR and ZVEI cooperate on elaboration of concepts and marketing
- VDI and NAMUR cooperate on standardization of **modular process plant design** in **VDI 2776**
- NAMUR and VDI/VDE GMA cooperate on standardization of **modular automation** in **VDI/VDE/NAMUR 2658**
- **International standardization** started in **IEC 63280**
- **PI as new partner** for technology development with clear IP Policies, training, and conformance testing

Source: Dr. Mathias Maurmaier, Siemens

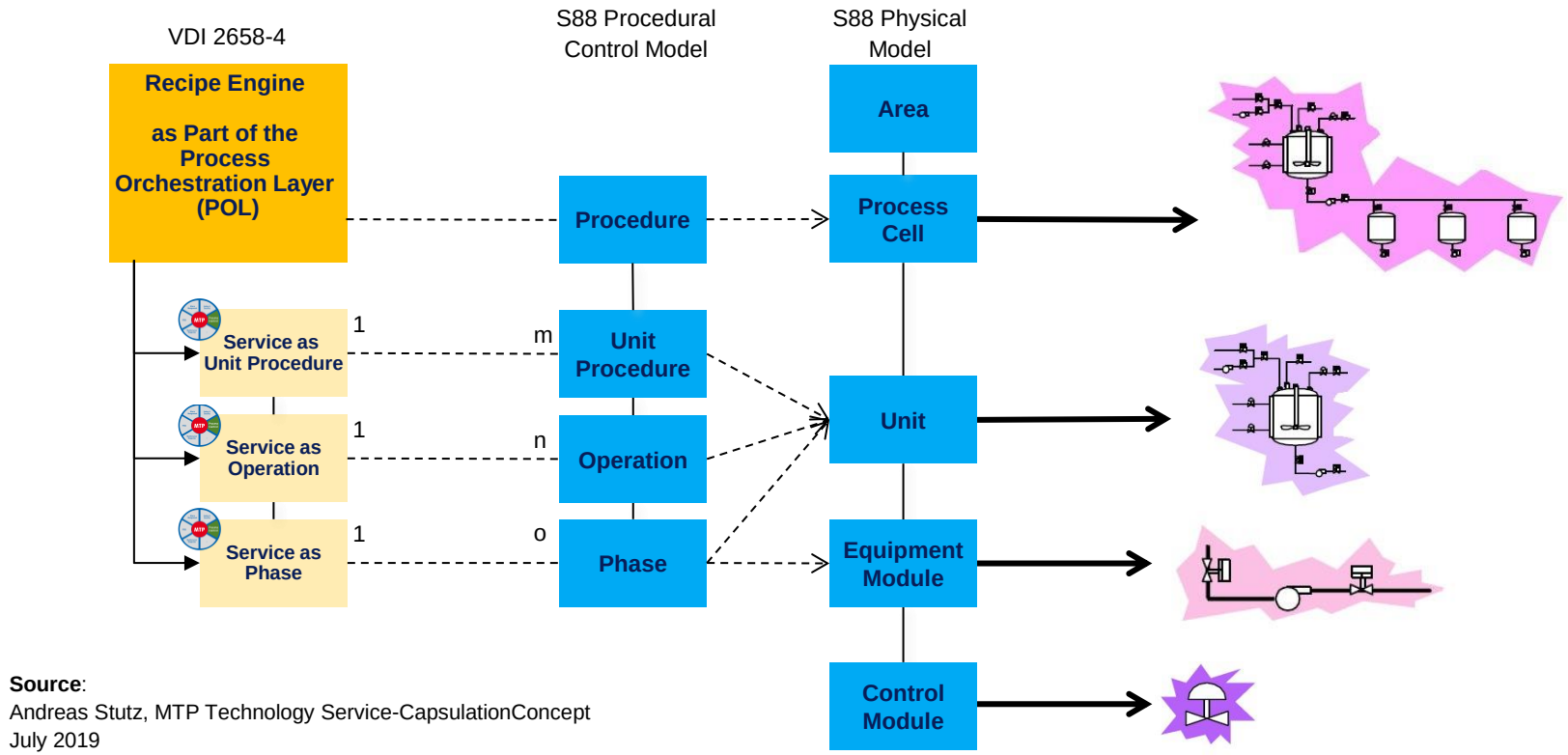
Process Control – Service State Machine

ISA88-compliant State Machine



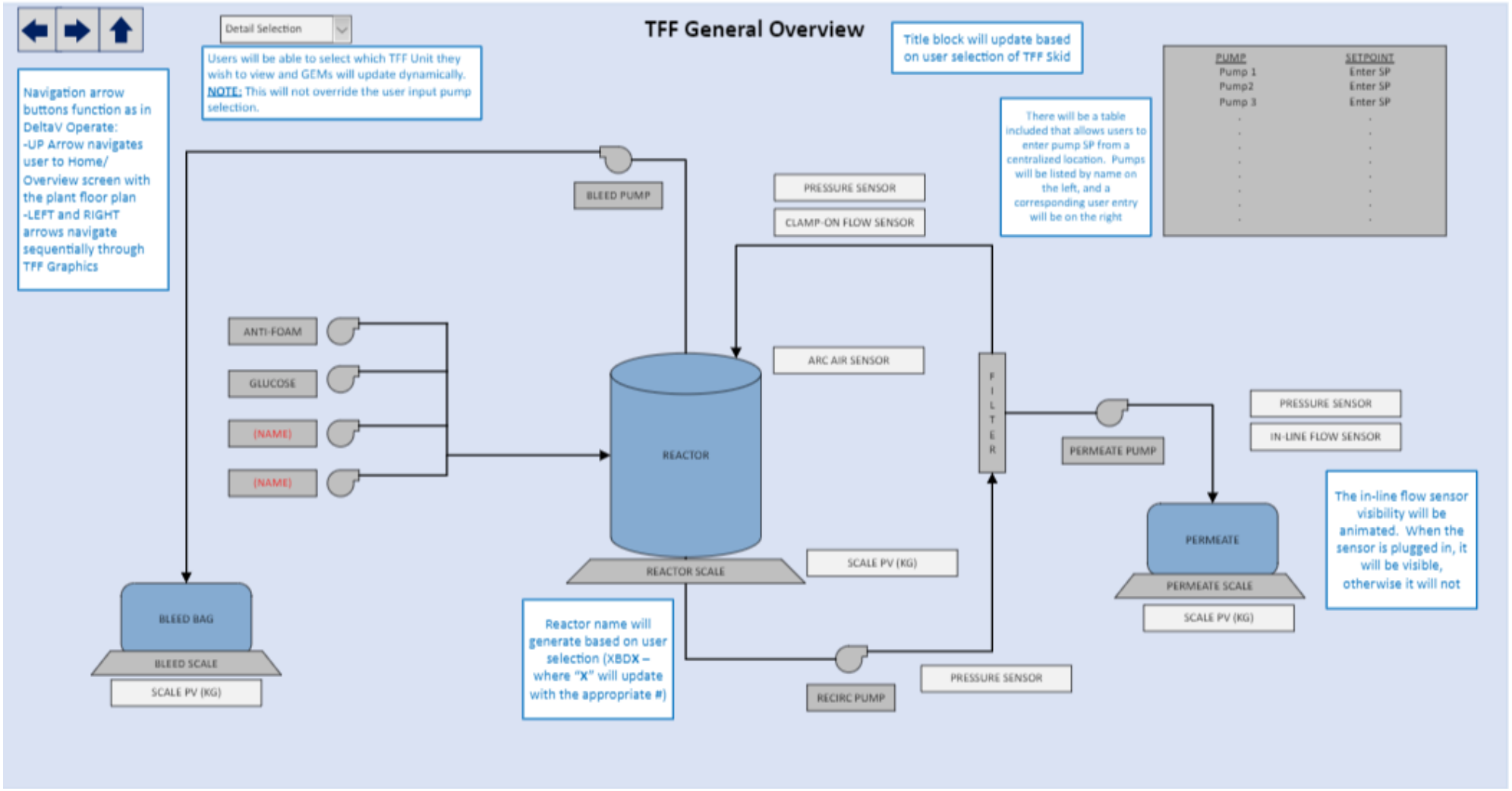
Source: K. WS. Bernshausen, Module Type Package - Modular Automation at the Example of a Pilot Plant, Namur Meeting, Nov 8 2018

MTP Services and the ISA 88 Procedural Control Model



Source:
Andreas Stutz, MTP Technology Service-CapsulationConcept
July 2019

DeltaV-Native Perfusion using Tangential Flow Filtration



Peripheral Equipment for Tangential Flow Filtration

Equipment resides on mobile carts

- The DeltaV (POL) is able to run the peripheral equipment for different services.

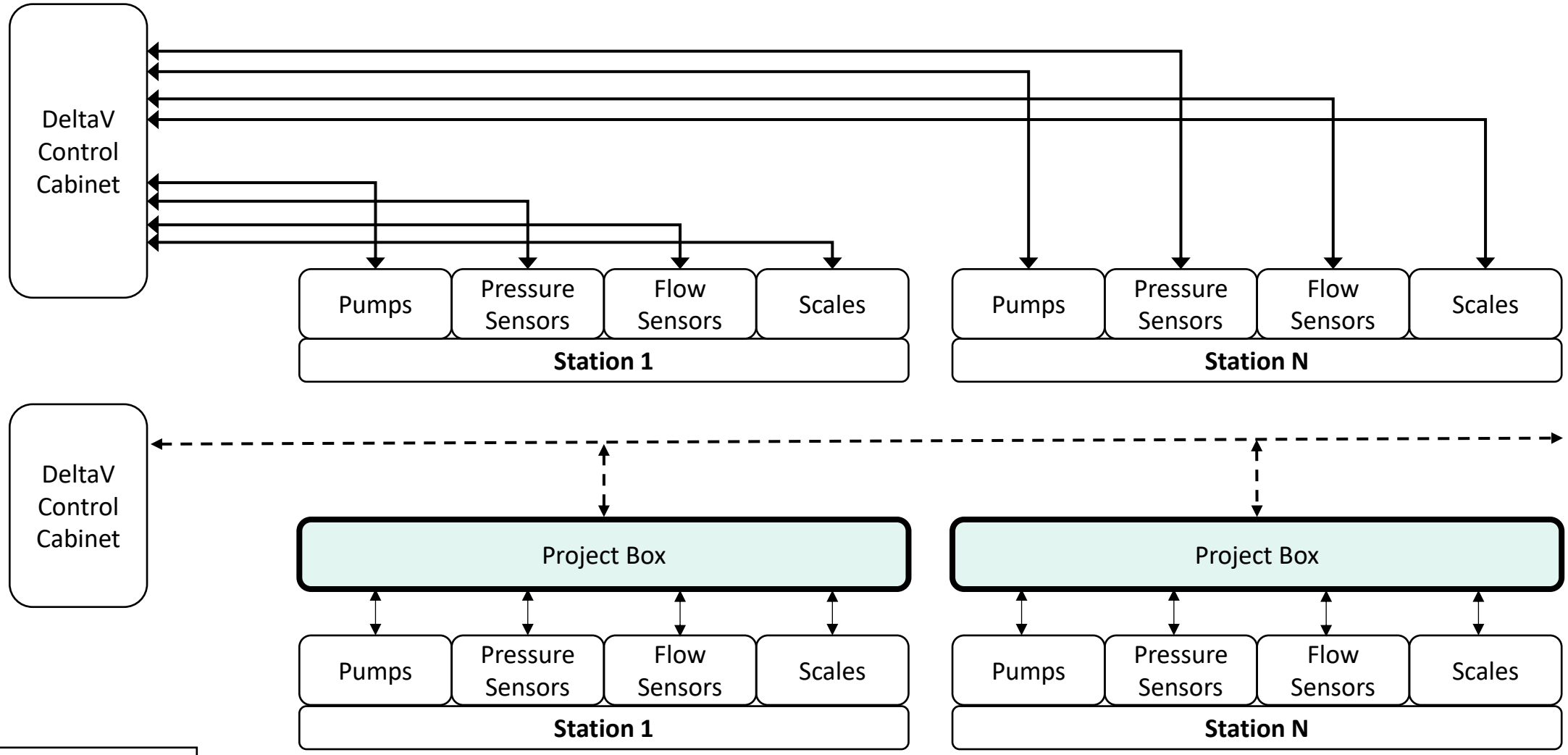
Services:

Weight Control
Pump Speed Control
Pneumatic Valves Control
Flow Control
Pressure Control

Software

Hardware

System design & architecture | the project box



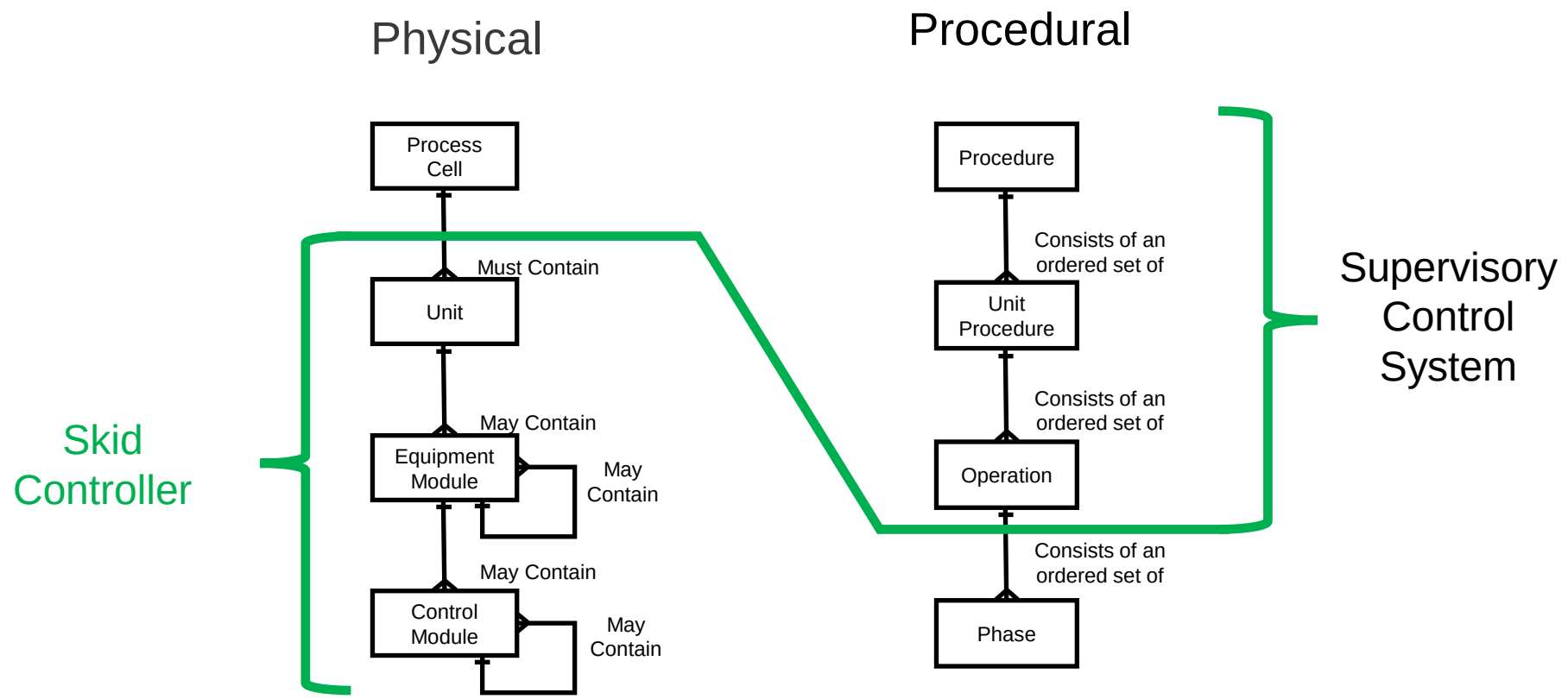
Why DeltaV-Native | comparing current vs. future states

Comparison	current state	future state
TFF Control Capability	recirc pump | clamp-on flow	recirc pump | clamp-on flow permeate pump | inline flow **any pump | any signal**
External I/O availability	4x Analog 4x Serial	+8x Analog +2x Serial +4x ModBus +3x Ethernet
equipment types	**Repligen compatibility** for TFF Serial & Analog with Sartorius	**any equipment** **any sensors** **PAT**
User Experience	In-person control Remote visibility	In-person control **via DeltaV** **Remote control (iPad)** Remote visibility

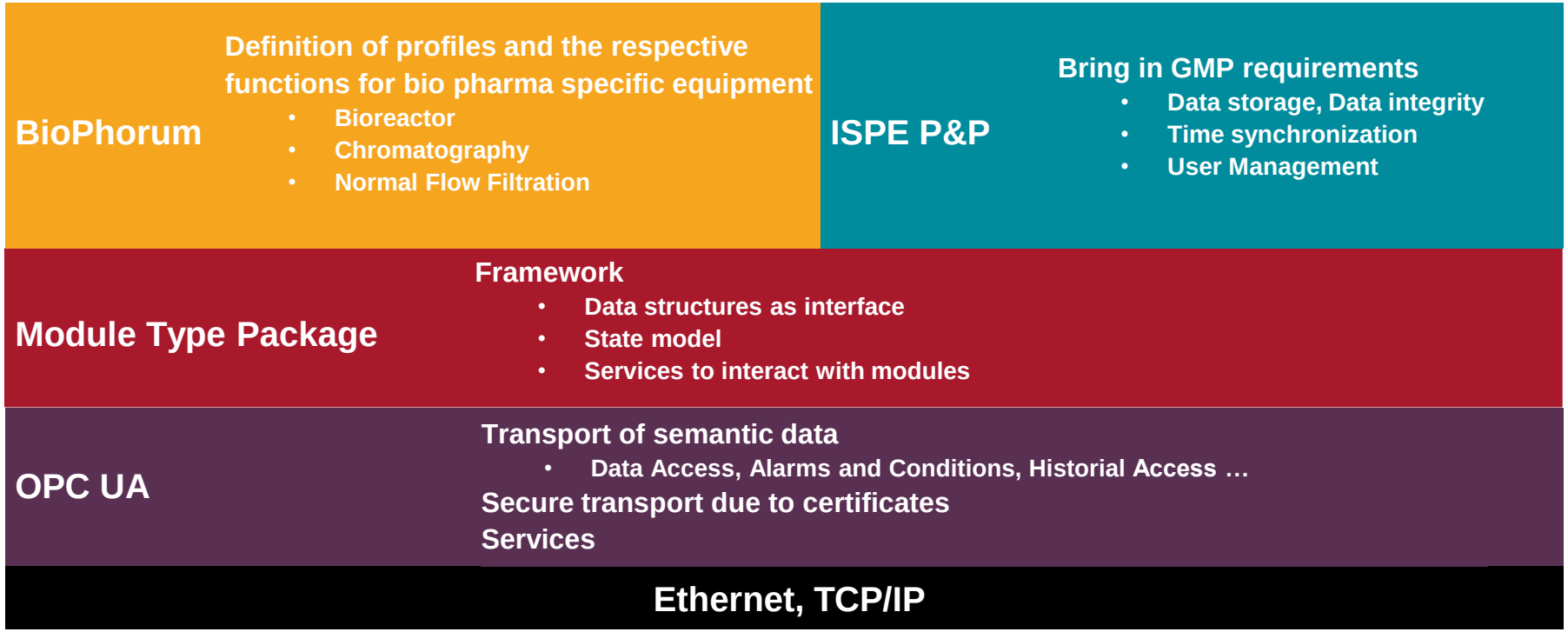
DeltaV-Native Perfusion **improves** automation capability at the 2L platform,
enabling and **accelerating** process improvements

Questions?

S88 Batch Model



MTP Basics



Stirred Tank Unit Interface Specification

Automated Facility: Stirred tank unit interface specification - BioPhorum

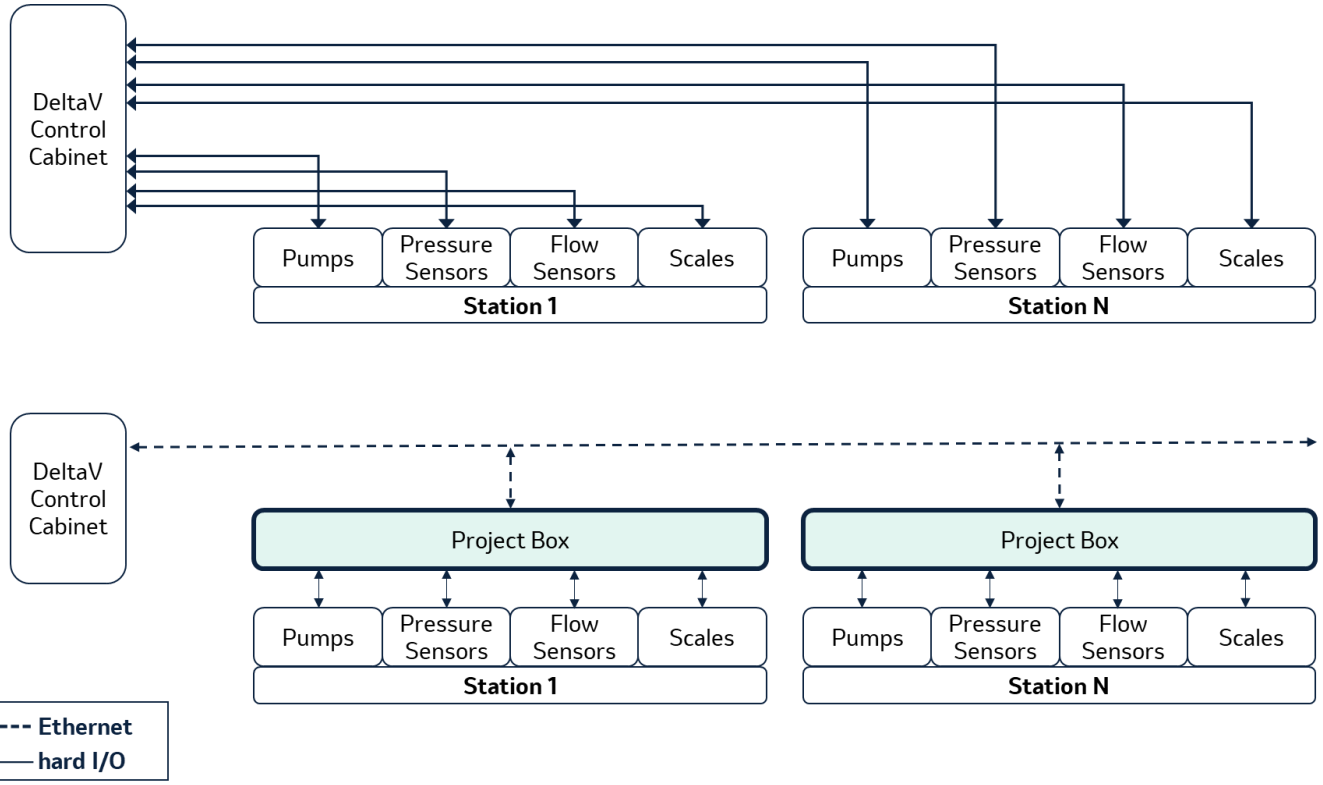
What is DeltaV-Native Perfusion TFF? *("Native TFF")*

Perfusion Control	Bioreactor Control **TFF / ATF Control**

Commercial off-the-shelf (COTS)	**Hybrid COTS**	**DeltaV-Native TFF**
Repligen, PendoTech, Millipore	**Levitronix Console**	**Control Associates custom build**
Pros: vendor support, minimize integration effort	**Pros**: vendor support, minimize integration effort, provide more operational flexibility	**Pros**: maximum operational flexibility, harness full automation capabilities of DeltaV
Cons: vendor support, lacks operational flexibility	**Cons**: vendor support, 1 point of failure	**Cons**: larger integration effort

Purpose: To develop a **DeltaV-native** bench-scale perfusion TFF control solution

System design & architecture | the project box *("slice I/O")*



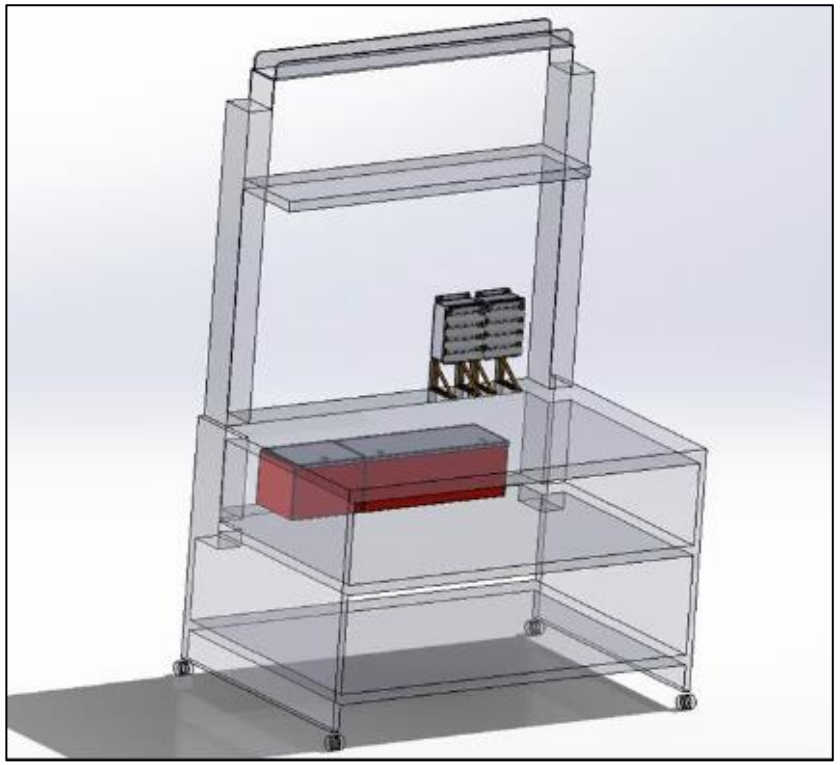


Figure: (L, top) Hard-wired equipment talking directly to the DeltaV controller (L, bottom) A project box consolidates hard-wired communication to an Ethernet signal that travels over the lab network to the DeltaV controller. (R) 3-D rendering of the project box. ***Note**: Picture is not to scale, represents a tentative configuration and only intended for visualization purposes.*