Advancing Facility Flexibility through Single Use and Automation

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2023 BPSA Single-Use Summit

Washington DC

We are expanding our network capability in support of the Biologics pipeline

	Pre-Registration		Registration & Launch + N	
Site	**Rahway** **Biologics Dev. Center**	**Schachen** **Biotech**	**Dunboyne** **BioNX**	**Dunboyne** **BioCEL**
Mission	Next-gen technologies are developed and scaled-up to support pre-clinical toxicology	Next-gen technologies are leveraged at MSD Schachen for early phase clinical supply	**Bio**logics I**N**novation **X**celeration **(BioNX)** facility for late-phase Clinical Supply and Launch	**Bio**logics **C**ommercialization and **E**xpedited **L**aunch and Long-Term Supply facility for Drug Substance

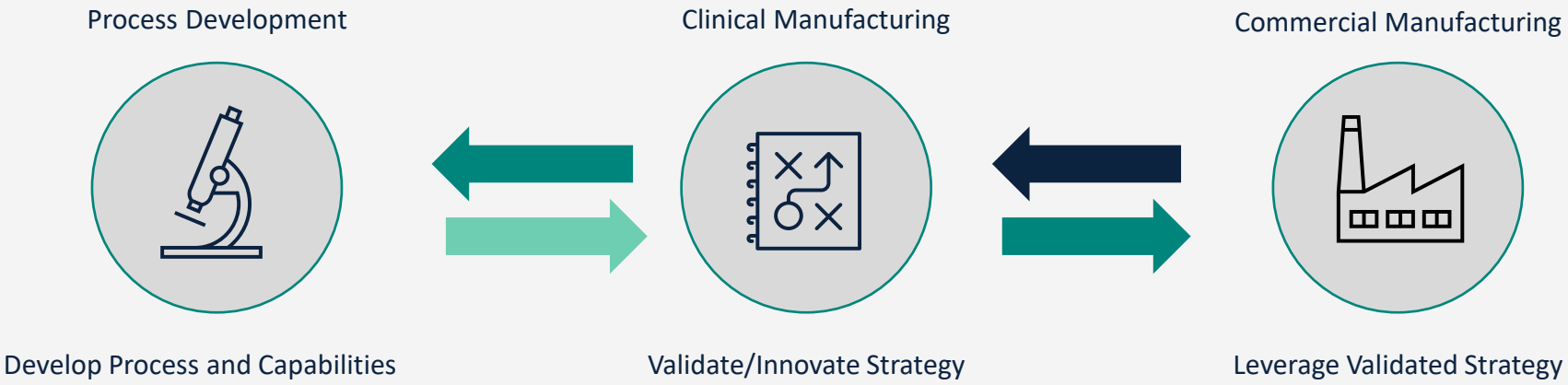
Age of disruption

Today's world of un-met medical needs and challenges means that we need to approach Building and transferring products differently

- Designing, Constructing and Qualifying new facilities can take over 3 years
- Development and Transfer of Processes is extremely resource intensive

Thousands of Hours are needed to develop and transfer the process between nodes

High administrative burden in modifying qualified systems and updating documentation



Switching to Automated Single Use Systems, with Podular / Modular facilities can enable speed and cost reductions

Biologics Innovation Xceleration Facility at MSD Dunboyne

Fastest Build in MSD Network History

- From Concept to Construction Complete was 21 months
- From Construction Complete to Engineering Batch was 9 months

Facility is based on the modular / podular concept – over 60% of the facility was manufactured offsite

Hiring of staff matched construction pace, with over 135 people hired in one year into the facility.

Created uncomfortable but achievable targets – leveraging it as unique talent development opportunity to bring key SME's from the network

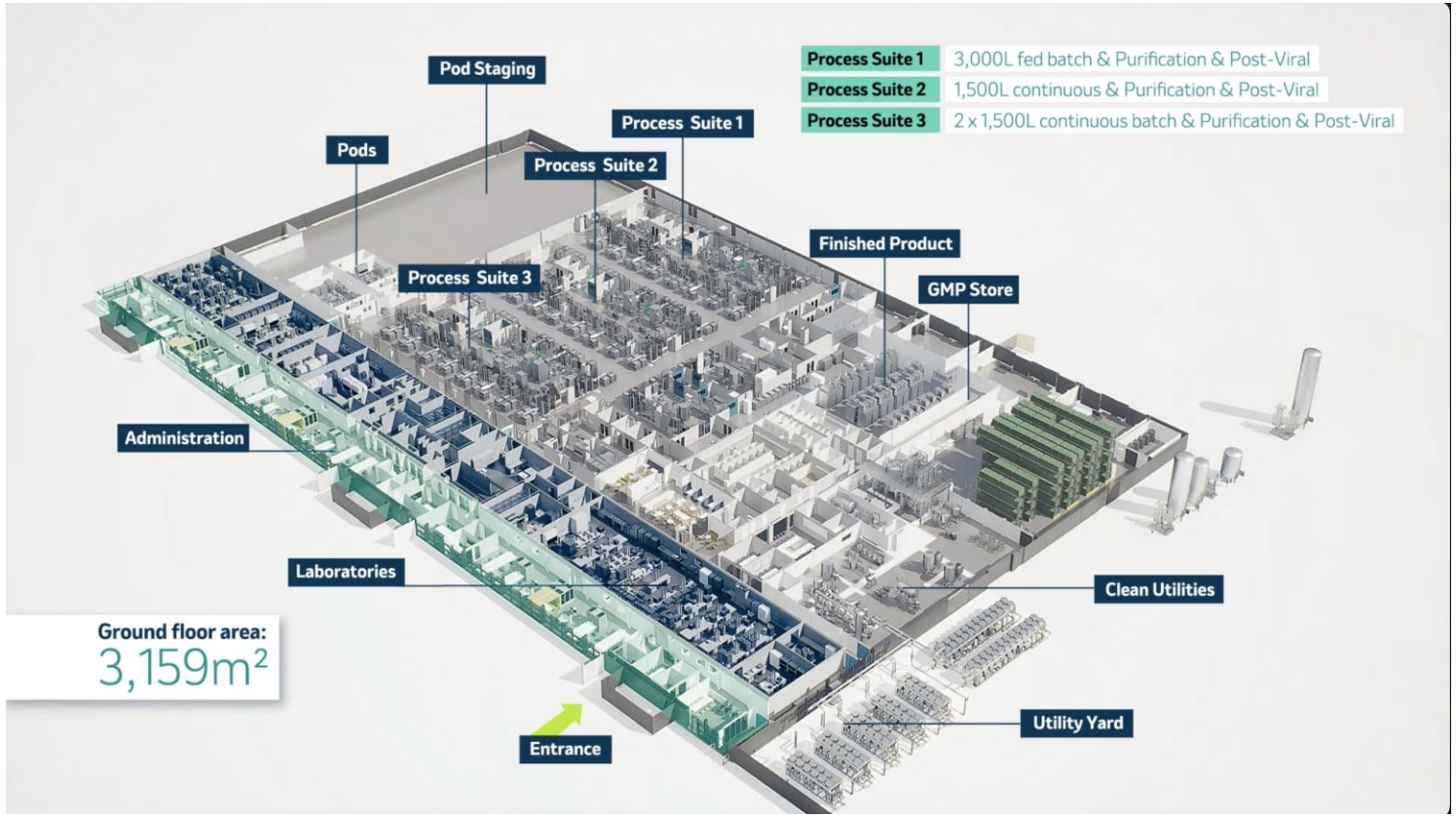
Cultural Shift in mindset and news ways of working to operate more in parallel on a risk-based approach

- 3 Production Trains at 3K Scale, capable of either Intensified Fed Batch or Continuous Manufacturing
- Scale-out possibility with Dual Reactor configuration
- Mixture of Manufacturing methods allow for optimizing COGs, Capacity vs Program Needs.
- Buffer Stock Blending to manage liquid volume
- Digital First facility, with integration between the ERP / MES / DCS layers enabling complete paperless manufacturing, testing, and release.

MSD Dunboyne - BioNX

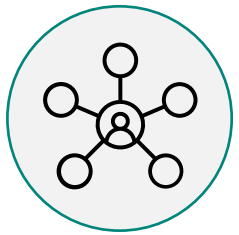
Sweating our assets to simplify

- A Digital Facility going beyond paperless
- " Lights Out Operations" Imagine setting up all of the process SU equipment, and once the process is started only needing to feed it more media/buffer and take samples!
- Advanced PAT Integration: Closed Loop Control.
- Wireless CTU's for flexibility in qualifying and movement.

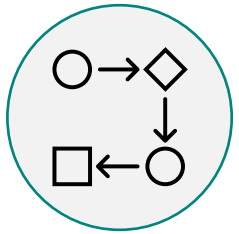


Simplicity

Simplicity



Standardize
After 3 times of doing the same thing-standardize formally



Digitize with Intent
Remove interdependencies with digital business processes

The rapid pace of technology development allows us to constantly simplify in new ways.

Imagine enabling new capabilities and flexibility like loading a new App on your phone

ISA-88 built for multi-product

Simplicity

The ISA-88 Model when implemented allows us to abstract the process from the automation and the equipment running on it.

Process Model	Procedural Model	Physical Model
Process	Procedure	Process Cell Suite / Building
Process Stage Protein A	Unit Procedure Primary Capture	Unit Chromatography
Process Operation Equilibration	Operation Bind & Elute	Equipment Module
Process Action Buffer Flush	Recipe Phase Equilibration	Control Module

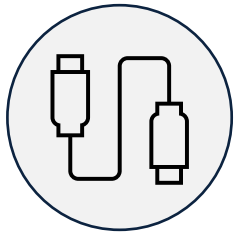
Automation Recipes are built on modules, allowing for adapting to different processes quickly

Utilize Early-stage and Late-stage binding to allow for equipment swap outs

Flexibility builds on simplicity

Flexibility

Parameterize
Variables of process that
can be in an automated recipe



Plug-n-Play
Seamless movement of equipment
and devices

Ethernet based equipment coupled with parametrization allows for flexibility to rapidly change parameters, but as well the physical layout of equipment.

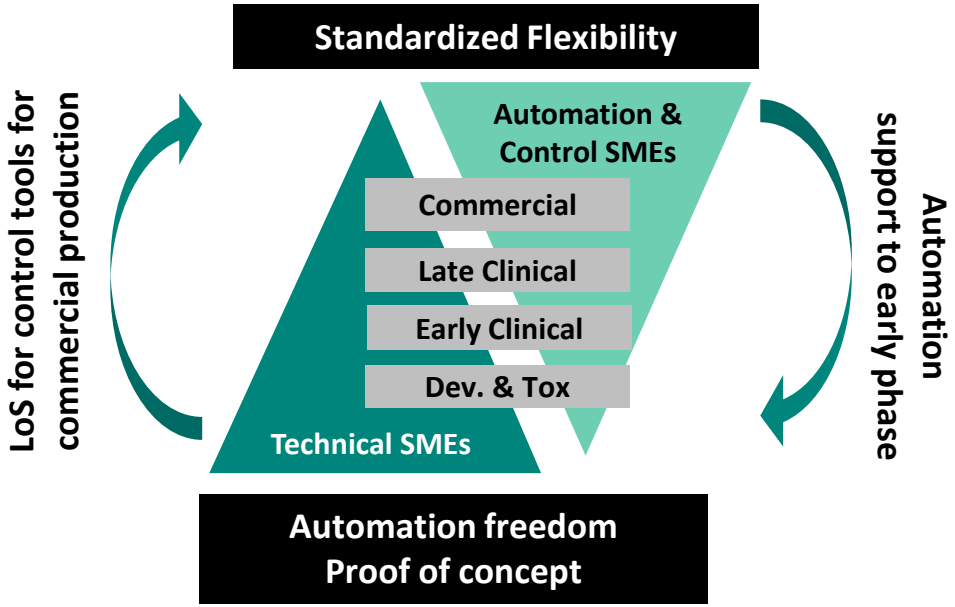
ERP to MES to DCS

Standardizing flexibility

Flexibility

Scale Out vs Scale Up while Standardizing Flexibility

- Utilizing S-88 Principles with lack of Product-specific automation enables Program-to-Program reuse
- Low customization, minimal qualification efforts, and standard structure enable integration with more systems without complexity
- Similarities in how we make a product allows for generic master batch records and SOPS, creating consistent approach which reduces operator errors and increases Right First Time.
- Allows agile iterative improvements over time, focusing on where flexibility is needed and isn't to maintain sustainability



Simplicity and flexibility enable agility

Agility

“Follow Me”
Right content, on right device at right time

Data Analysis
Aggregated data providing insights to trends

Standardizing on enterprise systems allows for a uniform approach that operators have with the process.

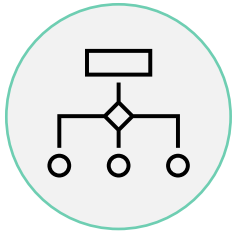
Most companies are very good at collecting data, but not as much at putting it to use.

Leveraging those enterprise systems allows for almost real-time visualization of the data across digital signage, ensuring tight coordination between areas, and escalation

Agility from many aspects

Agility

Technology
Flexibility in Automation
Integration of PAT



Business processes
Alarm Rationalization
Flexibility on "who"

Behaviors
Process Understanding Risk Based

With Integration of Advanced Analytics and PAT into the process – we move to Closed-loop control.

Increases process performance, reliability, and quality – reducing the amount and effort associated with the lifecycle in offline testing.

Business Processes aligned with that technology– allow people to flow to the work and focus on what is most important.

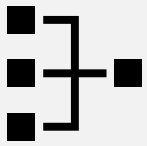
More focused staff to make better risk-based decisions.

Challenges

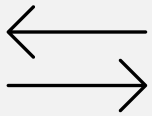
While we achieved an impressive speed, we were not without our challenges to over-come

The speed of the project required implementing new Ways of Working to enable more parallel activities.

Risk Based Approach taken regarding COTs system, but COTs while standard are not always error free, challenging the schedule

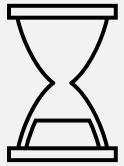


Design of Modular SU Assemblies can be challenging – balancing flexibility with supply chain.



Integration with OEM systems required more time due to challenges finding needed information. Native DeltaV systems went smoother.

Not all Instruments have Industrial Ethernet, and not all support every protocol, putting more effort in integration.



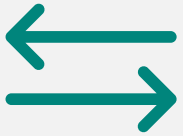
Longevity precision data not always available for SU sensors, needing additional controls to manage.

Summary

Single Use CM vs Stainless Steel Benefits

> 18 months faster build

> 30% COGs reduction



> 750 hrs savings / transfer

> 80% Carbon Footprint reduction

Digital Strategy & Platform Enabled

- Reduce supply chain risks, by having over 50% of the same components in use at other facilities
- Enable Lights-Out-Manufacturing –staffing only during normal business week, managing out of hours work by exception/escalation via automation
- 30-50% reduction of overall resources and administration needed to run plant
- Industry 4.0 Concepts (AI / ML…) can further improve efficiency / COGs

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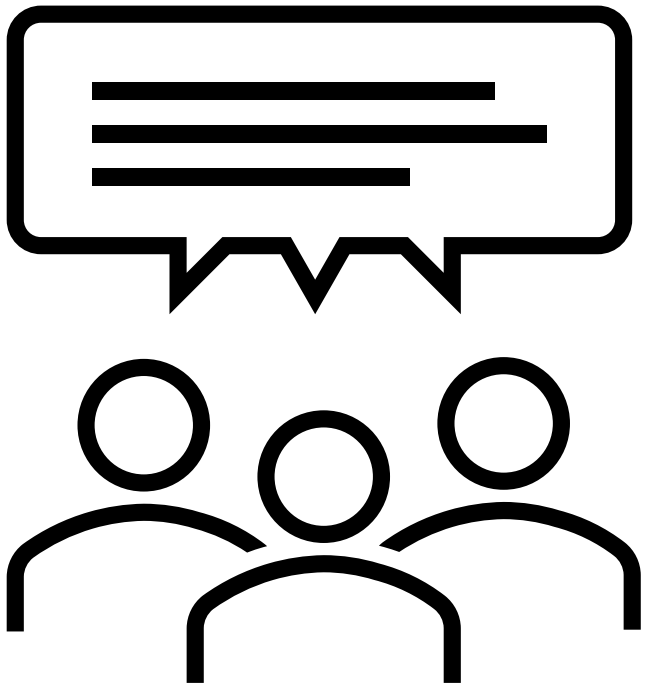
Questions - please defer to Panel Session



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