



**dcvmn**

Developing Countries Vaccine  
Manufacturers Network

DCVMN - 23 March 2021

# Vaccines for the World - Insights into Design and Execution of a BSL2 Fill-Finish Facility

Rutger Vandiest - Sr. Director, Head of Sales, CDMO  
Bavarian Nordic A/S

# Presentation overview

- Bavarian Nordic
  - Introduction to Bavarian Nordic
  - Viral vaccines
  - Challenges in working with live viral vaccines
- 
- IPS
  - Facility design - process architecture
  - Project team
  - Planning and Timelines
  - Challenges on project execution
- 
- Syntegon
  - Technological high-lights of the isolator line
  - Filling equipment
- 
- Bavarian Nordic
  - Summary

## Presenters:

### Bavarian Nordic

- Rutger Vandiest
- Sr. Director - Head of Sales, CDMO



### IPS

- Mark Miller
- Director of Engineering, EMEA



### Syntegon

- Matthias Angelmaier
- Global Product Manager  
Isolator and Processing Technology

**SYNTEGON**  
PROCESSING & PACKAGING



# Bavarian Nordic - Company overview

## Life-saving vaccines

Bavarian Nordic is a fully integrated biotechnology company developing, manufacturing and commercializing vaccines for the prevention and treatment of life-threatening diseases.

### FACTS

- Founded 1994, IPO 1998
- HQ: Hellerup - Denmark
- +700 Employees
- First product approved in 2013 (MVA-BN as smallpox vaccine)
- Commercial products, Long-term R&D and delivery contracts with the US government and Development partnerships with industry partners

By 2025, we aspire to be one of the largest pure play vaccine companies improving and saving lives by excelling in R&D innovation, manufacturing and commercialization

#### Develop innovative life-saving vaccines

Expand and advance portfolio of pipeline projects



#### A company driven by commercial excellence

Establish a full-scale commercial operation to expand the business and drive profitable growth

#### Best in class vaccine manufacturer

Expand manufacturing expertise and capacity

Hellerup, Denmark  
Headquarters



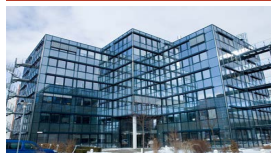
Kvistgård, Denmark  
Production site



Zug, Switzerland  
Commercial Strategy  
Global Sales



Martinsried, Germany  
R&D Facilities



Morrisville, NC, USA  
Global Clinical Regulatory  
Operations

# Products & pipeline

## Products



**Rabipur/RabAvert**  
Rabies



**Encepur**  
Tick-borne  
encephalitis (TBE)



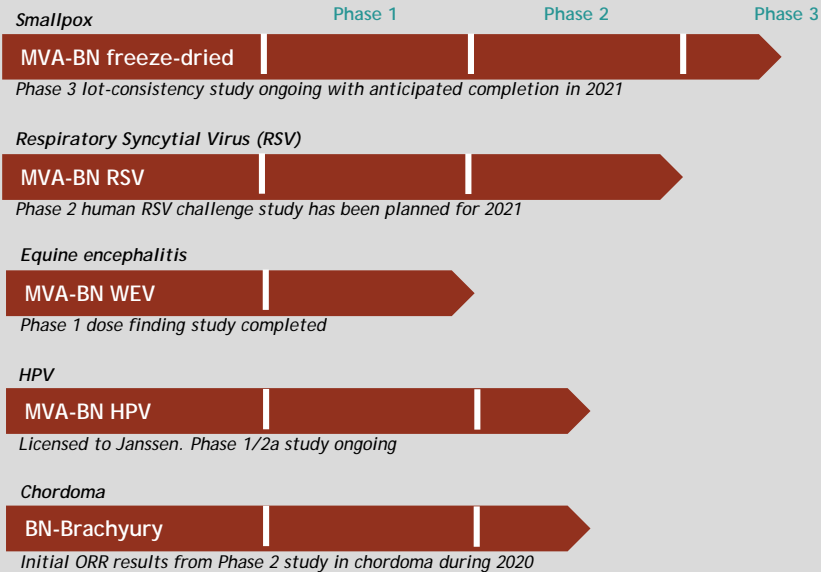
**JYNNEOS/IMVANEX/  
MVAMUNE**  
Smallpox &  
monkeypox



**MVABEA®**  
Ebola

Licensed to  
Janssen

## Pipeline



## Advancing COVID-19 vaccine program with AdaptVac

BN has entered a headsof agreement with AdaptVac, a joint venture betweenExpreS2ion Biotechnologies and NextGen Vaccines (spin-out from University of Copenhagen), to license their capsid virus like particle (VLP) based SARS-CoV-2 subunit vaccine.

# Live viral Vaccines at Bavarian Nordic

- Traditional activities for live viral vaccines manufacturing



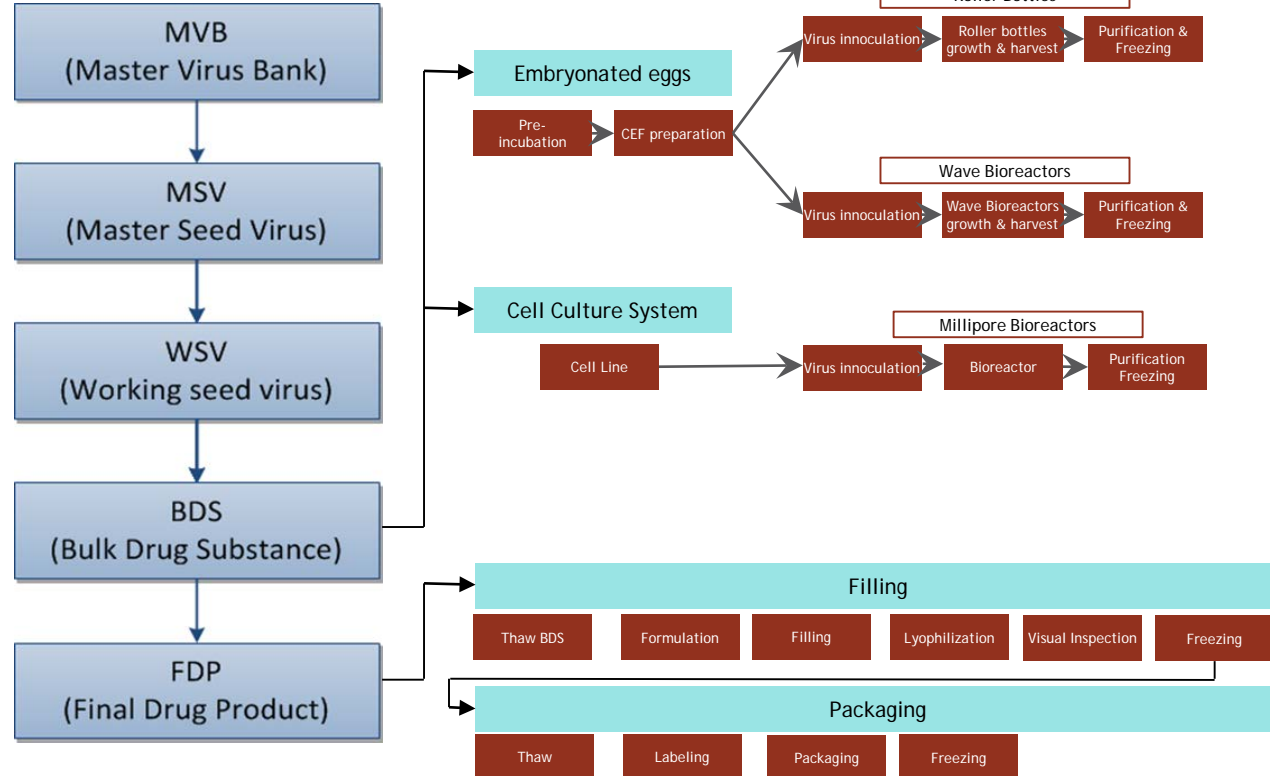
Bavarian Nordic  
Martinsried, Germany



Bavarian Nordic  
Kvistgaard, Denmark

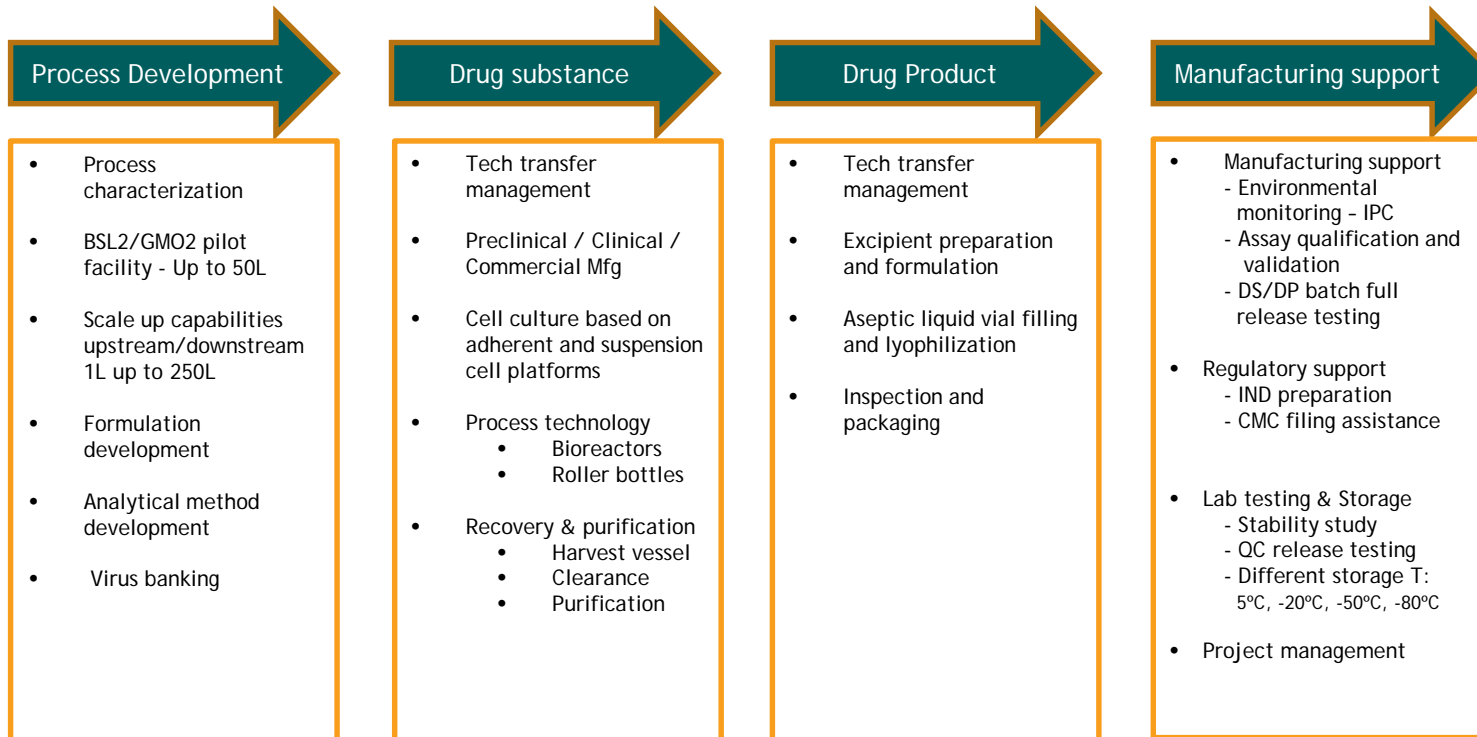


Bavarian Nordic  
Kvistgaard, Denmark



# Bavarian Nordic: Full CDMO Services

- EXPERTISE AND KNOWLEDGE - PASSION - SHARING - COLLABORATION



Experts in vaccines

Experience with transfer from and to external sites

Extensive experience working with external partners

EMA and FDA complaint site

BSL2/GMO2 classified facility

Large scale lyo capabilities

# Live, attenuated viral Vaccines



Live attenuated vaccines are produced by modifying a disease-producing (“wild”) virus or bacterium in a laboratory.

The resulting vaccine organism retains the ability to replicate (grow) and produce immunity, but usually does not cause illness.

They have been available since the 1950’s

- They elicit strong cellular and antibody responses with lifelong immunity with only one to two doses
- The immune response is virtually identical to natural infection
- Must replicate to produce an immune response
- A live attenuated vaccine virus could theoretically revert to its original pathogenic (disease-causing) form
- They are fragile and must be stored and handled carefully. They usually require refrigeration, which can make availability to remote areas/countries challenging
- They are generally contra-indicated in persons with weakened immune systems

## General Rule:

The more similar a vaccine is to the disease-causing form of the organism, the better the immune response to the vaccine

Source: CDC.gov, Principles of vaccination

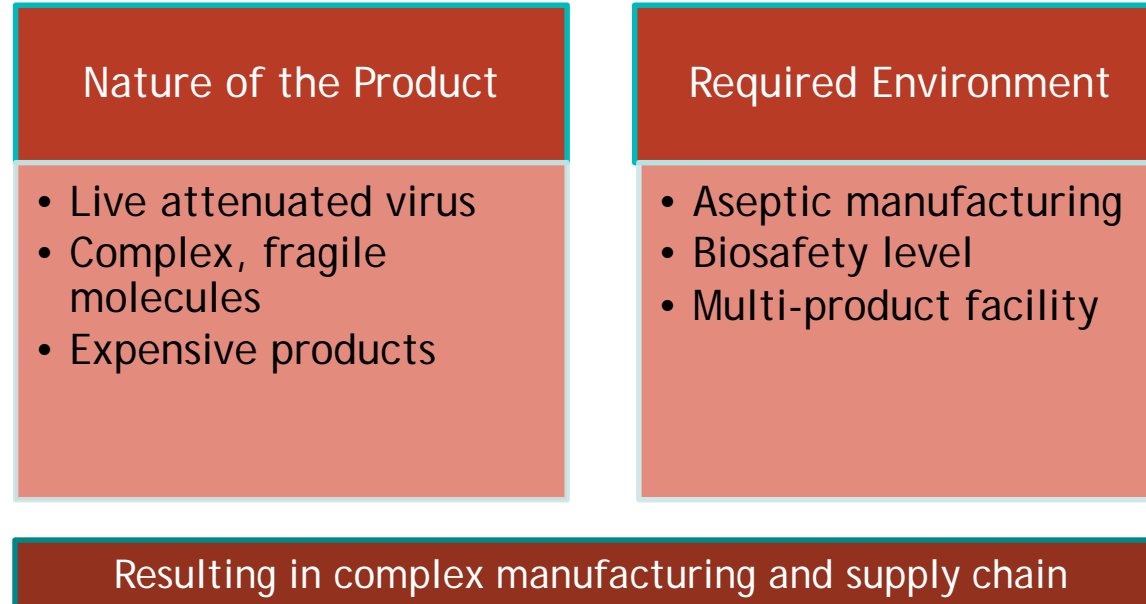
## Currently available live attenuated vaccines

- Measles
- Mumps
- Rubella
- Vaccinia
- Varicella
- Zoster (which contains the same virus as varicella vaccine but in much higher amount)
- Yellow fever
- Rotavirus
- Influenza (intranasal)
- Oral polio vaccine
- Live attenuated bacterial vaccines are bacille Calmette-Guérin (BCG) and oral typhoid vaccine.

The first vaccine used by Jenner is of this type: vaccinia virus (cowpox) inoculation of humans confers immunity to smallpox but does not cause smallpox.

# Complexity in Fill&Finish of Live viral Vaccines

- Complexity driven by



A high level of expertise is required!



# Basic Design concept for Fill&Finish



- Product considerations

Nature of the product	Design concept
Live attenuated virus	<ul style="list-style-type: none"><li>• Adequate Bio Safety Level</li><li>• Adequate cleaning and decontamination</li><li>• Full Single-use technology</li><li>• Full isolator technology</li></ul>
Complex, fragile molecules	<ul style="list-style-type: none"><li>• High speed filling line</li><li>• Low pressure peristaltic pumps</li><li>• Lyophilization capabilities</li><li>• Minimized transport between activities</li><li>• Cold storage capabilities for different T.</li><li>• Reduced TOR</li></ul>
Expensive products	<ul style="list-style-type: none"><li>• Minimize product losses</li><li>• Enable small bulk volumes</li></ul>

## Summary - take home messages



- Complex project
  - Very tight timeframe
  - Minimized facility space
- Goal achieved by:
  - Very clear design specifications
  - FDA Type C meeting very early in the design phase
  - Choice for proven technology
  - Strong project management
  - Aligned teamwork

Thank you to IPS, Syntegon and all involved and committed stakeholders!

Thank you for your attention!



- [Rutger.Vandiest@Bavarian-Nordic.com](mailto:Rutger.Vandiest@Bavarian-Nordic.com)

# Part II – Vaccines for the World – Insights into the Design & Execution of a BSL2 Fill-Finish Facility

March 23rd, 2021



**SYNTEGON**



## Facility Design & Project Execution



Mark Miller  
Director of Projects, IPS EMEA

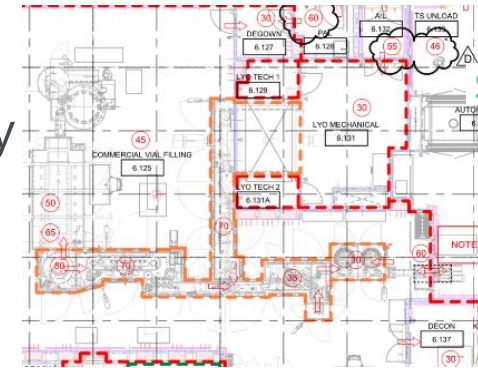
# Facility Design – Process Architecture

## Design Objectives

- Commercial & Clinical
- Multi-product
- FDA / EU GMP compliance
- GMO2 / BSL2 compliance

## Containment & GMP – EHS v's Quality

- Isolator technology
- Pressure regimes
- Uni directional flows

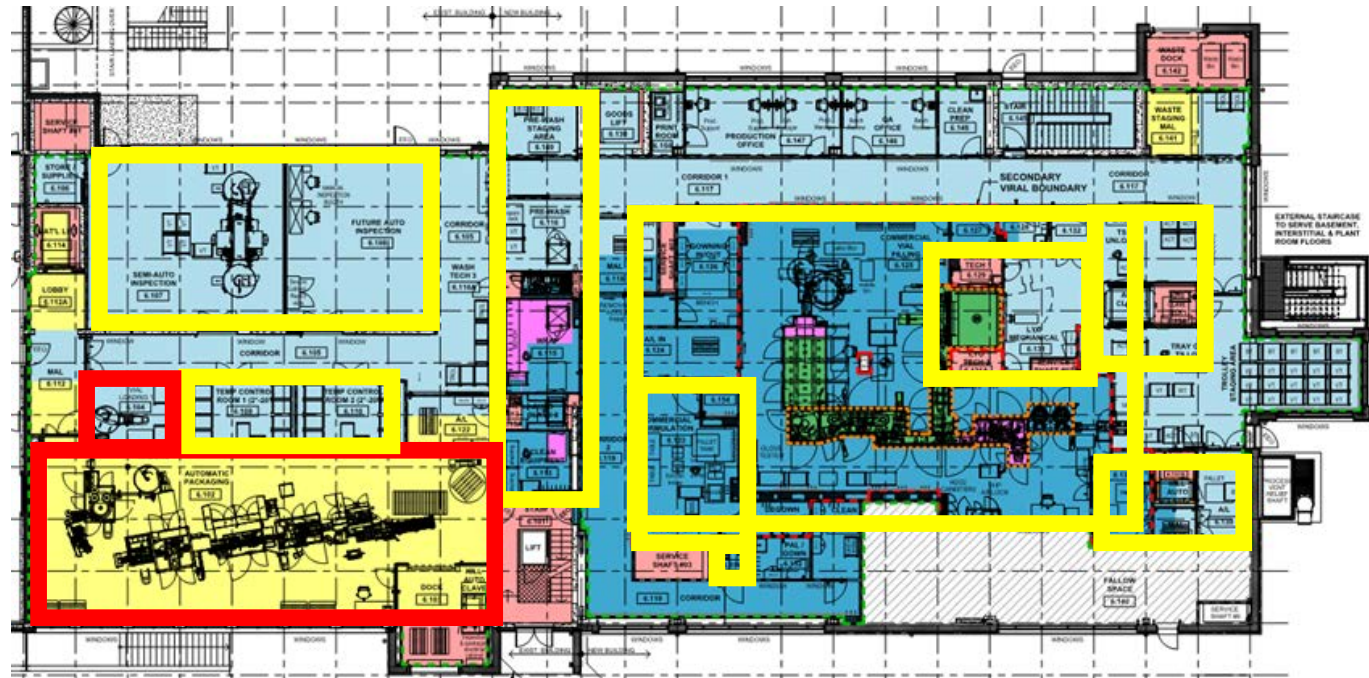


## Challenges

- Footprint constraints
- Refurbishment

## Functionality

- Cold Storage
- Formulation
- Filling
- Lyophilization
- Terminal Sterilisation
- Wash & Sterilisation
- Decontamination
- Inspection
- Packaging + Serialisation





**ips**

**SYNTEGON**

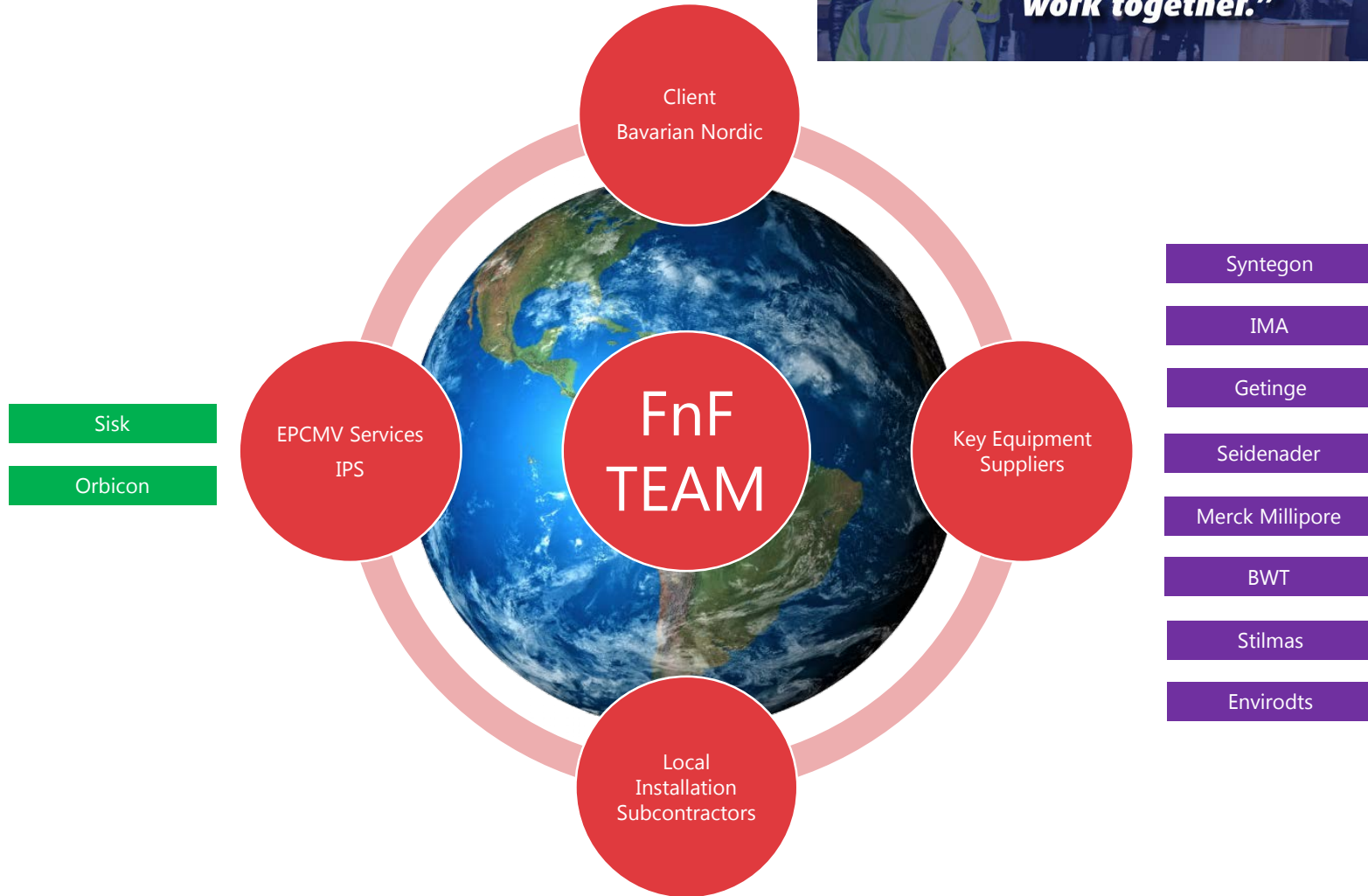




# Project Team



SYNTEGON

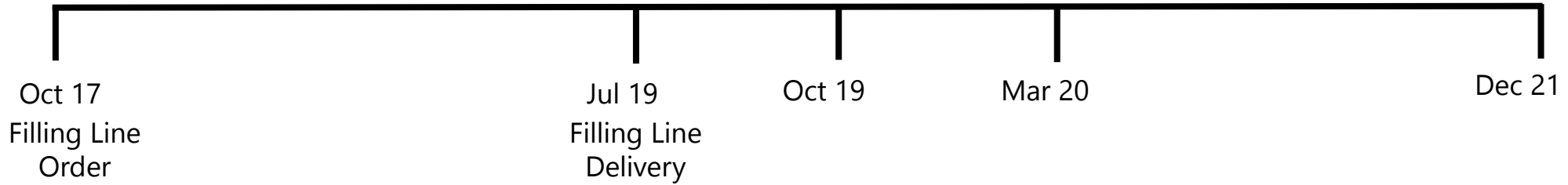




# Planning & Timelines



SYNTEGON



# Project Execution Challenges

- Basic Design changes
- Site noise constraints
- Local construction supply chain design capability
- Package Coordination – language, geography, culture



SYNTEGON





# Thank you!

Mark Miller

Director of Projects, IPS EMEA

[mamiller@ipsdb.com](mailto:mamiller@ipsdb.com)



**SYNTEGON**

PROCESSING & PACKAGING

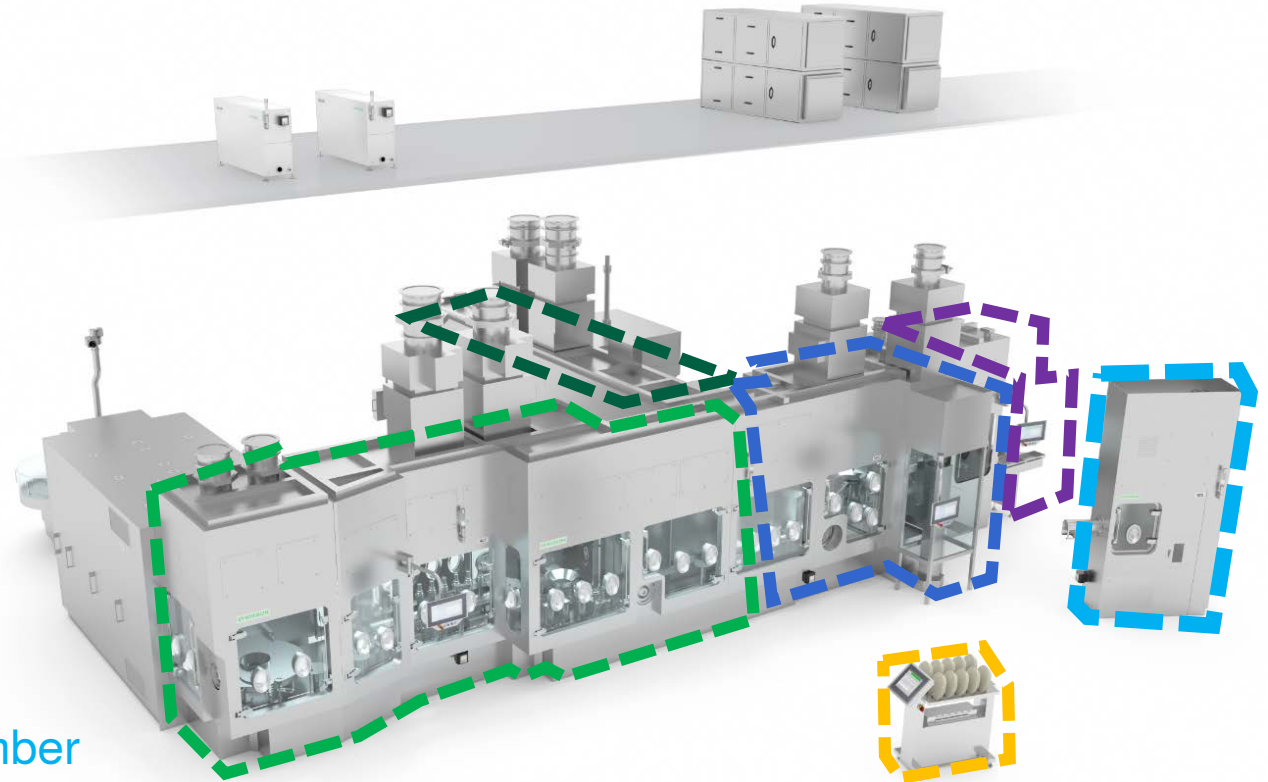
# Technological Highlights Isolator Line

DCVMN Webinar, March 23<sup>rd</sup>, 2021



# Line overview

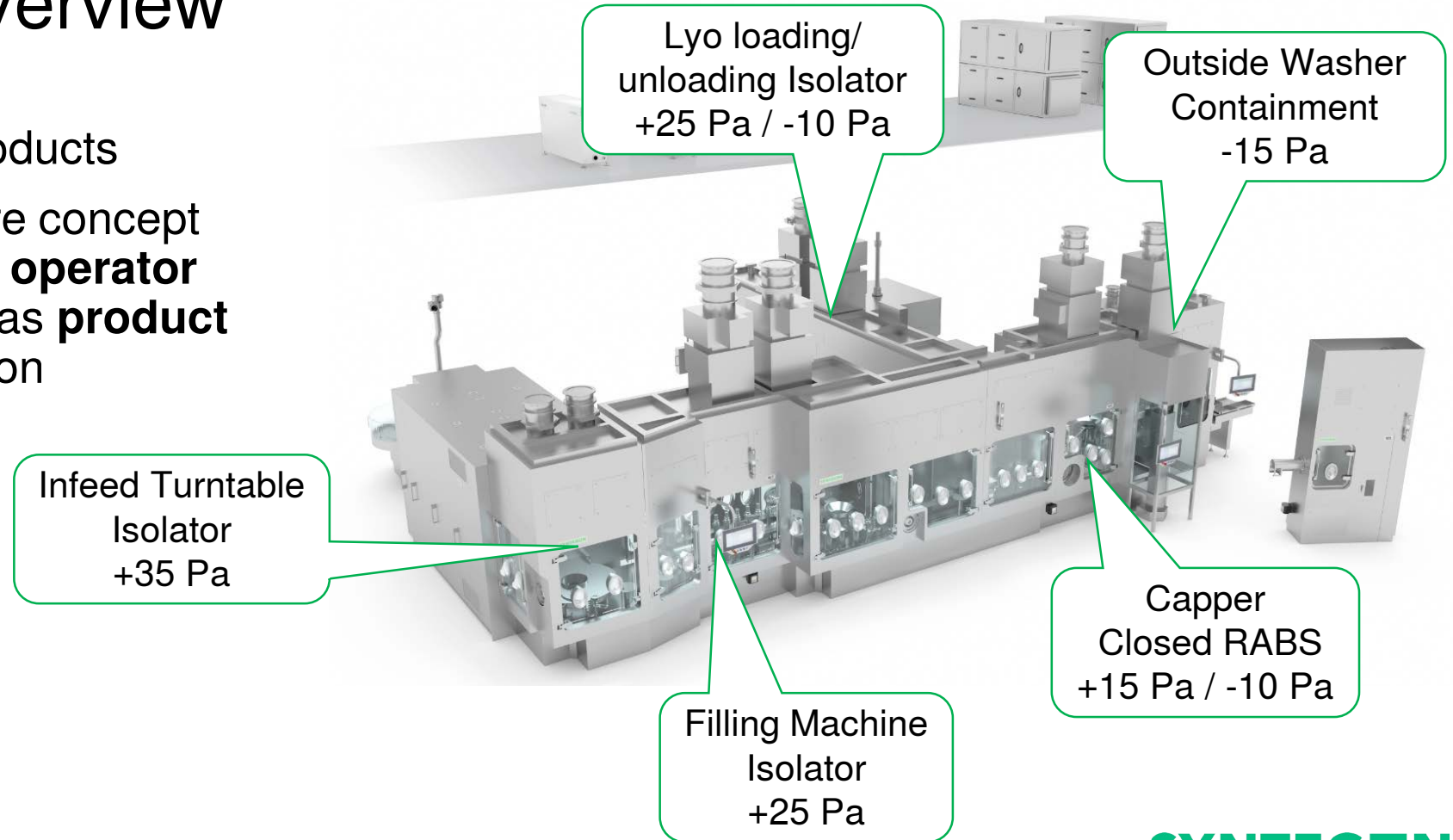
- BSL application
- Liquid and lyo products
- Vial filler with 100% IPC and Isolator
- Lyo loading/unloading Isolator
- Capper in Closed RABS
- Outside Cleaning in Containment
- Wireless Glove Testing
- Stand-alone Transfer Chamber ISS





# Line overview

- BSL products
- Pressure concept for both **operator** as well as **product** protection





# Fill-Finish Equipment

- **Usage of proven technology**
- High-speed filling machine up to 400pcs./min
- 100% IPC
- Focus on highest product yield
- Dose-In/Dose-Out function
- Optimized stoppering





# Fill-Finish Equipment



8-head peristaltic pumps

Filling needle movement

Environmental monitoring

100% IPC



# Focus on product and operator protection

- Dedicated pressure concept
- 2 dedicated VHP cycles
  - **Decontamination** as part of line changeover
  - **Inactivation cycle** for BSL 2 products
- Additional filter systems (SafeChange) for incoming and outgoing air





# Capping Machine

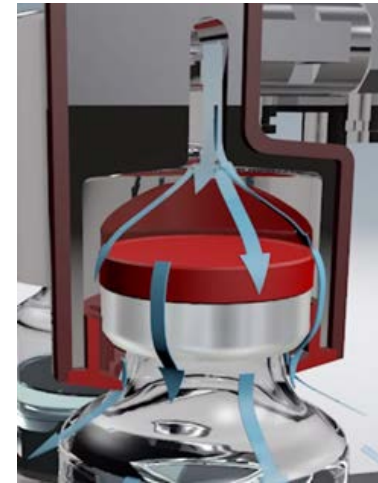
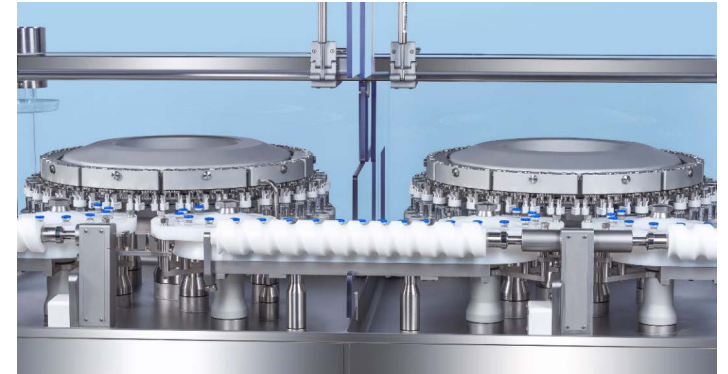
- Separated Closed RABS Segment
- VHP inactivation cycle
- Integrated Camera Systems
  - Crimping Quality
  - Stopper position check





# Outside decontamination of vials

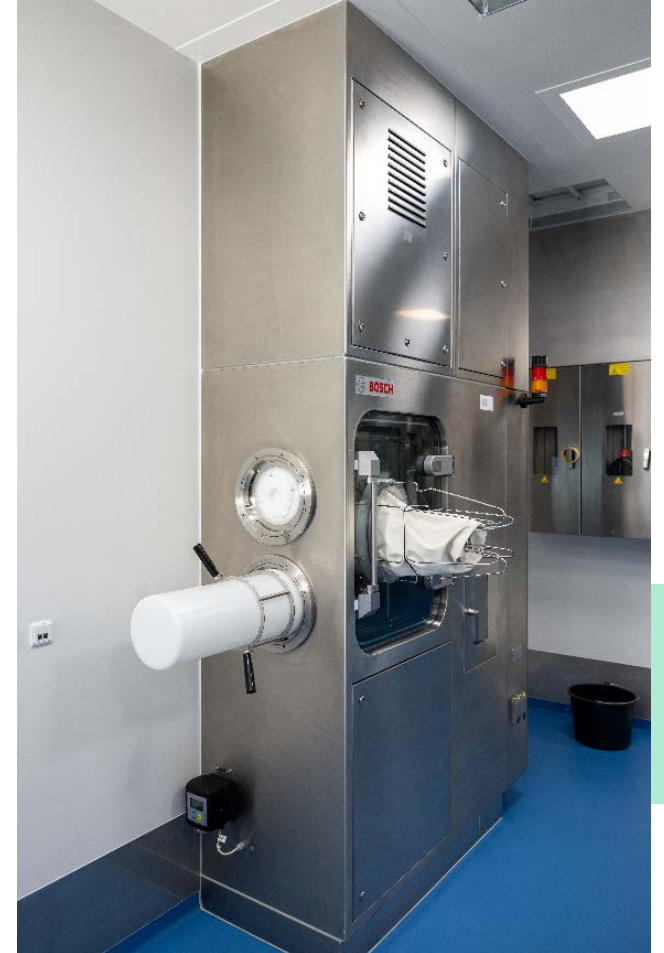
- Outside cleaning machine
- Containment execution
- 2 separated areas for cleaning and drying
- High-pressure cleaning of outer vial surfaces
- Vial neck area gets protected by active airflow

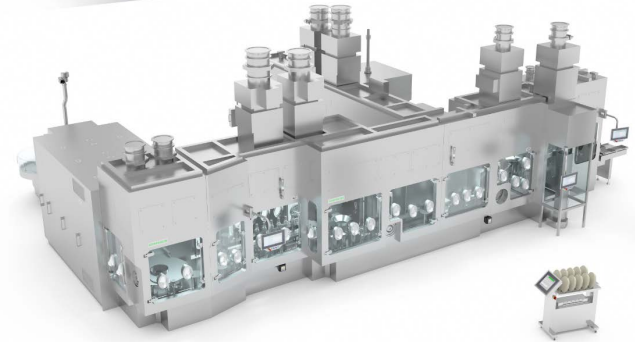


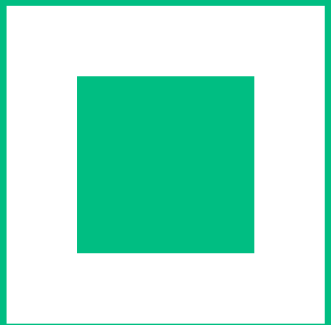


# Sampling and Material Transfer

- Usage of VHP transfer chamber
- Double functionality:
  - Material transfer via RTP port
  - Inactivation of outer surfaces of samples
- Customer specific racks and containers
- Rapid biodecontamination cycle time
- Simplified air handling with catalytic converter







THANK YOU!

ANY QUESTIONS?

E-MAIL: [MATTHIAS.ANGELMAIER@SYNTEGON.COM](mailto:MATTHIAS.ANGELMAIER@SYNTEGON.COM)