



#sharing challenges
and solutions in practice

Implementation of new freeze dryers in existing building infrastructure

CSL Behring Marburg

Conference

Part of PharmaCongress – Düsseldorf/Neuss, 31 May–1 June 2022

Project description and background

- **Case Study CSL Behring – Challenges due to limited space in the existing building during construction phase**
- The ILC-H69 (Increase Lyophilization capacity – building H69) project involves the installation of two new freeze dryers with automatic vial loading system and connection to existing filling line.
- The special challenges of this project are the extremely limited space in the existing building and the continuation of filling operations during the construction phase.
- These were mastered with the use of new planning tools:
 - 3D Planning
 - Laser-scan
 - Virtual Reality visualization
 - Feasibility Study for large component intake

What we will present to you

- Introduction of CSL and CSL Marburg
- Initial situation and scenarios
- Initial steps of project & scenarios
- Favored scenario
- Goals & user requirements
- Floor plans, initial and final situation
- Project challenges
- Realization
- Insights, examples and videos
- Cooperation between Production and Project
- Conclusions and outlook
- Your questions and exchange of ideas



Who is presenting to you ?

Matthias Klein

Value Stream Lead Packaging Marburg
Member of Site Operations Leadership Team

Former positions within CSL and predecessors:

- 2010 – 2021 Director Filling & Visual Inspection H69
- 2004 – 2009 Director Quality Management Production
- 1999 – 2004 Director Facility Validation/Qualification
- 1997 – 1998 Senior Manager Quality Assurance CSL
- 1994 – 1996 Plant Engineering Hoechst-Schering Crop-Science
- 1991 – 1993 Plant Engineering Hoechst Holland NV
- 1989 – 1991 Engineering Hoechst AG Frankfurt

Background: Dipl.-Ing., M.Sc.
Automation & Control Technology, University Darmstadt



Who is presenting to you ?

Steffen Mörl

Associate Director Project Excellence



Former positions within CSL and predecessors:

- 2021 – 2022 Associate Director Project Excellence, CSL Behring
- 2020 – 2021 Senior Project Manager, CSL Behring
- 2019 – 2020 Project Manager, CSL Behring
- 2016 – 2019 Senior Consultant Project Management, Campana & Schott
- 2010 – 2016 Project Manager, Areva
- 2008 – 2010 Project Engineer, Brunel

We operate globally

CSL is a leading global biotechnology company that develops and delivers innovative biotherapies that save lives, and help people with life-threatening medical conditions live full lives.



R&D Investments of **3.7** bio. US \$
in 5 years drive promising new products forward

1.700+ R&D Employees

270+ Plasma donation centres throughout Europe and North America

Manufacturing Sites



Marburg,
Deutschland

3,000

Employees

Core Products

- Coagulation factors
- Critical care products



Bern,
Schweiz

1,500

Employees

Core Products

- Immunoglobulins



Kankakee,
USA

1,600

Employees

Core Products

- Albumin
- Intermediate pastes



Melbourne,
Australien

1,000

Employees

Core Products

- Coagulation factors
- Critical care
- Immunoglobulins



Wuhan,
China

200

Employees

Core Products

- Immunoglobulins
- Albumin

CSL Behring Marburg at a glance

MARBURG
AT A GLANCE

30+

Nationalities
as the basis of our highly
qualified and diverse workforce

20+

Inspection days
per year

102

Countries
supplied from Marburg

625

Active licences
for 19 products

3,400

Final product releases
per year

8

Core products
with global sales >\$100m

183

Products approved
worldwide in the last 5 years

<2.00

Safety TRIFR
36 rolling avg: total recordable
incidents / 1 million working
hours

+\$700m

Site Operations Invest
in last 5 years

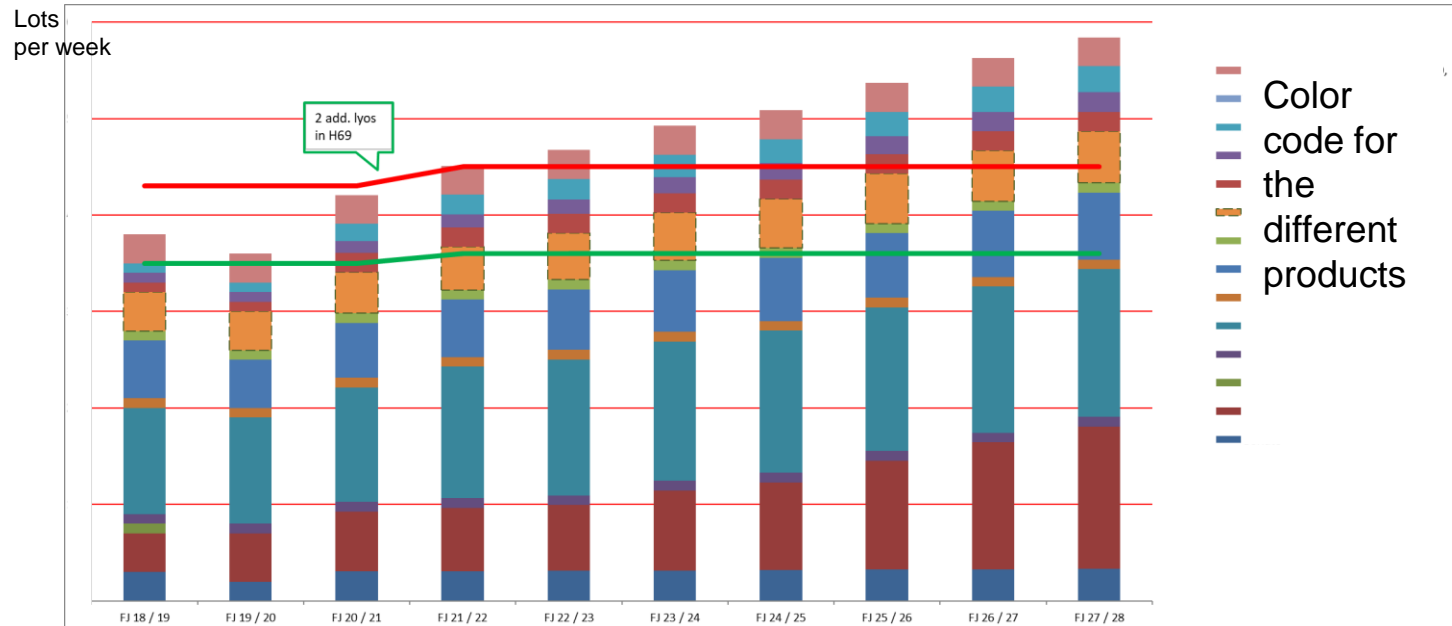
Driven by Our Promise™

Initial capacity situation 2017

- 10-year forecast revealed bottleneck for freeze-dried production capacities within the next 5 years

100% utilization capacity is "critical"

80% utilization capacity should be the "healthy" planning capacity, incl. time for maintenance shut down



Initial steps of project & scenarios

- Internal project request was initiated
- Order for a pre project study (strategy) addressed to
 - Project Engineering and
 - Production
- Scenarios and solutions were developed that included
 - Green field solutions
 - External supplies
 - Upgrade/expand of existing filling and freeze-drying lines
 - Do nothing option



- A favored version was selected



Favored scenario

- Highest benefit:
expanding of existing filling line in Building H69
- Main reasons:
 - Existing modern filling line available
 - Space for 2 new lyophilizers available
 - Infrastructure available
 - Shortest time for realization of project
 - Best costs of all alternatives
 - Business case showed a payback period < 4 years (NPV)
 - Bulk hold times are too short for external supply via CMO
 - CMO filling & freeze-drying capacities limited esp. for vial sizes > 100ml & 250ml
 - Know-how for aseptic filling & freeze-drying and Engineering project management available on site



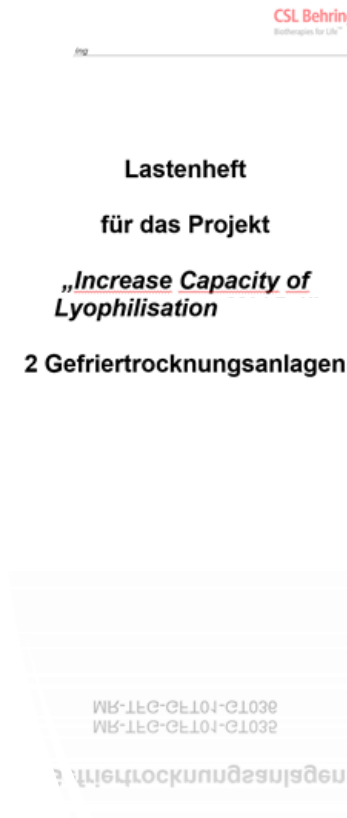
Goals & user requirements

- Assure patient supply for the future!
- State of the art design:
 - Aseptic technology → e.g. fully automated vial loading system
 - Full GMP- & EHS-compliant
 - EU & US market approval
- Available space must fit for the future product demand
 - 2 new Lyos and
 - Potential for future expansion
 - Design for multi purpose products
- Construction work in parallel to running aseptic filling
 - Safe separation of the construction and aseptic production areas
 - Needed higher sterility assurance
 - Additional (re-) qualification and monitoring program to assure aseptic filling area



Goals & user requirements

- One bulk batch per lyo-load
 - ~ 500 Liter drying capacity
- No human interventions in routine process
- High degree of process automation
- Integration of loading system to existing filling line
- Simulation of air flow in critical areas
 - CFD-Studies
- Shortest possible shut-downs for connecting new installations to filling line
 - Fully automated vial loading system
 - Utilities (HVAC, WFI, ...)
 - New lyophilizers
 - Synchronize routine with project shutdowns in order to minimize project specific shutdowns
 - Coordinate production schedule with Supply Chain Planning

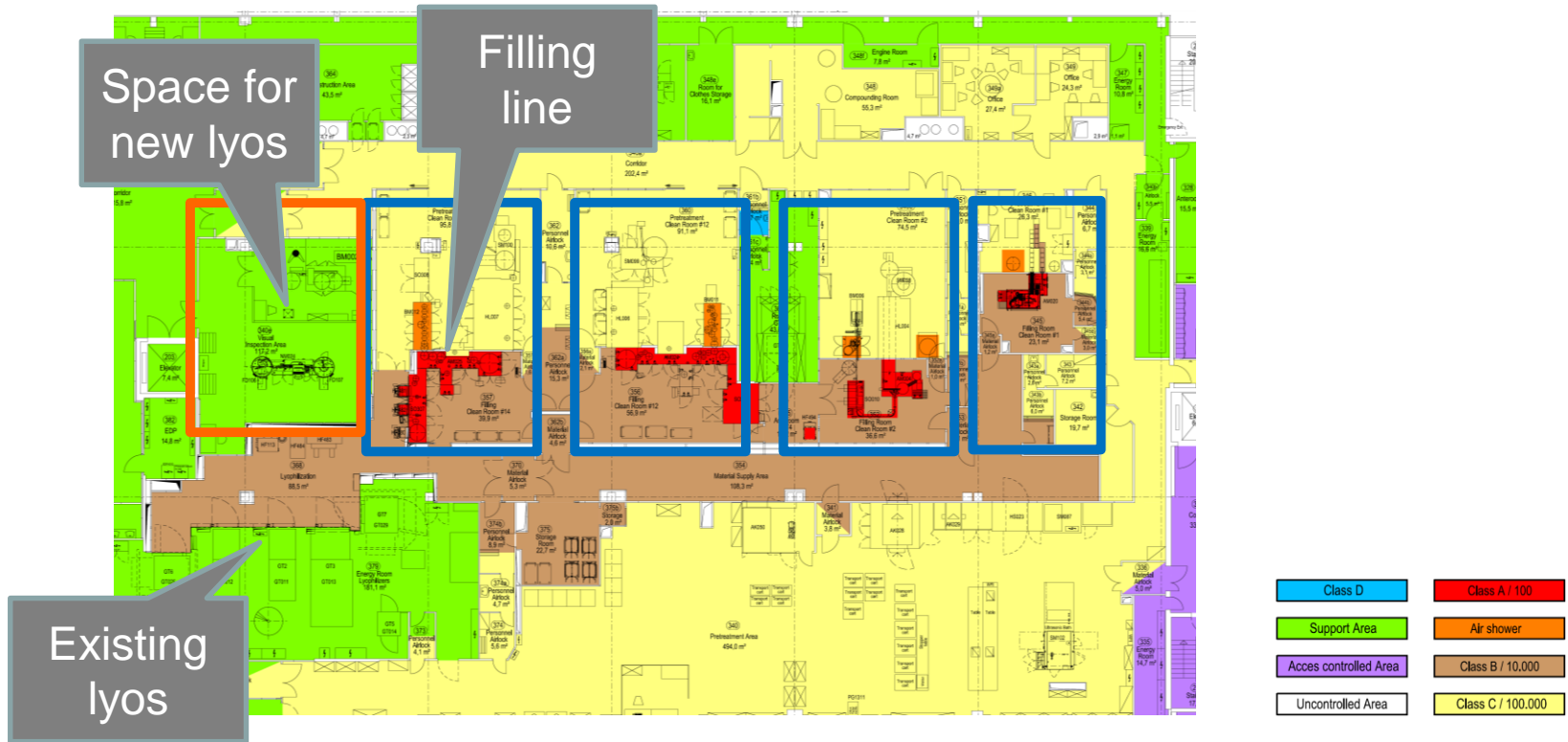


Project Engineering

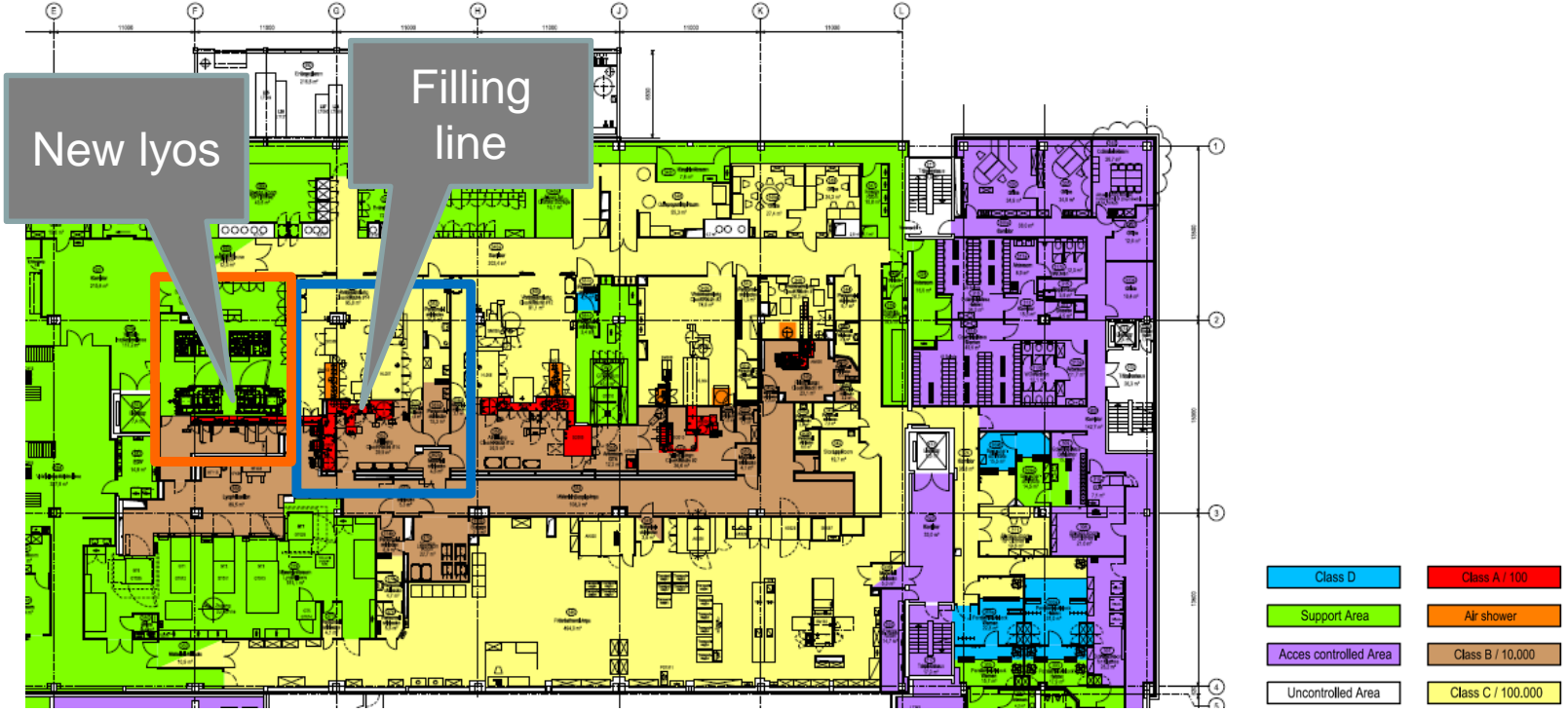
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Initial situation, filling lines in building H69



Final situation, filling lines in building H69



Project challenges

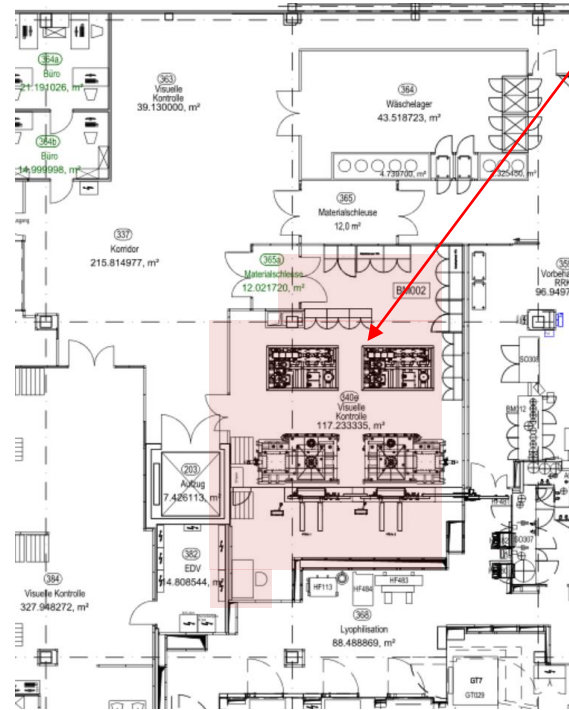
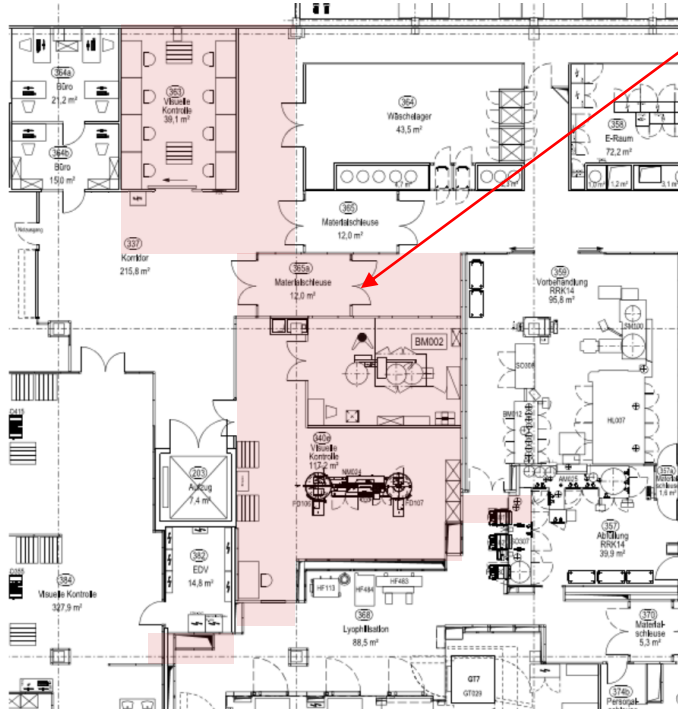
- No interruption of running production and synchronization with routine shut-downs
- Limited timelines
- Limited space
- Integration into an existing infrastructure
- Expanding of building infrastructure
- Load capacity of the floors & ceilings
- Relocation of rooms and air locks
- Unknown accuracy of existing building plans
- Integration and allocation of operators



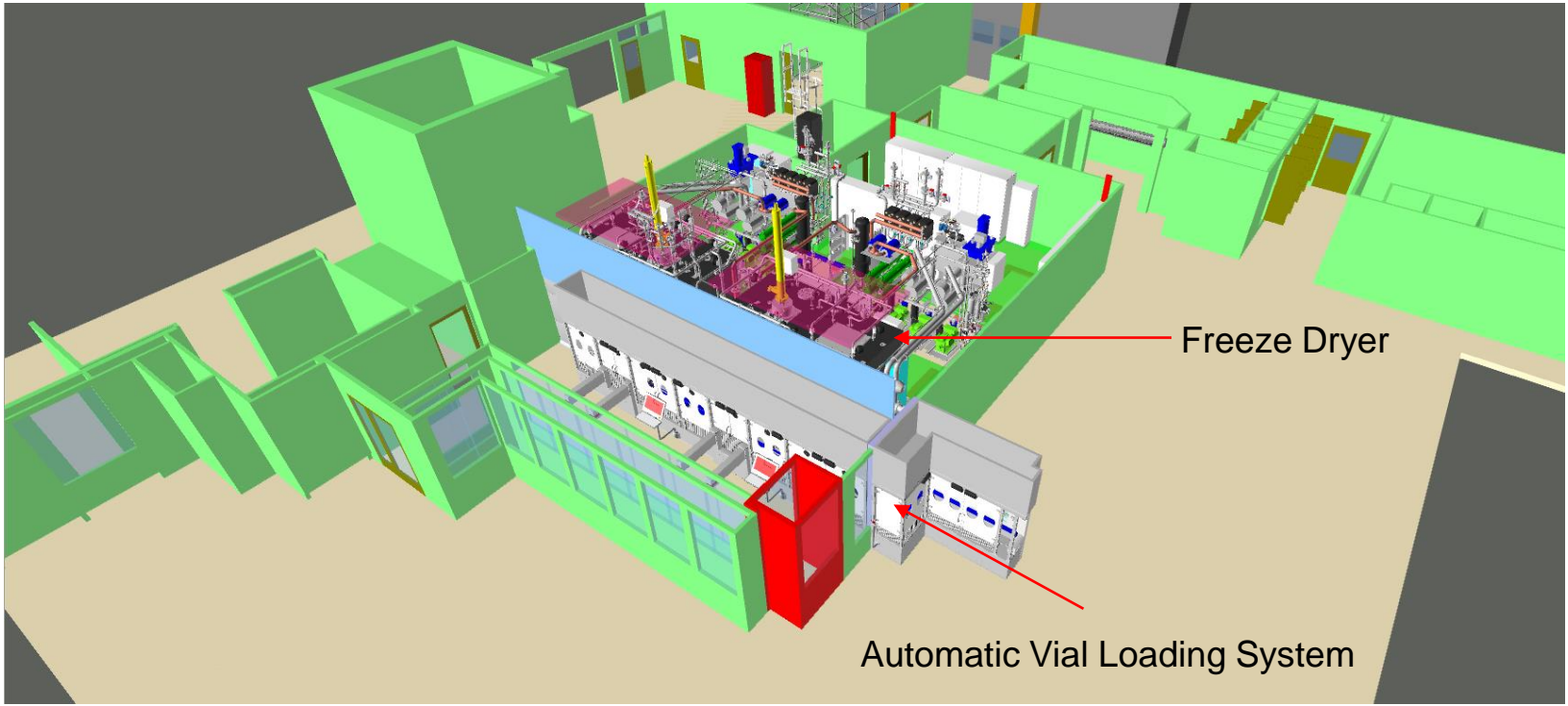
Transformation

Existing room layout

Modified room layout



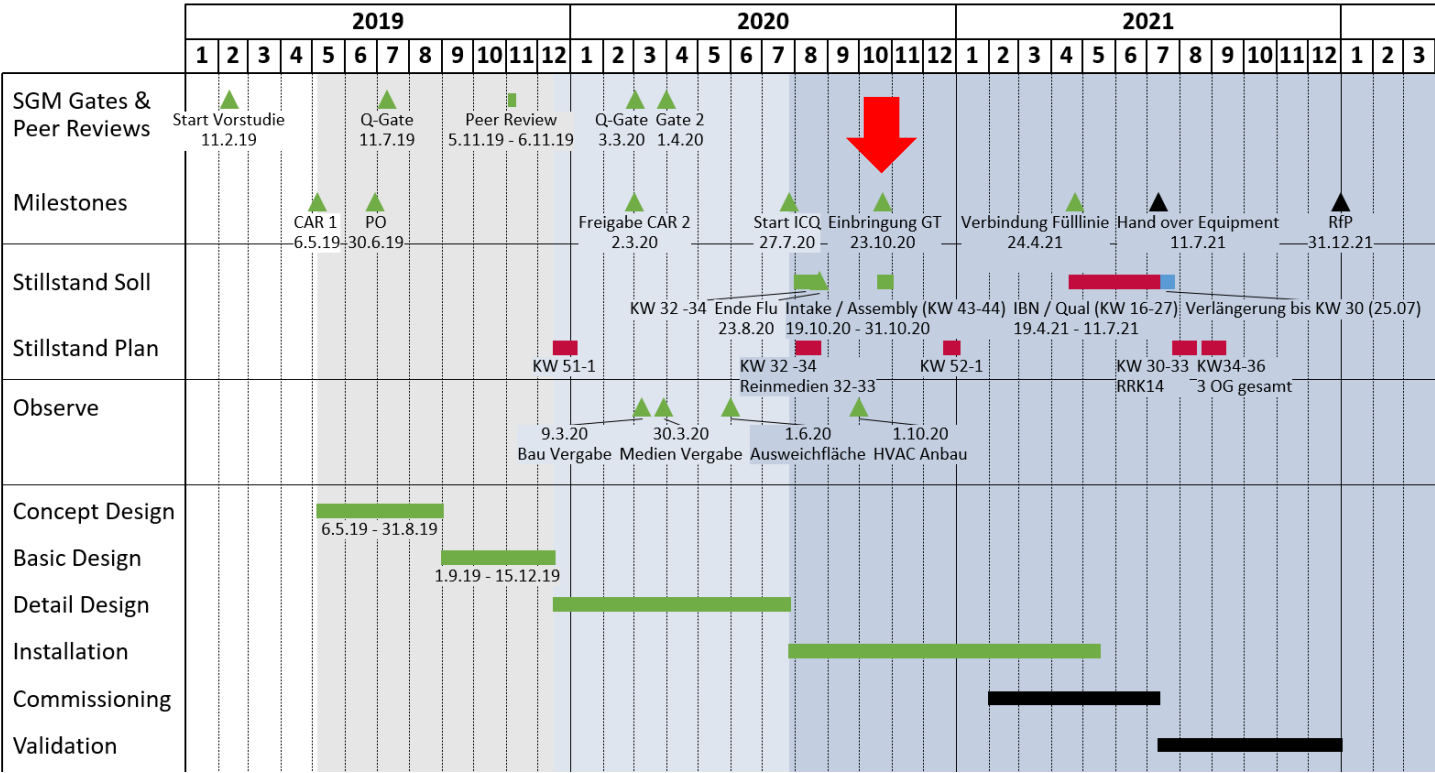
Layout Configuration



Freeze Dryer

Automatic Vial Loading System

Milestone Freeze Dryer Transport



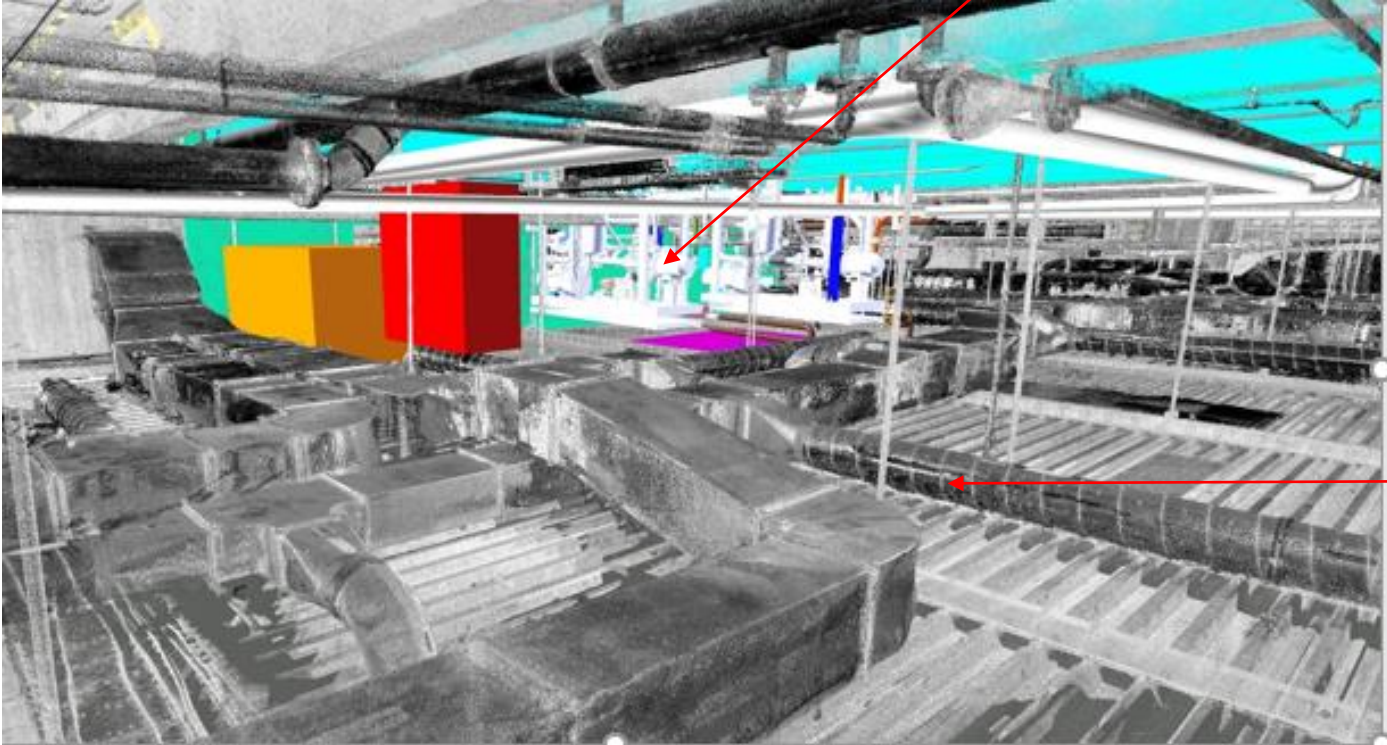
Supported by



Academy
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Information Source

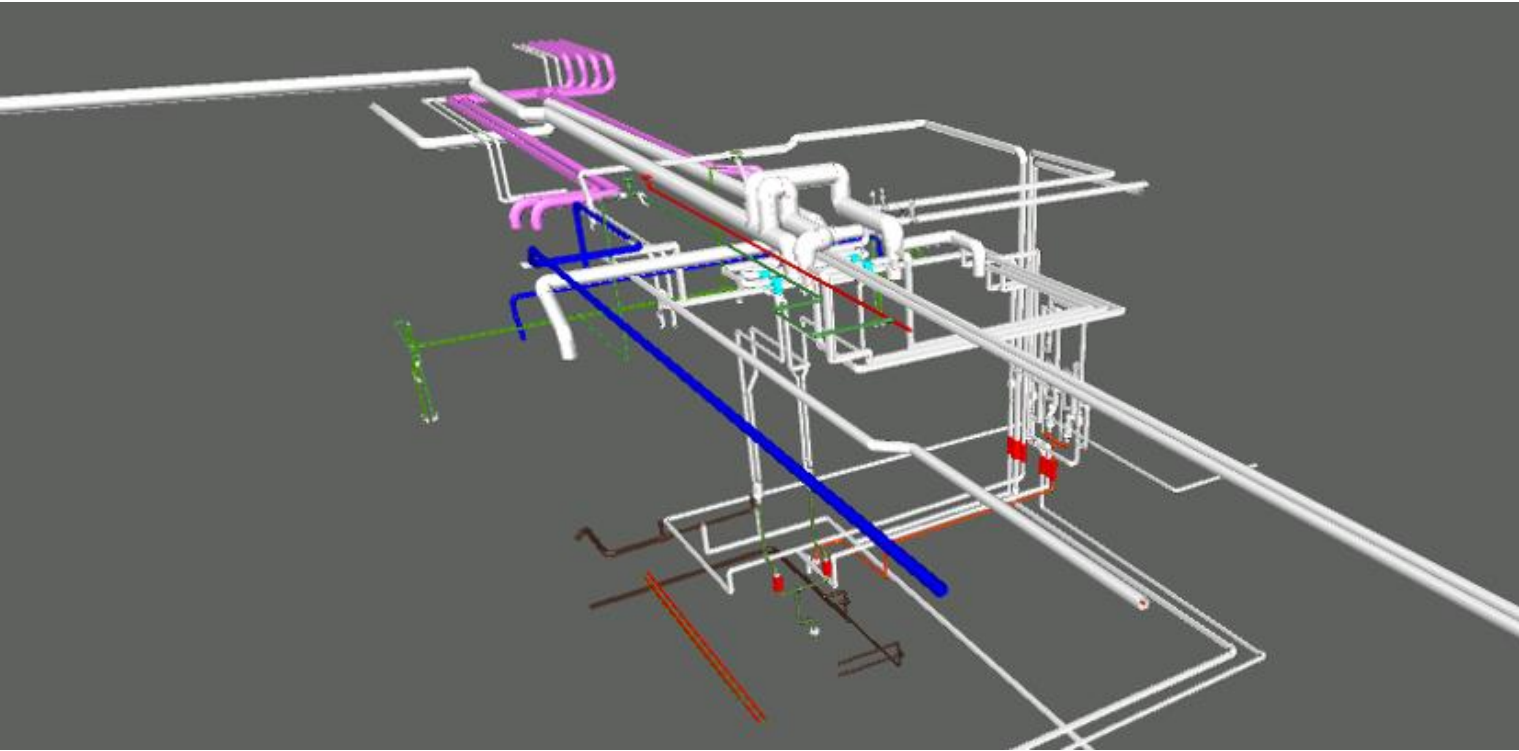
Detailed Design Layout

Detailed Design layout integration



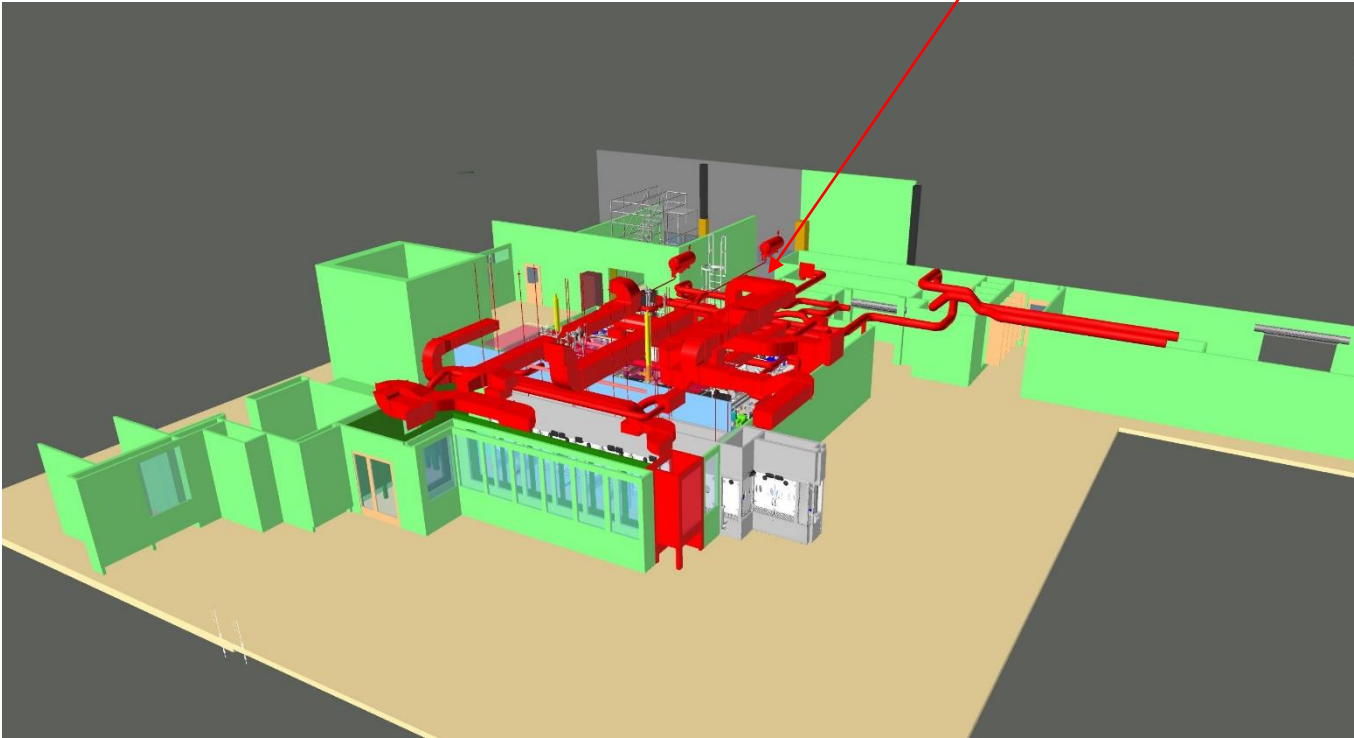
3D Scan

Existing & New Piping

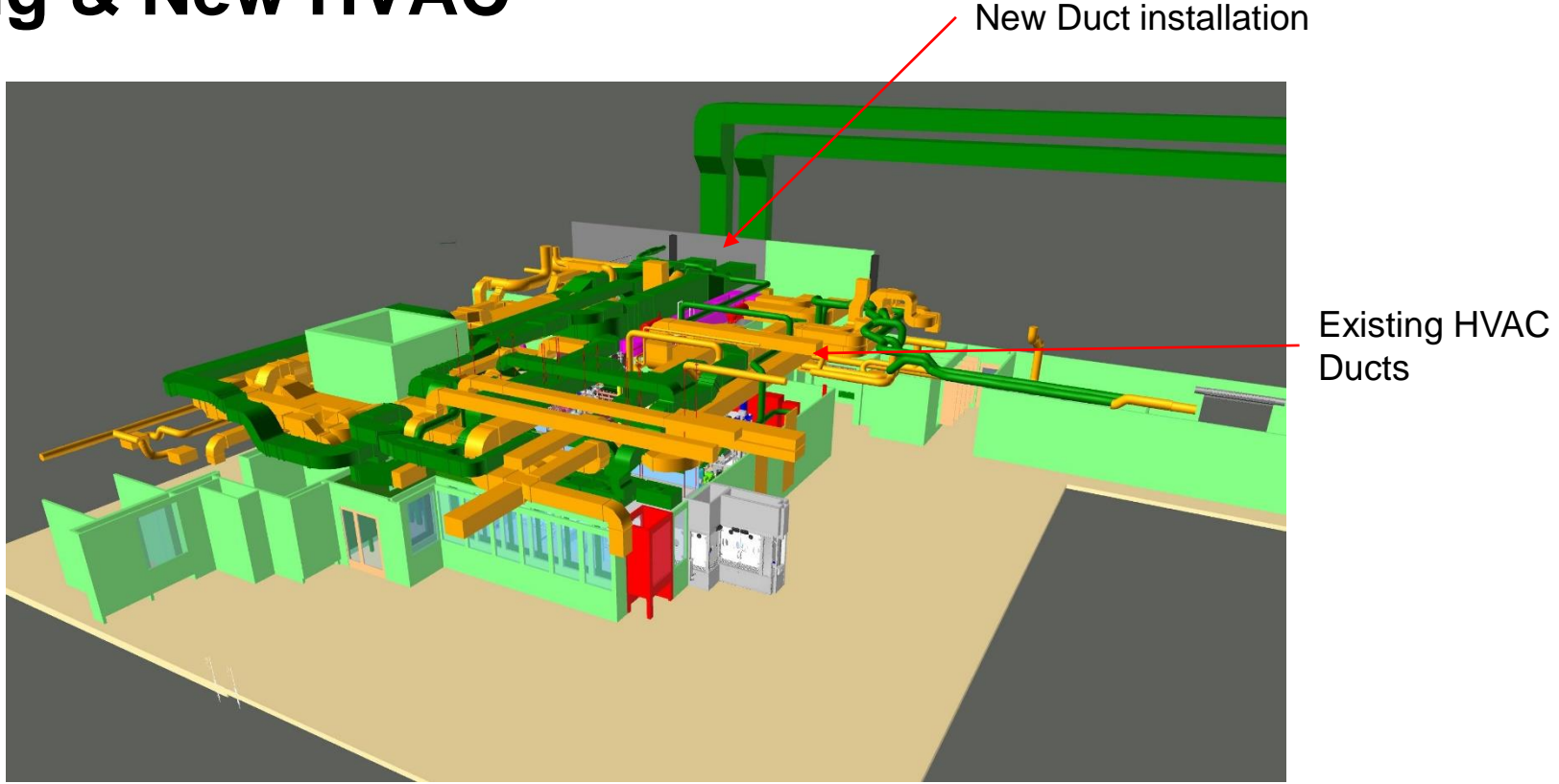


HVAC Dismantling

Dismantling Scope



Existing & New HVAC

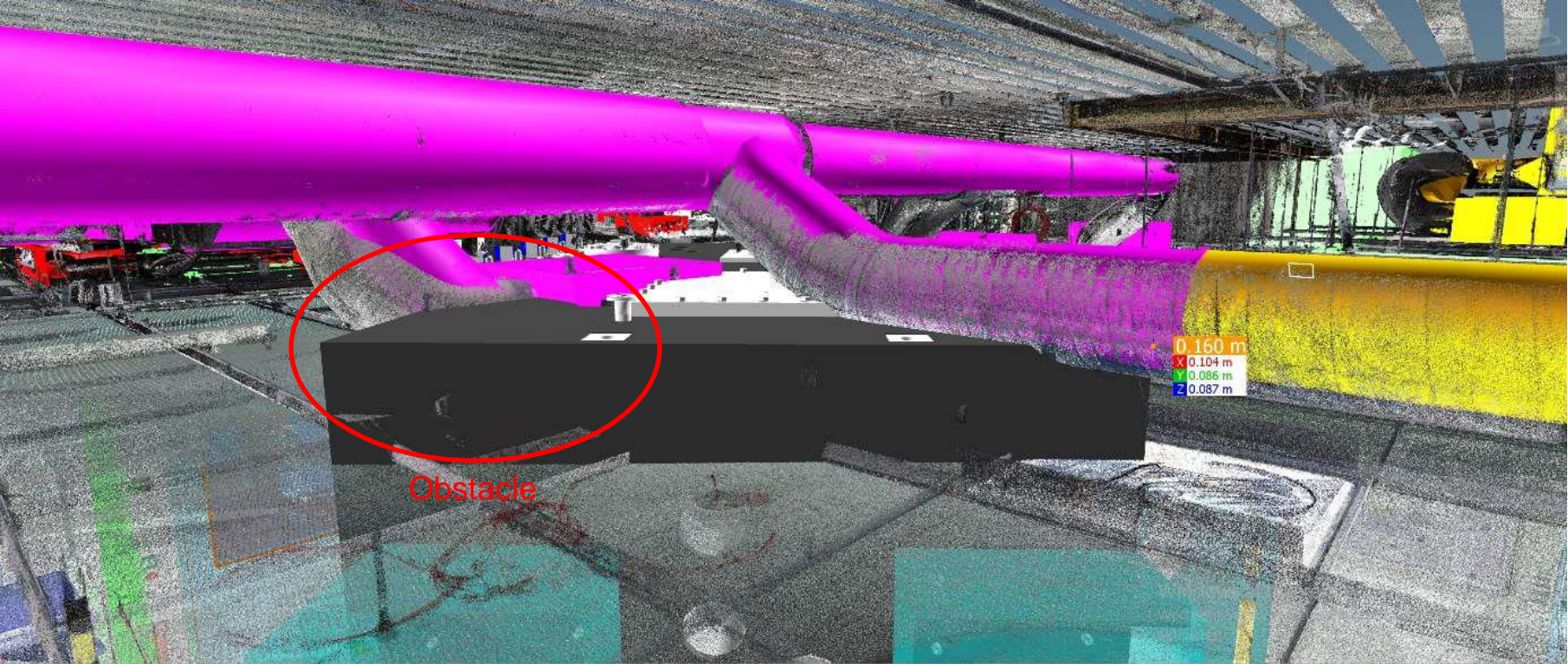


Layout & Feasibility Obstacles

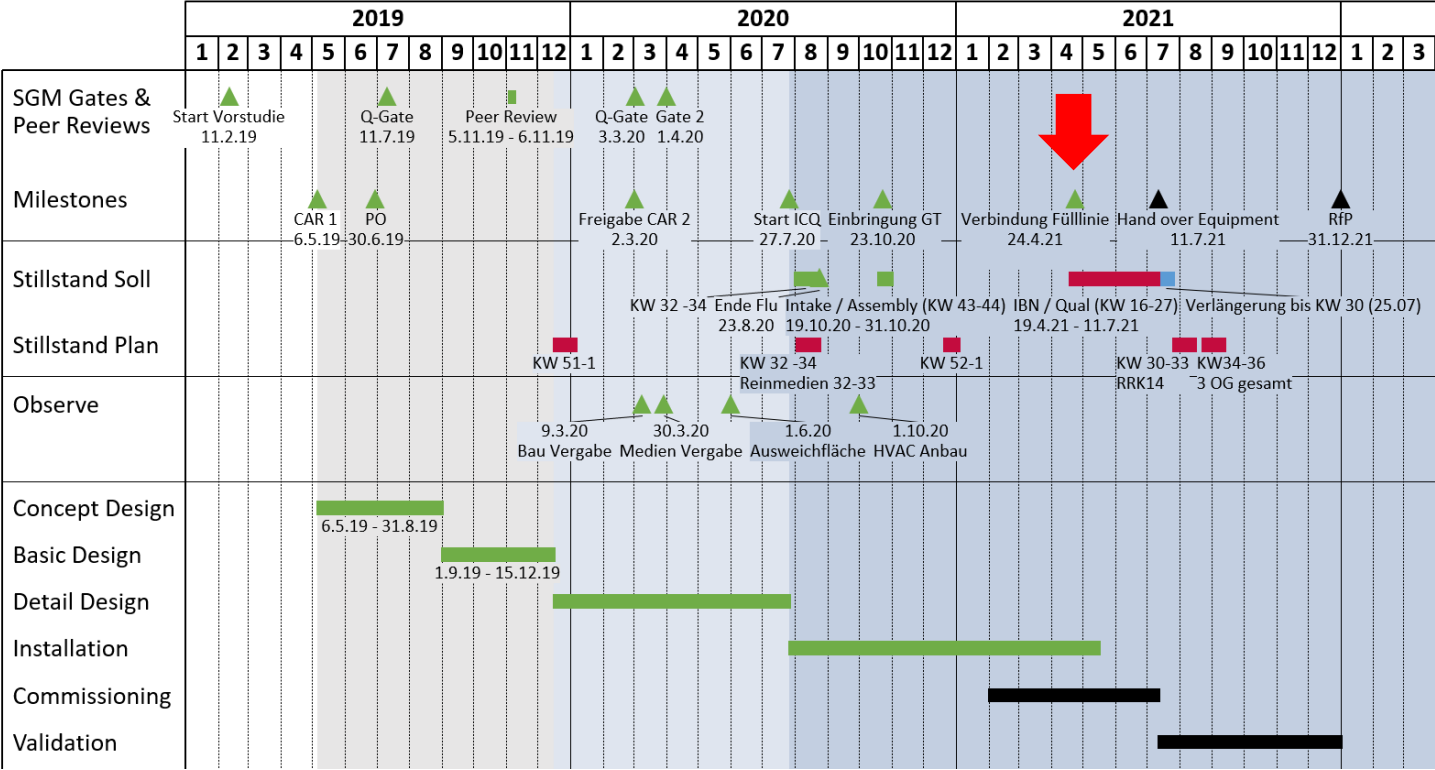


Windows aktivieren
Wechseln Sie zu den Einstellungen, um Windows zu aktivieren.

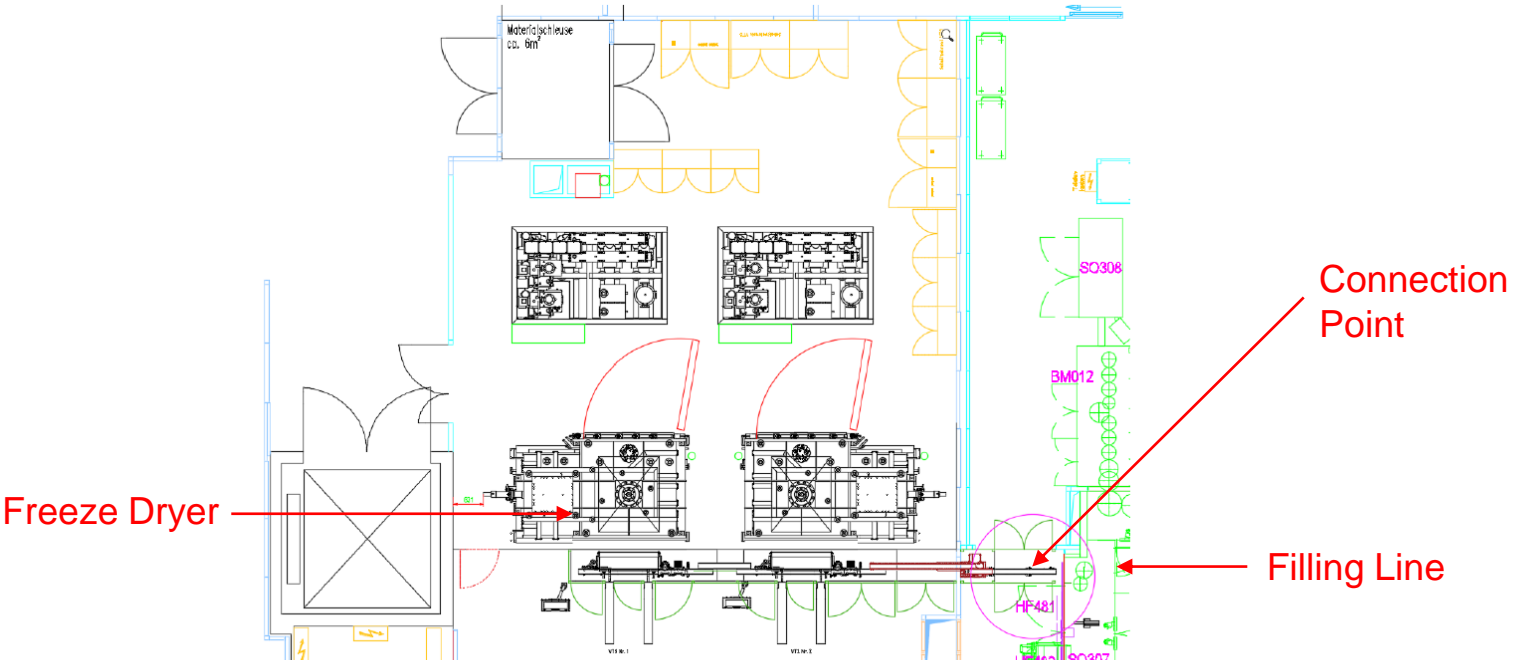
Layout & Feasibility Obstacles



Milestone Connection Filling Line



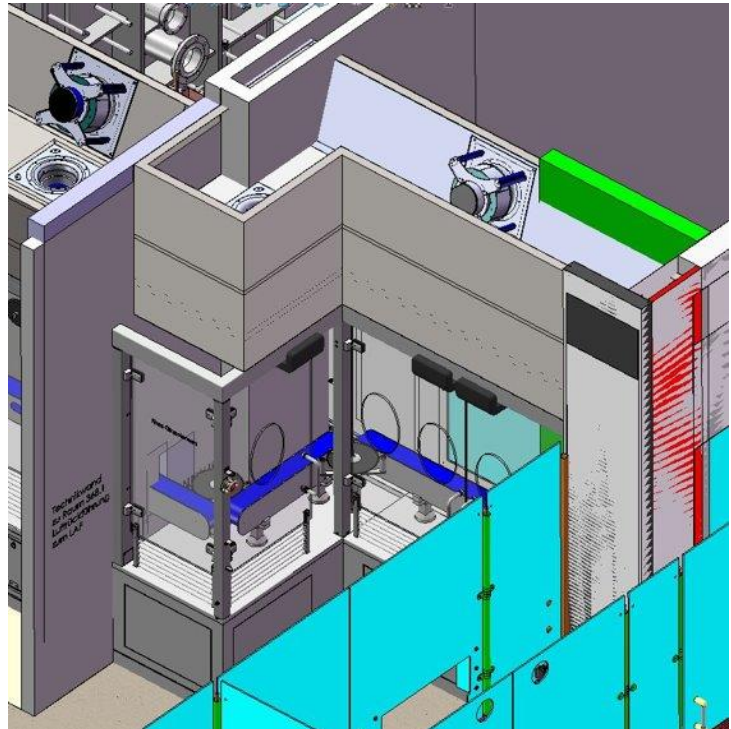
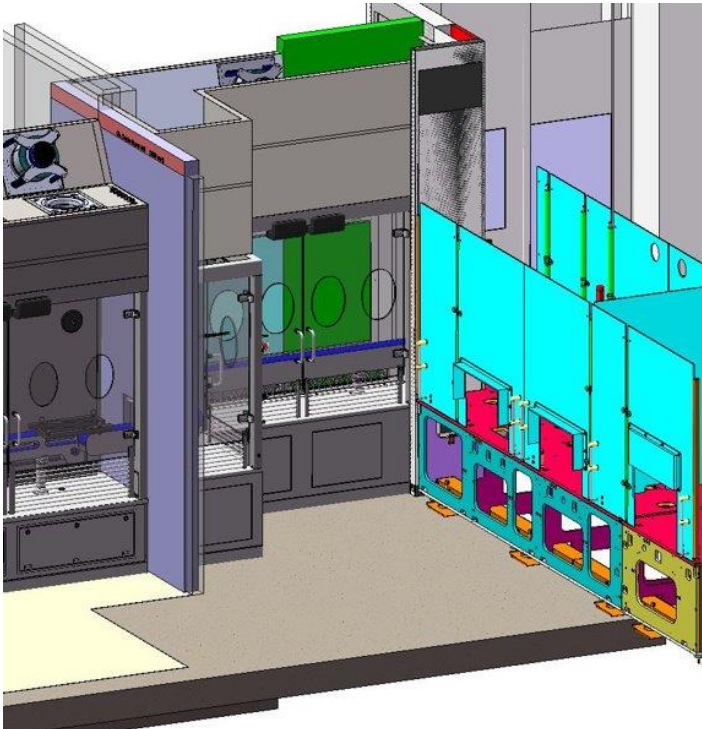
Planning



Mock Up



Final Layout



- Conclusions
 - Communication
 - Cooperation internal & external partners
 - Integration of operators
 - Project management methods
 - Use of modern tools



Looking forward to your questions and discussion