

# State of the Art Loading Systems

## Ride the waves of innovation

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# Presentation Overview

- Intro
  - Annex 1
  - Lyo System Configurations
- Motivation for Automation
- Nature of Loading System ( Fixed & Flexible & Mixed )
- Loading Sequences Capabilities
- Cold Shelf Loading Considerations
- Functional Integration with Filler & Capper
- Functional Integration with Freeze Dryer
- Containment ( LAF & RABS & Isolator )
- Environmental Monitoring
- Smoke studies
- Latest Features on Loading Systems
- Questions
- IMA Life

# Annex 1

## Main annex 1 items with respect to Lyophilisation Systems

- High risk operations on sterile products:  
Grade A with Grade B background
- Continuity of grade A , covering full vial-path
- Until caps are crimped: high risk operation for freeze dried products;  
air supply conform grade A requirements
- Minimize personnel
- Minimize particulate generation
- Minimal dwell time

# Lyo System configurations

1 - 7

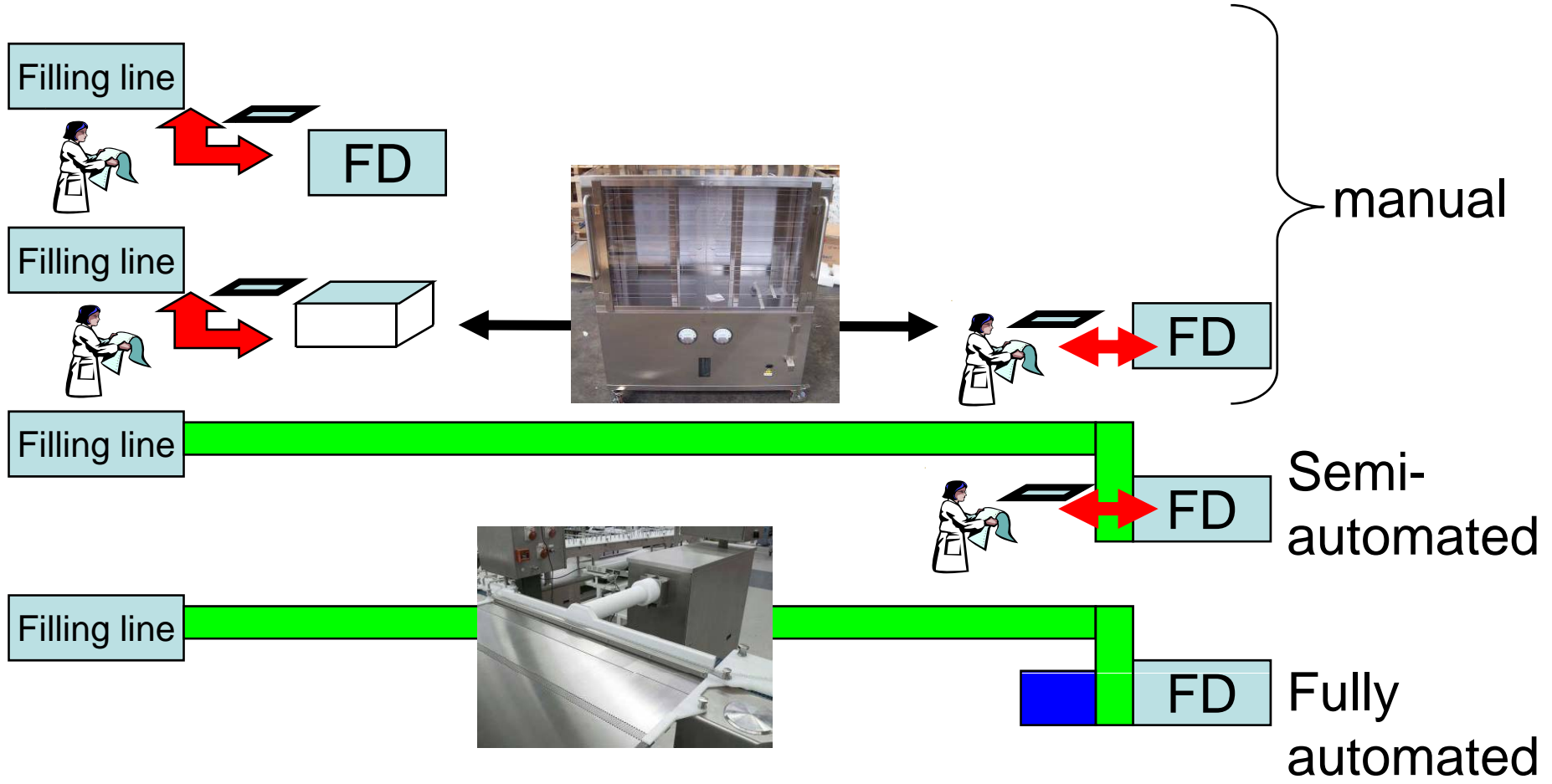
- Vial path between Filler and FD and between FD and Capper needs to be in Grade A containment.  
Capper needs to be in Grade A level infrastructure.
- Grade A Containment can be
  - Passive RABS ( Open system )
  - Active RABS ( Open system )
  - Closed RABS ( Closed system )
  - Isolator ( Closed system )
- Cleanroom environment :
  - Grade B for RABS
  - Grade C/D for Isolator

*Note : RABS definitions are according latest ISPE definitions*

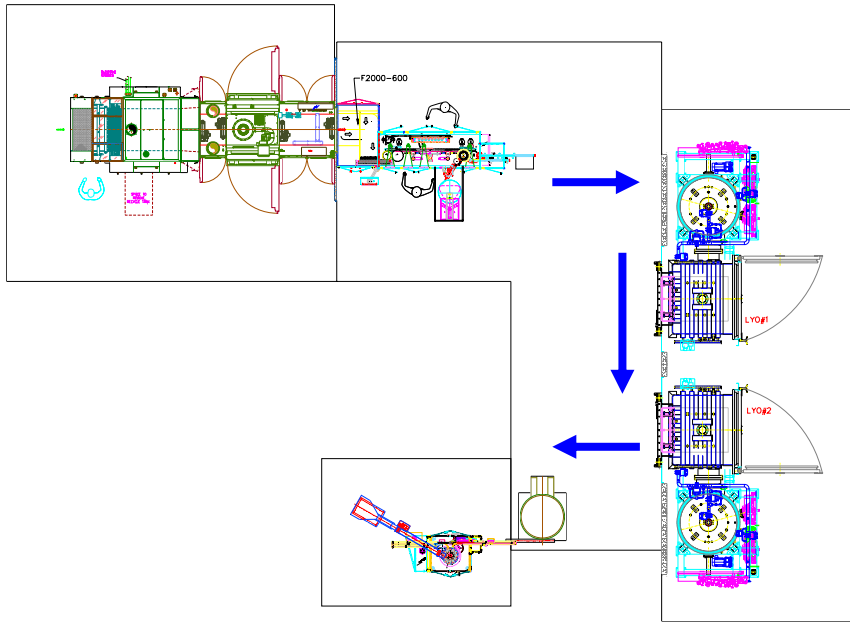
# Families of System configurations

Increasingly fitting with cGMP :  
EEC - Annex 1 or Chinese GMP

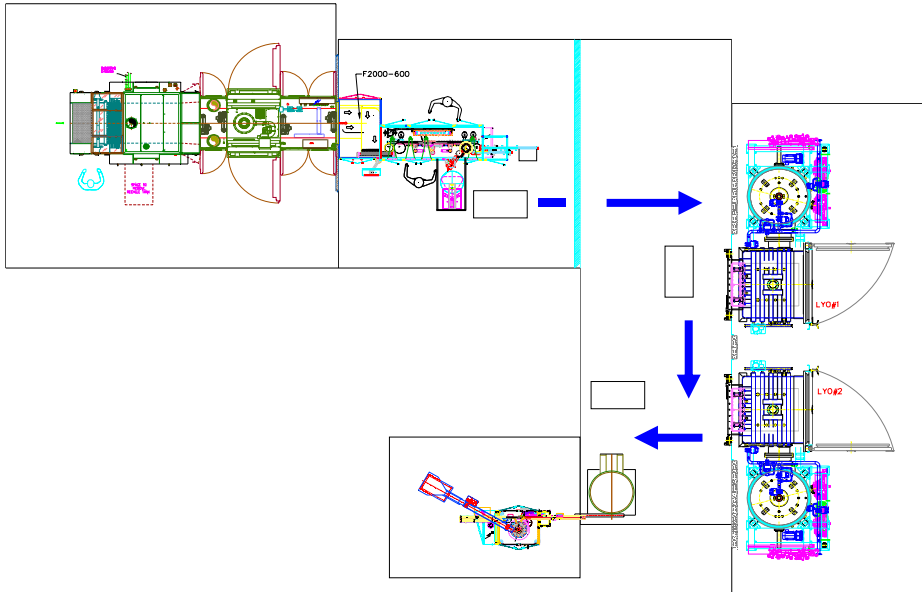
2 - 7



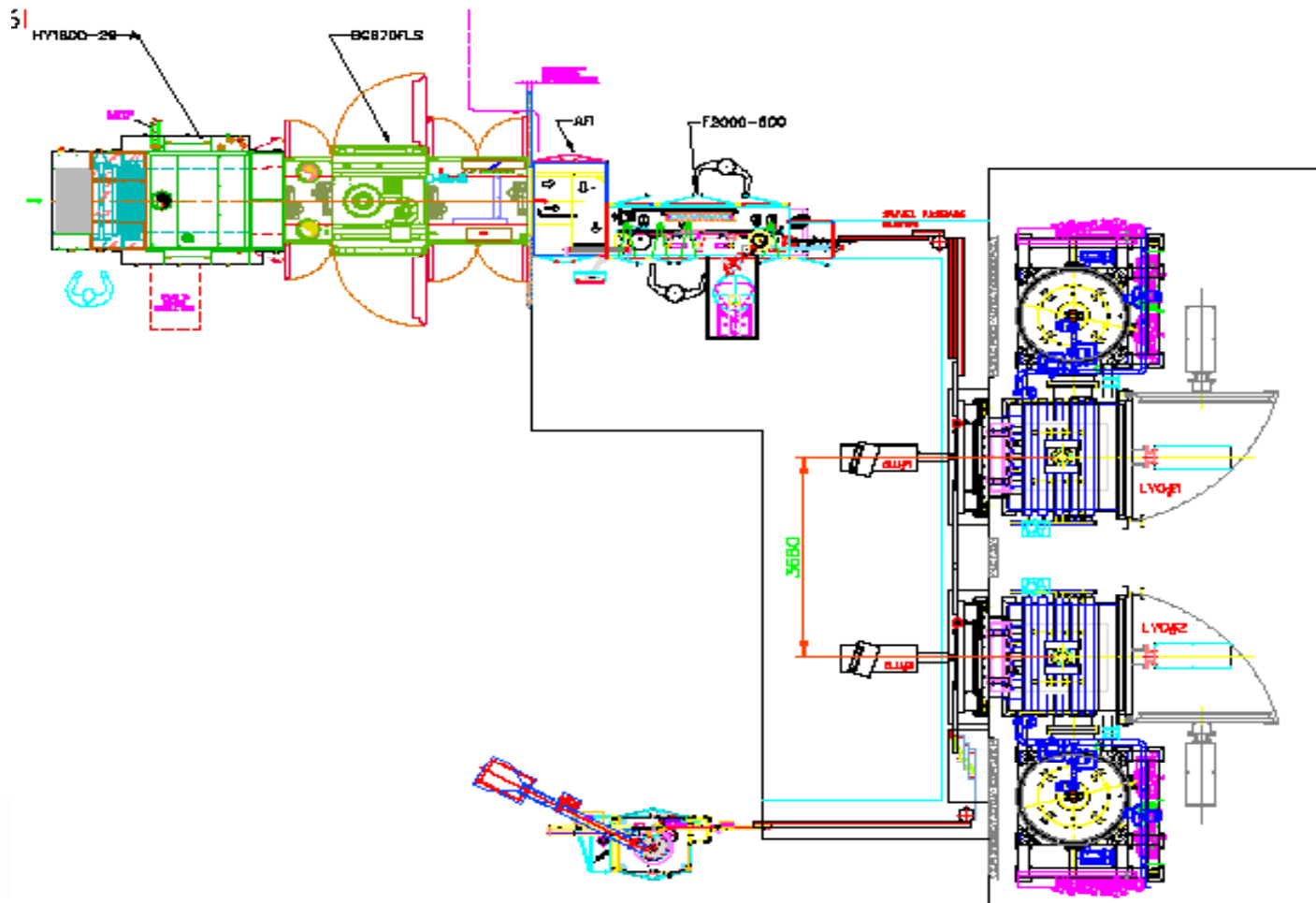
# LYO System in Manual Conf.



# LYO System in Manual with LAF Cart

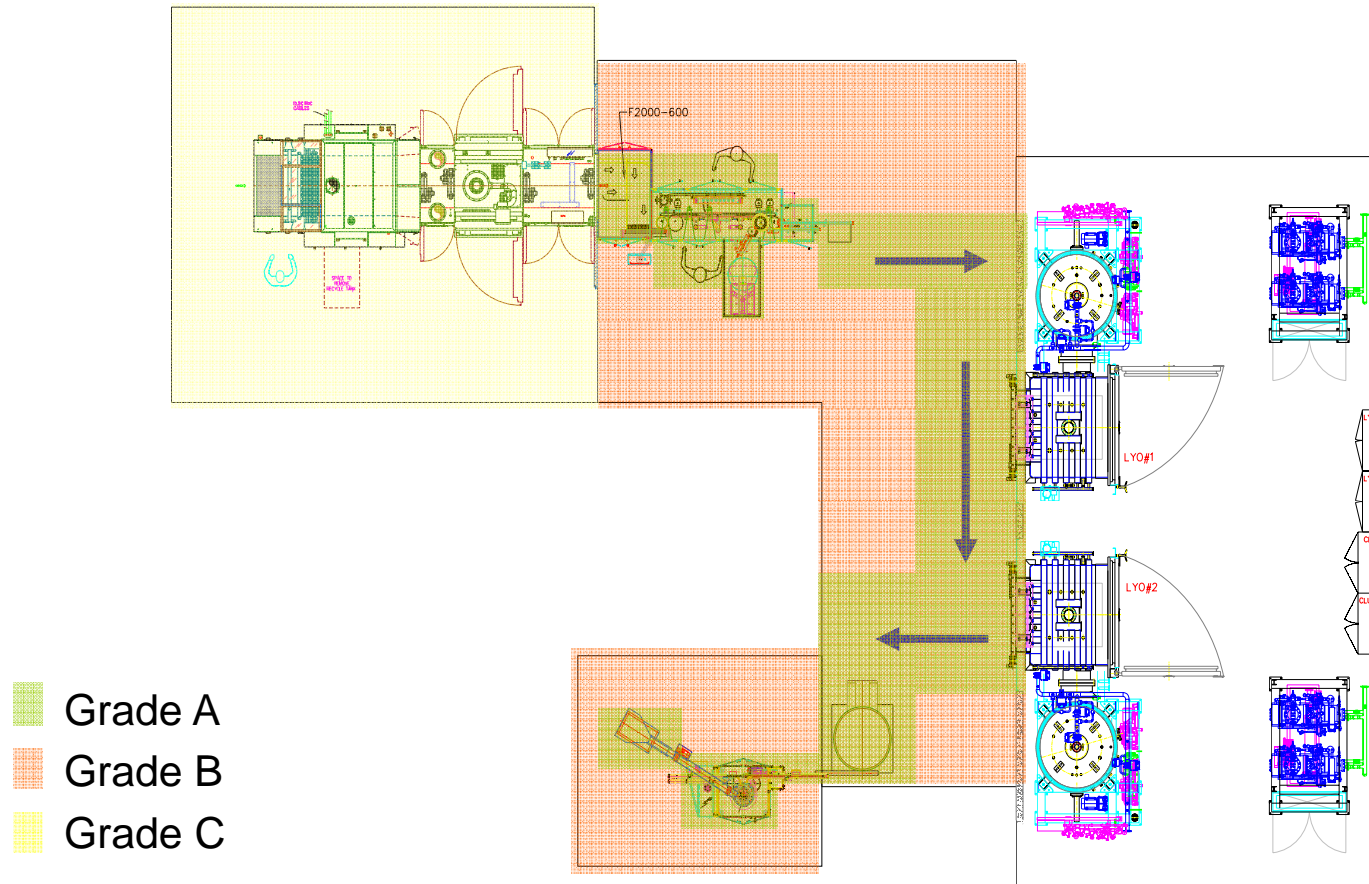


# LYO System in Automated Conf.

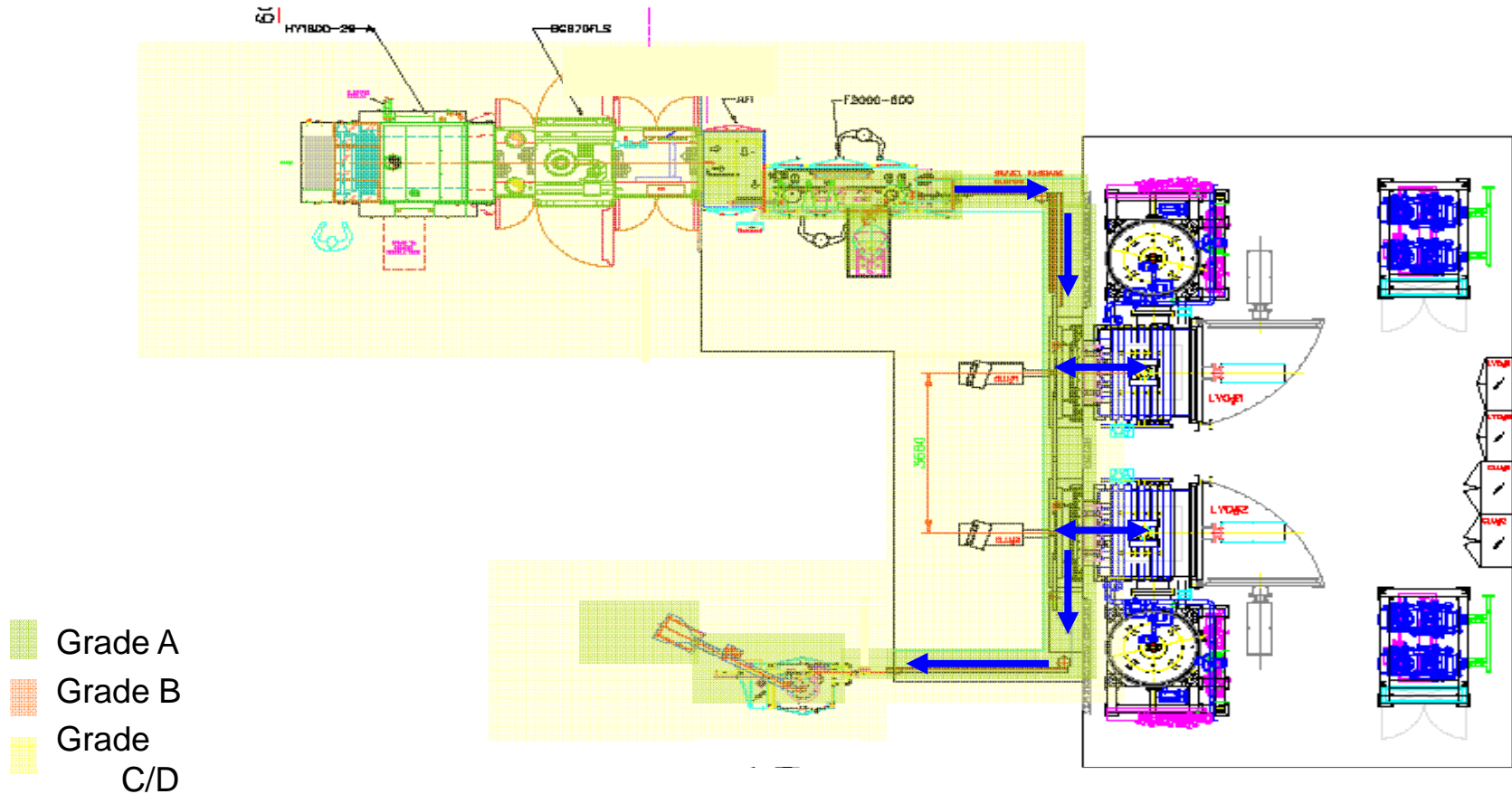




# LYO System in Full Manual Conf. under LAF



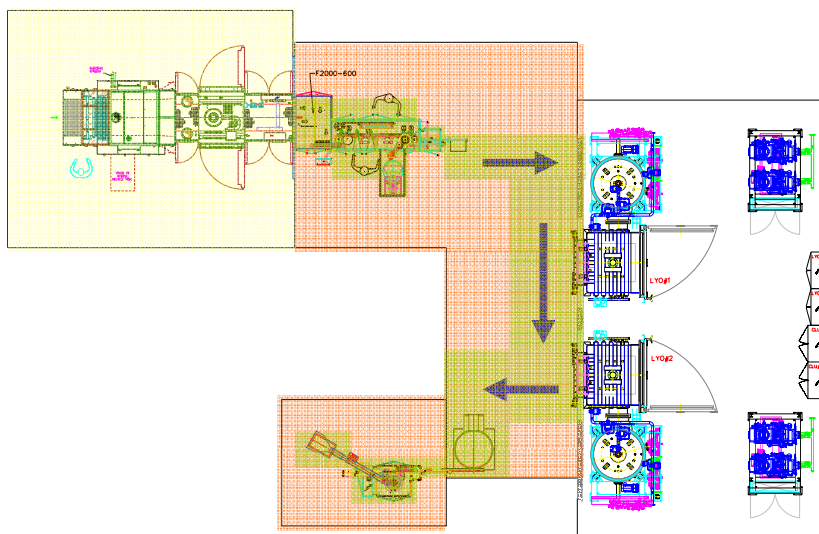
**LYO System in Automated Conf. under Isolator**



- Grade A
- Grade B
- Grade C/D

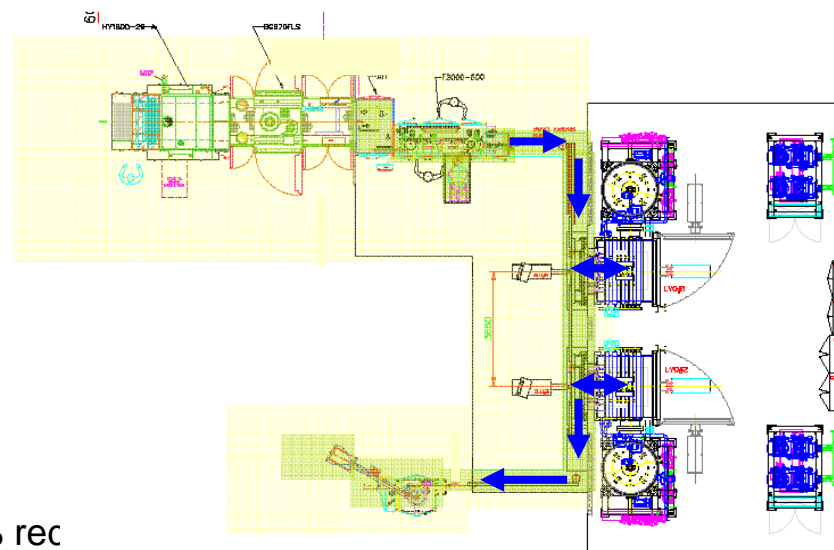


## Manual under LAF



- Grade A reduction ( around 50% )
- Minimize Grade B ( in case of RABS ) . If Isolator 100% rec
- Grade C
- The entire vial path is protected under RABS/Isolator

## Auto with Isolator



# Motivation for Automation

- Fewer clean room personnel
  - Greater assurance of product sterility ( SAL levels )
  - Reduction in bio-burden
  - Reduced operating costs
- Protection of operators
  - Potent products & Solvent products
- Repeatable standards
  - Reduction of classified room air
- Unattended operation possible
  - Increased equipment availability

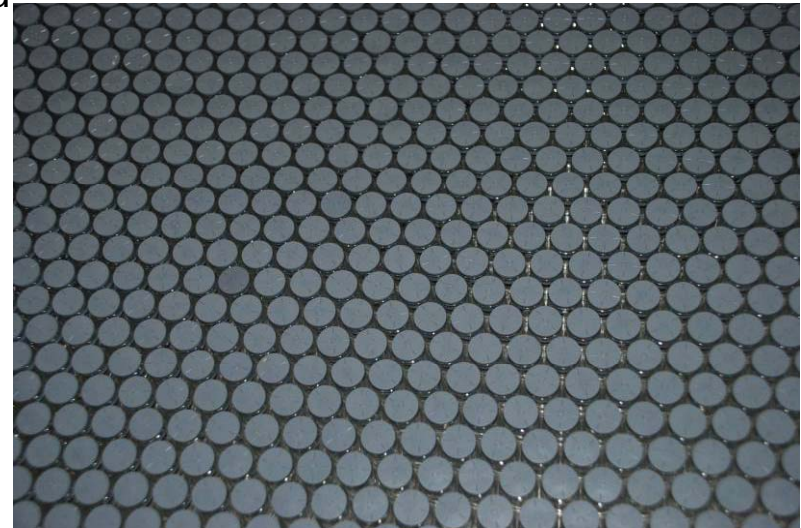
## Per Today

- Industry in both USA as Europe are regarding the use of automated systems as a standard requirement.
- Pacific region is increasingly requesting and using automated loading systems

# Nature of Loading

1 of 10

- **Constant Level loading :**  
Freeze Dryer is loaded or unloaded one shelf, or one row or several rows at a time, with vials at constant level. Loading is based on hexagonal loading patron
- **All Systems are Frameless Systems**
- **Can be 'Flexible' or 'Fixed' or 'Mixed' in nature**
  - **Fixed systems :**  
Systems build unto the freeze dryer and load each shelf one row or several rows at a time
  - **Flexible systems :**  
Systems using "Transporters" to load multiple FD one shelf at a time
  - **Mixed systems :**  
Combination of fixed and flexible . Mainly applicable for Passthrough FD

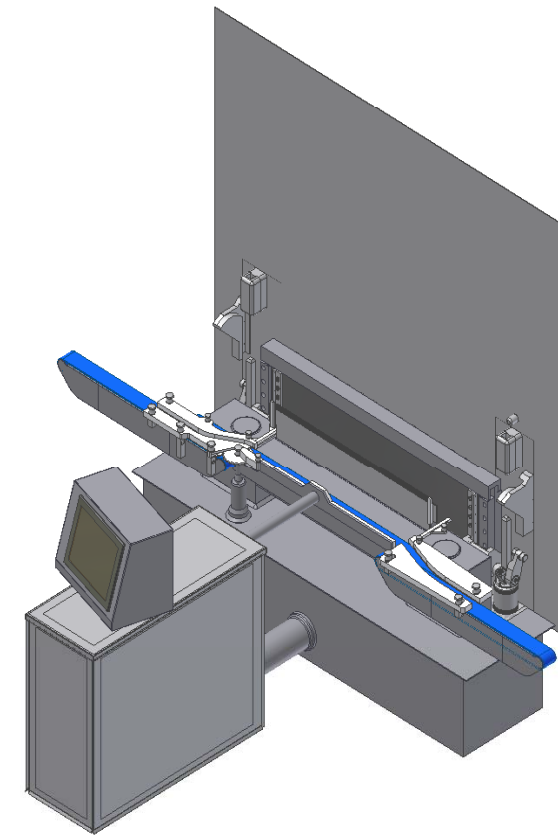
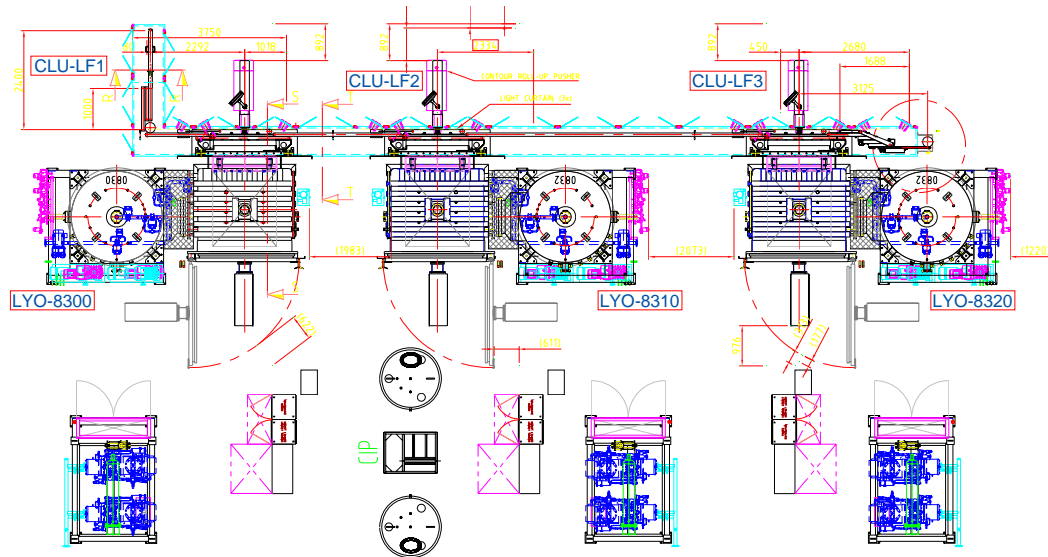


# Nature of Loading : Fixed

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## Fixed Loading Systems

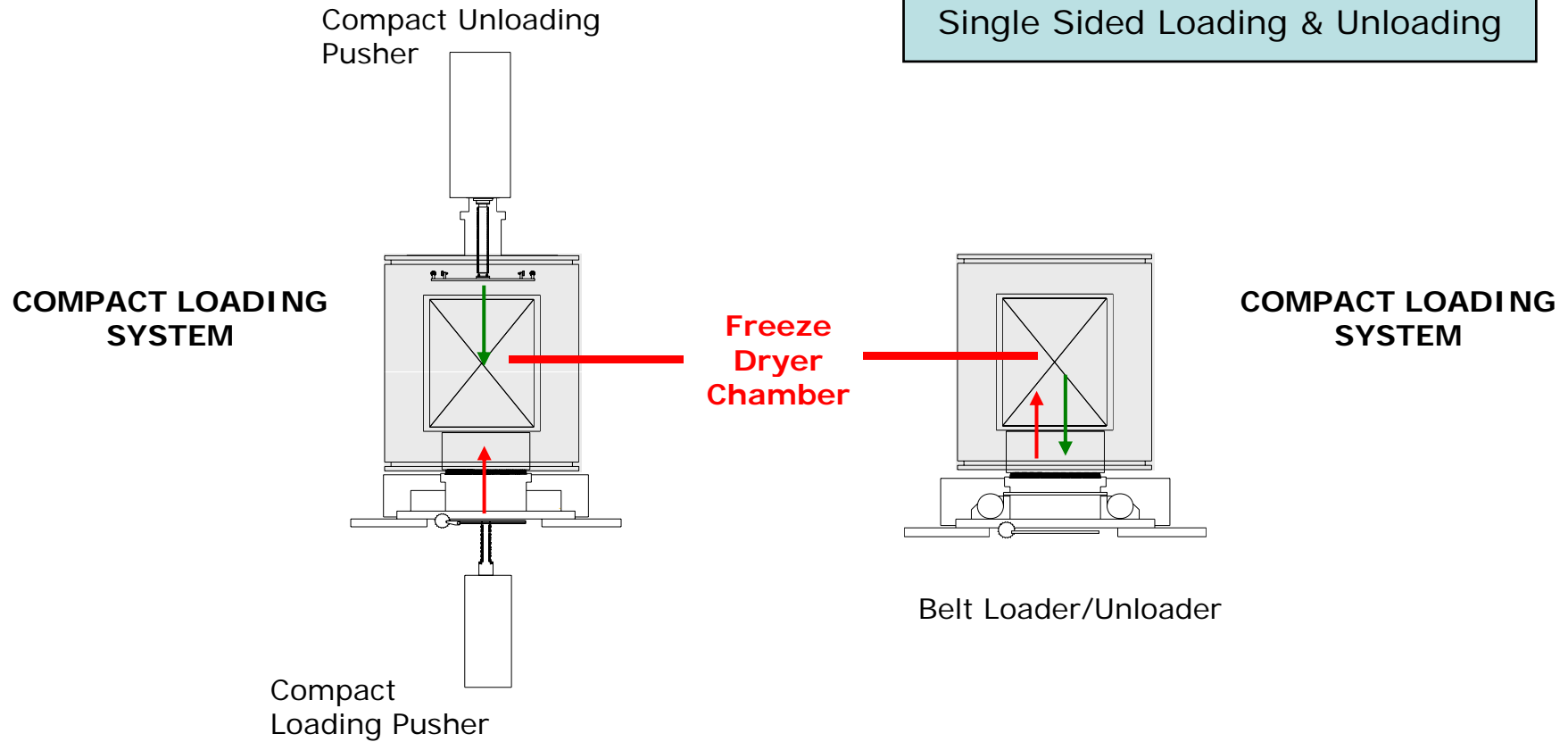
- Speeds up to 450 vpm
- One or 2 upto 4 Freeze Dryers, more depending on cycle times & logistics & Environment
- Choice on type of Loading Pusher
- Mainly Loading-Unloading from the same side
- Isolator or RABS



# Fixed Loading Systems

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Single Sided Loading & Unloading



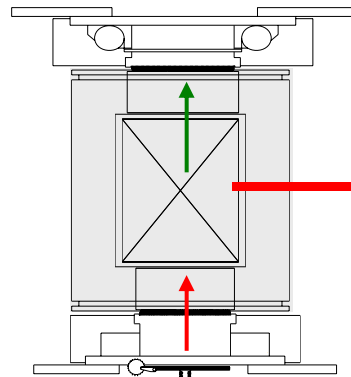


# Fixed Loading System Configurations

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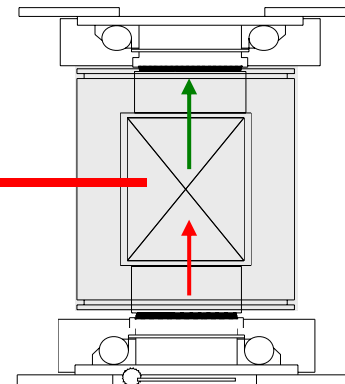
Pass Through  
Loading & Unloading

**COMPACT (UN)LOADER**  
Belt Unloader



Freeze  
Dryer  
Chamber

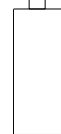
Belt Unloader



**COMPACT LOADER**  
Belt Loader/Unloader

Belt Loader

**COMPACT LOADER**  
Compact Loading  
Pusher

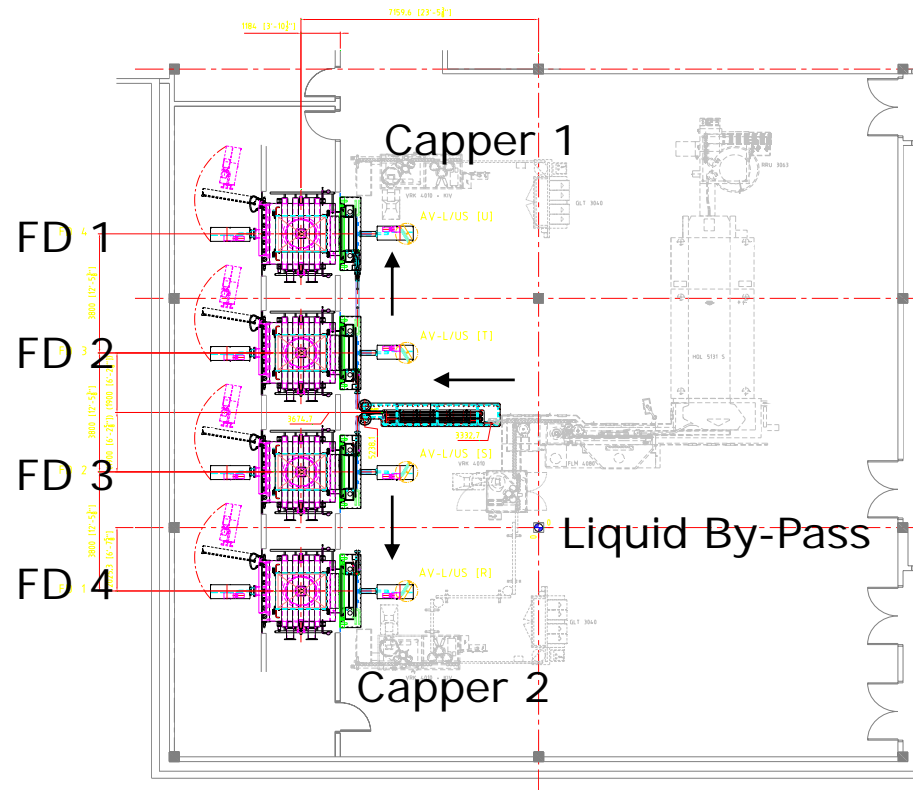




# Typical Lay-Out Fixed

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- 4 FD & 4 LS
- Loading Speed : 265/min – 10ml
- Unloading Speed : 265/min
- Multi-Lane Unloading
- Single Sided Loading & Unloading
- Two Cappers
- Liquid By-Pass
- Short Cycle Times
- Isolator split-up in 3 zones



# Nature of Loading Fixed : Video

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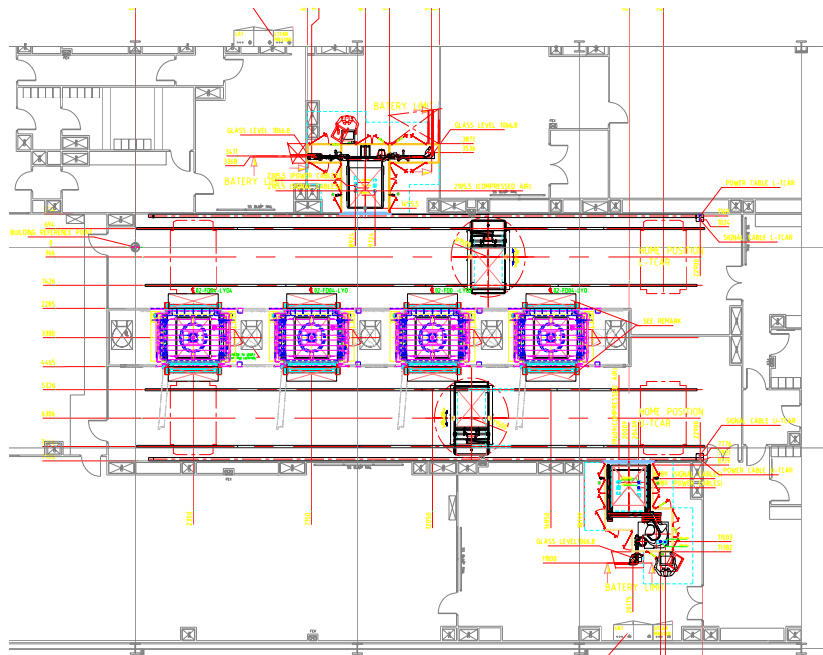
Video Fixed System

# Nature of Loading : Flex.

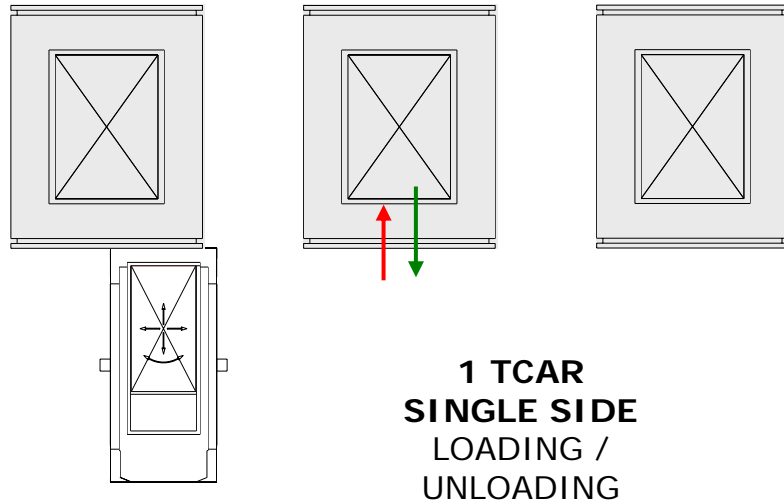
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## Flexible Loading Systems

- Capacities up to 450 vpm
- Mainly Multiple freeze dryers
- Mainly Loading-Unloading from the same side
- Suitable for Pass-Through systems

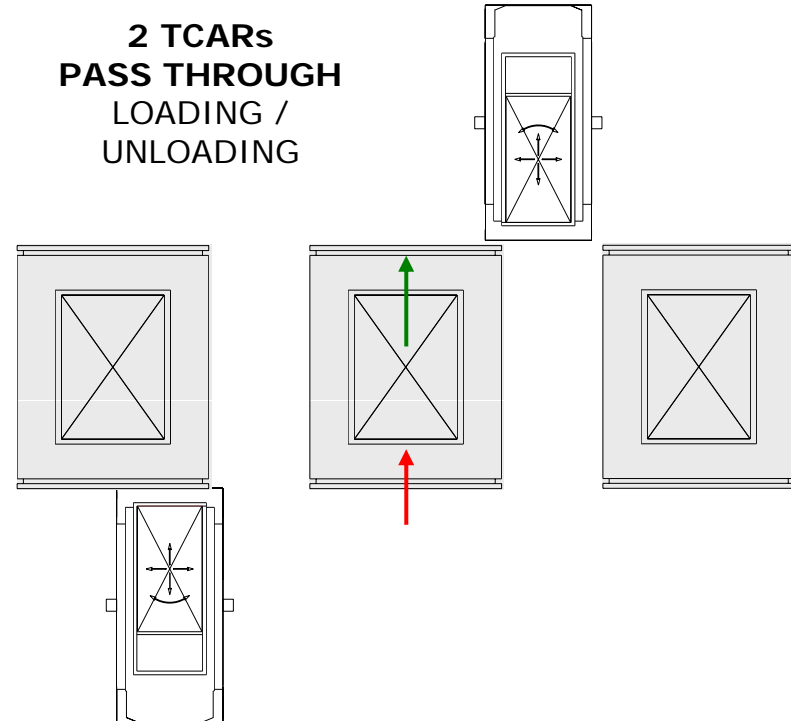


# Nature of Loading : Flex.



Flexible Loading & Unloading System

2 TCARs  
PASS THROUGH  
LOADING /  
UNLOADING

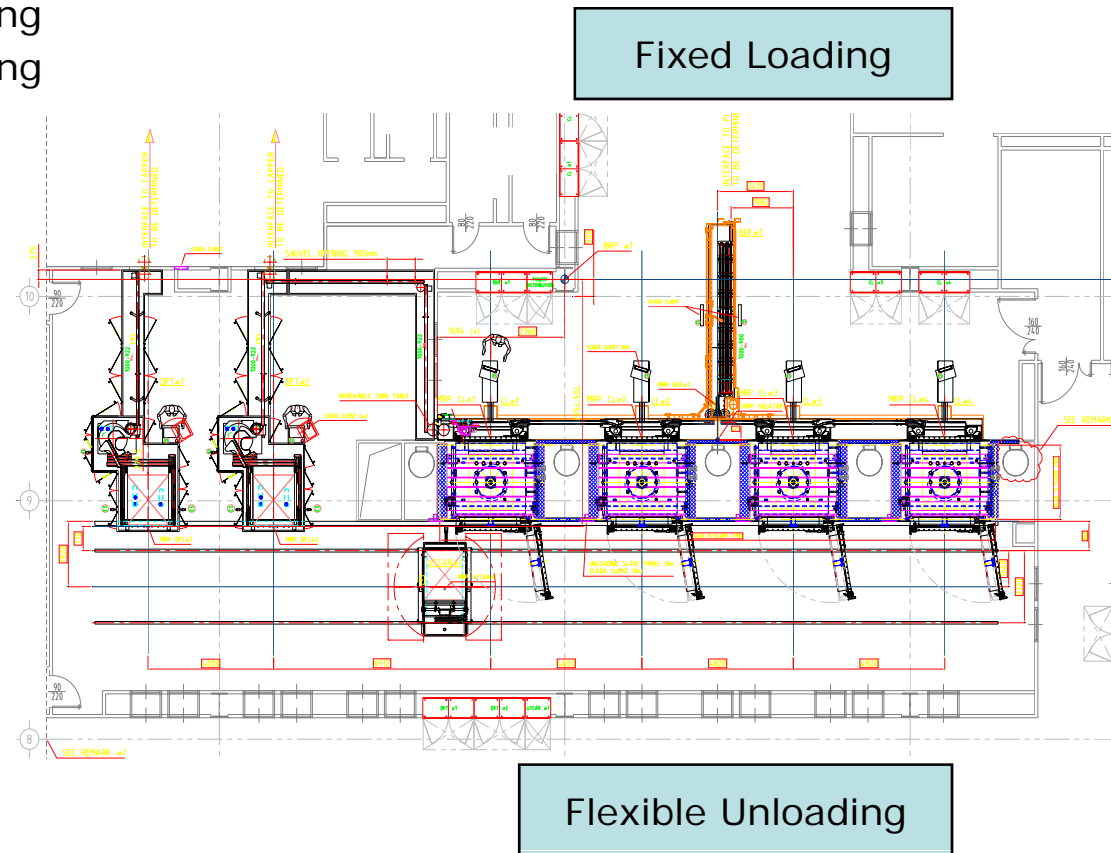


Video [Flexible System](#)

# Nature of Loading : Mixed

## Mixed Loading Systems

- Only Pass-Through to 450 vpm
- Fixed Loading & Flexible Unloading
- Flexible Loading & Fixed Unloading
- Mainly Multiple freeze dryers

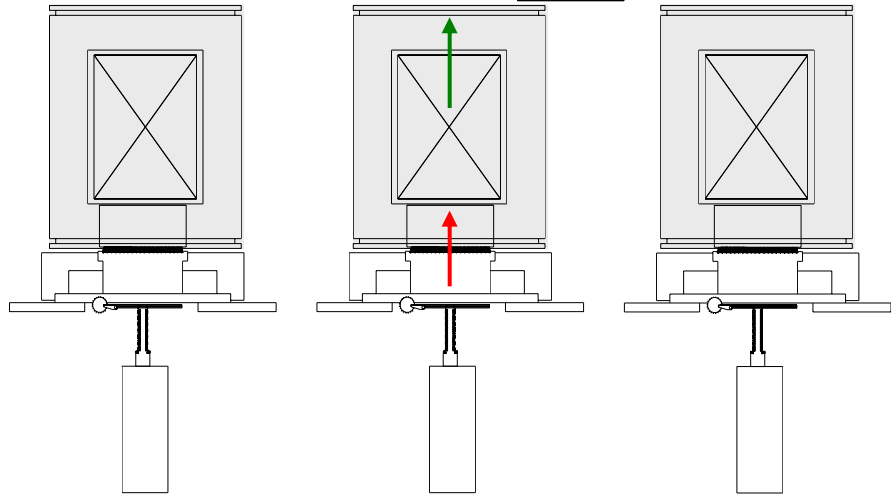
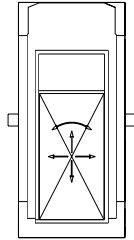


# Overview Mixed Configurations

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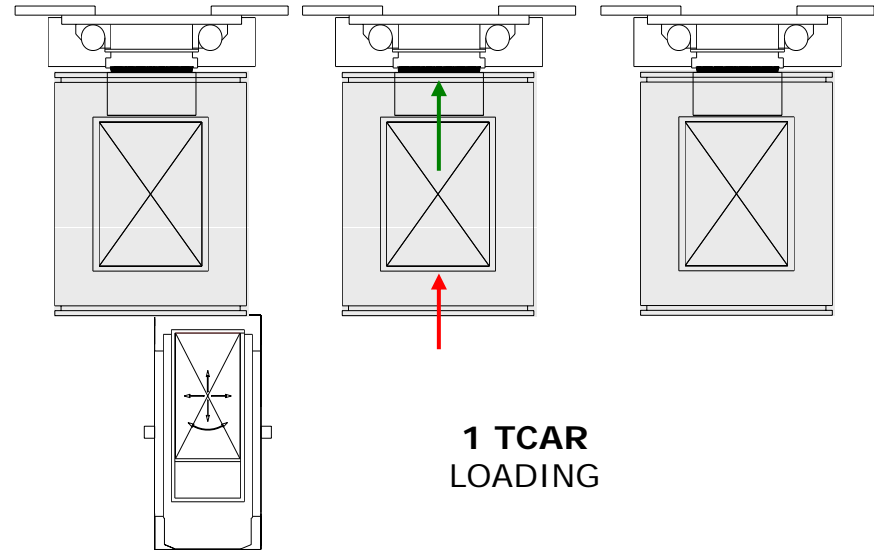
Mixed Loading & Unloading System

1 TCAR  
UNLOADING



3 Compact loaders  
LOADING

3 Compact loaders  
UNLOADING



1 TCAR  
LOADING

# Loading Sequence Capability

- **Row by Row Accumulative. (A)**  
Vials are loaded row by row on the bridging plate.  
The last row pushes forward the whole package onto the shelf.  
Suitable for loading at ambient shelf temperature ( 18 to 22 Degrees C )
- **Packaged row of vials ( positioned at leading edge of shelf ) (A)** Vials are loaded row by row or a packaged row of vials on the leading edge of the shelf. Every next row or packaged row of vials pushes forward the entire vial pack.  
Cold shelf loading
- **Packaged row of vials ( positioned at final shelf position ) (B)**  
Vials are gathered in packages of x nb. of rows on the bridging plate and are positioned as individual packages directly on its final position on the shelf.  
Cold shelf loading

Video [S1](#)

Video [S3](#)

Video [S2b](#)

Video [S2a](#)

# Cold Shelf Loading Considerations

1 of 3

- Increased nb. of systems equipped or prepared for cold shelf.
- More and more products unstable in solution
- URS Requirement on elapsed time ( Dwell time ) between point of fill at filler ) and positioning on shelf ( in FD )
- Airflow pattern during Loading Process
- Temperature of cold shelf
  - 4 Degrees C ( Condensation issues )
  - < 0 Degrees C ( Ice build up on shelf )
- Ingress between outside environment and inside FD



# Cold Shelf Loading Considerations

2 of 3

**Elapsed time between point of fill and positioning on shelf ( Dwell Time).**

- From filler , via buffer to Loading System
- From Loading System ( depending on chosen Loading Sequence ) into FD

**Calculation example : 2 ml vial on 400/min & Row width :1.324 mm**

- |   |         |
|---|---------|
| • Filler → Loader ( based on 15 mtr. Conveyor ) | 3 min.  |
| • Loader ( Based on row package )               | 13 min. |
| Total   | 16 min  |

# Cold Shelf Loading Considerations

3 of 3

## Airflow during Loading Process

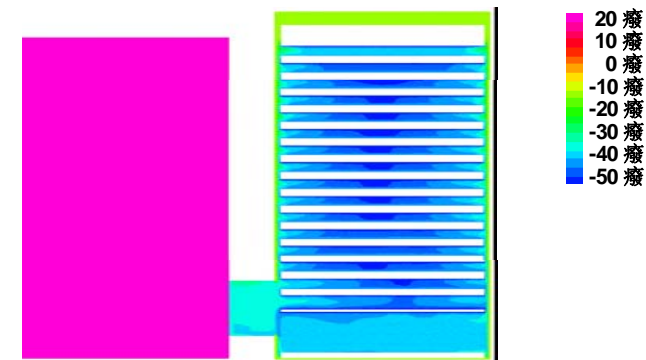
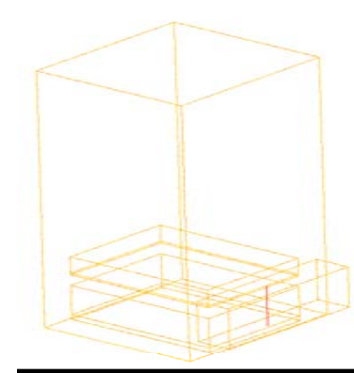
- Level of disturbance of uni-directional airflow is influenced by
  - Shape / seize and duration of Opening of slotdoor
  - Delta in Temp. between environment and shelf

## 4 Degrees C

- Condensation on shelf

## < 0 Degrees C

- Ice build-up on shelf
- Disturbance of Unidirectional Airflow



# Equipment : Functional Integration

1 of 2

## Fully automated Filling / Lyo Line :

### Target :

- Uninterrupted functioning of Filler in combination with Loading function of Loading & Unloading System
- Uninterrupted functioning of Capper in combination with Unloading function of Loading & Unloading System
- Optimisation of line Speeds.

### Note

- Loading of Freeze Dryer is an intermittant process
- Filling of vials is continous or intermittant process
- Unloading of Freeze Dryer is an semi continuous proces
- Capping of vials is a continuous proces

# Equipment : Functional Integration

2 of 2

Integration track between filler and Loader is depending on :

- Vial diameter(s) icw with speed(s)
- Position of switches
- **Storage of “wrongly filled” vials required Y/N**
  
- Method of IPC on filler.
  - or statistical check weighing
  - or 100% weighing
- **Method of Loading ( Loading Sequence )**

# Integration with Freeze Dryer

1 of 2

- Integrated design
- Flexible Docking Plate
- Vertical Sliding Slotdoor
  - Minimum opening
  - Fast acting design
- Sunken rail principle.

# Containment Solutions

1 of 7

- LAF system
- RABS System ( following ISPE definition of Sept. 08-2005 )  
( Restricted Access Barrier System )
  - Open ( Active and Passive )
  - Closed
- Isolator System

# Containment Solutions

2 of 7

Open RABS

- **Passive RABS**
  - Air intake from customer HVAC system. Barrier of supplier is docked unto clean room ceiling of customer.
  - Air flow underneath machine into clean room
- **Active RABS**
  - LAF unit is integrated with barrier
  - Air intake is from clean room
  - Air flow underneath machine back into clean room

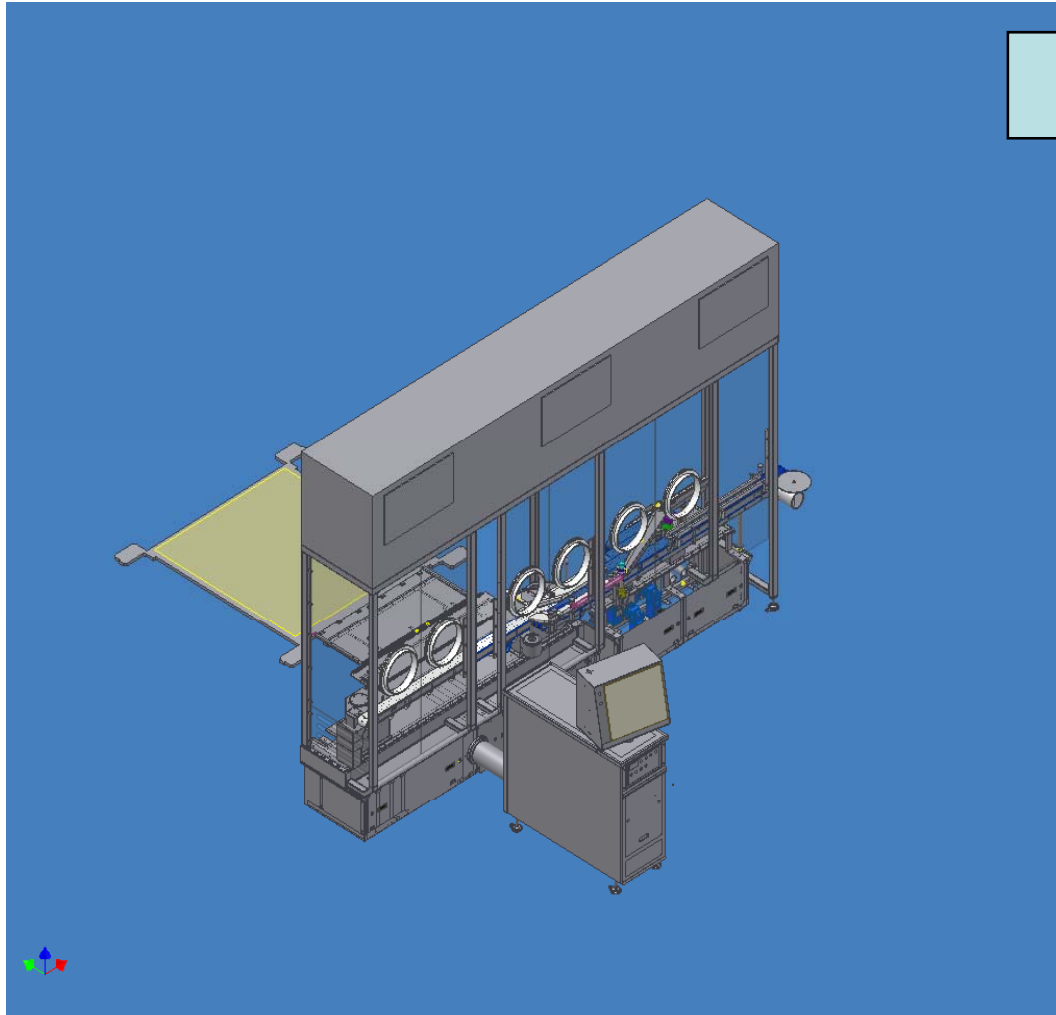
Both systems configured with

- Gloves for intervention during production with doors closed
- Doors interlocked and individually monitored ( locked doors optional )
- Environmental Monitoring preparation

# Containment Solutions

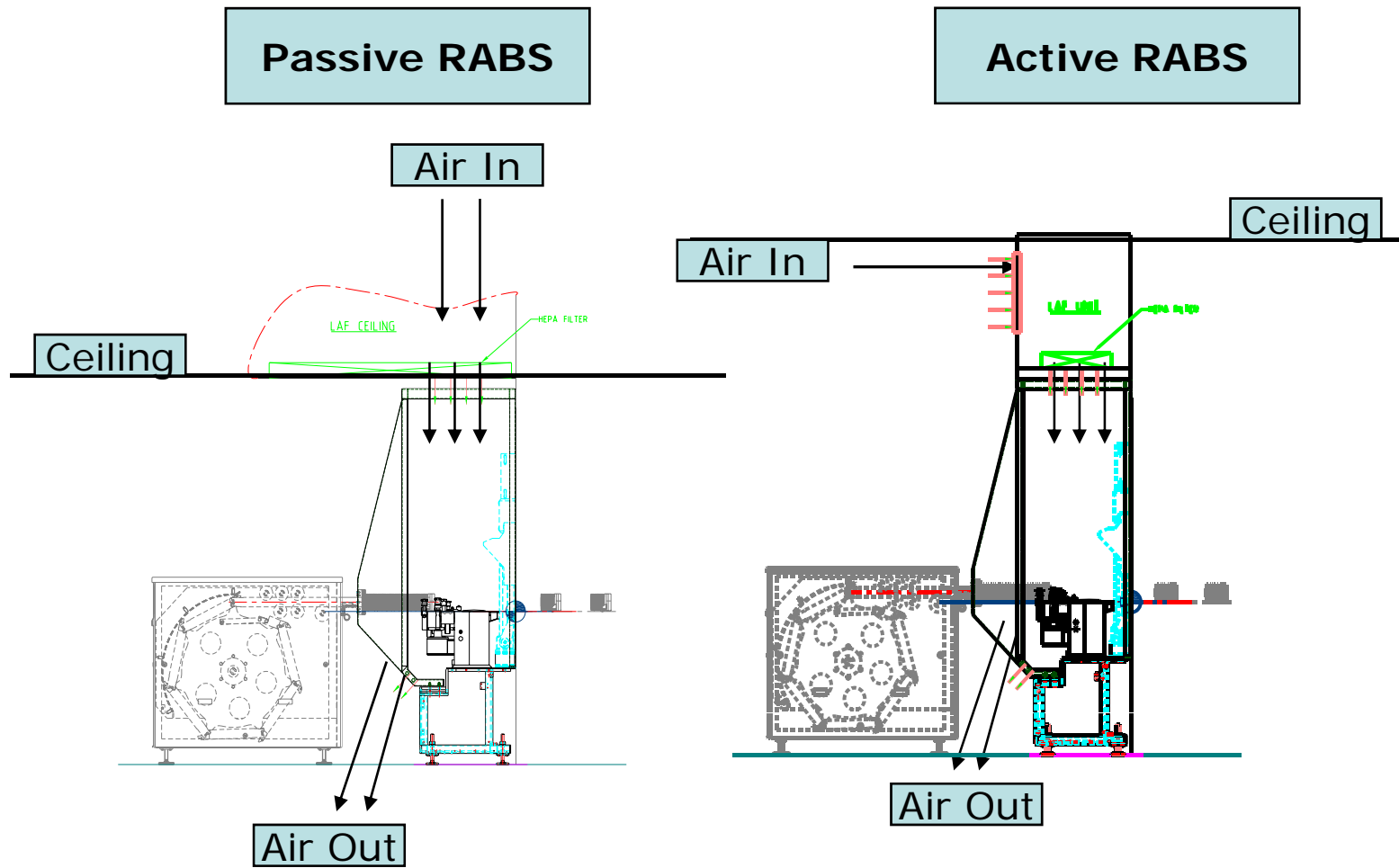
3 of 7

Active RABS





# Containment Solutions



# Containment Solutions

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## Closed RABS

- Barrier based on closed recirculation system
- Closed recirculation based on single wall ( windows and doors ) principle
- Air intake ( make-up air only ) from customer HVAC system or Clean room.
- Possibility for environmental control like Temp. and RH

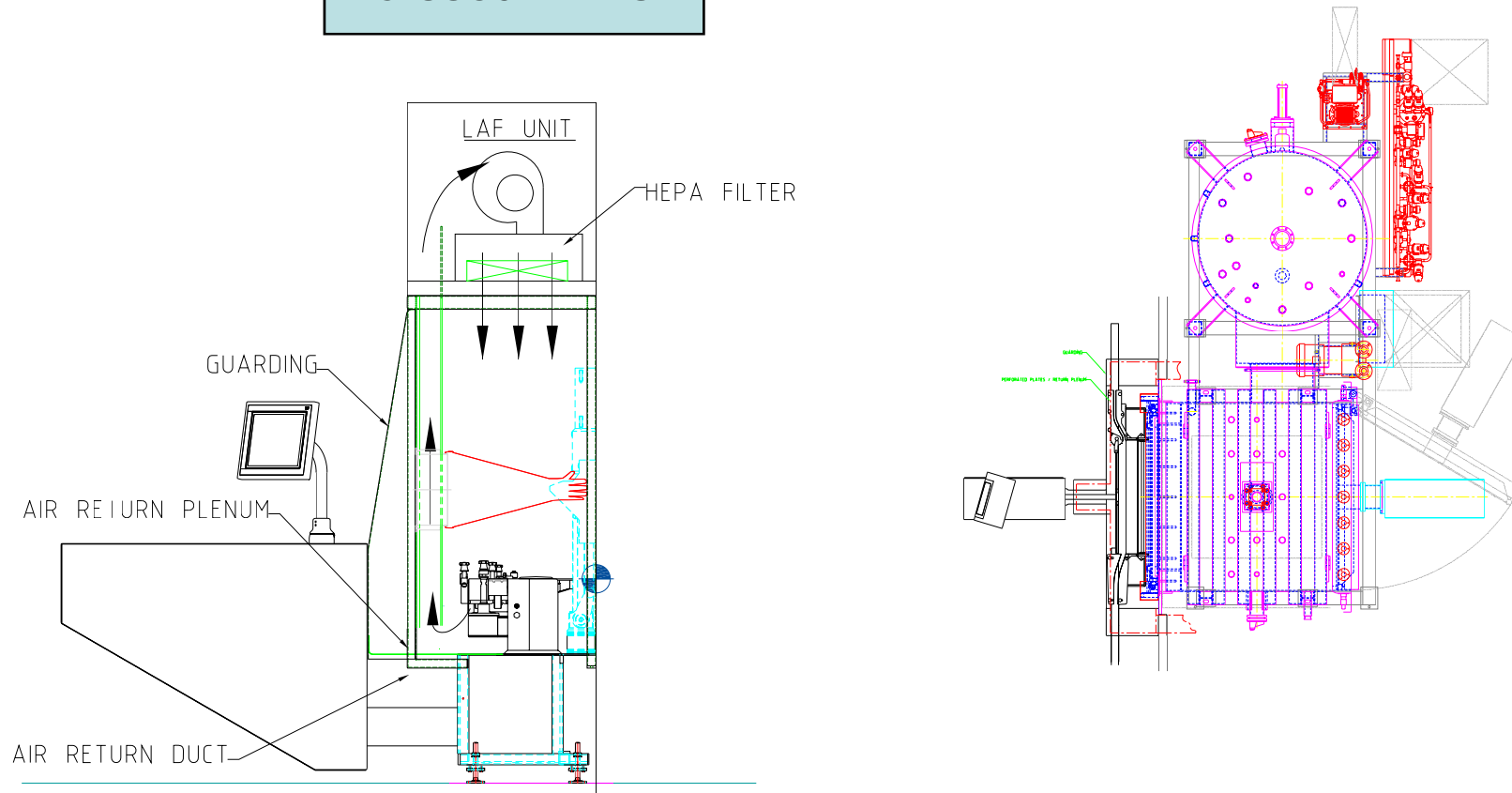
Systems configured with

- Gloves for intervention during production with doors closed
- Doors interlocked and individually monitored ( locked doors optional )
- Environmental Monitoring preparation

# Containment Solutions

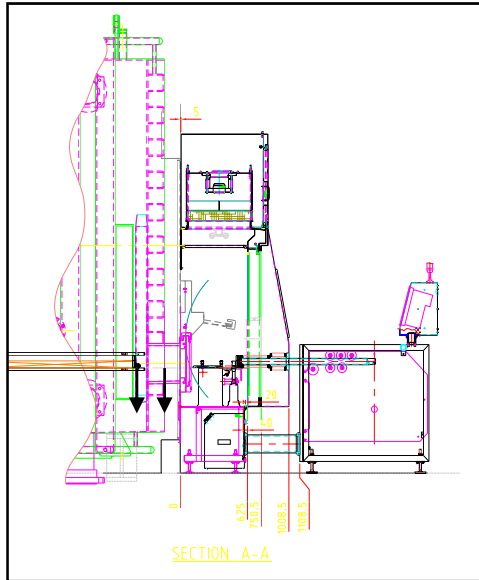
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## Closed RABS

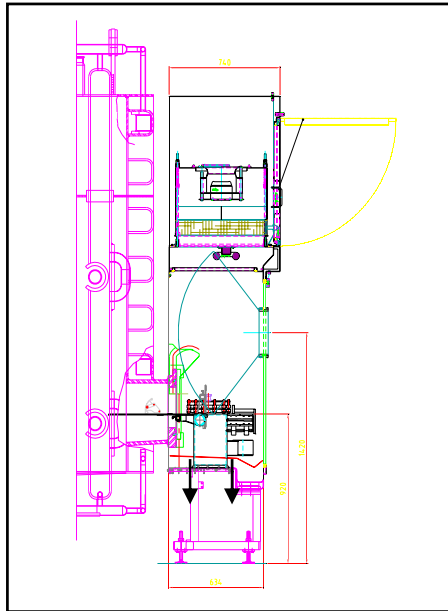


# Containment Solutions

## Isolator



Double Wall / Compact Pusher



Single Wall / Belt Pusher



# Environmental Monitoring

- Integral part of RABS/Isolator system
- Machine Supplier is most knowledgeable on preferred position of probes
- **Viable Sampling:**
  - Active ( Sampling port & Monitoring device )
  - Passive ( Petri dishes )
  - Location : Critical positions / Subject to chosen LS system
- **Non-Viable Sampling:**
  - Isokinetic probes & Particle Counters
  - Location : Critical positions / Subject to chosen LS system

# Smoke Studies

- Smoke study is performed
  - In case of design changes on Standard Equipment
  - Customer requirements

[Video](#) CLU

# Latest Features on Loading Systems

1 of 4

Vial Sampling  
Video



Bad Zone Handling  
Video





# Latest Features on Loading Systems

2 of 4

Spacer Handling  
Video



FIFO Buffer  
Video





# Latest Features on Loading Systems

3 of 4

Emptying FIFO Buffer



Reject  
Fallen Vial & Stopper



# Latest Features on Loading Systems

4 of 4

High Speed Single Lining  
Video



# Questions

???????

# IMA Life Aseptic Filling / Lyo line

Fully automated and Integrated aseptic operation

Filling lines



Bologna & Florence, Italy

Freeze dryers



Tonawanda, USA

Loading Systems



Dongen, NL



Freeze dryers



Beijing, China



# IMA LIFE Loading Systems

IMA Life Loading Systems are Configured to Order Solutions

***IMA Life Loading System are integrated equipment ,  
designed and produced by IMA Life***

- 18 Years of experience and innovation on Loading Systems
- More 64 references world wide
- 8 off Fully Integrated Systems ( Filling Line + LS + FD )
- Wide range of solutions
  - Available shelve packages and loading sequences
  - Cold shelf loading loading / flammable solvents / Toxic.