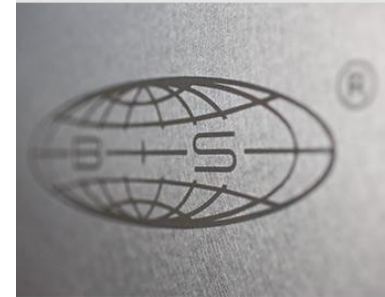




PDA Brazil Chapter Aseptic Processing Workshop

Sep 18 - Sep 22, 2017 |
CRQ - Pinheiros | São Paulo, Brazil





RABS

Restricted Access Barrier System Training Session

- Passive RABS
- Active RABS
- Closed RABS
- Isolator



Frank Härterich
B+S Germany

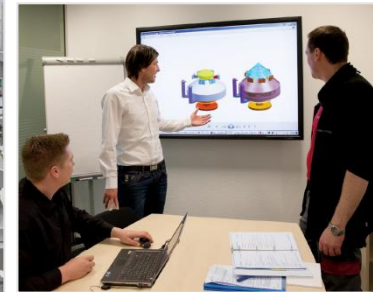
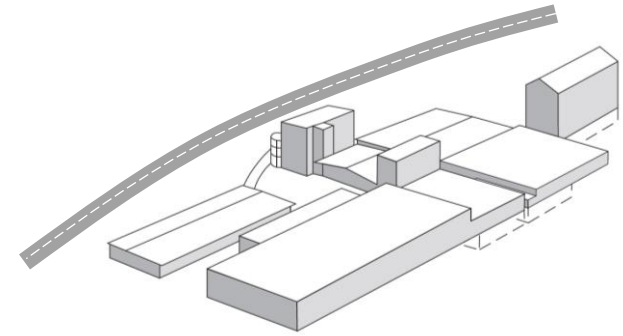


B+S Ilshofen / Germany



B+S Ilshofen / Germany

- Production capacity: approx. 400 machines / year
- Turnover: approx. 180 million Euro / year
- Export: approx. 90%
- Pharm. Industry: approx. 98%
- Employees: approx. 1,400
 (of which approx. 150 trainees)
 (of which approx. 240 design)
 (of which approx. 650 production)
 (of which approx. 50 QA/QM/QC)
- Company area: approx. 90,000 m²



What we do - Production program

Cleaning



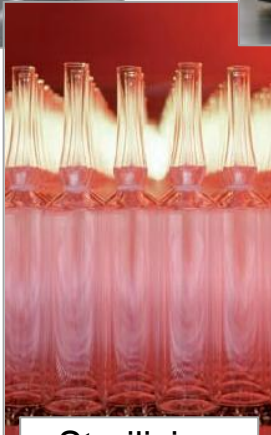
Filling



Inspection



Tray-loading



Sterilizing



Closing



Labelling



Assembly

What we did - Projects realized since 1967



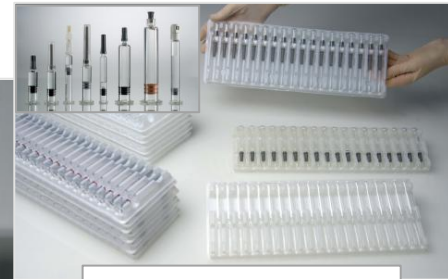
More than 160 ampoule lines



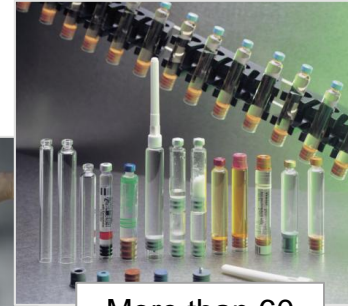
More than 400 vial/bottle lines



More than 150 syringe lines (nest)



More than 50 syringe lines (bulk)



More than 60 cartridge lines

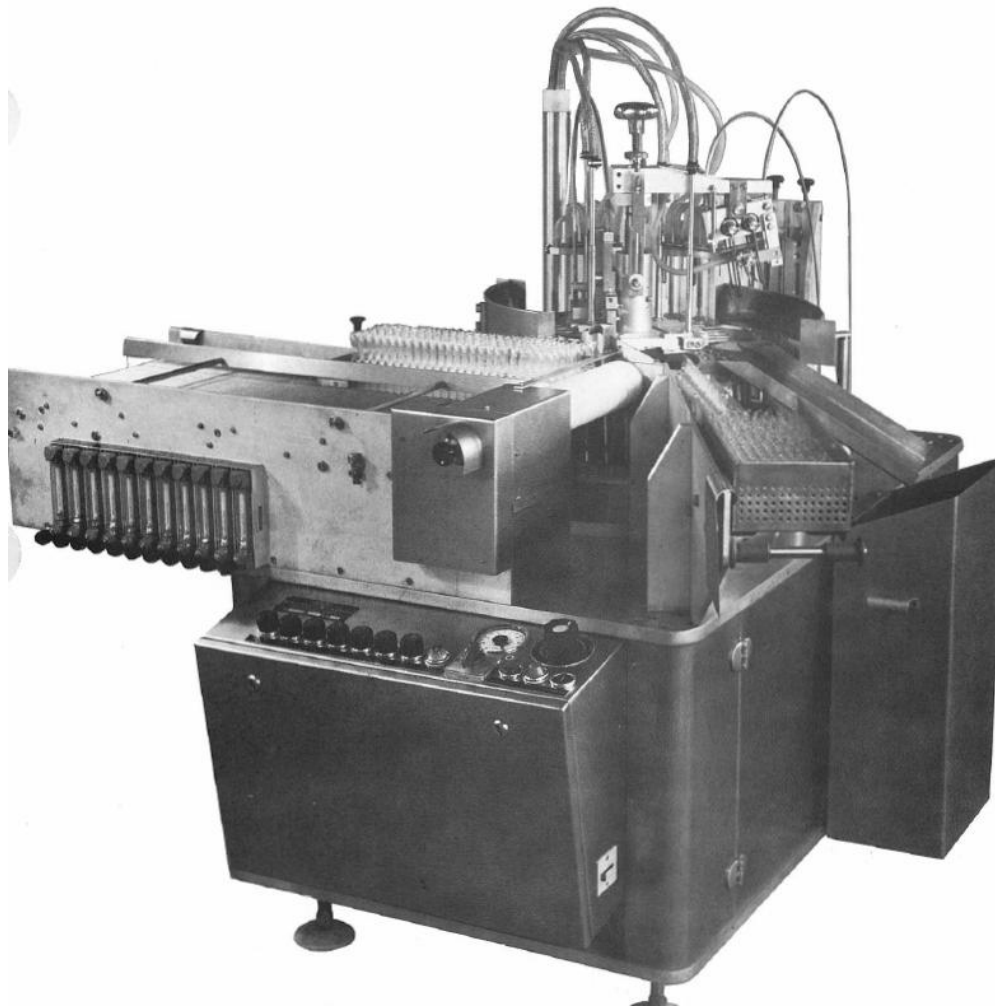
A total of more than 13,000 machines worldwide



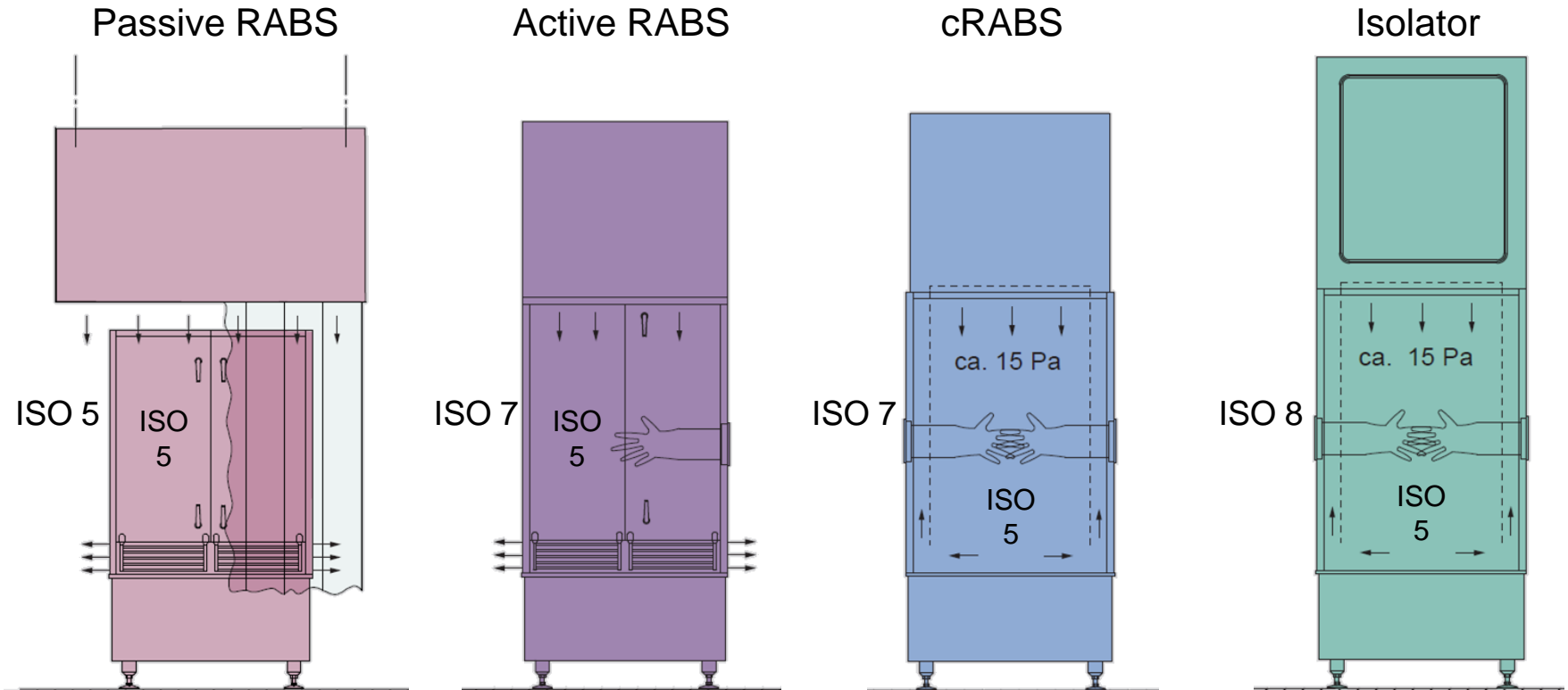
Barrier Technology

1. Passive RABS
2. Active RABS
3. Closed RABS
4. Isolator Technology
5. Comparison of the systems
6. Summary

RABS ?



RABS – Restricted Access Barrier System



Definition of „RABS“ Restricted Access Barrier System - DESIGN

- rigid wall enclosures
- unidirectional airflow system, providing an ISO 5 / Class A – environment in the critical area (inside the machine)
- ISO 7 / Class B – surrounding room conditions
- automation as far as possible, i.e. CIP/SIP; IPC remote or automated sampling
- well documented; appropriate line clearance and disinfection;
- extended ISO 5 / Class A conditions adjacent to outside of barrier

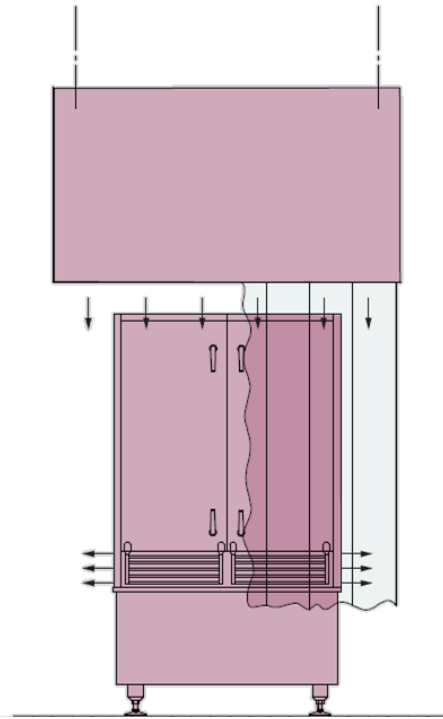
Definition of „RABS“ Restricted Access Barrier System - OPERATION

- automation as far as possible, i.e. CIP/SIP; IPC remote or automated sampling
- Sterilization of all product contacting parts
- manual bio-decontamination / high level of disinfection
- glove ports and/or half suits
- closed door operations
- rare open door interventions

Barrier Technology

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Passive RABS



- Laminar flow system to cover the processing area
- Ceiling integrated or ceiling mounted
- Air flow is guided by the machine guard or curtain
- Intervention is possible by using glove ports or by opening doors

-
- + lower investment for RABS
 - + Doors can be opened following SOPs
 - Airflow not dedicated to the machine area only
 - Risk for turbulences
 - Use of curtains is not the best practice
 - Environment around RABS ISO 5 (A) recommended
 - Higher costs for the surrounding room

Example of Passive RABS installations

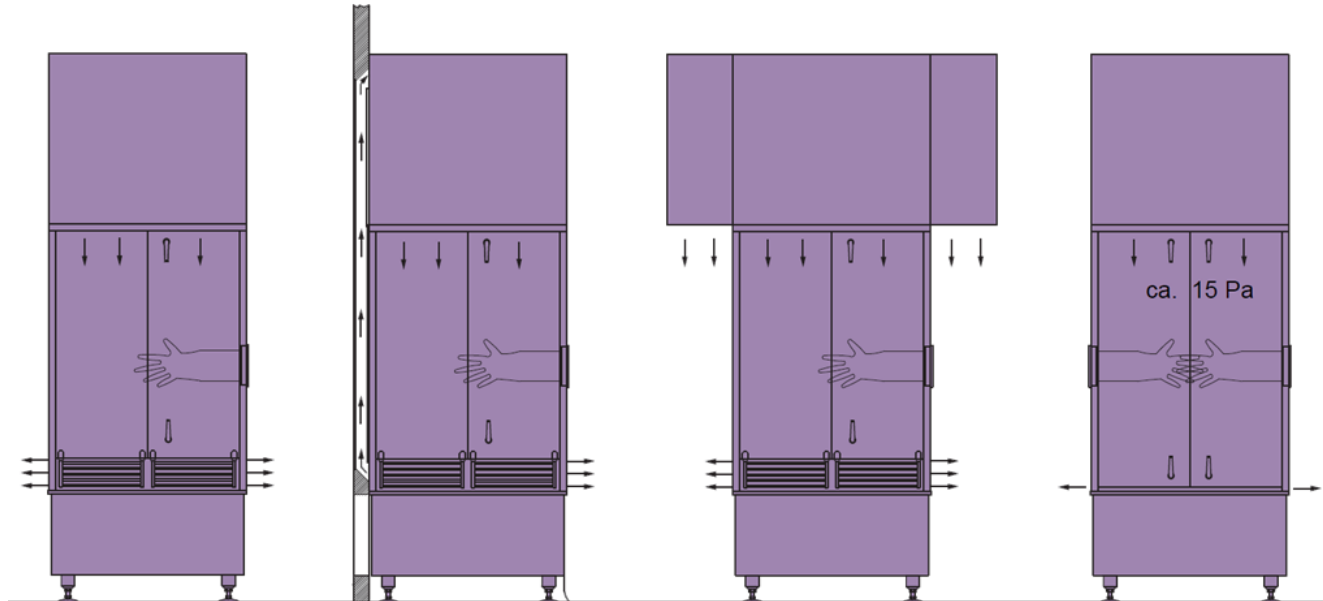


Barrier Technology

1. Passive RABS
2. **Active RABS**
3. Closed RABS
4. Isolator Technology
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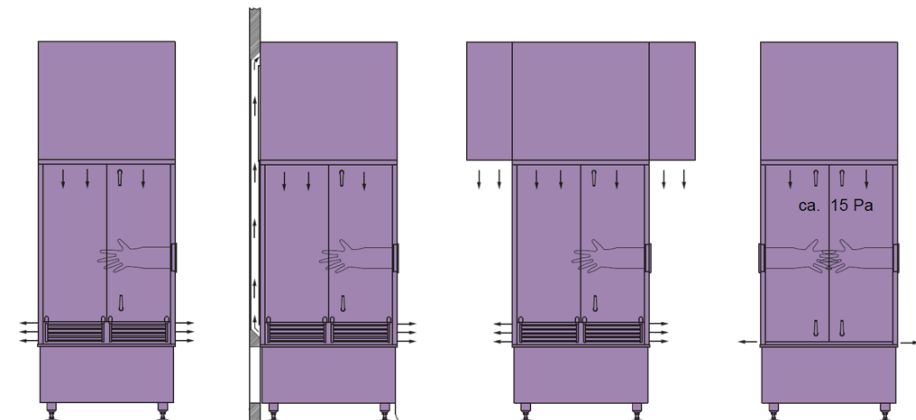
Active RABS

- Laminar flow unit located on top of the RABS
- Air intake from the room or pre-preped from building AHU
- Environment around RABS ISO 7 (B)
- Air discharge below the open containers at the level of the table plate
- Interventions via glove



Active RABS

- + Airflow dedicated to the machine / processing area
 - + Easier to control and validate
 - + Overpressure possible
 - + Wall mounting and adjacent LF units possible
 - + Doors can be opened following SOPs
- LF units designed according to the machine shape
 - Environment around RABS ISO 7 (B) recommended
 - No air conditioning (humidity, temperature)
 - Higher costs for the surrounding room



Example of Active RABS installations



Example of Active RABS installations

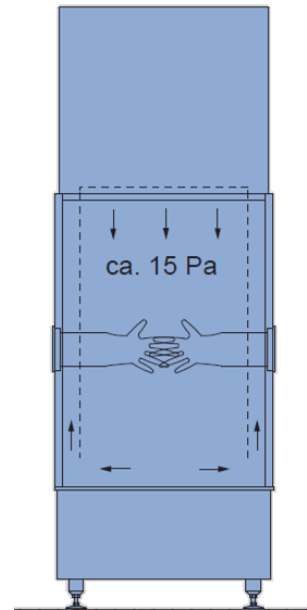


Barrier Technology

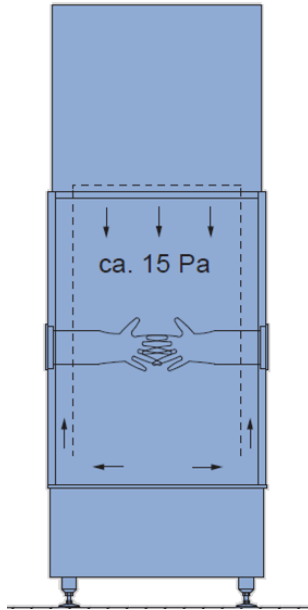
1. Passive RABS
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Closed RABS

- Closed machine guard with recirculating air handling system
- Closed and integrated system
- Machine guard equipped with air return ducts/double doors
- Intervention via gloves – Door opening critical, depending on use
- Air conditioning options available

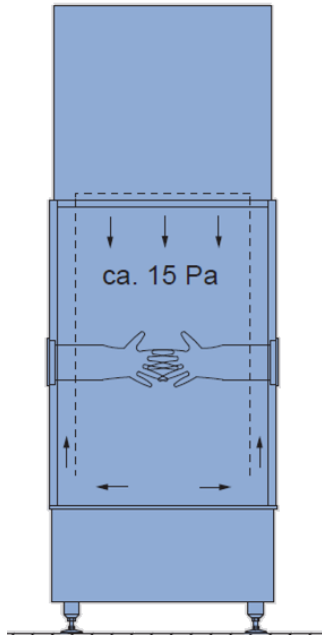


Special features and options for Closed RABS



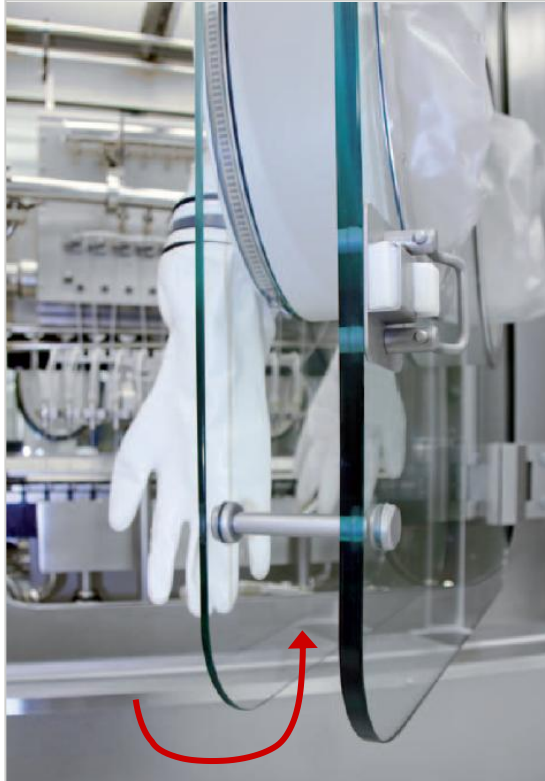
- Temperature control and monitoring
- Pressure control – positive + as well as negative – pressure
- Return air filtration
- Ring extraction around mouseholes

Closed RABS



- + Recirculating air, dedicated to the machine /processing area
 - + Overpressure and underpressure possible
 - + Wall mounting possible
 - + Operator and product protection
 - + Air conditioning possible
-
- Environment around RABS ISO 7 (B) still required
 - Higher investment for the closed RABS
 - Component loading (stoppers, caps) via ports

Example of Closed RABS installations



Air recirculation by double pane doors



Developed among others for powder filling machines (for example Antibiotics)

Example of Closed RABS installations



Partial Closed RABS in powder filling section
Open RABS in infeed and discharge section



Reasons for closed RABS instead of open active RABS?

→ depending on products (active / toxic)

Operator Protection → negative pressure possible

→ reduction/avoidance of fumes in the room

→ reduction/avoidance of powder dust in the room
(also dried out liquid spills)

Product Protection → controlled overpressure possible

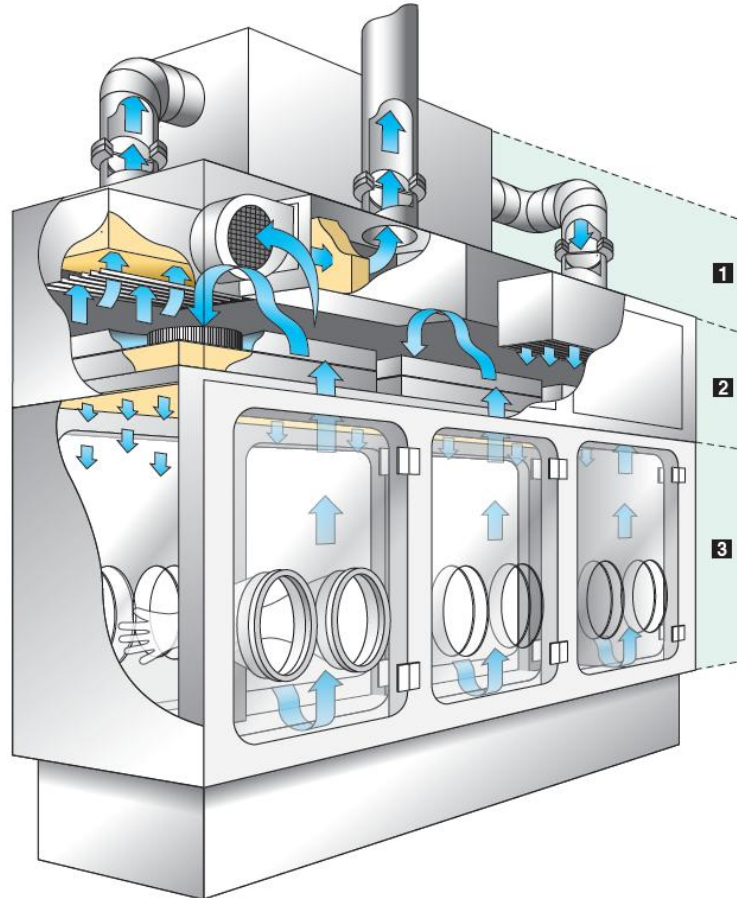
→ controlled humidity and temperature

→ *Closed RABS is often/mainly used for powder processing lines.*

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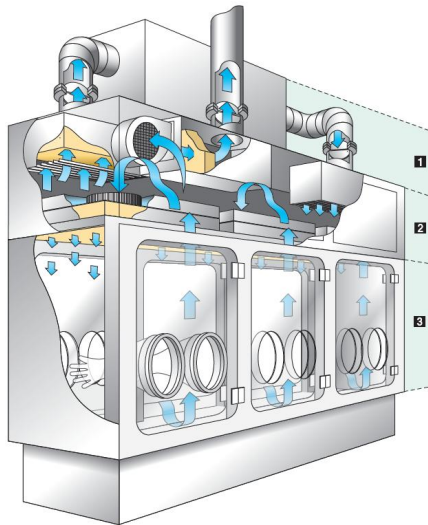
Isolator



1. Air treatment equipment:
Preparation of sterile air
2. Air circulation unit with air flow control:
Controllable air flow (Laminar Flow) for the displacement of any particles and return of the air.
3. Process area
The gloves integrated in the machine guard permit manual intervention in the work area without impairing the clean room class A (class 5 acc. to ISO14644). Opening the doors leads to an immediate production stop.

Isolator

- + Lower costs for surrounding room (C)
- + More comfortable for operators due to simpler dress
- + Aseptic area minimized
- + Highest product safety
- + Automated H₂O₂ decontamination



- Higher investment costs for the isolator
- Door opening during production not possible
- Initial qualification requires more efforts
- Additional space required in technical area

Isolator

ISOLATOR

VHP (H₂O₂) gassing /
decontamination essential

different protective areas

protecting the product

- aseptic production
- operating with higher pressure
- SAL at least 10⁻⁶
(SAL= Sterility Assurance Level)

protecting personnel

- processing toxic or infectious products
- operating with lower pressure
- isolator = containment

High speed filling and closing machine under Isolator



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Comparison of the systems

Pro RABS

- High flexibility in regards of frequent size change / small batches
- Low investment costs
- Qualification is less extensive, thus sooner ready for production
- Manual intervention is possible

Pro Isolator

- Provides a higher sterility assurance level than RABS (at least factor 100)
- Reduced number of positive samples from environmental monitoring
- Clean room area reduced
- Clean room class required for the surrounding is lower
- Gowning costs are reduced, less time for gowning is needed
- Active substances can be processed
- High operator protection by simple means (return air filter)

Summary investment costs (EUR)

	Cleanroom A / B / C / D incl. airlock	cRABS	Cleanroom D incl. airlock	Isolator incl. H₂O₂
Investment costs (€)	950.000	500.000	600.000	1.650.000
Conditioning	350.000	incl.	250.000	incl.
IQ/OQ, cycle, micro biology	20.000	40.000	20.000	250.000
Subtotal (€)	1.320.000	540.000	870.000	1.900.000
Total (€)	1.860.000		2.770.000	

Summary yearly costs (EUR)

	cRABS	Isolator incl. VHP
Cleaning and clothing	300.000	180.000
Utilities		
Requalification		
Monitoring		
Total (€)	300.000	180.000

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Summary

- The use of Passive RABS for filling machines is not common anymore
- Most RABS for liquid filling machines are Active Open RABS
- Most RABS for powder filling machines are Closed RABS
- Authorities „encourage“ the use of Isolator systems

Decision for the kind of RABS needs to be evaluated case by case.



Flexible Production – using Isolators

VARIOSYS®



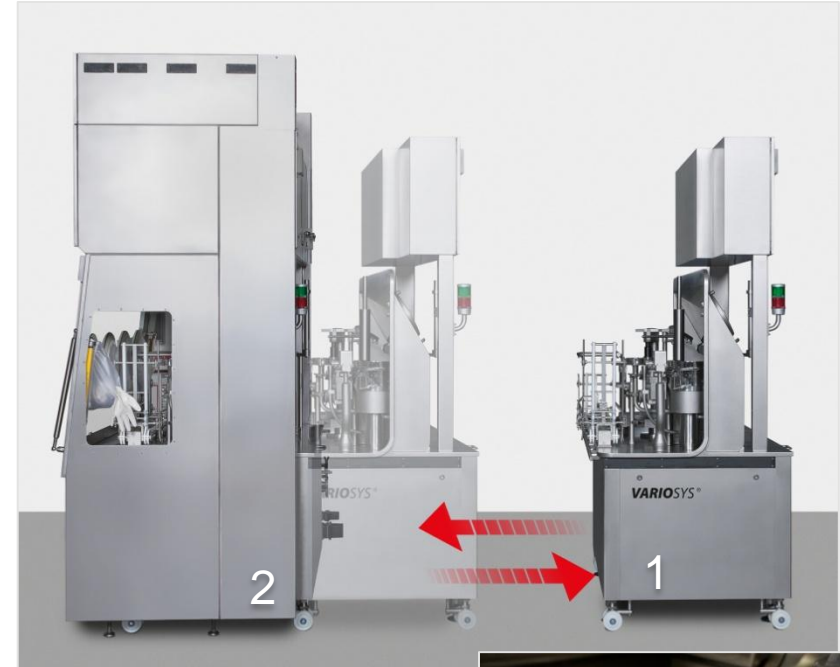
The lock-and-key principle

1. Exchangeable basic modules (“L-flange”)

- Standardized size
1.65 m x 2.50 m x 1.25 m (width x height x depth)
- Mounted on castors

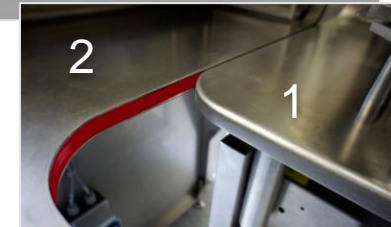
Basic modules provided by B+S

- Blank, multi-purpose module
- Semi-automatic processing
- Nest filling process - syringes, vials and cartridges
- Vials in bulk processing
- Ampoules in bulk processing

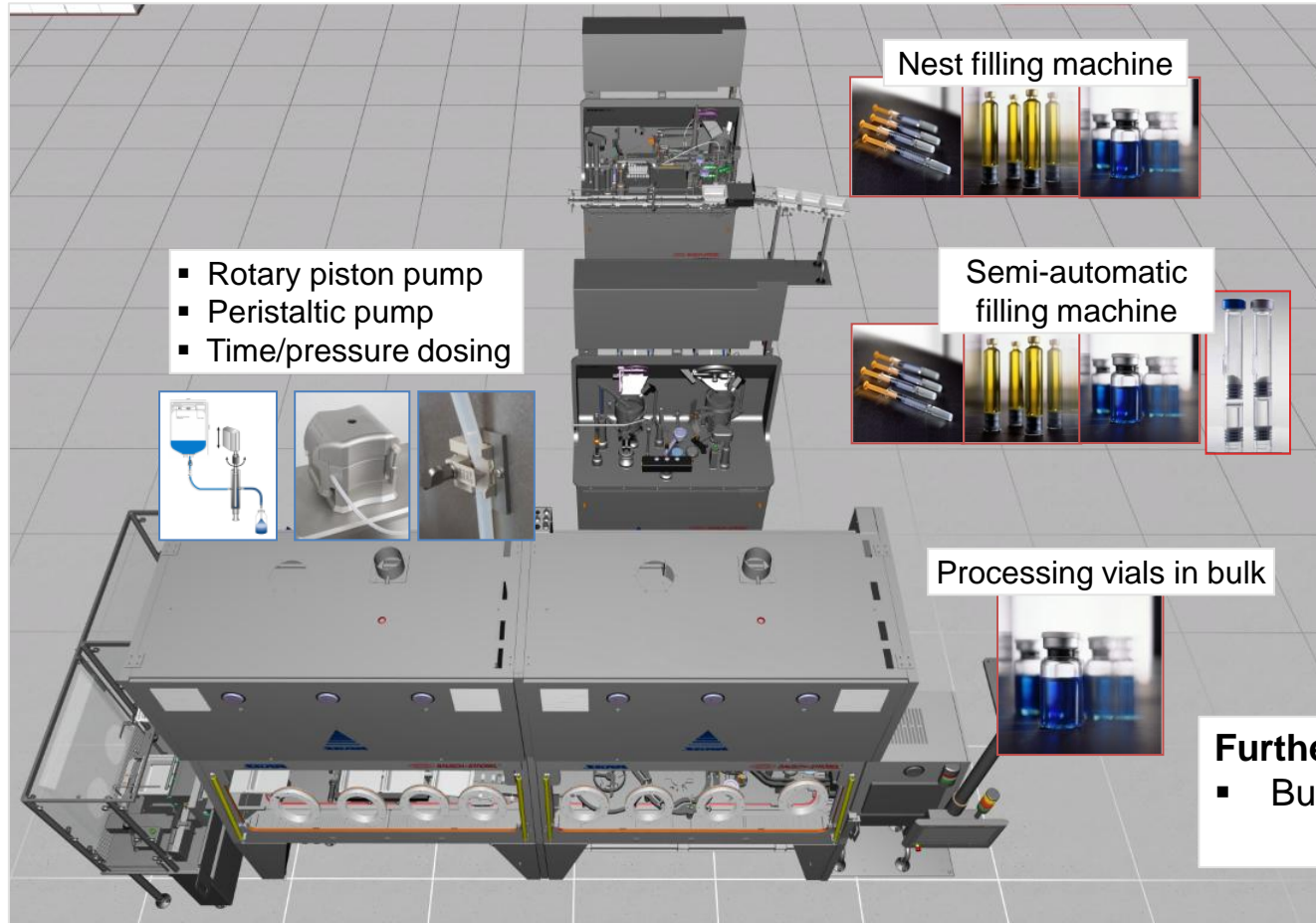


2. Isolator

- Connected with module via inflatable gasket
- Standardized size
1.90 m x 2.90 m x 1.50 m (width x height x depth)



Flexible processing line



- Rotary piston pump
- Peristaltic pump
- Time/pressure dosing

Nest filling machine



Semi-automatic filling machine



Processing vials in bulk



Further modules available:

- Bulk ampoule processing

One room fits all

VarioSys® fits in one room. You no longer need to invest in several filling rooms with several machines for processing different containers. Instead, you can set up a combination of production modules tailored to your requirements in one room only.

	VarioSys filling room	Vial filling room	Syringe filling room	Cartridge filling room	Ampoule filling room	I.V. bag fill. room
Vials	X	X				
Syringes	X		X			
Cartridges	X			X		
Ampoules	X				X	
I.V. bags	X					X
Lyo	X	X				
Liquid/powder	X	X				

Questions about

VARIOSYS®

Contact us

For the optimal processing of your product!



We shall be pleased to answer your questions!