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Manufacturing Aspects

Syringe Processing – State of the art and latest technologies

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Bulk Processing


- Challenges:
 - Syringes not stable
 - Siliconization has to be adapted to each format
 - Not very flexible for new components (tip cap, LLA)
 - Syringes with needle cannot be processed in the tunnel
 - Can be done with autoclaves → high effort, batchwise process
- Advantages
 - Proven sterilization process
 - Proven transfer to the filling area
 - Cheaper packaging material
 - Full control of the manufacturing / siliconization process







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Bosch Syringe Product Portfolio

Container	Bag Opening	Tub Opening	Filling, Sealing	Guarding	Downstream Processing
<p>SCF Syringes</p> 	<p>ABO 5000</p>	<p>Low to Mid Speed</p> <p>ATO 3000</p> <p>ATO 5000</p> <p>High Speed</p> <p>ATO 5000</p>	<p>Low Speed</p> <ul style="list-style-type: none"> - FXS 2021 (5400sph) - FXS 2051 (11280sph) <p>Medium Speed</p> <ul style="list-style-type: none"> - FXS 3050 (10800sph) - FXS 3100 (18600sph) <p>High Speed</p> <ul style="list-style-type: none"> - FXS 5100 (36000sph) - FXS 5160 (57600sph) <p><i>Output based on 0,5ml Syringes in a 160 Nest</i></p>	<p>Clean Room installation</p> <ul style="list-style-type: none"> - RABS - cRABS - Isolator 	<ul style="list-style-type: none"> - Denester - Rod Insertion and Labeling - Renester - Buffer - Inspection



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FXS 3100 – Line in RABS

ABO LF-hood ATO LF-hood FXS LF-hood

ABO 5000 Clear separation of the cleanroom areas (two base frames) ATO 5000 FXS 3100 Stopper supply for double bags (pre-sterilized)

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FXS 3100 Isolator Line with Automatic Bag and Tub Opening

Clear separation of the cleanroom areas (two base frames)

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Automatic Bag Opening Connected to Automatic Tub Opening



Automatic Bag Opening

Requirements

- Up to 6 tubs/bags per minute
- Clear separation of clean room areas
- Protection of the tub (by the bag) as long as possible
- Safe separation of tub and bag
- No contact bag outside – tub outside
- Minimizing the risk of particles
- Only one piece of waste



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Automatic Bag Opening



Clear separation of the cleanroom areas (two base frames)



ABO

C

ATO



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Automatic Bag Opening – Basic Configuration



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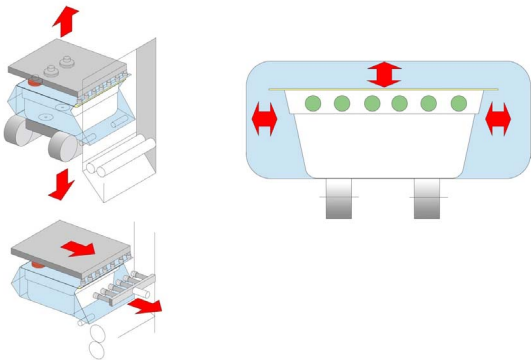
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Aseptic Tub Transfer – a Bundle of Measures



The diagram illustrates the aseptic tub transfer process. On the left, two views of a tub being moved by a robotic arm are shown with red arrows indicating the direction of movement. On the right, a top-down view of the tub is shown with a white bag covering its top surface. Red arrows indicate the bag's position relative to the tub's edges.

No contact bag outside – tub
outside, especially at the top
of the tub.

Protection of the tub (by the
bag) as long as possible.
Removal just before the
transfer.

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Automatic Bag Opening – Basic Configuration



The photograph shows a close-up of an automatic bag opening process. A white bag is being opened by a mechanical arm. A blue callout box points to the top of the tub, indicating that the bag should not touch it. Another blue callout box points to the side of the bag, indicating that it should not touch the outside of the tub.

Outside of the bag
does not touch the
outside of the tub


No contact of the bag
to the top of the tub

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Tub Opening

Requirements

- Up to 6 tubs/min
- Minimum particle generation
- Reliable gripping of the cover sheet
- Absolute reliable functionality

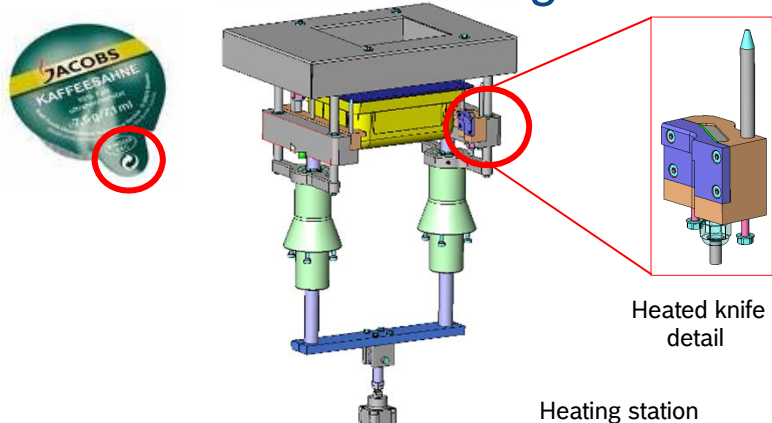



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Coffee Cream Concept – pre-Determined Breaking Line



The diagram shows a green Jacobs coffee cream lid with a red circle highlighting a specific feature on its top surface. To the right, a 3D CAD model of a heating station is shown, with a red circle highlighting a component. A callout box provides a detailed view of this component, labeled 'Heated knife - detail', which is a blue and brown assembly with a vertical rod. The main assembly is labeled 'Heating station'.

Heating station

Heated knife - detail

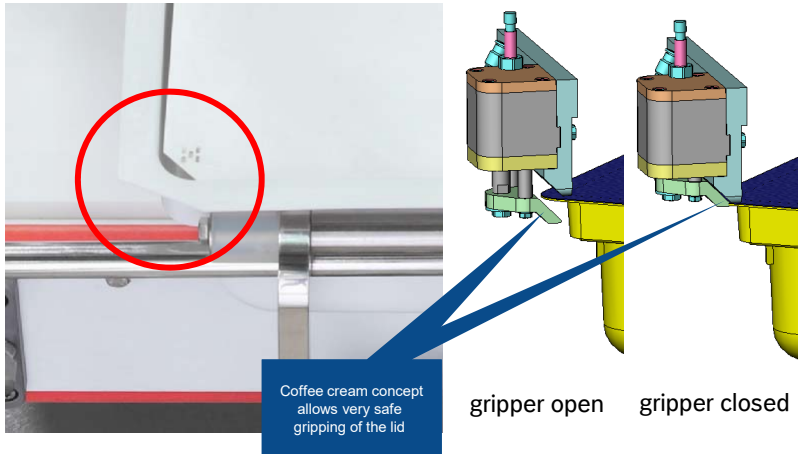
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Tub Opening – Detail



The photograph on the left shows a white tub opening with a red circle highlighting a detail. To the right, a 3D CAD model shows two gripper mechanisms in 'gripper open' and 'gripper closed' states. A blue callout box points to the gripper mechanism with the text: 'Coffee cream concept allows very safe gripping of the lid'.

Coffee cream concept allows very safe gripping of the lid


gripper open gripper closed

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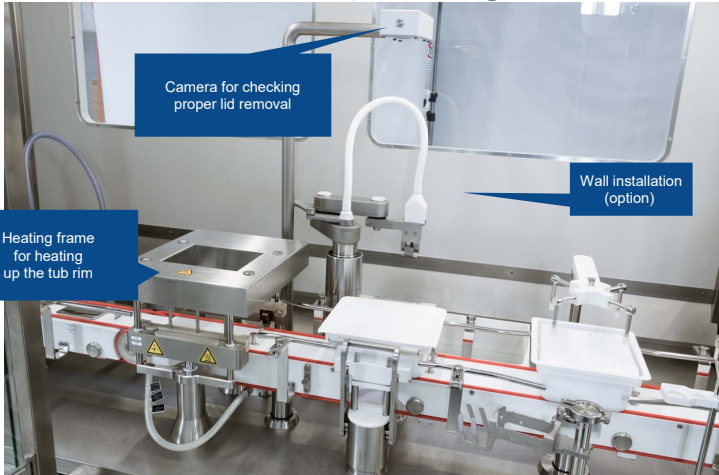
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Automatic Tub Opening




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Requirements

- Syringe specific requirements:
 - Up to 600 syringes / min
 - Precise transport system
 - No contact of the insertion tube with the syringe
 - Suitable for all available filling systems
 - Stopping immediately after filling
 - Transport of the tub



In Process Checkweigh under Isolator – Detail



Weighing cells

Gripper for syringes



Filling Area



Allows continuous filling and stoppering even during transition from nest to nest

Stoppering immediately after filling → minimum exposure time of the product to the environment.



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Time Pressure Filling (TPF)



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Peristaltic Pump



Individual stopper presence check with sensors to check rod position



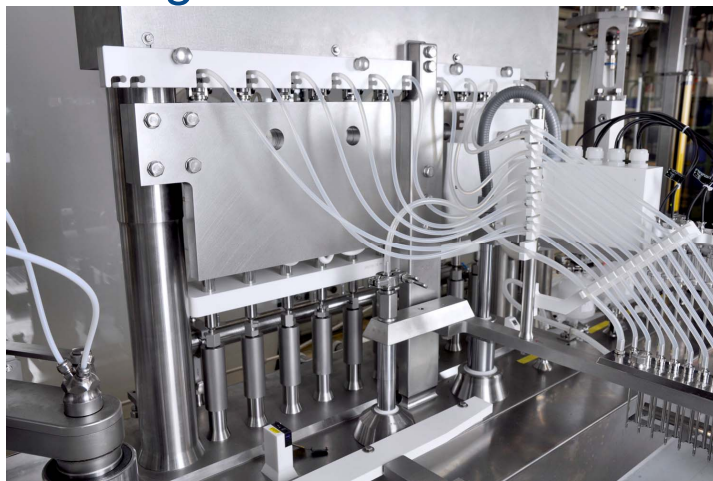
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Combi Filling Station

Combination filling station with up to 4 filling systems possible (piston pump, time pressure, peristaltic pump and rolling diaphragm pump).




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Vacuum Filling / Stoppering



Pump station, reinforced for vacuum filling

Filling needles

Rods for stoppering

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CIP/SIP Cabinet



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Basic Configuration Stopper Supply



Detection of stopper presence perrow (not individual):
When one or more stopper(s) is (are) not present in vent tube
→ rod is not lifted
→ sensor is blocked

Stopper supply, made of stainless steel

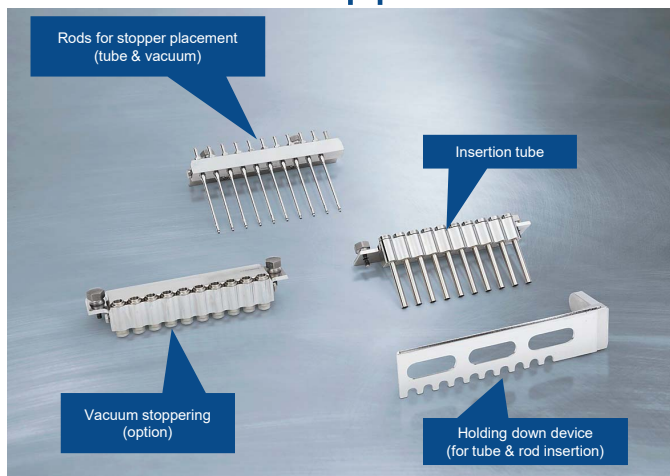


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Size Parts Stopper Placement



Rods for stopper placement (tube & vacuum)

Insertion tube

Vacuum stoppering (option)

Holding down device (for tube & rod insertion)



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RABS Stopper Supply Including Sliding Pane



Stopper loading from operation side

Easy logistics / no crossing of the line



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Nested Syringe Filling Machine with Isolator



Stopper supply with exchangeable Port

Wash down air ducts



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Isolator Stopper Supply



Exchangable port for stopper supply

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Exchangeable Port for Stopper Supply

- Port Getinge La Calhène



Outside view



Inside view

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Exchangeable Port for Stopper Supply

- Port from Sartorius stedim for BD TSCF stoppers (former IDC)



Outside view



Inside view

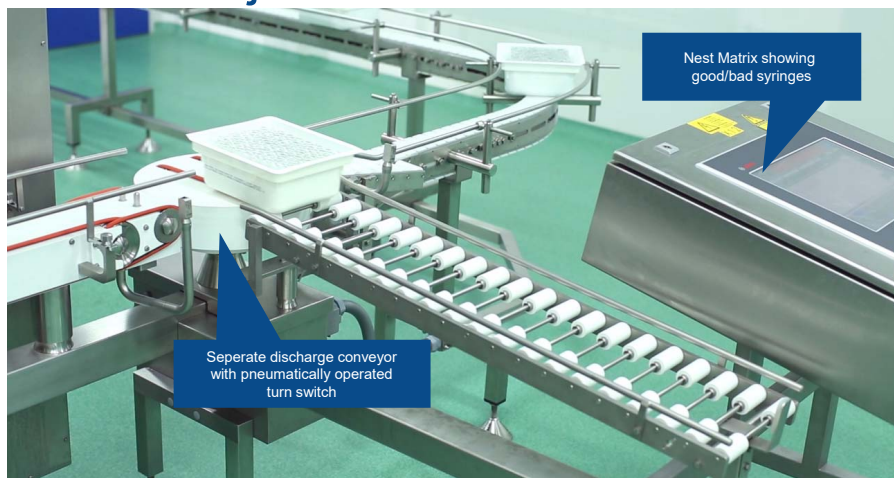


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Tub Reject




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Topics for Mock-Up (Selection)



- Positioning and number of gloves
- Media connections
- Stopper supply
- Position of particle and microbiological monitoring
- Handling inside the barrier system: Start up of line, line clearance and trouble shooting

Conclusion: After the mock-up major adaptations of the machine design can be necessary for optimized barrier system use.

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Mock Up for Isolator & RABS



ABO

ATO

FXS

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Rod Insertion and Labeling



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New Trends – Packaging Material – Pre-Sterilized (Selection)

- Tub & nest approach (syringes, vials and cartridges)



Packaging material pictures by Gerresheimer



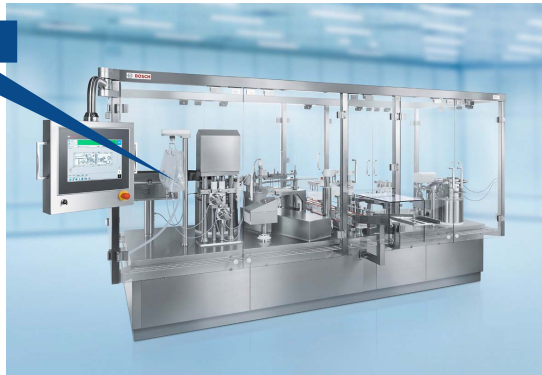
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Filler for Nested Syringes, Vials and Cartridges

Single use filling system
PreVAS



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Flexible Filler for Clinical Trials



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Manufacturing Aspects

Case study for high-viscous product

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Summary

- There is a huge variety in filling and stoppering of syringes compared to e.g. vials
- The specific set-up is depending on the fill product and the syringe components
- Adapting the specific process of filling and stoppering on a production machine is quite challenging
- Bulk syringe processing is an exception
- Processing nested syringes is state of the art

