Introduction, Background and History of BFS Technology

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AGENDA

1. **Basics of BFS Technolgy**
2. **History of BFS**
3. **Comparison BFS Technology with Traditional Aseptic Technology**
4. **Container Designs**
5. **Packaging Options**
6. **Summary**

1. Basics of BFS-Technology

BFS Definition

BFS is an production process based on extrusion blow molding of polymer containers.

However BFS aseptically produces filled & closed containers using compact and fully automated machines that:

-1- Continuously melt polymer granules & extrudes a sterile, formable polymer parison

-2- **B**low the molten polymer into a container using sterile air

-3- **F**ill a sterile liquid into the container

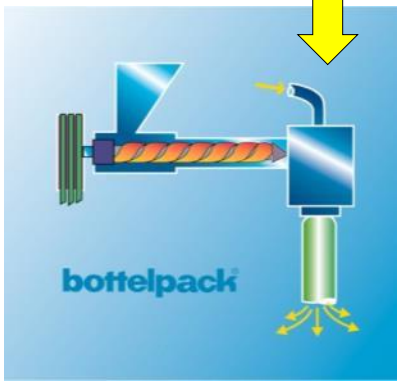
-4- **S**eal the container tightly immediately after filling

1. Basics of BFS Technology

BFS Process (Shuttle Typ) BFS is simple & straight forward

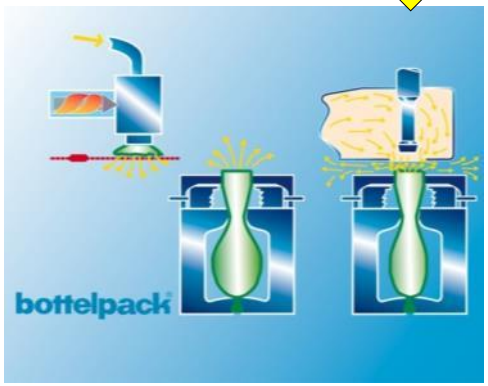
Med. Grade Polymer

Sterile Air



Melting polymer & Extrusion of parison with sterile air

Sterile Air

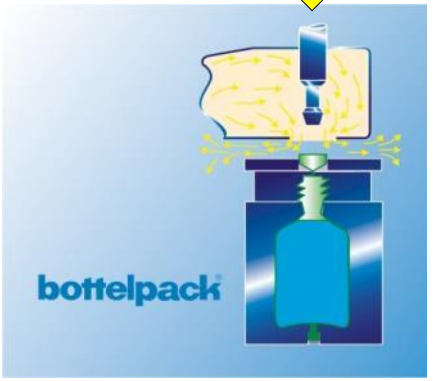


Transfer in mold and cutting with overpressure of sterile air

1.Sterile Air
2. Sterile Formulation

Container blow forming with vacuum or sterile air & filling

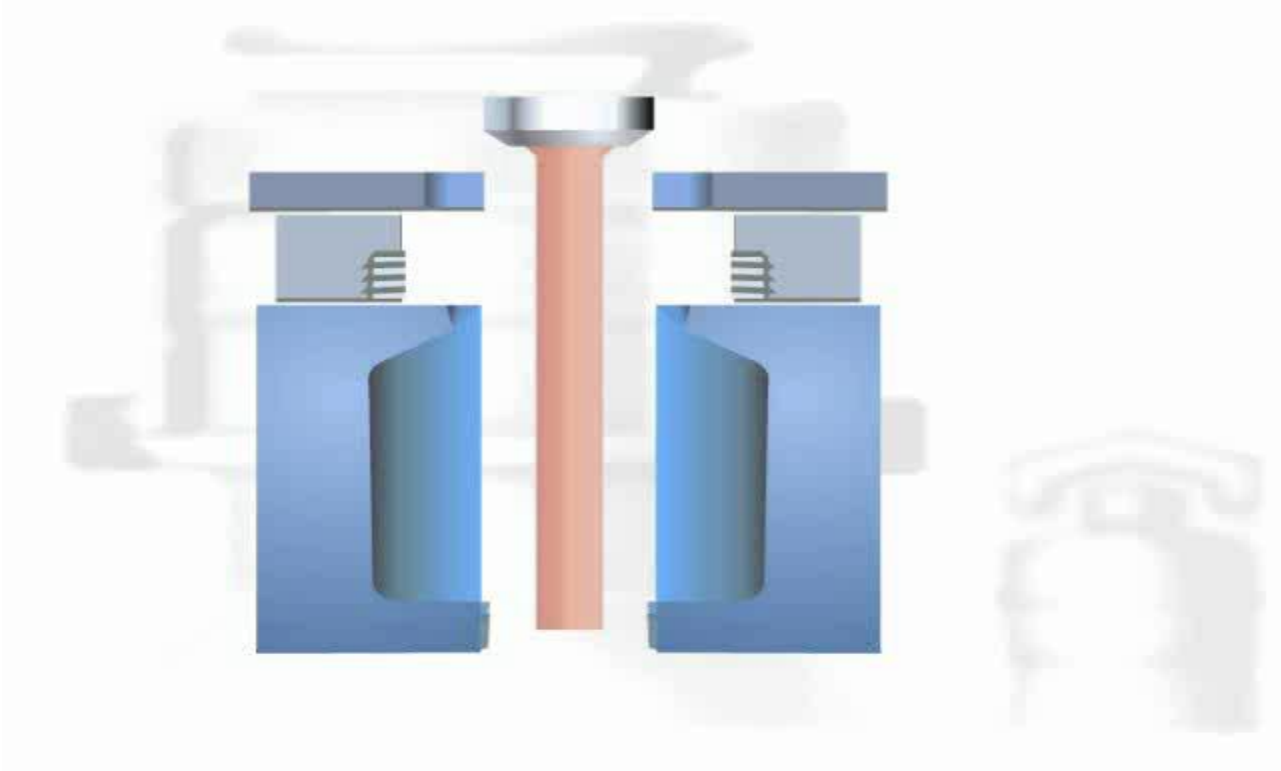
Sterile Air



Container closing

1. Basics of BFS-Technology

Process-Overview (Shuttle Process)



1. Bascis of BFS-Technology

- Extrusion of Polyethylene- (PE) or Polypropylene- (PP) or PET Granules
- Container Sizes between 0,2 ml and 1000 ml
- Aseptic Filling
- The shuttle BFS process: 12-16 sec
- Rotary BFS process 2,5 -3,5 sec
- Using molds with up to 30 cavities
- Output depending on equipment up to 30.000 pieces/hour
- Mainly Time-Pressure-Dosing Systems

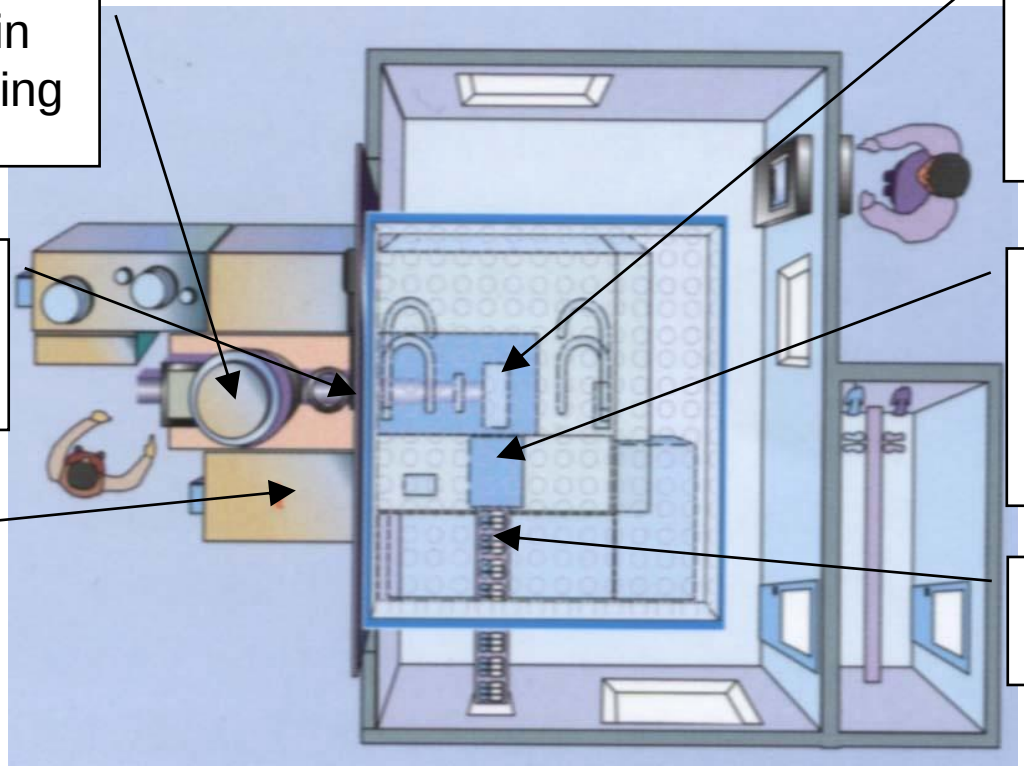
1. Basics of BFS-Technology

Process-Overview (Shuttle Process)

Granules/Resin Hopper for feeding granules

Extruder for melting Granules

Switchbox for Technical-equipment



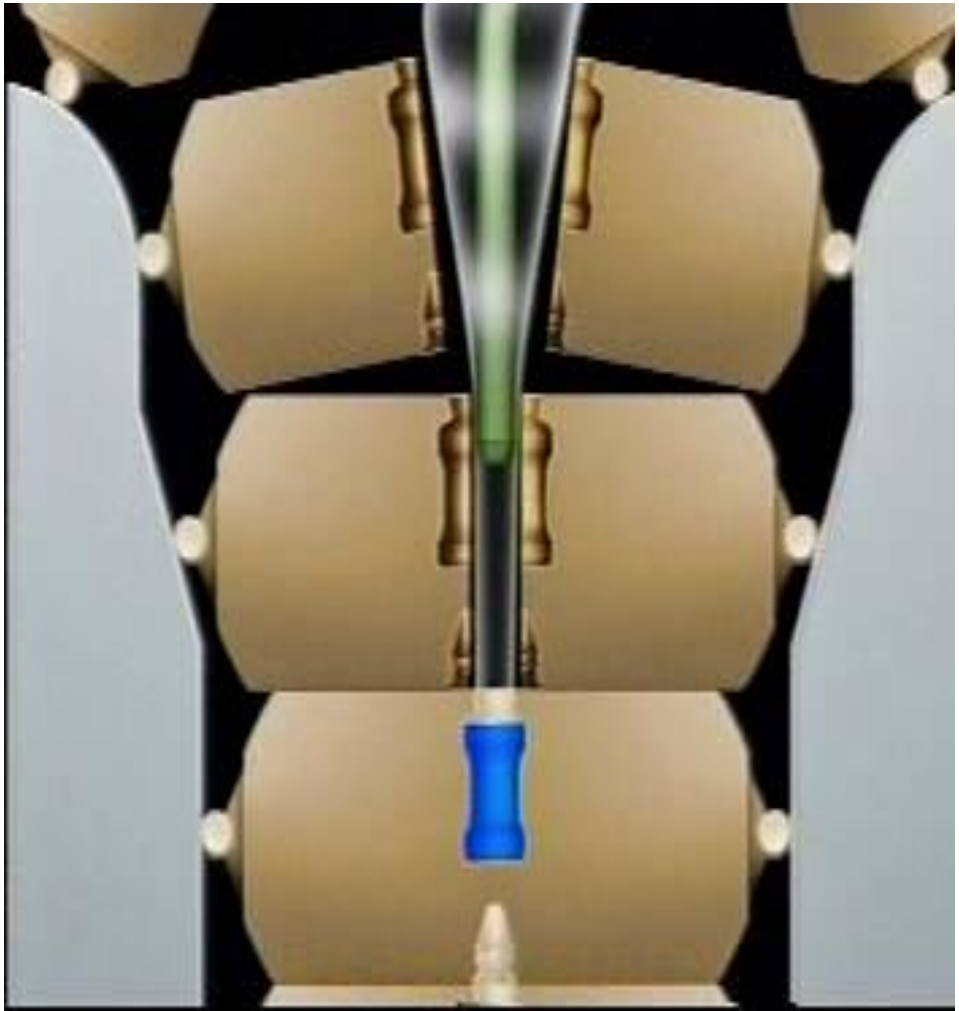
Parsion head for manufacturing Endless-Tubing

Air shower For filling Blow-Fill-Seal-Process

Conveyor belt and Punching

1. Basics of BFS-Technology

Process-Overveiw (Rotary Process)



Process-Overview (Rotary Process)

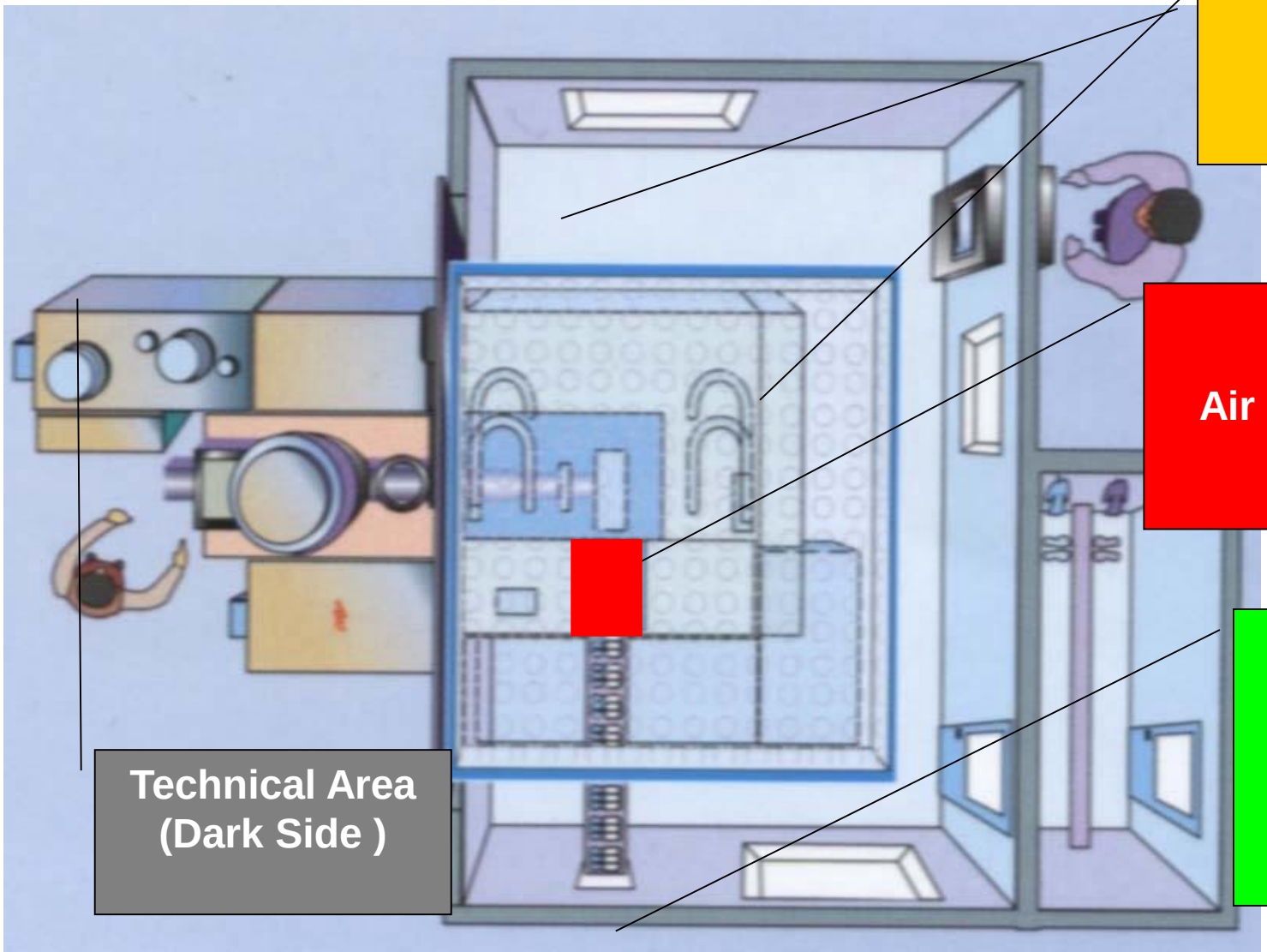
BFS-Technology
Type 460 ***located in clean room class C***

Parison head for Manufacturing Endless-Tube/Parison Dosing needles are located in the Parison

Outlet and Punching Device

Moulds are mounted on rotating chain, therefore continuous process

1. Basics of BFS-Technology



Class 100 000
ISO 8
Class C
Environment

Class 100
ISO 5
Air shower class A

Sekondary Packaging

"House class" E/F

Technical Area
(Dark Side)

2. History of BFS Technology

established since 1964

1st application for IV Solutions sold in 1965
1st application for Eye drops sold in 1971
1st application for Single dose Eye drops sold in 1976
1st application for Inhalation Therapy sold in 1981
1st application for Cough Syrup sold in 1982

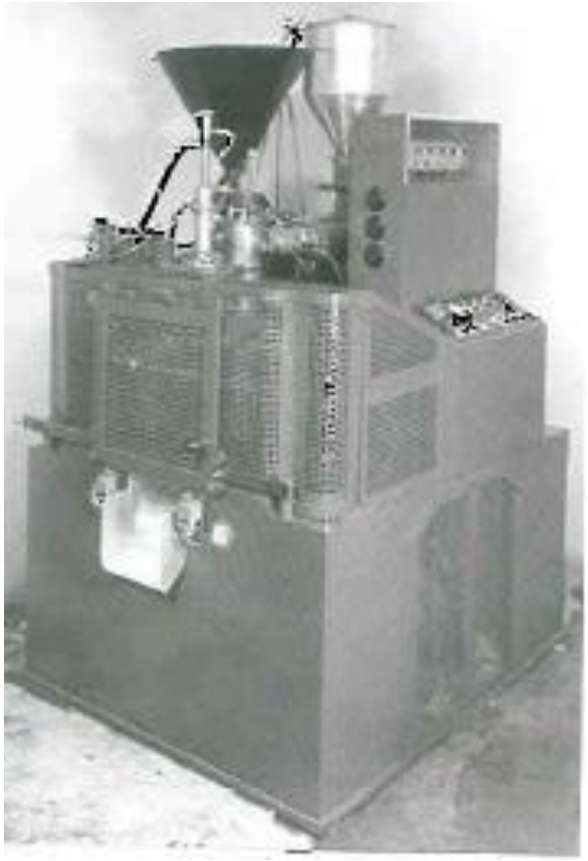
more than 1800 BFS machines sold worldwide

Approx. 10 Billion of BFS containers produced worldwide/Year

2. History of BFS-Technology:

First BFS-Equipment 1964

Type 301



1. Basics of BFS-Technology

BFS-Equipment Type (Shuttle Typ)

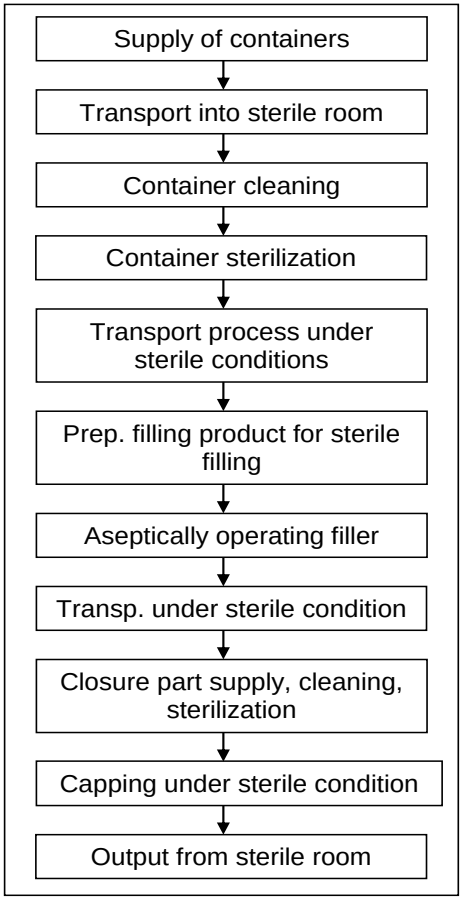
3. Comparison of sterility assurance between BFS- and traditional aseptic filling

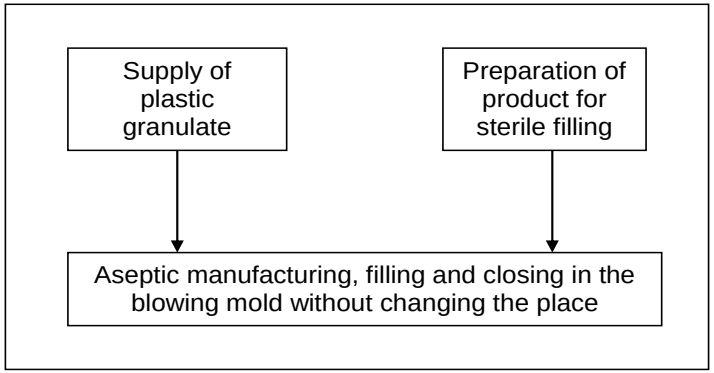
Summary:

- No Interventions in class A/B areas for BFS Technology during production and at rest
- Equipment runs with a lot of Interventions out of the Clean room for Dark/White separated machines (Remote Control)
- Integrated SIP / CIP / DIP Processes for high security during equipment preparation
- Running of long filling times/big batches with BFS-Technology (up to one week is possible)
- Long Media Fill History without Media fill failures: Regular Media Fills with up to 50.000 containers without contamination
  No Handling of empty containers

3. Comparison of sterility assurance between BFS- and traditional aseptic filling

CONVENTIONAL TECHNOLOGIES VS. BFS





4. General Container Design Examples

Infusion up to 2000ml

Ophtalmic & Inhalation & Rinsing

Injection

Injection with Luer Connection

Irrigation, rectal, vaginal

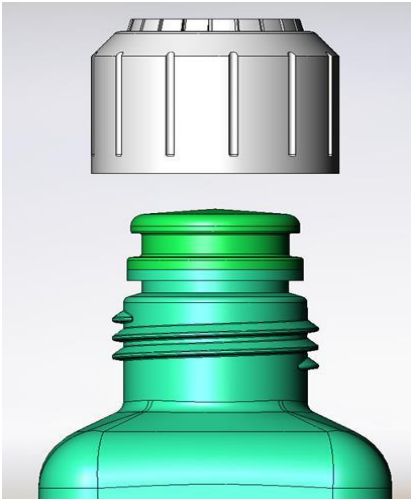
4. General Container Design Examples

ENHANCED SVP CONTAINER DESIGNS

BIOLOGICALS AND VACCINES

IRRIGATION / ORAL APPLICATIONS

- Large openings with easy-to-use caps allow fast applications (surgery, eye wash, …)
- Also applicable for oral medical solutions and e.g. electrolyte drinks
- Dedicated machine and mould design for large openings

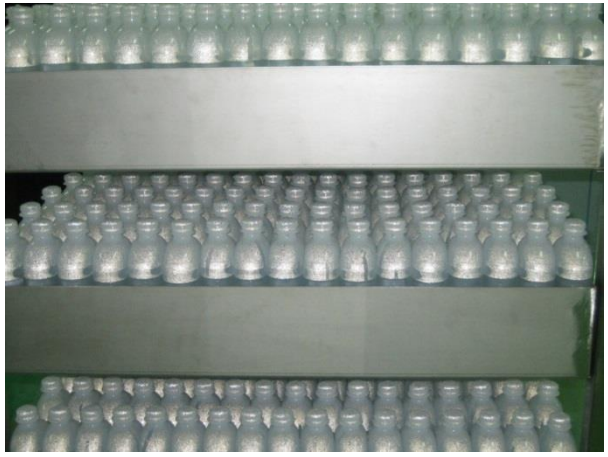


INNOVATIVE LVP CONTAINER DESIGNS

- Outstanding container characteristics, easy and safe to use: easy empty bottle design / „standing pouch“
- Machines designed to operate on large scale batches
- Higher production efficiency / OEE compared to conventional technologies

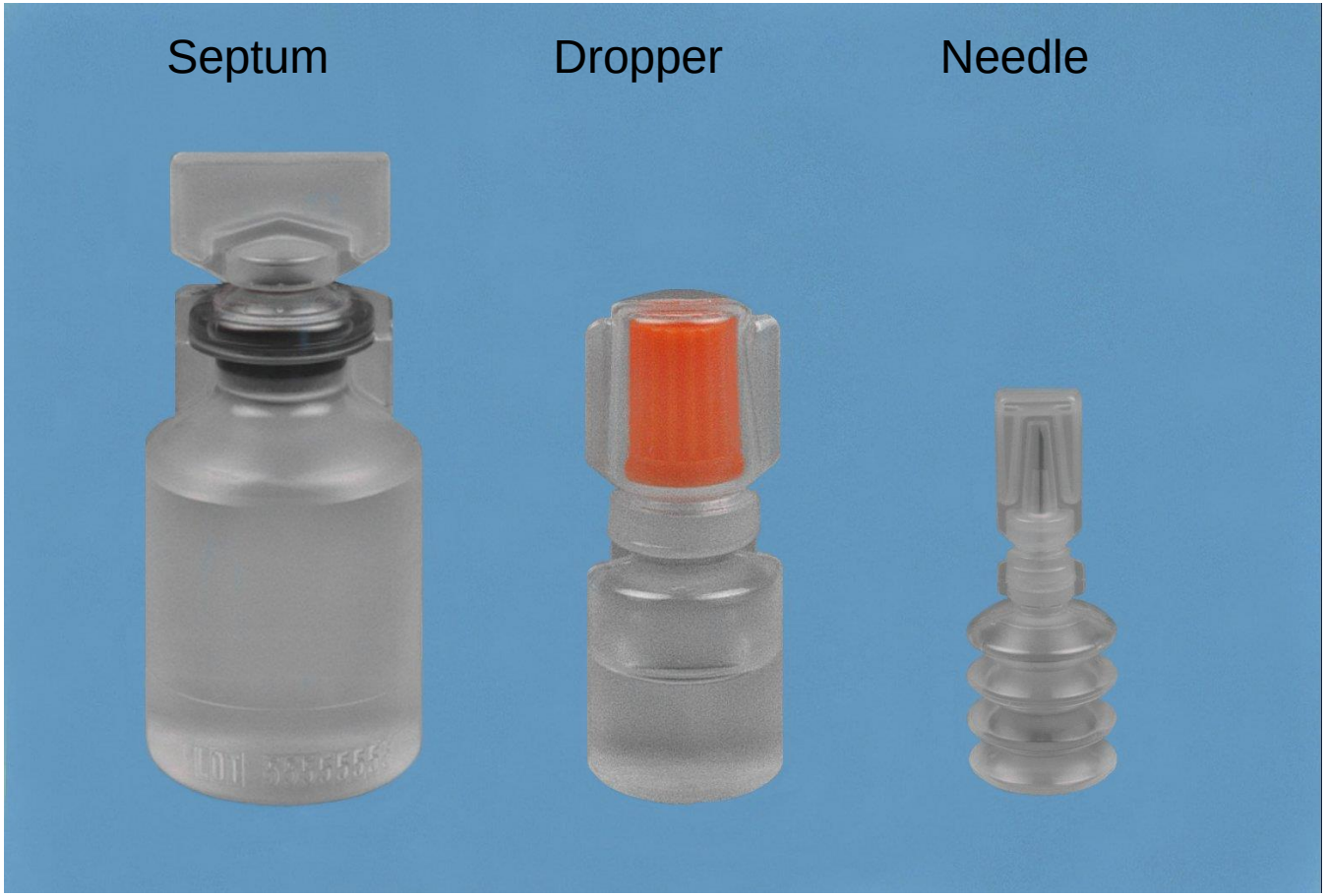
INNOVATION ON PRIMARY PACKAGING MATERIAL AND CAPS

- Different BFS grade soft PP materials of global resin suppliers available
- Different BFS grade LDPE materials with high sterilization temperatures available
- Different BFS cap designs and applicators for various appications (LVP)



4. General Container Designs Examples

Containers with Inserts



5. Packaging Options

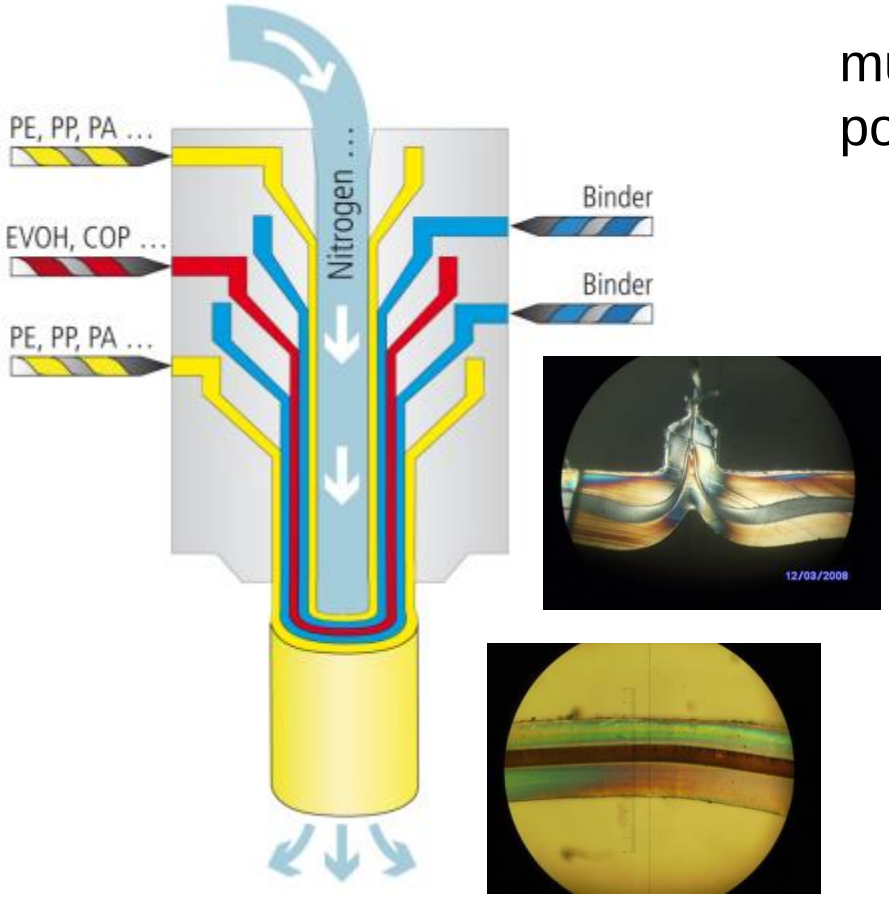
secondary packaging examples

Container in aluminium bag

Container in Blister for sterile surface

5. Packaging Options

CoEx principle



multilayer wall from up to 5 polymers with different (barrier) properties:

EVOH - excellent O_2 barrier properties for food and pharmaceutical packaging

PA - good gas barrier properties and chemical resistance, used for packaging of cosmetics and chemicals

mod. COP special inner layer for low adsorption

Binder (tie layer; adhesive):
e.g. with acrylic acid modified PE or PP

6. Summary 1/3

Some key features

Topic	Bfs feature
• Product sterility	• very compact machines, minimal class 100 area & human interference; optional terminal sterilization by autoclaving
• Endotoxin content	• Rigorous polymer processing (high temp & shear stress by extrusion-process)
• Particulate matter	• Typically a factor of 10 lower than glass/ elastomer packaging
• Heat stress on formulation	• Can be minimized to fit even biotech products
• Min. product volume requirements	• Down to 50 to 100 µl

6. Summary 2/3

Some key features

Topic	Bfs feature
• Container material compatibility	• Med grade polyolefines e.g. PP, PE
• Container material supply assurance	• Various independent Polymer suppliers
• Test containers for early pharmaceutical development	• Bfs test kit available
• Extractables from polymers	• Low risk, various extractables dossiers available
• Semipermeable containers	• Optional: increase barrier against mvt, oxygen ingress or light by secondary packaging or dedicated CoEx- design

6. Summary 3/3

Some key features

Topic	Bfs feature
• User & production friendly container design	• Easy opening, no breakage, high mechanical robustness, collapsible high design flexibility from 0.1 to 1000 ml
• Multidose containers	• Elastomer closures or screw caps available
• Authorities (FDA, EMEA et al.)	• Well known as advanced aseptic processing;
• Anti counterfeiting	• Tamper evidence & dedicated design
• Environment	• Halogen free polyolefines; mono materials
• Cost of goods	• very cost effective

Thank you very much for your Attendance!

非常感谢您的参与！