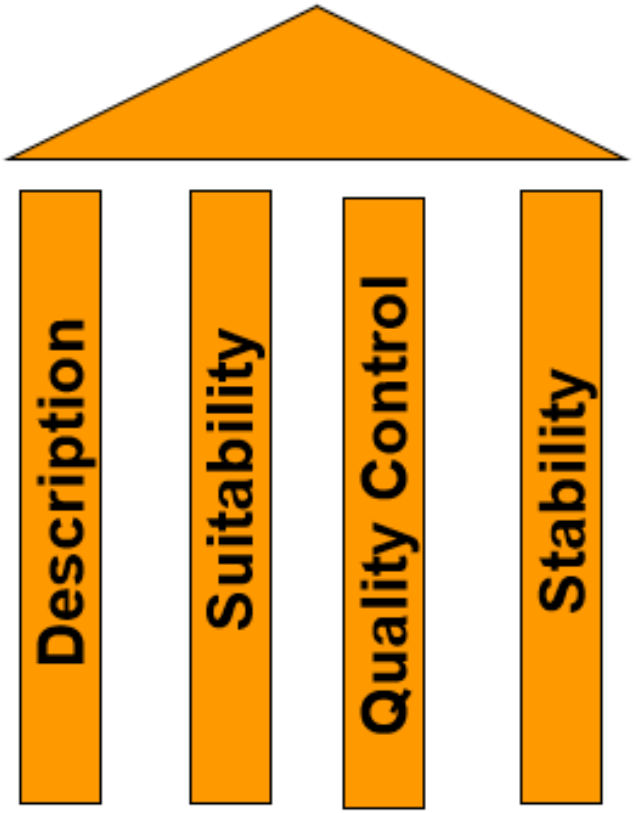
Primary container closure systems, part II: **Blow-fill-seal containers**

- Requirements
- Overview BFS-container closure systems
- Advantages and disadvantages

Blow-fill seal (BFS) Containers allow a wide range of applications & designs.

Examples of BFS containers

Drug product requirement are grouped into 4 sectors.



General Requirements

Description
incl. container closure system (CCS)

Suitability
of packaging system for the intended use
e.g. protection, compatibility, safety, performance

Quality Control
incl. packaging components

Stability
of dosage form and container closure system

Key requirements have to be addressed in different phases of Packaging Development.

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Definition of core requirements → Design concepts → Lab-scale manufacturing → Verification tests → Scale-up

chemical
- sorption
- degradation
- light sensitivity
- E&L
- oxidation
- etc.

physical
- loss of water
- particulate matter
- handling forces
- etc.

functional
- filling volume
- delivered volume
- terminal sterilization
- usability
- etc.

Example Permeation: Assay-Changes of mt 5% have to be justified explicitly.

physical
- **loss of water**
- particulate matter
- handling forces
- etc.

In general, *significant change* for a drug product is defined as one or more of the following (as appropriate for the dosage form):

- A 5 percent change in assay from its initial value, or failure to meet the acceptance criteria for potency when using biological or immunological procedures

or:

A 5 percent loss in water from its initial value is considered a significant change for a product packaged in a semipermeable container after an equivalent of 3 months' storage at 40°C/NMT 25 percent RH. However, for small containers (1 mL or less) or unit-dose products, a water loss of 5 percent or more after an equivalent of 3 months' storage at 40°C/NMT 25 percent RH may be appropriate if justified.

Source: FDA Guidance for Industry, Q1A(R2) Stability Testing of New Drug Substances and Products)

BFS containers cover many dosage forms from oral via ophthalmic to infusion.

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General container examples

Ophtalmic & Inhalation
0,1 ml to 20 ml

Orals (1 ml to 500 ml)

Injection (1 ml to 20 ml)

Astra Zeneca
Ropivacain 10 ml

BBraun NaCl 10 ml

Infusion 50 ml to 2000ml

Polymer materials, additives and designs allow customized containers, e.g. Branding by color.

BFS Containers provide easy, tamper evident openings.

Standard twist-off

CR-twist-off

Dual twist-off

Never opened
(Application based on permeation)

Female Luer Lock

Piercing

Male Luer Lock

Hook lock

BFS containers design features facilitate oral administration, e.g. by spoon-type applicators.




There are various options with dual chamber containers.

3 ml and 10 ml
VZ 2719a

2x 100 ml
(food application)

A comparison for glass vs. polymer ampoules.

Summary

	Glass ampoules	Polymer ampoules
Typical materials	various borosilicates	various LDPE, PP
Special materials	soda lime, (alumosilicates)	HDPE, COC, COP, multilayer
Internal surface treatment/ coatings	possible	not possible
Extractables	inorganic /1/	organic /2/
Tamper evidence	yes	yes
Transparency	high	low
Design options	limited	high
Connectivity	low	high
Needle stick prevention	low	high

