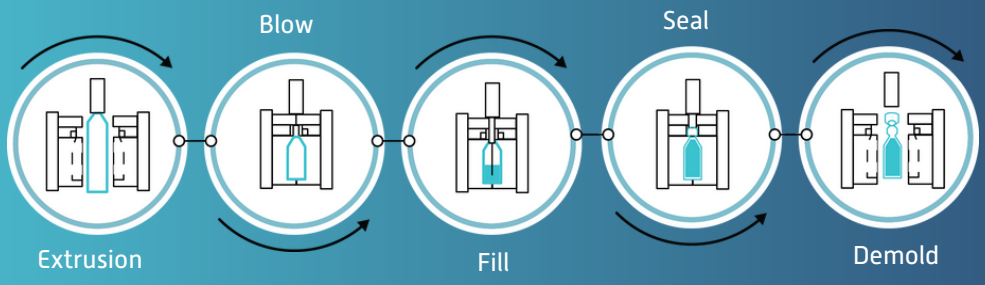
Blow-Fill-Seal technology
TEMPERATURE MANAGEMENT

Blow-Fill-Seal (BFS) is an advanced aseptic process for which temperature management is essential. It performs the primary packaging for a wide product variety: nebulized inhalation drugs, ophthalmic OTC products and injectable medecine.

THE BLOW-FILL-SEAL PROCESS



Plastic is extruded at 170 – 220°C depending on the resin being used. The cooling process starts as soon as the plastic parison leaves the extruder head.

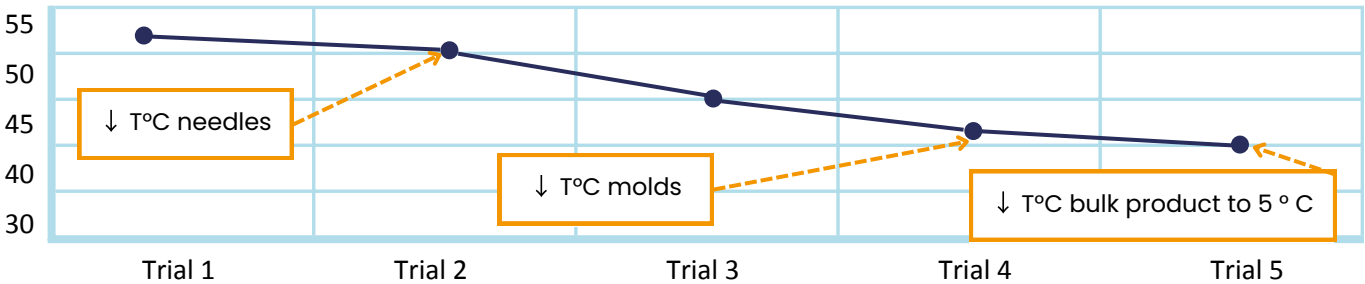
The temperature controlled metal copper alloy moulds continue the cooling process as they close and form the primary container.

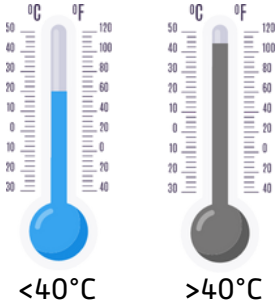
THE TEMPERATURE STABILITY: THE CHALLENGE HAS BEEN MET

Biological products (including biological substances such as vaccines or monoclonal antibodies) are to some extent sensitive to heat. Many parameters influence the temperature of the drug product during the filling BFS process. By running design of experiments (DOE) to identify these key parameters (cooling temperature, filling speed, etc.) in combination with the use of additional accessories of the filling machine (chilled tank, refrigerated needles, etc.), **we succeeded to limit the heat shock bellow 40°C along the filling process, as reported with a thermochrome indicator. The drug product is then rapidly cooled down to the storage temperature.**

We internally validated our parameter setup on a vaccine candidate for COVID-19 for which no impact was detected in quality and functionality of the RBD domain of the spike protein antigen [1].

Evolution of product temperature during trials of DoE – Filling volume at 0.5mL





Instantaneous confirmation of BFS process stability and optimized parameters with a thermochrome T°C ~ 40°C

0.5 ml

[1] Fontayne A ; Blow-Fill-Seal technology and vaccine delivery. European Biotechnology 2022 Dec. 36-37.

WHAT IS OUR SOLUTION?

Every biological product is different in composition and the formulation impacts the behaviour of the molecule along the filling BFS process, mainly by its fluidic parameters, including the viscosity. At Unither, our R&D team can operate different tests to see how your formulation reacts to the BFS process considering your needs in the type of vial, the filling volume and the storage conditions.

FIRST BLOW-FILL-SEAL WORLDWIDE LEADER

Capacity
5 villion SDU / year
Rapid scale-up capacity

Unique offer
Worldwide locations
& Dual sourcing supply

5 manufacturing sites
- Amiens (France)*
- Coutances (France)*
- Nanjing (China)
- Gannat (France)
- Rochester (USA)

* vaccine fill and finish

Authorizations
- FDA (USA),
- EMEA (Europe),
- ANVISA (Brazil),
- SKFDA (South Korea),
- and most of other authorities worldwide

BLOW-FILL-SEAL TOP ADVANTAGES

Sterile
Preservative-free

Mono-material LDPE
No risk of contamination of other components, no additives (colorants, stabilizers, plasticizers, etc.)

Safe aseptic filling process recognized by top regulators worldwide (FDA, EMA, etc.)

ISO 5 / Class A conditions International Organization for Standardization (ISO) & GMP EU cleanroom standard

ABOUT US

Unither Pharmaceuticals is a world-leading CDMO that specializes in the development and manufacturing of liquid single-dose forms (mainly eye drops, saline solutions, and asthma medications in BFS unit doses and OTC and Rx formulations in stick packs) for pharmaceutical companies and generic manufacturers. Unither Pharmaceuticals employs around 2,000 people across 8 manufacturing facilities in France, the United States, Brazil, and China.

HOW CAN WE COLLABORATE?

You have an existing product with new packaging (interactions with the plastic)
> compatibility test with single doses (specifications)
> product - polyethylene interactions
> or a product in development with BFS packaging?

CONTACT US

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Blow-Fill-Seal technology
EXTRACTABLES AND LEACHABLES

BLOW-FILL-SEAL (BFS)

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DEFINITIONS

Extractables are compounds that can be extracted from a material under stress or accelerated conditions, e.g. the use of aggressive solvent and/or high temperature.
Leachables are compounds that can migrate from the material under normal manufacturing, storage and use conditions.

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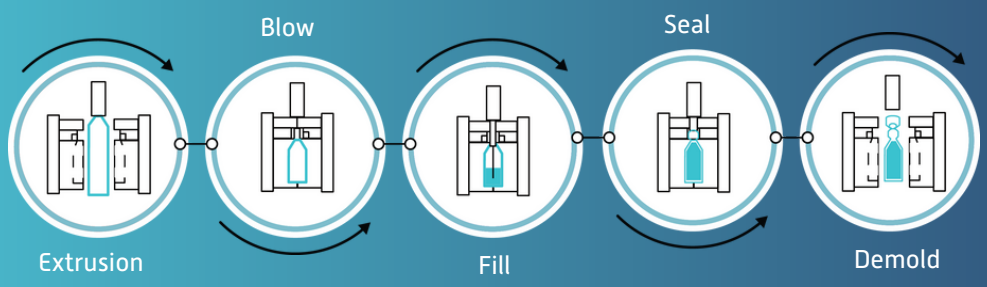

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THE IMPORTANCE OF EXTRACLABLES & LEACHABLES TESTING

Products may be administered through a variety of routes of administration and posology that may expose patients to several substances of concern. To provide patients with safety products, extractable and leachable substances need to be examined as part of the drug development process.
LDPE is compliant to Ph. Eur. 3.1.4 and is therefore manufactured without the use of metal catalysts and does not include additives such plasticizer, dye, stabilizer, preservative ….
UNITHER has already demonstrated that polyethylene-related extractables are under toxicological threshold, generic studies are available.

HOW DO WE OPERATE?

At UNITHER, our R&D team offers a package of service for your Blow-Fill-Seal products:

- Gather prior knowledge to accurately define the study strategy and parameters
- Lead the extractable studies including extraction and analytical operations, toxicological assessment
- Summarize the results and conclude on the toxicological risk
- If necessary, conduct any leachable study

UNITHER has multiple capabilities to carry out these studies:

- Climatic chambers
- Own analytical laboratory for method development
- Analytical & Toxicological partners for specific services

Throughout the whole process, you will have one main point of contact, an Analytical Development Scientist that will provide you with:

- Project management
- Meetings follow-up
- Coordination of operations and service providers
- Redaction of study protocols and reports

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