PureTain®

# PureTain® Single-Use Solutions

Assemblies, Containers, Tubing

Parker

ENGINEERING YOUR SUCCESS.

PureTain®

# Single-Use Solutions For Bio-Processing

Biopharmaceutical manufacturing, for instance of vaccines and therapeutics using viral vectors, mRNA, mAB and other recombinant proteins as well as cell and gene therapy solutions requires excellent protection of the valuable product in enclosed processes. Growing pressure to reduce development and processing times while increasing efficiency and decreasing complexity call for advanced technology solutions.


Long-standing experience in polymeric materials and clean-room production in Central Europe combined with extensive know-how of biopharma processes and validation procedures makes Parker your perfect partner to identify and maximize the potential of utilizing single-use systems (SUS) in your manufacturing operations.

**Our experts are able to specifically assist you in**

- Developing customized solutions tailored to perfectly fit your production environment
- Setting up a suitable validation procedure according to the safety level required by the specific use of the SUS (incl. leakage testing, particles, endotoxins and sterility)
- Management and coordination of your project from the initial idea through to implementation in volume production processes

As an independent open-architecture supplier, Parker offers you maximum flexibility of working with standardized components from established brands. Thanks to our in-house product design and tooling capabilities, we are able to address unique requirements and develop tailored components and solutions to meet your needs, drawing on in-depth materials engineering expertise.

Our PureTain® single-use systems are manufactured in European and North American clean room production locations under an ISO 9001 certified Quality Management System. With this global manufacturing footprint, Parker is able to support our global customer base with a local supply chain.

# Application and Product Overview

Parker's single-use solutions are able to support every stage of your biomanufacturing process. During upstream and downstream process steps of a typical biomanufacturing process, engineered single-use systems deliver superior process performance and product protection.

## Media Bottles, Caps and Tubing

Parker offers PureTain® PETG media bottles from 60ml to 1000ml, non-sterile or gamma-irradiated. The validation guide includes E&L data and is available upon request. Bottles are leakage-tested and can be integrated into customer-specific bottle assemblies.

For glass bottles, Parker's PureTain® portfolio includes flexible cap solutions featuring cap, venting, filling, and draining tailored to specific process needs.

**Discover our PureTain® Products**

- → PETG Media Bottles
- → Thermoplastic Tubing (TPE)
- → Platinum-Cured Silicone Tubing
- → Tubing Manifolds
- → Bottle Caps

## Cell Culturing Solutions

Single-use Erlenmeyer flasks play a key role in achieving consistent cell density and cell growth rate. Parker provides ready-to-use sterile Erlenmeyer flasks with or without vented caps and fully integrated filling and draining options, enabling closed system configurations which eliminate contamination risks.

**Discover our PureTain® Products**

- → Erlenmeyer Flasks
- → Erlenmeyer Flask Assemblies

## Freezing Containers

Parker´s patented container sealing system guarantees maximum protection of valuable products during low-temperature storage and transportation, validated at -85 °C for single-use bottles.

Parker also offers accessories such as protection caps and integrity seals around the container cap.

In addition to the single-use bottle solutions, Parker offers freezing bags featuring a single-layer EVA film.

**Discover our PureTain® Products**

→ Freezing Bottles

→ Freezing Bags

## Sampling Solutions

From small-volume 2-ml sampling to larger-volume 1000-ml sampling, Parker offers highly flexible product configurations from bags to rigid containers. From single-container to multi-container solutions or combinations of all options.

**Discover our PureTain® Products**

→ Sampling systems

→ Sampling Bottles

→ Sampling Bags

# Application and Product Overview

Parker's single-use solutions are able to support every stage of your biomanufacturing process. During upstream and downstream process steps of a typical biomanufacturing process engineered single-use systems deliver superior process performance and product protection.

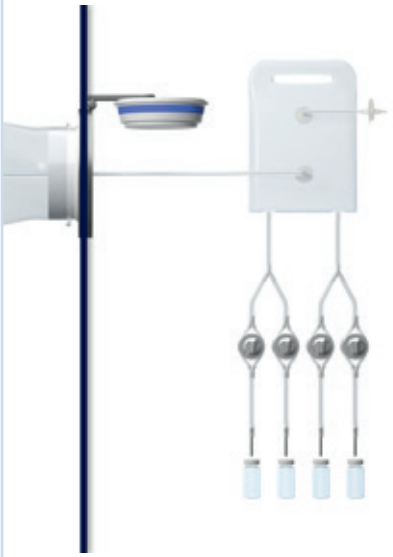
## Bulk Filling and Transportation Solutions

An efficient and safe filling process requires a single-use system that perfectly fits the process, avoiding leakage as well as potential handling mistakes. Parker's unique product design capabilities help process engineers address and mitigate potential risks, from filling to draining of bulk substance.

**Discover our PureTain® Products**

→ Bottle Assemblies

→ Bag Assemblies



## Final Filling Solutions

From the product vessel to the needle – Parker's single-use solutions ensure an aseptic product transfer and filling process. Our overmolding technology enables seamless fluid transfer including molded ports and pump-head manifolds with highest dose control and integrity.

**Discover our PureTain® Products**

→ Final Fill Manifolds

→ Isolator Transfer Sets

→ PUPSIT Assemblies

## Solutions for mRNA Processes

mRNA manufacturing processes require flexible manifolds designed for small batch sizes featuring small diameter tubing, dispensing, filtration, product storage, and sampling. In addition, we assist our customers with tailored carboys for UF/DF applications etc.

**Discover our PureTain® Products**

→ Tubing Manifolds mRNA

→ Carboy Assemblies

## Solutions for CGT

Parker offers flexible tubing and bag manifolds e.g., for cell storage/ freezing, cell expansion, cell modification, and sampling. Bags are available with different film layers and volumes in sizes of 2 ml and larger.

**Discover our PureTain® Products**

→ Erlenmeyer Flasks

→ Erlenmeyer Flask Assemblies

→ Sampling Bags

→ Freezing Bags

→ Tubing Manifolds CGT

→ Bag Assemblies

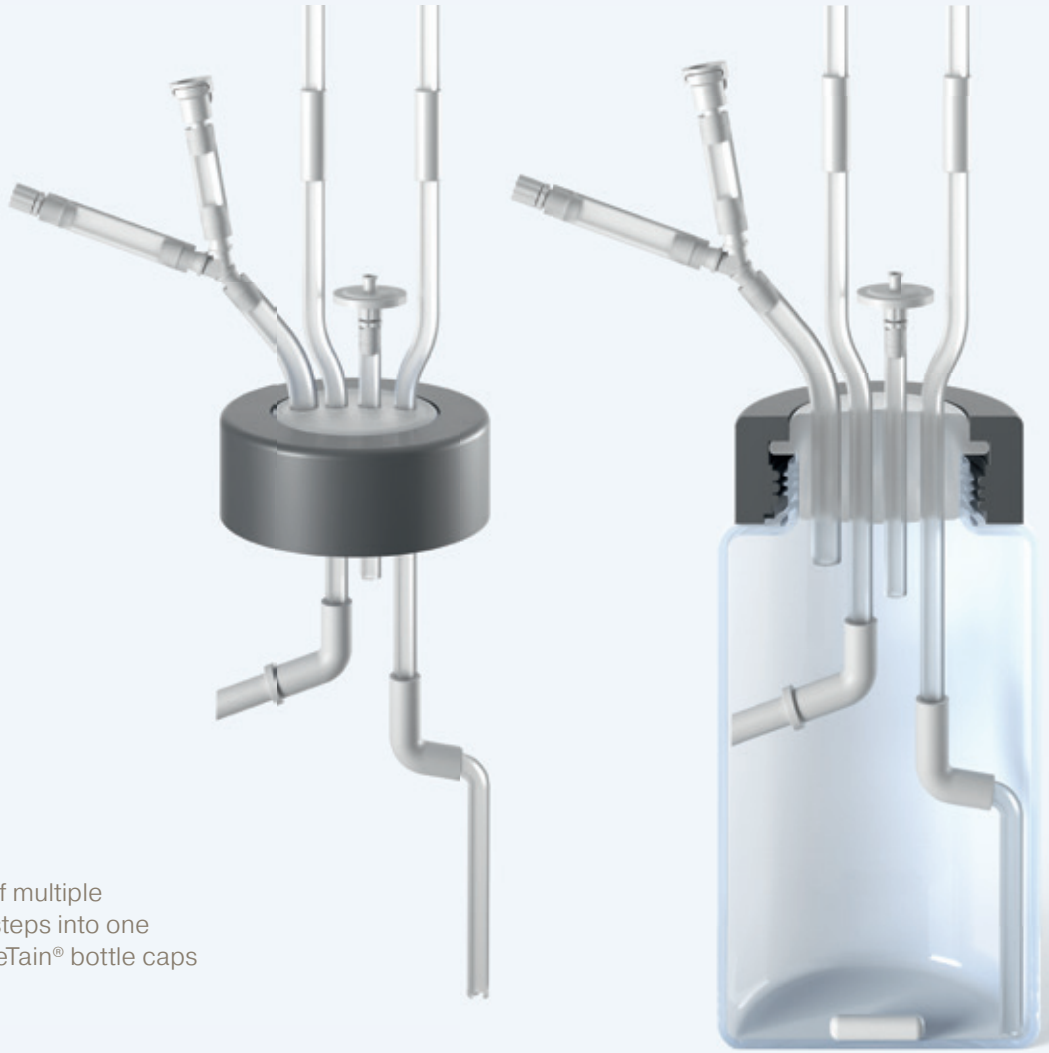
# Application and Product Overview
# Upstream

## Product Development

Parker provides the tools that are needed to achieve a perfect end-to-end process starting as early as in a laboratory environment. The opportunity to integrate multiple processing steps in a lab-scale bioreactor significantly facilitates the simulation of subsequent production complexity. Excellent process control is achieved by means of smart in-container product management features such as an overmolded tube guide ensuring a continuous, unimpeded mixing process, for instance while adding an adjuvant to the fluid mix.

Even on a laboratory scale, maximum mitigation of the contamination risk is achieved by seamless integration of tubing through the tube-to-container interface.

Parker's PureTain® bottle caps that are used for this purpose feature an open architecture enabling easy integration of previously validated components resulting in significant time and cost savings. Scalable from 125 milliliters to 20 liters, they perfectly fit all types of glass bottles or containers that are used as early as in the initial development stages.



Integration of multiple processing steps into one unit with PureTain® bottle caps

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## Media Preparation and Buffering

Our open architecture allows us to provide single-use container solutions that benefit with maximum flexibility, efficiency and compatibility. When combining custom manifolds with Parker's custom container solutions, our overmolding technology is utilized for secure tube-to-tube connections and includes the secure connection between the container and tube as well.

As a result, the product can be transferred into the container through the tubing system in a laminar flow process without mechanical stress.

Multiple containers connected to a central feeding line featuring fully overmolded interfaces

Due to Parker's patented integrity seal technology, customers are able to work with containers instead of the commonly used bags, which ensures tamper-proof storage and transportation. In addition, the utilization of containers improves handling processes combined with clear and reliable monitoring and evaluation of fill levels.

## Fermentation & Sampling

During upstream processes samples have to be taken for the purpose of verifying the initial properties of the targeted product.

Integrated sampling lines can consist of a sampling manifold, valves or tailored sampling systems. They typically consist of sampling containers or bags, centrifugation tubes or syringes and a connecting manifold.

Sampling system with an overmolded tube-to-container interface utilizing containers of various size factors

# Application and Product Overview
# Downstream

## Cell Harvest and Collection

For harvesting and collection operations involving centrifugal applications, Parker offers overmolded star manifold configurations that securely connect containers to a central feeding/draining line.

The tubing into the containers is seamlessly integrated in the manifold via an overmolded stopper, which provides excellent protection against leakage and contamination.

Overmolded star-manifolds deliver excellent sealing performance during challenging centrifugation applications

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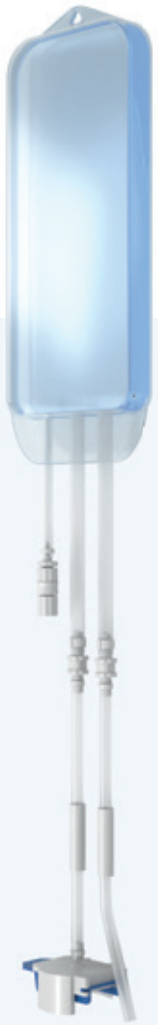
## Sampling

Most single-use systems have one or more integrated sampling lines. They can be equipped with valves, sampling manifolds or special sampling systems. Sampling manifolds consist of sampling bags, sampling flasks, centrifugation tubes or syringes. An aseptic luer sampling port can be provided to remove test material using needle-free luer-lock syringes. This facilitates taking of multiple samples and significantly reduces the number of manipulations required in a process.

The manifolds are delivered in preassembled sterile condition ready for use. Only one connection has to be made, thus limiting the risk of contamination associated with multiple connections.



Sampling bag system with customized filling and draining features

Sampling system with centrifugation tubes

Closed sampling container with overmolded stopper and Parker´s patented integrity seal

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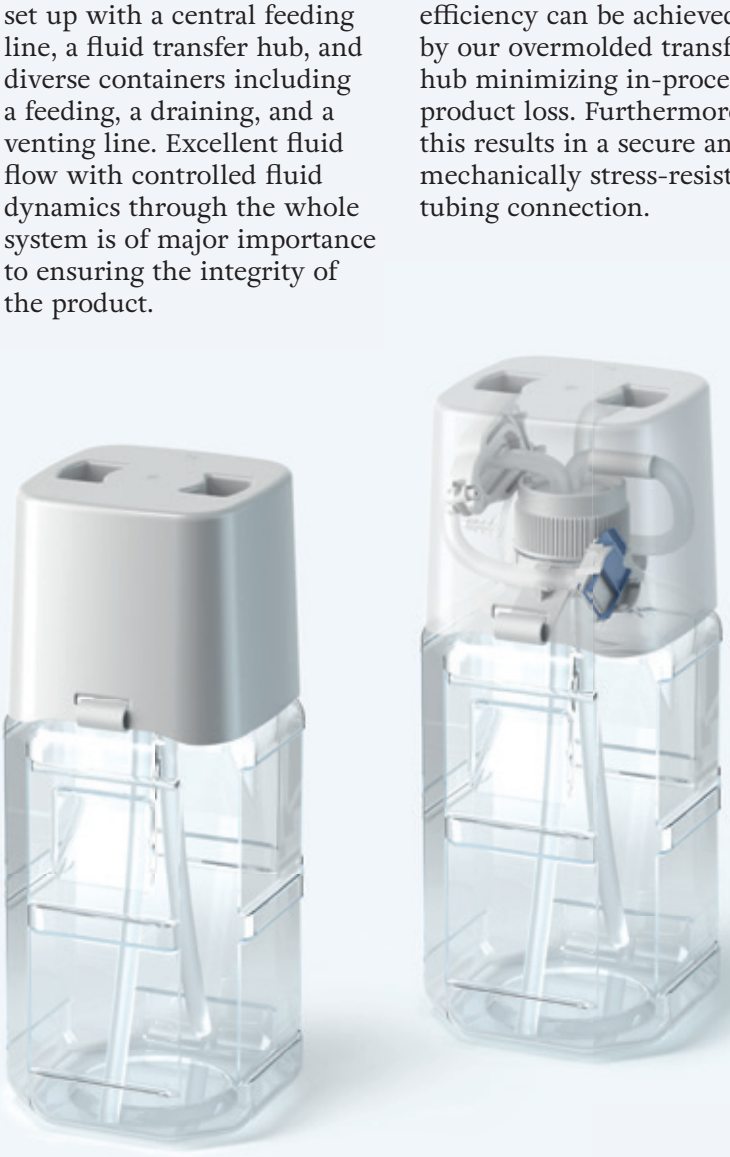
## Bulk Filling and Transportation

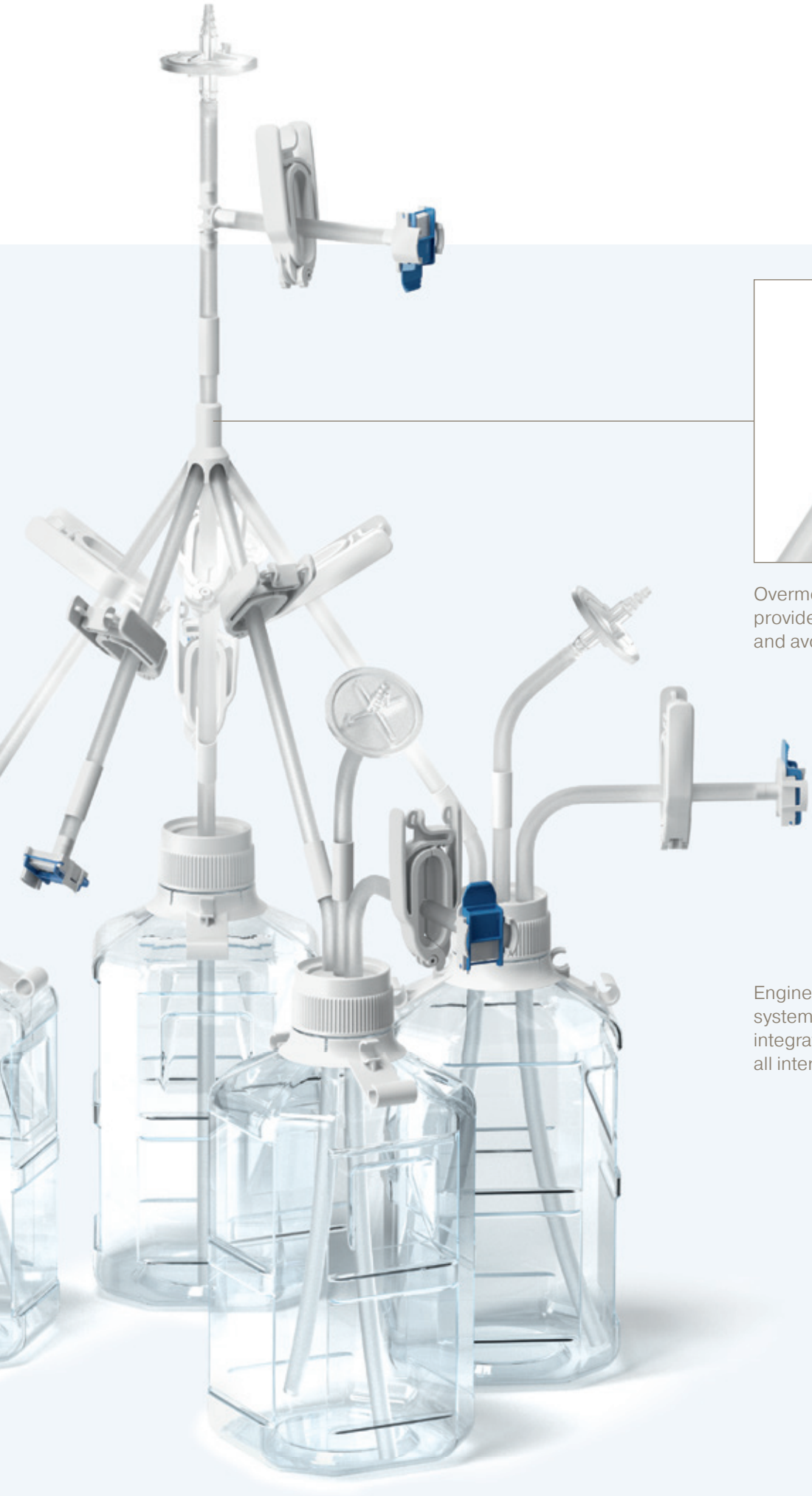
Engineered fluid management systems for bulk drug substance management can provide the highest level of protection for high-value products. Such systems are set up with a central feeding line, a fluid transfer hub, and diverse containers including a feeding, a draining, and a venting line. Excellent fluid flow with controlled fluid dynamics through the whole system is of major importance to ensuring the integrity of the product.

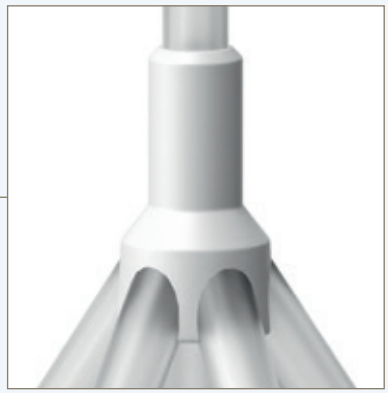
The high-value product is protected against contamination by means of overmolded interfaces enabling a closed system approach. Maximum draining efficiency can be achieved by our overmolded transfer hub minimizing in-process product loss. Furthermore, this results in a secure and mechanically stress-resistant tubing connection.

For the protection of components during transfer and storage operations, dedicated, customized solutions are available.



Customized protection caps ensure secure handling of components during transportation and storage operations





Overmolded fluid transfer hub provides laminar product flow and avoids dead zones

Engineered bulk filling system featuring seamless integration of tubing across all interfaces

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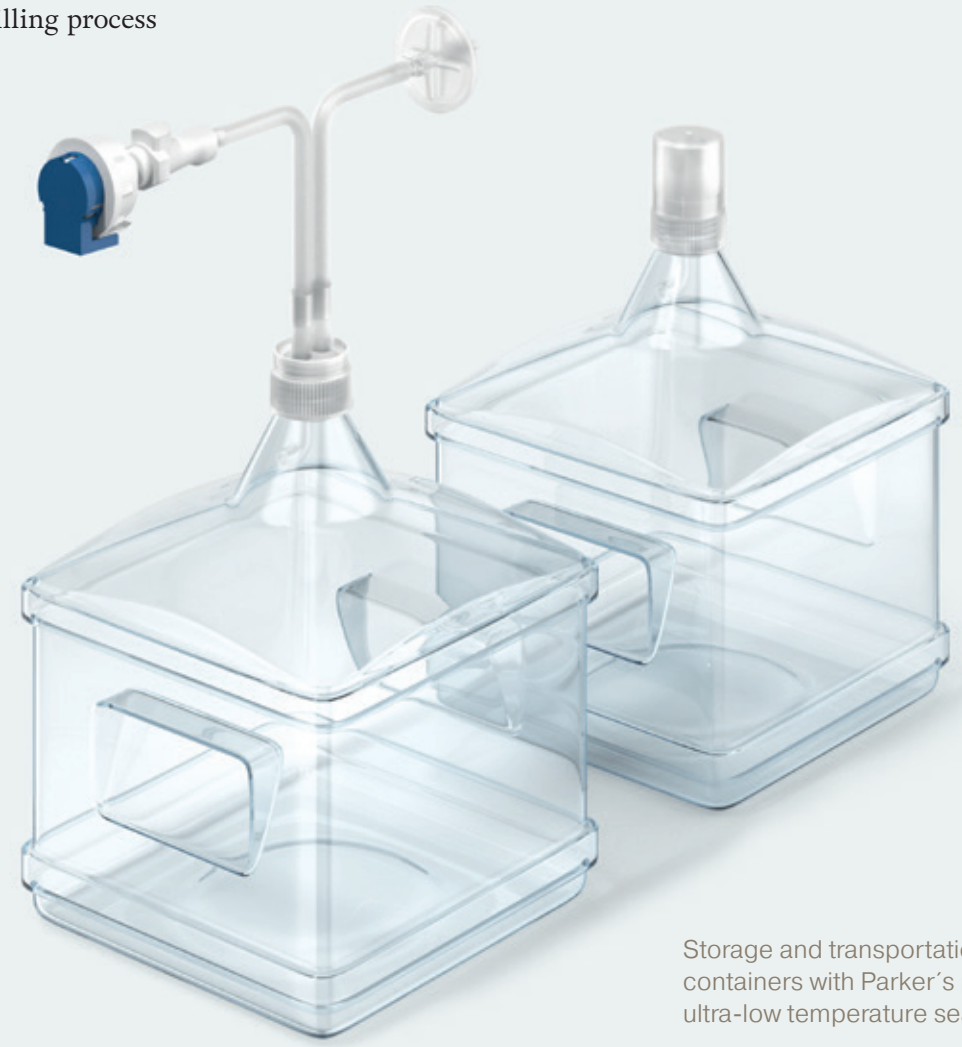
## Freezing Containers

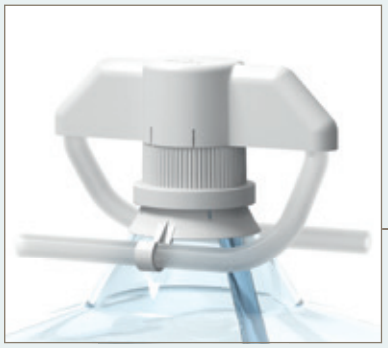
Parker's innovative container sealing concepts for cold-chain transportation have been validated at -85 °C and successfully tested at -120 °C.

A protective cap prevents tube damage during low-temperature transportation. Various container sizes and tubing configurations are available. Integrated anti-foam tube configurations ensure maximum filling process control.

Excellent, reliable sealing performance at ultra-low temperature mitigates the risk of contamination. A patented energizer element equalizes differences in the thermal behavior of components and delivers perfect sealing performance at ultra-low temperatures.



Storage and transportation containers with Parker´s patented ultra-low temperature sealing



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## Final Fill

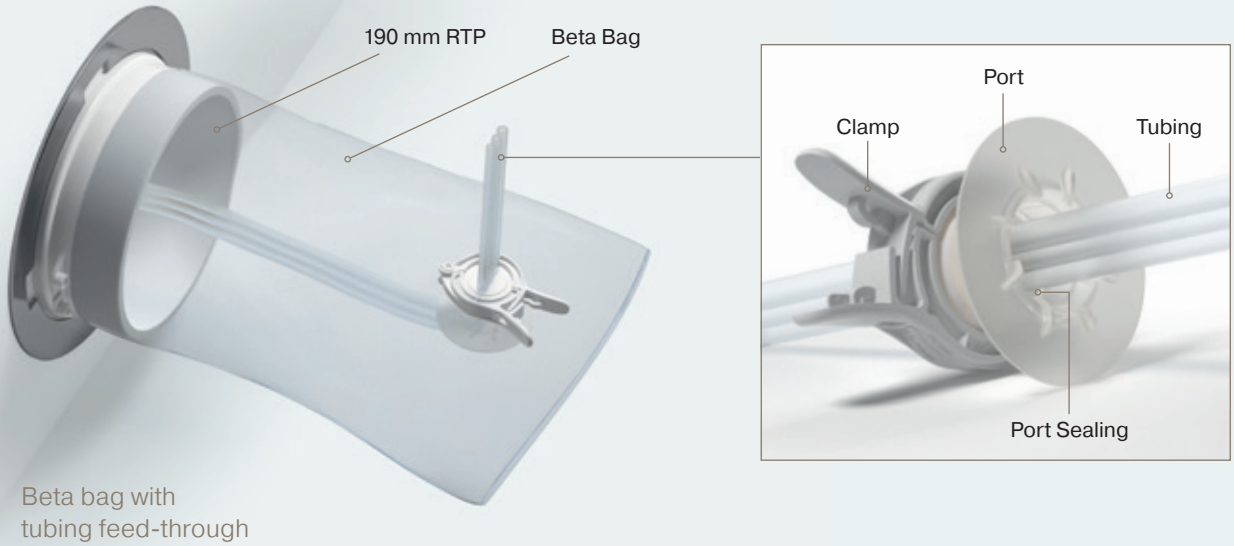
The utilization of single-use systems in the final fill process is steadily increasing. Parker's final fill solutions effectively meet the stringent requirements for this final process step. Molded connections on all critical joints ensure high product yields, maximum safety, and accuracy for final filling processes. Various types of tubing, aseptic connectors, bags, and needle configurations are available and allow for the configuration of systems as needed. Molded stopper solutions are used in transfer applications with beta bags, eliminating leak points and dead zones.

Parker's single-use systems for the final fill process enable customers to flexibly and reliably respond to the demands of manufacturing a variety of drug products and fill volumes.

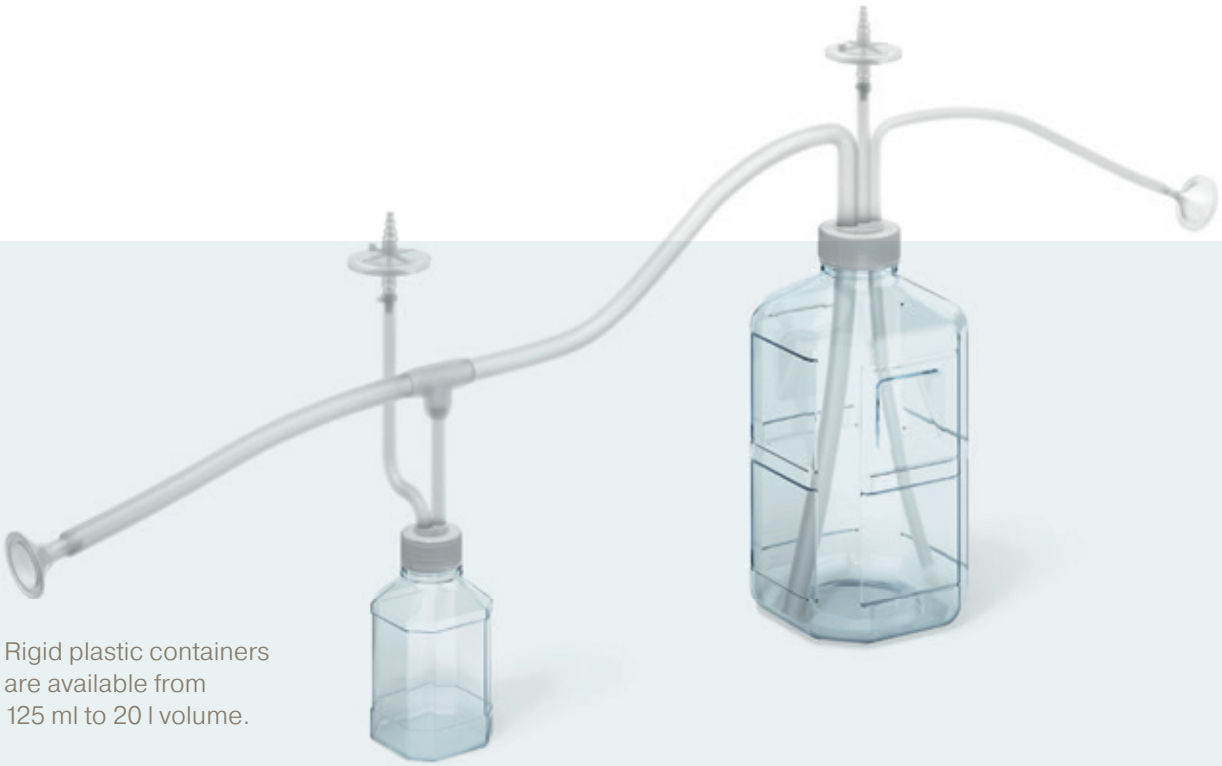
Molded connections on all critical joints achieve maximum safety and accuracy for final fill processes and are 100% leakage-tested.

Molded Y-connections can combine different tubing sizes in one joint. Parker´s proprietary micro-overmolding technology allows for combining tubing diameters by overmolding down to an inner diameter of 0.8 mm. This offers significant advantages in reliable fluid flow management for final fill applications using peristaltic pumps.

Final fill set with vented 5-liter bag and micro-overmolded Y-connections for reliable and smooth media flow using peristaltic pumps

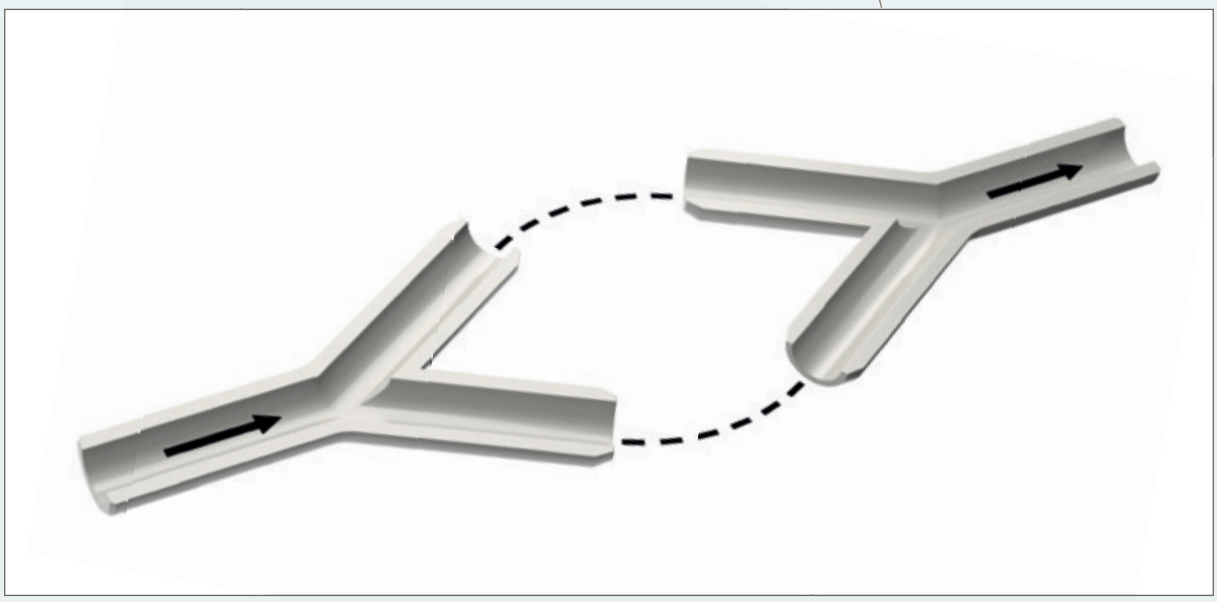



Beta bag with tubing feed-through



Rigid plastic containers
are available from
125 ml to 20 l volume.

Micro-overmolded
Y-connections mitigate
the risk of leakage
during final fill operations



Molded Y-Connections combining different tubing diameters

# Overmolding Technology

## The Right Choice for Critical Processes

Our overmolding solutions ensure both maximum safety to prevent contamination due to validated and completely closed systems and fully controlled fluid path dynamics as a result of smooth transitions between the tubing and connector. Depending on specific customer requirements, Parker is able to offer its entire overmolding portfolio in pharma-grade silicone or TPE materials.

**Our overmolding technology is suitable for the following solutions:**

- Tube-to-tube connections
- Overmolded labels
- Tube-to-container connections (molded stoppers)
- Tube-to-hose barb connections (e.g. vent filters and connectors)
- Container integrity seals

Molded Stopper

Overmolded Label

Integrity Seal and Tamper Evidence Seal

**These technology pillars enable the creation of product systems with numerous advantages:**

- Mitigation of the contamination risk due to seamless tubing integration and a closed system approach
- Excellent process control due to in-container product management features
- Simulation of operational complexity due to functional integration of multiple processing steps in one unit
- Open architecture enabling integration of pre-validated components for maximum reduction of development time and costs
- Scalability of lab scale form factor from 125 milliliters up to 20 liters including compatibility with any type of bottle/container

PureTain®



Molded Tri-Clamp and Vent Filter



Molded X-/T-/Y-Connections



Molded Bag Port Connection

# Validation Guidelines And Procedures

The provision of customized single-use consumables entails project-specific validation in practically every customer project as the configuration of any system is unique to some extent.

Achieving the right balance between product safety, regulatory requirements and commercial aspects for customized single-use consumables requires in-depth knowledge of all applicable regulations and standards as well as of the technical aspects and risks associated with any product, from the raw materials through to the production technology used.

**The scope of our validation capabilities encompasses:**

- Particle testing
- Bioburden
- Endotoxins
- Leakage (pressure decay testing)
- Sterility
- Shelf-life
- Packaging
- Transportation / shipping

## Sterility ISO 11137

If requested, our single-use consumables are sterilized to achieve a sterility assurance level (SAL) of 10-6, which corresponds to the probability of one in a million items being nonsterile. Validation is performed according to the ISO 11137-2 VDmax 25 method. Based on the annual production volume of every item, the sterilization dose is audited quarterly during routine production runs.

## Leakage Testing

Parker performs leakage testing using pressure decay (destructive and non-destructive). Pressure decay testing is done with a dedicated device inside a clean room class 7. The device has a sensitivity of 1 Pa monitoring air loss inside single-use assemblies after they have been pressurized and the pressure has been stabilized. The acceptance limits for the pressure decay test are product-specific and heavily depend on the component materials and size as various tubing materials for instance behave differently during a pressure decay test. The test result requires in-depth understanding of material performance characteristics. The submergence air bubble test is performed to verify if the acceptance limits used for every product during pressure decay testing are suitable. Parker pressure decay test results can be used to establish a correlation to integrity testing done after manipulation at the customer's site.

## Shelf Life

All sterile products require shelf life testing of the product's packaging as well as its functionality in order to verify the impact of aging on the materials. In order to avoid delays entailed by real-time aging studies of the product(s), accelerated aging tests according to ASTM F 1980:2007 are performed. In accelerated aging tests, it is important not to select excessively high temperature settings even though this reduces testing time and cost. Plastic components in particular may change in terms of mechanical properties and surface characteristics if temperatures for accelerated aging are set too high. Typical shelf life is 24 months but may be extended based on the customer's project-specific requirements.

## Applicable Regulations and Standards

- ISO 14644: Clean-Room Environmental Controls
- ISO 11137: Sterilization of Medical Devices
- ISO 11737-1: Bioburden
- ISO 11737-2: Sterility Test
- E.P. 2.6.14 and USP<85>: Bacterial Endotoxins Test
- E.P. 2.9.19 and USP<788>: Particulate
- ASTM F 1980:2007: Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices

- Materials of Construction free of animal-derived ingredients or meeting EMEA410.01 rev.03)
- USP <661> Extractables / BPOQ Protocol
- ISO 10993 Biocompatibility
- USP class VI
- Transportation Validation (ISTA-2A or ASTM D7386-12)
- ISO 9001: Quality Management
- ADI-free certification (Animal Derived Ingredients)

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