

Single-use hose systems

Using single use hose systems in pharmaceutical and biotechnology applications

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1. Definition of single-use systems

The term 'single-use systems', or 'disposal systems' (systems that can be thrown away), describes systems that are only intended to be used one time and then replaced.

In contrast to this, components made of stainless steel or glass can be reused after they have been properly cleaned.

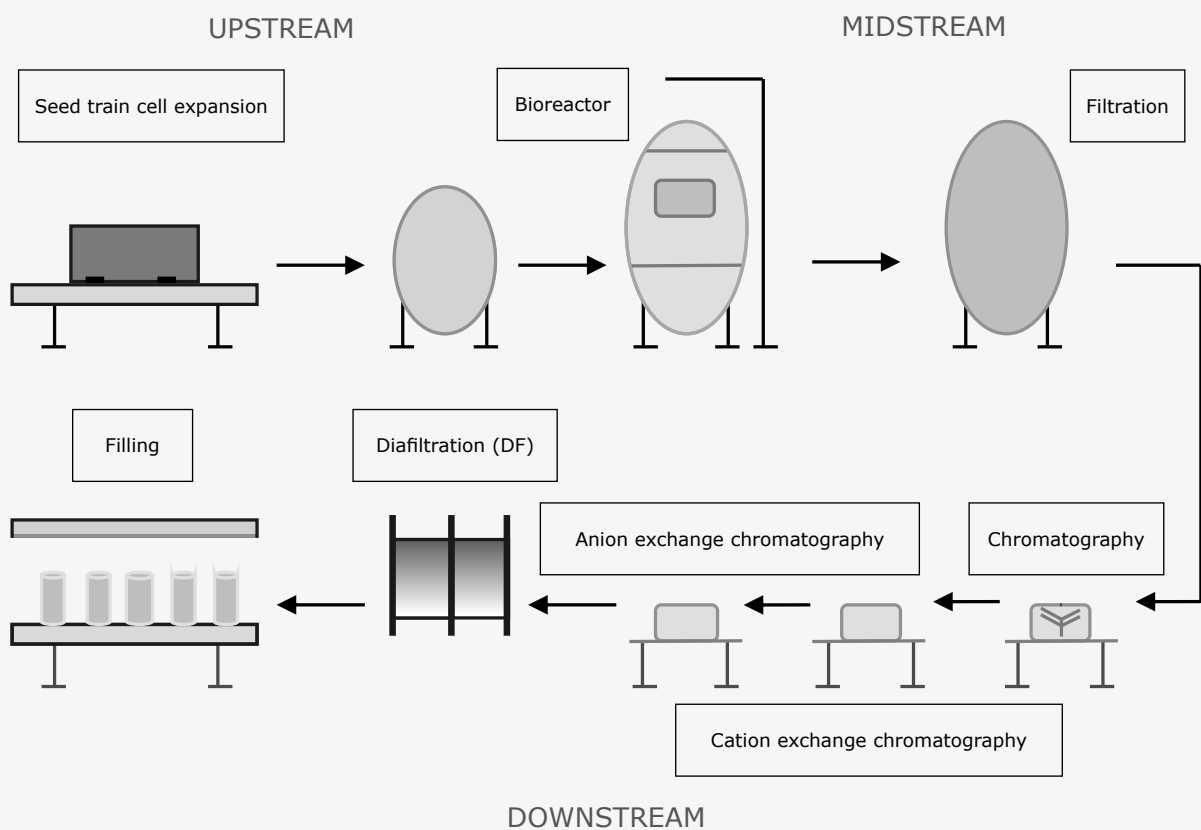
Single-use systems have the advantage over these reusable systems that the initial investment is lower and also energy costs for cleaning processes (CIP, SIP) can be eliminated.

The parts that come in contact with the product consist of materials approved by the Food and Drug Administration (FDA), such as silicone, polyethylene or polycarbonate. Single-use systems are generally manufactured in class 7 cleanrooms and may also be beta or gamma sterilised, which means that they can be used immediately (ready-to-use systems).



2. Application and processes

Single-use systems are today used in the majority of biopharmaceutical processes (or 'bioprocesses') with animal cell cultures. These processes are divided into upstream and downstream processes.



The **upstream** process (USP) includes the initial phase in which the microbes/cells, e.g. bacteria or mammalian cell lines, are bred in bioreactors.

This includes all steps associated with inoculum development: media preparation, cell culture and cell separation, as well as harvest. In biotechnology, 'inoculum' is the term for the quantity of reproductive cells with which a fermenter is inoculated. When the cells have reached the desired density, they will be harvested and sent into the bioprocess downstream.

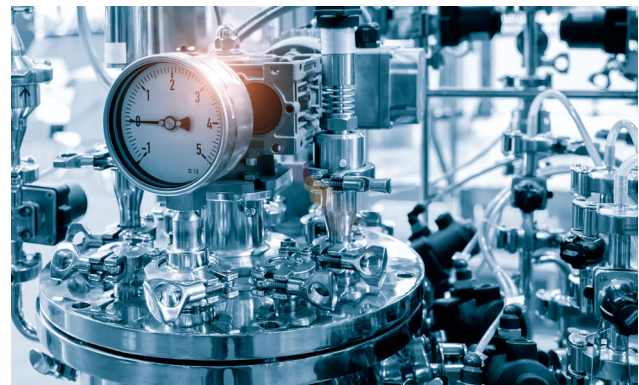
Single-use systems have been used widely in the upstream process for many years (e.g. single-use filters, mixers and bioreactors or single-use plastic bags for storage purposes).

The **downstream** process (DSP) covers the part of a bioprocess in which the cell mass from the upstream is processed in order to meet requirements for purity and quality.

The objective of the downstream process is to isolate and purify a biotechnological product in order to create a form suitable for the intended purpose. The end product in this process is typically recovered from an aqueous solution. End products may include, for example, whole cells, organic acids, amino acids, solvents, antibiotics, industrial enzymes, therapeutic proteins or vaccines.

Due to the variety in size and quality of the products, different classification principles are used in recovery and purification. While single-use systems already see widespread use in the upstream process, they have only recently been increasingly used in the downstream process (e.g. single-use bioreactors for microorganisms).

The final step of the downstream process is formulation (the optimal combination of an active ingredient with certain auxiliary ingredients) and filling. Here, single-use systems are used for mixers, transfer systems, dosing systems and filling needles, among other things.



3. Pros and cons of single-use systems

Single-use systems have the following advantages over reusable equipment made of glass or steel:

- shorter production times (no need for sterilisation and purification procedures)
- higher flexibility (product changes can be performed more quickly)
- higher production security (minimised risk of product cross-contamination)
- lower initial investment in a production plant

Some studies also show that the energy costs for purification (CIP, SIP) of permanent systems are currently higher than those of single-use systems. Thus single-use systems have a better carbon footprint.

On the other hand, they have the following disadvantages:

- Single-use systems (especially in the downstream process) frequently form bottlenecks with higher volumes
- the running costs for consumables are much higher
- potential supply chain issues
- large quantities of waste



4. Leachables and extractables

Leachables and extractables (L&E) refer to chemical substances that in the worst-case scenario, migrate out of plastic under process conditions and damage the product. In the extractables study (extraction study), the quantity of organic and inorganic substances that can be extracted from the analysed material by adding extraction solvents is recorded. The objective of the extractable study is to simulate a “worst-case scenario” and use the data obtained to support process developers and toxicologists in validation studies.

The leachables study (leachables = leachable components), records those substances that migrate from the analysed material to the sample under real-life conditions. It may also include the assessment of possible secondary reaction products in a drug. Currently the lack of regulations for standardised tests to prove L&E or corresponding analysis protocols is the biggest weak spot.

Markert had extractable studies performed for the products SIL300PTFE, SIL200 and SIL300.



5. Other approvals (BSE, TSE, GMO, ADI)

The pharmaceutical industry may require manufacturers to confirm that their products are free of BSE/TSE/GMO, or animal components and materials originating from animals or cell cultures:

- **BSE** (Bovine Spongiform Encephalopathy): the spongiform change that occurs in the brain matter of cattle
- **TSE** (Transmissible Spongiform Encephalopathy): spongiform brain damage that can be transmitted
- **GMO** (Genetically Modified Organism): genetically modified organisms

The “**ADI-free**” certificate verifies that the raw materials used in the production of elastomer do not contain any animal-derived ingredients (ADI).

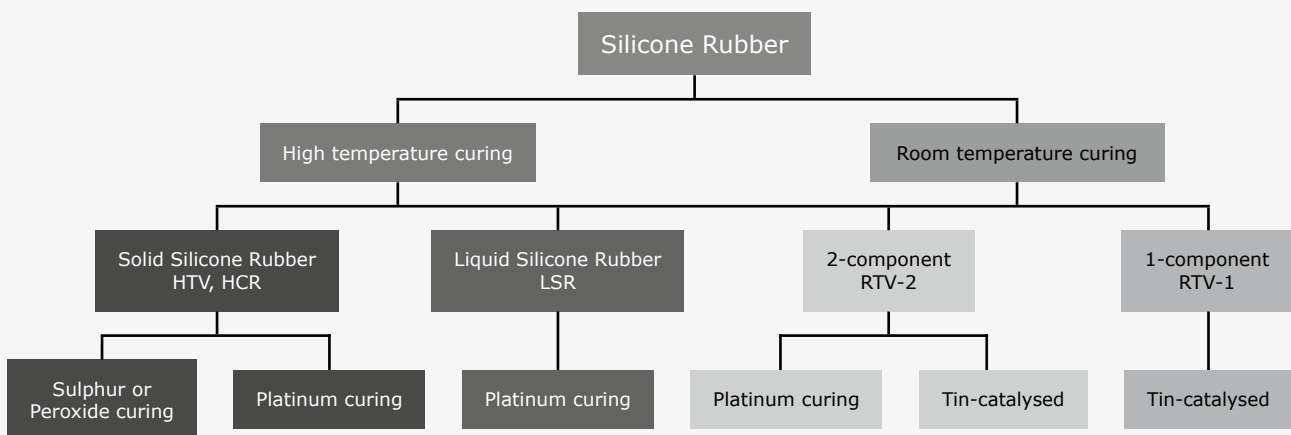


6. Silicone hoses in single-use systems

Its exceptionally good properties make silicone the material of choice in pharmaceutical applications. The material is relatively soft and can withstand a wide range of temperatures.

Numerous types of silicone are safe to use, meaning they are biocompatible.

Silicones available on the market today differ in both the pharmaceutical approvals and especially the cross-linking process on which their processing is based.



A distinction is made between platinum-cross-linked and **peroxide-cross-linked** silicones. Materials that use peroxide to cross-link are exposed to a radical reaction. In doing so, the peroxide group and thus the cross-linking of the silicone is activated. The waste products that form in this process do not dissolve, however, but remain in the end product.

This results in the distinct smell typical of silicone and the ability to leach by-products out of the material.

This is the major risk in using peroxide silicone in pharmaceutical applications.

Platinum-cross-linked silicones have been established very successfully for several years:

In these silicones, platinum is used as the catalyst in an addition reaction with silanes. The silane is fully integrated into the silicone and there are no by-products or break-down products that form.

This means that platinum-cross-linked silicone hoses are completely safe for pharmaceutical applications. It does not take on the unpleasant odour or contain substances that can be leached out in application. The material properties of platinum-cross-linked silicone are comparable to those of materials cross-linked using peroxide.

Silicone hoses used in the pharmaceutical industry are frequently exposed to intense radiation when they are sterilised (gamma radiation or E-Beam). Some studies have shown that gamma or E-Beam radiation has a considerable deteriorating effect on the mechanical properties of peroxide-cross-linked silicone such as hardness, elasticity or ultimate elongation. This deterioration in mechanical properties is not pronounced in platinum-cross-linked silicone.

However, cross-linking notwithstanding, not all silicones are the same. The raw material HCR (abbreviation for High Consistency Rubber, Heat Cured Rubber or HTV, High Temperature Vulcanising) or LSR (Liquid Silicone Rubber) is typically used to manufacture silicone hoses or silicone preforms. HCR is largely cross-linked using peroxide, while LSR is cross-linked with platinum, and has a much lower viscosity. Due to the advantages of platinum-cross-linked silicone described above, LSR is predominantly used as the base material for silicone products in pharmaceutical applications. This is cross-linked through extrusion and made into the desired shape.

LSR (liquid silicone) is offered by various manufacturers and in different qualities. Known and established manufacturers include:

- Wacker
- DuPont
- Dow Momentive Inc
- Shin-Etsu Chemical Co. Ltd. Tokyo
- Elkem in Oslo, Norway

7. Packaging, batch tracking and dimensions

Single-use hoses are typically (depending on the area of application) packaged in cleanrooms in accordance with ISO 14644-1, class 7. The entire process must be set up to allow for the tracking of batches. The systems or components are packed once, but usually twice in PE bags (suitable for gamma sterilisation).

Single-use hoses are available in a wide variety of dimensions. Custom dimensions are generally needed depending on the production process, so there is no uniform standard. The most common dimensions are listed below.

Dimension in mm / inner diameter x wall thickness				
1.6 x 1.6	3.0 x 1.0	3.0 x 1.5	3.0 x 4.0	3.2 x 1.6
3.2 x 2.4	4.0 x 2.0	4.0 x 2.4	4.0 x 3.0	4.8 x 1.6
4.8 x 2.0	4.8 x 2.4	5.0 x 1.5	5.0 x 2.5	5.0 x 3.0
6.0 x 2.0	6.0 x 3.0	6.4 x 1.6	6.4 x 2.4	6.4 x 3.2
7.9 x 2.4	7.9 x 3.2	8.0 x 1.6	8.0 x 2.0	8.0 x 3.0
8.0 x 4.0	8.5 x 3.25	9.5 x 2.4	9.5 x 3.2	9.6 x 3.2
10.0 x 2.5	10.0 x 3.0	10.0 x 4.0	12.0 x 3.2	12.7 x 3.2
15.9 x 3.2	16.0 x 5.0	19.0 x 3.2	20.0 x 5.0	25.4 x 4.8

Dimensional tolerances are defined in ISO 3302-1. Three tolerance classes, E1 through E3, are defined here, with E1 representing the lowest tolerances (E1: fine degree of accuracy, E2: moderate degree of accuracy, E3: rough degree of accuracy). Accuracy class E2 generally applies to standardised single-use hoses. Unique products may be manufactured with much lower tolerances (up to a factor of 10).

8. Why Markert Marsoflex

The Markert Group endeavours to be the number one in filter and hose technology, with leadership in quality and innovation. These two pillars of our company vision make us who we are.

For us, innovation means offering the broadest range of approved products on the market and extensive product features for hose assemblies.

Quality is reflected in the materials we use for hoses, their design, their connections and our comprehensive testing of the final product.

Markert Marsoflex in this context stands for:

Expertise

Experienced specialists with comprehensive product and applications knowledge ensure technically outstanding products. In the jungle of extractables studies and standards such as EN1761/EN12115, EN10204 3.1, DNV, TRbF-131/2, USP XXXVI class VI, FDA 21 CFR 177 and 3a Sanitary Standard and platinum cross-linked silicone, we provide clarity. And we draw up the best solution for you.

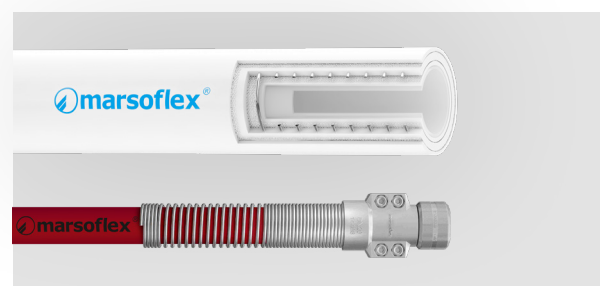
Your advantage: all the answers on industrial hose lines from a single source



Flexibility

From dry coupling and special materials to custom hose assemblies, we offer a comprehensive product range, engineered for your application by competent specialists.

Your advantage: flexible and fast product solutions



Stock availability

With several million euros worth of product in stock, multiple decentral PTFE lining warehouses close to customers and automated forming facilities, we combine our high quality with short delivery times.

Your advantage: rapid availability

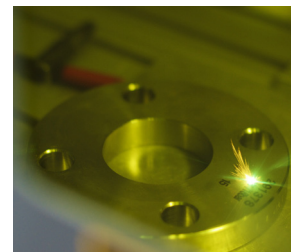


Quality

The hazard potential of hose assemblies is frequently underestimated. To ensure our hoses meet all relevant requirements such as the PED Pressure Equipment Directive, leave our plant with all technical properties inspected, and provide reliable service in their intended applications, we provide:

- Our own pressing, tightness and laser technology
- 100% pressure and seal testing
- 100% material traceability

Your advantage: quality you can rely on



Customer proximity

Whether for examining your system, working out technical solutions or the regular inspection of your installed hose assemblies:

We are close by, either through our regional sales and applications specialists or with our own service team.

Your advantage: specialists in your area



9. Contacts

Do you have questions about any of the matters discussed, or are you looking for specialist consulting on hoses and fittings? Contact our field representatives at any time.

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