SEALING SOLUTIONS FOR APPLICATIONS IN THE PHARMACEUTICAL INDUSTRY

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CHALLENGES FOR SEALS IN THE PHARMACEUTICAL INDUSTRY

The purity requirements for the product and the process are particularly high in the pharmaceutical industry because the synthesis of pharmaceuticals must prevent germs from entering the product and unwanted by-products from being produced. Resistance to cleaning agents, solvents, steam and the product media themselves also play an important role in the synthesis process. Pharmaceutical-specific applications therefore require sealing solutions that reliably prevent contamination and can come into contact with the product without hesitation. Given the large number and special features of plants and processes in the pharmaceutical industry, there are many challenges for a sealing system that plant engineers must overcome. The following diagram provides an overview of these challenges.

CHALLENGES FOR SEALS IN THE PHARMACEUTICAL INDUSTRY

TEMPERATURES AND PRESSURES
The organic synthesis process generates high temperatures and pressures. For instance, very low temperatures can occur in the production of vaccines or proteins, as well as in the separation of blood. That require seals that remain very flexible under cold conditions.

CIP/SIP RESISTANCE
The sealing materials must withstand aggressive media such as CIP/SIP cleaning agents.

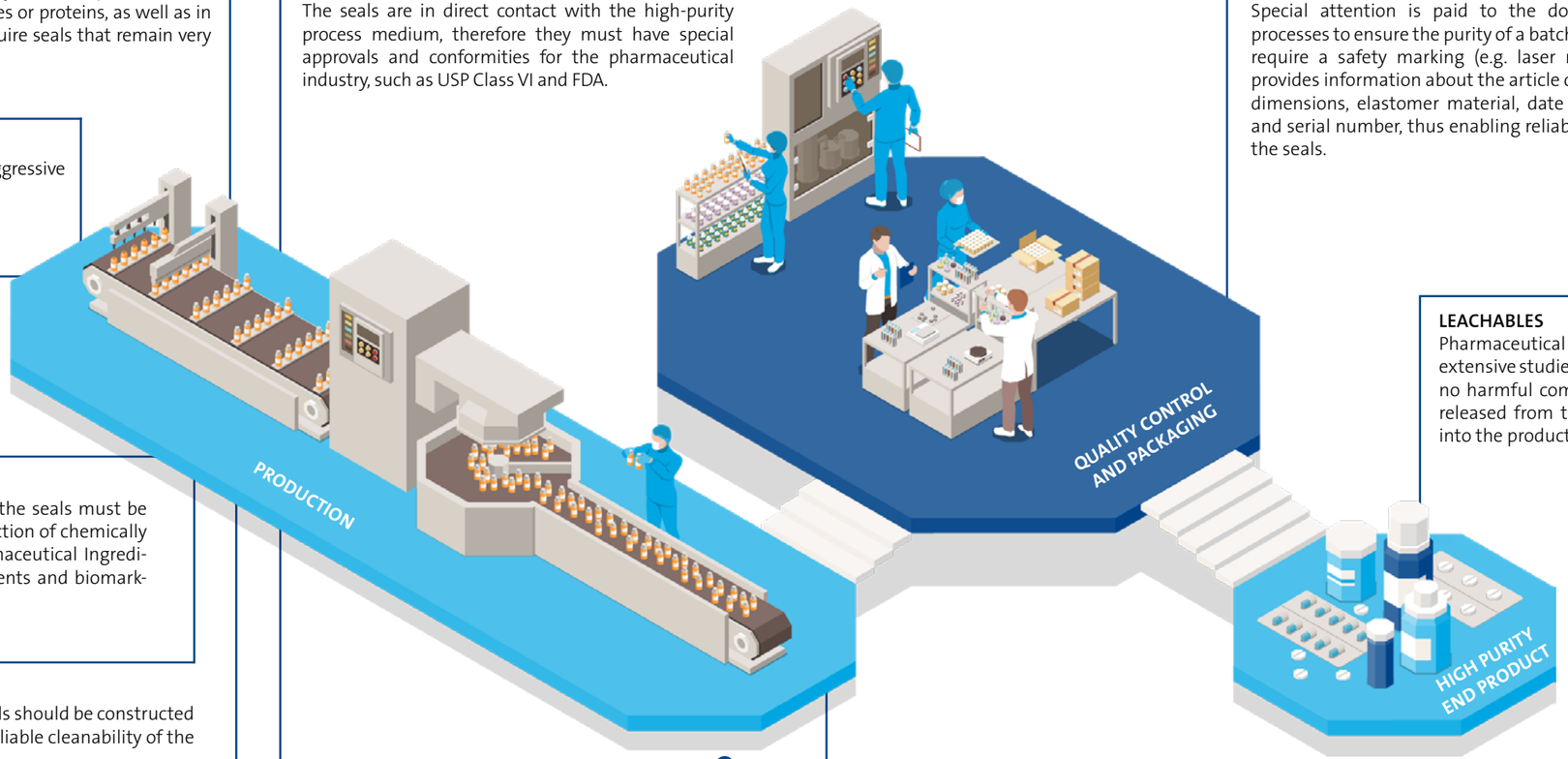
POWDERY MEDIA
Seals often must also be able to withstand powdery media, such as those found in tablet presses.

AGGRESSIVE CHEMICALS
Chemicals and toxic substances, which the seals must be able to withstand, are used in the production of chemically manufactured agents, API (Active Pharmaceutical Ingredients) or in vivo diagnostics (contrast agents and biomarkers).

HYGIENIC DESIGN
Due to the strict hygiene regulations, seals should be constructed according to hygienic design to ensure reliable cleanability of the equipment and thus sterile processes.

EXTRACTABLES
Pharmaceutical manufacturers are obliged to conduct extractables studies due to the high purity requirements. Extractables are chemical compounds that are extracted from a packaging material under certain conditions (e.g. at elevated temperature or different solvents) and migrate into the product.

CONFORMITIES AND APPROVALS
The seals are in direct contact with the high-purity process medium, therefore they must have special approvals and conformities for the pharmaceutical industry, such as USP Class VI and FDA.



PURIFIED WATER (WFI AND DI WATER)
Both WFI water (water for injection, demineralized ultrapure water) and DI water (deionised water) place enormous demands on elastomeric materials. Here, sealing materials must be used that are resistant to these media in long-term use.

TRACEABILITY
Special attention is paid to the documentation of processes to ensure the purity of a batch. Seals therefore require a safety marking (e.g. laser marking), which provides information about the article description, type, dimensions, elastomer material, date of manufacture and serial number, thus enabling reliable traceability of the seals.

LEACHABLES
Pharmaceutical manufacturers are required to conduct extensive studies on leachables. The goal is to ensure that no harmful components of an elastomeric mixture are released from the packaging materials and transferred into the product during storage.

DIRECT CONTACT WITH HIGH PURITY PRODUCTS
The synthesis of pharmaceuticals in the pharmaceutical industry is not allowed to produce any unwanted by-products or allow foreign substances to enter the product, as the purity requirements for the process and the product are particularly high. Sealing solutions that reliably prevent contamination and are allowed to come into contact with the product without causing concern are needed.

EXTRACTABLES AND LEACHABLES STUDIES

The issue of purity plays a major role in the production of pharmaceutical products. But how do you guarantee the required process purity in terms of the sealing materials?

The classic approvals alone are not sufficient as proof of the purity of a sealing material, as they do not provide any information about possible interactions of the process medium with the seal used. This is where extractables and leachables studies come into play because they pursue a common goal: to ensure and verify process purity.

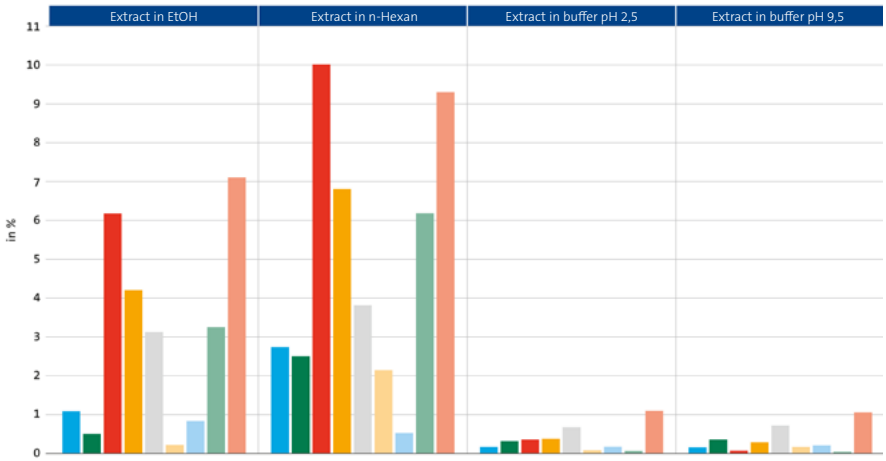
In an **extractables study**, the interactions between the pharmaceutical product and the elastomer are investigated. These often occur in a medium with a higher solvent strength than the product and at high temperature. The objective of this study is to identify all possible extractable components of the elastomer that can migrate out of elastomeric sealing materials during the production, filling and packaging of food and pharmaceutical products. This will provide information on how an O-ring for sealing an inhalation spray head behaves in contact with the drug, for example.

The **leachables study** in turn looks at what influences the environment has on the material. The leachable components of an elastomeric compound that can migrate into the product during storage with a long contact time are documented.

In two separate extractables studies, Freudenberg Sealing Technologies investigated whether its own EPDM materials and Fluoroprene® XP are suited for use in the pharmaceutical industry and meet the high purity requirements. The study on EPDM materials also included a benchmark with comparable USP Class VI certified compounds from competitors.

Results of the EPDM extractables study

When the extraction values of black EPDM materials are compared **(Figure 1)**, the two materials from Freudenberg as well as EPDM 4 are the clear winners in the benchmark comparison, with the latter showing significantly higher TOC values. Among the white materials, EPDM 253815 and EPDM 5 prevailed. But the latter shows excessive extraction values in EtOH and n-hexane, and thus only EPDM 253815 is recommended overall.



MATERIAL	COLOR	HARDNESS SHORE A
EPDM 291 (Freudenberg)	black	70
EPDM 292 (Freudenberg)	black	85
EPDM 1	black	70
EPDM 2	black	80
EPDM 3	black	70
EPDM 4	black	75
EPDM 253815 (Freudenberg)	white	70
EPDM 5	white	70
EPDM 6	white	70

Figure 1:
Extraction quantities in relation to original sample weight

The TOC value (Total Organic Carbon) indicates the amount of total carbon and is therefore an indication of the organic contamination. As shown in **Figure 2**, Freudenberg's EPDM 253815 clearly has a lower carbon content compared to the other two white materials, EPDM 5 and EPDM 6. The black EPDM 291 and EPDM 292 also have very low TOC values. The study shows clear differences from the competitors in favor of Freudenberg's materials.

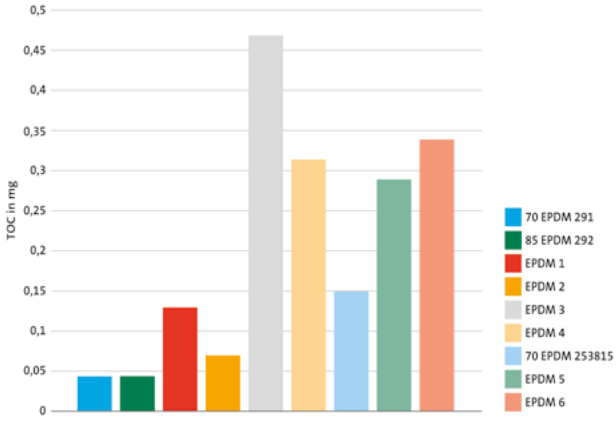


Figure 2:
TOC values in relation to original sample weight (buffer pH 2,5)

Results of the Extractables study for fluorinated materials
Freudenberg Sealing Technologies has conducted its own extractables study to test whether the material Fluoroprene XP® is suited for use in the pharmaceutical industry and meets the high purity requirements. To this end, two fluorinated material variants were selected and compared with two EPDM materials, see **Figure 3**. Fluoroprene XP® performed even better in the study than EPDM: No migrated substances were detected when it was stored in ethanol and n-hexane for 24 hours. In addition, TOC investigations were conducted as a measure of organic contamination. The result: The TOC values in the phosphate buffers were also outstandingly good with Fluoroprene XP®. In the phosphate buffer with a pH value of 9.5, they were only a fifth of the already pure values of the EPDM materials.

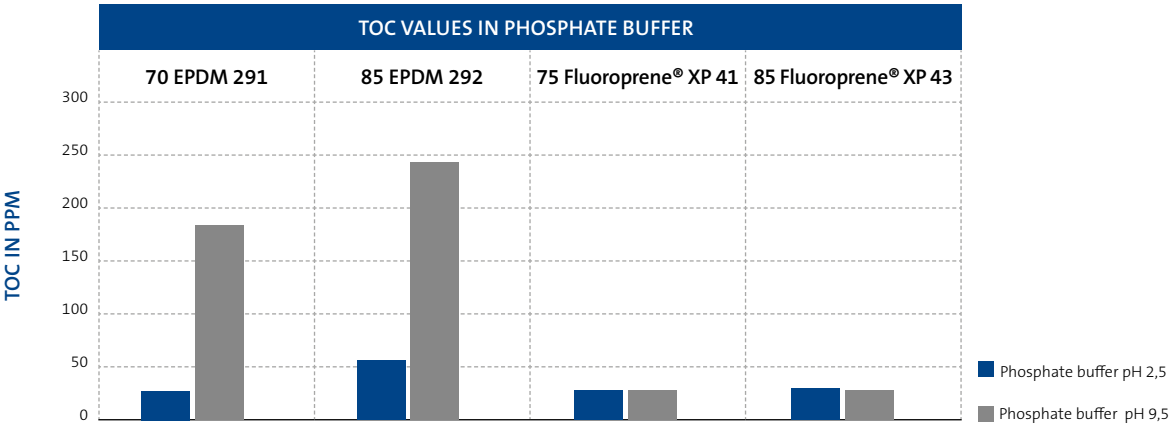


Figure 3:
TOC values in Phosphate buffer

EVERYTHING FROM A SINGLE SOURCE – YOUR BENEFITS

MATERIAL EXPERTISE

- Extensive expertise in the area of premium quality elastomer and plastic materials
- In-house development and production of high-performance materials with all relevant approvals
- Own accredited test laboratory for analyses
- Extractables and Leachables studies

DESIGN EXPERTISE

- Development and calculation based on the Finite Element Method (FEM)
- In-house test bench for perfect matching of valve seals to the respective CIP/SIP process
- Customer-specific solutions according to Hygienic Design

OUR KNOW-HOW
on sealing solutions for the pharmaceutical industry

MANUFACTURING EXPERTISE

- Own production sites worldwide
- Production of prototypes without tool costs. Short-term requirements can be met and small series can be made available from original materials by the Freudenberg Xpress® Service

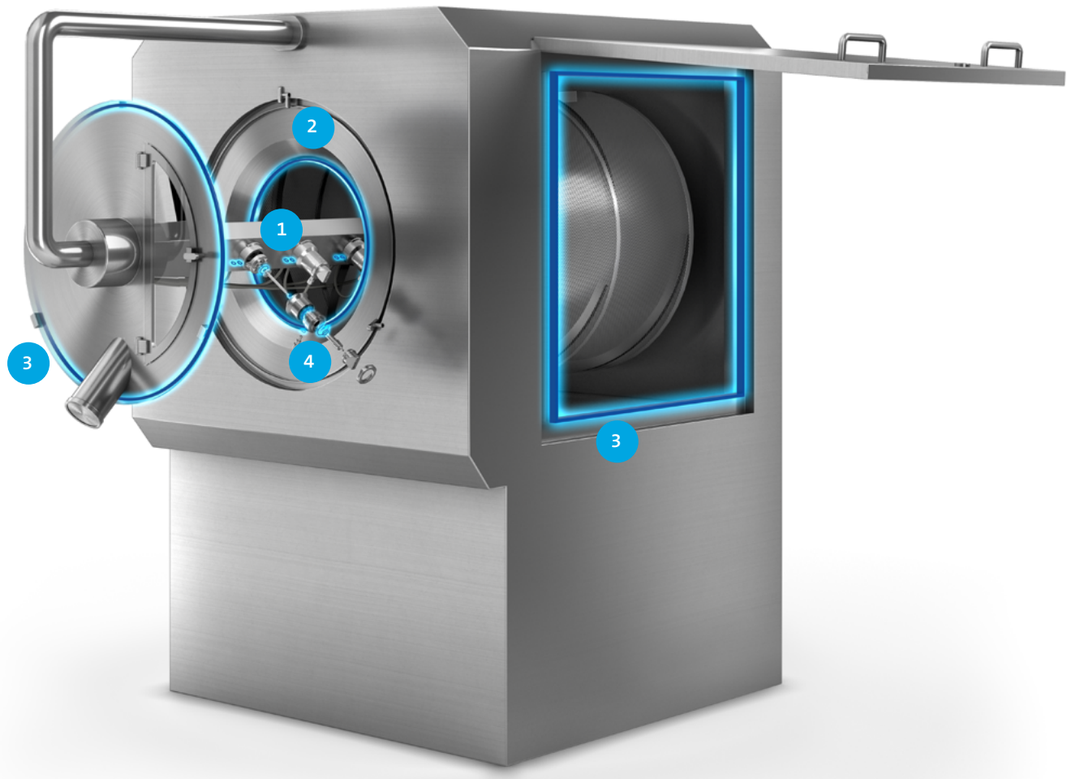
CONSULTING AND SERVICE EXPERTISE

- Expertise on the selection of materials and the hygienic design of sealing solutions
- Application consulting through countless tests (CIP/SIP database) and cooperation with cleaning agent manufacturers
- Global stocking program allows for fast delivery
- Laser marking
- Individual packaging concepts (individual and kit packaging, customer-specific packaging bags)

OUR SEALING SOLUTIONS FOR APPLICATIONS IN THE PHARMACEUTICAL INDUSTRY

The pharmaceutical industry makes use of many different applications and processes, all of which have individual requirements. Freudenberg Sealing Technologies supplies the right innovative sealing solutions. The portfolio includes all sealing products, from customer-specific molded parts to standardized clamp seals. Mixers, coaters and pumps, including their pipe connections, and many other machines in the pharmaceutical industry are sealed hygienically and reliably. The following pages will give you an overview of our sealing solutions for applications in the pharmaceutical industry.

COATER



VIEW ALL SEALING SOLUTIONS IN A COATER HERE AS A 3D ANIMATION!

1

HYGIENIC USIT®

Freudenberg's Hygienic Usit® sets new purity standards in open and closed manufacturing processes because it prevents the formation of germs under the screw head. Metal washers that are not suited for the pharmaceutical industry due to a lack of hygiene can therefore be completely replaced. The elastomer bead is available in three high-quality materials, 70 EPDM 291 (black), 70 EPDM 253815 (white) and 75 Fluoroprene® XP 45 (blue). All materials are suited for direct contact with the process media and are compliant with EU (Reg.) 1935/2004 and FDA requirements. EPDM also has USP Class VI approval. The materials are also resistant to the cleaning and sterilization media used in CIP/SIP processes.

2

V-RING

V-Rings protect the bearing in the drive system of a coater from various media and prevent contamination of the product by lubricants. Freudenberg Sealing Technologies offers V-Rings in various designs. They act axially, are easy to install and are ideal for use even if the shaft is highly deflected. During installation, they are stretched over the shaft and pushed onto their subsequent seat. Freudenberg manufactures V-Rings made of high-performance materials such as EPDM, VMQ and Fluoroprene® XP especially for the pharmaceutical industry.

3

PROFILE AND INFLATABLE SEAL

Freudenberg's profiles are resistant to high temperatures, cleaning products, and other media such as water, steam, disinfectants, alkaline solutions, and acids. Resistance and durability are the most important features. We also develop customized profiles for your individual needs that are perfectly adapted to your installation space situation. Our experts will be happy to advise you on this. Freudenberg Sealing Technologies also offers high-quality inflatable seals, e.g. for doors of coaters, made of various high-performance materials that have all the relevant approvals and offer impressive chemical resistance.

4

O-RING

Freudenberg Sealing Technologies offers O-rings made of the high-performance materials 75 Fluoroprene® XP 41, 70 EPDM 291 and 70 VMQ 117055 especially for the hygienic requirements of the pharmaceutical industry. They not only convince users due to their universal applicability, as in the spray nozzles of a coater, for example, but also their broad chemical and thermal resistance, combined with international approvals for the pharmaceutical industry. As a standardized sealing element, O-rings are available in all dimensions according to DIN ISO 3601 as well as in special sizes.

MIXER

VIEW ALL SEALING SOLUTIONS IN A MIXER
HERE AS A 3D ANIMATION!

1

GUIDE RING

The guide rings from Freudenberg Sealing Technologies, for example, are made of the premium material PTFE Y005, have a uniquely low tendency to extrusion and thus guarantee a long service life. Guide rings are used as sealing elements for pistons, among other purposes, to compensate for lateral forces in machines.

2

RADIAL SHAFT SEAL

Freudenberg offers various radial shaft seals for sealing rotating shafts. The Radiamatic® HTS II is a special development made of PTFE and can be used for a wide range of applications in the pharmaceutical industry. Industry-specific developments with regard to media resistance as well as innovative sealing lip designs for freedom from dead space in accordance with hygienic design and material variations make Freudenberg radial shaft seals the ideal choice.

3

FLAT GASKET

Freudenberg Sealing Technologies offers highly media-resistant flat gasket types that meet the special requirements of the pharmaceutical industry. Thanks to their industry-specific approvals, the stamped or plotted flat gaskets made of PTFE or ePTFE cover all applications in the pharmaceutical industry.

4

COVER SEAL AND PROFILE

Freudenberg Sealing Technologies offers seals in various geometries and materials for easy sealing of doors and container covers, for example, FEP-encapsulated or elastomer O-Rings that have all the relevant approvals and can therefore safely come into contact with the process medium. Furthermore, profiles are also available that are highly resistant to high temperatures, cleaning agents and other media such as water, steam, disinfectants, alkaline solutions and acids.

TABLET PRESS

Rotary tablet presses are mainly used to press a powder or granulate into the form of a tablet. The mixture is filled and pressed into the shape of a tablet using two punches. Our polyurethane **wipers** prevent the release of dust or powder. They are wear-resistant against such abrasive materials. Furthermore, the lubrication system and pressing area must be reliably separated from each other so that the tablet is not contaminated. To prevent this, our **bellows** are used in addition to the wipers. Similar to the wipers, these must not only withstand the lubricants, but also the dynamic requirements. Freudenberg Sealing Technologies has also developed special polyurethane U-cups that are used to seal the tablet stamp. The pressing chamber must also be completely sealed so that no germs can enter the process through gaps in the windows and doors of the system. This can be prevented by our **inflatable seals**. They permanently guarantee easy opening and closing of the doors. Furthermore, dynamically applied axial seals prevent powder or dust from depositing underneath the turntable. The flexibility and wear resistance of the seal play an important role in this respect. We supply **O-rings** in the material 70 EPDM 291 for the sealing at the filler neck, which meets the necessary requirements according to USP Class VI, FDA and EU (Reg.) 1935/2004.

FILLING MACHINE

Solid, liquid, semi-solid and sterile drugs can be packaged during the filling of active pharmaceutical ingredients. These are different processes and packaging units. The processes do have one thing in common, however: they must be lean and clean. From filling to sealing the product, contamination of the product must be avoided and purity must be guaranteed. This requires an effective cleaning CIP system and a hygienic design of the system. If powders, granulates or lumpy products are filled in large quantities, modern precision filling scales are used. Smooth surfaces, no dead spaces and good cleanability are a must for the parts in contact with the product. The same challenges are of particular importance when filling highly viscous and shear-sensitive products such as ointments and creams. For dosing pumps or dosing valves in filling machines, we offer you **piston seals** and **O-rings** made of pharma-specific high-performance materials that ensure highly precise and hygienic filling of products.

GRANULATOR

Granulation is used to shape powdery solids. This process simplifies and optimizes both product handling and further processing. Depending on the initial substance and the application area, different processes are used – wet, melt or dry granulation. For example, Freudenberg offers the Radiamatic® HTS II **radial shaft seal** for hygienic sealing of rollers, mixing tools, or choppers in agglomeration or granulation equipment. This special development made of PTFE with FDA and USP Class VI approvals convinces customers thanks to its media resistance and its dead space free sealing lip design. By using **O-rings** made of 70 EPDM 291 and **clamp seals** made of 70 VMQ 117055 or 75 Fluoroprene® XP 41, connections and connecting lines can also be sealed both reliably and hygienically.

STERILIZER

Hygiene and absolute purity are essential in the pharmaceutical industry. Therefore, sterilizers are often used to kill microorganisms on objects at any stage of development. During the sterilization process, especially the seals in the door must withstand particularly high temperatures. Freudenberg offers **profiles** for doors that meet these requirements. They are resistant to high temperatures, cleaning agents and other media such as water, steam, disinfectants, alkaline solutions and acids. We also develop **customized profiles** that meet your individual needs, which are perfectly adapted to your installation space situation. Our experts will be happy to advise you on this. Freudenberg Sealing Technologies also offers high-quality **inflatable seals** made of various high-performance materials that have all the relevant approvals in the pharmaceutical industry.

HOMOGENIZER

In the pharmaceutical industry, homogenizers are used for cell disruption in order to get at their contents, e.g. organelles, proteins, DNA or other biomolecules. In mechanical disruption processes, temperatures and pressures must be taken into account. Temperature changes (repeated freezing and thawing) are part of the process or result from the movement when applying the necessary forces. When pressing through valves, high pressures are generated or a rapid pressure release is used to destroy the cell walls. Non-mechanical methods use chemical effects to break through the cell membrane. To get to the content of the cell, different chemicals are used to extract, dissolve or saponify components of the cell membrane. This requires special sealing solutions, such as **O-rings** and **piston seals** that can withstand aggressive media, high pressure loads and product media. The appropriate sealing solutions range from high-quality plastics such as polyamides, PTFE and PEEK to premium elastomers such as EPDM and Fluoroprene® XP.

MEASUREMENT AND REGULATION TECHNOLOGY

Sensors and measuring devices are often used to control and monitor the individual processes in reactors or mixers. If the seals are installed near the media, they must meet certain regulations for use in the pharmaceutical industry. In addition, the sealing material must have high chemical and thermal resistance. High temperatures can easily occur and aggressive cleaning agents are often used. A good, long-lasting sealing effect and the smallest possible influence on the values to be measured are therefore important. Freudenberg Sealing Technologies offers a broad portfolio of **hygienic elastomer seals** for sensors. 70 EPDM 291 and 75 Fluoroprene® XP 41 are available for **O-rings** and customized parts. **Flat gaskets** made of ePTFE are also well suited for such uses.

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