High Purity Water Systems for the Biopharmaceutical Industry

Improving security, flexibility and operation costs
Pall's total turnover is more than $1.5 billion. Our staff of more than 10,000, many of whom are scientists and engineers, are 100% focused on providing separation and purification solutions to global industries.

As the largest division of Pall, the Biopharmaceuticals group is already the world leader in separation systems and consumables used in pharmaceutical, biotechnology, plasma processing, vaccines, cosmetics and other healthcare markets.

Sales of high purity water systems to our pharmaceutical industry customers is a strategic part of our business and our reputation depends upon it.

We are totally committed to your success.
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Improving security, flexibility and operational costs for filtration and purification processes

Turnkey project management
Each manufacturing process has specific needs from its high purity water supply. Pall therefore customizes every project to meet the unique requirements of the user. We offer our customers total capability from initial consultation to design, engineering, manufacturing and installation with first class service and back up support. We believe in supplying "what you want" not "what we have".

Pall also has a reputation for creating membrane and process technology. We develop and manufacture some of the core separation modules used in our systems. Our design engineers continually seek new and innovative ways to provide optimized solutions though application of our advanced know-how.

Whatever the water supply, whatever the process demands, wherever in the world and whatever the time constraints, Pall will provide professional and efficient turnkey management.

Validation & pharmaceutical industry standards
Being in the forefront of Biopharmaceutical supply for three generations, Pall maintains the most comprehensive standards for its manufactured products and systems. Personnel receive the highest level of training and support infrastructure to make sure that approaches are both current and realistic according to applications and local needs.

Our high purity water projects are handled with proper attention to documentation requirements from DQ through IQ, OQ and acceptance testing in accordance to latest GAMP standards and with respect to CFR21 Part 11 where applicable.

Materials compatibility is in line with USP Biological Safety Test Standards where needed and general guidelines such as the ISPE Baseline Guides, cGMP, and ASME Bioprocessing are always central principles of our design philosophy.
Water requirements in pharmaceutical processing

Pall’s high purity water systems are designed to comply with international codes and regulations governing medicinal product manufacture referred to in various regional Pharmacopeia as, for example, USP, EP and JP. These regulations specify standards of purity for a number of waters including Purified Water, Highly Purified Water and Water For Injection. These waters are used in the preparation of compendial dosage forms in a variety of applications from bulk primary processing, media make up, equipment and container rinsing to use in final formulations. Controls include microbial and total organic carbon (TOC) and in the latter cases, endotoxin.

Non-compendial water used in pharmaceutical processing must also meet specified criteria. This water may be used applied in early stages of synthesis or cleaning and as the feedwater to high purity water treatment systems. Typically this water must meet at least potable (drinking water) standards and usually has additional limits specified (for example hardness, silica, total bacteria count).

Pretreatment

Raw water supply varies in quality. Typical impurities which need to be reduced or controlled include

- Particulates
- Inorganics
- Micro organisms
- Dissolved gases
- Organic compounds

Pretreatment reduces the effect of potential variations in feedwater quality, minimizing the operating and maintenance requirements in the final treatment stages. Typically it has little effect on some parameters indicative of final water quality such as anions, total bacteria count, TOC and volatile components but pretreatment must be effective to minimize plant operating costs.

Microfiltration

Crossflow microfiltration (MF) is a highly efficient way to remove small suspended solids, large colloids, and microorganisms from large volumes of water.

New generations of membranes in robust materials and large area format, which are unique to Pall, provide excellent economy and exceptionally stable performance independent of variability in feed water.

Operating pressures are lower than UF (typically 1 to 2 bar) and the systems use backwash and air scrubbing techniques to minimize requirements for chemical regeneration.

- Removes turbidity, suspended solids, bioburden
- Reduces silt density index (SDI) to protect RO/NF and ion exchange
- Compatible with chlorine and other chemicals which may be present in feed
- Minimal waste stream
- Low operating cost
- Stable filtrate and low chemical compared to multimedia filters
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**Ultrafiltration**

Ultrafiltration membranes, when incorporated in our systems, retain particles, bacteria, viruses, pyrogens (endotoxins), colloids and large organic molecules. Dissolved salts and smaller organic molecules pass freely through these systems. A wide variety of proprietary membranes are available to Pall, but the two most common applications for pharmaceutical water processing are in pretreatment (eg colloid removal) and for pyrogen control in both low and high temperature distribution using both hollow fiber and ceramic technologies.

Full process review and skilled design optimization mean that Pall can apply UF in its systems with considerable advantages to end users.

Benefits include
- Excellent protection when used in prefiltration
- Steam in place options available for pyrogen applications
- Sanitary and cleanable designs where required in final processing

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Top: End view of 'Microza' 6KD hollow fiber ultrafiltration module showing packing of unique double skinned fibers
Centre: Membralox® Ceramic ultrafiltration membrane elements are used for de-pyrogenation in hot water distribution loops post RO
Bottom: Magnified view showing Membralox ceramic membrane structure
Left: Aria Microfiltration System
Reverse Osmosis

Reverse osmosis (RO) is the finest level of membrane separation in liquids. The RO membranes used in Pall® systems act as an efficient barrier to all dissolved salts and inorganic molecules as well as most organic compounds (organics typically greater than 100 daltons in molecular weight).

Water passes freely through, while salts are rejected typically from 98% to over 99%.

Pall has optimized the pretreatment, design and staging of RO systems in single or multipass arrangements for stable and low fouling performance and for extremely high recovery (water conversion) rates without the use of chemicals.

Benefits include
- Compact and modular design
- No added chemicals
- Very high rejection rates producing high purity filtrate
- Maximum efficiency in throughput
- Recovery rates as high as 95%

Nanofiltration

Pall also uses nanofiltration (NF) water technology with similar but slightly more open membranes than RO. The modules have higher unit capacity and lower operating pressures for greater economy where higher passage of monovalent ions and some small organics is not an important factor.

These systems are used typically to produce softened process water and for removal of high levels of common organic compounds found in some waters.

Other technologies

Membrane systems listed above can meet most requirements for process water, purified water and highly purified water or water for injection (WFI) quality.

Some regulations still demand that WFI must be prepared using distillation. Pall systems can be used in parallel or in series with distillation and are often employed to take load off existing distillation installations. Distillation can be incorporated into systems when required.

Other important features of Pall’s high purity water systems include, according to process requirements, ozone dosing, ultraviolet (UV) treatment, carbon filters, ion exchange (softeners) and chemical dosing. Pall’s own cartridge filters are also employed to protect tank vents, and as highly effective prefiltration or point-of-use guard filters.
Storage and distribution

Total system design ensures that water is purified, stored and distributed with quality maintained to specification all the way. Tank designs take into account sizing, choice of material and microbiological considerations. Additional components such as heat exchangers, filters, UV, ozone and point-of-use valves are selected on technical merit, simplicity, efficiency and cost effective maintenance. Loop pressure and flow rates are carefully designed and controlled to meet microbiological and safety considerations.

Microbiological protection

High quality water has to be properly handled and protected from contamination right up to point-of-use.

The hydrophobic vent filters in Pall systems provide high sterility assurance and generous air flow rates with minimum risk of blockage by wetting. Integrity testing of the filters is achieved with minimum fuss and maximum confidence.

Final water quality at point-of-use is ensured by high flow rate, long life sterilizing grade filters capable of absolute removal of even the smallest organisms which may be encountered in practice.

Pall Advanced Separations Systems

Pall Advanced Separations Systems (PASS) is an independent engineering and procurement entity for Pall’s global separations systems business. To successfully deliver high purity water systems that meet stringent customer requirements we have excellence in:

- Process System Design
- Documentation
- Systems Fabrication
- Project Management

Pall also has many experts in its SLS support laboratories (46 labs at the time of writing) handling microbiological and contamination analysis. This experience includes many years of handling and identifying water-borne organisms.

We can provide these services to our customers as part of service contracts, or on demand according to the project requirements. We are also developing new tools to detect and document cleanliness of equipment and water.

PASS will provide the following

- Installation Support
- Systems Design
- Document Preparation
- Validation/Qualification
- Risk Analysis
- Operator Training
- Spare Parts
- Service Contracts
- After-Market Service
Why choose a pharmaceutical water system from Pall?

**Trusted Partner for Biotech Processing and Pharmaceutical Production.** Pall is the broadest based filtration, separation and purifications company in the world. We have the highest reputation for technical excellence, product quality and customer support to the pharmaceutical industry and we are committed to remain the leader.

**Total Solution Provider For Pharmaceutical Water Production**
Within Pall’s experience is more than 20 years in supply and service of bespoke systems for the production of all grades of pharmaceutical water. We are recognized experts in microbiological protection and control as well as in pharmaceutical process engineering.

**Optimized Process Solutions using Membrane Technology**
Unique access to a comprehensive range of membrane technologies developed in house and sourced from alliance partners means a head start in providing the best answer for each specific request. Whether it is superior prefiltration technology for lifetime and process consistency, optimal water conversion using staged RO or high temperature ceramics, Pall has significant process advantages to offer.

**Excellence in Engineering and Validation**
Understanding regulatory demands in the pharmaceutical industry is a key aspect of Pall’s business. Matching this with strengths in system engineering, project management and validation support ensures each system is supplied in accordance with GAMP and ISPE and to user’s specifications in a timely and efficient process.
A bespoke system for the production of USP purified water to very low endotoxin levels. The system incorporates pre-treatment, double reverse osmosis and ultrafiltration.
Pall Corporation has offices and plants throughout the world in locations including:
Argentina, Australia, Austria, Belgium, Brazil, Canada, China, France, Germany, India, Indonesia, Ireland, Italy, Japan, Korea, Malaysia, Mexico, the Netherlands, New Zealand, Norway, Poland, Puerto Rico, Russia, Singapore, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, United Kingdom, the United States and Venezuela. Distributors are located in all major industrial areas of the world.