BOSCH
Invented for life

High Purity Media Systems

For generation, storage and distribution of PW, WFI and pure steam

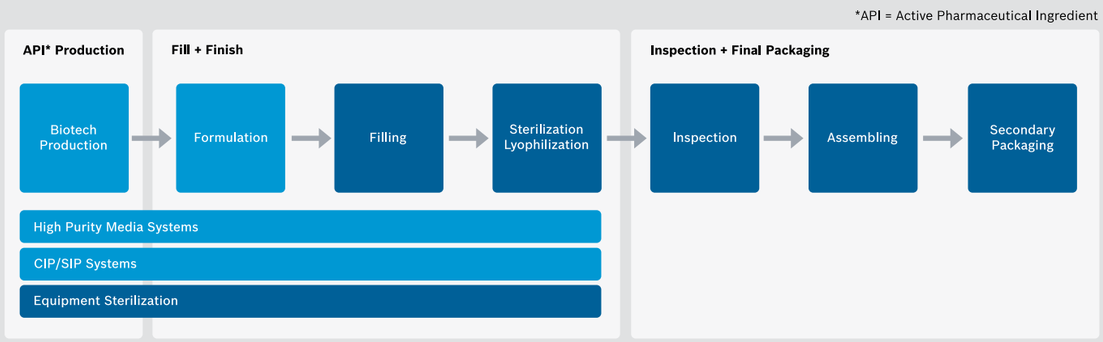
Pharma Specialist at Bosch

At Robert Bosch Packaging Technology GmbH, Pharmatec in Dresden is the competence center for pharmaceutical process systems and plants for the production of liquid active substances or medicinal products. In addition, Pharmatec develops and manufactures complete systems for generation, storage and distribution of high purity media for pharmaceutical use and the biotechnology industry.

Since 1993, Pharmatec has been one of the technology leaders in this segment of plant construction and benefits greatly from the integration in the Bosch family. Its technological expertise and method competence in research, development and project management provide a resilient foundation to meet the requirements of ”Industry 4.0” with all its options.

The enormous advantages of this far-reaching networking and online integration of industrial production processes makes Pharmatec, together with Robert Bosch Packaging Technology GmbH, beneficial to the pharmaceutical and biotech sector – with fully developed and modern solutions for the production, handling, filling and packaging of pharmaceutical active substances or medication.

*API = Active Pharmaceutical Ingredient



Line competence under a single roof: Pharmatec Bosch Packaging Technology

Product life cycle at Bosch

In the interests of its customer companies, Robert Bosch Packaging Technology GmbH has high service requirements: Over the entire product life cycle, we therefore offer all planning and production phases linked together with one another as well as with After Sales Service and Support Offering.

During **consulting and project development**, customer requirements are in the foreground, which are analyzed based on the planned production processes and coordinated with the customer.

Project management is the responsibility of a Pharmatec Project Manager who serves as a central contact person. He synchronizes the activities of all project partners in the framework of scheduling and technical planning.

For the **production process**, Pharmatec engineers implement the detailed plant concept for production. They inspect the design of all system components, coordinate suppliers and service providers until, after the first complete assembly, all functional tests have been completed.

Assembly on-site by highly qualified specialists also includes the integration of the systems in the technical infrastructure as well as repeated extensive testing up to acceptance by the customer.

For **quality assurance**, in each Pharmatec project all work steps from planning up to final inspection are documented extensively and transparently – including endoscopic recordings of the welding seams, test reports, inspection reports and material certificates.

After Sales Services are available to the customer after commissioning for the entire life cycle of his plant. Apart from technical support, this also covers the instruction and advanced training of operating staff and consultation services for operation or conversion of the plant.

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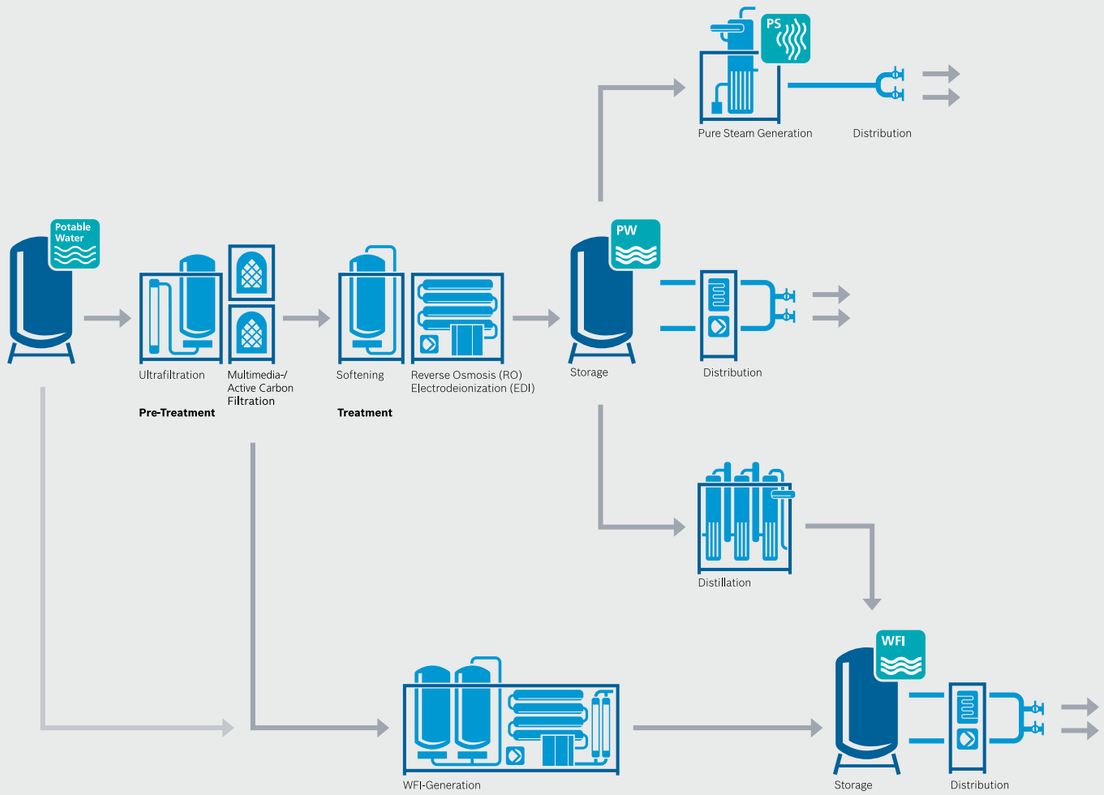

Ultrapure water is essential for the pharmaceutical industry and biotechnology production processes: It must be available at all times for all stages of the production process in sufficient quantities and at the required levels of quality. This requirement applies to the manufacture of active substances (API) and biomolecules as well as to the production of medicines. Quality defects in the pure water supply can therefore result in loss of production or even legal problems. Ultimately, pure water quality is regulated by law in all countries and is closely monitored by the responsible authorities.

For many years now, Pharmatec has supplied high purity media systems for customers across all continents, customized to their individual requirements and compliant with internationally valid regulations. The product portfolio ranges from compact generation units for water treatment for pharmaceutical purposes, to pure steam generators, up to complete supply systems for biotechnological production processes. State-of-the-art membrane or distillation systems are used to produce pure water (PW), water for injection (WFI) and pure steam (PS).

The modular design of these plants makes it possible to design the exact capacities required to meet customer demands and to deliver even highly complex systems fully assembled. The company engineers provide the benefits of their many years of experience and support the customer in all project phases, from concept design to commissioning of the plant.

High-quality components guarantee quality and safety of a generation unit for pharmaceutical water

Pre-treatment

The first quality stage for pharmaceutical water is Aqua Purificata or purified water (PW). This is the base medium for producing higher grades of pharmaceutical water or pure steam. Depending on the origin and quality of the available drinking water, this level of purity requires several treatment stages using various procedures.

The Pharmatec unit design is therefore based on a modular system which enables all customer-specific requirements to be met. The tendency for the water quality of some regions to fluctuate between seasons is of particular importance, and can only be compensated for using highly efficient treatment stages. The conceptual design of these stages therefore requires specific parameters for operational and maintenance criteria as well as detailed drinking water analyses.

This important stage in the chain of treatment for drinking water is used to reduce hardness components, impurities and biological deposits. Water treatment begins with a suitable filtration stage to remove particulate turbidity followed by various procedures to extract substances such as chlorine, iron or manganese from the water.

Removal of colloids and bacteria by means of ultrafiltration

Row water ultrafiltration
An additional ultrafiltration stage to remove colloids and bacteria is implemented if required before the softening equipment, which is integrated as standard, separates off calcium and magnesium. Sanitization is a particularly important part of this microbiologically critical treatment stage, and it is normally achieved in Pharmatec units by means of hot water systems.

Membrane processes

Generation Unit for Purified Water

The pharmaceutical industry generally requires water in two levels of purity for production: Clean water in PW quality and water for injection (WFI). Technically the high WFI quality can be produced via filtration or distillation processes.

Treatment
The softened water is then processed to PW quality using membrane-based process steps. In the first step, the water passes a reverse osmosis stage to separate out salts and other impurities.

To ensure the required low conductivity, an electrodeionization module (EDI) is used next to reduce the remaining proportion of salts, carbon dioxide and other ions by at least 95 percent. If the feed water contains high levels of carbon dioxide, a membrane degassing unit can be connected upstream of the EDI module. Additional options include a second reverse osmosis stage, UV radiation, a heat exchanger and various monitoring or analysis functions.

Ultrafiltration
The initial medium of this "cold" treatment technology is clean water in PW quality. The multistage separating process with hollow fiber polysulfone membranes achieves a separation limit far below the size of bacteria, viruses and pyrogens. Ultrafiltration therefore delivers ultra-pure water which, depending on regional regulations, satisfies the quality criteria for WFI.

Complete system for WFI generation
The new compact system series for WFI generation is based on the "cold" reverse osmosis membrane process, which is combined with an electrodeionization module and a further ultrafiltration stage. For sterilization, the unit is equipped with an integrated sanitization unit which, depending on customer requirements, operates with hot water or chemical additives. To monitor all production parameters, the MWFI systems can be equipped with various sensors and measuring instruments which control the water or filter quality during the entire production process. In addition to standard measurements, such as residual hardness, conductivity and TOC content, an inline germ count can also be integrated into the system in order to increase the safety and efficiency of the production. Depending on the design of the system, the maximum capacity of the MWFI systems is between 1,000 and 20,000 liters of WFI per hour.

Package Unit for WFI generation

PW-Unit

Unit	400	1 100	2 000	3 300	6 600	9 900	13 300	16 500
Output * of	220	550	1 250	2 500	4 500	7 500	10 500	11 500
Output * to	550	1 250	2 500	4 500	7 500	11 500	14 500	20 000

* Output l/h PW

MWFI Generation Unit

Unit	1 000	2 000	3 000	5 000	7 500	10 000	12 000
Output *	1 000	2 000	3 000	5 000	7 500	10 000	12 000

* Output l/h WFI

Thermal processes

Pharmatec units use natural circulation to their advantage: During the phase transition from water to steam, particles, endotoxins, pyrogens or other impurities remain in the water and the sterile steam is converted to ultrapure water in WFI quality in the subsequent condensation stage. Multiple-Effect Distillation Units are a widespread solution for the generation of water for injection (WFI), particularly in Europe, and comply with all worldwide applicable quality requirements.

Distillation units
Multiple-Effect Distillation Units for producing WFI also use the natural circulation process. Heating steam is only required to heat the first column, and all other modules are heated using the heat of the preceding process stages, ensuring energy efficiency.

The pure steam from the first column is condensed in the next one, transferring its vaporization enthalpy to the feed water in this column, which is then vaporized in turn. This process continues through to the last column. Upon request, the distillation units can be designed for additional pure steam generation: In "Dual Mode", steam is available as an option instead of WFI, and in "Triple Mode", which features a large starting column, steam production is possible in parallel with water production. Additional options such as preheaters, consumption-based output control, degassing modules or additional sensors and interfaces are available for communication or control to meet specific customer requirements.

Multiple-Effect Distillation Unit

Multiple-Effect Distillation Unit

Unit	501	1 101	1 501	2 201	3 301	5 001	6 001	8 001	10 001	12 001
Output * at 4 bar(g) **	350	750	950	1 600	2 000	3 000	3 600	5 200	6 000	7 200
Output * at 6 bar(g) **	450	950	1 250	1 900	2 800	4 000	5 000	7 000	8 200	9 600
Output * at 8 bar(g) **	500	1 100	1 500	2 200	3 300	5 000	6 000	8 000	10 000	12 000

* Output l/h WFI ** Heating steam pressure

Pure Steam Generator

Unit	500	1 000	1 500	2 500	3 500	5 000
Output * at 4 bar(g) **	70	190	260	400	600	910
Output * at 6 bar(g) **	300	630	950	1 490	2 220	3 050
Output * at 8 bar(g) **	500	1 000	1 500	2 500	3 500	5 000

* Output kg/h pure steam at 3 bar(g) pure steam pressure ** Heating steam pressure

Pure Steam Generator

Pure steam generation
Sterile steam is indispensable for the biotechnology and pharmaceutical industries, used for example in cleaning and sterilizing production systems or in autoclaves. The pure steam is produced from PW-quality water in a distillation column heated by industrial steam. Non-condensable gases in the pure steam are eliminated via thermal degassing or an integrated membrane degassing module.

Process safety over the entire life cycle

The comprehensive Pharmatec expertise ensures stable production conditions over the entire life cycle of the high purity media infrastructure. It starts with the needs-based system design and technical planning that is consistently oriented towards the requirements of the customer and his production processes.

During the entire operating lifetime Pharmatec services are available for regular maintenance, inspection, sanitization or cleaning processes. This reduces the risk of production losses to a minimum and possible technical faults will be corrected timely. For this an advanced remote service system is ready beside experienced staff.

In case of changed requirements for system layout or performance engineering specialists of Pharmatec will develop tailor-made solutions on request for extension or conversion of the installed pure media systems.

Infrastructure for the highest possible requirements

High purity media system for generation, storage and distribution of PW (cold and hot)

Storage and distribution of water for pharmaceutical use (PW, WFI) are two of the most critical areas in the pharmaceutical production process. Precise analysis of the requirements for plant design and planning is necessary to ensure that water is available at all points of use without any loss in quality: This analysis includes close monitoring of pressure or supply quantity intervals in day-to-day operation. Storage tanks feed the consumption points via a continuously circulating loop. The piping system supplies all points of use with high purity media and an optional point of use management system optimizes water consumption across the system.

Cold storage
Pure water tanks, adapted to the capacity of the generation unit and peak consumption levels during production, are available for cold storage and distribution of pure water in PW quality. To protect against contamination, ozone can be added to the pharmaceutical-quality water in the tank. This keeps the tank contents permanently germfree. During production times, a UV unit in the feeding system ensures that the dissolved ozone in the water is removed upstream of all consumption points.

Hot storage
Water for injection (WFI) is heated during storage and continuously circulated. The water temperature during storage and distribution is between 80 °C and 85 °C. Cold points of use are realized via sub-loops with integrated cooling modules.

Hygiene
Storage and distribution systems are periodically sanitized or sterilized with pure steam in accordance with customer specifications to maintain water quality. Various processes can be used. Sanitization with ozone or hot water at over 85 °C are used for cold storage; pressurized water sanitization at over 121 °C is used for hot storage.

Monitoring
Temperature, volumetric flow, pressure and conductivity are mandatorily monitored to ensure water quality. Online TOC measurement can be optionally implemented. All measured values relevant to quality are recorded on paperless recorders and/or made available for supervisory automation systems as required by the customer.

High purity media system with storage tank and central distribution skid for PW and WFI

Distillation unit, storage tank and skid for generation, storage and distribution of WFI

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