



Cold WFI in Best Quality

GENERATE, STORE AND
DISTRIBUTE WFI.

Freshly
Thinking.

WFI. COLD. SAFE. PERFECT FOR THE ENVIRONMENT AND BALANCE.

For many pharma and biotech companies, the admission of cold processes for the production of WFI is good news. The safe procedure of OSMOTRON® WFI from BWT impresses both ecologically and economically.



THE BASICS OF WATER FOR INJECTION

For pharma and biotech companies which, for example, require water for injection (WFI) mainly cold, the revised European Pharmacopoeia (Ph. Eur.) monograph 0169 represents a big opportunity. As a result of this change, membrane processes to create the critical raw material of WFI are now also permitted, alongside distillation, in the area of validity of the European Pharmacopoeia, as has already been the case with the United States Pharmacopoeia (USP) for some time (01).

IN THE PH. EUR. AND THE USP, THE REQUIREMENTS ON THE PURITY OF WFI ARE DEFINED AS FOLLOWS:



TOC

≤ 0.5 ppm C



NO₃

Ph. Eur. ≤0.2 ppm



CONDUCTIVITY

Ph. Eur. ≤1.1 μS/cm (20°C)
USP ≤1.3 μS/cm (25°C)



PYROGENE

Ph. Eur. ≤0.25 EU/ml
USP ≤0.25 I.U./ml



CFU

≤10 KBE/100 ml

THE WORDING OF THE GUIDELINES OF THE EUROPEAN PHARMACOPOEIA AND BWT'S SOLUTION

in a superior concept. The commented text of the European Pharmacopoeia also forms the table of contents and guide for this brochure.

„Water for injections [...] is produced either by [...] a purification process that is **equivalent to distillation (02)**. Reverse osmosis, which may be single-pass our **double-pass (02)**, coupled with other appropriate techniques such as **electrodeionisation, ultrafiltration (03)** or nanofiltration, is suitable. Notice is given to the supervisory authority of the manufacturer before implementation. For all methods of production, correct operation **monitoring (04)** and **maintenance (06)** of the system are essential. In order to ensure the appropriate quality of the water, validated procedures, in-process monitoring of the electrical conductivity, and **regular monitoring (05)** of total organic carbon and microbial contamination are applied. The first portion of water obtained when the system begins to function is discarded. Water for injections in bulk is **stored and distributed (07)** in conditions designed to prevent growth of microorganisms and to avoid any other contamination.”

INHALT

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OF COURSE, WITH CRITICAL UTILITIES FROM THE RIGHT PARTNER. BWT.

Medical end products and their production must meet the highest requirements. This also applies to the water used. The impressive solutions from BWT provide safety along the whole life-cycle.

BWT is the market-leader for critical utilities and a well-established company that has been working successfully with its systems and services in the pharmaceutical and biotech industry for decades. The customers benefit from their extensive experience, and will continue to do so in the future. In the interests of customers, BWT organises all the core process and competencies in-house. From the development and planning, construction and production, to service and maintenance.



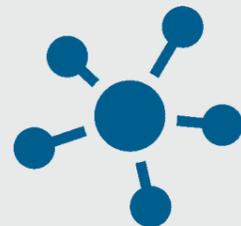
FULL PORTFOLIO

Standardised systems from pre-treatment to distribution. Lower risk, higher safety and good calculability.



WELL OVER 1.000 OSMOTRON®

Compact, integrated systems generate PW and HPW from drinking water, all over the world.



SUPERIOR HPW SYSTEMS

A large number of cold HPW systems from BWT have been reliably producing WFI-quality water for years.



HUNDREDS OF THERMAL SYSTEMS

Extensive experience with the planning, implementation and support of projects with WFI and pure steam.

*Production.
Continual
and safe.*

AN INSIGHT INTO THE WORLD OF THE BEST SYSTEMS FOR CRITICAL UTILITIES.



BWT has not made it everywhere yet. But it certainly is wherever customers need solutions. With branch offices and partners all over the world, and over 100 experienced and highly-qualified service technicians on site.



The safe systems of BWT are made at the group's own production sites on three continents. The sites in Switzerland, USA and China are ISO 9001 certified and ensure extremely high quality.



At all locations, and always together with the customer: before the delivery of each system, the full performance FAT provides extensive proof of the system's quality and output.

OSMOTRON® WFI. TRIPLY IMPRESSIVE.

Safer. More ecological. And more profitable.



01 THE DIRECT ROUTE FROM DRINKING WATER TO WFI

The system for the cold, membrane-based generation of WFI is called OSMOTRON® WFI. Its compact frame has everything you need to reliably make drinking water into the best water for injection purposes. The standardised system clearly exceeds the requirements of the applicable regulations.



100%
SAFETY & QUALITY

	 TOC ppm C	 NO ₃ ppm ³	 CFU KBE/100 ml	 CONDUCTIVITY µS/cm (20°C)	 PYROGENE EU/ml
OSMOTRON® WFI ¹	≤ 0.02	≤ 0.002	≤ 1	≤ 0.1	≤ 0.06
SAFETY FACTOR ²	25x	100x	10x	10x	4x

¹ Long term values of so-called HPW Systems in production and test operation
² Mathematical distance between Ph. Eur. Regulations and produced quality

MORE SAFETY AT THE WHOLE SITE

The usually needed upstream PW or Permeate generation for distillation units can be omitted, as drinking water is sufficient for the OSMOTRON® WFI. Consequently, consumption points which just need PW, can also be supplied with commercially produced WFI. The higher quality provides extra safety and a headstart due to the additional and early alarm and action limits.



02 EXTREMELY ECONOMICAL – AND THEREFORE ECOLOGICALLY VALUABLE

The yield is much better than with conventional systems, as just one system is in operation, instead of two, and therefore less water is discarded. In addition, much less energy is consumed during the production. In distillation systems, the water is evaporated with much energy efforts. Heat exchangers then ensure that the steam is condensed again. Depending on the design of the system, powerful cooling may then be required. The normal, continual production operations are therefore very energy-intensive. The OSMOTRON® WFI impresses with its much lower consumption and better energy balance. When assessing the total energy consumption, it is key what quantities and temperatures of WFI are required at the various points of consumption. Due to the use of antiscalant in connection with a two-stage reverse osmosis process, water softening is not necessary. No salt is need, so as a result there is no chlorinated sewage water. This measure also contributes to the aforementioned high yield.



20%
less waste water



80%
energy saving



0%
completely no
need for salt

THE EARTH IS KNOWN AS THE BLUE PLANET – BUT DESPITE THAT, ONLY A SMALL AMOUNT OF THE AVAILABLE WATER IS POTABLE. THE SOLUTION OF BWT FOR PRODUCING COLD WFI HELPS PRESERVE RESOURCES AND THE ENVIRONMENT. HOWEVER, SUSTAINABILITY MUST ALSO BE PROFITABLE – AND THE OSMOTRON® WFI ALSO SETS NEW STANDARDS HERE.



03 WHEN LESS IS MORE

The conventional process takes much longer. The final stage of distilling impresses with its high yield. Unlike the OSMOTRON® WFI, the conventional process is not supplied with drinking water, but in most cases with purified water (PW). In the future it is possible, that only an OSMOTRON® WFI system will be positioned between the drinking water supply line and the WFI tank, instead of a membrane system, a tank and a distilling unit.

The space requirement is also much lower, as is the required investment volume. This reduction of the process stages does not just lead to space and cost savings, but also has ecological benefits.

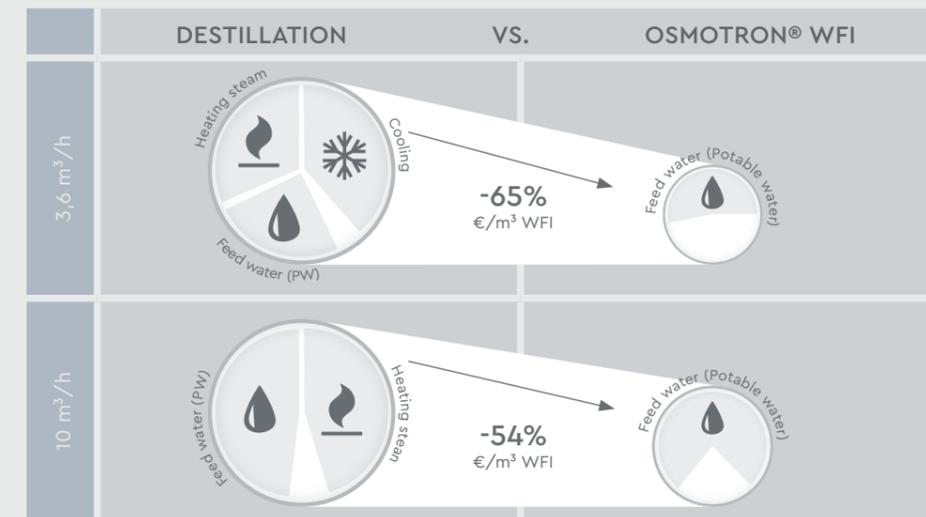


70%
space



50%
investment

COMPARISON OF THE COSTS PER M³ WFI: THE FIGURES SHOW A CLEAR TREND

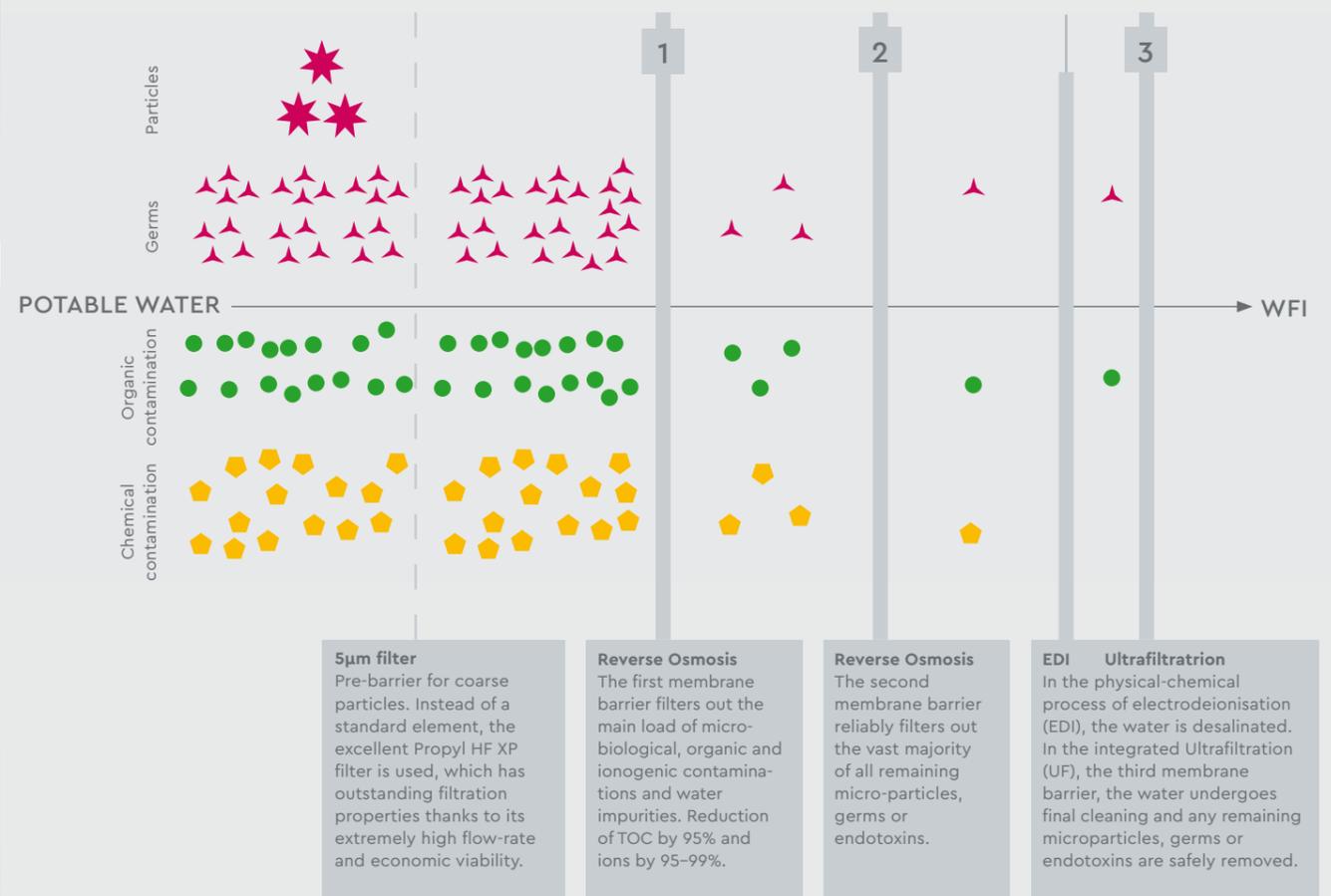


The main cost components are listed below. 300 operating days of 20 hours. Other costs to take into account are depreciation (10 years), maintenance as well as expendable and wear materials. Source: PharmaTEC 04/2016 "Freiheit für die WFI-Erzeugung" [Freedom for WFI production], p. 42-44



TRIPLE SAFETY. SIMPLY IMPRESSIVE.

WFI is subject to the highest demands. Consequently, BWT has also specified the highest standards for the OSMOTRON® WFI. As a result, a triple membrane barrier is used. For maximum safety and higher efficiency.



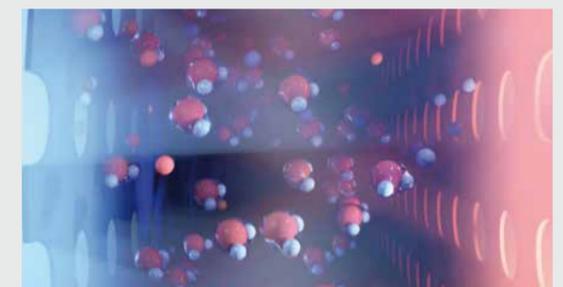
FUNCTIONING PRINCIPLE OF THE FILTER, REVERSE OSMOSIS AND ULTRAFILTRATION

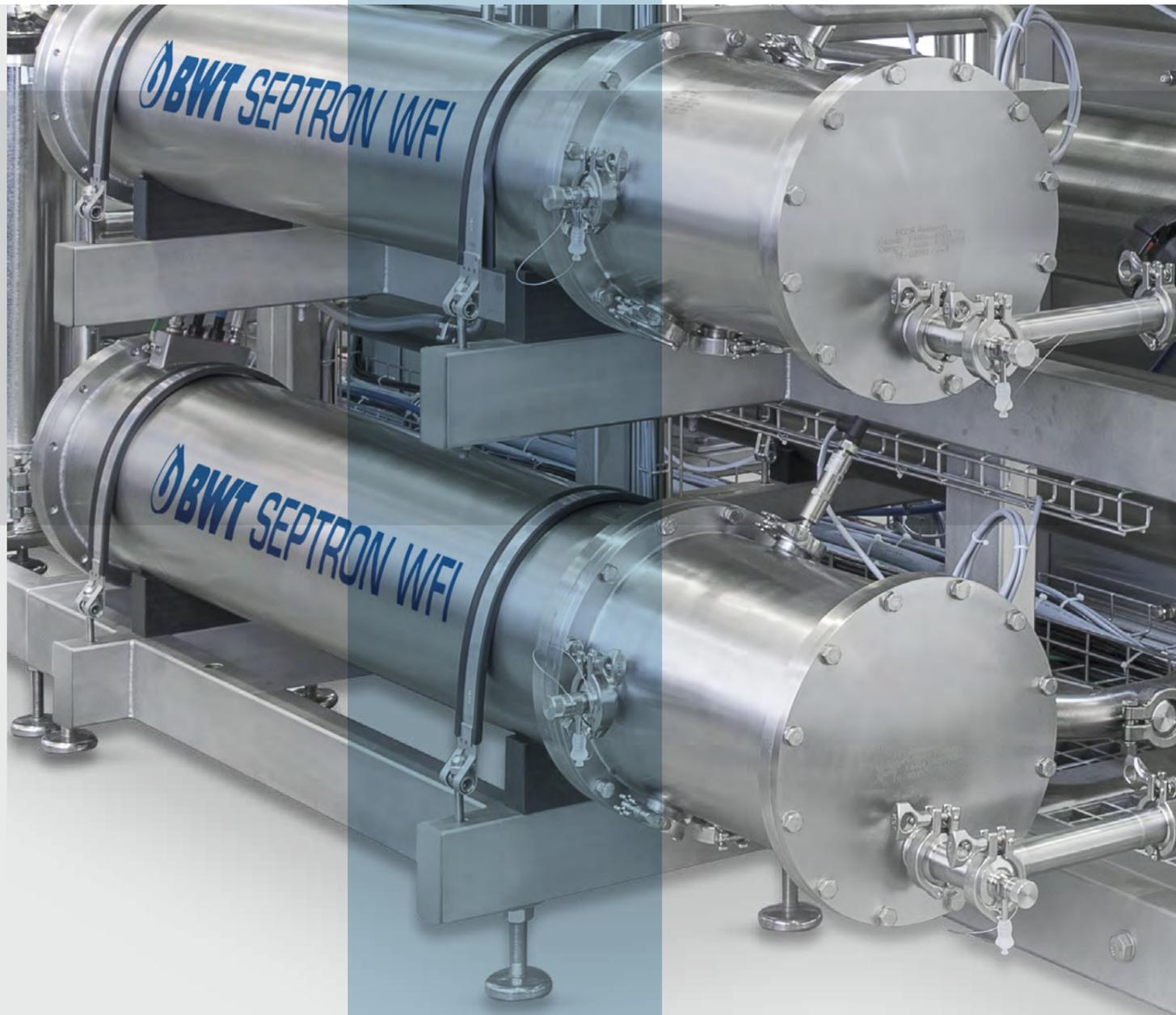
The water passes through the barriers while undesired parts are retained in the filter, or rinsed out with the concentrate flow during reverse osmosis.



FUNCTIONING PRINCIPLE OF ELECTRODEIONISATION

Due to the generated electric field, anions and cations are removed by the ion-exchange membrane, while the water flows through the SEPTRON® WFI.





SEPTRON® WFI. THE CENTREPIECE FOR THE BEST WATER QUALITY.

The electrodeionisation module with unique integrated ultrafiltration ensures the best results. After the double barrier of two-stage reverse osmosis, it represents the final preparation stage for WFI.

PERFECTED FOR MEMBRANE-BASED WFI

The SEPTRON® Module has been developed specifically for the purification of water in the pharmaceutical & biotech industry. The special requirements for cold WFI Systems were taken into account inside in the design of the SEPTRON® WFI.

- » Sampling after EDI and after UF
- » Safe retention of endotoxins with MWCO acc. to USP <1231>
- » Testability of UF integrity when installed
- » Δp – Measurement for both stages
- » Highest yield



EXCLUSIVE SWISS QUALITY

Thousands of SEPTRON® modules are used worldwide. The modules are produced exclusively in Switzerland. Every single module is also tested and certified there. Due to the spiral-wound design, there are no dead spaces or seals. The design, production and performance of the modules meet the needs and requirements of customers in the pharmaceutical, biotech and cosmetics industries.

- » 316L stainless steel housing
- » Seal-free spiral wound membrane technology
- » 100% routine inspection of the modules at the production site: performance test with certificate
- » Excellent TOC reduction, high CO₂ and SiO₂ reduction
- » Highest yield

EFFICIENT AND VERIFIABLE SAFE ULTRAFILTRATION

For the highest microbiological quality and safety, hundreds of SEPTRON® are equipped with an integrated UF. It is the final barrier to eliminate even the smallest risk from the purified water. The integrated design convinces with highest yield and efficiency with minimum space requirement. Integrity is checked, proven and documented as part of the service when installed. The preventive exchange for maximum risk minimization is also part of the routine maintenance by technicians of BWT. The change is contact-free, a GMP-compliant operation is always secured in this way.





AQU@VIEW
AUTOMATION

SANITIZATION AND
CLEANING.



THERMAL



CIP

MONITORING.
ONLINE & OFFLINE.



CONDUCTIVITY



TOC



SAMPLING



CFU/BACTERIAL
COUNT

CHECK OF OPERATION.
BASIS: RELEVANT PROCESS
PARAMETERS.



PRESSURE



FLOW RATE



TEMPERATURE

THE RIGHT STRATEGY. RISK CONTROLLED.

BWT places emphasis on the importance of monitoring and maintenance to ensure long-term safe system operation. So does the European Pharmacopoeia.

A HOLISTIC RISK-BASED APPROACH TO THE WHOLE LIFE-CYCLE

In manufacturing, systems must continually provide the required quality. Operational safety must also be ensured and risks detected early, so that suitable action can be taken. The requirement for continual, extensive monitoring as well as regular, preventive maintenance is therefore undisputed. In the Ph. Eur. both are explicitly required. With OSMOTRON® WFI, the focus from the beginning was therefore on "quality by design". This helps ensure long-term quality and availability. The whole system can be thermally sanitized at >80°C and also has CIP inlets for chemical cleaning. The main load of the feed water concerns reverse osmosis. This can then be individually sanitized and cleaned.

AQU@VIEW AUTOMATION. NOTHING IS OVERLOOKED. THANKS TO INTEGRATED MONITORING.

The Ph. Eur. and EMA require the measurement of the most relevant process parameters. BWT goes one step further: the OSMOTRON® WFI records and saves the data from all instruments in the automated AQU@VIEW system.

This is the basis for the

- » Diagnosis and analysis
- » Alarm and action limits
- » Cumulative presentation of current and historic data on one screen
- » Continual status check of passive components like filters and membranes
- » Automatic sanitization
- » Verification of intervals

These characteristics form the basis for the simplification of operation and preventative maintenance. Data integrity is ensured by the AQU@VIEW audit trail and operator actions are recorded in line with 21 CFR, Part 11.



CENTRAL
CONTROL POINT



ALARMS & ACTIONS



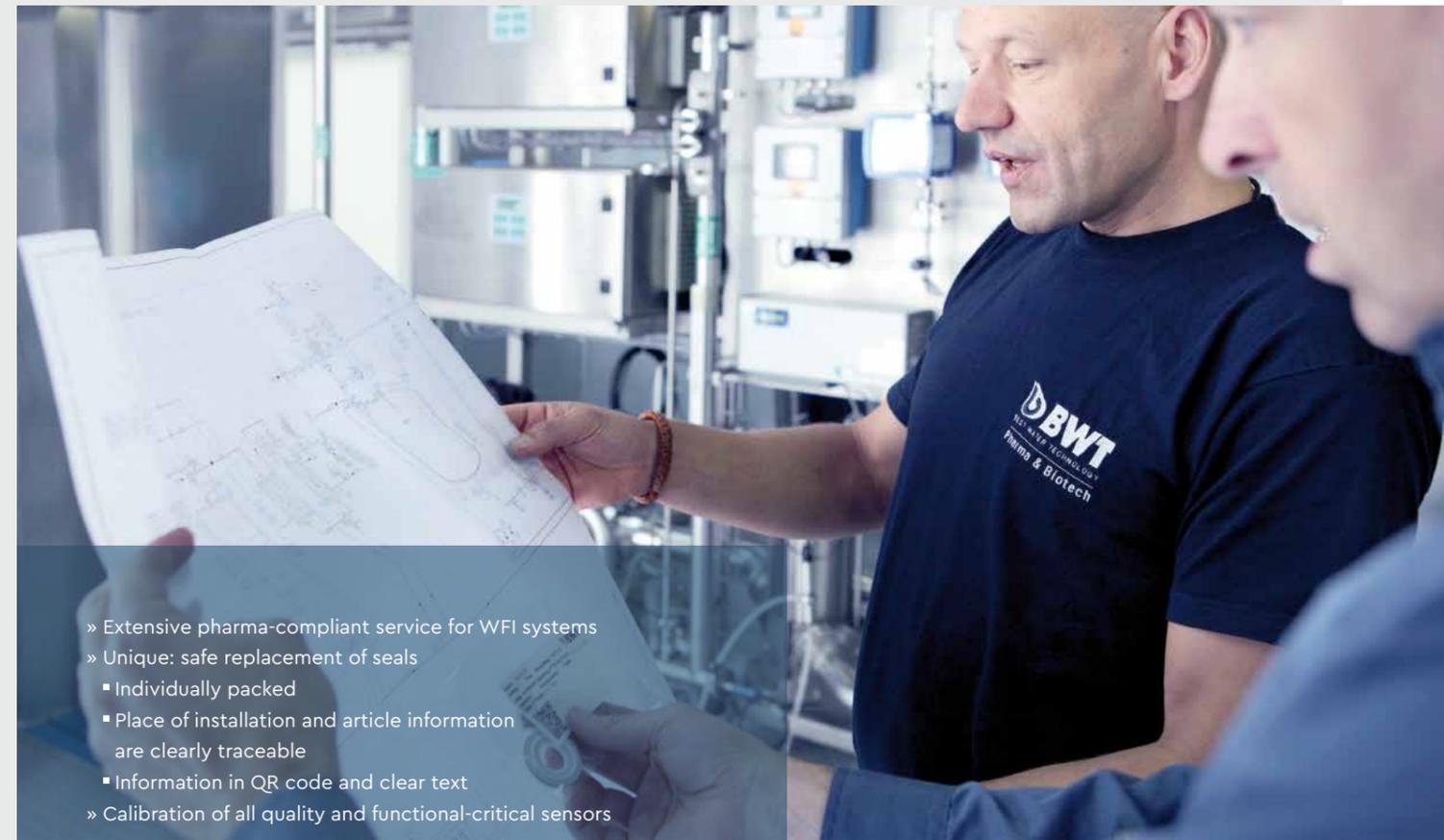
ALL PARAMETERS



LOGBOOK



DATALOGGER



- » Extensive pharma-compliant service for WFI systems
- » Unique: safe replacement of seals
 - Individually packed
 - Place of installation and article information are clearly traceable
 - Information in QR code and clear text
- » Calibration of all quality and functional-critical sensors



- » Developed for critical utilities and pharma requirements.
- » A library with standardised and validated software modules.
- » Transparent. The source codes are open, commented and structured.
- » Reliable, flexible and future-proof.

AQU@SERVICE WFI. MAINTENANCE THAT COVERS EVERYTHING.

Maintenance is also emphasised in connection with risk control. BWT has been focusing for years on preventative maintenance, to ensure the product quality and high readiness to use critical utility systems, in order to minimise risks and downtime and avoid unplanned stoppages.

The service engineer analyses the process data before maintenance. He discusses the results with the customer and, where necessary, takes suitable action.

During the construction of the OSMOTRON® WFI, the operating comfort and ease of servicing were important points. All samples and components are easy to reach. This simplifies the correct and swift performance of all work.

For each customer and system there is an individual, tailor-made service package. With AQU@SERVICE WFI, all the requirements on service calls for WFI systems in general, and cold WFI systems in particular, are taken into account.



GMP MAINTENANCE



CALIBRATION



EXCHANGE OF
FILTER, SEAL &
MEMBRANE



FILTER INTEGRITY



DOCUMENTATION

OSMOTRON® WFI. SAFETY, BIT-BY-BIT.

The objective was clear from the overall concept to the smallest detail. To find the solution for the safe and efficient production of WFI. Objective achieved.

High-quality, pharma-conform brand products are systematically used. All pumps, sensors, valves or membranes come from renowned manufactures, often world leaders in their sector. The process is extremely robust and therefore suitable for a large range of feed water qualities (e.g. silicic acids or high salt content). The whole system has been independently extensively

tested in cooperation with a renowned Swiss University of Applied Sciences. The adjustment of the output depending on the tank level makes the operation particularly efficient. The water and energy consumption is reduced and the components are less stressed, which extends their life-span.



OSMOTRON® WFI.

Environmental compatibility and economy: excellent.

Highlights:

- » Easy handling
- » Low operating costs
- » No need to increase the salt content of waste water
- » High safety
- » High yields
- » Up to 15 m³/h WFI on one skid

LOOPO WFI. ENSURE PERMANENT WFI QUALITY. WITH THE RIGHT STORAGE AND DISTRIBUTION.

Water for injection has to be distributed from the producer OSMOTRON® WFI to the point of consumption. During storage and distribution, LOOPO WFI ensures and maintains the quality at all times.

LOOPO WFI was developed according to the requirements from the question and answer sheet of the European Medicines Agency (EMA). As a result, the LOOPO has all the components

- » sanitize it with ozone
- » to sterilise the distribution system with overheated water at 121° Celsius and

The ozone is produced electrolytic by the STERITRON® cell from purified water, without adding extra external substances. This process is extremely safe: this way, there is no risk that contamination could get into the system.

To ensure safe storage, the tank is continually sanitized with the ozone released in the WFI. Before the WFI gets into the loop and is distributed towards the points of consumption, the ozone is removed by a BEWADES® UV lamp until the ozone level is below the detection limit. The LOOPO WFI constantly ensures the quality of WFI. The proof is provided by the use of measuring and analysis devices to check the relevant parameters like TOC, conductivity and bacterial count. Furthermore, the use of high-quality pharma-conform components such as pharma pumps, ensures maximum safety.

LOOPO WFI.

It has everything needed for the secure storage and distribution of WFI on a compact frame.

Highlights:

- » Continual sanitization of the WFI tanks
- » Sanitization of the distribution system with ozone
- » Sterilisation of the distribution system with overheated water 121 °C
- » Online measuring technology (TOC, conductivity, bacterial count)
- » All components including automation on a compact frame
- » BWT AQU@Sense MB Online bacterial count monitoring



AQU@SENSE MB.

The use of an "online real-time microbiology analyzer" saves time. In operation, it measures the microbiology in real time. Due to the immediate recognition of problems, action can be taken quickly and errors rectified. This averts the danger of delays in product approval.



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FOR YOU AND PLANET BLUE.