

PHARMA & BIOTECH

# BWT Pharma & Biotech



Pharmaceutical Water Requirements

For You and Planet Blue.

 **BWT**  
BEST WATER TECHNOLOGY

# Pharmaceutical Waters

### Potable water

#### **Potable water/water intended for human consumption**

Potable water, or water intended for human consumption, is also used as feed water for the production of purified water and water for injections. Potable water may be used to rinse product-contacting surfaces of equipment.

#### **Potable water (treated)**

Treated potable water has the same uses as potable water and water intended for human consumption but has been treated to reduce its microbial content.

### Purified Water (PW)

#### **Purified Water in bulk**

Is used as an excipient in the preparation of non-sterile products and as a starting material in the preparation of water for injection and pharmaceutical-grade pure steam. It is also used for rinsing purposes (cleaning of containers) and in the preparation of cleaning solutions.

#### **Purified Water in containers**

Is Purified Water in bulk that has been filled and stored in conditions designed to assure the required microbiological quality. It must be free from any added substances.

### Highly Purified Water (HPW)

Is used in the preparation of medicinal products where bacterial endotoxins need to be controlled, except where water for injection is required. Current methods for the preparation include double-pass reverse osmosis, reverse osmosis combined with ultrafiltration and distillation.

### Water for Injection (WFI)

#### **Sterilized Water for injection**

Is used for dissolving or diluting substances or preparations for parenteral administration.

#### **Water for injection in bulk**

Is used in the manufacture of parenteral and ophthalmic products. It is also used for final rinsing of containers (e.g. primary packaging materials) and manufacture of these products.

### Pure Steam (PS)

Pure steam is evaporated above 100°C and used for humidification and sterilisation of e.g. porous goods. The level of steam saturation or dryness, and the amount of non-condensable gases are to be determined by the Pure Steam application. The condensate must comply with the respective WFI requirements.

## USP\* /Ph. Eur.\*\*

Purified Water			
Parameter	Unit	USP	Ph. Eur. (Bulk)
TOC	ppm C	0.50	0.5
Conductivity	$\mu\text{S}/\text{cm}@20^{\circ}\text{C}$	–	$\leq 4.3$
Conductivity	$\mu\text{S}/\text{cm}@25^{\circ}\text{C}$	$\leq 1.3$	–
Nitrate ( $\text{NO}_3$ )	ppm	–	$\leq 0.2$
Heavy metals	ppm as Pb	–	$\leq 0.1$
Aerobic bacteria	CFU/ml	$\leq 100$	$\leq 100$

Highly Purified Water			
Parameter	Unit	USP	Ph. Eur. (Bulk)
TOC	ppm C	n.c.st.	0.5
Conductivity	$\mu\text{S}/\text{cm}@20^{\circ}\text{C}$	n.c.st.	$\leq 1.1$
Nitrate $\text{NO}_3$	ppm	n.c.st.	$\leq 0.2$
Aerobic bacteria	CFU/100ml	n.c.st.	$\leq 10$
Bacterial endotoxins	I.U./ml	n.c.st.	$\leq 0.25$

Water for Injection			
Parameter	Unit	USP	Ph. Eur. (Bulk)
TOC	ppm C	0.50	0.5
Conductivity	$\mu\text{S}/\text{cm}@20^{\circ}\text{C}$	–	$\leq 1.1$
Conductivity	$\mu\text{S}/\text{cm}@25^{\circ}\text{C}$	$\leq 1.3$	–
Nitrate ( $\text{NO}_3$ )	ppm	–	$\leq 0.2$
Aerobic bacteria	CFU/100ml	$\leq 10$	$\leq 10$
Bacterial endotoxins	EU/ml	$\leq 0.25$	–
Bacterial endotoxins	I.U./ml	–	$\leq 0.25$

Pure Steam (condensate)			
Parameter	Unit	USP	Ph. Eur. (Bulk)
TOC	ppm C	0.50	n.c.st.
Conductivity	$\mu\text{S}/\text{cm}@25^{\circ}\text{C}$	$\leq 1.3$	n.c.st.
Aerobic bacteria	CFU/100ml	$\leq 10$	n.c.st.
Bacterial endotoxins	EU/ml	$\leq 0.25$	n.c.st.

n.c.st. = no comparable standard

\* current United States Pharmacopoeia, \*\* current European Pharmacopoeia

# Conductivity According to USP

## Three-stage Philosophy

### 1. In-line Measurement:

A conductivity measurement without temperature compensation corresponding to a measured temperature. If the conductivity is below  $1.3 \mu\text{S}/\text{cm}$  at  $25^\circ\text{C}$  (or values according to Table A) the measurement is completed. If not, stage 2 is required.

### Advantages of the in-line Measurement in Stage 1

- Real-time information for conductivity and temperature
- Immediate limit value alarm
- Data output for recording and documentation of the water quality
- Calibrated measurement
- Avoiding of errors due to sampling, handling & transport

### 2. Laboratory Measurement:

If the  $\text{CO}_2$  concentration of the sample is at equilibrium with the air and the conductivity is below  $2.1 \mu\text{S} / \text{cm}$  at  $25^\circ\text{C}$  the measurement is completed. If not, stage 3 is required.

### 3. Laboratory Measurement:

Add saturated KCl to the sample from stage 2 and measure pH and conductivity. The measured conductivity must be below the conductivity value shown in Table 1 at the measured pH. If this is the case, the measurement is completed. If not, the water does not conform to the standard.



**Table A****Stage 1:** Conductivity limits as a function of the temperature**Stage 3:** Conductivity limits as a function of the pH value

Stage 1	
Temp. °C	µS/cm
0	0.6
5	0.8
10	0.9
15	1.0
20	1.1
25	1.3
30	1.4
35	1.5
40	1.7
45	1.8
50	1.9
55	2.1
60	2.2
65	2.4
70	2.5
75	2.7
80	2.7
85	2.7
90	2.7
95	2.9
100	3.1

Stage 3	
pH	µS/cm
5.0	4.7
5.1	4.1
5.2	3.6
5.3	3.3
5.4	3.0
5.5	2.8
5.6	2.6
5.7	2.5
5.8	2.4
5.9	2.4
6.0	2.4
6.1	2.4
6.2	2.5
6.3	2.4
6.4	2.3
6.5	2.2
6.6	2.1
6.7	2.6
6.8	3.1
6.9	3.8
7.0	4.6

## Systems and Turnkey Solutions?

### We've got what you're looking for!

With BWT systems and turnkey solutions you benefit from the industry leading product lines combining best process engineering, premium components and technologies, highest quality manufacturing and assembly, cGMP compliant documentation and validation, validated automation solutions and comprehensive services for the entire life-cycle.

### Pre-treatment

Drinking water is mandatory as the basis for the production of pharmaceutical water, but such water is not available everywhere in the necessary quality and quantity. The use of BWT ULTRASTIL systems is a reliable method for the production of drinking water from raw water and as an optimal pre-treatment stage to protect downstream PW/HPW processes.

#### ULTRASTIL Raw-Water Ultrafiltration

- High recovery robust dead end ultrafiltration
- Optimal reduction of colloidal impurities (SDI15)
- Best retention rate for particles, germs, bacteria and viruses
- Continuous operation of downstream process equipment
- Significant lifetime extension of downstream disposable filters and membranes
- Compact space saving skid design



ULTRASTIL

## PW/HPW Generation

Purified Water or Highly Purified Water is one of the most critical raw materials for pharmaceutical production and related industries. As such the qualities at the point of use are regulated in the different international pharmacopeia's such as USP, EP, JP etc.

To safely achieve the defined qualities and maintain appropriate safety, alarm and action levels, it is important to deliver highest qualities to the storage & distribution systems. BWT pre-validated and tested PW/HPW generation products allow an optimal choice and technology for any kind of PW/HPW generation need, project requirement and budget. All systems are optional available with the unique SEPTRON® BIOSAFE the only integrated EDI/UF technology guaranteeing premium microbiological quality and safety.

### SEPTRONLINE – standard compact PW/HPW systems

- Integrated RO, SEPTRON® EDI
- Small footprint
- Semi-automatic chemical sanitization
- Attractive pricing
- Easy modular upgrade option within the series
- Separate pre-treatment, ELITE RS hygienic softening with SANISAL salt
- 0.15 - 0.3 m<sup>3</sup>/h and 0.4 - 2.4 m<sup>3</sup>/h series

### OSMOLINE – standard compact PW/HPW systems

- Open skid RO, SEPTRON® EDI
- Small footprint
- Automatic hot water sanitization >80°C
- Multijoint bloc valve technology
- Easy modular upgrade option
- Attractive pricing
- 0.4 - 2.4 m<sup>3</sup>/h series



SEPTRONLINE



OSMOLINE

### OsmoVision – innovative integrated high efficiency PW/HPW system

- Open skid pre-treatment, softening, RO, SEPTRON® EDI
- Maximum recovery for lowest operating cost
- Free chlorine & CO<sub>2</sub> tolerance by patented process design
- Continuous chemical sanitization without added substances
- MULTIJOINT diaphragm bloc valve technology
- 0,5 - 10m<sup>3</sup>/h single skid or >10m<sup>3</sup>/h multi skid solutions



OsmoVision

### OSMOTRON® – the world best-selling PW/HPW system

- Open skid pre-treatment, softening, RO, SEPTRON® EDI
- 316L SS execution
- Automatic hot water sanitization >80°C
- MULTIJOINT diaphragm bloc valve technology
- Easy modular upgrade option within the series
- 0,5 - 10m<sup>3</sup>/h single skid or >10m<sup>3</sup>/h multi skid solutions



OSMOTRON®



## PW/HPW Storage and Distribution

Storage Tanks fed by BWT PW/HPW generation systems enable buffering of peak consumptions. Selection of the optimal tank size allows sizing of the PW/HPW generator for the most continuous efficient generation mode.

In storage and distribution systems the objective is to maintain the chemical and microbiological quality of the PW/HPW at constant high level to ensure that user points are supplied with the quality exceeding the requirements defined per USP/EP and providing sufficient safety margin to set alarm and action levels.

### **LOPO C – standardized compact distribution, control, monitoring and sanitization for ambient temperature PW/HPW storage and distribution systems**

- Open-skid system including STERITRON electrolytic ozone generators and BEWADES ozone destruct UV technology
- Calibrated online analytical instrumentation for flow, pressure, temperature, conductivity and ozone
- Optional calibrated TOC analyzer
- 316L SS execution
- Continuous sanitization of the storage tank by electrolytic produced ozone
- Automatic and easy periodic sanitization with ozone of the complete storage/distribution system up the user points
- Optimal energy efficiency
- NO insulation requirement for tank and loop piping



LOPO C

## WFI / Pure Steam Generation

Water for injection (WFI) is the most critical raw material for parenteral pharmaceutical production. As such the qualities at the point of use are regulated in the different international pharmacopeia's such as USP, EP, JP. The EP is permitting distillation as the only method to produce WFI. Although some pharmacopeia's allow alternative production technologies, distillation is the technology of choice and industry standard for the generation of WFI.



For Pure Steam the USP has set the quality requirement for condensate of the pure steam identical to WFI quality.

### 1 **MULTITRON – high efficiency multi effect distillation**

- 316L SS construction
- Up to eight columns increasing the efficiency
- Preheaters included
- Integrated cooler / condenser
- Optional variable WFI capacity control

### 2 **VAPOTRON – fast reaction pure steam generator**

- 316L SS construction
- Constant pure steam pressure at maximum demand
- Optional preheater
- Optional Degasifier
- EN 285 compliant

MULTITRON multi effect distillation systems and VAPOTRON pure steam generators are available as individual units or as the unique COMBITRON system producing water for injection and pure steam in parallel.

## WFI Storage and Distribution

### 3 **LOOPO H – standardized compact distribution, control, monitoring and sanitization for hot WFI storage and distribution systems**

- Open skid system including DTS (Double Tube Sheet) heat exchanger
- Calibrated online analytical instrumentation for flow, pressure, temperature, conductivity
- Optional calibrated TOC analyzer
- 316L SS execution
- Optional automatic periodic sanitization with superheated water 121°C of the complete storage/distribution system up the user points
- Optional POU (point of use) DTS coolers and POU operator interface panels

## Validation, Qualification & Documentation – Successful Inspection Guaranteed

BWT Pharma & Biotech systems are qualified in accordance with the requirements of FDA, cGMP, cGAMP, cUSP and cPh. Eur. The design and the documentation are based on the 'ISPE Engineering Guide – Water and Steam Systems' and 'Commissioning and Qualification of Pharmaceutical Water and Steam Systems'. The systems are designed and built in accordance with the actual regulations of PED, EMC, LV and the Machinery Directives and carry the CE symbol.

During each project, a validation engineer accompanies all project activities in order to ensure optimal coordination of all steps, from the URS (User Requirement Specification) through all stages of the V model to the FAT/SAT. All IQ/OQ checks and tests are as far as possible and practical executed in our workshop before the factory acceptance test. BWT systems leave the factory only after successful FAT, which verifies the execution, functionality and quality of the system. This procedure permits simple and fast installation and commissioning of the system on the customer's premises and limits the implementation risk at site.

Providing a compliant and uniform technical & qualification documentation BWT will ensure clients compliance and comfort during inspections and audits. Transparent and well-structured information permits easy operation and maintenance of the systems. High quality drawings with standard tag numbering provide the basis for quick assistance and support by our experienced service engineers.



## Automation

The automation and control system is the brain and heart of every clean utility system. Executing the projects according to cGAMP requirements is the basis for best performance and results.

### **AQU@VIEW automation products**

are available for all systems and provide high quality process control with validated open source software and interface graphics. All based on international well recognized premium control products such as Siemens or Rockwell.

Based on the approved P&ID, control concept and electrical wiring diagrams a detailed functional logic (FL) document is developed. Describing well-structured all functions, controls, sequencers, set-points, alarms, priorities etc. the FL is essential basis for the qualified programming and OQ testing. Transparent documented PLC program descriptions will provide a logical and easy to understand program structure that is free of any dead code.

Independent PLC-CPU's for each skid unit provide maximum independence and safety as well as enabling all loop checks, alarm checks, operational parameter etc. during the functional FAT. This ensures a perfect tested system before shipment to site.

BWT AQU@VIEW offers many value added optional features to enhance system control and comfort.

Comfortable visual interface graphics and innovative applications such as **AQU@VIEW Data Logger** in combination with **AQU@VIEW Audit Trail** allow GMP compliant monitoring of the entire system.

Embedded in your factory DCS system you can interface via **AQU@VIEW Data Export** Ethernet connection with each of the individual systems and extract and monitor all available data.

**AQU@VIEW Remote Operation** allows complete replication of the system HMI to your office computer or remote tablet and granting you comfortable access and information of the system status. Wherever you are.

**AQU@VIEW Remote Assistance** enables skilled BWT engineers to support your operators via a safe VPN (Virtual Private Network) Internet connection in case of emergency.

With **AQU@VIEW POU Management** you can control and optimize all automatic user points in your clean media distribution system to ensure optimal supply and prioritizing.

## Customer Services

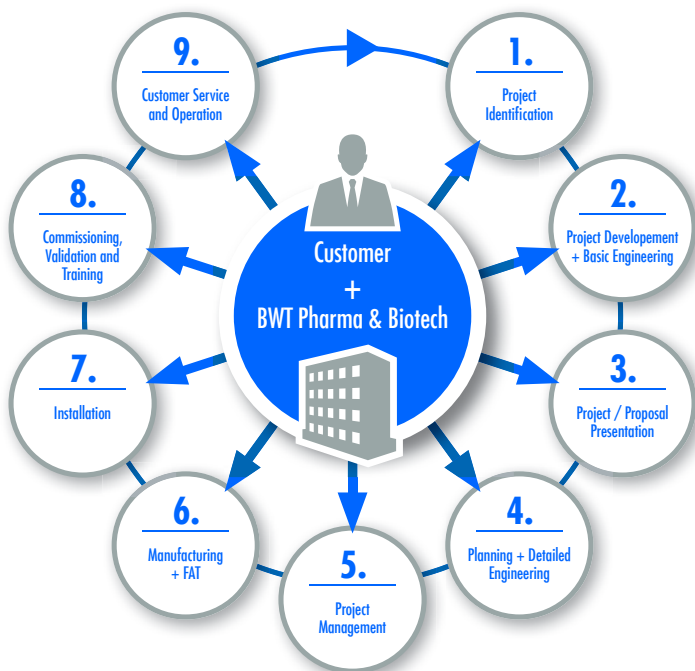
Consistent performance in quality and quantity of the clean utility systems as well as maximum availability are critical to any pharmaceutical or related production process. To safely ensure the performance during the entire system life cycle regular and well documented maintenance as well as calibration of quality relevant process instrumentation is necessary.

### **AQU@SERVICE – customer service products**

With maximum flexibility, ranging from **AQU@SERVICE GMP** scheduled preventive maintenance to **AQU@SERVICE Complete** full service packages including all wear and spare parts, allows you to configure your individual service demand.

Experienced and well trained field service engineers will provide cGMP conform service, maintenance of the complete installation and, with **AQU@SERVICE Calibration**, the routine calibration of all quality relevant instrumentation. An excellent documentation of all service activities and calibrations is self-evident.





With **AQU@SERVICE Documentation** BWT keeps your system documentation up to date with all reports, calibration certificates, change controls, data sheets and manuals of updated parts and many more, for perfect inspections and audits.

Expert know-how combined with modern tools will support and service your installation around the globe – wherever you are. Our international team is available for you 365 days per year on a 24/7 basis and, with our **AQU@SERVICE Hotline**, assisting you in all questions regarding your clean media systems.

Together with local critical spares **AQU@SERVICE Parts** provides you with a central warehouse to supply validated high quality wear and spare parts for optimal system availability.

**With BWT Pharma & Biotech AQU@SERVICE you can rely on one partner and one single point of contact for your clean media installation – wherever you are!**

## BWT – The Company

Best Water Technology Group (BWT) is Europe's leading water technology company. Our water partner network comprises the group's 3,300 employees and thousands of plumbers, planners, architects and hygiene experts. Our Research & Development teams, using state-of-the-art methods, work on new processes and materials to create products that are both ecological and economical. Looking ahead, a key development issue is a reduction in the products' use of operating resources and energy consumption and the resulting minimisation of CO<sub>2</sub> emissions.

Whether at the place where the water pipe enters the building ('point of entry') or at the tapping point ('point of use'), BWT's trend-setting 'Made in Europe' products have proved their quality millions of times over in the treatment of: drinking water, mineral water and ultrapure water for the pharmaceutical industry; water for swimming pools; heating and process water; boiler and cooling water; and water for air-conditioning. BWT's wide-ranging innovations guarantee maximum safety, hygiene and health in the daily use

of water – that precious elixir of life. These innovations, among others, include: SEPTRON<sup>®</sup>, the world's first electrodeionisation module (EDI) with spiral wrap; manganese oxide activation (MDA) – a method for effective manganese removal; AQA total bipolar technology for chemical-free limescale protection; SANISAL – the world's first regeneration salt for softening water systems, which also works as a disinfectant; and the new, revolutionary Mg<sup>2+</sup> technology that improves the taste of filtered water, coffee and tea. Through its unique, high efficiency membranes for fuel cells and batteries, BWT is creating a cleaner, more sustainable energy supply for the 21<sup>st</sup> century.

BWT – For You and Planet Blue signifies that our mission is to take ecological, economical and social responsibility, to provide our customers and partners with the best products, systems, technologies and services in all areas of water treatment and, at the same time, to make a valuable contribution to preserving the global resources of our blue planet.



**BWT** | For You and Planet Blue.  
BEST WATER TECHNOLOGY

Find us on [www.bwt-pharma.com](http://www.bwt-pharma.com)