



## **BWT AQU@SENSE MB**

The Key to a Successful  
Contamination Control Strategy  
in Pharmaceutical Water

# TIME TO TAKE NEW PATHS

The AQU@Sense MB allows you to meet the requirements for continuous germ load monitoring in pharmaceutical water fully automatically.

## Flow Cytometry

Flow cytometry is not just a high-precision method for counting all living microorganisms; it can do much, much more.

- It detects individual microorganisms, microorganisms in larger conglomerates, or bio film fragments and tells you the exact number of living cells.
- It creates a fingerprint of a microbiological population and can show any changes to it.

## The Benefits

- Time saved for approval and troubleshooting
- Greater process reliability through trend analyses
- No "false positives" or "negative" results

## "Out of the Box" Measurements

- All the solutions required for up to 1000 measurements are placed in a hermetically sealed cartridge,
- which takes just a few minutes to replace.
- Up to 99% of the cartridge is recycled.







### Online or Offline

Fixed installation  
or manual sampling

### Specific

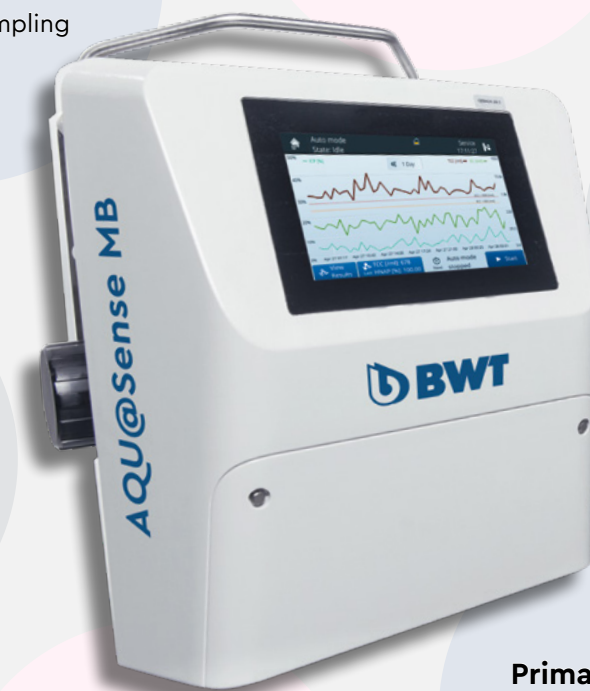
The staining method  
provides maximum speci-  
ficity for living organisms.  
No disruption caused by  
particles.

### Electronic Documentation

21 CFR Part 11-compliant  
electronic documentation

### Fully Automatic

Up to 1000 measurements  
without any manual  
intervention



### Proven Technology

The standard for drinking  
water and food for many  
years now

### Primary Validation

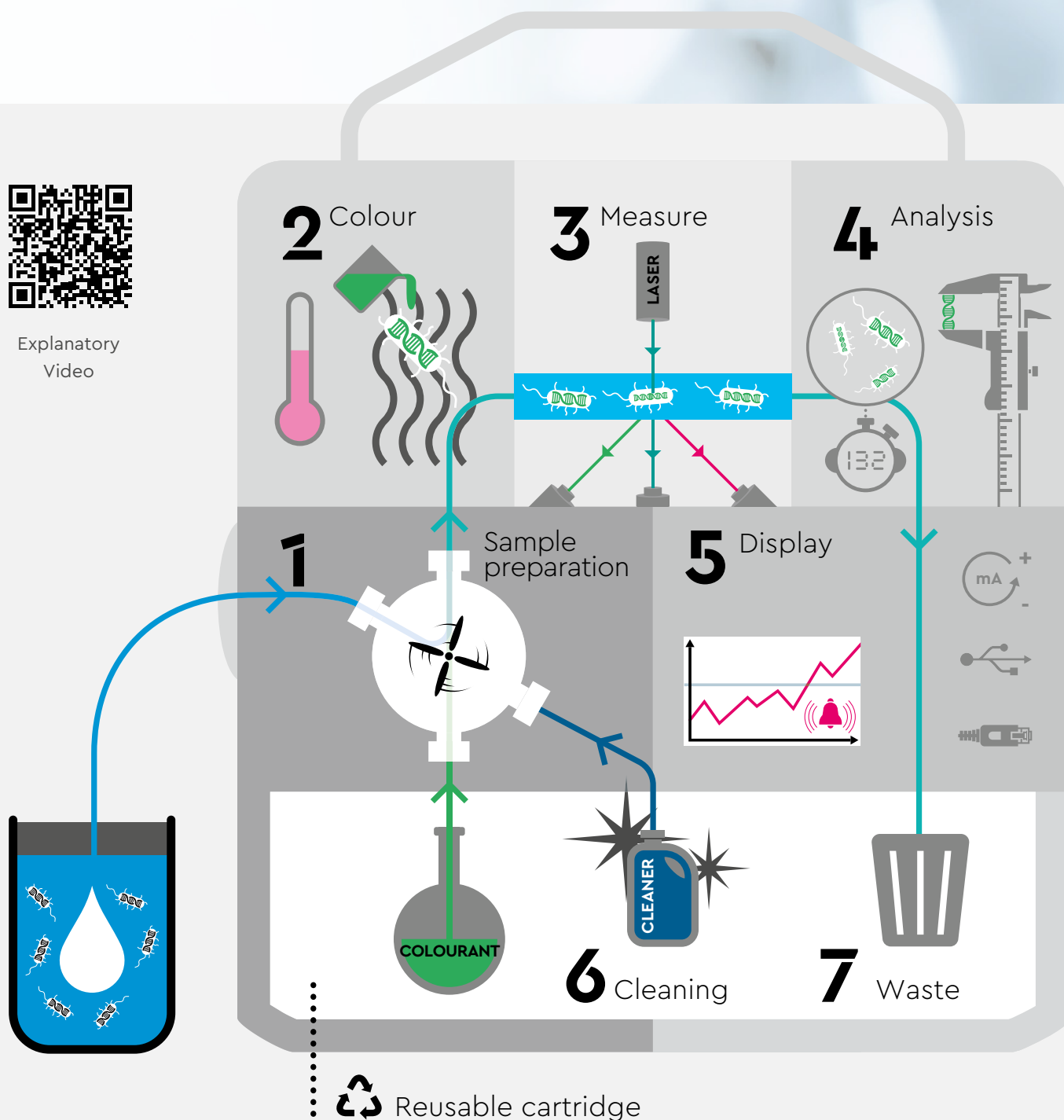
In accordance with Ph.Eur.  
and USP requirements

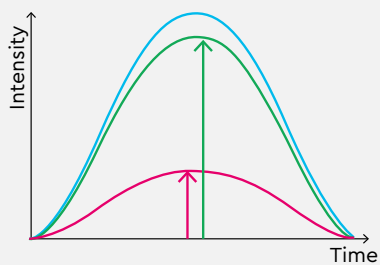
# FLOW CYTOMETRY

Quick, exact, reproducible and specific for intact cells

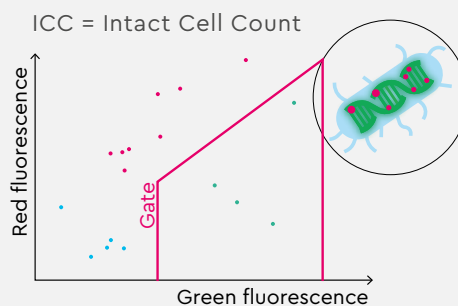


Explanatory  
Video



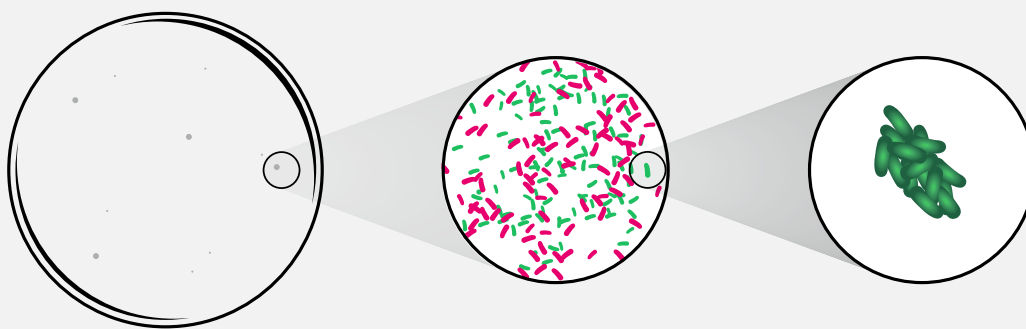


Precise identification of intact microorganisms by evaluating scattered light (blue line) and fluorescence signals (green and red lines)



The "DOT plot" compares the two fluorescence signals. The area under the gate shows a signal for each intact organism. This DOT plot is a kind of fingerprint for a population.

### The bottom line: flow cytometry counts every single living cell



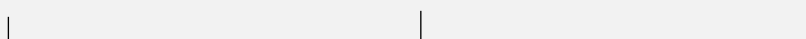
**You See Practically Nothing**

**But It Is There**

Many living organisms do not grow on the plate, but they can be stained.

**In Abundance**

Most microorganisms occur as conglomerates. They would each form just a single colony.



# CONTAMINATION CONTROL STRATEGY

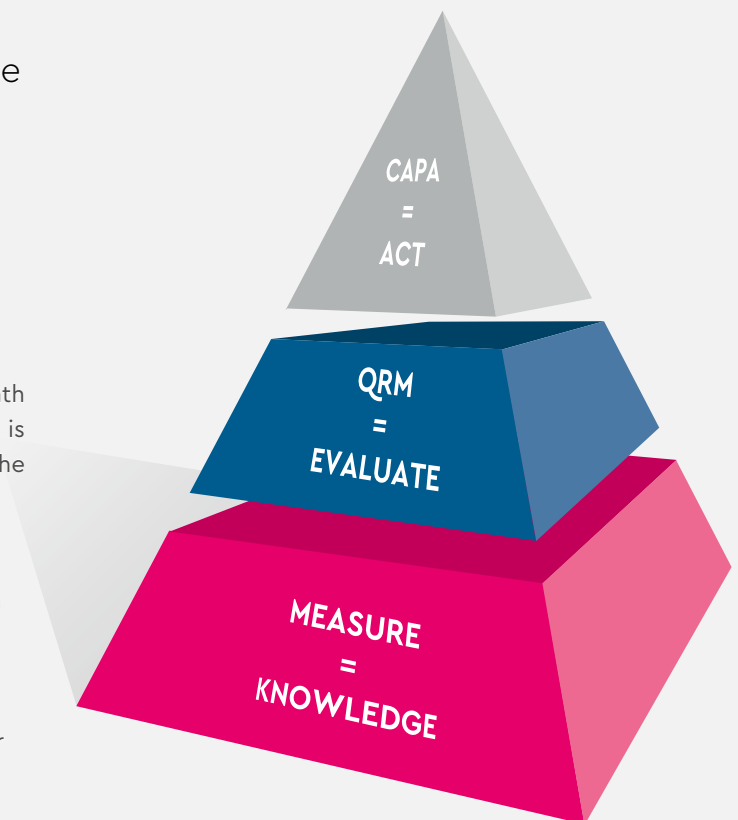
Annex 1 sets it out plainly: every system operator needs to have control over all their processes at all times, and must be able to prove that they are functioning correctly. That means seamless, risk-based monitoring has to be ensured.

## The Three Levels of a CCS

The basis for all the other steps on the path towards establishing a comprehensive CCS is accurate knowledge of the actual situation in the system.

In a data-driven approach, that means:

- Recording knowledge of the current situation for all process steps promptly
- Carrying out an assessment based on a risk analysis
- Taking suitable measures (CAPA) to correct or prevent errors





# Chapter 5.1.6 and USP

Good Manufacturing Practice (GMP) is a production standard. Many countries have legislative requirements for GMP.

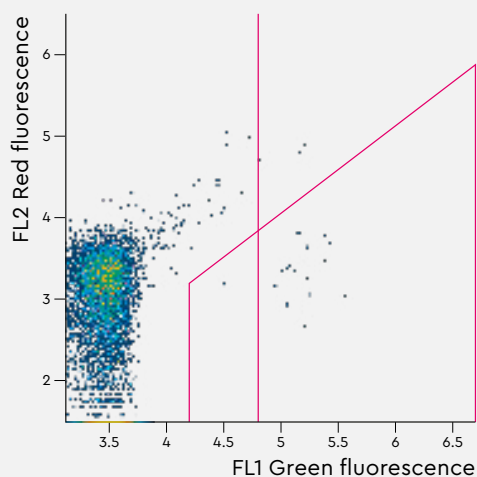
## The Plate Count Is Not the Solution

The conventional plate count (HPC) has many disadvantages, particularly regarding the time required to obtain measurement results. The use of an alternative method is recommended in Ph. Eur., Annex 1, provided that the information can deliver a scientifically sound measurement for assessing microbiological quality. The AQU@Sense MB meets these requirements.

## Alternatives Are Already Available Today

A variety of technologies for determining biological quality quickly and accurately are already available on the market.

The AQU@Sense MB uses flow cytometry technology, which is probably the most advanced technology currently available and can also be used for online bioburden monitoring. It does not just show the presence of microbiological contamination, but also provides an exact cell count. Furthermore, the measurement includes additional information about the population of the microorganisms.



A typical measurement result of flow cytometry.

# TECHNOLOGY YOU CAN TRUST

Primary validation has shown that flow cytometry significantly outperforms the conventional plate count in some areas under comparable conditions.

Flow cytometry is an established microbial counting technique. It has been used in laboratories and to assess drinking water for many years now. The AQU@Sense MB is the first flow cytometer that enables online monitoring of water quality in pharmaceutical systems. The basis for the validation of this application is a primary validation in accordance with the applicable regulations (Ph.Eur. 9.2, chapter 5.1.6 and USP 41, chapter 1223). This was carried out by BWT in collaboration with bNovate, Eindhoven University of Technology (TU/e) and the University of Applied Sciences Northwestern Switzerland (FHNW).



**Regulatory  
requirements**

**Preliminary  
studies**



**Validation  
masterplan**

**Experimental  
work**





## Results

The AQU@Sense MB passed the primary validation in full!

Parameter	Results
Accuracy	✓
Precision	✓
Specificity	✓
Quantification limit	✓
Linearity	✓
Measurement range	✓
Robustness	✓
Ruggedness	✓

## Your Next Steps...

Risk-benefit analysis  
Validation for intended use

**n|w** Fachhochschule  
Nordwestschweiz

**TU/e** EINDHOVEN  
UNIVERSITY OF  
TECHNOLOGY

Evaluation

Statistical  
analysis

Documentation



# ONE INSTRUMENT, MULTIPLE APPLICATIONS

The AQU@Sense MB can be used online or offline as a standalone device.

## IN PROCESS CONTROL

### Requirements for the method

- Specific
- Reproducible
- Quick
- Cost-effective

### Benefits of AQU@Sense MB

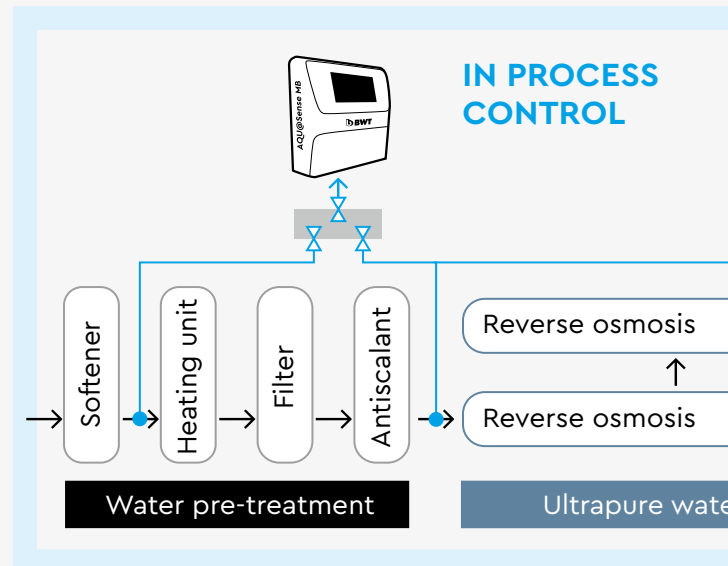
- Keep a global overview and control each step of production
- Monitoring of all process steps for biological contamination, from the incoming water to the end product
- Early detection (trending) of signs of contamination with microorganisms to take preventative measures
- Reduced costs for water samples and associated tests
- Time saved during investigations

### Trend Monitoring

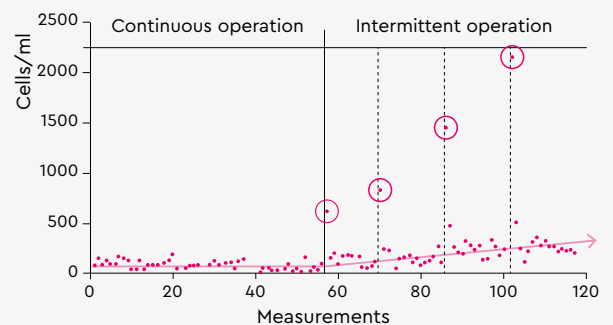
The AQU@Sense MB lets you monitor microbiological contamination changes promptly, long before critical values are reached.

### Sanitization Monitoring

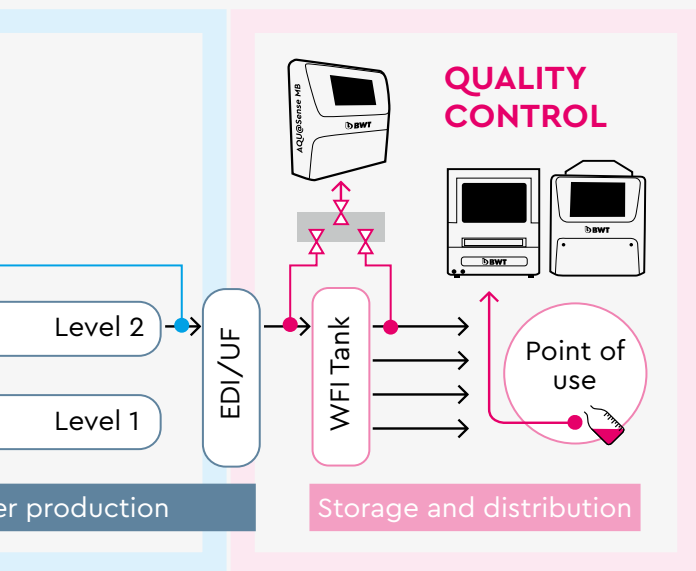
- Sanitization effect immediately demonstrable
- Faster approval following maintenance



### Trend Monitoring



Detecting changes in the system continuously and rapidly.



## QUALITY CONTROL UNIT

### Requirements for the method

- Validated
- Specific
- Reproducible
- Correct

### Benefits of AQU@Sense MB

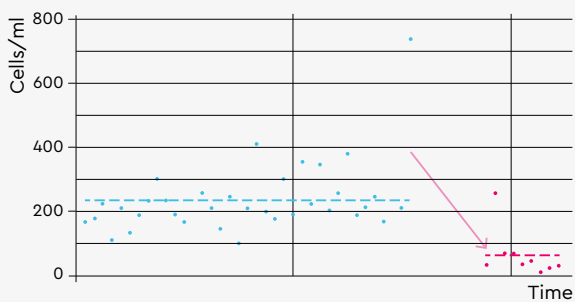
- Immediate proof of quality
- Immediate intervention when problems occur
- Rapid analysis

### Assess different results correctly

- Total bioburden background signal
- Detection and trend analysis of individual cells from conglomerates or bio film fragments.

### Sanitization Monitoring

Sanitization effect immediately demonstrable



- Permeate (before sanitization)
- Permeate (after sanitization)



# SO TIME IS ON YOUR SIDE

Do you want to investigate yesterday's problem or shape tomorrow's success?

The AQU@Sense MB gives you the data you need, quickly, reliably and conclusively. The AQU@Sense MB is not just a high-precision technology for counting all living microorganisms; it can do much, much more.

- It detects both individual organisms and organisms in larger conglomerates or biofilm fragments and tells you the exact number of living cells contained within them.
- It creates a fingerprint of a microbiological population in your system and can show any changes to it.

## **Automatic Digital Documentation**

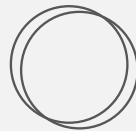
- No manual processes requiring time-consuming documentation.
- Analogue and digital interfaces to control systems
- Simple visualisation of results for further evaluations

## **Minimal Maintenance**

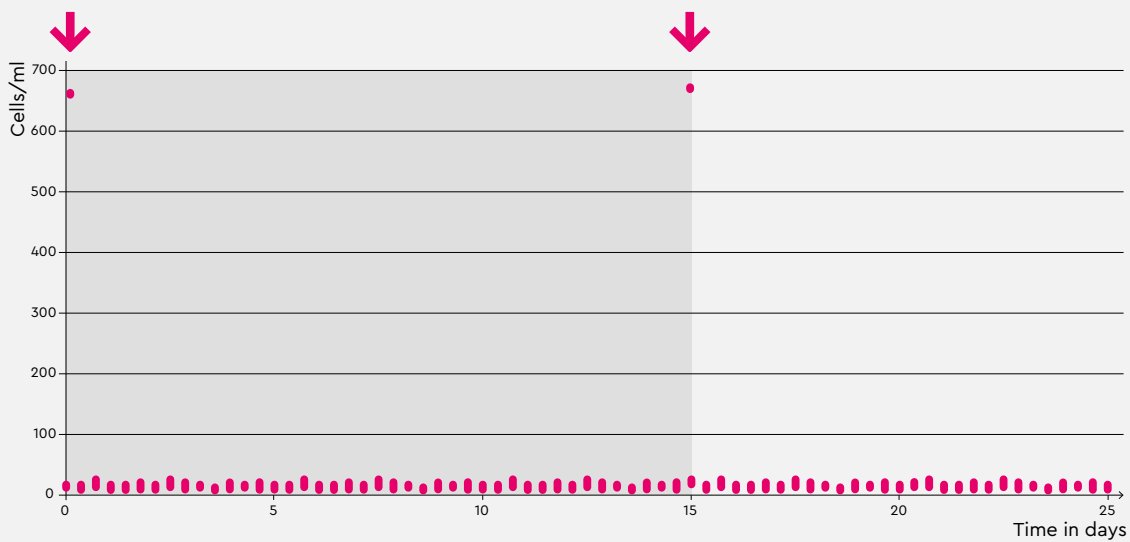
- Menu-guided cartridge replacement in minutes following 1000 measurements
- No calibration



With AQU@Sense MB  
you would notice  
this result within  
**20 Minutes.**



With HPC you  
would only notice  
this result after  
**1 to 2 weeks.**



# SERVICE AND SUPPORT

## Minimal Maintenance

The AQU@Sense MB is designed in such a way that scheduled maintenance is required just twice per year. It is performed by qualified BWT staff as part of the fully documented AQU@Service.

## Benefits

- No calibration required
- SST based on standard maintenance
- High availability as maintenance can be planned
- Transparency with maintenance and operating costs known in advance
- Hotline

## Service Range

- Integration planning
- System integration
- Documentation
- Control system programming
- Automation adjustment
- Testing
- Project execution
- Change control
- Expertise/suggestions for improvement



Hotline  
061 755 83 00





## TECHNICAL DATA

### General

<b>Measuring principle</b>	Flow cytometry
<b>Degree of protection</b>	IP65
<b>Ambient temperature</b>	+5 °C to +35 °C
<b>Humidity</b>	10 to 90% RH
<b>Dimensions (W × D × H)</b>	350 × 240 × 373 mm
<b>Weight</b>	14 kg

### Connections

<b>Outputs</b>	4 digital outputs and 2 × 4 to 20 mA analogue outputs, freely configurable
<b>Inputs</b>	4 digital inputs
<b>Sampler input</b>	¼" Swagelok tube fitting, male
<b>Sampler output</b>	¼" Swagelok tube fitting, male
<b>Energy supply</b>	DC 18 V, 1.4 A, ax. 20 W
<b>Memory card</b>	32 GB
<b>Data export</b>	USB and Ethernet

### Measurements

<b>Sample volume</b>	90 µl
<b>Measurement type</b>	Continuous or manual
<b>Measurement interval</b>	30 min. to 6 hrs
<b>Analysis duration</b>	20 min.
<b>Cartridge contents</b>	Max. 1000 measurements
<b>Sample flow</b>	100 to 200 ml per min.
<b>Max. sample temperature</b>	40 °C
<b>Sanitation capacity</b>	Ozone up to 100 ppb Hot water up to 85 °C (without running measurement)



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FOR YOU AND PLANET BLUE.