

Specifications for Water for Injection (WFI)

Information from Biochrom AG

Water for Injection (WFI) by definition is water that is intended for use in the manufacture of medicines for parenteral administration whose solvent is water (WFI in bulk), or water that is used to dissolve or dilute substances or preparations for parenteral administration (heat-sterilised WFI). WFI in bulk from Biochrom AG is sterile-filtered and intended for *in vitro* use. WFI in bulk is suitable for use in the manufacture of media for biopharmaceutical production or for the manufacture of buffers. All solutions produced by Biochrom AG for cell culture and buffers are based on WFI in bulk water quality.

WFI in bulk and heat-sterilised WFI are manufactured according to the same criteria. The two specifications differ in a few parameters: WFI in bulk has very low conductivity at the time of bottling and a very low concentration of organic components. Other parameters are the same for both specifications. An overview of the individual parameters can be illustrated in a table.

Biopharmaceutical production methods often require large quantities of "pharmaceutical-grade" ultra pure water. However, this water is only approved as Water for Injection (WFI) for the manufacture (direct or indirect) of medicines if it is of reproducible quality and satisfies the relevant specifications. Depending on local water quality, several processing steps are required in order to manufacture pharmaceutical quality water from the raw material "drinking water". The microbiological, chemical and physical parameters to be observed are specified in the European Pharmacopoeia (Ph. Eur.) and elsewhere. Validation of WFI manufacture, storage and shipping is a legal requirement.

The sterile-filtered WFI in bulk from Biochrom AG is sterile-filtered and bottled aseptically in a class A cleanroom environment. It has very low conductivity and a very low concentration of organic components (TOC, total organic carbon). In order to ensure that the water is of sufficient quality, in addition to the in-process monitoring of the electrical conductivity, the microbiological parameters are also regularly monitored, and the following parameters are amongst those that are determined: number of colony-forming units (CFU) of aerobic bacteria¹ or the level of bacteria endotoxins². These WFI in bulk parameters are within the appropriate limits (cf. table).

All parameters for both specifications are listed in the table on the next page for comparison purposes.

¹ under normal conditions the number of CFU aerobic bacteria should not exceed 10 microorganisms per 100 ml, determined by means of membrane filtration, using agar medium S and at least 200 ml WFI in bulk after 5 days' incubation at 30-35 °C

² Value for bacteria endotoxins must be below 0.25 EU/ml water

Tab.: Comparison of typical parameters for WFI in bulk from Biochrom AG and sterilised WFI

Parameter	WFI in bulk from Biochrom AG	Sterilised WFI*
Manufacture from drinking water or from purified water	x	x
Manufacturing process: Distillation	x	x
Product-contacting parts (quartz glass, neutral glass or suitable metal)	x	x
Appearance	colourless, clear	colourless, clear
(CFU) bacterial count, aerobic bacteria	Sterile (Sterile-filtered)	Sterile (Heat sterilisation in closed container)
Total organic carbon (TOC, ppb)	≤ 500	No data
Conductivity, at 20 °C (µS/cm)	≤ 1.1 at 20 °C	≤ 25 at 25 °C in containers of maximum 10 ml nominal volume (NV) ≤ 5 at 25 °C in containers with more than 10 ml NV
Nitrate (ppm)	≤ 0,2	≤ 0,2
Endotoxins (EU/ml)	< 0,25	< 0,25
Acid and alkaline solutions	***	x
Oxidisable substances	***	No data
Chloride	***	≤ 0.5 ppm in containers of maximum 100 ml NV
Sulphate	***	x
Ammonium ppm	***	≤ 0,2
Calcium, Magnesium	***	x
Residue on evaporation (percent)	***	0.004 (max 10 ml), 0.003 at more than 10 ml measurement volume

* All data in the Ph.Eur.

** At the time of bottling

***No specification acc. to Ph.Eur.