



## Milli-Q Advantage Compliance Report

The Milli-Q® Advantage water purification system from Millipore has been designed to be compliant with water quality standards in the laboratory.

The values reported in the Tables below were obtained with a Milli-Q Advantage water purification system (lot n° F7BN146811) equipped with a Q-Gard 1 (QGARDT1X1, lot n° F7PN93689), a Quantum EX (QTUM0TEX1, lot n° F7NN84696), and a Millipak 40 (MPGP04001, lot n° F7DN39762) at the point of delivery. This Milli-Q Advantage system was fed by an Elix 5 UV (lot n° F4SN68699C) water purification system, equipped with a Progard (PROG000S2, lot n° F7HN38145) and connected to a reservoir (TANKPE100, lot n° F6CN24961).

Analyses were performed in an ISO 9001:2002 certified laboratory of Millipore (R&D Center, Saint-Quentin-Yvelines, France), or in an accredited laboratory (Sumika Chemical Analysis Service Ltd, Japan, ISO9001 and ISO17025 certified). Methods and validated equipments utilized are described after the Tables. Tables are organized by Standards and Norms, followed by Pharmacopeiae and Guidelines.

### Water quality specifications

#### 1- Norms and Standards

ASTM D1193 – Type I

Parameters	Resistivity (MΩ.cm) - 25°C	Conductivity (µS/cm) – 25°C	TOC (µg/L)	Total silica (µg/L)	Chloride (µg/L)	Sodium (µg/L)
Specification	> 18	< 0.056	< 50	< 3	< 1	< 1
Values in water produced by Milli-Q Advantage	18.2	0.055	4.2	< 0.5 (QL)	< 0.5 (QL)	< 0.5 (QL)
Method	A	A	B	C	D	D

QL: quantification limit

Chinese National Standard – Grade 1

Parameters	Conductivity (mS/m) - 25°C	Conductivity (µS/cm) - 25°C	Resistivity (MΩ.cm) - 25°C	UV absorbance 254 nm (AU)	Total silica (mg/L)
Specification	< 0.01	< 0.1	> 10	< 0.001	< 0.01
Values in water produced by Milli-Q Advantage	0.0055	0.055	18.2	0.0004	0.0006
Method	A	A	A	E	F

ISO 3696 – Grade 1

Parameters	Conductivity (µS/cm) - 25°C	UV absorbance 254 nm (AU)	Silica (mg/L)
Specification	< 0.1	< 0.001	< 0.01
Values in water produced by Milli-Q Advantage	0.055	0.0004	0.0006
Method	A	E	F

## 2- Pharmacopeiae

European Pharmacopeia (EP) – Purified water

Parameters	Conductivity (µS/cm)	TOC (µg/L)	Bacteria (cfu/mL)	Heavy metals (mg/L)	Nitrates (mg/L)
Specification	< 1.1 at 20 °C	< 500	< 100	< 0.1	< 0.2
Values in water produced by Milli-Q Advantage	Pass	Pass	Pass	Pass	Pass
Method	A	G	H	I	J

Japanese Pharmacopeia (JP) – Purified water

Parameters	Acidity & Alkalinity	Chloride	Sulfate	Nitrate	Nitrite	Ammonium	Heavy metals	KMnO4 reducing matters	Dry residue 105°C
Specification	Color change	AgCl precipitate test	BaSO4 precipitate test	Specific test	Specific test	< 0.05 ppm Specific test	Specific test	Specific test	< 1 mg in 100 mL
Water produced by Milli-Q Advantage	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
Method	K	L	M	N	O	P	Q	R	S

US Pharmacopeia (USP) – Purified water

Parameters	Conductivity (µS/cm) – 25 – 30 °C – non compensated	TOC (µg/L)
Specification	< 1.3	500
Suitability test	Pass	Pass
Method	T	G

## 3- Guidelines

CLSI C3-A4 – Clinical Laboratory Reagent Water (CLRW) grade

Parameters	Resistivity (MΩ.cm) - 25°C	TOC (µg/L)	Bacteria (cfu/mL)
Specification	> 10	< 500	< 10
Values in water produced by Milli-Q Advantage	18.2	4.2	< 1
Method	A	B	H

## Methods and equipments

The following methods and equipments were used for the measurements reported in the Tables. All equipment utilized in Millipore R&D was qualified according to the Millipore ISO standard procedures. Specific information on calibration and qualification frequency can be requested upon demand.

### Method A

Conductivity measured in-line using a Thornton 200CR (N° 604070449). Measurement done in quadruplicate. (Millipore).

### Method B

The Total Organic Carbon (TOC) was measured utilizing an on-line TOC analyzer using a combination of persulfate, phosphoric acid and UV 185 nm for the oxidation process. (Millipore).

### Method C

Total silica measured by graphite furnace atomic absorption (GFAAS Varian SpectrAA 880Z). Method ASTM D1197 and JIS K0555. (Sumika Chemical Analysis Service Ltd (SCAS), Japan).

### Method D

Concentrations of chloride and sodium were obtained using an ion chromatography system Dionex ICS 3000. Chloride analysis: A AS19 (2 x 250 mm) column, with a AG19 (2 x 50 mm) guard column, and ASRS Ultra II 2 mm suppressor were used for the chloride analysis; Spex Certiprep standard 1000 ppm AS-CL9-2X/2Y, lot n° 1-50CL-2; Calibration with 0.1, 0.5, 1 and 2 ppb solutions.

Sodium analysis: A CS12A 3 x 150 mm column, with a CG12 3 x 30 mm guard column, and CSRS 300 2 mm suppressor were used for sodium analysis; Spex Certiprep standard 1000 ppm CS-NA2-2Y, lot n° 12-141NA; Calibration with 0.1, 0.5, 1 and 2 ppb solutions. (Millipore).

### Method E

UV Absorbance measured at 254 nm in a 1 cm length quartz cell, using a Shimadzu Pharmaspec UV1700 spectrophotometer. Measurement done in quadruplicate. (Millipore).

### Method F

Silica measurement using the hetero poly blue method 8186. Hach Spectrophotometer DR/2500 (N° serie 030100004582). (Millipore).

### Method G

#### TOC USP

Tests were performed with an on-line TOC analyzer using a combination of persulfate, phosphoric acid and UV 185 nm for the oxidation process. The instrument is certified by the manufacturer to pass the USP suitability test, monography <643>. (Millipore).

### Method H

Heterotrophic plate count method. Bacterial count was obtained from a 100 mL water sample collected under standard operating conditions of sampling for microbiology. The sample was filtered through a 0.45 µm HAWG (Millipore) membrane, using a Milliflex apparatus. The filter was placed in contact with R<sub>2</sub>A medium (Millipore), and the plate was incubated for 72 hrs at 37 °C. Samples were collected in duplicate. (Millipore).

### Method I

Heavy metals. The method described in the European Pharmacopeia IV was used. (Millipore).

### Method J

Nitrates. The method described in the European Pharmacopeia IV was used. (Millipore).

### Method K

Acidity and Alkalinity. The method described in the Japanese Pharmacopeia was used. (SCAS).

### Method L

Chloride. The method described in the the Japanese Pharmacopeia was used. (SCAS).

### Method M

Sulfate. The method described in the Japanese Pharmacopeia was used. (SCAS).

#### Method N

Nitrate. The method described in the Japanese Pharmacopeia was used. (SCAS).

#### Method O

Nitrite. The method described in the Japanese Pharmacopeia was used. (SCAS).

#### Method P

Ammonium. The method described in the Japanese Pharmacopeia was used. (SCAS).

#### Method Q

Heavy metals. The method described in the Japanese Pharmacopeia was used. (SCAS).

#### Method R

KMnO<sub>4</sub> reducing matters. The method described in the Japanese Pharmacopeia was used. (SCAS).

#### Method S

Dry residue. The method described in the Japanese Pharmacopeia was used. (SCAS).

#### Method T

Conductivity USP, monography <645>. A Thornton 200CR instrument was used (N° 604070449). (Millipore).

## References

### **ASTM D1193 – 06 Standard Specification for Reagent Water**

Active Standard ASTM D1193 Developed by Subcommittee: D19.02

Book of Standards Volume: 11.01

ICS Number Code 71.040.30

**CLSI.** Preparation and testing of reagent water in the clinical laboratory; Approved guideline – Fourth edition. C3-14, Vol 26, N° 22, Clinical and Laboratory Standards Institute.

### **ISO 3696**

#### **Laboratory water for analytical purpose – Specification and test methods**

Edition: 1 | Stade: 90.93 | TC 47

ICS: 71.040.30 USP

### **The European Pharmacopoeia 6<sup>th</sup> Edition**

Author: Council of Europe European (COE) - European Directorate for the Quality of Medicines (EDQM)

Publication Date: 23 July 2007

### **The Japanese Pharmacopoeia Fifteenth Edition. (JP XV)**

Official from March 31, 2007 .

Edited by Society of Japanese Pharmacopoeia. 2007

### **The United States Pharmacopeia : USP31-NF26**

by authority of the United States Pharmacopoeial Convention

### **Chinese National Standard**

GB6682