



Is Ultrapure Water Validatable

Harry Yao, Ph.D.
RephiLe Bioscience, Ltd.

What is Ultrapure (UP) Water

Contaminant	Parameter (units)	Type 1	Type 2	Type 3
Ions	Resistivity (MΩ-cm)	> 18.0	> 1.0	> 0.05
	Silica (ppb)	< 10	< 100	< 1000
Organics	TOC (ppb)	< 20	< 50	< 200
Particles	particles > 0.2 um (#/ml)	< 1	NA	NA
Bacteria	Bacteria (cfu/ml)	< 1	< 100	< 1000
	Endotoxin (EU/ml)	< 0.001	NA	NA

Published Standards:

- ASTM: American Society for Testing and Materials
- CLSI: Clinical and Laboratory Standards Institute
- CAP: College of American Pathologists
- ISO: International Organization for Standardization
- *USP: United States Pharmacopoeia*
- *EU: European Pharmacopoeia*



What Grade of Water Do I need

Type II for some Pharmaceutical analysis

- TOC analysis: conductivity <1 $\mu\text{S}/\text{cm}$, TOC <100 ppb

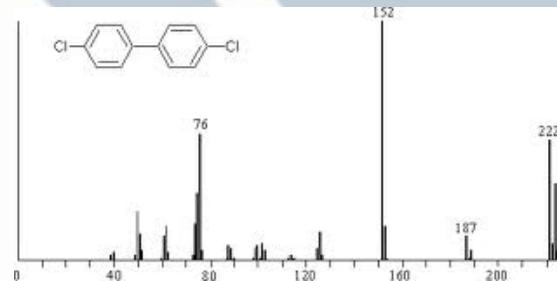
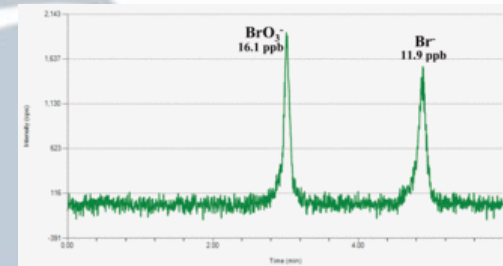
Type I water for more assurance in analysis

		EP	USP	ISO3696	ASTM
Conductivity ($\mu\text{S}/\text{cm}@25^\circ\text{C}$)		<4.3	<1.3	0.1	0.056
Resistivity ($\text{M}\Omega\cdot\text{cm}$)	0.23	0.77	10	18	
TOC (ppb)	<500	<500	/	<50	
Bacteria (cfu/ml)	<100	<100	/	<1	
Particle $>0.22\mu\text{m}$ (/ml)	/	/	/	/	/

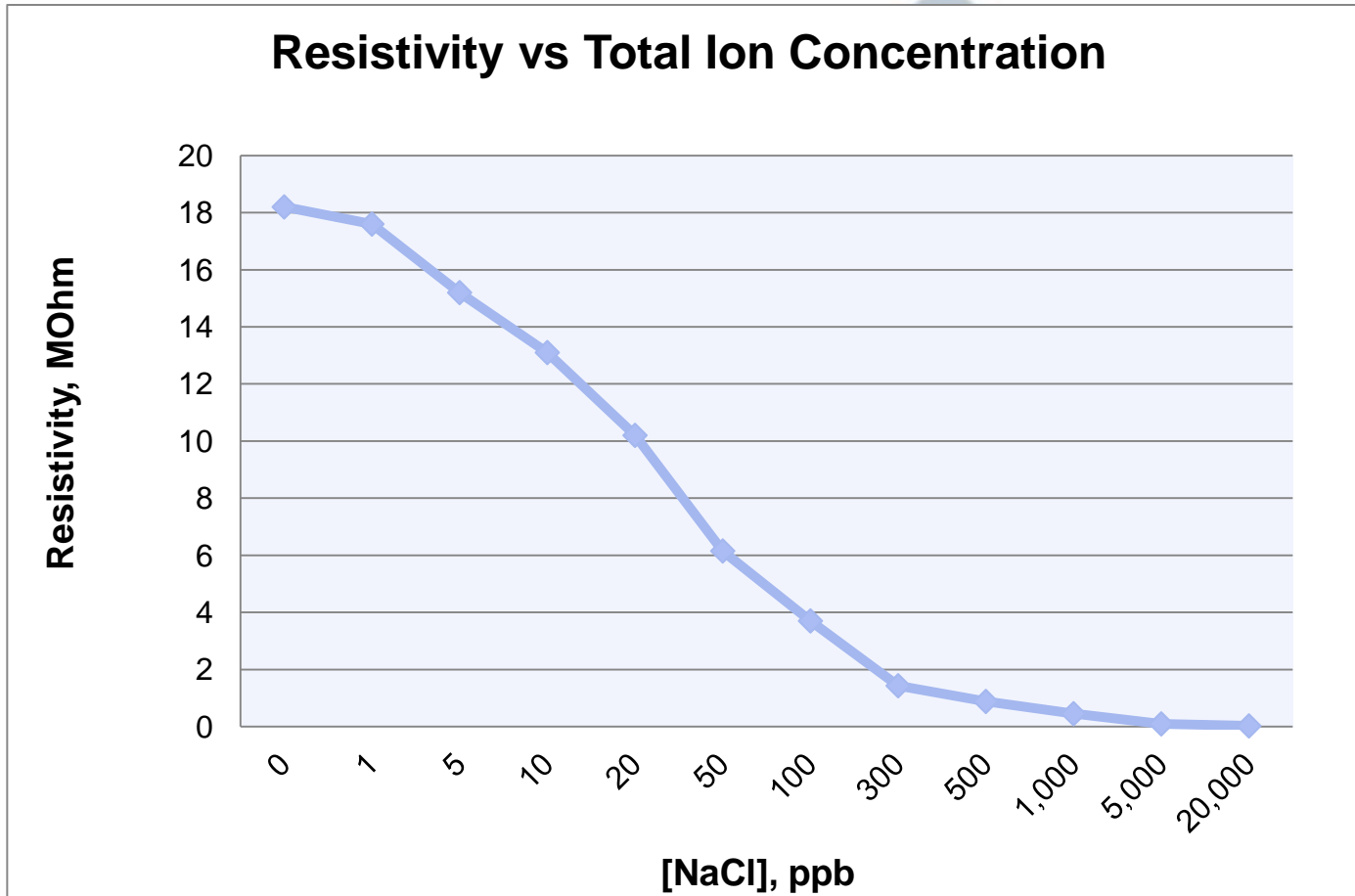
Ultrapure (UP) Water

In sample dilution, standards, mobile phase, blanks, buffer, media, rinse solutions

- ICP-Mass: bias
- LC-Mass: Na⁺ and K⁺ adduct peaks
- IC: baseline, chelates
- HPLC: additional peaks, baseline, resolution
- IVF: +pyrogen, bacteria

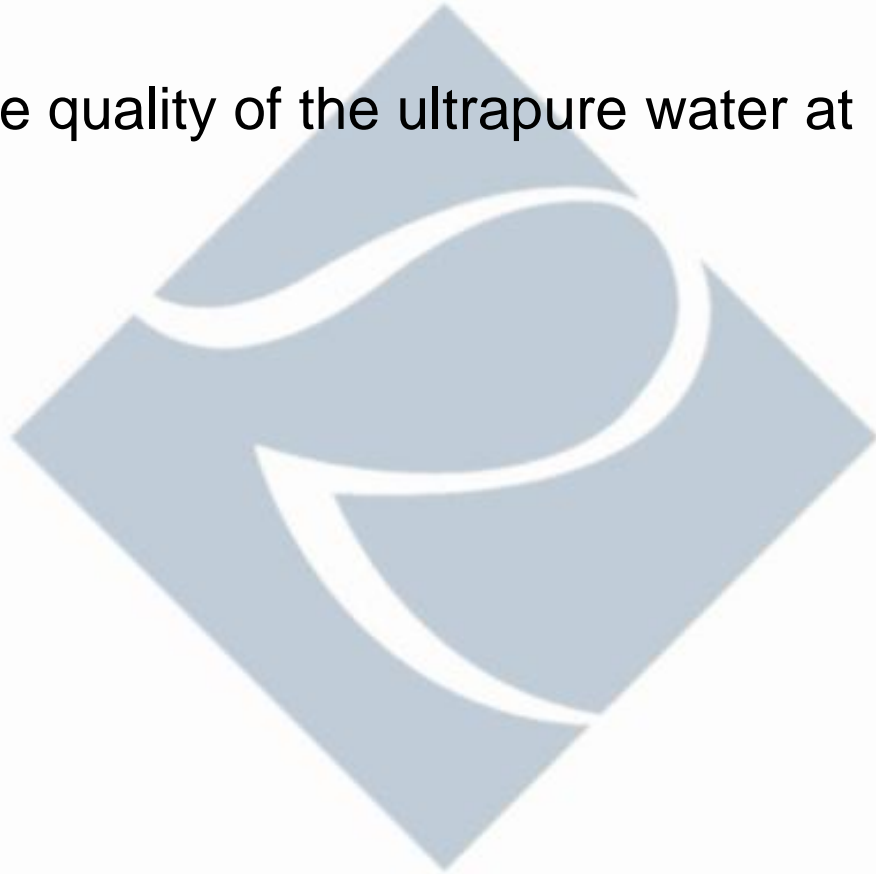


What Does Resistivity Mean



What Determines Its Quality

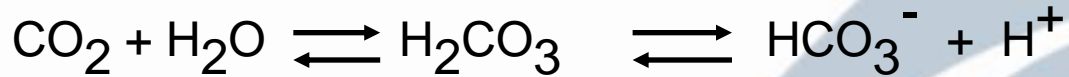
- What determines the quality of the ultrapure water at POU?



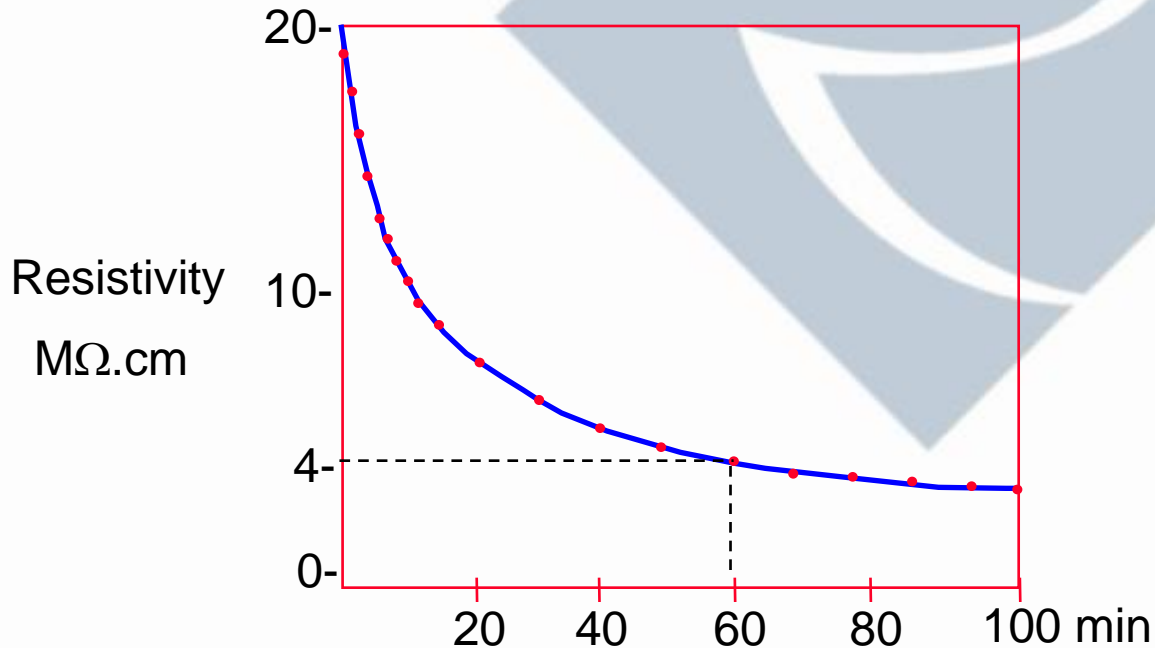
UP Water Cannot Be Stored

- Water quality deteriorates quickly upon storage

CO₂ in the air dissolves in UP water quickly



At equilibrium, $[\text{H}^+]$ from $\text{H}_2\text{CO}_3 = 2 \times 10^{-6}$ mol/L (pH 5.7)

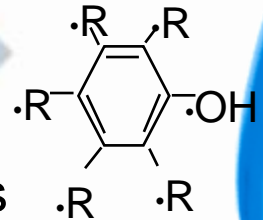


UP Water Is Validatable

Validation is for both the system and the product

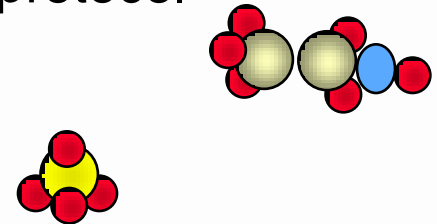
- IQ, OQ –validate functionality of the system
- PQ – validate performance of its product: UP Water
- **Must be measured in-line** with a calibrated meter

- Resistivity
- TOC
- pH measurement is not feasible and meaningless



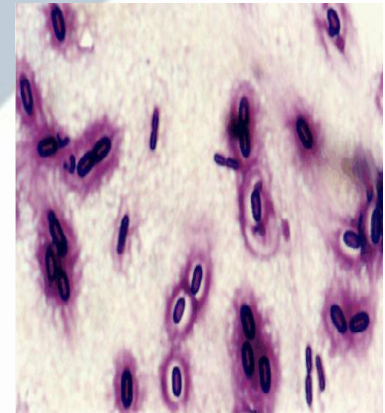
No other ions, thus pH is 7

- Other parameters as required by your protocol
 - Bacteria count
 - Endotoxins
 - Particle count



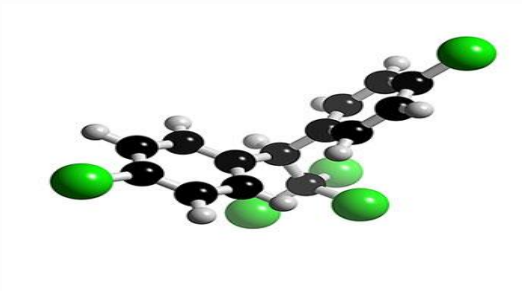
Delivery of UP Water

- Not suitable with carboys
- Must use low extractable plastics or 316 stainless steel tubing
- 0.2 μm final filter at delivery point is needed to remove bacteria
- Resistivity must be detected and validated at the farthest delivery point in a multi point of delivery system
- A UP system must have periodic recirculation to prevent microbial growth



Storage of Pure Water

- With specially designed PP, PE or stainless steel water tanks
- Protect water from airborne contaminants with a tank vent filter with CO₂ scavenger
- UV lamp in the tank can effectively inhibit microbial growth
- Storage time: 1 day





THANK YOU