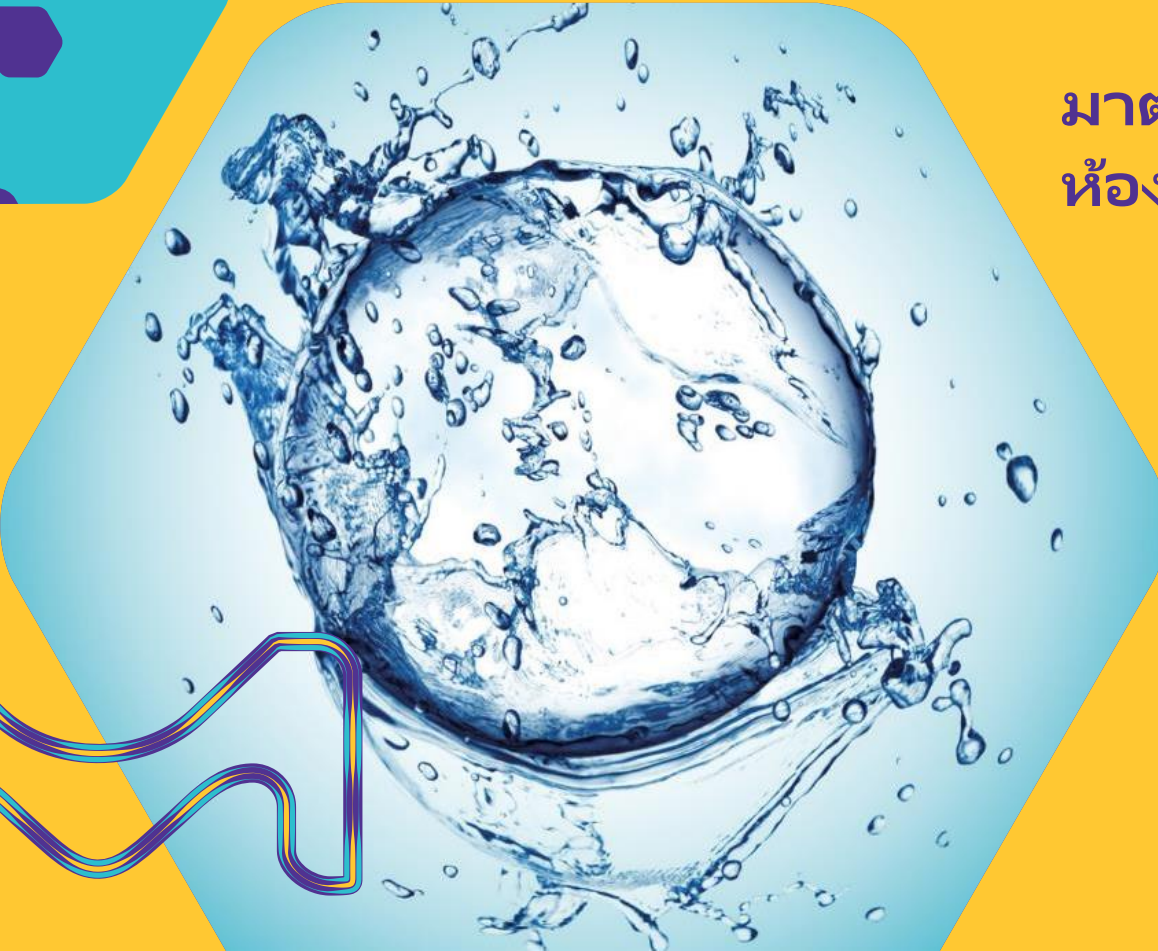


Milli-Q® Lab water Applications

มาตรฐานน้ำบริสุทธิ์สำหรับงาน
ห้องปฏิบัติการ

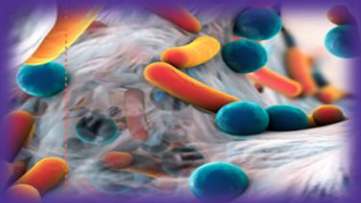
Arpa Suveatvatanakul
Senior Sales Specialist, Lab Water Solutions

MERCK



Common water contaminants

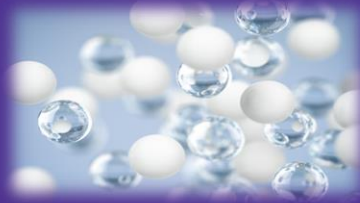
Bacteria & bacterial by-products



Bacteria: *Ralstonia pickettii*, *Pseudomonas aeruginosa*

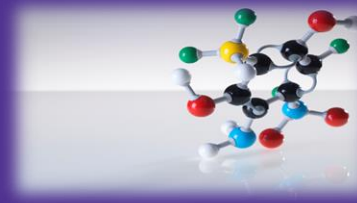
Bacterial by-products: alkaline phosphatase...

Ions



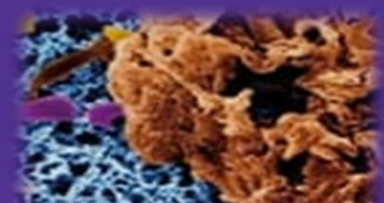
Ca^{2+} , K^{+} , Na^{+} , Cl^{-} , Fe^{2+} ...

Organics



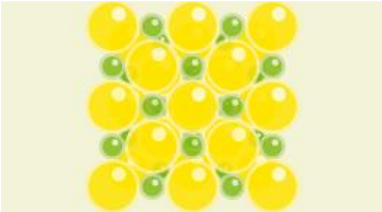
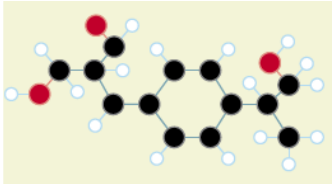
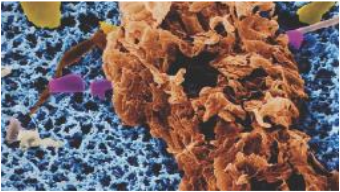
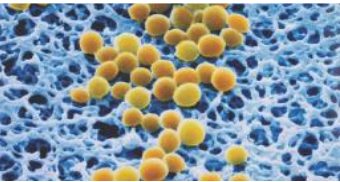
Dissolved biological molecules, VOCs, pesticides, plasticizers...

Particulates



Silica, Pollen, Salt Crystals...

Water Contaminants

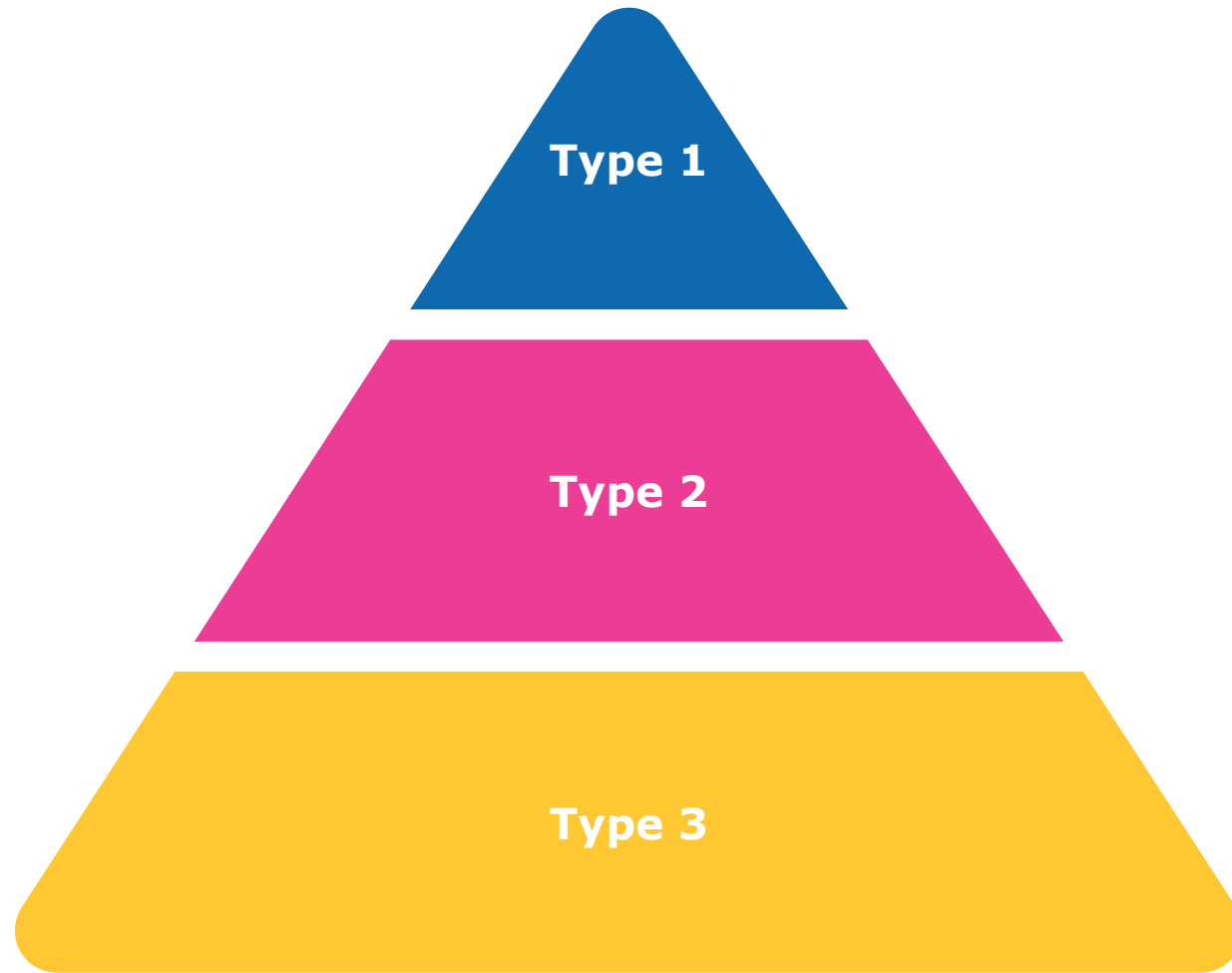
Inorganic Ions		Cations Na+ Ca+2	Anions Cl- HCO-3
Organics		Natural Tannic Acid Humic Acid	Man Made Pesticides Herbicides
Particles (Colloids)		Non Dissolved Solid Matter (Small deformable solids with a net negative charge)	
Microorganisms (Endotoxin)		Bacteria , Algae , Microfungi (Lipopolysaccharide fragment of Gram negative bacterial cell wall)	

Measurement of Contaminants

Contaminants	Measurement	Unit
Inorganic Ions	Conductivity (Resistivity)	$\mu\text{s}/\text{cm}$ $\text{M}\Omega.\text{cm}$
Organics	Total Oxidizable Carbon (TOC)	ppm (mg/L), ppb ($\mu\text{g}/\text{L}$)
Particles (Colloids)	Silt Density Index / Fouling Index	Rate of pluggage of $0.45\ \mu\text{m}$ membrane.
Bacteria	Colony count on $0.45\ \mu\text{m}$ Membrane.	cfu/ml

water quality types and norms

Laboratory water types



- **Ultrapure water**
- Targeted contaminant removal

- **Critical applications:**
HPLC, LC-MS, GFAA ,
ICP-MS, GC-MS,
Molecular Biology ...

- **Pure water**
- Consistent water quality

- **Standard Applications:**
Preparation of buffers,
microbiology media,
glassware rinsing

- **Pure water**
- Final quality subject to incoming water quality

- **Basic lab needs:**
Non-critical rinsing,
heating baths...

Laboratory Water Purity Specifications

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)	< 10	< 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

Laboratory Water Purity Specifications

Regulatory Agencies with Published Standards



- ASTM: American society for Testing and Materials
- ISO: International Organization for Standardization
- CLSI: Clinical and Laboratory Standards Institute
- CAP: College of American Pathologists
- USP: United States Pharmacopoeia
- EP: Euporean Phamacopoeia

ASTM* Standards

	Electrical Conductivity $\mu\text{S}/\text{cm}$ at 298 K (25 °C)	Electrical Resistivity M Ω -cm at 298 K (25 °C)	pH at 298 K (25 °C)	Total Organic Carbon (TOC), max, $\mu\text{g}/\text{L}$	Sodium, max, $\mu\text{g}/\text{L}$	Chlorides, max, $\mu\text{g}/\text{L}$	Total silica, max, $\mu\text{g}/\text{L}$	Maximum heterotrophic bacteria count, mL	Endotoxin, EU/mL
Type I	0.0555	18	N. A.	50	1	1	3	-	-
Type IA	0.0555	18	N. A.	50	1	1	3	10/1000	< 0.03
Type IB	0.0555	18	N. A.	50	1	1	3	10/100	0.25
Type IC	0.0555	18	N. A.	50	1	1	3	100/10	N. A.
Type II	1.0	1.0	N. A.	50	5	5	3	-	-
Type IIA	1.0	1.0	N. A.	50	5	5	3	10/1000	< 0.03
Type IIB	1.0	1.0	N. A.	50	5	5	3	10/100	0.25
Type IIC	1.0	1.0	N. A.	50	5	5	3	100/10	N. A.
Type III	0.25	4.0	N. A.	200	10	10	500	-	-
Type IIIA	0.25	4.0	N. A.	200	10	10	500	10/1000	< 0.03
Type IIIB	0.25	4.0	N. A.	200	10	10	500	10/100	0.25
Type IIIC	0.25	4.0	N. A.	200	10	10	500	100/10	N. A.
Type IV	5.0	0.2	5.0 to 8.0	No limit	50	50	No limit	-	-
Type IVA	5.0	0.2	5.0 to 8.0	No limit	50	50	No limit	10/1000	< 0.03
Type IVB	5.0	0.2	5.0 to 8.0	No limit	50	50	No limit	10/100	0.25
Type IVC	5.0	0.2	5.0 to 8.0	No limit	50	50	No limit	100/10	N. A.

*ASTM (American Society for Testing and Materials)

ISO® (International Organization for Standardization) - Several industry sectors

ISO 3696 standard

Parameter	Grade 1	Grade 2	Grade 3
pH @ 25 °C	Not applicable	Not applicable	5.0 – 7.5
Conductivity (µS/cm) @ 25 °C, max	0.1	1.0	5.0
Oxidizable substances, Oxygen (O) level (mg/l), max	Not applicable / Specific test to perform	0.08	0.4
254 nm absorbance (1 cm path), (AU), max	0.001	0.01	Not specified
Dry residue (mg/kg) after evaporation at 110 °C	Not applicable / Specific test to perform	1	2
Silica (SiO ₂), (mg/l), max	0.01	0.02	Not specified

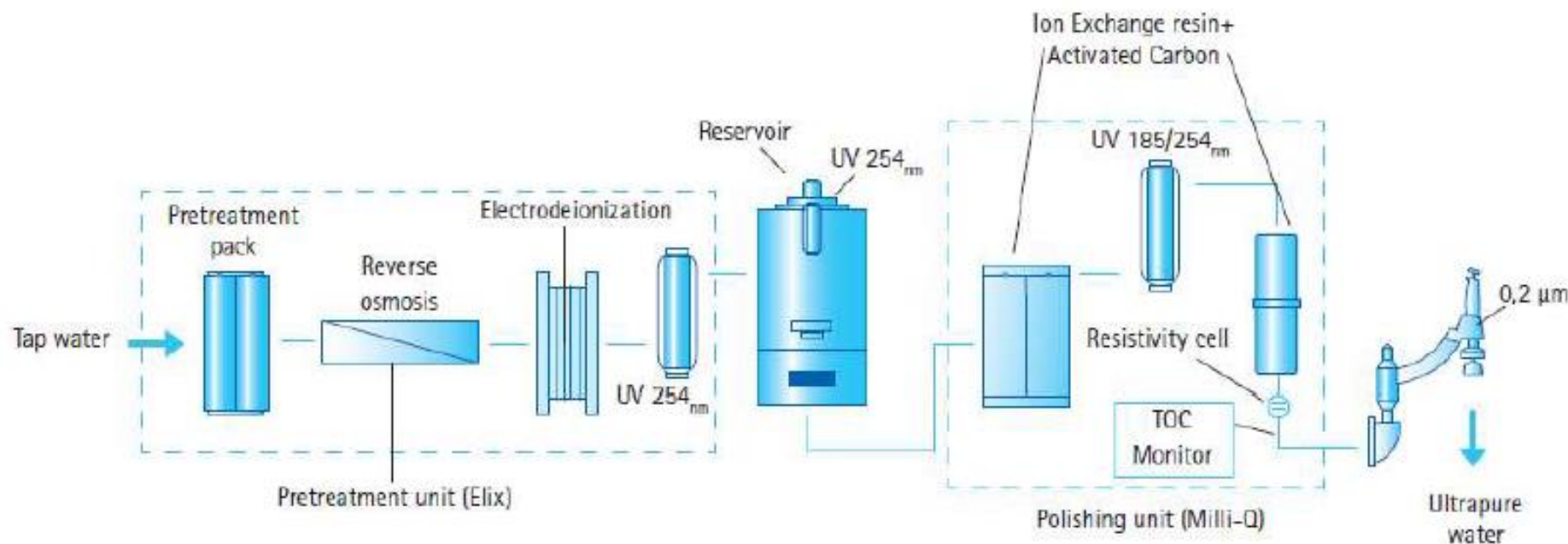
US and European Pharmacopoeia

Summary specifications	USP Purified Water	EP Purified Water	EP Highly Purified Water
Source water	Drinkable water according to EPA, EU		
Conductivity	< 1.3 $\mu\text{S}/\text{cm}$ @ 25 °C*	< 4.3 $\mu\text{S}/\text{cm}$ @ 20 °C	< 1.1 $\mu\text{S}/\text{cm}$ @ 20 °C
TOC (ppb of C)	500 **	500 **	500 **
Bacteria Action level, max	FDA specifications: < 100 cfu/mL	< 100 cfu/mL	< 10 cfu/ 100 mL
Pyrogens (EU/mL)	NA	NA For dialysis < 0.25	< 0.25

* Refer to USP 32 <645> or EP Monographies

** Refer to USP 32 <643> or EP Monographies

Optimal Purification Change



	RO	EDI	UV-254	UV-254	IX	AC	UV-185	0.22μm/ (UF)
Ions	X	X			X			
Organics	X					X	X	
Particles	X							X
Bacteria	X		X	X				X
Enzymes/endotoxins								(X)

Versatile solutions



Tap water

Pretreatment



Pure water



- Microbiology media
- Titration, pH
- ELISA
- Kjeldahl
- Washers, autoclaves

Polishing



**Ultrapure water
(Type 1)**



- HPLC, LC-MS
- Ion Chromatography
- Elemental analysis (AAS, ICP)
- Molecular Biology



**Water for trace
elemental analyses**

- Ultra-trace ICP-MS, GF-AAS

Lab Water Solutions

💧 Ultrapure Water - Type 1

FROM TAP TO PURE & ULTRAPURE WATER

Milli-Q® IQ
7003/05/10/15



Milli-Q® EQ
7008/16



Milli-Q® SQ
240/240L/240XL/
240C/240CI



FROM PURE TO ULTRAPURE WATER

Super-Q®



Milli-Q®
IQ 7000



Milli-Q®
EQ 7000



Milli-Q® SQ
200/200P



🔥 Pure Water - Type 2

FROM TAP TO PURE WATER

Milli-Q®
HX 7000
Series



Milli-Q®
HX 7000 SD
Series



Milli-Q® IX
7003/05/10/15



Elx® Essential



Milli-DI®



💧 Pure Water - Type 3 & RO

FROM TAP TO PURE WATER

Milli-Q®
HR 7000
Series



RiOs™ Essential I



Milli-Q® SR
240/240L/240XL



💧 CLRW Biomedical Water

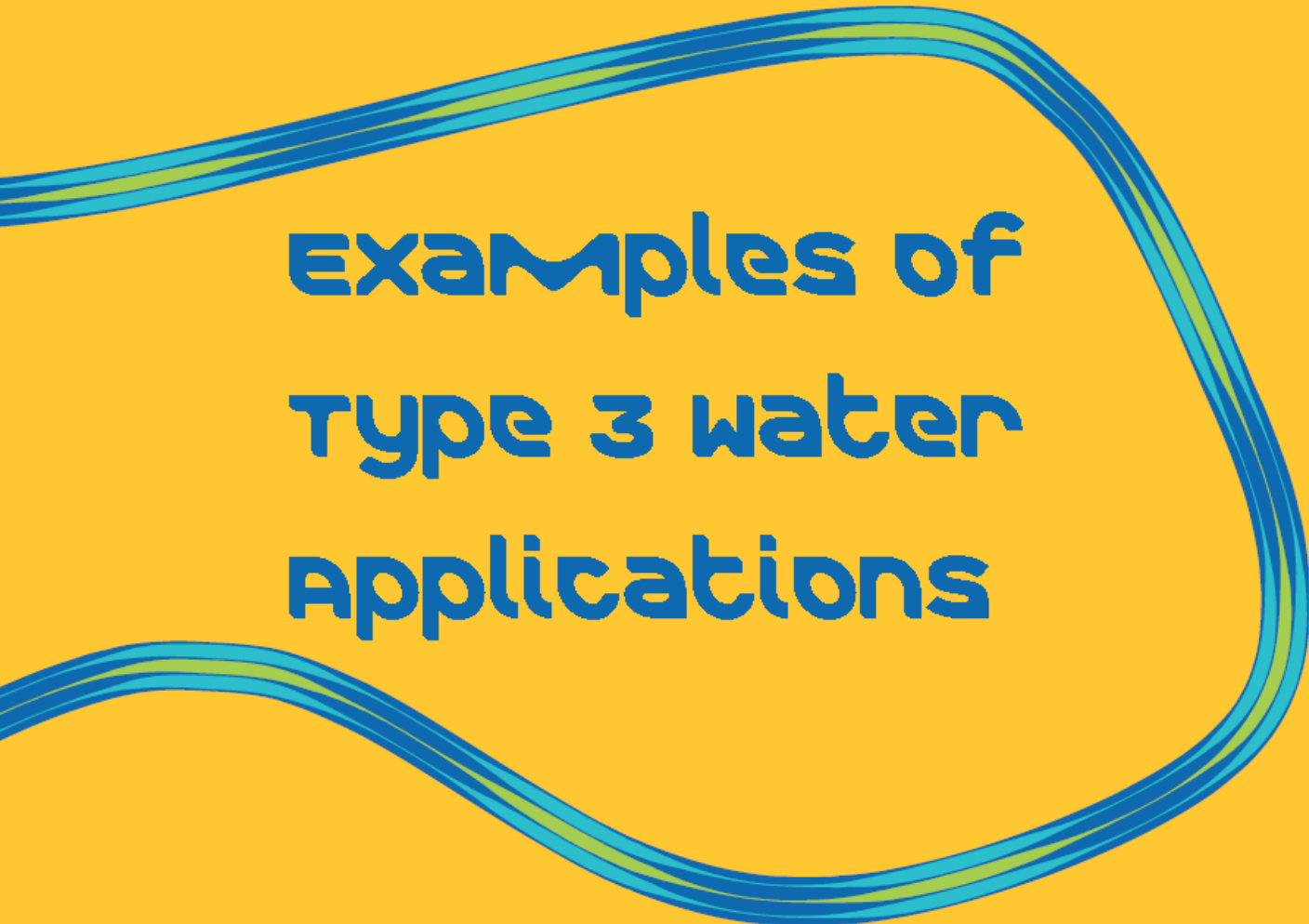
PURE WATER FOR BIOMEDICAL LABS

Milli-Q®
CLX 7000
Series



AFS®, AFS® D,
AFS® E
(AFS®, analyzer-
feed-systems)





examples of type 3 water applications

Type 3 – Animal Facilities

Academia, Pharma

For rodent facilities, avoid:

- **hardness** (clogs water lines)
- **particles** (clog water lines)
- **bacteria** (<1 coliform/100 mL), viruses
- potentially harmful or carcinogenic **chemicals** (heavy metals, chlorination by-products, pesticide residues)
- daily **variations** in water quality
- high levels of **organics** (= “food” for bacteria)

Water quality:

Reverse-osmosis, followed by a maintenance level of disinfectant biocide (chlorine, acidification or ozone)

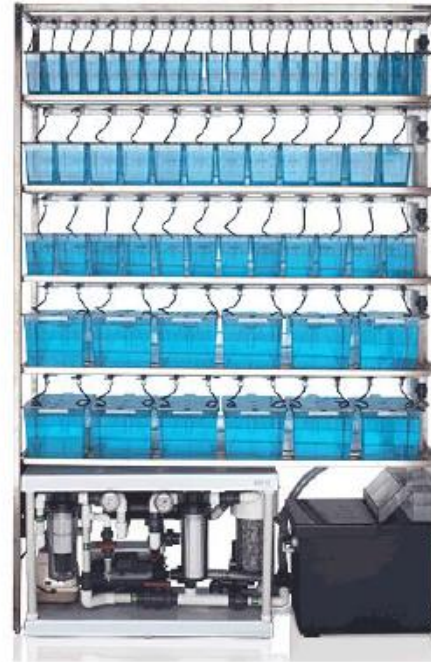


Milli-Q®

Type 3 - water for fish tanks

Academia, Pharma

TECNIPLAST
Innovation through passion™



Zebrafish



Water purified by **RO** for water make-up and replenishment



Milli-Q®

TYPE 2 OR 3 – GLASS-WASHING FINAL RINSE

Water quality selected based on specific applications

Typical glass-washing machine cycle:

- Initial rinse with tap water
- Wash with softened water + detergent.
- Multiple rinses with softened water
- **Final rinse(s) with Type 2 or 3 water**
(sometimes Type 1) to ensure contamination removal



Miele
PROFESSIONAL

GETINGE
LANCER



Milli-Q®

TYPE 2 OR 3 – Autoclaves / sterilizers

Used to sterilize equipment and reagents

1. vacuum is applied (trapped air is a very poor medium for achieving sterility)
2. superheated steam is applied under high pressure

Also used to degrade DEPC (used to remove RNases)

Purified water is required to produce pure superheated steam

- **Hard water** forms scale deposits on heating elements (reduces heat exchange efficacy)
- **Particles and metals** may deposit inside the autoclave and on what is being autoclaved
- **Bacteria and endotoxins** should be avoided



Tuttnauer
Heat Sterilizers & Incubators Control Systems

Milli-Q®

Type 2 (or 3) - stability testing

pharma, cosmetics,
FOOD & BEV

Stability testing is a routine procedure performed on medications (Pharma), cosmetics, etc.

Involved at various stages of product development.

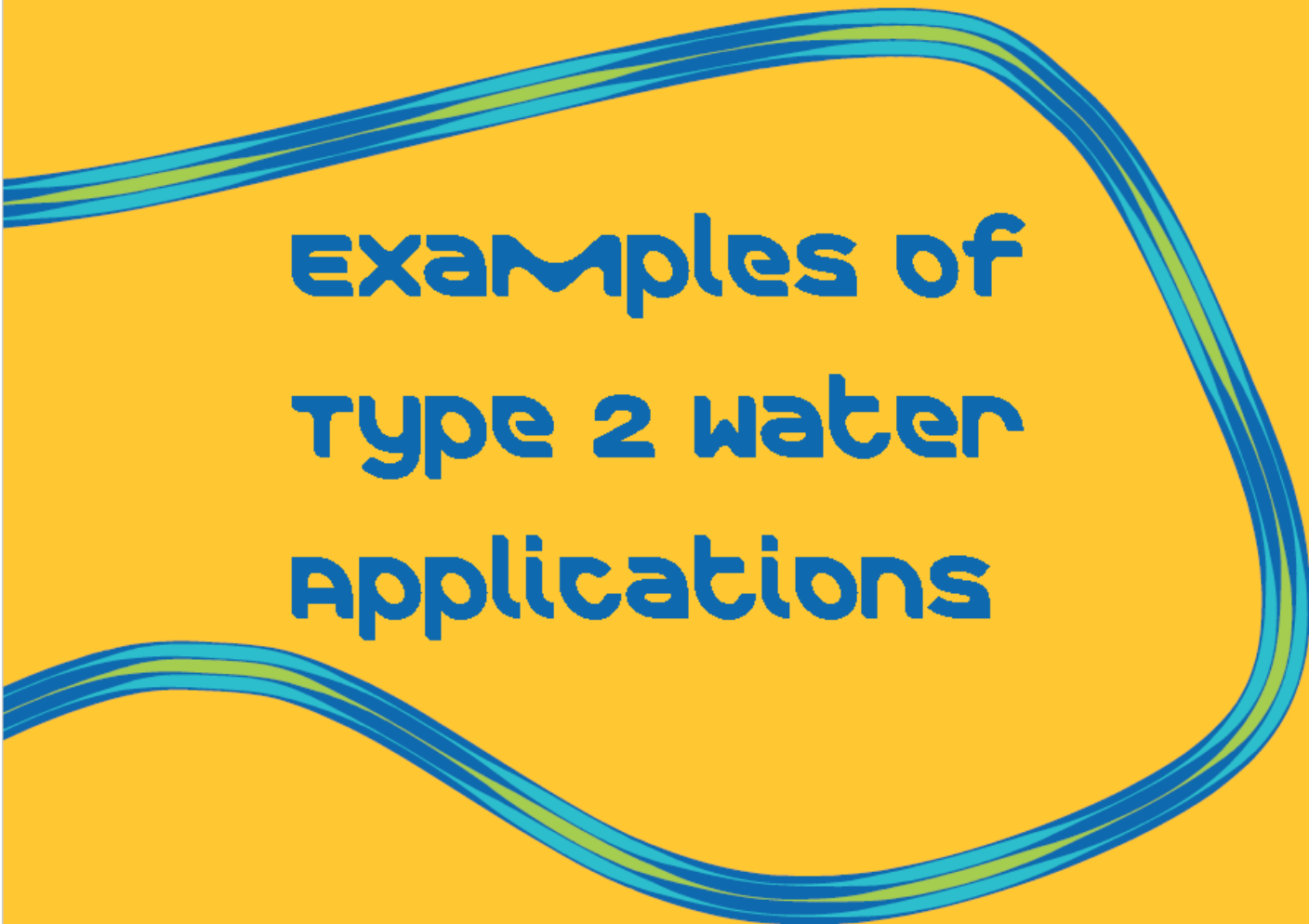
- In early stages, accelerated stability testing (at relatively high temperature and/or humidity) : "**worst case**" evaluation to determine degradation products after long-term storage.
- Testing under more gentle conditions (those recommended for long-term shelf storage), and slightly elevated temperature, used to determine a product's **shelf life and expiration dates**.



schunk company



Milli-Q®



Examples of Type 2 Water Applications

Type 2 – weathering chambers

industry (plastic, automotive...),
pharma, cosmetics

Accelerated Weathering: test materials stability to outdoor exposure, photo-degradation, fading and photo-chemical reactions.

Used to test many materials / components for industry (automotive industry, paints, plastics, cosmetics ...)

Water quality required:

- **Type 2 (+ Q-Gard optional)**
- Avoid **particles, metals, silica** : may deposit on the samples or the inside of the instrument, and affect the results



Ci4000 Weather-Ometer®



Q-Sun Xe

Milli-Q®

Type 2 – histology / histo-pathology

Hospitals, Medical offices..

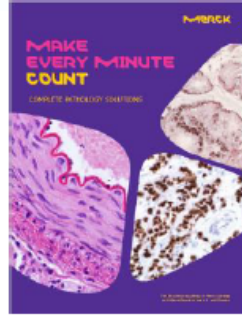
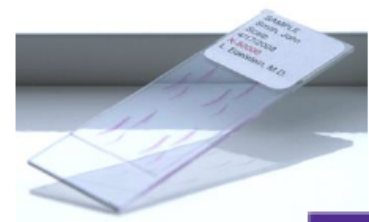
Histology is used to diagnose some cancers (biopsies), infections...

Water is used:

- in stainers, tissue processors, in tissue floatation baths, water baths
- to prepare reagents : buffers, stains, rinsing solutions

Water should not contain:

- **particulates, hardness and silica**: may adhere to tissue sections; deposit inside stainer and tissue processor
- **bacteria**: may generate artifacts on slides; may grow inside stainer and tissue processor tubings
- **organics**: may interfere with the staining process; “food” for bacteria
- **chlorine**: may have a bleaching effect on stains
- **ions** (calcium, etc.) and metals: known to interfere with a variety of stains; in addition, many stains are very sensitive to pH variations



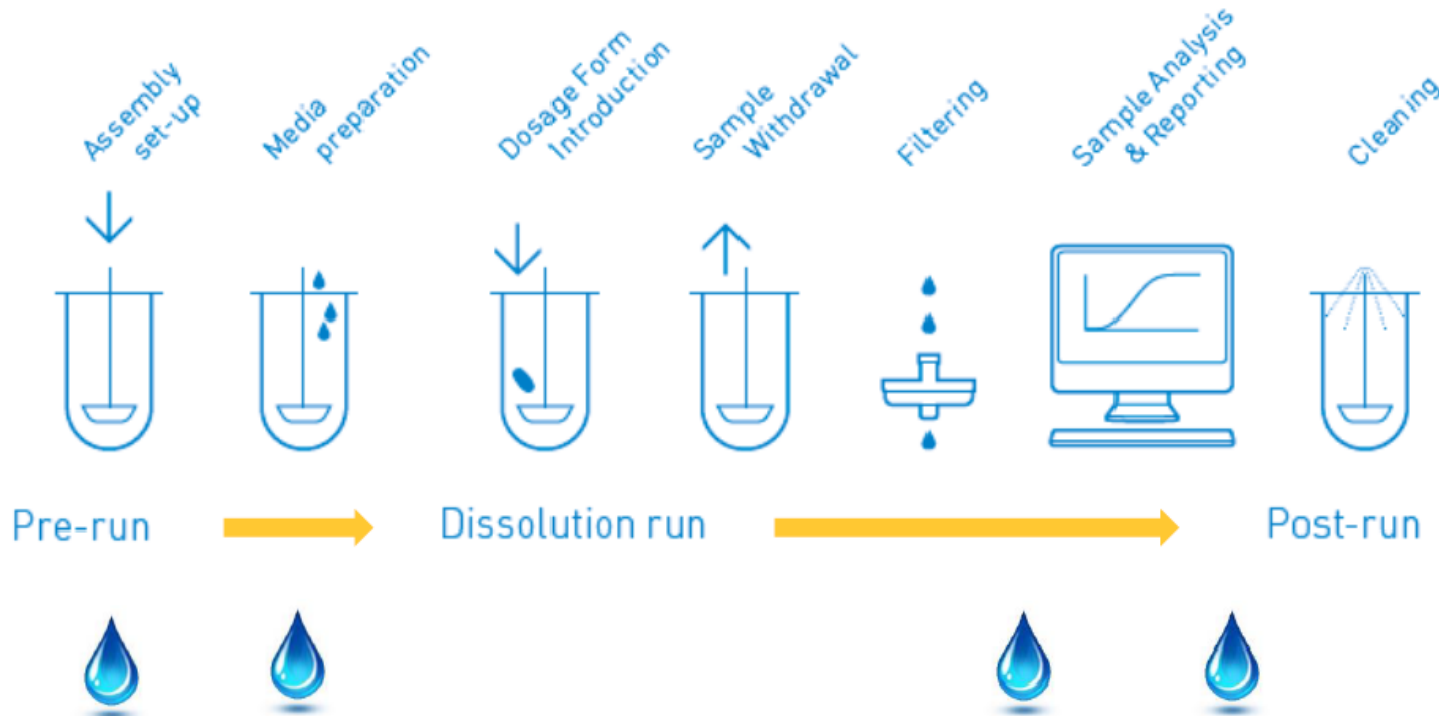
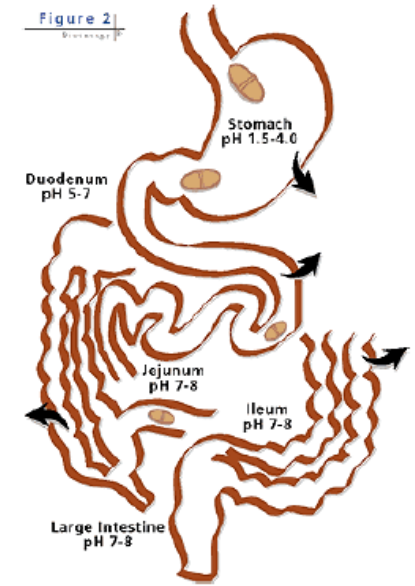
Application Note

Milli-Q®

Type 2 - Dissolution Testing

pharma

In vitro assessment of the dissolution of drugs in the gastro-intestinal tract
Drug (tablets) must deliver active ingredient in proper dose, rate and location



Large volumes of water are needed

- for the water bath (if used)
- to prepare the dissolution media
- to rinse the vessels between experiments, to flush the lines of automated systems (if used)

Water may also be needed for the detection

water quality for dissolution testing

Identifying these labs:



Type 2 water is recommended



But Type 1 water will be needed if HPLC (or UHPLC, or LC-MS) is performed for the analysis of the samples !



Milli-Q®

Biochemical oxygen Demand (BOD)



water facilities, industry, environment



Purified water is used for blanks and dilutions. Various dilution levels of the samples need to be prepared (usually 6 of each) because **tests cannot be repeated!**

The dilution water should:

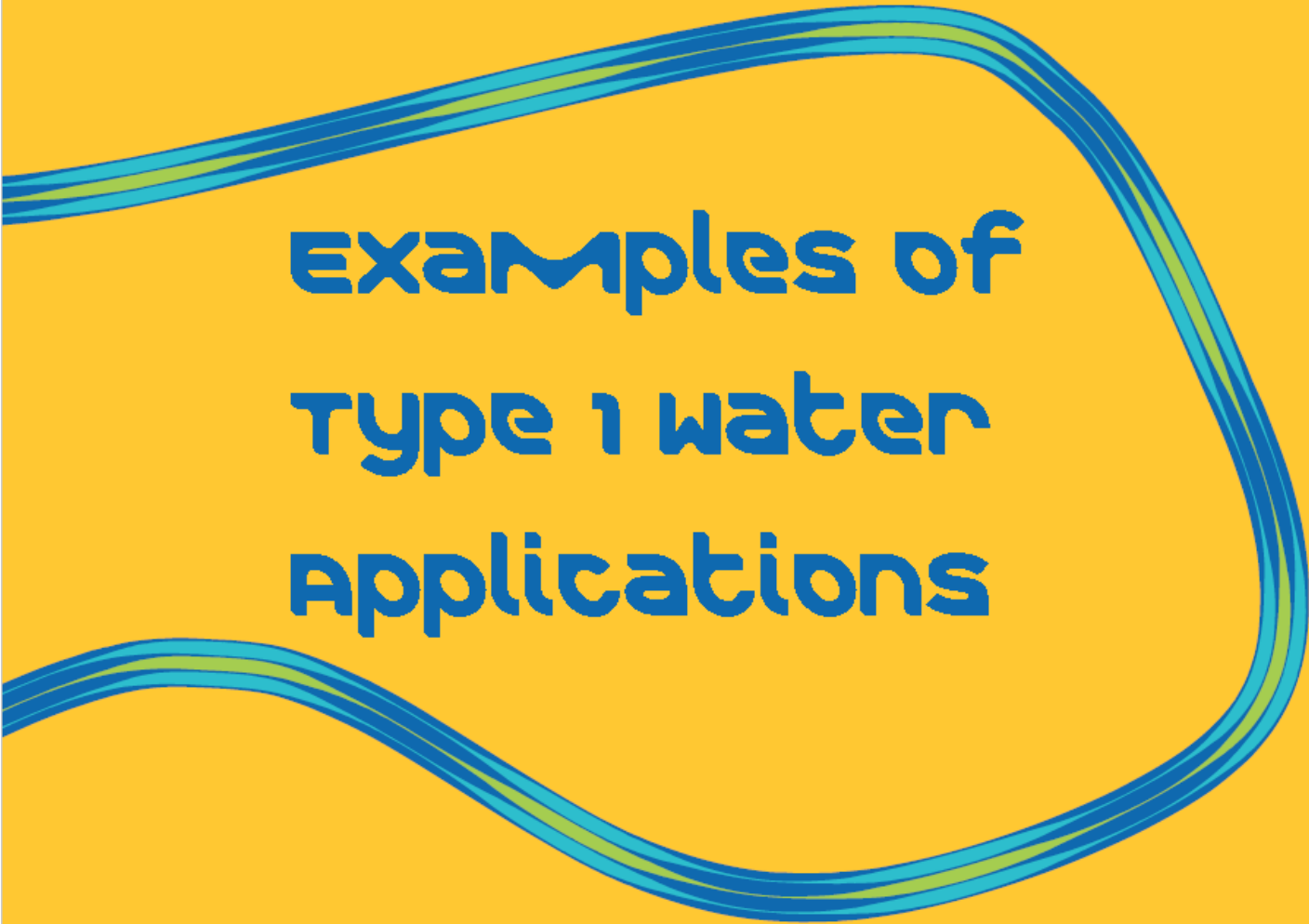
- Not contain any **organics** (contributes to BOD)
- Not be toxic to the bacteria (**chlorine, copper, mercury**)

Blanks

- Most norms require that the oxygen depletion of BOD blanks be **< 0.20 mg/L**

Article (Direct-Q 3 UV)





examples of type 1 water applications



Milli-Q®
Lab Water Solutions

water in analytical chemistry

ions with varying degrees of sensitivity

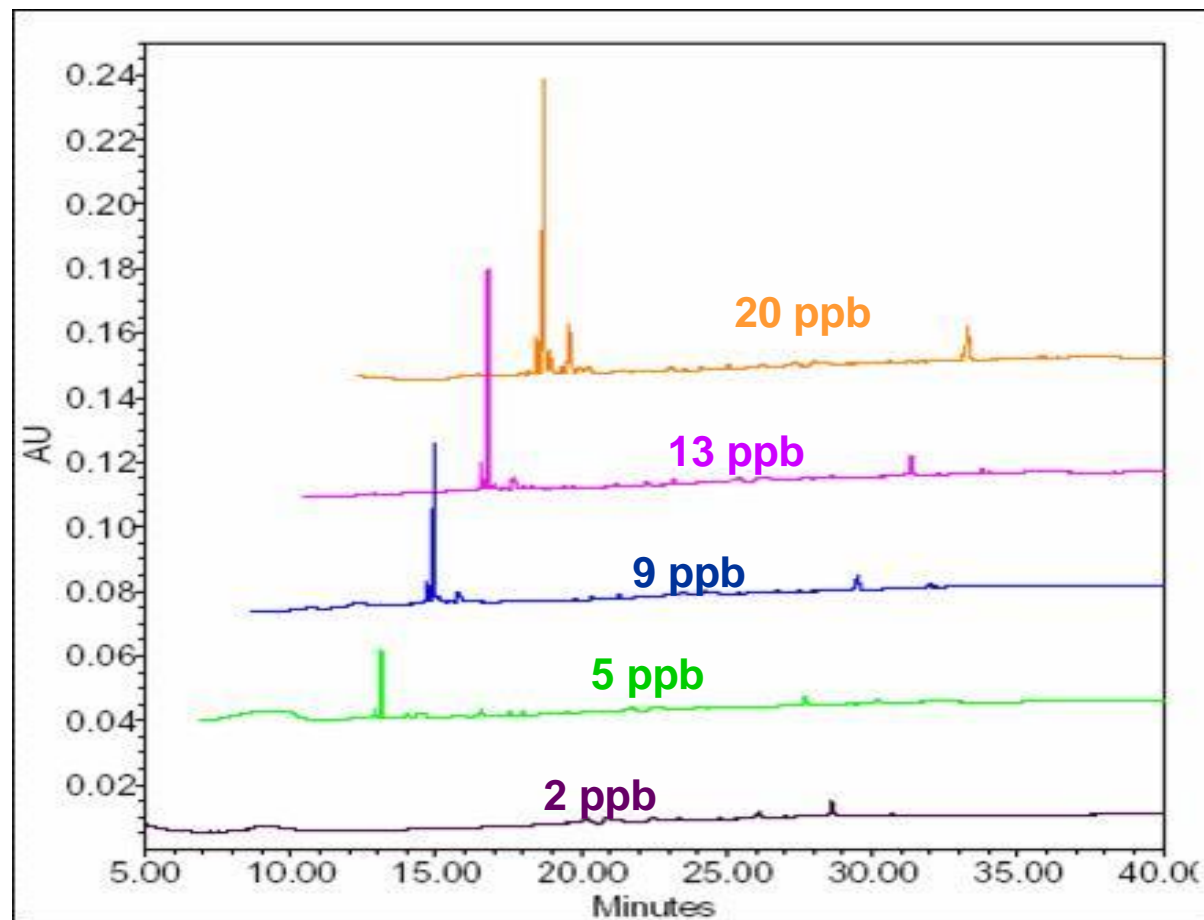


- Inductively Coupled Plasma – Optical Emission Spectrometry (ICP-OES)
- Inductively Coupled Plasma – Mass Spectrometry (ICP-MS)
- Flame Atomic Absorption Spectroscopy (FAAS)
- Graphite Furnace Atomic Absorption Spectroscopy (GF-AAS)
- Ion Chromatography (IC) combined with UV-Vis spectroscopy or electrical conductimetry.

Effect of organic on HPLC baselines:

Particles

Bacteria

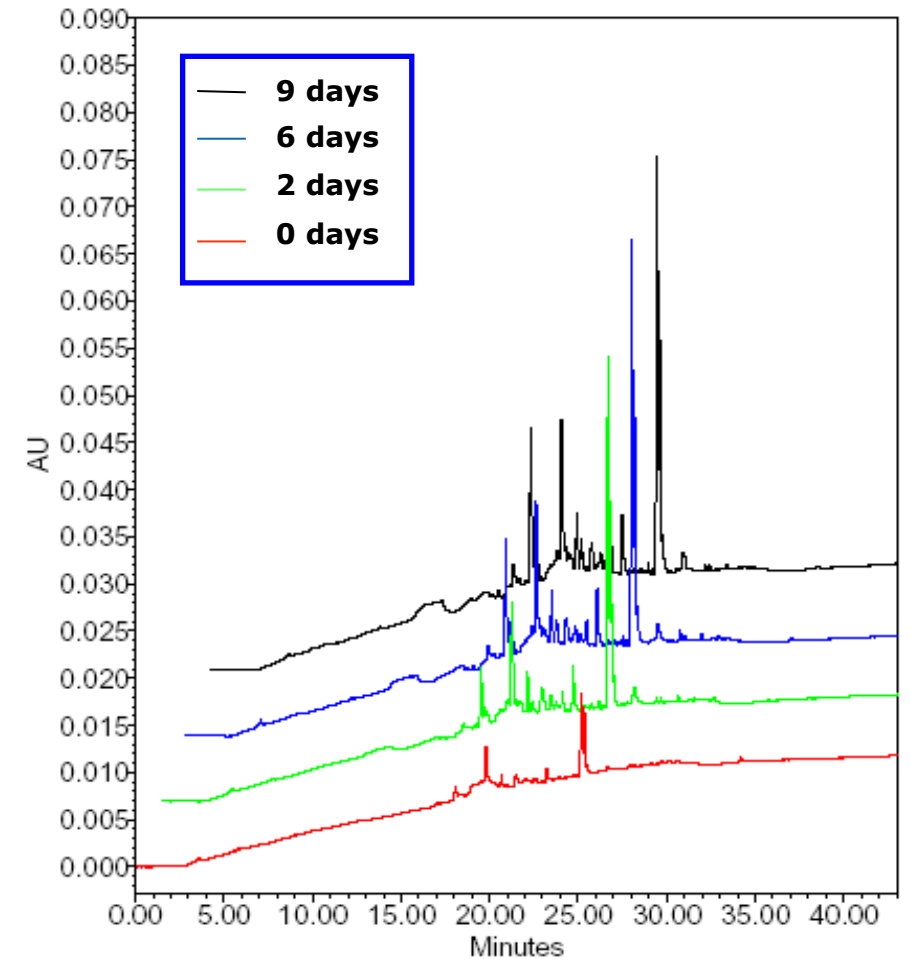


Tip: Use water with
TOC < 5 ppb

Increasing TOC level results in more extraneous peaks

Effect of water storage

- Milli-Q® water was stored in a plastic carboy, then HPLC analysis was performed (214 nm)
- Water samples : 60 mL trace enrichment by accumulation on a C₁₈ column at 1 mL/min



Effects of water contaminants on HPLC and LC-MS

Organics

- Noisy or drifting baselines
- Unknown (ghost) peaks
- “Pollution” of the column (reduced lifetime)

Ions

- Formation of adduct peaks if Na^+ or K^+ are present (concern for LC-MS)

Particles

- May increase system back-pressure (UHPLC)
- Damage pumps and injector

Bacteria

- Behave as particles (back-pressure)
- By-products include organics and ions

Milli-Q® IQ Element

ppm

ppb

ppt

Sub ppt

ion concentration

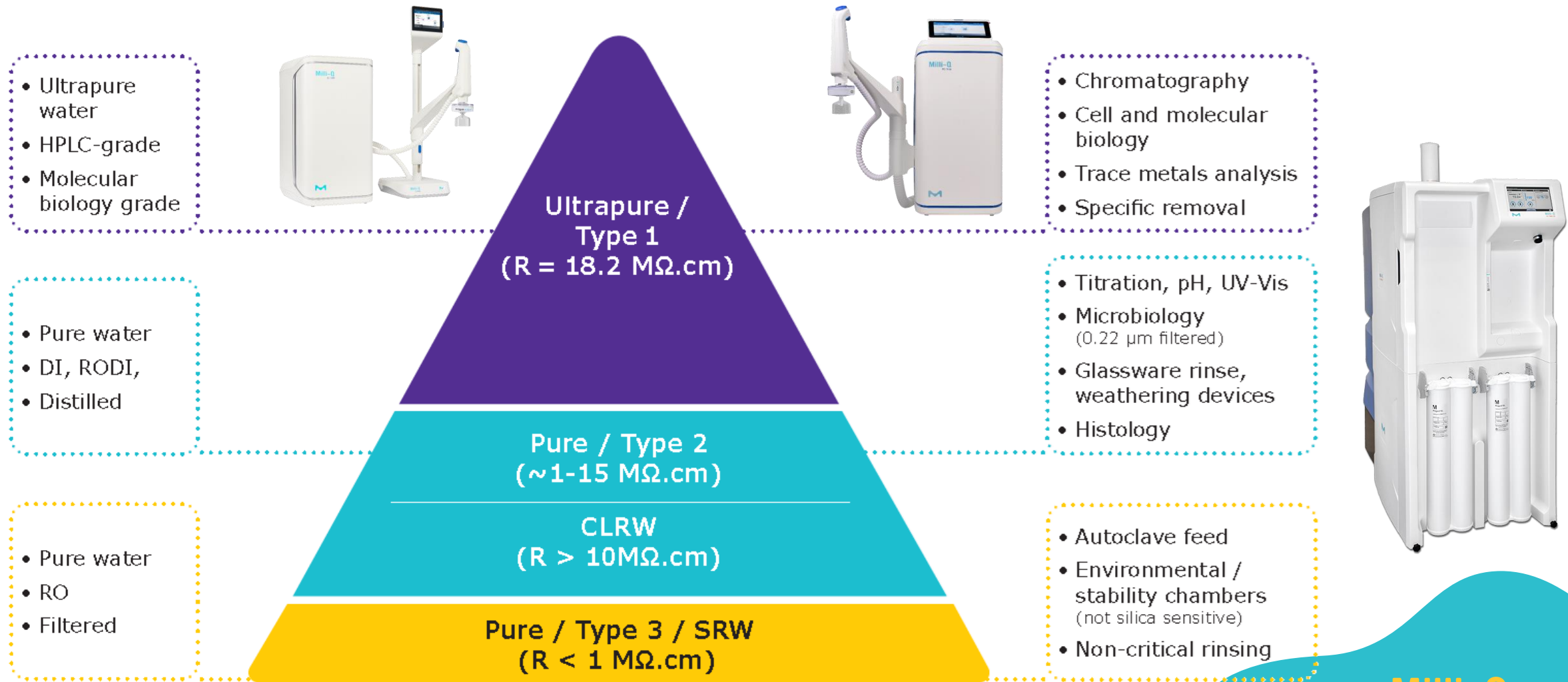
***Datasheet;
Posters 82 and 89***

**1 ppt = 1 ng/L
similar to:
1 sec / 317 centuries**



The pyramid of quality

3 Qualities of Water, fitting all laboratories' needs



MERCK

Thank you!



Milli-Q®
Lab Water Solutions