



**Water Purification 101
From Tap to Pure
Understanding the What, Why, and How**

*Brian Hagopian
Mar Cor Purification / Fluid Solutions
May 20, 2008*

Today's discussion will cover

- Contaminants found in water (What)
- Do they have to be removed? (Why)
- How to remove them (How)



Basic Groups of Contaminants

- Suspended Solids or Particles
- Dissolved Salts or Ions
- Organic Materials- low molecular weight organics
- Colloidal Materials- high molecular weight organics
- Bacteria and Other Living Organisms
- Dissolved Gases

ENGINEERING PHARMACEUTICAL INNOVATION



Basic Groups of Contaminants

- Suspended Solids or Particles
 - Materials that do not dissolve in water
 - Can be any shape, but are generally considered hard, spherical particles
 - Moving water holds more particles
 - Larger particles will settle out by themselves

ENGINEERING PHARMACEUTICAL INNOVATION



Basic Groups of Contaminants

- **Dissolved Salts or Ions**
 - **Materials that dissolve in water, forming free floating ions**
 - **Add positive and negative charges to the water**
 - **Change how much electricity water can transmit**

ENGINEERING PHARMACEUTICAL INNOVATION



Basic Groups of Contaminants

- **Organic Materials- low molecular weight organics**
 - **Materials containing carbon**
 - **Small in size (MW in the hundreds/thousands)**
 - **Little change in electrical conductance of water**
 - **Extremely difficult materials to remove**
 - **Many substances are manmade: alcohols, fertilizers, pesticides, THM's**

ENGINEERING PHARMACEUTICAL INNOVATION



Basic Groups of Contaminants

- Colloidal Materials- high molecular weight organic molecules
 - Contain carbon
 - Large in size (MW in 10,000 to 5,000,000 range)
 - Not really dissolved or particulate
 - Most carry a small negative charge
 - Form a stable suspension in water
 - Abundance measured by silt density index

ENGINEERING PHARMACEUTICAL INNOVATION



Basic Groups of Contaminants

- Bacteria and Other Living Organisms
 - Exist in equilibrium with their environment
 - Abundance is based on the amount of food available
 - Capable of rapid multiplication under the right conditions

ENGINEERING PHARMACEUTICAL INNOVATION



Basic Groups of Contaminants

- **Dissolved Gases**
 - **Not removed by most purification processes**
 - **Least understood and least studied water based contaminant group**
 - **Carbon dioxide is troublesome because it ionizes when it dissolves**

ENGINEERING PHARMACEUTICAL INNOVATION



Why do we care about contaminants?

- **Because organizations say we should?**
 - CAP – College of American Pathologists
 - NCCLS – National Committee of Clinical Laboratory Scientists
 - ASTM – American Society for Testing and Materials
 - USP – US Pharmacopoeia
 - FDA – US Food and Drug Administration
 - SEMI – Semiconductor manufacturing standards
 - HIMA – Health Industries Manufacturing Association
 - ISPE – Baseline guides

ENGINEERING PHARMACEUTICAL INNOVATION



LABORATORY GRADE WATER USE CAP/NCCLS/ASTM STANDARDS

PARAMETER	CAP/NCCLS			ASTM			
	TYPE 1	TYPE 2	TYPE 3	TYPE 1	TYPE 2	TYPE 3	TYPE 4
Conductivity (max)	<0.1	<0.2	<0.5	0.056	1.0	0.25	5.0
Resistivity (min)	>10.0	>2.0	>1.0	18.0	1.0	4.0	0.2
pH	---	---	---	---	---	---	5.8-8.0
Silica (ppb)	<500	<100	<1000	3	3	500	----
Sodium (ppb)	---	---	---	1	5	10	50
Chlorides	---	---	---	1	5	10	50
Total Organic Carbon (ppb)	---	---	---	100	50	200	---
Bacteria (cfu/ml)	<10	10	---	Separate specification, only where bacteria control is required Type 1 : 10/1,000 ml Type 2 : 100/1,000 ml Type 3 : 10,000/1,000 ml			

ENGINEERING PHARMACEUTICAL INNOVATION



PHARMACEUTICAL GRADE WATER

PARAMETER	USP PURIFIED	USP WFI
Total Organic Carbon (ppb)	500	500
Conductivity	<1.3 @ 25°C	<1.3@25°C
Bacteria	None given, but recommended to be 100/ml	None given, but recommended to be 10/100 ml
Endotoxins	----	<0.25 EU/ml

ENGINEERING PHARMACEUTICAL INNOVATION



SEMICONDUCTOR GRADE WATER

Page 1 of 3

PARAMETER	ATTAINABLE	ACCEPTABLE	ALERT	CRITICAL
Resistivity	18.2	18.2	17.9	17.5
TOC (online, ppb)	<1	<2	5	10
THM (ppb)	<2	<5	---	---
Particles by laser 0.05 to 0.1 micron 0.1 to 0.2 micron 0.2-0.3 micron 0.3-0.5 micron >0.5 micron	<100/1000 ml <50/1000 ml <20/1000 ml <10/1000 ml <1/1000 ml	<500/1000 ml <300/1000 ml <50/1000 ml <20/1000 ml <4/1000 ml		
Bacteria (cfu/1000 ml)	<1	<6	25	>25
Silica (total, ppb)	<0.5	<3	>5	>10

ENGINEERING PHARMACEUTICAL INNOVATION



SEMICONDUCTOR GRADE WATER

Page 2 of 3

PARAMETER	ATTAINABLE	ACCEPTABLE	ALERT	CRITICAL
Phosphate (ppb)	<0.02	<0.1	>0.01	>0.5
Silicate (ppb)	<0.05	0.1	<0.02	>0.5
Sodium (ppb)	<0.01	0.05	>0.02	>0.5
Potassium (ppb)	<0.02	<0.1	>0.02	>0.5
Ammonium (ppb)	<0.06	0.1	<0.02	>0.5
Calcium (ppb)	<0.02	<0.1	>0.01	>0.2
Magnesium (ppb)	<0.02	<0.1	<0.01	>0.2
Fluoride (ppb)	<0.1	<0.1	>0.02	>0.5
Chloride (ppb)	<0.02	0.1	<0.02	>0.5
Bromide (ppb)	<0.02	<0.1	>0.01	>0.5
Nitrate (ppb)	<0.02	<0.1	<0.01	>0.5

ENGINEERING PHARMACEUTICAL INNOVATION



SEMICONDUCTOR GRADE WATER

Page 3 of 3

METAL ION CONTAMINANTS, ALL ARE MEASURED IN PARTS PER TRILLION				
Aluminum (ppt)*	7	50	>0.0	200
Barium (ppt)*	2	10	>50	100
Boron (ppt)*	300	<2000		
Chromium (ppt)*	8	30	>30	50
Copper (ppt)*	5	50	>50	>200
Iron (ppt)*	10	100	200	>200
Lithium (ppt)*	4	30	100	>100
Magnesium (ppt)*	2	20	100	>200
Manganese (ppt)*	4	30	>30	100
Nickel (ppt)*	5	50	>50	100
Sodium (ppt)*	10	60	>200	>500
Strontium (ppt)*	2	10	>10	>10
Zinc (ppt)*	8	60	>50	>100

ENGINEERING PHARMACEUTICAL INNOVATION



Why do we care about contaminants?

- We care when contaminants interfere with what we're trying to do
- Water is the most abundant single ingredient coming into contact with our product
- Pure water variability decreases repeatability
 - Bacteria and cell fragments interfere with cell and tissue culture work
 - Bacteria and cell fragments interfere PCR processes
 - Ions interfere with buffer prep, atomic analysis, etc.

ENGINEERING PHARMACEUTICAL INNOVATION



How do we remove these contaminants?

- Particle removal equipment
- Ion removal equipment
- Bacteria removal equipment
- Organics removal equipment



Particle Removal Technologies

- Nominally rated particle filters
- Absolute membrane filters
- Ultrafilters
- Reverse Osmosis



Particle Filters

- Particles are classified by “micron or micrometer size”
- For reference, 1 mil = 25 microns
- 25 microns is smallest particle visible to naked eye
- Remove particles from 1 to 200 microns
- Particle filters are rated using a ‘nominal’ or 80 - 99% removal efficiency
- Filters can be permanent or disposable

ENGINEERING PHARMACEUTICAL INNOVATION



Absolute Membrane Filters

- An order of magnitude finer than particle filters
- Removes particles from 1 micron down to 0.05 microns in size
- Removes bacteria, spores, yeasts, etc.
- Pharmaceutical industry uses these filters to produce “sterile” filter products
- Filters can be integrity tested

ENGINEERING PHARMACEUTICAL INNOVATION



Ultrafilters

- An order of magnitude finer than absolute membrane filters
- Pore size is defined by Molecular Weight Cut Off (MWCO)
- Retention varies from 5,000 to 5,000,000 MWCO based upon membrane composition *and* the containment being removed

ENGINEERING PHARMACEUTICAL INNOVATION



Ultrafilters

- Removes particles, bacteria, some/ all large colloidal organics, and cell fragments
- Most are not Integrity testable, so they can have defects and let bacteria through
- Cross flow device- some water goes to waste
- May need added driving force to operate

ENGINEERING PHARMACEUTICAL INNOVATION



Reverse Osmosis

- An order of magnitude finer than ultrafilters
- Approximately 200- 500 MWCO
- Removes particles, bacteria, colloids, many organics, AND most ions
- Performance measured by salt rejection
- Pumps needed to add driving force

ENGINEERING PHARMACEUTICAL INNOVATION



Reverse Osmosis

- Cross flow device- send more water to drain than ultrafilters
- Not Integrity testable- defects can let bacteria through
- Many types cannot tolerate free chlorine
- Lots of buzz about RO, both positive and negative
- Lots of regulations surrounding its generation of “reject water”

ENGINEERING PHARMACEUTICAL INNOVATION



Inquiring minds want to know

Why does Reverse Osmosis
remove ions smaller than its pore
size?

Asked a little differently, how can a 200 MWCO reverse
osmosis membrane remove over 90% of ions that are
much smaller than 200 MW?

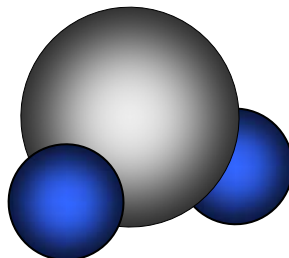
ENGINEERING PHARMACEUTICAL INNOVATION



Reverse Osmosis

We need to understand the water molecule
a little bit better to answer the question

Negative End



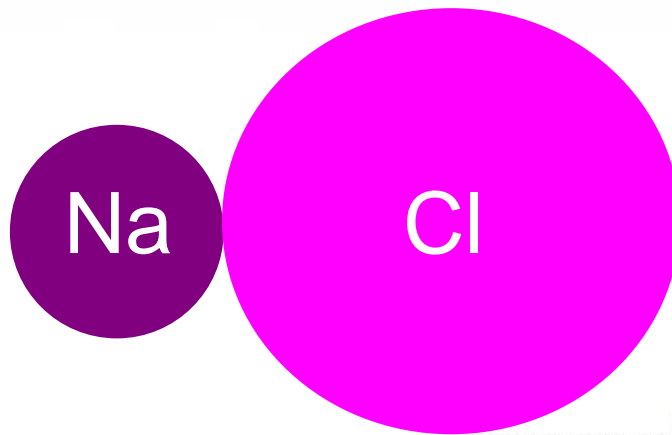
Positive end

ENGINEERING PHARMACEUTICAL INNOVATION



Reverse Osmosis

Lets consider a typical salt molecule



ENGINEERING PHARMACEUTICAL INNOVATION

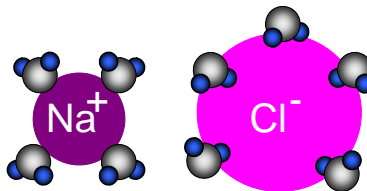


Reverse Osmosis

In solution



Water separates and surrounds ions



Making them larger and easier to remove

ENGINEERING PHARMACEUTICAL INNOVATION



Ion Exchange

- Used to remove dissolved ions from water
- Can shed particles
- Can generate bacteria
- Resins are attacked by chlorine

ENGINEERING PHARMACEUTICAL INNOVATION



Ion Exchange

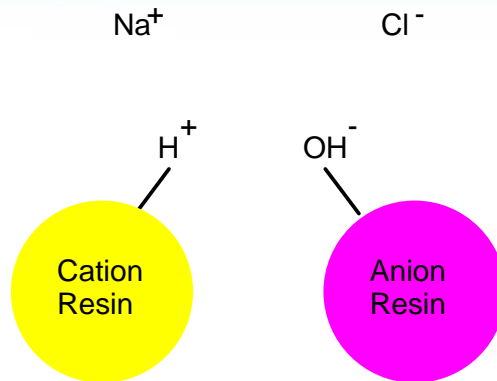
- There are hundreds of types, so lets keep it simple
 - Cation exchange resin (+)**
 - Anion exchange resin (-)**

ENGINEERING PHARMACEUTICAL INNOVATION



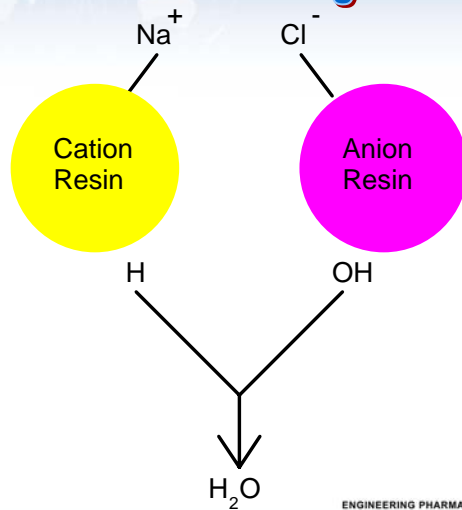
Ion Exchange

How Ion Exchange Works



Ion Exchange

How Ion Exchange Works



Ion Exchange

Salts are attracted to resins based on size and charge.

- **Greater size**
- **Greater attraction to resin**
- **Greater charge**

ENGINEERING PHARMACEUTICAL INNOVATION



Carbon Filters

- Removes small organics
- Complements reverse osmosis
- Removes disinfectants present in water
 - chlorine / chloramine
 - downstream design must account for this
- Place where bacteria can grow
- Many different types of carbons

ENGINEERING PHARMACEUTICAL INNOVATION



UV Sanitizers

- Irradiate water, denature DNA, prevent multiplication
- Adds nothing to water
- Produces 254 nm radiation
- Particles interfere with operation

ENGINEERING PHARMACEUTICAL INNOVATION



TOC Reducing Sanitizers

- Use shorter wavelength than UV unit, 185 nm
- Oxidize organics into acids, making for easier removal
- Particles interfere with operation

ENGINEERING PHARMACEUTICAL INNOVATION



Electro Deionization

- Uses electricity to keep resins clean
- Generates a waste stream during operation
- Can produce 2-16 megohm water
- Requires softened RO water feed

ENGINEERING PHARMACEUTICAL INNOVATION



Distillation

- Only process that removes water from its contaminants
- Heat kills all bacteria
- The gold standard in the pharmaceutical industry
- Can carry through materials with similar or lower boiling points

ENGINEERING PHARMACEUTICAL INNOVATION



Ozone

- Powerful oxidizing agent
- Kills bacteria
- Reduces Total Organic Carbon levels
- Dangerous gas that must be properly vented

Table 1 - Removal Capabilities of Various Water Purification Processes

	Coarse Particle Filters	Absolute Membrane Filters	Ultrafilters	Reverse Osmosis	Carbon Filtration	Ultraviolet Disinfection	Deionization
Particles	F	G-E	E	E	N	N	N
Dissolved Ions	N	N	N	G-E	N	N	E
Small Organics	N	N	N	F-G	G-E	N	P
Colloids	N	F-P	G-E	E	P-F	N	P
Bacteria	P	E	E	E	A	G	A-P

N = None P = Poor F = Fair G = Good E = Excellent A = Adds contaminants to systems

In Summary

- We discussed
 - “What” contaminants are present in water
 - “Why” they need to be removed
 - “How” to remove them
 - However, this is an introductory level discussion, so.....

ENGINEERING PHARMACEUTICAL INNOVATION



In Summary

- We did not discuss
 - Best equipment sequences for effective removal
 - Unit process limitations
 - Conveying water to points of use
 - Many other important details and considerations

ENGINEERING PHARMACEUTICAL INNOVATION



For additional information

Brian Hagopian
VP of Research and Development
Mar Cor Purification / Fluid Solutions
160 Stedman Street
Lowell, MA
(978) 453-9600
e: BHagopian@mcpur.com
www.mcpur.com
www.fluid-solutions.com

ENGINEERING PHARMACEUTICAL INNOVATION

