

Supplementary Training Modules on Good Manufacturing Practice

Water for Pharmaceutical Use

Part 1: Introduction and treatment



Water for Pharmaceutical Use

Objectives

1. Introduction to Water for Pharmaceutical Use
2. Review WHO GMP guidance
3. Sources and types of water for pharmaceutical use
4. Storage of bulk, untreated raw water
5. Pre-treatment of water



Water for Pharmaceutical Use

Principles (1)

- Like any starting material, water must conform to Good Manufacturing Practice norms
- It must be “potable” and comply with WHO Guidelines for drinking-water quality



Water for Pharmaceutical Use

Principles (2)

1. Potential for microbial growth
2. Systems must be properly validated
3. Water for parenteral use could be contaminated with pyrogens or endotoxins
4. Specifications and periodic testing is required

Annex 5, 7.2.4 Excipients,



Water for Pharmaceutical Use

Types of water used in pharmaceutical processes

1. Purified water
2. Water for Injections – PFW & WFI
3. Softened Water
4. Water for Final Rinse
5. Pure, or clean Steam
6. Water for cooling Autoclaves



Water for Pharmaceutical Use

Why purify raw water?

1. Although reasonably pure, it is always variable
2. Seasonal variations may occur in water
3. Some regions have very poor quality water
4. Must remove impurities to prevent product contamination.
5. Control microbes to avoid contaminating products



Water for Pharmaceutical Use

Contaminants of water (1)

- There is no pure water in nature, as it can contain up to 90 possible unacceptable contaminants
- Contaminant groups:
 1. *Inorganic compounds*
 2. *Organic compounds*
 3. *Solids*
 4. *Gases*
 5. *Micro-organisms*



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Contaminants of water (2)

Treatment depends on water's chemistry and contaminants, influenced by:

1. Rainfall
2. Erosion
3. Pollution
4. Dissolution
5. Evaporation
6. Sedimentation
7. Decomposition



Water for Pharmaceutical Use

Contaminants of water (3)

Problem minerals

1. Calcium and magnesium
2. Iron and manganese
3. Silicates
4. Carbon dioxide
5. Hydrogen sulfide
6. Phosphates



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Contaminants of water (4)

Further problem minerals

1. Copper
2. Aluminium
3. Heavy metals
 - *Arsenic, lead, cadmium*
4. Nitrates



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Contaminants of water (5)

Micro-organisms – Biofilm

1. Algae

2. Protozoa

- *Cryptosporidium*

- *Giardia*

3. Bacteria

- *Pseudomonas*

- *Gram negative, non-fermenting bacteria*

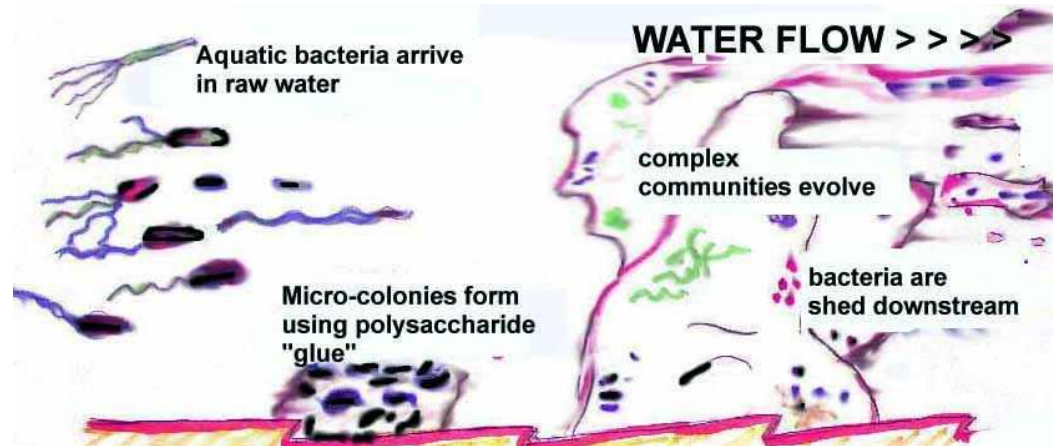
- *Escherichia coli and coliforms*



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Biofilm formation

1. Free swimming aquatic bacteria use *polymucosaccharides* to colonise surfaces
2. Complex communities evolve which shed micro-colonies and bacteria



Water for Pharmaceutical Use

Turbidity

1. Silt, clay, and suspended material cause turbidity
2. Small particles include "colloids"
3. Removal of colloids is usually the first step in water treatment



Water for Pharmaceutical Use

Water hardness

<i>Water hardness classification</i>	<i>mg/L or ppm as CaCO_3</i>
Soft	0-60
Moderate	61-120
Hard	121-180
Very Hard	> 180



Water for Pharmaceutical Use

Source of raw water

1. Rain water
2. Surface or ground water
3. Well or borehole
4. Municipal or civil – “tap water”
5. Purchased in bulk



Water for Pharmaceutical Use

Well water

1. Inspect exposed parts of the well
2. Depth of well

Check:

1. Nearby septic systems
2. Hazardous materials usage (pesticides, fertilizers, etc)
3. “Potability”
4. Well maintenance



Water for Pharmaceutical Use

Raw water storage

1. May be required prior to pre-treatment according to local circumstances
2. Check material of construction
 - *Concrete, steel are acceptable but check corrosion*
 - *Plastics or plastic linings may leach*
3. Check cover
 - *To keep out insects, birds and animals*
4. Check disinfection practices



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WHO water treatment guidance

The following should be monitored

- Sources of water
- Treatment procedures
- Water treatment equipment
- Treated water tests
- Monitoring records required

Annex 1, 17.42



Water for Pharmaceutical Use

Pre-treatment steps

1. Primary filtration and multi-media filter
2. Coagulation or flocculation
3. Desalination
4. Softening



Water for Pharmaceutical Use

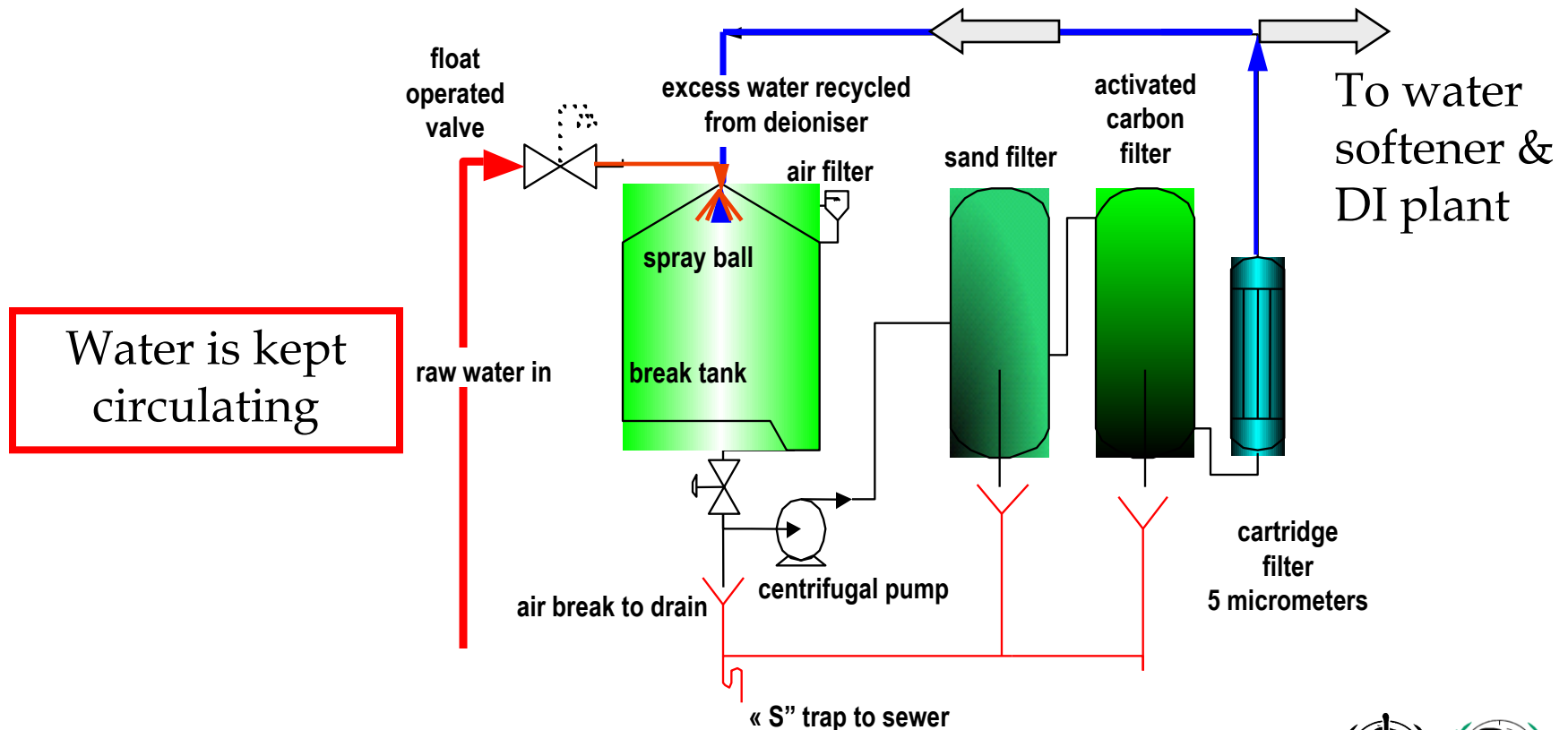
Chlorine removal Activated-carbon (AC) filtration or bisulphite

1. AC removes chlorine but bacteria can then grow
2. AC filtration can remove organic impurities
3. Bisulphite leaves sulphate residues but is anti-microbial



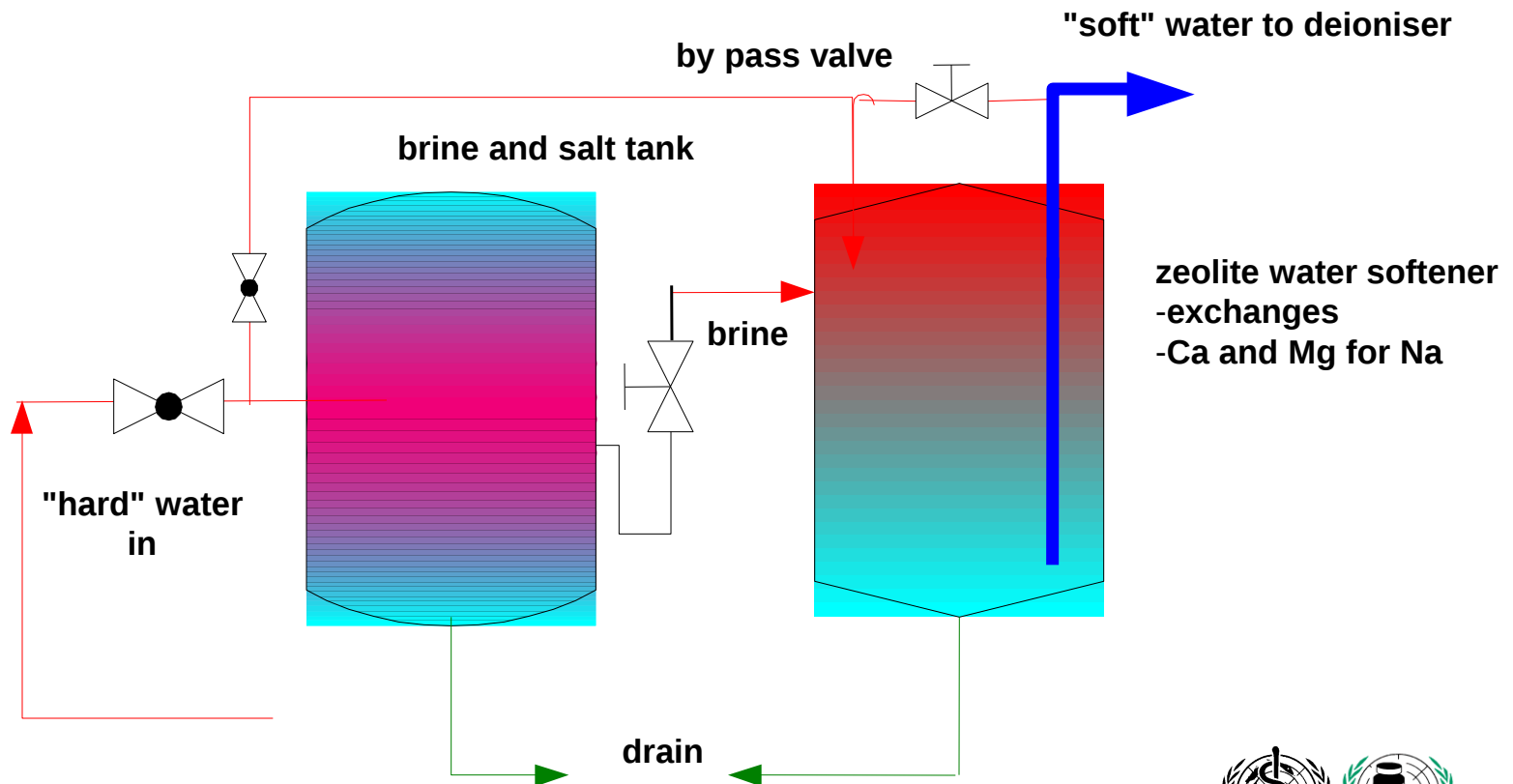
Water for Pharmaceutical Use

Pretreatment – schematic drawing



Water for Pharmaceutical Use

Water Softener – schematic drawing



Water for Pharmaceutical Use

Water pre-treatment complex

External raw water storage



Pretreatment room