Membrane Based WFI Requirements and Guidance

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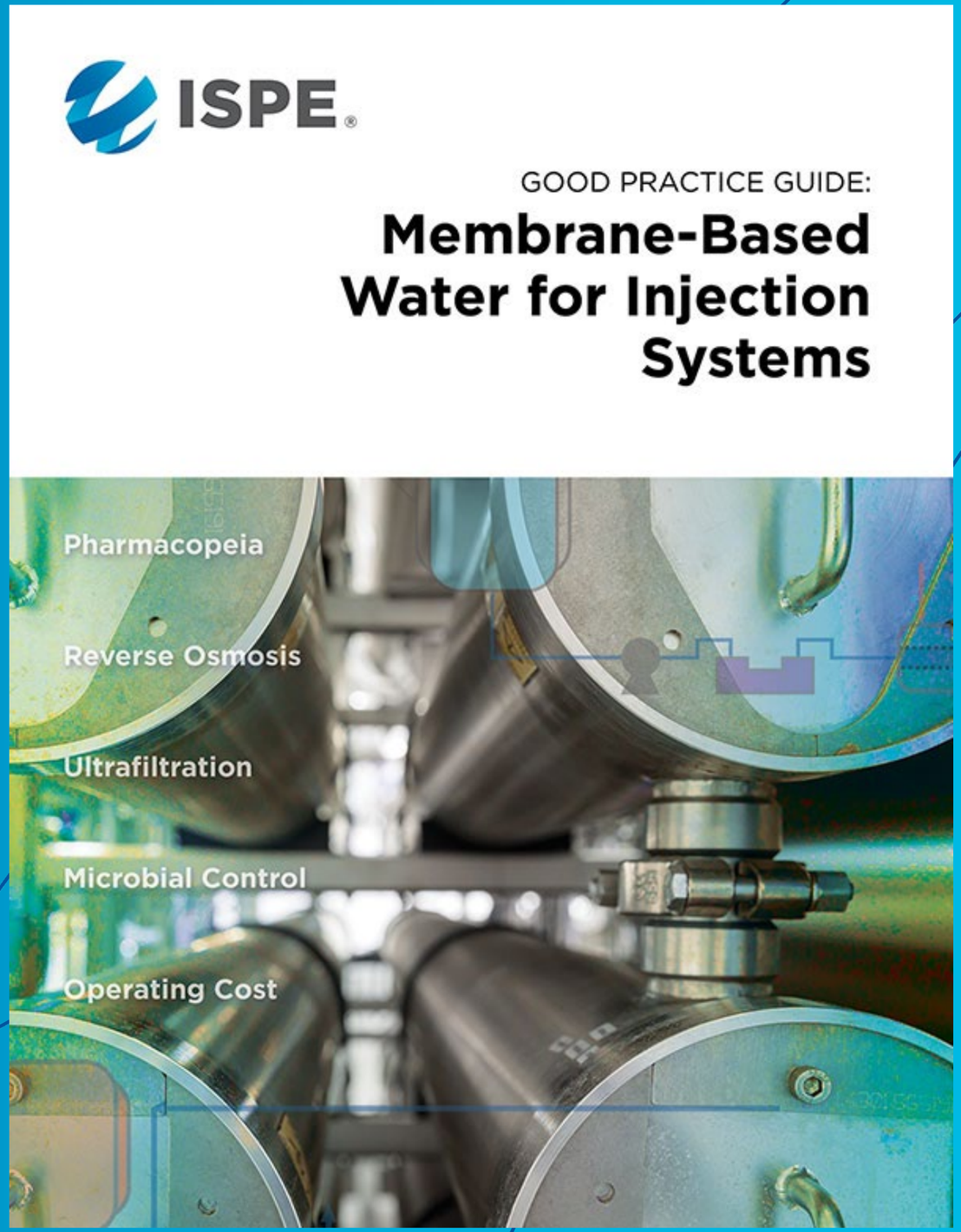
Good Practice Guide:

Membrane-Based Water for Injection Systems



Why is membrane-based WFI production appealing?

Reduced carbon footprint

Reduced capital costs

Reduced operating costs

Potential for improved water quality

Reduced space requirement

Utility plant impact

WFI Regulatory History

1820 USP 1…… “Let water be distilled….’

1942 USP XII….. WFI shall be produced by distillation

1975 USP…….WFI produced by distillation or reverse osmosis

2005 USP……”distillation or a process that is equivalent or superior to distillation in removal of chemicals and microorganisms’

2017 Ph. Eur. “distillation or reverse osmosis, which may be single-pass or double-pass, coupled with other appropriate techniques such as electro-deionization, ultrafiltration or nanofiltration”

Guide Pharmacopeial Guidance

All require CQA attainment for conductivity, TOC, micro and endotoxin
some plus additional CQA

China….new membrane-based allowance in 2025 (PW feed?)

Japan…...membrane alternates allowed, RO or UF

International Pharmacopeia….membrane alternates allowed

India……no process restrictions (PW feed)

Brazil…..no process restrictions

Mexico…no process restrictions

Russia…no process restrictions if from drinking water

Korea….membrane alternates allowed

Generation Pretreatment Process Options

Media filter
Cartridge/bag filter
Screen filter
Ultrafilter
Softener
Antiscalant
Electric scale control
Activated carbon
Chemical dechlorination/chlorination
pH adjustment

Generation Final Treatment Process Options

Nanofiltration

Reverse osmosis

Ion exchange

Electrodeionization

Ultraviolet light

Microfiltration

Ultrafiltration

Membrane degasification

Generation System Design

No single recommended solution

Ph. Eur. requires reverse osmosis for compliance

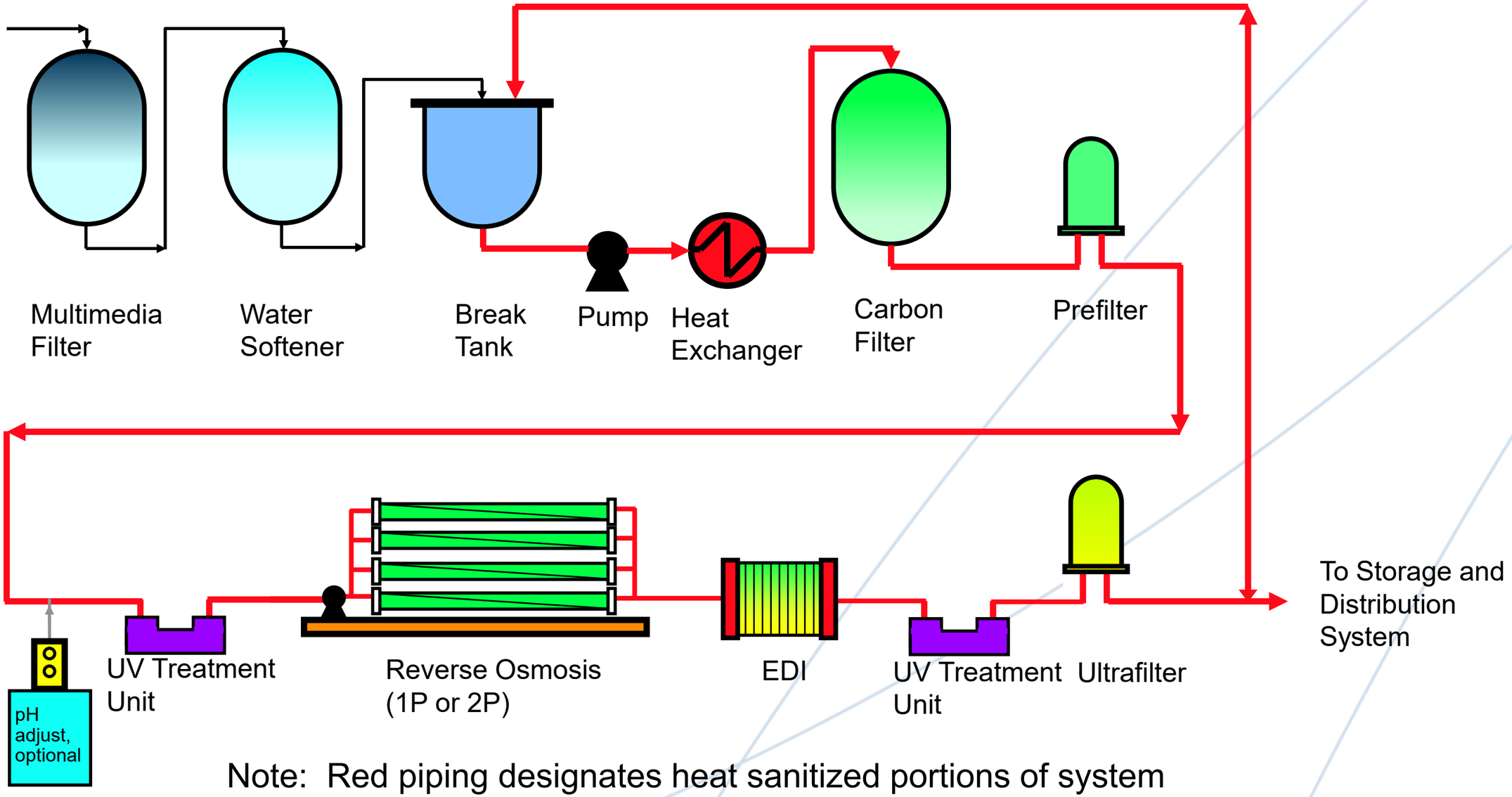
No requirement for multiple membrane barriers, but recommended in guide

Most configurations include pretreatment, reverse osmosis, electrodeionization, ultrafiltration and hot water sanitization

Hygienic construction recommended

Multiple sanitization methods recommended

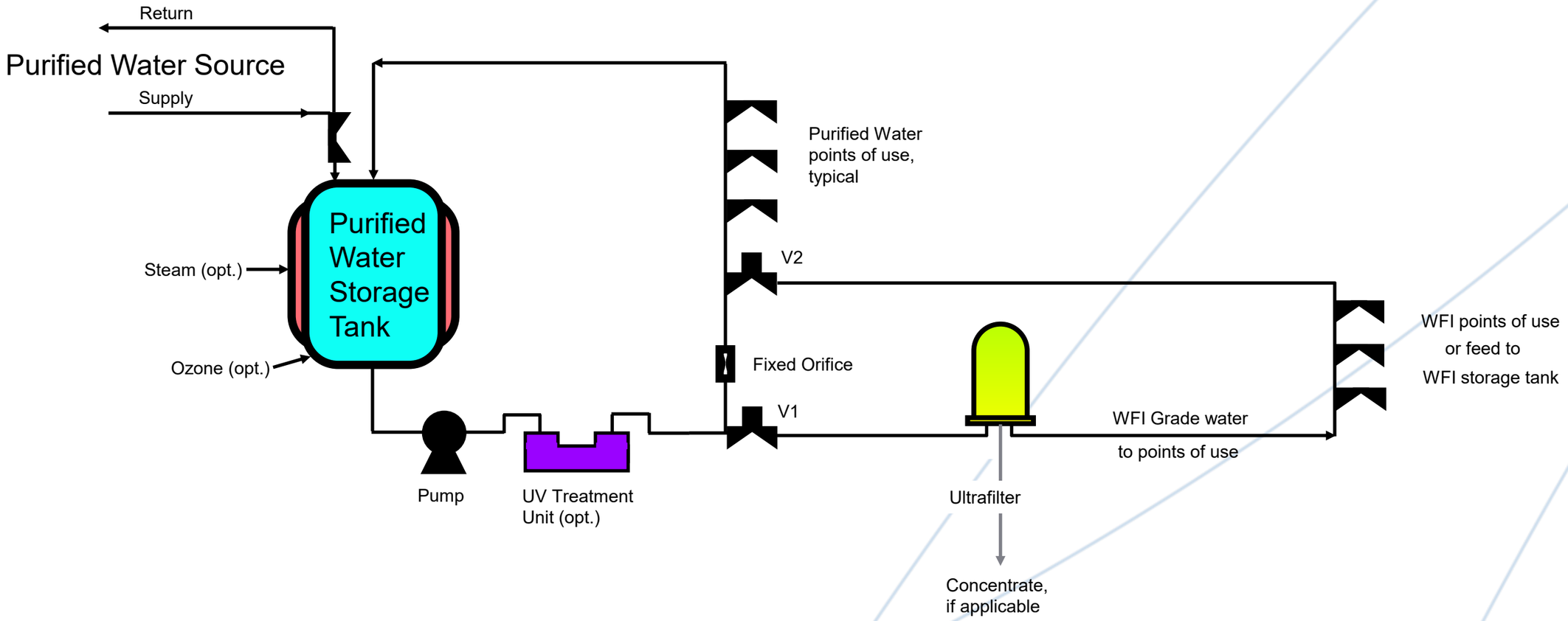
Figure 5.16: Example 1- RO/EDI/UF Membrane System



Note: Red piping designates heat sanitized portions of system

Figure 5.11

Purified Water and WFI Water from a single storage tank



Storage and Distribution

Continuously sanitizing environment preferred

- ozone
- heat

Frequent sanitization if intermittent

Evaluate tank turnover, turbulence, vessel design/construction for intermittent

Minimize dead legs

Appropriate instrumentation

Figure 6.1

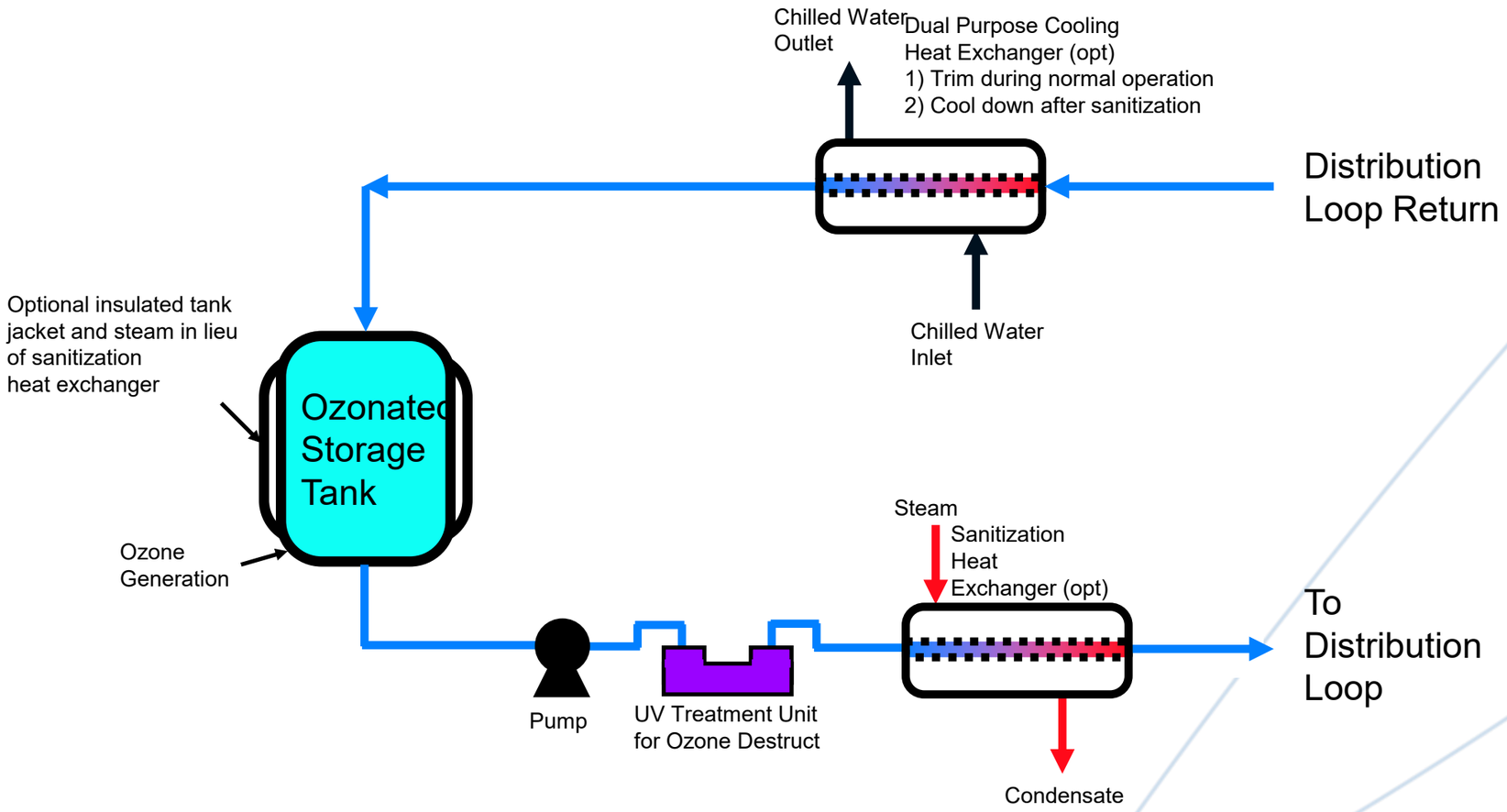


Figure 6.1 - An example showing a continuously ozonated storage tank with ambient temperature WFI distribution featuring heat sanitization capabilities as a backup sanitization method. Heat exchanger locations are for illustrative purposes and may vary.

Total cost of Ownership

Utilization is a key TCO factor

- standby utility costs greater factor for low utilization

Utility costs variable and significant factor

Equipment life is a significant factor due to depreciation costs

Distillate temperature (hot versus ambient) is a significant factor

- ambient distillate temperature used for VC

Water recovery is a major consideration

Sampling practice vary and can impact costs significantly

Utility plant capital costs not considered, but a significant factor

Summary

Guide is comprehensive

Guide is well balanced - risks defined as well as advantages

No single solution

Guide has significant design information, but is not overly prescriptive

Questions?