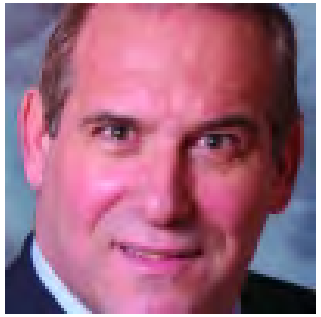
Everything You Wanted to Know about Pharma Water & Steam Systems…but Were Afraid to Ask! Webinar

Speakers:
Nissan Cohen
Gary Zoccolante

21 November 2019
Hosted by ISPE

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Speakers



Nissan Cohen
Owner
Biopharmaceutical Water Doc

Nissan is a worldwide expert, with 40 years' experience, in Total Organic Carbon (TOC), high purity, ultrapure, reclaim and recycle water systems, with profound expertise in instrumentation, automation, and organic contamination oxidation systems using ozone, UV, ion exchange and catalysts.



Gary Zoccolante, BSME
President
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Gary has over 40 years of experience in the design, operation and troubleshooting of pharmaceutical water systems. He has been involved in the development of equipment for pretreatment, reverse osmosis, deionization, ultrafiltration, and distillation.

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POLL

Are you currently using the ISPE Water and Steam 2nd Edition?

- ❑ Yes
- ❑ No
- ❑ We're still using the 1st edition



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The Guide: A Quick Introduction

Nissan Cohen
Owner
Biopharmaceutical Water Doc

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Introduction to the Guide Update

Brief background

Why Revise the Guide?

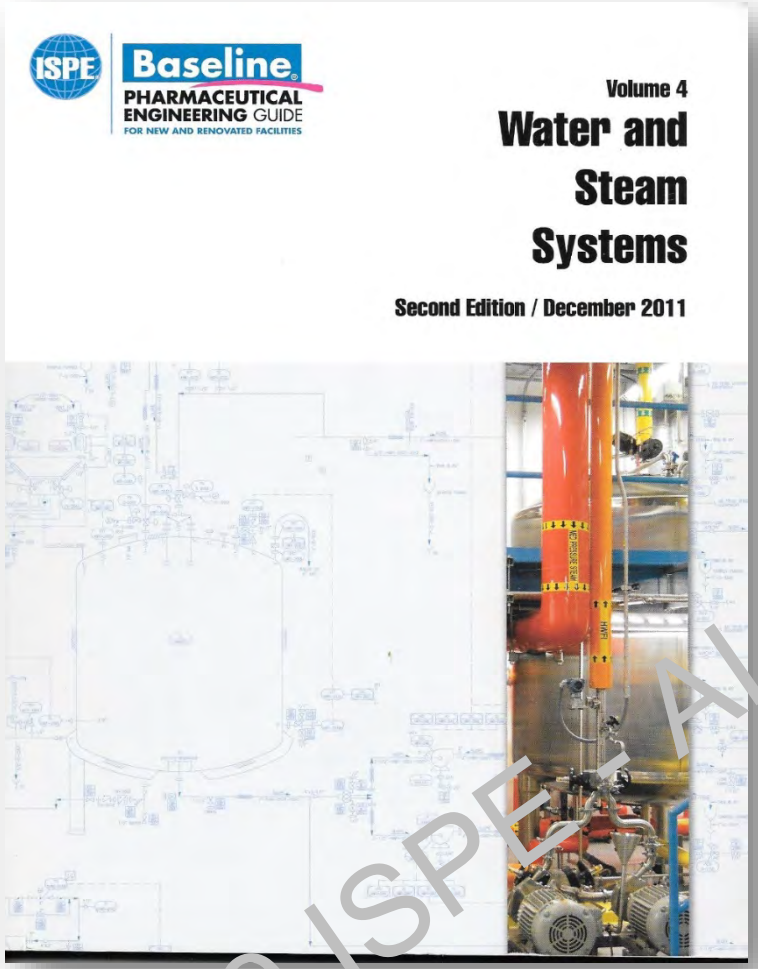
Revision Team

Revision Guidelines

Large and small changes

Next Steps

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Water and Steam Guide 2011

<u>Background from 2011</u>

FDA reviewed

Sponsored by ISPE Technical Doc

Guidance provided by CU COP steering committee

10 Different chapter leaders and 42 Team members

13 Chapters, 260 pages appendix included

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2011 Guide Overview

Section	Title	Number of Pages
Forward	Forward	1
Chapter 1	Introduction	4
Chapter 2	Key Design Philosophies	5
Chapter 3	Water Options & System Planning	12
Chapter 4	Pretreatment Options	22
Chapter 5	Final Treatment Options **Non-Compendial waters, Compendial Purified Water, Compendial Highly Purified Water**	24
Chapter 6	Final Treatment Options: WFI	26
Chapter 7	Pharmaceutical Steam	14
Chapter 8	Storage & Distribution Systems	22
Chapter 9	Laboratory Water	26
Chapter 10	Rouge	26
Chapter 11	Control and Instrumentation	13
Chapter 12	Commissioning/Qualification	4
Chapter 13	Microbial Considerations for pharmaceutical water systems	33
Appendix 1	References	3
Appendix 2	Glossary	**14**

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2011 Guide

Difficulty with FDA review process

- Over 1 year delay as guide was in review
- FDA reviewers were not SMEs on the pharmaceutical water and steam systems

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Why Update Water and Steam Baseline Guide?

Baseline Guide widely recognized as authoritative

Some content needed updating and amending

- Written over a decade ago in 2008 - 2010, technology changes
- Recently released guidelines created gaps (e.g. ASTM, BPE, GPGs for C&Q of water and steam, Ozone, Sampling, Risk-Based Management
- Expansion of Global Standards (e.g. USP, Eur. Ph., WHO, JP, China P, PIC/s, ICH)

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Why Update Water and Steam Baseline Guide?

- Additional content / information required
  - Eur. Ph. non-distilled WFI water generation added
  - Elimination of High Purity Water
  - Artificial Intelligence
  - Redefine the chapter contents
- Overall Improvements
  - Smaller working groups and defined timelines
  - Initiation to Publication just less than 18 months
- Industry acceptance and perception
  - Risk-Based Approach
  - Lean Manufacturing and Flexible Designs
  - Most comprehensive document in existence

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Core Team

This Baseline® Guide Third Edition was produced by a Task Team led by

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Revision Guidelines

Chapter Leaders had the same set of basic directions

- Emphasize “revision” not “rewrite”.
- Purpose of revision is to update the document, remove duplication, and fine tune.
- Avoid imperative words like “all, shall, must” but utilize “many, could, and typical”.
- The revision process is a team effort driven by Chapter Leader

- All chapters managed differently based on strengths
- Some divided the chapter based upon individual strengths.
- Entire group reviewed the chapter Group members provided input to leader who then made revisions.
- Leaders personality impacted performance.

- All chapters were reviewed by Co-chair task leaders

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3rd Edition Completion Status

Received approx. 800 comments

Comments addressed and revisions made

Responses provided to reviewers

3rd Edition is 260 pages

Reviewed by ISPE (Guidance Documents Committee)

Published September 2019

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Significant Changes

Redefinition of all chapters

Content reduced, refined, and enhanced to meet global needs

Greater Flexibility is designs and configurations especially for non-distilled WFI generation

Incorporation of all major pharmacopeias and mention of India, Brazil, and Mexico pharmacopeias

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Summary of Revisions (Ch. 1- 4)

Introduction: revised for consistency with other baseline guides, regulatory, and new content.

Key Philosophies: clarified the correlation between design and operating ranges as well as alert and action levels.

System Options and Planning: expanded to include ICH, China P, requirements.

Pretreatment: enhanced to include pretreatment options utilized globally and definitive options for water purification with flexible alternatives

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Summary of Revisions (Ch. 5 - 6)

Chap 5: Final Treatment options for Compendial PW, WFI: enhanced and rewritten to include final treatment options and improved final treatment technologies.

Chap 6: Systems for the Production of Compendial PW, WFI, and non-compendial: Completely new written chapter focusing on non-distilled WFI and module technology employed to produce PW, WFI and non-compendial waters

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Chapter 7: Pure Steam

Incorporation of USP Standards

Prepared from water meeting Drinking Water Standards of EPA, WHO, major and minor pharmacopeias where applicable.

No added substance

Pure steam quality is determined by the attributes of its condensate.

Steam “Dryness” and amount of “Non-condensable Gasses” are determined by the application.
- References

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Chapter 7: Pure Steam

Incorporation of International Standards

- Pure or Clean steam – Eur. Ph.
  - Meets Eur. Ph. sterilizer guidelines of EN 285 and HTM 2010:2015 for dryness and non-condensable gases

Incorporation of ASME BPE guidance documents.

Defined industry baseline practices on types of steam and applications.

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Chapter 8: Storage & Distribution

- Content upgraded
  - General Overview
  - System Components
  - Microbial Concerns
  - Design Examples
- Content Simplified or Moved
  - Installation Materials and Methods Referenced to other Industry Standards (e.g. BPE)
  - Microbiological moved to separate chapter
- Enhanced Design Examples
  - Better Graphics
  - Definitive Advantages / Disadvantages

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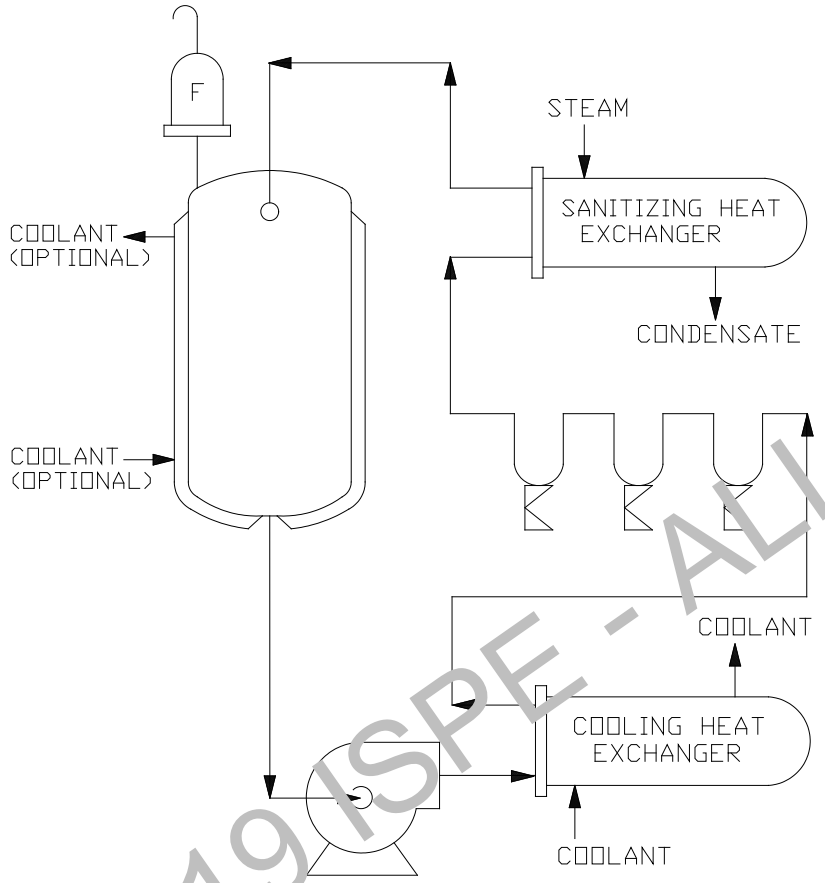
Chapter 8: Section Example

8.3.1 Tanks

When properly designed, storage tanks can offer a number of advantages over tankless systems, including reserve capacity during a purification outage, atmospheric air break for loop return, or to facilitate service of the upstream water purification equipment, as well as minimizing purification system instantaneous demand capacity. Careful consideration should be given to sizing, based on various factors including associated costs. The storage tank also may be used as a contact chamber for sanitization using ozone.

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Chapter 8: Section Example



Advantages:

Well suited if water is generated at ambient temperature and used at ambient temperature
Well suited for small systems.
Moderate capital and operating costs
Non-metallics may be suitable based on application

Disadvantages:

Microbial control is a concern.
Periodic sanitization is required
Sanitization can limit water availability
Additional equipment may increase capital cost
If the tank is supplied with hot water, then this design is not energy efficient.

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Chapter 9 – Lab Water

ISPE recognized the need for guidance on lab water systems

Provides overview of different lab water purification and distribution designs

Includes step-by-step guidance on the type of system to best meet user needs

Compares water quality requirements for laboratory grade waters and compendial waters

Discussions included on monitoring and compliance

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Chapter 10 – Rouge

Condensed and compacted from 2011 version

Intended to provide an understanding of this phenomenon in stainless steel

Detailed explanations on types of rouge

Provides guidelines on how to address the presence of *rouge* and what may be the consequences for the water/steam systems and/or production equipment.

Provides suggested methodology for rouge remediation (de-rouging)

Conclusions emphasize a well-balanced approach for dealing with rouge

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Summary of Revisions (Ch. 11-12)

Instrumentation revised to incorporate updates in instrument technologies

- Advancements in Rapid Microbial Monitoring
- Statistical Process Control
- Artificial Intelligence
- Continuous data acquisition and alert/action limits

C&Q: updated to reflect the ISPE GPG Approaches for Commissioning and Qualification of Water and Steam Systems,

- Evolving approaches to C&Q (e.g. risk based, enhanced commissioning) CPP & CQA assignations

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Chapter 13 – Microbiology

The most comprehensive document on microbials in water systems

Detail included from pretreatment through use point management

- mechanisms driving biofilm proliferation
- microbial control strategies
- microbial sampling and monitoring,
- compendial compliance issues

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Key Points for Discussion

- Design Philosophies and System Planning
  - Establishing appropriate quality attributes
  - Operational Ranges
  - Establishing Life Cycle Costs
- Pretreatment Options
  - Alternative Filtration Options
  - Quality Pretreatment = Reliable Final Treatment
  - Alternative Materials of Construction
  - Optimizing Regeneration/Backwash Frequency

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Key Points for Discussion

- Final Treatment Options
  - Configurations to achieve compendial classifications
  - Use of different modules to attain non-distilled WFI
  - ME vs VC Distillation Comparison
- Storage and Distribution
  - Optimization of Equipment Sizing
  - Alternative Distribution Examples Pros/Cons
  - Materials of Construction
  - Design configurations for optimization

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Key Points for Discussion

Instrumentation and Control

- Selecting a Control Strategy
- Online Instruments and 24/7 operations
- Statistical Process Control and EWPS

Microbiological Considerations

- Alternative Sanitization Methods
- Microbial Enumeration
- Speciation when needed
- Frequency of Sanitization

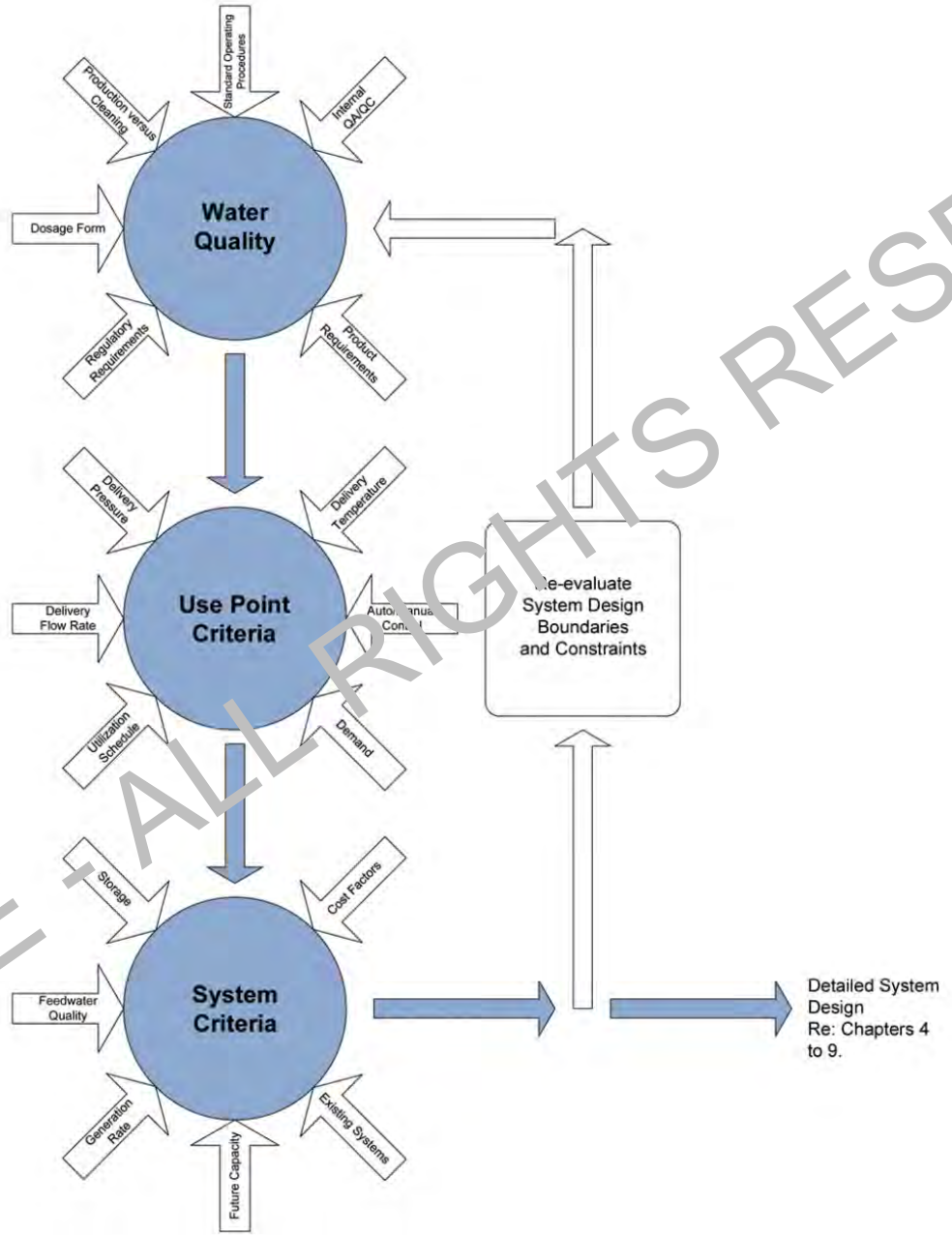
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Guide Use for System Design

Gary Zoccolante, BSME
President
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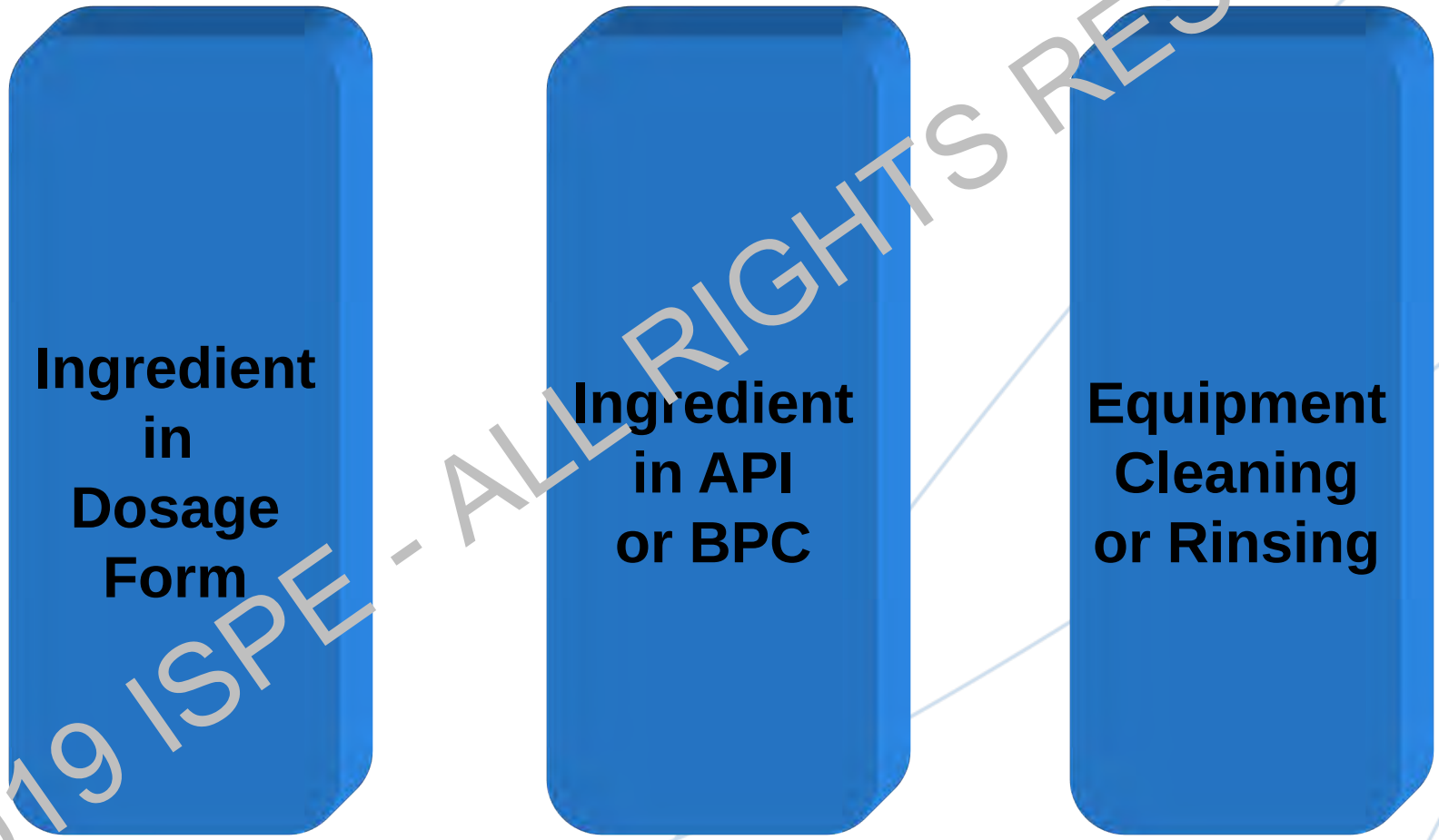
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System Planning



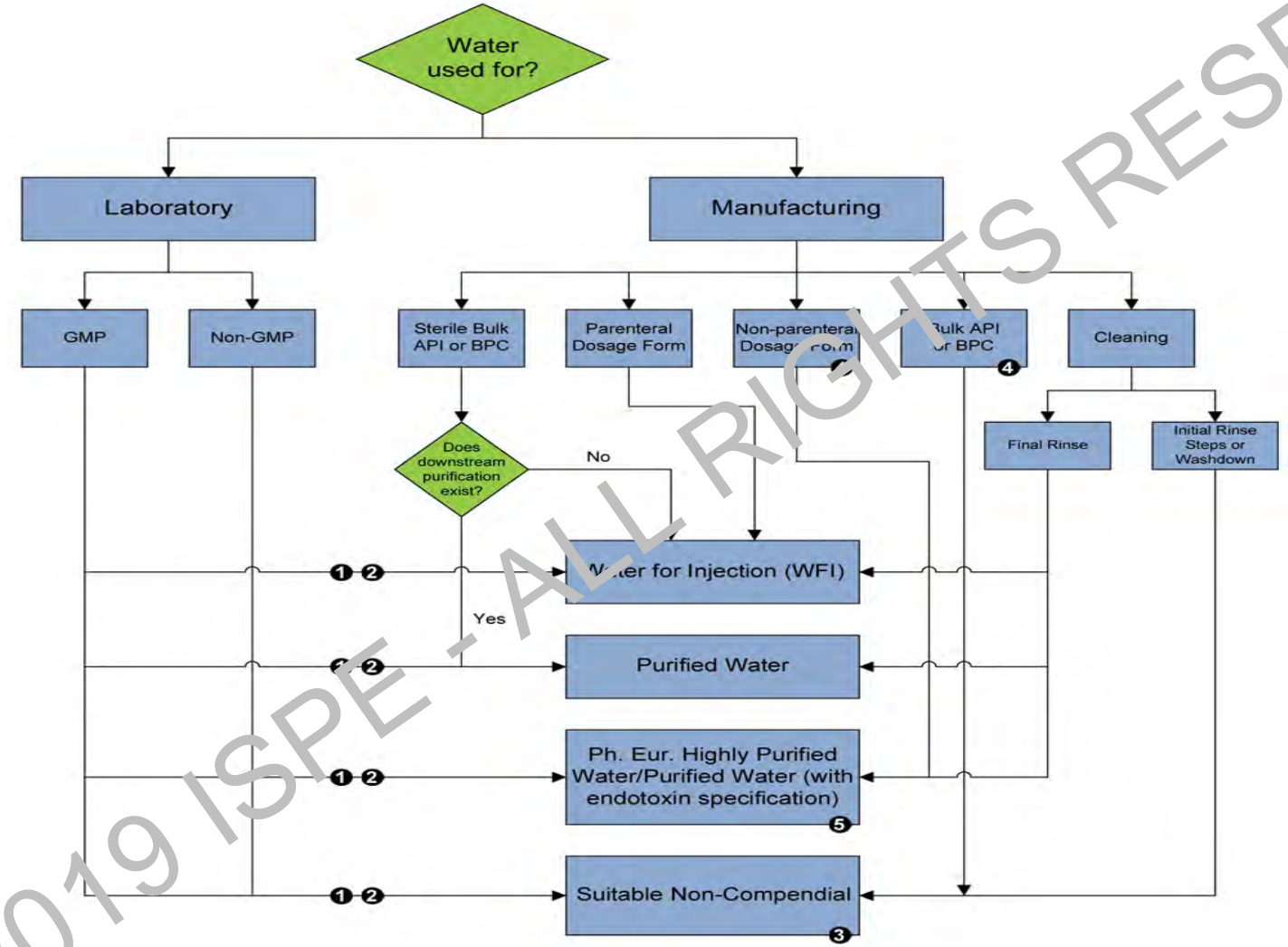
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Pharmaceutical Water Categories



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Fig. 3.1 Pharmaceutical Water Quality Decision Tree



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Water for Injection Questions

What countries require distillation?

What are advantages and disadvantages of multiple effect and vapor compression stills?

Where is membrane based WFI allowed?

Do membrane based systems have special requirements?

Are redundant membrane barriers required?

Are redundant membrane barriers a good idea?

Is Purified Water required for WFI final treatment feed?

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Pharmacopoeial Water Grade Summary

United States
Europe
Japan
China
Brazil
India
Mexico
WHO

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Table 9.3 Specifications

Organization / Reference	European Pharmacopoeia 9.8 (2019)			Japanese Pharmacopoeia XVII (2016)			US Pharmacopeia 42 (2018)		Indian Pharmacopoeia (2018)		Chinese Pharmacopoeia (2015)		Brazilian Pharmacopoeia 5 (2010)			Pharmacopoeia of the United Mexican States 12 (2018)			International Pharmacopoeia	
Water Grade or Type	Purified Water	Water for Injections	Highly Purified Water[5]	Water	Purified Water	Water for Injection	Purified Water	Water for Injection	Purified Water	Water for Injections	Purified Water	Water for Injection	Purified Water	Water for Injection	Ultrapure Water	Purified Water Level 1	Purified Water Level 2[7]	Water for Injection	Purified Water	Water for Injections
Specified Source and Purification Approaches	Drinking Water Source; Dist or IX or RO or other suitable methods	Drinking Water Source; Distillation or purification process equivalent	Highly Purified Water (HPW) from the Ph. Eur. effective 01APR2019 Commission Suppressed	Japanese Drinking Water (Water Supply Law, Ordinance No.101, Article 4, 2003)	"Water" Source; RO, UF, Deionization, Distillation, or a combination thereof	Water or Purified Water Source; Distillation or RO-UF	Drinking Water Source; Suitable process	Drinking Water Source (US,EU,Japan, WHO); Distillation or equiv/superior process	Drinking Water Source; Dist or DI or RO or other suitable methods	Purified Water Source; Distillation or equiv/superior process	Drinking Water Source; Dist or DI or RO or other suitable methods	Purified Water Source; Distillation	Drinking Water Source; Dist or DI or RO or other suitable methods	Properly treated water Source; Distillation	Purified Water Source; Supplemental purification with Dist, DI, RO, other	Drinking Water Source; Dist or RO or DI or Other	Drinking Water Source: e.g. 1P/2P RO; UF, DI, EDI	Potable Water Source: Dist or equivalent	Suitable water source; Dist, DI, RO, or other suitable methods	Potable or Purified Water Source; Distillation
Description	Clear and colourless liquid	Clear and colourless liquid		*	Clear and colourless liquid having no odor	Clear and colourless liquid having no odor	*	*	Clear, colourless, odourless liquid	Clear, colourless, odourless liquid	Clear, colourless liquid, odourless	Clear, colourless liquid, odourless	Clear, colorless, tasteless, odorless liquid	Clear, colorless, tasteless, odorless liquid	Clear, colorless, tasteless, odorless liquid	Transparent and colorless liquid	Transparent and colorless liquid	Transparent and colorless liquid	Clear, colourless liquid; odourless	Clear, colourless liquid; odourless
pH value at 25°C (inclusive range)	*	*		*	*	*	*	*	*	*	*	* - 7.0	*	*	*	5.0 - 7.0	*	*	*	*
Acidity or Alkalinity	*	*		*	*	*	*	*	MRed - not red, BTBlue - not blue	MRed - not red, BTBlue - not blue	MRed - not red, BTBlue - not blue	*	MRed - not red, BTBlue - not blue	MRed - not red, BTBlue - not blue	*	*	*	*	MRed - not red, BTBlue - not blue	MRed - not red, BTBlue - not blue
Conductivity µS/cm @25°C, max	5.1[1]	1.3[1]		*	2.1[2] [1.3[1] in JP Info Ch 21]	2.1[2] [1.3[1] in JP Info Ch 21]	1.3[1]	1.3[1]	5.1[1]	1.3[1]	[1]	1.3[1]	1.3 (Alt to NH_3, Ca/Mg, Cl, NO_3, SO_4)	1.3 (Alt to NH_3, Ca/Mg, Cl, NO_3, SO_4)	0.1	5.1[1]	1.3[1]	1.3[1]	*	*
TOC (as C), max	0.5 mg/L (500 ppb)[3] [Alt to Ox Sub]	0.5 mg/L (500 ppb)[3]		*	0.50 mg/L (500 ppb)[3]	0.50 mg/L (500 ppb)[3]	Instrument response to 0.50 mg/L standard (500 ppb)[3]	Instrument response to 0.50 mg/L standard (500 ppb)[3]	0.5 mg/L (500 ppb)[3] [Alt to Ox Sub]	0.5 mg/L (500 ppb)	0.50 mg/L (500 ppb)[3] [Alt to Ox Sub]	0.50 mg/L (500 ppb)[3]	0.50 mg/L (500 ppb)[3] [Alt to Ox Sub]	0.50 mg/L (500 ppb)[3] [Alt to Ox Sub]	0.05 (50 ppb) [Optional, application-specific]	0.5 mg/L (500 ppb)[3] [Alt to Ox Sub]	0.5 mg/L (500 ppb)[3]	0.5 mg/L (500 ppb)[3]	*	*
Oxidisable Substances (Permanganate Red. Subst.)	Negative to test of 0.1 mL of 0.02M $KMnO_4$ [Alt to TOC]	*		*	*	*	*	*	Negative to test 0.1 mL of 0.02M $KMnO_4$ [Alt to TOC]	*	Negative to test of 0.10 mL of 0.02M $KMnO_4$ [Alt to TOC]	*	Negative to test of 0.2 mL of 0.02M $KMnO_4$ [Alt to TOC]	Negative to test of 0.2 mL of 0.02M $KMnO_4$ [Alt to TOC]		Negative to test of 0.1 mL of 0.02M $KMnO_4$ [Alt to TOC]	*	*	Negative to test of 0.5 mL of 1% $KMnO_4$	Negative to test of 0.2 mL of 0.02M $KMnO_4$
Residue after evaporation on heating at 105°C, mg/100mL, max	*	*		*	*	*	*	*	*	*	1	1	*	*	*	*	*	*	1 (5mg from 500mL)	1 (5mg from 500mL)
Heterotrophic Bacteria Count cfu/mL, max	Action Level 100 [in monograph, mandatory]	Action Level 0.1 (10cfu/100mL, 200mL test) [in monograph, mandatory]		*	Action Level 100 (R2A) [in Info Ch 21, non-mandatory]	Action Level 0.1 (10cfu/100mL) (R2A) [in Info Ch 21, non-mandatory]	100 (optimal medium) [in Info Ch 1231, non-mandatory]	0.1 (optimal medium) (10cfu/100mL, 200mL test) [in Info Ch 1231, non-mandatory]	100 (R2A) Absence specified pathogens [in monograph, mandatory]	0.1 (10cfu/100mL, 200mL test) [in monograph, mandatory]	100 (R2A) [in monograph, mandatory]	0.1 (R2A) (10cfu/100mL, 200mL test) [in monograph, mandatory]	1 (100cfu/100mL) using any valid method; also absence of E. coli and P. aeruginosa [in monograph, mandatory]	0.1 (10cfu/100mL) 200mL, using any valid method) [in monograph, mandatory]	0.01 (1cfu/100mL, 200mL test) [in monograph, mandatory]	*	*	*	*	*
Bacterial Endotoxins EU/mL or IU/mL (note ≤ or <)	<0.25 (dialysis solutions only)	<0.25		*	*	[illegible]25	*	<0.25	≤ 0.25 (dialysis solutions only)	≤ 0.25	*	<0.25	*	≤ 0.25	*	*	*	< 0.25	*	≤ 0.25
Chloride µg/L, max	*	*		*	*	*	*	*	*	*	*	*	pass	pass	*	*	*	*	pass	pass
Sulfate, ppm, max	*	*		*	*	*	*	*	*	*	*	*	pass	pass	*	*	*	*	pass	pass
Calcium and Magnesium ppm, max	*	*		*	*	*	*	*	*	*	*	*	1	1	*	*	*	*	pass	pass
Carbon Dioxide ppm, max	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	pass	pass
Ammonia ppm, max	*	*		0.05[6]	*	*	*	*	*	*	0.3	0.2	0.2	0.2	*	*	*	*	pass	pass
Nitrates ppm, max	0.2	0.2		*	*	*	*	*	0.2	0.2	0.06	0.06	0.2	0.2	*	0.2	0.2	0.2	pass	pass
Nitrites ppm, max	*	*		*	*	*	*	*	*	*	0.02	0.02	*	*	*	*	*	*	*	*
Aluminium ppb, max	10 (dialysis solutions only)	10 (dialysis solutions only)		*	*	*	*	*	10 (dialysis solutions only)	10 (dialysis solutions only)	*	*	*	*	*	*	*	*	*	*
Heavy Metals ppm, max	0.1	*		*	*	*	*	*	0.1[4]	*	0.1	0.1	*	*	*	0.1	*	*	pass	pass

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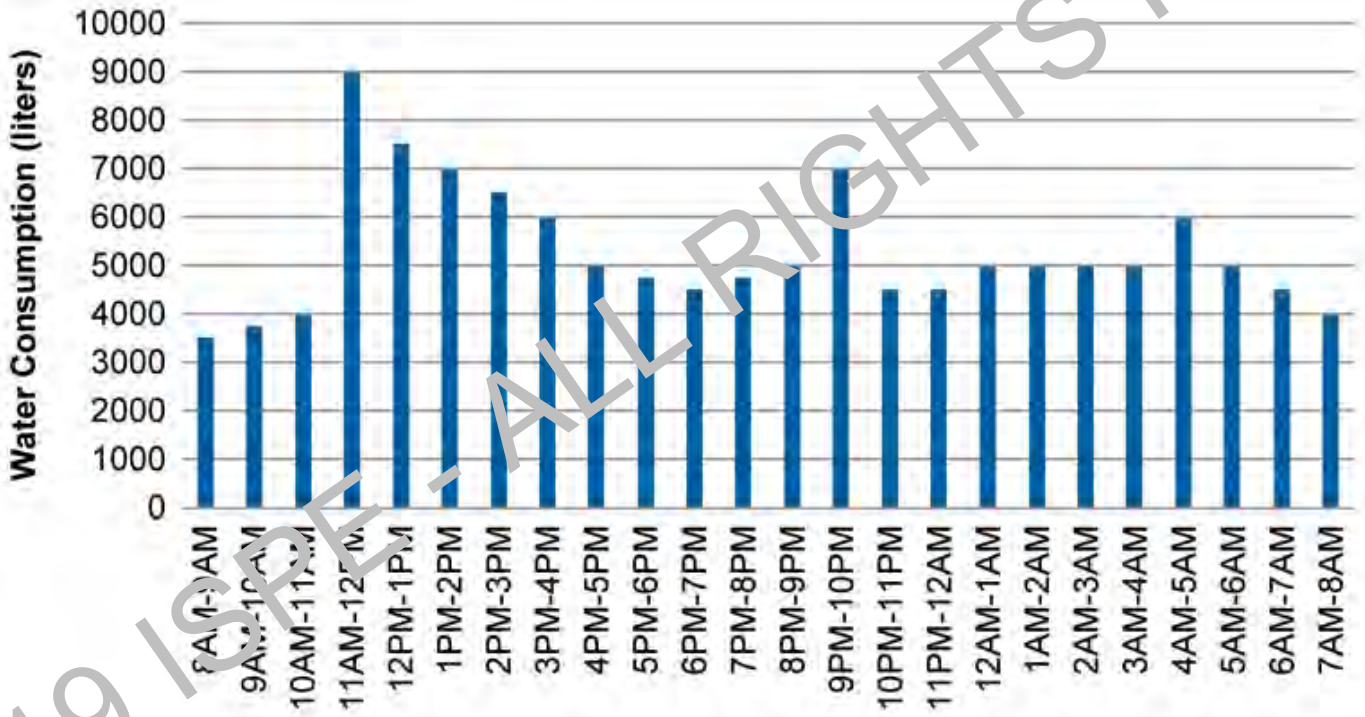
Table 3.2: Point of Use Criteria

ID (Tag)	Temp. °F (°C)	Press. PSIG (BARG)	Type A = Auto M = Manual	Equipment Name (Purpose)	Flow Rate			Daily Use			Comments
					Demand	Diversity	Design	Demand	Diversity	Design	
					GPM (LPM)	Factor	GPM (LPM)	GPD (LPD)	Factor	GPD (LPD)	
					GPM (LPM)	Factor	GPM (LPM)	GPD (LPD)	Factor	GPD (LPD)	
WFI-1	181-185 (83-85)	60-65 (4-4.5)	M	CIP Wash Tank	10.6 (40)		10.6 (40)	317 (1200)	1	317 (1200)	Assume a recirculating cycle in 4 steps for total of 23 minutes
WFI-2	68-74 (20-23)	35-40 (2.4-2.75)	A	Stopper Washer	5.3 (20)	0	0	122 (460)	1	122 (460)	Assume one cycle per day. 100liters/ rinse, 3 rinse/ cycle @ 2lpm for 60mins.

Guide Reference p. 32

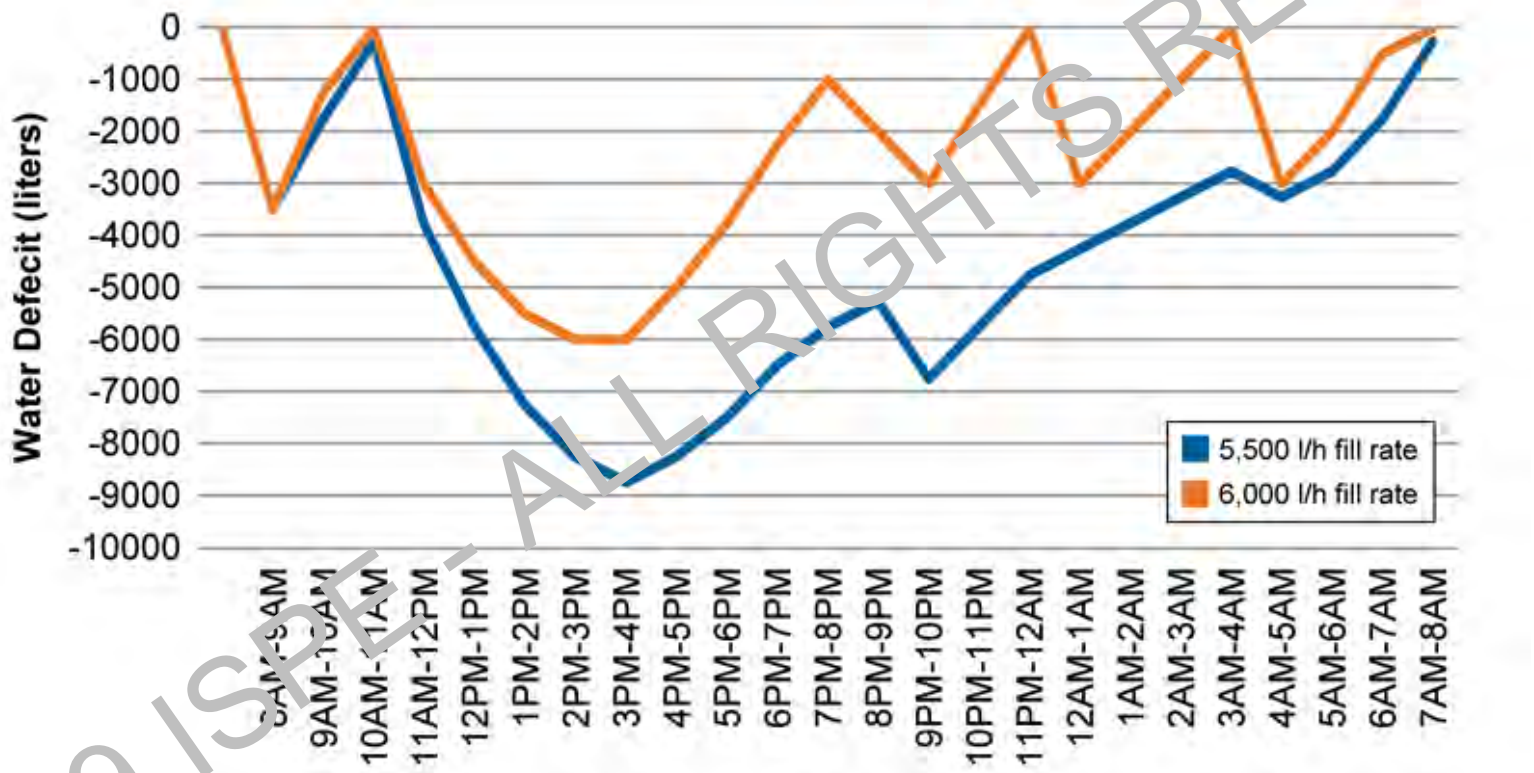
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Fig 3.3 Water Consumption Graph



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Fig 3.4 Storage Tank Capacity Determination



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System Unit Process Selection

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Pharmaceutical Water Generation System Detail Design

Pretreatment (Chapter 4)

- Protect primary purification units
  - Normal feed water conditions
  - Feed water upset conditions
- Specific contaminant reduction to meet final water specification

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Table 4.1 System Pretreatment Selection

Common Impurities	Chlorine Injection	Media Filter	Ultrafiltration	Cartridge/Membrane Filtration	Chlorine Dioxide	Ozone	Activated Carbon Filtration	Antiscalant	Ion Exchange Softeners	Ion Exchange	Electric Scale Control	Ultraviolet Light	Sodium Hydroxide Injection	Reverse Osmosis (RO)	SBS (Sodium Bisulfite)
Turbidity		X[1]	X	X		X									
Particulates/Suspended Solids		X	X	X											
Hardness								X	X	X	X			X	
Iron		X[2]								X	X				
Dissolved Silica								X			X			X	
Colloidal Silica		X	X	X											
Carbon Dioxide													X		
Trihalomethanes (THMs)			X			X	X							X	
Total Organic Carbon (TOC)			X			X	X					X		X	
Microorganisms	X		X		X	X					X	X		X	
Pyrogens			X			X								X	
Free Chlorine							X					X			X
Chloramines							X					X			X
Ammonia									X[3]	X[3]				X[4]	

Notes:
X = Commonly employed
1. With a highly turbid water supply, media filters may be supplemented with coagulation, flocculation, and sedimentation to achieve drinking water standards.
2. For iron removal, typically a green sand media is employed.
3. Refer to discussion in Section 4.10.1 for further detail.
4. Used with acid injection to convert ammonia to ammonium ion to be removed by RO (See Chapter 5).

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Pharmaceutical Water System Detail Design

Final Treatment

- Primary ionic reduction
  - Conductivity spec
  - Specific ion
- Primary organic reduction to meet TOC specification
- Primary microbial/endotoxin control

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Final Treatment Options

- Primary Treatment (Chapter 5)
  - Ion Exchange
  - Reverse Osmosis
  - Distillation
- Polishing Process Options
  - UV
  - MF
  - UF
  - Membrane Degas

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Table 5.1 Multiple Effect Still Utility Requirements

Effects	1	3	4	5	6	7	8
Steam lb/h	9,800–10,200	3,300–3,700	2,600–3,000	2,100–2,500	1,900–2,300	1,500–1,800	1,340–1,600
kg/h	4,445–4,626	1,496 – 1,678	1,179 – 1,360	952–1,134	86–1,043	682–818	609–727
Coolant MBtu/h	7.9–8.1	2.0–2.2	1.4–1.6	1.0–1.2	0.8–1.0	0.07–0.1	0
kW	2,313–2,371	585–644	409–468	293–351	234–293	20.5–29.3	0

Note: MBtu is 1,000 BTU (British Thermal Units).

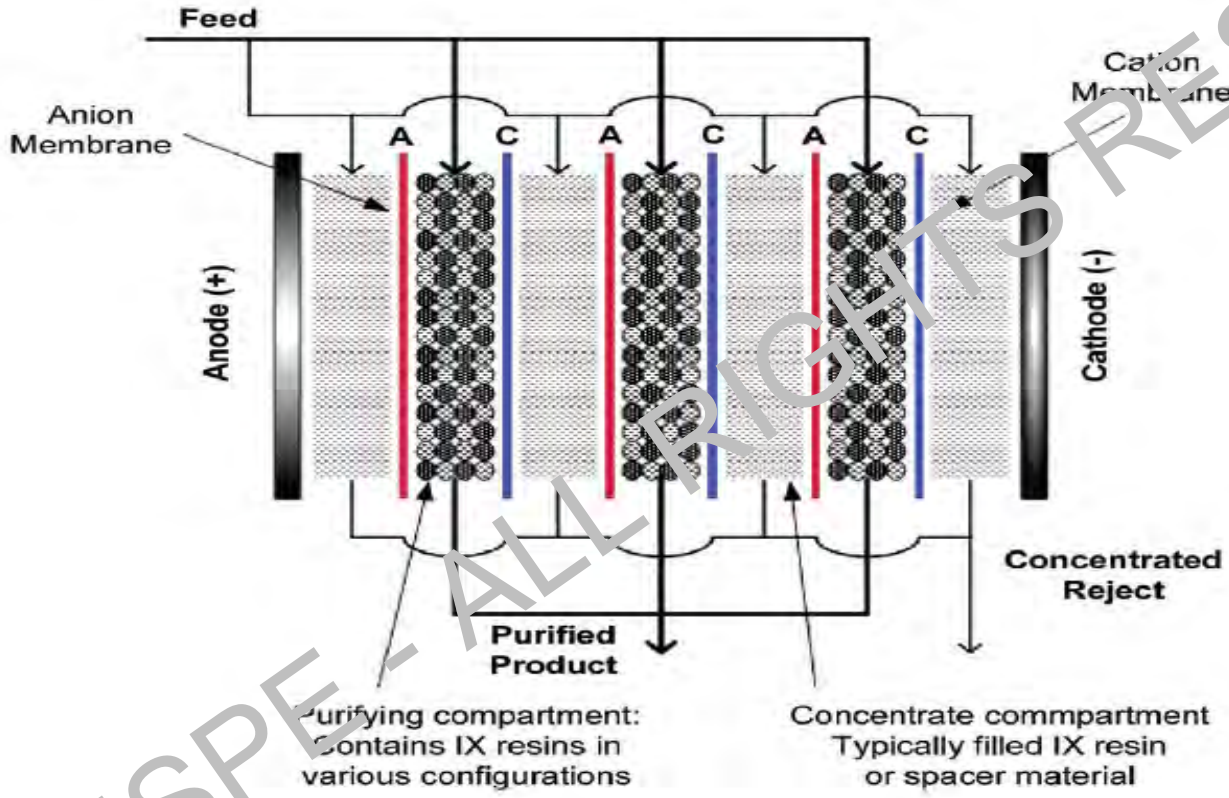
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Table 5.2: VC Utility Consumption per 1,000 Gallons (3,785 liters) of WFI Produced

Capacity Range 200 GPH (757 LPH) to 7200 GPH (27,255 LPH)	Minimum	Maximum
Electricity kWh	44	80
Steam Lb/Hr	[illegible]	1100
Kg/Hr	408	498
Coolant GPM	2	4
LPM	7.6	15.2

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Typical CEDI Process Drawing



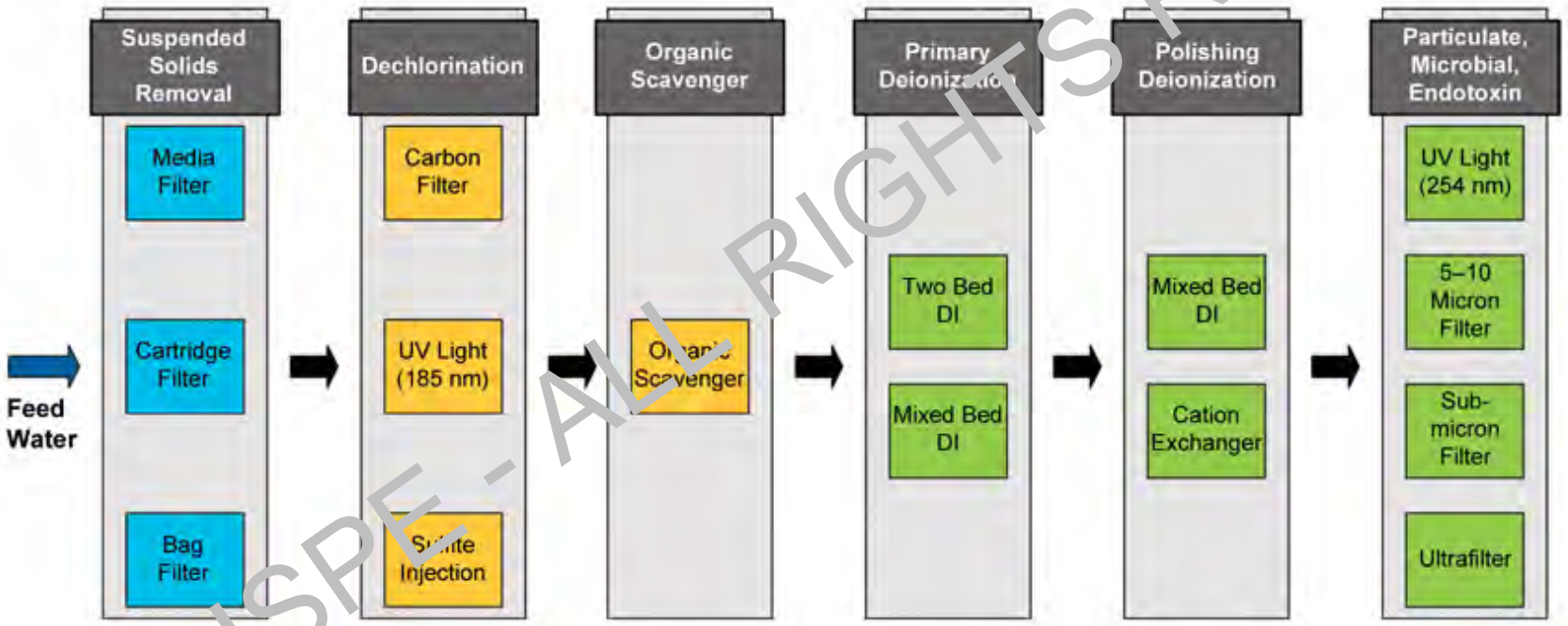
Guide Reference: Figure 5.2

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System Process Technology Maps

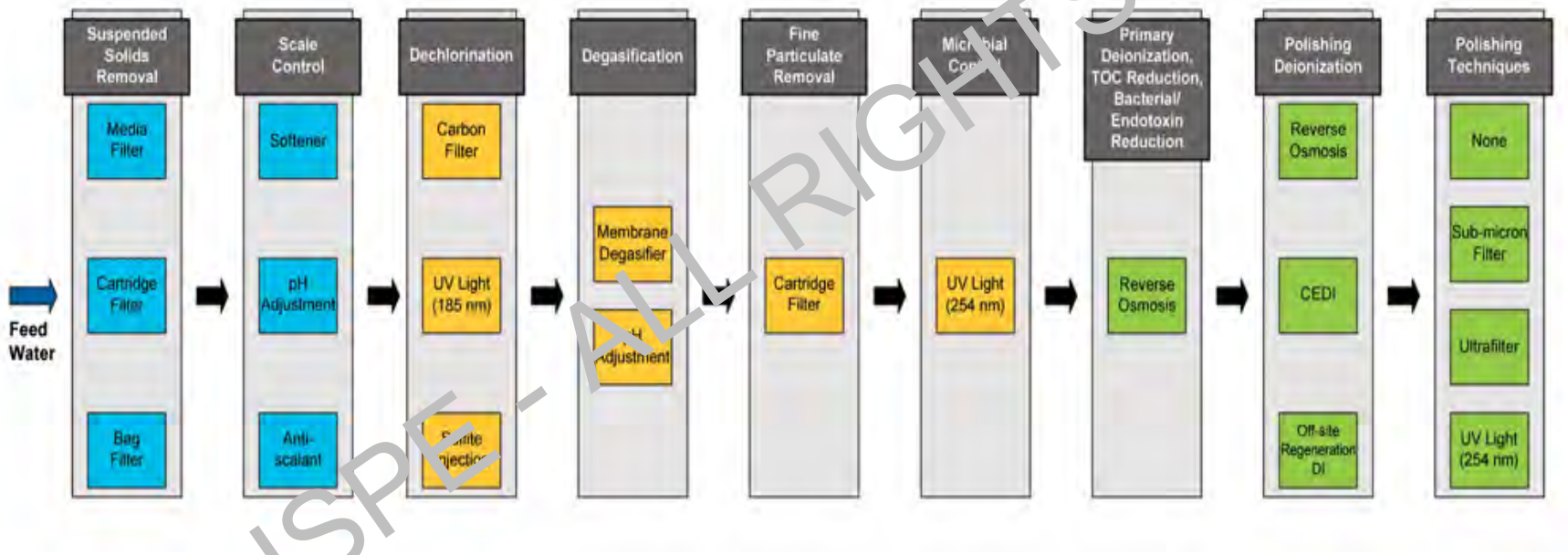
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Fig. 6.2 Deionization Technology Map



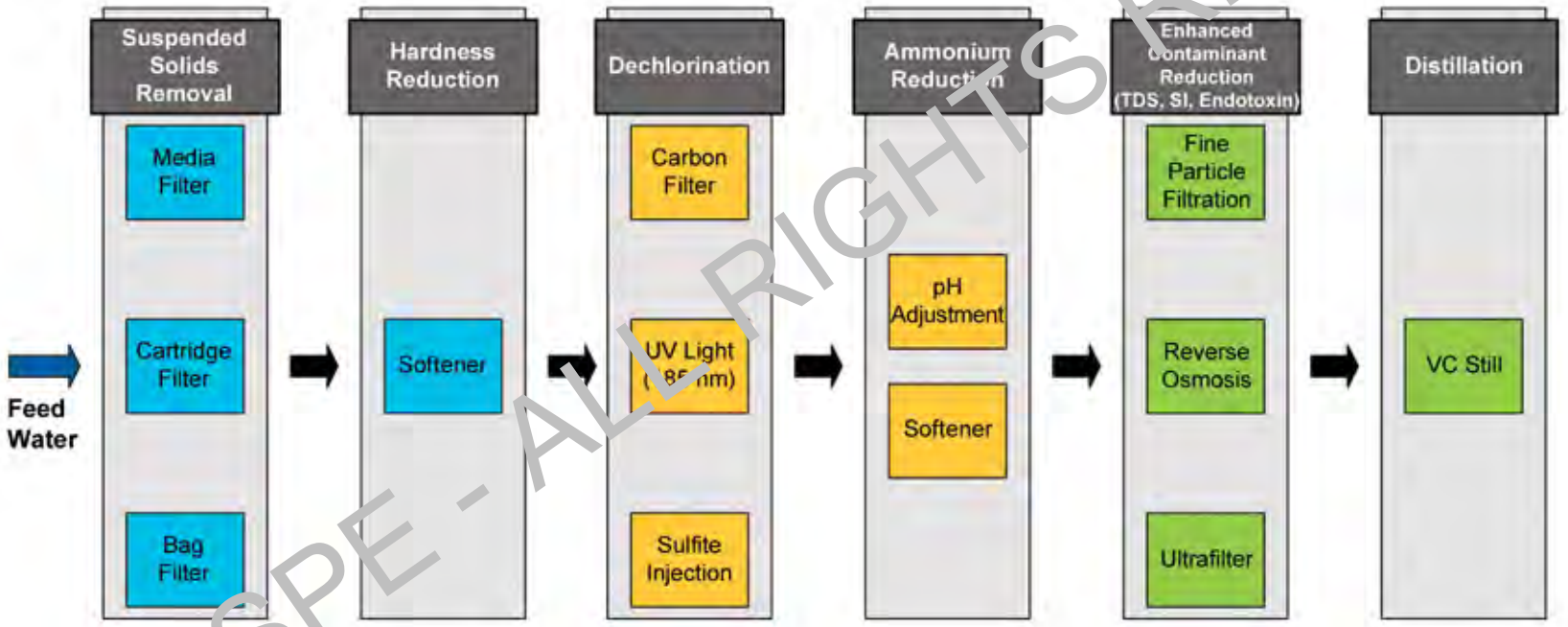
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Fig. 6.1 RO Technology Map



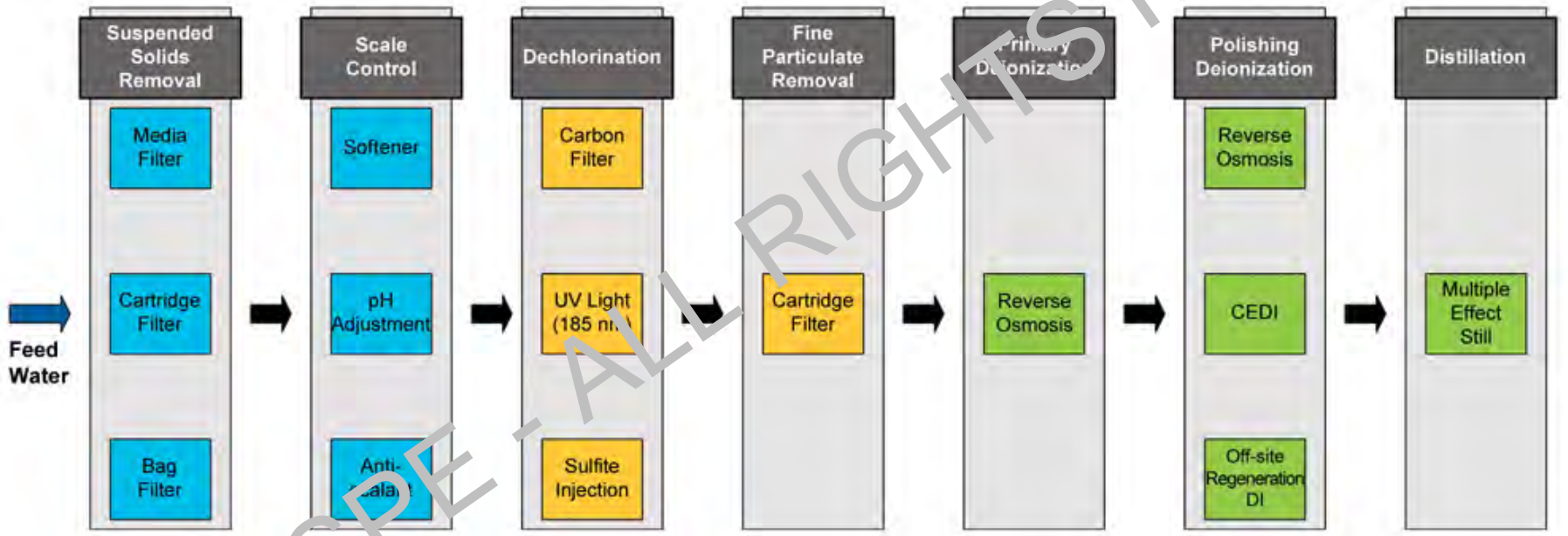
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FIG 6.3 VAPOR COMPRESSION STILL TECHNOLOGY MAP



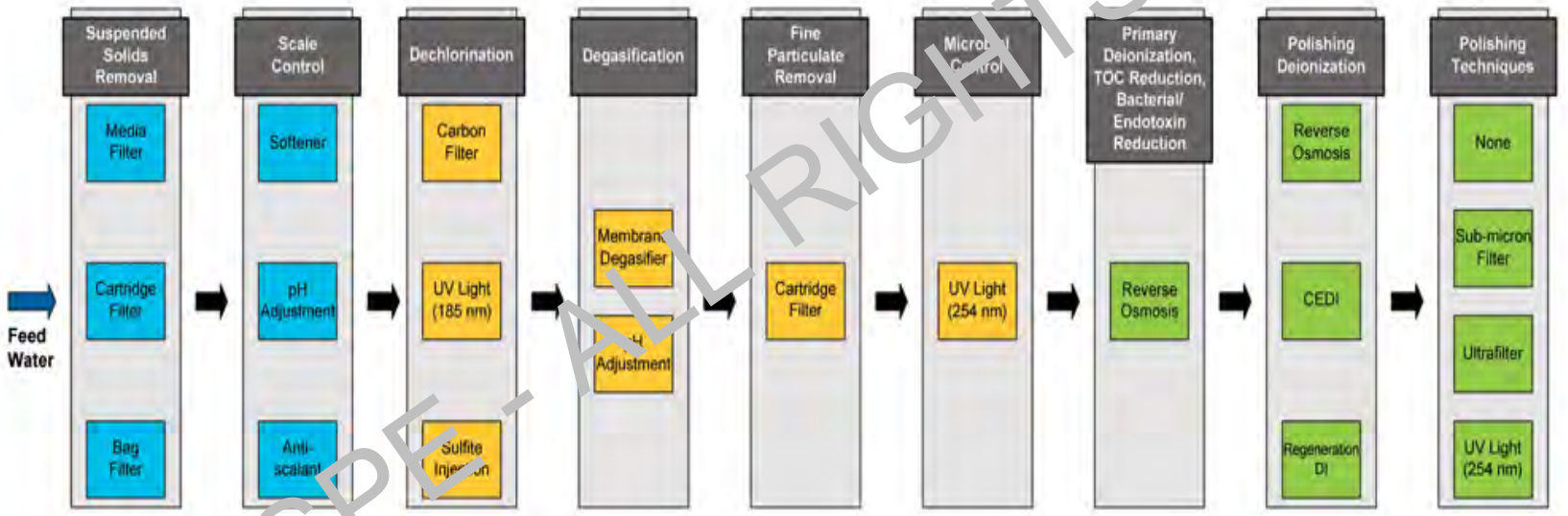
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Fig. 6.4 ME Still Technology Map



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Fig. 6.5 Membrane Based WFI Technology Map

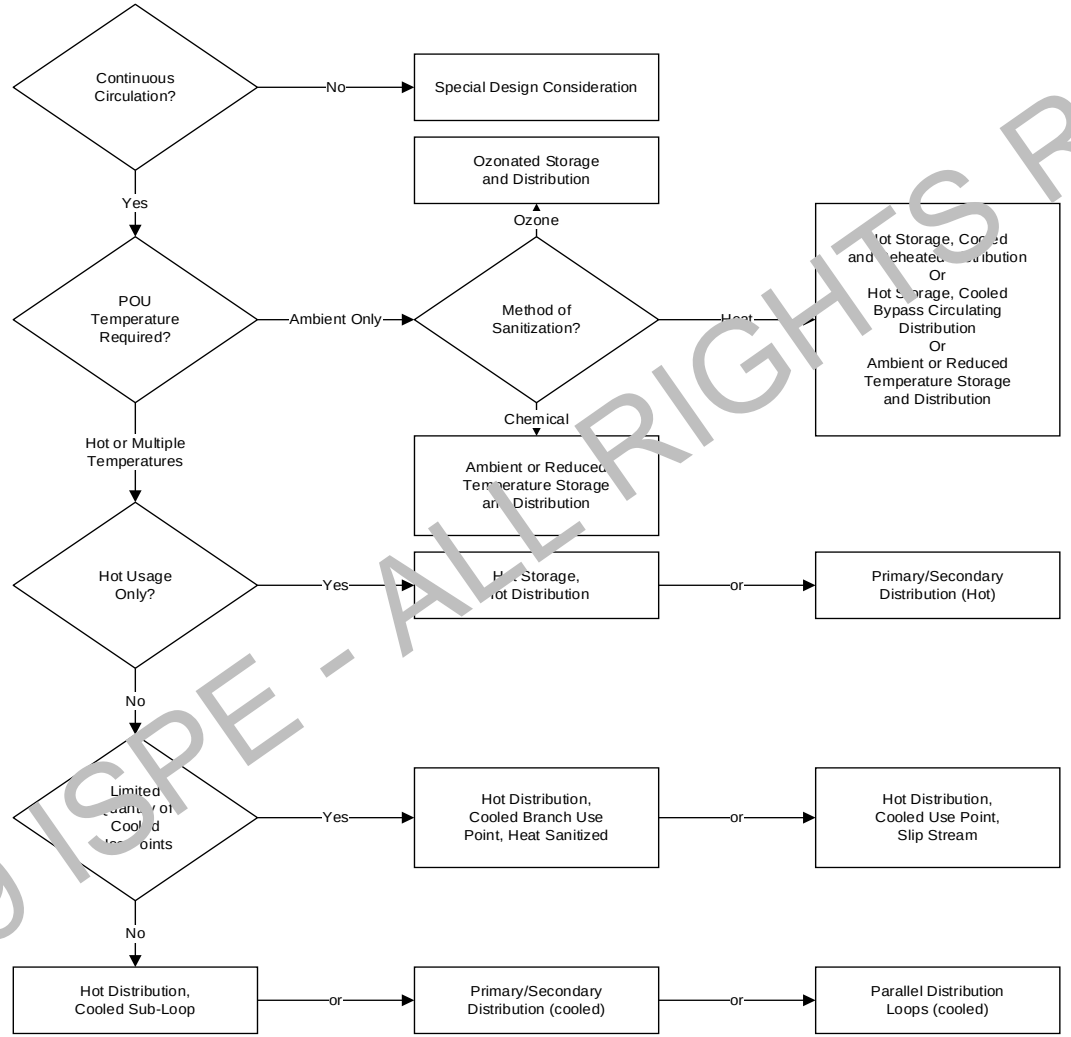


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Storage and Distribution Design and Sanitization Strategy

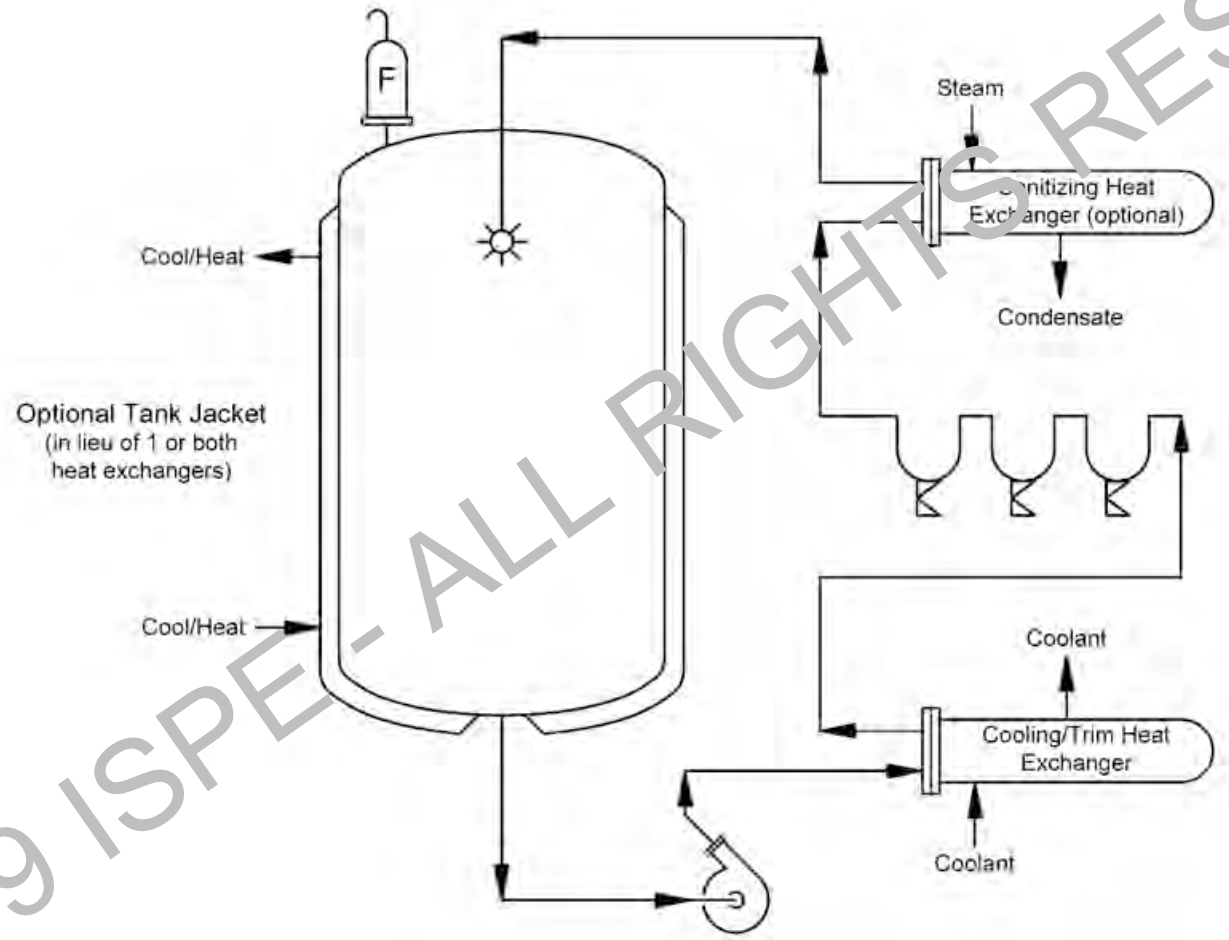
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Fig. 8.1 Storage & Distribution Decision Flow Chart



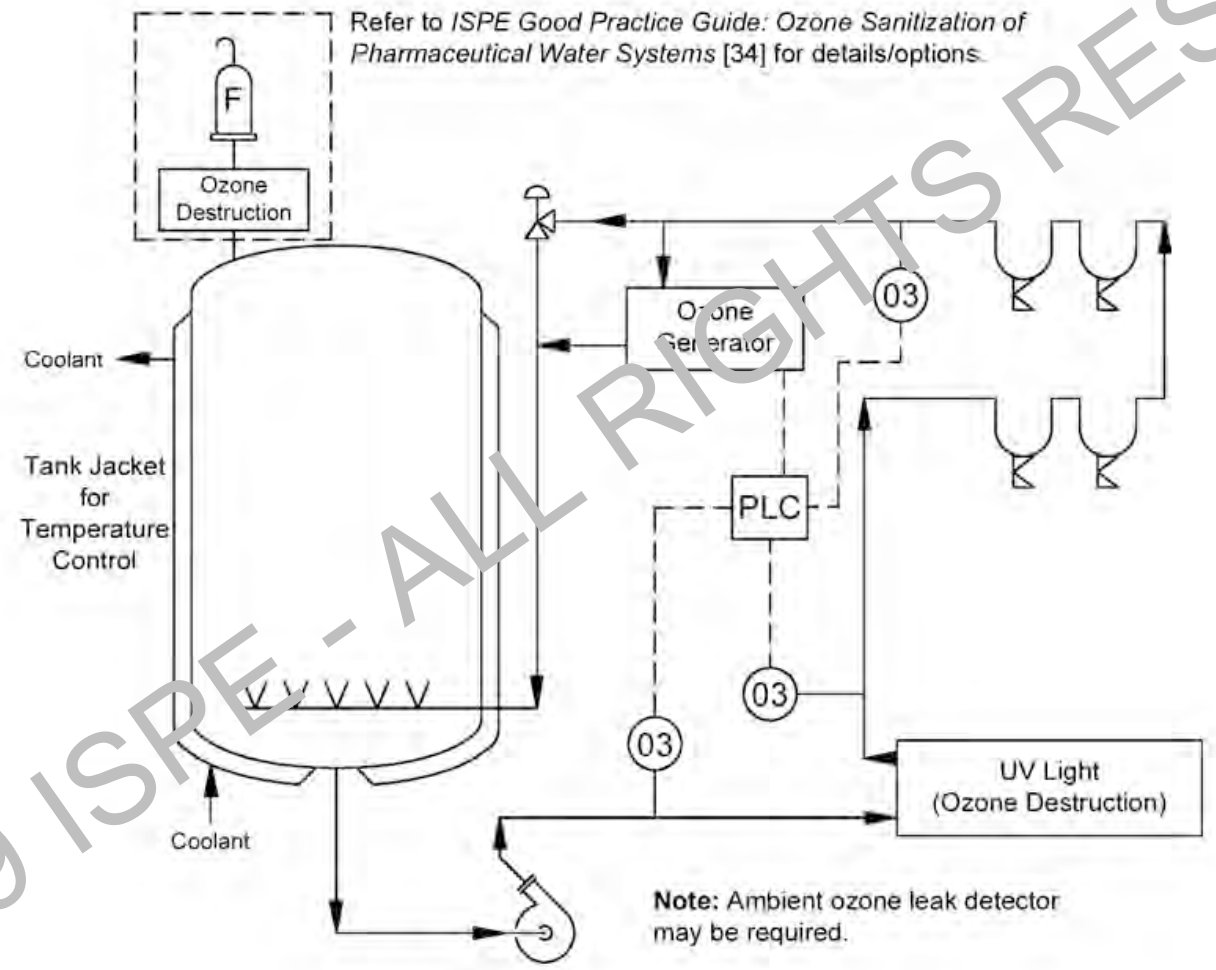
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Fig. 8.3: Ambient/Reduced Temperature Storage & Distribution



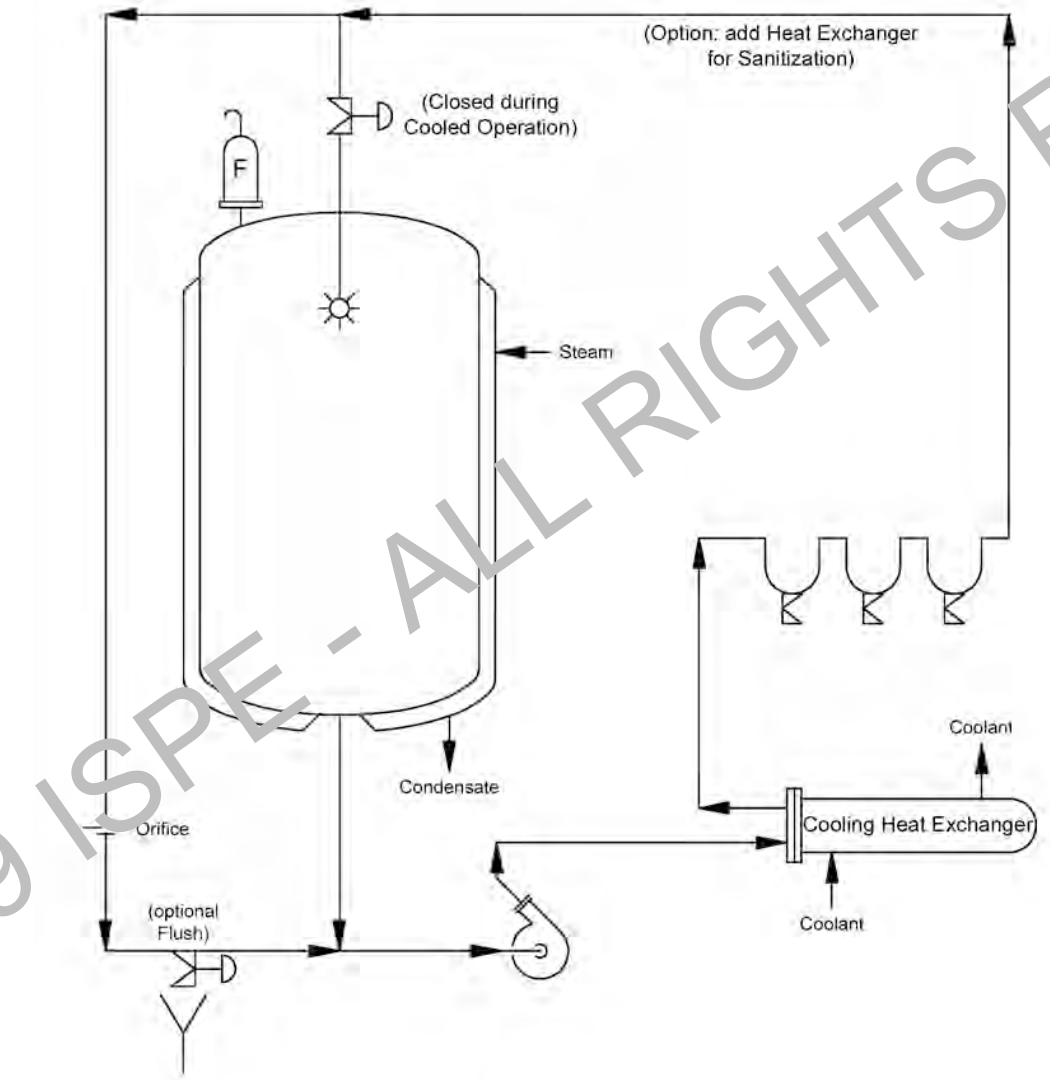
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Fig. 8.5: Ozonated Storage and Distribution



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Fig. 8.9: Hot Storage, Cooled Bypass Circulating Distribution



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Table 8.1: System Components Comparison

Item	Type	Industry Practice	Advantages	Disadvantages
Heat Exchangers	Concentric Tube	Common in sanitary applications	Simple design, low pressure drop	Limited surface area
	Plate and Frame (Single Wall)	Common in pretreatment	Cost, large surface area	Drainage, not "fir… in … out," gask…
	Plate and Frame (double Wall)	Common in sanitary applications	Improved integrity	Co…
	Tube and Shell-Single Tubesheet	Common in pretreatment	Cost	Cont…mination potential
	Tube and Shell-Double Tubesheet	Common in sanitary applications	Highest integri…	…ost
Pumps	Centrifugal with Single Seal	Common for purified and WFI	…ost, …plicity	Seal integrity
	Centrifugal with Double Seal	Common for WFI	Seal …tegrity	Cost, maintenance
	Positive Displacement-Rotary	Can be used for hi… pres…200 ps…	High pressure	Cost, pulsation
	Positive Displacement-Diaphragm	Can be used …r suctio… lift	Suction lift/priming	Limited flow, pulsation
Tanks	Single Shell	Co…mon fo… ambient operation No he… sanitization	Cost, easy inspection	Sweating, flexibility
	Insulated …th…	Common for cold or for ambient Operation with heat sanitization	Energy, safety	Cost, Difficult To Inspect and Repair (DTI&R)
	…acketed 1/2 Pipe (and a…rnative)	Common for hot applications and/or heat sanitization	Thermal efficiency	Welding, cost, (DTI&R)
	Jacketed-Dimple Wall	Common for hot applications and/or heat sanitizations	Cost, less welding	Thermal efficiency (DTI&R)
Reli… Devices	Rupture Disc	Common for sanitary applications	Monitorable, integrity, suitable for pressure and/ or vacuum service	Cost, failure causes shutdown
	Relief Valve	Common for sanitary applications	Cost	Not monitorable, can result in potential contamination. Suitable for vacuum rated tanks only unless used with vacuum relief.
Valves	Diaphragm	Common for sanitary systems	Integrity	Cost, not suited for steam.
	Butterfly	Common in pretreatment	Cost	Stem, crevices
	Ball	Common in pretreatment and CS	Cost, CS service	Stem, crevices
	Plug, Gate, Globe	Common in pretreatment	Cost	Stem, crevices
	Rising Stem Sanitary	Common in sanitary throttling	Integrity, leak detection, performance	Angle design

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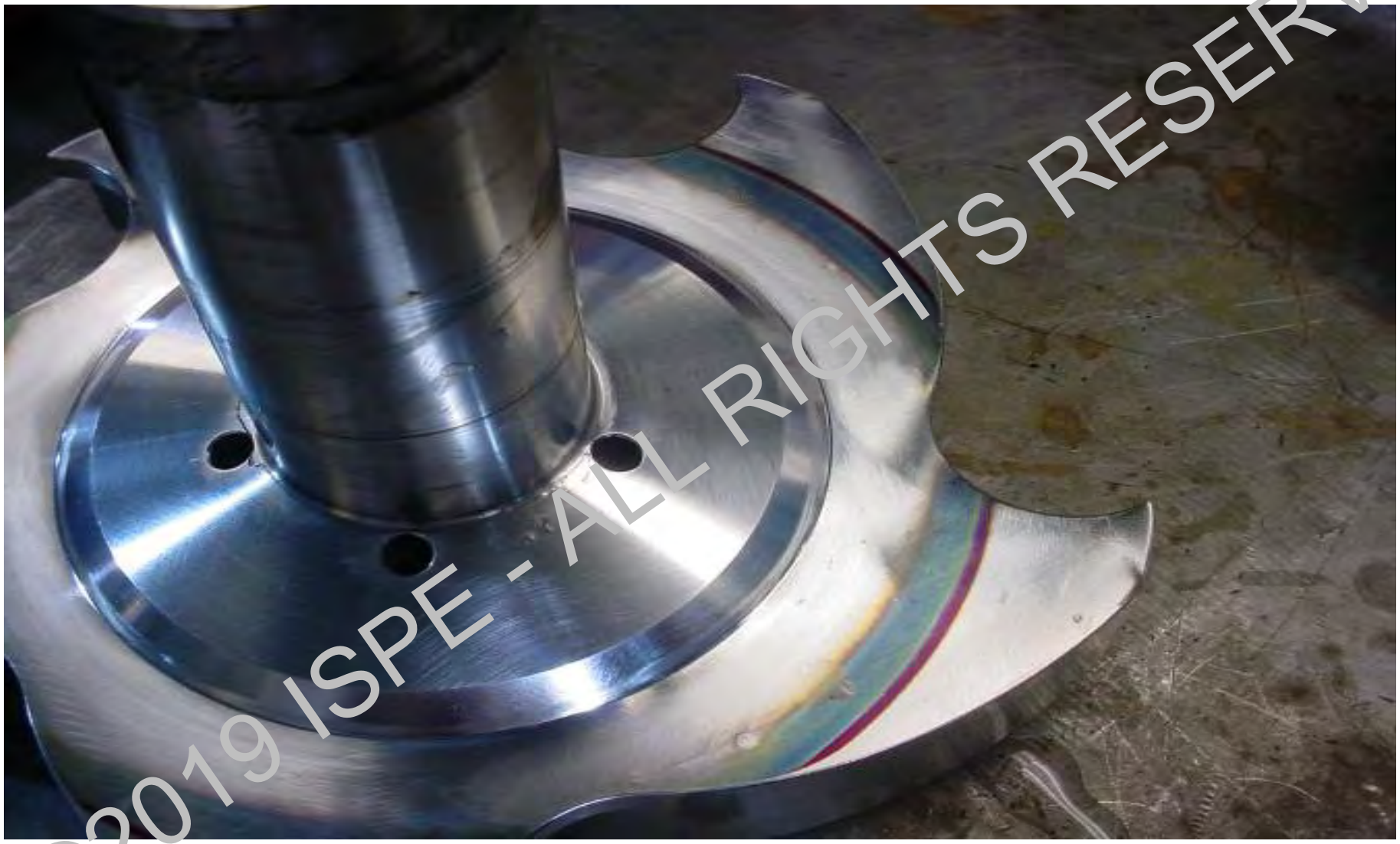
Table 8.2 Distribution Piping Materials Comparison

	Polyvinylidene Fluoride (PVDF)	Polypropylene (PP)	316L Stainless Steel
Material Cost	High	Medium	High
Installation Cost[1]	High	Medium	Medium
Steam Sanitizable	Yes[2]	No	Yes
Hot Water Sanitizable	Yes[3]	No[3]	Yes
Ozone Sanitizable	Yes	Yes[4]	Yes
Chemical Sanitizable	Yes	Yes	Yes
Rouging Susceptibility	No	No	Yes
Corrosion Resistance	High	High	High
Availability	Medium	Medium	High
Extractables	Low	Low	Low
Degree of Thermal Expansion	High	High	Low
Joining Method • **Hygienic Clamp** • **Solvent/Glue**[5] • **Thermal Fusion/Weld**	Yes No Yes	Yes No Yes	Yes No Yes
Support Requirements	High	High	Low
Typical Usage	Medium	Medium	High

Notes:
1. Based on skilled labor requirements, ease of welding, ease of visual inspection, shop fabrication requirements, etc.
2. Steam pressure and temperature control are critical and need to be kept below the manufacturer's ratings.
3. Sanitization of PP can only be performed at low temperatures (e.g., 60°C (140°F)). For PP and PVDF nearly continuous support along the entire length is needed.
4. Limited tolerance; may be beyond manufacturers recommendations.
5. Materials using solvents and glues are not recommended and may result in elevated TOC.

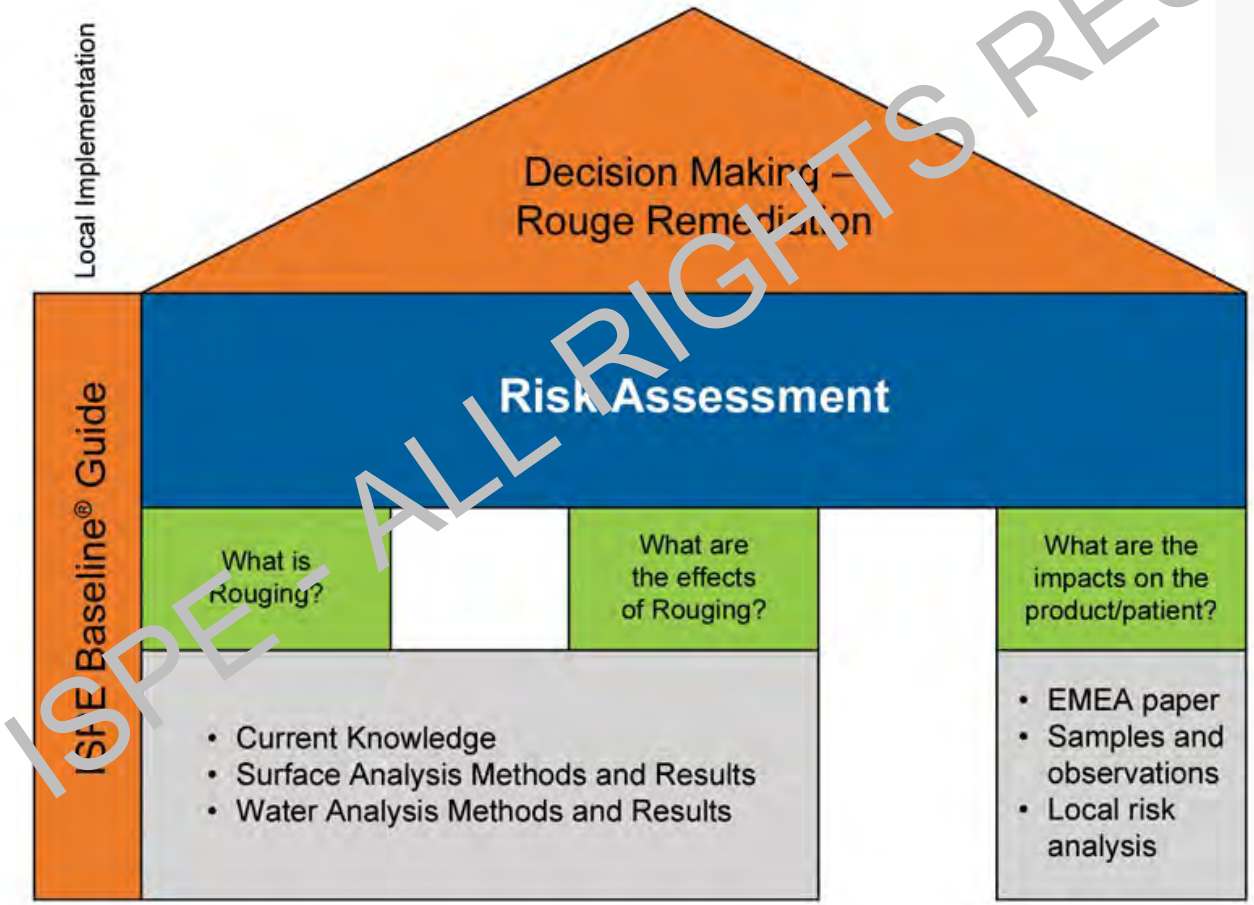
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AL6XN Impeller after 2 Years 80°C Service



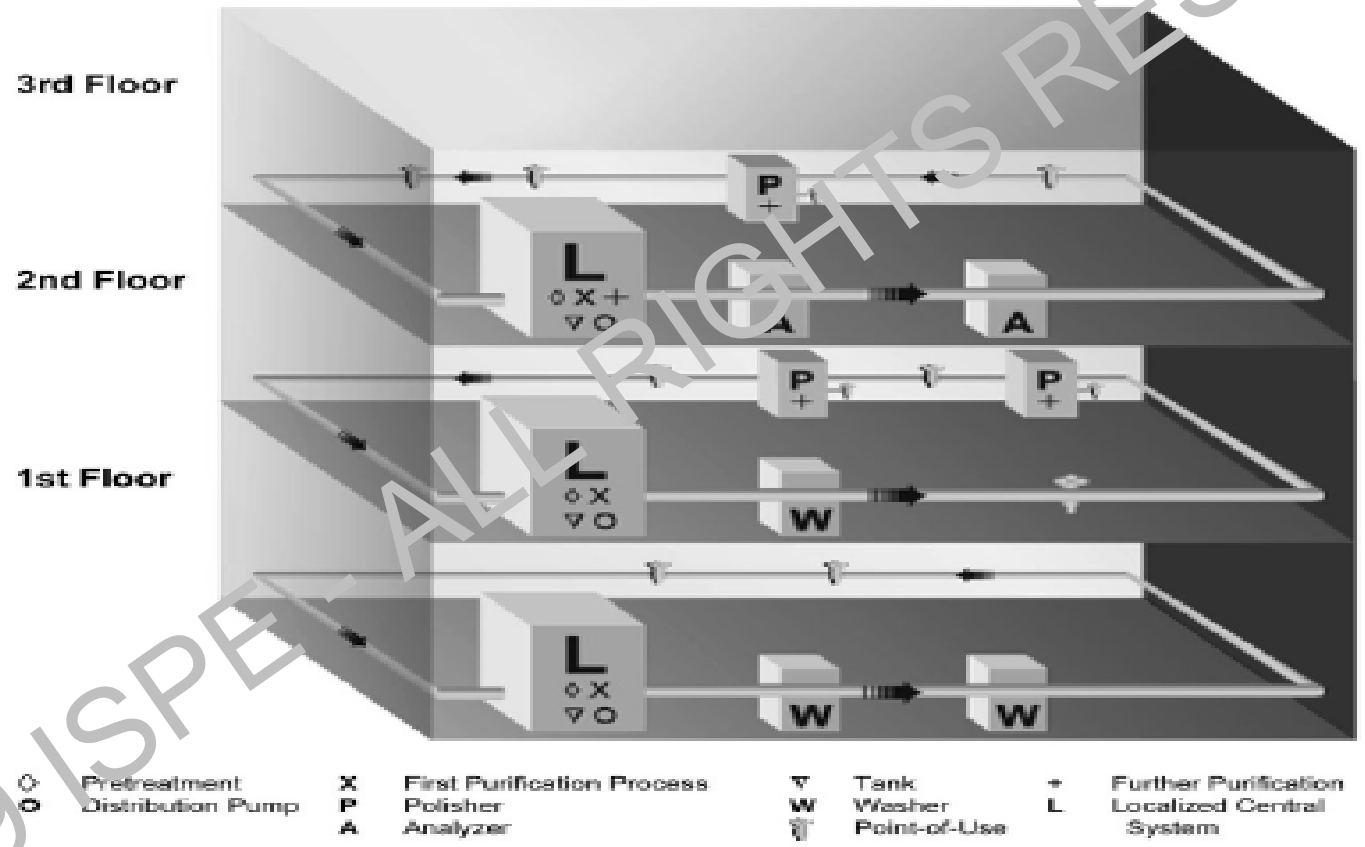
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Rouge Risk Assessment



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Example of Localized Systems

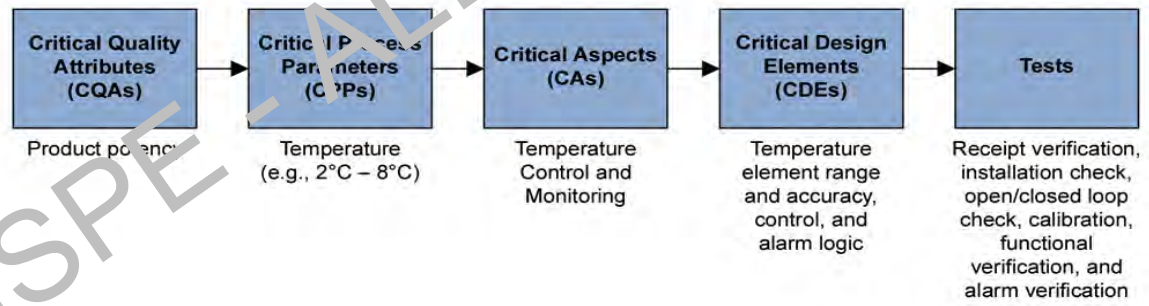


Reference: Figure 9.2 (p. 172)

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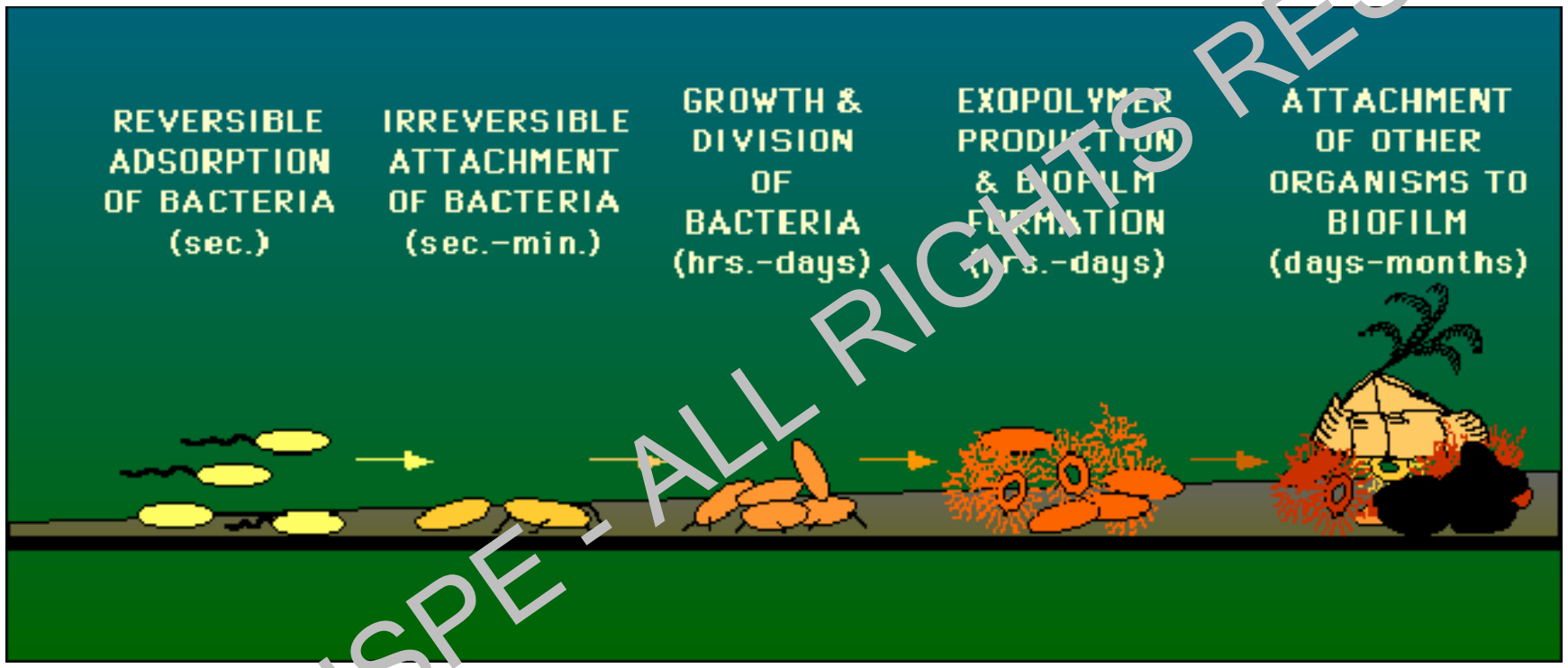
Critical Design Element (CDE) – Definition

- Design function or feature of an engineered system that is necessary to consistently manufacture products with the desired quality attributes.
  - Examples of automation design functions include alarms and data management.
  - Examples of engineering design features include components, instruments, and materials of construction.
- CDEs are identified and documented based on technical understanding of the product CQAs, process CPPs, and equipment design/automation.
- CDEs are verified through C&Q.



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Biofilm Formation



Mark Wiencek, Rohm & Haas Company, Spring House, PA 19477

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WRAP UP

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POLL

Do you have plans to implement changes recommended in the new Water and Steam 3rd Edition?

- ❑ Immediately
- ❑ Within the next 6 months to 1 Year
- ❑ Within the next 1 to 3 years
- ❑ Unsure
- ❑ I have no plans to implement changes at this time



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Q&A

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Upcoming Webinars

- 11 December 2019 - Data Science Tools for Successful Technology Transfer
- 23 January - One Size Does Not Fit All: Strategies for Bringing Advanced Therapy Medicinal Products to Market

Topic Ideas or Feedback?

Send to ispeak@ispe.org

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