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

Speakers:
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21 November 2019
Hosted by ISPE
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 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.
POLL

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

- Yes
- No
- We’re still using the 1st edition
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
Water and Steam Guide 2011

Background from 2011
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
## 2011 Guide Overview

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<th>Number of Pages</th>
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</table>
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
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)
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
Core Team

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

Brian Pochini Sanofi
Nissan Cohen Biopharmaceutical Water Doc
Gary Zoccolante Plymouth Rock Water Consultants

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Anders Widov  Wipha AB  Sweden
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Paul Whitehead  VWS Limited  United Kingdom
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
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
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
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.
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
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
Chapter 7: Pure Steam

Incorporation of International Standards
  Pure or Clean steam – Eur. Ph.

Incorporation of ASME BPE guidance documents.
Defined industry baseline practices on types of steam and applications.
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
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.
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.
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
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
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
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
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
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
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
System Planning

Water Quality

Use Point Criteria

System Criteria

Detailed System Design
Re: Chapters 4 to 9.

Re-evaluate System Design Boundaries and Constraints

Delivery Flow Rate

Dosage Form

Quality System

Functional Quality

Cost/Value Matrix

Cost/Time Matrix

Cost/OEE Matrix

OEE/Time Matrix

OEE/Cost Matrix

Time/OEE Matrix

OEE

Time

Cost
Pharmaceutical Water Categories

- Ingredient in Dosage Form
- Ingredient in API or BPC
- Equipment Cleaning or Rinsing
Fig. 3.1 Pharmaceutical Water Quality Decision Tree
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?
Pharmacopoeial Water Grade Summary

United States
Europe
Japan
China
Brazil
India
Mexico
WHO
Table 9.3 Specifications

<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Water Grade or Type</td>
<td>Purified Water</td>
<td>Water for Injections</td>
<td>Highly Purified Water(1)</td>
<td>Water</td>
<td>Purified Water</td>
<td>Water for Injections</td>
<td>Unpurified Water</td>
<td>Water for Injection</td>
</tr>
<tr>
<td>Specified Source and Purification Approaches</td>
<td>Dialysis Water or other suitable methods</td>
<td>Dialysis Water or other suitable methods</td>
<td>Dialysis Water or other suitable methods</td>
<td>Dialysis Water or other suitable methods</td>
<td>Dialysis Water or other suitable methods</td>
<td>Dialysis Water or other suitable methods</td>
<td>Dialysis Water or other suitable methods</td>
<td>Dialysis Water or other suitable methods</td>
</tr>
<tr>
<td>Description</td>
<td>Clear and colourless</td>
<td>Clear and colourless</td>
<td>Clear and colourless liquid, odourless</td>
<td>Clear and colourless liquid, odourless</td>
<td>Clear and colourless liquid, odourless</td>
<td>Clear and colourless liquid, odourless</td>
<td>Clear and colourless liquid, odourless</td>
<td>Clear and colourless liquid, odourless</td>
</tr>
<tr>
<td>pH value at 25°C (pH range)</td>
<td>5.0 to 7.0</td>
<td>5.0 to 7.0</td>
<td>5.00 mg/L</td>
<td>5.00 mg/L</td>
<td>5.00 mg/L</td>
<td>5.00 mg/L</td>
<td>5.00 mg/L</td>
<td>5.00 mg/L</td>
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<td>综合实力 or Alkalinity</td>
<td>≤ 0.25 mg/L</td>
<td>≤ 0.25 mg/L</td>
<td>≤ 0.25 mg/L</td>
<td>≤ 0.25 mg/L</td>
<td>≤ 0.25 mg/L</td>
<td>≤ 0.25 mg/L</td>
<td>≤ 0.25 mg/L</td>
<td>≤ 0.25 mg/L</td>
</tr>
<tr>
<td>Conductivity at 25°C (μS/cm)</td>
<td>≤ 2.0 (Alt to Ox Sub)</td>
<td>≤ 2.0 (Alt to Ox Sub)</td>
<td>≤ 2.0 (Alt to Ox Sub)</td>
<td>≤ 2.0 (Alt to Ox Sub)</td>
<td>≤ 2.0 (Alt to Ox Sub)</td>
<td>≤ 2.0 (Alt to Ox Sub)</td>
<td>≤ 2.0 (Alt to Ox Sub)</td>
<td>≤ 2.0 (Alt to Ox Sub)</td>
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<td>Total Oxidisable Substances (Permanganate Reduction Value)</td>
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<td>≤ 0.5 mg/L</td>
<td>≤ 0.5 mg/L</td>
<td>≤ 0.5 mg/L</td>
<td>≤ 0.5 mg/L</td>
<td>≤ 0.5 mg/L</td>
<td>≤ 0.5 mg/L</td>
<td>≤ 0.5 mg/L</td>
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<tr>
<td>Residual after evaporating on heating at 180°C, mg/100mL, max</td>
<td>≤ 0.10</td>
<td>≤ 0.10</td>
<td>≤ 0.10</td>
<td>≤ 0.10</td>
<td>≤ 0.10</td>
<td>≤ 0.10</td>
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<tr>
<td>Bacterial Endotoxins (E. coli, nL)</td>
<td>≤ 0.25 to 25.0 unit/mL (500 mL)</td>
<td>≤ 0.25 to 25.0 unit/mL (500 mL)</td>
<td>≤ 0.25 to 25.0 unit/mL (500 mL)</td>
<td>≤ 0.25 to 25.0 unit/mL (500 mL)</td>
<td>≤ 0.25 to 25.0 unit/mL (500 mL)</td>
<td>≤ 0.25 to 25.0 unit/mL (500 mL)</td>
<td>≤ 0.25 to 25.0 unit/mL (500 mL)</td>
<td>≤ 0.25 to 25.0 unit/mL (500 mL)</td>
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<td>Bacterial Resistance</td>
<td>E. coli or S. aureus (K12 or J1)</td>
<td>E. coli or S. aureus (K12 or J1)</td>
<td>E. coli or S. aureus (K12 or J1)</td>
<td>E. coli or S. aureus (K12 or J1)</td>
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### Table 3.2: Point of Use Criteria

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<tr>
<th>ID (Tag)</th>
<th>Temp. °F (°C)</th>
<th>Press. PSIG (BARG)</th>
<th>Type</th>
<th>Equipment Name (Purpose)</th>
<th>Flow Rate</th>
<th>Daily Use</th>
<th>Comments</th>
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<td></td>
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<td></td>
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<td>Demand</td>
<td>Diversity</td>
<td>Design</td>
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<td>GPM (LPM)</td>
<td>Factor</td>
<td>GPM (LPM)</td>
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<td></td>
<td></td>
<td>GPM (LPM)</td>
<td>Factor</td>
<td>GPM (LPM)</td>
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<td>WFI-1</td>
<td>181-185 (83-85)</td>
<td>60-65 (4-4.5)</td>
<td>M</td>
<td>CIP Wash Tank</td>
<td>10.6 (40)</td>
<td>1</td>
<td>317 (1200)</td>
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<td>WFI-2</td>
<td>68-74 (20-23)</td>
<td>35-40 (2.4-2.75)</td>
<td>A</td>
<td>Stoper Washer</td>
<td>5.3 (20)</td>
<td>0</td>
<td>122 (460)</td>
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</table>

Guide Reference p. 32
Fig 3.3 Water Consumption Graph
Fig 3.4 Storage Tank Capacity Determination
System Unit Process Selection
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
### Table 4.1 System Pretreatment Selection

<table>
<thead>
<tr>
<th>Common Impurities</th>
<th>Chlorine Injection</th>
<th>Media Filter</th>
<th>Ultrafiltration</th>
<th>Cartridge/Membrane Filtration</th>
<th>Chlorine Dioxide</th>
<th>Ozone</th>
<th>Activated Carbon/Filtration</th>
<th>Antiscalant</th>
<th>Ion Exchange (Softeners)</th>
<th>Reverse Osmosis (RO)</th>
<th>DI Membrane</th>
<th>Steam-Circle Injection</th>
<th>Reverse Osmosis (RO)</th>
<th>SRS (Sodium Bicarbonate)</th>
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<tr>
<td>Turbidity</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>X</td>
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<td>Particulates/Suspended Solids</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td></td>
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<td>Hardness</td>
<td></td>
<td></td>
<td></td>
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<td>X</td>
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<td>X</td>
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<td>Iron</td>
<td>X</td>
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<td>Dissolved Silica</td>
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<td>Carbon Dioxide</td>
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<td>Trihalomethanes (THMs)</td>
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<td>Total Organic Carbon (TOC)</td>
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<td>Microbiological Organisms</td>
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<td>X</td>
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<td>Ammonia</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td></td>
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<td></td>
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</tbody>
</table>

**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 6).
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
Final Treatment Options

- Primary Treatment (Chapter 5)
  - Ion Exchange
  - Reverse Osmosis
  - Distillation

- Polishing Process Options
  - UV
  - MF
  - UF
  - Membrane Degas
Table 5.1 Multiple Effect Still Utility Requirements

<table>
<thead>
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<th>Effects</th>
<th>1</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<td>Steam lb/h</td>
<td>9,800–10,200</td>
<td>3,300–3,700</td>
<td>2,600–3,000</td>
<td>2,100–2,500</td>
<td>1,900–2,300</td>
<td>1,500–1,800</td>
<td>1,340–1,600</td>
</tr>
<tr>
<td>kg/h</td>
<td>4,445–4,626</td>
<td>1,496–1,678</td>
<td>1,179–1,360</td>
<td>952–1,134</td>
<td>86–1,043</td>
<td>682–818</td>
<td>609–727</td>
</tr>
<tr>
<td>Coolant MBtu/h</td>
<td>7.9–8.1</td>
<td>2.0–2.2</td>
<td>1.4–1.6</td>
<td>1.0–1.2</td>
<td>0.8–1.0</td>
<td>0.07–0.1</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: MBtu is 1,000 BTU (British Thermal Units).
Table 5.2: VC Utility Consumption per 1,000 Gallons (3,785 liters) of WFI Produced

<table>
<thead>
<tr>
<th>Capacity Range</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 GPH (757 LPH) to 7200 GPH (27,255 LPH)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electricity kWh</td>
<td>44</td>
<td>80</td>
</tr>
<tr>
<td>Steam Lb/Hr</td>
<td>926</td>
<td>1100</td>
</tr>
<tr>
<td>Kg/Hr</td>
<td>408</td>
<td>498</td>
</tr>
<tr>
<td>Coolant GPM</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>LPM</td>
<td>7.6</td>
<td>15.2</td>
</tr>
</tbody>
</table>
Typical CEDI Process Drawing

Guide Reference: Figure 5.2
System Process Technology Maps
Fig. 6.2 Deionization Technology Map
Fig. 6.1 RO Technology Map
FIG 6.3 VAPOR COMPRESSION STILL TECHNOLOGY MAP
Fig. 6.4 ME Still Technology Map
Fig. 6.5 Membrane Based WFI Technology Map
Storage and Distribution
Design and Sanitization Strategy
Fig. 8.1 Storage & Distribution Decision Flow Chart

- Continuous Circulation?
  - Yes
    - Ozonated Storage and Distribution
  - No
    - Special Design Consideration
- POU Temperature Required?
  - Yes
    - Method of Sanitation?
      - Chemical
      - Ambient or Reduced Temperature Storage and Distribution
  - No
    - Hot Usage Only?
      - Yes
        - Primary/Secondary Distribution (Hot)
      - No
        - Limited Quantity of Use Points
          - Hot Distribution, Cooled Sub-Loop
          - Hot Distribution, Cooled Branch Use Point, Heat Sanitized
- Hot or Multiple Temperatures
- Hot Usage Only?
  - Yes
    - Primary/Secondary Distribution (Hot)
  - No
    - Hot Distribution, Cooled Branch Use Point, Heat Sanitized
Fig. 8.3: Ambient/Reduced Temperature Storage & Distribution
Fig. 8.5: Ozonated Storage and Distribution

Refer to ISPE Good Practice Guide: Ozone Sanitization of Pharmaceutical Water Systems [34] for details/options.

Note: Ambient ozone leak detector may be required.
Fig. 8.9: Hot Storage, Cooled Bypass Circulating Distribution
<table>
<thead>
<tr>
<th>Item</th>
<th>Type</th>
<th>Industry Practice</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat Exchangers</td>
<td>Concentric Tube</td>
<td>Common in sanitary applications</td>
<td>Simple design, low pressure drop</td>
<td>Limited surface area</td>
</tr>
<tr>
<td></td>
<td>Plate and Frame (Single Wall)</td>
<td>Common in pretreatment</td>
<td>Cost, large surface area</td>
<td>Drainage, not “fit in a tight spot”</td>
</tr>
<tr>
<td></td>
<td>Plate and Frame (double Wall)</td>
<td>Common in sanitary applications</td>
<td>Improved integrity</td>
<td>Cost</td>
</tr>
<tr>
<td></td>
<td>Tube and Shell-Single Tube sheet</td>
<td>Common in pretreatment</td>
<td>Cost</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tube and Shell-Double Tube sheet</td>
<td>Common in sanitary applications</td>
<td>Highest integrity</td>
<td>Cost</td>
</tr>
<tr>
<td>Pumps</td>
<td>Centrifugal with Single Seal</td>
<td>Common for pumped and WFI</td>
<td>Cost, Complexity</td>
<td>Seal integrity</td>
</tr>
<tr>
<td></td>
<td>Centrifugal with Double Seal</td>
<td>Common for WFI</td>
<td>Seal integrity</td>
<td>Cost, maintenance</td>
</tr>
<tr>
<td></td>
<td>Positive Displacement-Rotary</td>
<td>Can be used for high pressure</td>
<td>High pressure</td>
<td>Cost, pulsation</td>
</tr>
<tr>
<td></td>
<td>Positive Displacement-Diaphragm</td>
<td>Can be used for suction</td>
<td>Suction limitations</td>
<td>Limited flow, pulsation</td>
</tr>
<tr>
<td>Tanks</td>
<td>Single Shell</td>
<td>Common for ambient operation</td>
<td>Cost, easy inspection</td>
<td>Sweating, flexibility</td>
</tr>
<tr>
<td></td>
<td>Insulated 1/2&quot; S/S (and alternative)</td>
<td>Common for cold or hot operation with heat sanitation</td>
<td>Energy, safety</td>
<td>Cost, Difficult To Inspect and Repair (DTIR)</td>
</tr>
<tr>
<td></td>
<td>Jacketed 1/2&quot; S/S (and alternative)</td>
<td>Common for hot applications and/or heat sanitization</td>
<td>Thermal efficiency</td>
<td>Welding, cost, (DTIR)</td>
</tr>
<tr>
<td></td>
<td>Jacketed Double Wall</td>
<td>Common for hot applications and/or heat sanitizations</td>
<td>Cost, less welding</td>
<td>Thermal efficiency (DTIR)</td>
</tr>
<tr>
<td>Reels/ Devices</td>
<td>Rupture Disc</td>
<td>Common for sanitary applications</td>
<td>Monitorable, integrity, suitable for pressure and/or vacuum service</td>
<td>Cost, failure causes shutdown</td>
</tr>
<tr>
<td></td>
<td>Relief Valve</td>
<td>Common for sanitary applications</td>
<td>Cost</td>
<td>Not monitorable, can result in potential contamination. Suitable for vacuum relief. Tanks only unless used with vacuum relief.</td>
</tr>
<tr>
<td></td>
<td>Diaphragm</td>
<td>Common for sanitary systems</td>
<td>Integrity</td>
<td>Cost, not suited for steam</td>
</tr>
<tr>
<td></td>
<td>Butterfly</td>
<td>Common in pretreatment</td>
<td>Cost</td>
<td>Stem, valves</td>
</tr>
<tr>
<td></td>
<td>Ball</td>
<td>Common in pretreatment and CS</td>
<td>Cost, CS service</td>
<td>Stem, valves</td>
</tr>
<tr>
<td></td>
<td>Plug, Gate, Globe</td>
<td>Common in pretreatment</td>
<td>Cost</td>
<td>Stem, valves</td>
</tr>
<tr>
<td></td>
<td>Rising Stem Sanitary</td>
<td>Common in sanitary throttling</td>
<td>Integrity, leak detection, performance</td>
<td>Angle design</td>
</tr>
</tbody>
</table>
### Table 8.2 Distribution Piping Materials Comparison

<table>
<thead>
<tr>
<th></th>
<th>Polyvinylidene Fluoride (PVDF)</th>
<th>Polypropylene (PP)</th>
<th>316L Stainless Steel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Material Cost</td>
<td>High</td>
<td>Medium</td>
<td>High</td>
</tr>
<tr>
<td>Installation Cost¹</td>
<td>High</td>
<td>Medium</td>
<td>Medium</td>
</tr>
<tr>
<td>Steam Sanitizable</td>
<td>Yes²</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Hot Water Sanitizable</td>
<td>Yes³</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Ozone Sanitizable</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Chemical Sanitizable</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Rouging Susceptibility</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Corrosion Resistance</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Availability</td>
<td>Medium</td>
<td>Medium</td>
<td>High</td>
</tr>
<tr>
<td>Extractables</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Degree of Thermal Expansion</td>
<td>High</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Joining Method</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hygienic Clamp</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>• Solvent/Glue⁴</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>• Thermal Fusion/ Weld</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Support Requirements</td>
<td>High</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Typical Usage</td>
<td>Medium</td>
<td>Medium</td>
<td>High</td>
</tr>
</tbody>
</table>

**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 manufacturer’s recommendations.
5. Materials using solvents and glues are not recommended and may result in elevated TOC.
AL6XN Impeller after 2 Years 80°C Service
Example of Localized Systems

Reference: Figure 9.2 (p. 172)
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.
Biofilm Formation
WRAP UP
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
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