



# SPS Training Presentation Abstracts

## Understanding Biofilm in High Purity Water Systems

**Abstract:** Biofilm represents the predominant form of microbial growth on this planet. From sewage treatment plants to high purity water systems, it's simply the way bacteria have most successfully adapted to survival. Science is slowly unraveling the mysteries underlying how these microbes manage to survive and even thrive in austere environments such as high purity water. All the while, those who manage and monitor those water systems and are otherwise accountable for the quality of this water must try to understand these mysteries in order to foil these microbes' tenacity for survival. From this presentation you will learn in layman's language, the basics of:

- ▲ Where these microorganisms come from and some of their traits
- ▲ How biofilm develops in pure water systems.
- ▲ What strategies work and don't work to control biofilm and why.
- ▲ Ways to monitor for their presence in a water system.
- ▲ Why conventional plate counts underestimate the total count (which is neither a good nor bad thing).
- ▲ What manufacturing and health significance these microorganisms might have.

**Duration and Audience:** This presentation lasts between 90 minutes and a half day, depending on the depth of coverage. It is targeted toward non-microbiologists and has benefited engineers, utility managers and operators, quality assurance personnel (who are responsible for water but don't understand much about it), and laboratory personnel (including microbiologists, most of whom don't understand biofilm and its impact on their test results). I try to throw in enough "myth busters" to make it interesting for everyone, even if they THINK they understand biofilm.

## Practical Water System Design and Operation Issues Impacting Microbial Control

**Abstract:** This presentation is a companion to and picks up where "Understanding Biofilm..." leaves off. This presentation focuses on a number of hot issues, buzz words, facts and myths about water system pretreatment and distribution system design and operations from a microbiological perspective. This is an interactive presentation where a combination of planned topics and audience questions constitute the main discussion points. Points that will be covered include:

- ▲ Piping composition and smoothness
- ▲ Disinfection using heat, ozone, hydrogen peroxide and other chemicals
- ▲ Loop vs branched distribution systems, deadlegs and flowrate
- ▲ UV sanitization and TOC reduction
- ▲ Filtration, where, when, and how to use
- ▲ Microbiological pitfalls in pretreatment and final purification

**Duration and Audience:** This presentation lasts between 60 minutes and a half day, depending on the nature and number of audience questions. It too is targeted toward non-microbiologists and has benefited engineers, utility managers and operators, quality assurance personnel (who are responsible for water but don't understand much about it), and laboratory personnel (microbiologists or not, who also don't understand biofilm and its impact on their test results). This presentation contains plenty of "myth busters" to make it interesting for everyone, even if they THINK they understand biofilm.

## Validation of Microbial Enumeration Methods for Water

**Abstract:** This presentation focuses on the why's and how's of validating microbial test methods for monitoring water systems. It provides the basis for understanding what your microbial monitoring data actually mean and how it can be used for both process control (through Alert and Action Level comparisons) and quality control (when the water is used as an ingredient in product formulations or for product equipment contact) – two concepts that are often (incorrectly) considered interchangeable. Points that will be covered include:

- ▲ Why water enumeration method validation is so misunderstood, by users and regulators alike
- ▲ Why it bears no resemblance to any other microbial test validation approach
- ▲ What to look for in a valid test method
- ▲ What enumeration methods/approaches are available, how they work, and their advantages/disadvantages
- ▲ How to establish meaningful and useful alert and action levels and specifications, if needed
- ▲ How to defend the choice of methods and control levels/specifications to regulatory authorities

**Duration and Audience:** This presentation lasts between 3 and 5 hours, depending on the interest and background of the audience. It is targeted mainly at lab personnel responsible for this testing as well as their management. However, Quality Assurance personnel and those in Regulatory Affairs who may be explaining/defending the company's water monitoring decisions to regulatory authorities will also benefit as would utility management staff in understanding the meaning of data or alerts received from the laboratory.

## Optimizing Microbial Monitoring of Water Systems

**Abstract:** Of all the things that can go wrong with a pharmaceutical water system, it's the microbiological quality that is responsible for the most product recalls and the sharpest focus of attention from FDA and other regulatory agencies. That microbiological quality is most often revealed by culturing water samples from a water system, but the choice of the optimal enumeration test method is not in any FDA guidance document or USP monograph or test chapter -- it is up to the user to determine. This presentation will help guide the user in understanding how to determine the optimal testing approach to assess the true microbial quality of their water as well as the microbiological "health" of the system that produced it. This presentation will cover:

- ▲ Determining the purpose of the testing: QA/In-Process Control, QC/Water Release, or both
- ▲ Understanding why the purpose of data determines the usable options for sampling and testing approaches
- ▲ Understanding the various cultural and instrumental approaches, including advantages and disadvantages
- ▲ Understand the intricacies of the various cultural approaches including media and incubation conditions as well as advantages and disadvantages of each
- ▲ Understanding performance-based Alert and Action Levels and how they differ from Specifications
- ▲ Understanding how the method used has an impact on the Alert and Action Levels and Specifications

**Duration and Audience:** This presentation lasts between 1 and 2 hours, depending on the interest and background of the audience. It is targeted mainly at lab personnel responsible for this testing as well as their management. However, Quality Assurance personnel and those in Regulatory Affairs who may be explaining/defending the company's water monitoring decisions to regulatory authorities will also benefit as would utility management staff in understanding the meaning of data or alerts received from the laboratory.

## The Logic of Water System Validation

**Abstract:** Water system validation is often perceived as a meaningless exercise, a requirement only for pharmaceuticals and stemming from pharmaceutical product recalls in the 1970's and 80's that were caused by unvalidated water systems. Back then, demonstrating consistent microbiological control at the use points was the singular objective, and the purification process was a black box that typically worked because chemical purity requirements were poorly defined. Times have changed. The USP now has water conductivity and TOC specifications, the incoming water now could have chloramines instead of just chlorine in it, and non-pharmaceutical industries are seeing the financial value of water system validation in avoiding costly maintenance, downtime, and product quality problems. Nowadays, the validation of the chemical purification process is equally important to microbial control and each affects the other. Some of the intermediate purification steps may be the only control of certain contaminants (e.g. the ammonia from chloramines). That means that this black box may have to be opened up to the rigors of validation. This process often detects errors in design that emphasize the need for competent, experienced water system designers and fabricators. This presentation is intended to show that expert water system design and fabrication is the foundation for water system "success". It will also show that well-designed water system validation protocols are cost-effective "insurance" that can be created and implemented by the users with a reasonable understanding of the chemistry and microbiology of how the unit ops are intended to work. It's really only a matter of logic and financial common sense. Participants will receive guidance to help them determine for their own water systems the following:

- ▲ What validation attributes and specifications are important for each unit op and use point
- ▲ What sampling should be done to assess those attributes
- ▲ How long and how frequently should the validation sampling be done
- ▲ What can affect those test results and what it means
- ▲ Why poorly designed or maintained systems can't be validated and cause unending headaches
- ▲ When validation is finally over, is it really over?

**Duration and Audience:** This presentation lasts between 1 and 2 hours, depending on the interest and background of the audience. It is targeted mainly at validation and lab personnel responsible for writing protocols and executing this testing as well as their management and those who approve the protocols and final packages. Quality Assurance personnel and those in Regulatory Affairs who may be explaining/defending the company's water system validation approach to regulatory authorities will also benefit as would utility management staff in understanding the meaning of data and the value of change control.

## Pharmaceutical Water System Excursions: Types, Impact and Response

**Abstract:** This presentation focuses on the delineating the types of water system excursions that can occur related to process controls (alert and action levels) and limits (raw material specifications) for both microbiological and chemical water attributes. It gives guidance on how to assess the impact of such excursions on the water uses during the excursion period as well as the relative regulatory risks associated with these excursions and their frequency.

**Duration and Audience:** This presentation requires about 45 minutes. It is targeted for utility as well as quality assurance personnel, and those in Regulatory Affairs who may be explaining these excursions, impact assessments, and related CAPA's to regulatory authorities.

## Update on Latest USP Pharmaceutical Water Developments

**Abstract:** This presentation gives the latest developments in USP related to actions by the USP Pharmaceutical Water Expert Committee. By its nature (and the nature of USP in general), it is in continuous revision and is kept updated relative to committee initiatives. Being a member of the USP Water Expert committee, the presenter has first hand knowledge of recently approved and upcoming changes to all issues within USP related to water and Pure Steam. This presentation also covers the most recent harmonization developments with EP and JP which the USP Expert Committee is leading.

**Duration and Audience:** This presentation requires at least 60 minutes, but can be scaled back to 45 minutes if harmonization portion is not included. The intended audience is dependent on the subject matter initiatives before USP at the time. Currently, that would include engineers and utility personnel (because of current Pure Steam initiatives) as well as quality assurance and laboratory personnel. Because of efforts in heretofore “unregulated” areas like hemodialysis, Regulatory Affairs personnel might also benefit from attending. The committee’s ongoing efforts with packaged waters should be of specific importance to LVP manufacturers. There is a significant discussion of an update to the general information chapter <1231> Water for Pharmaceutical Purposes (the presenter is the primary author of those revisions) which should be interesting to anyone wanting to know more about high purity water issues. A new general information chapter on water system instrumentation is under consideration that should be of interest to TOC and conductivity instrument users and makers.

## USP-ology: Understanding the “Big Red Book”

**Abstract:** As widely used and referenced as the USP is (or should be), it is frequently underused, misused or misinterpreted out of a lack of awareness of its content and applicability or even that a more recent revision is in effect. This presentation is intended to present the basic organization of the book, what parts are legally binding and what parts are informational and not legally binding, along with some little-known facts. Also covered will be the revision process, including USP’s companion review journal Pharmacopeial Forum, USP Supplements, and the Expert Committee role in the revision process.

**Duration and Audience:** This presentation lasts about 45 minutes. The intended audience for this presentation is anyone who does or should be using the USP as a reference book. This includes all personnel in QA and QC organizations as well as Regulatory Affairs, Compliance and Product Research & Development personnel.

## Author’s Perspective on What USP’s Chapter <1231> Really Says About Water (& Why)

**Abstract:** Water seems to be so simple, but yet as the closest thing to a universal solvent and the very basis of life on this planet, it affects just about every industry as well as the consumers of their products, and not always in good ways. As it turns out, purifying water and keeping it pure for uses in the pharmaceutical, biotechnology, and device industries is sufficiently challenging and complex enough for USP to have formed the Pharmaceutical Waters Expert Committee (PWEC) whose sole functions are related to this deceptively complex solvent called “water” and what its compendium has to say about this subject. The broad-reaching impact of water on FDA-regulated industries gives this Expert Committee a pivotal role in the quality of FDA-regulated products. This session will address the recent developments related to water within USP, in particular, the newly revised <1231> “Water for Pharmaceutical Purposes”. But in addition, the unique role of the USP book in FDA enforcement will also be covered. Attendees will learn:

- ▲ Recent landmark changes to bulk water monographs
- ▲ What drove USP (and its author) to revise this pivotal informational chapter again
- ▲ An overview of the organization of this chapter and its main sections
- ▲ A highlighting of the content of each section having major changes and additions since the last rewrite
- ▲ A detailed discussion of critical new or expanded material with insight into the rationale behind it
- ▲ How this chapter was intended to be used, and how it has been misused by FDA and practitioners

**Duration and Audience:** This presentation lasts about 1.5 to 3 hours depending on audience interest. The intended audience for this presentation is anyone who is associated with water systems, including their control, their uses, and their monitoring. This includes all personnel in Utility Maintenance, QA and QC organizations as well as Regulatory Affairs, who may be explaining/defending the company’s water usage and monitoring decisions to regulatory authorities.

## Water System Microbiology 101:

### The comprehensive short course for everyone who tests & maintains water systems

This course begins with presenting a basic understanding of biofilm, how it thrives in high purity water systems, what environmental influences it is susceptible and resistant to and the health and manufacturing significance of these organisms. It delves into the confusing and often opinionated issues of microbial enumeration and how the methods and their data can be used to effectively (or ineffectively) control the microbial content and quality of the water. With this understanding, a number of water system design and operation issues that impact microbial control will be discussed. Discussion will not be limited by the prepared subject matter – all attendee's questions (and problems, if any) with their own water systems will be addressed. Points that will be covered include:

- ▲ How biofilm develops in pure water systems
- ▲ What strategies work and don't work to control biofilm and why
- ▲ Ways to monitor for their presence in a water system
- ▲ What to look for in a valid test method
- ▲ What enumeration methods/approaches are available, how they work, and their advantages/disadvantages
- ▲ How to establish meaningful and useful alert and action levels and specifications, if needed
- ▲ How to defend the choice of methods and control levels/specifications to regulatory authorities
- ▲ What are some microbiological pitfalls in pretreatment and final purification
- ▲ What is the impact on biofilm growth and control from such things as:
  - ▲ Piping composition, smoothness and flow rate
  - ▲ Looped vs branched distribution systems and deadlegs
  - ▲ Disinfection using UV, heat, ozone, hydrogen peroxide and other chemicals
  - ▲ Filtration, where, when, and how to use

**Duration and Audience:** This in-depth presentation covers the same material covered in the first 3 presentations (without the redundancy), and lasts between 1 and 1½ days (7 – 10 hours) depending on the technical interest level and intended audience. The terminology used will be understandable by non-microbiologists and should be of tremendous benefit to quality assurance personnel (who are responsible for water but don't understand much about it), and laboratory personnel (including microbiologists, most of whom don't understand biofilm and its impact on their test results). This would be a very important course for anyone involved in water system design, operation, testing, validation, compliance or troubleshooting.

## Customized Training Programs

We recognize that your training needs may require a topic other than those listed above or perhaps a combination of topics that are listed. SPS is able to accommodate your training needs to cover a wide variety of topics in addition to those listed above for which existing presentation materials already exist. If an assessment (or test) is needed to measure the retention of the presented material, one can be prepared at whatever difficulty level you desire. However such assessments do not already exist for the above presentation topics. Customized presentation topics include, but would not be limited to:

- ▲ The microbiology of raw materials used in biopharmaceutical manufacturing
- ▲ Aseptic techniques for the microbiology laboratory
- ▲ Aseptic techniques for use in manufacturing sterile products
- ▲ Microbiological control techniques for use in manufacturing non-sterile products
- ▲ Sterilization and depyrogenation processes -- how they work and how their effectiveness is validated
- ▲ Antimicrobial preservatives, how they work, how to assess their effectiveness, and how microbes can still win
- ▲ Rapid microbiological methods as alternatives to compendial methods for products, raw materials, and water
- ▲ Microbial identification – phenotypic vs genotypic, advantages and disadvantages