Ozone Sanitization of Pharmaceutical Water Systems
Disclaimer:
This Guide aims to describe practices associated with ozone sanitization of high purity GMP pharmaceutical water storage and distribution systems. ISPE cannot ensure and does not warrant that a system managed in accordance with this Guide will be acceptable to regulatory authorities. Further, this Guide does not replace the need for hiring professional engineers or technicians.

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Preface

The purpose of this document is to provide guidance when considering, designing, and operating an ozone system for the purpose of sanitizing a high purity GMP pharmaceutical water system. While the use of ozone as a sanitant in GMP high purity water storage and distribution systems is widely accepted, there is little design and operating guidance for such systems. It is the intent of this Good Practice Guide to provide such guidance.

This Guide includes a comprehensive assortment of design and operating considerations that system designers and owners should be aware of.

This is not a requirements or specification document. Based on user requirements and risk assessments design, teams will have to establish their own system requirements and specifications.

The reason for considering the use of ozone is that there may be a wide range of possible cost and operating advantages. The significance of these advantages may vary depending upon the site and project; however, as with all methods of sanitization, the use of ozone technology will place specific requirements on the system design and operation and also may impact the chemical attributes of the water. Some of these requirements and impacts might be considered disadvantages.

This Guide discusses these ozone-specific requirements, advantages, and disadvantages. It also steps the reader through system design, operation, and control. As with any system design, it is the responsibility of the design team and owner to evaluate these possible advantages and disadvantages, taking into consideration the design guidance outlined in this document and determine which method of sanitization, ozone or other, is best for their particular application.
Acknowledgements

Core Team Contributors

Tony Harrison       Pharmagaph       United Kingdom
Joe Manfredi        GMP Systems, Inc.  USA
Teri C. (T.C.) Soli, PhD  Soli Pharma Solutions, Inc.  USA
Philip E. Sumner, P.E. (Team Leader)  Pfizer Inc.  USA

Contributors

Stefan Aebi           Novartis Pharma AG       Switzerland
Ben Battat            IN USA, Inc.                   USA
Anthony Bevilacqua, PhD  Mettler Toledo Thornton, Inc.  USA
Will Brown             MECO                       USA
Vince Ciufia           OSTI Inc.                  USA
Nissan Cohen           Rohrback Cosaco Systems, Inc.  USA
Ken Gethard, PhD       Schering Plough Global  USA
Ismail Gobulukoglu, PhD  Aquafine Corporation    USA
Michelle M. Gonzalez, P.E.  BioPharm Engineering Consultant  USA
David M. Gray          Mettler-Toledo Thornton, Inc.  USA
Richard Kettlewell     GlaxoSmithKline         United Kingdom
Bill LaVoice           Aquafine Corporation   USA
Neil McCarthy          Pfizer Inc.               Ireland
Robert Neri            Sanofi                    France
Reune Runyon           Apaco AG/Innovatec       Switzerland
Barbara Schilling      Ozonia North America    USA
Cameron Sipe           Pfizer Inc.             USA
Hans Sundstrom         MKS Instruments         USA
Robert Vecchione       Christ Aqua Pharma & Biotech NA  USA
Peter Vishton, P.E.    Technology Engineer Consultant  USA
Gary Zoccolante        Siemens Water Technologies Corp.  USA

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1 Introduction

The reason for considering the use of ozone as the primary sanitizing agent for a pharmaceutical water distribution system is that there may be a wide range of possible operating and cost advantages. The significance of these advantages may vary depending upon the site and project. However, as with all methods of sanitization, the use of ozone technology will place specific requirements on the system design and operation.

This Guide discusses these ozone-specific requirements, including associated advantages and disadvantages. It also steps the reader through system design, operation, and control. As with any system design, it is the responsibility of the owner and the design team to evaluate ozone’s applicability taking into consideration the design guidance outlined in this Guide.

Ozone has been used extensively by many firms, while others have little or no experience with ozone as a sanitant. The reasons may include a lack of knowledge regarding system design and operation, concerns about compatible materials of construction, and safety and environmental issues. It has been reported that misunderstanding of the “added substance” issues with compendial waters also has been a potential deterrent. For this reason, there is also discussion of this issue in this Guide.

1.1 Purpose

The purpose of this Guide is to provide detailed guidance relating to design and operation of pharmaceutical water systems using ozone for sanitization as well as describing the principles that allow this sanitization approach to be effective.

1.2 Scope

The scope of this Guide includes designs and practices associated with ozone sanitization of high purity GMP pharmaceutical water storage and distribution systems. Other ozone applications are not considered (e.g., drinking water, cooling towers).

1.3 Structure of This Guidance

This ISPE Good Practice Guide: Ozone Sanitization of Pharmaceutical Water Systems is presented in the following sections:

- Introduction
- Use of ozone in the pharmaceutical industry
- Regulatory and industry guidance documents
- Ozone characteristics
- Effectiveness of ozone for microbial control
- Ozone generation
- Ultraviolet light for ozone destruction
- Ozone sensors
1.4 Background

This ISPE Good Practice Guide: Ozone Sanitization of Pharmaceutical Water Systems describes established design methodologies and practices to allow expanded use of ozone based on knowledge of the principles and benefits.

For more than 100 years, ozone has been used to sanitize municipal drinking water and reduce its organic content, and its use for pharmaceutical water systems extends beyond 30 years, yet its use is still to some extent limited in pharmaceutical applications [1].

Pharmaceutical water is used as a utility and ingredient for Good Manufacturing Practice (GMP) processes, and for the production of drug products and drug substances including Active Pharmaceutical Ingredients (APIs). Depending on the application, the purities of these waters are usually categorized as Purified Water (PW), Highly Purified Water (HPW), or Water for Injection (WFI) for which the world pharmacopoeias have monographs. In addition, water may be produced as a final product, such as USP packaged waters, including:

- Sterile water for injection
- Sterile water for irrigation
- Sterile water for inhalation
- Sterile purified water
- Bacteriostatic water for injection
- Water for hemodialysis (which also may be produced as a bulk water)

The USP monographs for bulk purified water and water for injection also provide for packaged options where microbial control within the package and inertness of the packaging are very important.

Because of the potential importance of the microbial content of water to the manufacturing of products, cleaning and some laboratory activities in pharmaceutical or biopharmaceutical facilities, water systems that produce and distribute these waters generally should be under a continuous state of control to minimize microbial content, biofilm buildup, and endotoxins.
Controlling microbial presence and proliferation within the storage and distribution sections of pharmaceutical water storage and distribution systems is typically accomplished by heat, sanitizing chemical solutions, or ozone. To heat sanitize, the storage and distribution systems are heated either continuously or on a periodic basis as validated. To sanitize using chemical solutions, these solutions are periodically circulated throughout the system followed by rinsing. This Guide focuses on the use of ozone as a sanitant.