Points to Consider for Implementation of Pre-Use Post-Sterilization Integrity Testing (PUPSIT)

Points to Consider for Implementation of Pre-Use Post-Sterilization Integrity Testing (PUPSIT) Team

Authors

The authors formed a multicompany consortium comprising more than 50 subject matter experts from 25 biopharmaceutical manufacturing companies and filter suppliers to consider the different aspects of implementing PUPSIT. The experts are experienced in sterile filtration and authors drew upon their collective experiences, current company practices, consultations with stakeholders and colleagues, and a review of current regulatory guidelines.

Steve Ensign, Eli Lilly and Company

Will Peterson, Merck Sharp & Dohme

Hal Baseman, ValSource

Dieter Bachmann, Johnson & Johnson

Stephanie Ferrante, Millipore Sigma

Jeff Gaerke, CAI

Maik Jornitz, G-CON Manufacturing Inc.

Tina Morris, Parenteral Drug Association

Thao Le Vinh, Glaxo Smithkline

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Allan Elder, BioPhorum (retired)

Jannika Kremer, BioPhorum

Ali Wilson, BioPhorum

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I. Introduction and Scope

Pre-use/post-sterilization integrity testing (PUPSIT) has been a widely debated topic for the last several years. To a large extent, the debate has been due to the fact that scientific data were not available to provide additional clarity that could inform appropriate risk-based decisions and commensurate actions. To gain clarity on this and other topics related to sterile filtration, PDA and BioPhorum formed the Sterile Filtration Quality Risk Management (SFQRM) consortium in late 2017. The consortium goals are to fill existing gaps in scientific data with studies and industry guidance that would provide professionals and license holders with the ability to make informed decisions about quality risk management strategies.

In total, 25 manufacturers and filter suppliers have contributed to the work of the Consortium, deploying their filtration experts, pooling their collective knowledge and applied science experience to address these questions. This effort has been supported by many of the best independent filtration experts currently working in the industry who have contributed to and driven the Filtration Interest Group in PDA for many years. Both PDA and BioPhorum have prioritized this program and combined their approaches to deliver this comprehensive body of work. We hope that collectively the publications aid decision-making, create greater certainty and confidence and above all alignment between suppliers, manufacturers and regulators alike on these important questions.

This paper marks the fourth in a series designed to share the learnings of the consortium, as gained through the exploration of sterilizing filtration through science and risk management.

The series comprises four publications:

- PDA Journal: Datamining to Determine the Influence of Fluid Properties on the Integrity Test Values ***(1)***
- PDA Journal: Test Process and Results of Potential Masking of Sterilizing Grade Filters ***(2)***
- PDA Points to Consider for Risks Associated with Sterilizing Grade Filters and Sterilizing Filtration ***(3)***
- PDA Points to Consider for Implementation of Pre-Use Post-Sterilization Integrity Testing (PUPSIT) (this publication)

The result of the group's collaboration, this collection should be considered holistically to determine best practices in addressing the quality risk management of sterilizing filtration, filtration process control, and PUPSIT. For additional information on how the work of the consortium and the resulting publications, listed above, fit together to provide an overall evaluation of PUPSIT, see the article titled "The Use of Scientific Data to Assess and Control Risks Associated with Sterilizing Filtration" presented in the *PDA Letter* ***(4)***.

The purpose of this document is to provide the reader with points to consider on how best to implement and execute a pre-use/post-sterilization integrity test (PUPSIT) of the final sterilizing grade liquid filters for products that are not terminally sterilized.

Variations in the filtration design, set-up, operation, process stream attributes, and manufacturing operational philosophies all have a significant impact on how pre-use post-sterilization integrity testing (PUPSIT) is incorporated into a manufacturing process. Because of this, there is not a "one size fits all" solution for PUPSIT implementations. Instead there are several attributes related to the integrity test operation that one must consider in determining how best to design, implement, and run PUPSIT for a specific application.

By considering the various filtration/integrity test characteristics discussed in this document, it is expected that the reader will be able to determine how to implement PUPSIT for their specific application in a robust manner that mitigates the risk of compromising the sterility of the system.

Note: This document will only cover a primer on sterilizing filtration in general and filter integrity testing, and the reader is assumed to have basic knowledge of this material. For additional reading, refer to PDA *Technical Report No. 26: (Revised 2008): Sterilizing Filtration of Liquids* ***(5)***.