Points to Consider for Risks Associated with Sterilizing Grade Filters and Sterilizing Filtration

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Points to Consider for Risks Associated with Sterilizing Grade Filters and Sterilizing Filtration Team

Authors and Contributors

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 sterile filtration risk management. 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.

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Introduction

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 judgments and commensurate actions. To gain clarity on this and other topics related to sterile filtration, the Parenteral Drug Association (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 also been supported by many of the best independent filtration experts currently working in the industry that have manned 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, which includes two research articles, two Points to Consider documents, and articles in the *PDA Letter*. We hope that collectively the publications aid decision-making and create greater certainty, confidence and, above all, alignment between suppliers, manufacturers, and regulators alike on these important questions.

This paper marks the third in a series designed to share the learnings that the consortium gained through the exploration of sterilizing filtration through science and risk management. In particular, it describes the process and outcomes of the consortium's Quality Risk Management (QRM) team tasked with identifying risks and preventive controls associated with sterilizing-grade filter manufacturing and use in the drug product manufacturing process.

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 (this publication)
- PDA Points to Consider for Implementation of Pre-Use Post-Sterilization Integrity Testing (PUPSIT) ***(3)***

As a 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 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," published in the *PDA Letter* ***(4)*.**

The criticality of sterilizing filtration in the production of parenteral drug products cannot be understated. For certain medicinal products, such as biopharmaceuticals, sterilizing filtration marks one of the final steps by which patient safety is assured. To ensure this operation is performed successfully each and every time, parenteral drug manufacturers must command a complete understanding of the quality-related risks involved and make sure scientific and engineering principles are adequately applied to control those risks. These risk controls, combined with product and process knowledge, comprise the control strategy for sterilizing filtration ***(5, 6)***. Control strategies have been discussed at length in regulation, published literature, and in industry discourse in forums offered by both PDA and BioPhorum, among others. Since sterilizing filtration is itself both a control over the critical quality attribute (CQA) of sterility and a discrete manufacturing unit operation, the associated control strategy must be particularly robust.

With patient protection as its guiding light, the QRM team set out to fully map all quality-related risks and related controls associated with sterilizing filtration. This effort entailed a comprehensive risk assessment and control mapping exercise performed by a seasoned QRM facilitator and subject matter experts from the consortium, with more than a dozen pharmaceutical and biopharmaceutical companies and four filter manufacturers represented on the team. This paper summarizes the process and outcomes of that exercise and is intended to serve as a QRM implementation guide for both manufacturers of sterilizing grade filters and companies or sites performing sterilizing filtration.

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