



Points to Consider for Aseptic Processing

Part 1

January 2015

PDA Points to Consider for Aseptic Processing Task Force

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Introduction

This document presents the views of the Parenteral Drug Association (PDA). The document is designed to communicate PDA's thoughts and encourage further dialog with industry, health authorities, and suppliers of technology and materials while taking into consideration the changes and needs of the modern, global, sterile, healthcare product manufacturing industry. It does not represent a standard or regulatory guidance.

In 2003, PDA issued *Points to Consider for Aseptic Processing*. Much has been learned by the industry since that document was published. In an effort to address the impact of this knowledge gained, PDA has assembled a task force of subject-matter experts from industry with the purpose of revising that report. The revision provides positions on current topics, best practices, and areas of clarification that are important to the manufacturing of quality sterile products.

Many of the topics have been included in the revision as a result of input from PDA members at conferences and meetings. It is the intention of the task force to issue Part 1 of the revised report, which addresses initial topics, and then publish subsequent parts on other subjects. Parts may be added as additional input is received from industry and members. It is anticipated that the scope of the revised report may be further broadened to include other related topics.

The revised report topics are organized into categories. Each topic discussion begins with a problem statement in the form of a question about issues or points needing clarification in that specific topic. Recommendations from the PDA task force are then presented as an answer to the question. The rationale and references for each recommendation follow.

Primarily, the topics align with those addressed in the 2003 report, although the revision addresses some additional topics. Part 1 and Part 2 of this revision are meant to replace the 2003 *Points to Consider for Aseptic Processing*.*

***Note:** For comparative purposes, the Chapters and Topics are organized in this document in the same order as the 2003 document. Not all Topics are included. Chapter III, as well as potential additional Topics within Chapters I-II and IV-VII, will be addressed in Part 2 of this *Points to Consider*, which PDA will publish subsequently.

Part 1 of the revised report presents points to consider on topics related to the physical environment in which aseptic processing is conducted, monitoring of that environment, cleanroom personnel, and material transfer. It also includes points to consider on aspects of filter-integrity testing and water for injection (WFI) preparation. Part 2 is expected to include points to consider in topics related to aseptic-process simulation and validation, “modern” blow fill seal technology, additional restricted access barrier systems (RABS) and isolators, cleaning, disinfection and sterilization, and critical utilities.

As the task force contemplated specific areas to discuss in the revision, five guiding and linked principles for improvement in sterile healthcare products emerged that the task force used to develop these points:

1. Science- and risk-based approaches should be used to obtain information needed to make decisions related to the evaluation, design, qualification, operation, and monitoring of sterile product manufacturing processes. Risk- and science-based approaches should be used to develop and implement control strategies and acceptance criteria designed to ensure the establishment and maintenance of manufacturing conditions that affect the sterility of products. Sterile drug-product-manufacturing processes and testing requirements should have a basis in and relevance to risks to product quality and patient safety. Risk management and assessment methods should be developed not only to identify risk, but also to allow the improvement of processes and control strategies.

2. Where feasible, the use of newer technologies should be considered to mitigate or reduce risks to product quality identified in manufacturing processes and operations. It is important that companies involved in the manufacture of sterile drug products be encouraged to identify and consider the use of modern technologies and that regulatory guidance enable this by presenting expectations that encourage the use of these technologies. Technologies and facility, equipment, and process designs that protect products and product contact surfaces from personnel and environmental contact and that provide more reliable and useful information are particularly beneficial in order to reduce the risk of microbiological contamination during aseptic processing.
3. The effectiveness of certain traditional testing and monitoring methods as control strategies should be reevaluated. As technology has been introduced and knowledge has been acquired, the usefulness and value of testing procedures have changed. Testing and monitoring should be designed and performed, and the results should be evaluated, based on scientific value, risk to product quality and patient safety, and usefulness to determination of process control. Where testing and monitoring approaches and methods no longer meet the needs or are not optimal, their replacement or modification should be considered. The use of outdated testing and monitoring methods has the potential to add risk, provide a false sense of control, be ineffective, and deploy resources in a manner that may not be efficient or optimal, thus detracting from the development and use of more effective testing and monitoring approaches.
4. New product/container presentations, therapies, and technologies present challenges to traditional and existing methods for the development, manufacture, validation, and testing of sterile products. To meet these challenges, an emphasis on thorough technical and process understanding, science, and risk will become important to design effective means to ensure product quality. Companies should be encouraged to seek out the most effective means rather than try to fit traditional methods to these new products, technologies, and therapies.
5. When scientific approaches are similar and agreed upon, global health authority requirements and guidance should be consistent in technical language and definition. It is important that harmonized technical and regulatory language, where possible, be consistent with approaches presented in other similar guidance. This practice should promote clarity of global regulatory expectations and reduce the risk of misunderstanding and redundant efforts.

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