Points to Consider for Aseptic Processing

Part 2

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PDA Points to Consider for Aseptic Processing Part 2 Task Force

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Introduction and Scope

The following document presents the views of the Parenteral Drug Association (PDA) expert task force, with the concurrence of the PDA Science Advisory Board and Board of Directors. The document is designed to encourage further dialog with industry, health authorities, and suppliers of technology and materials, taking into consideration the changes and needs of the modern, global sterile health care product manufacturing industry.

In 2003, PDA issued a Points to Consider (PtC) for Aseptic Processing. Much has been learned by the industry since the publishing of that document. In an effort to address the impact of this gained knowledge, PDA established an expert task force comprised of subject-matter experts from industry, with the purpose of developing a revision of these PtC. The documents have also been subjected to peer review by other experts and regulators. The revision provides positions on the current topics, best practices, and areas of clarification which are important to the manufacturing of quality sterile products. Part 1 of the revision was published in January 2015. Part 2 of the Revision completes the PtC by covering additional topics identified by the task force.

Many of the topics have been included as a result of input from PDA members at conference sessions and meetings. It is the intention of the task force to issue an initial revision and then to supplement the PtC as additional input is received from industry and members. The scope of the PtC has been broadened beyond aseptic processing to include topics related to terminal sterilization conditions. These other related topics may be reflected in one or more supplements or addendums to this revision, published at a later date.

Note: For comparative purposes, the Chapters and Topics are organized in Part 1 and 2 of the PtC in the same order as the 2003 document. Part 2 begins with additional Topics in Chapters I and II, all of Chapter III, and then moves on to Chapter VI-VII. Parts 1 and 2 together comprise the complete PtC.

The PtC is not meant to be an all-inclusive instructional guide on sterile product manufacturing nor is meant to restate regulatory and health authority positions. Rather, the PtC addresses specific questions and positions which the task force felt required further explanation, clarification, and in some cases modification. The recommendations are nonprescriptive and, along with the accompanying rationale, designed to encourage critical risk-based thinking that companies can use to develop their own process control strategies.

As the task force contemplated specific areas to discuss in the revision, five guiding and linked principles for improvement in sterile health care products emerged. These include:

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 sterile product manufacturing processes. Risk and science based approaches should be used to develop and implement control strategies and acceptance criteria designed to assure the establishment and maintenance of manufacturing conditions which affect the sterility of products. Sterile drug product manufacturing processes and testing requirements should have a basis in and relevance to risk to product quality and patient safety. Risk management and assessment methods should be developed to not only identify risk, but allow for the improvement of processes and control strategies.

2. The use of **technology** should be implemented to mitigate or reduce the risk to product quality identified in manufacturing processes and operations. It is important that companies involved with the manufacture of sterile drug products be encouraged to identify and consider the use of technology and that regulatory guidance help by presenting expectations which encourage the use

of technology. Technologies which have become more prominent since the development of current industry guidance include barrier technology, RABS (restricted access barrier systems), isolators, closed vial filling, blow fill seal technology, automation, rapid microbiological testing, continuous monitoring systems, continuous process control systems, and novel sterilization, decontamination methods, and other technologies in various stages of development and use. Technologies, facility, equipment and process designs which protect product and product contact surfaces from personnel and environmental contact, through the use of barriers or through the elimination of personnel interventions, are particularly beneficial to reduce major sources of 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 acquired, the usefulness and value of testing procedures have changed. Testing and monitoring should be designed, performed, and its results evaluated based on scientific value, risk to product quality and patient safety, and usefulness to the determination of process control. Where testing and monitoring approaches and methods no longer meet the needs or are not optimal given, their replacement or modification should be considered. The use of "outdated" testing and monitoring methods have the potential to add risk, provide false sense of control, be ineffective, and deploy resources in an manner which 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 and therapies,** such as cell therapies, personalized medicine, and alternate therapies present challenges to existing and traditional methods for development, manufacture, validation, and testing of sterile products. To meet these challenges, an emphasis on science and risk will become important components to design effective means to assure product quality. Companies should been encouraged to seek out the correct and optimal means, rather than continue to try to fit traditional methods to these new products, technologies, and therapies.

5. It is important that **harmonized technical and regulatory language,** where possible, be used and be consistent with approaches presented in other similar guidance. Where scientific expectations are similar and agreed upon, requirements and guidance should be consistent in technical language and definition, thus reducing the risk of misunderstanding of global regulatory expectations.

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