



Points to Consider for Aseptic Processing

Part 2
May 2016

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 a 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 be 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.

Table of Contents

I. PHYSICAL ENVIRONMENT	1
TOPIC K.1: BLOW/FILL/SEAL PROCESS DESIGN AND OPERATION	2
What are the unique environmental contamination control considerations for the Blow/Fill/Seal (BFS) process?	
TOPIC K.2: PLASTIC RESIN STORAGE AND HANDLING	4
What are the unique container and resin control considerations for the BFS process?	
TOPIC K.3: BLOW/FILL/SEAL PROCESS SIMULATION	5
What are the unique process simulation considerations for the BFS process?	
II. ENVIRONMENTAL MONITORING AND CONTROL	6
TOPIC E: INVESTIGATION AND DOCUMENTATION OF ENVIRONMENTAL MONITORING EXCURSIONS	7
How are environmental monitoring excursions investigated and documented?	
TOPIC F: ROOMS CLASSIFICATION/ZONING FOR TERMINALLY STERILIZED SOLUTION PRODUCTS	8
What is the appropriate cleanliness grade for areas used in the manufacturing of terminally sterilized products?	
TOPIC G: DISINFECTION PROGRAM FOR GRADE A/B ROOMS	10
How is a disinfection program for a Grade A/B room designed and qualified?	
III. VALIDATION (PROCESS SIMULATION)	11
TOPIC A: ACCEPTANCE CRITERIA	12
What are the acceptance criteria for aseptic process simulations?	
TOPIC B: DURATION OF PROCESS SIMULATIONS VS. PRODUCTION	14
What is the appropriate duration of an aseptic process simulation run? How should process simulation address multiple shifts and campaign production runs?	
TOPIC C: INCUBATION TEMPERATURES	16
What are suitable incubation conditions for process simulations?	
TOPIC D: INCUBATION OF NONINTEGRAL AND REJECTED UNITS	17
Should nonintegral media fill units and/or units which are otherwise procedurally deemed 'rejected' units (during routine operations), be incubated and evaluated as part of the media fill study?	
TOPIC F: PROCESS SIMULATION RECONCILIATION	19
What are the reconciliation/accountability requirements for process simulation?	
TOPIC G: INVERT UNITS PRIOR TO OR DURING INCUBATION	20
Should process simulation units be inverted prior to or during some or all of the incubation period?	
TOPIC H: AEROBIC VS. ANAEROBIC	21
When should anaerobic process simulations be performed?	
TOPIC I: PROCESS SIMULATION BOUNDARIES	22
What are the boundaries for aseptic process simulation? Can the process simulation be performed in discrete segments?	

TOPIC J:	FILL VOLUME	23
	What fill volume should be used for process simulations in order to assess potential contamination?	
TOPIC K:	INTERVENTIONS — TYPE AND FREQUENCY	24
	What types of interventions are required for process simulations, and with what frequency?	
TOPIC L:	VIDEO RECORDING	26
	Should aseptic process simulation be video recorded and how long should recordings be kept?	
TOPIC M:	INVALIDATION OF PROCESS SIMULATION	27
	Under what conditions can a process simulation run be aborted or invalidated?	
TOPIC N:	NUMBER OF PROCESS SIMULATION RUNS REQUIRED	28
	How does a manufacturer determine the appropriate number of process simulation tests to be performed?	
TOPIC O:	INFREQUENTLY USED LINES	29
	How many aseptic process simulation runs should be performed for infrequently used lines or processing areas?	
TOPIC P:	SPECIAL CONSIDERATIONS FOR MEDIA FILLS IN ISOLATORS AND OTHER ADVANCED ASEPTIC PROCESSES (i.e., CLOSED VIAL FILLING)	30
	What are the special considerations for media fills in isolators and other advanced aseptic processes (i.e., closed vial filling)?	
TOPIC Q:	HOLD TIMES FOR STERILE BULK	31
	Should hold times for sterile bulk be included in the process simulation for aseptic filling?	
VI.	CLEANING, DISINFECTION, AND STERILIZATION	32
TOPIC A:	DISINFECTION PROGRAM	33
	Is a disinfectant rotation program necessary?	
TOPIC B:	STERILIZATION OF DISINFECTANTS AND CLEANING AGENTS	34
	How do you ensure that disinfectants and cleaning agents (detergents) used in aseptic processing areas (Grade A/B) are free from contaminants?	
TOPIC C:	HOLD TIMES FOR STERILIZED WRAPPED PARTS, COMPONENTS AND OTHER MATERIAL	35
	How should hold times be determined for sterilized wrapped parts, components and other material?	
TOPIC D:	FREQUENCY OF REQUALIFICATION OF STERILIZATION PROCESSES	36
	How frequently should sterilization processes be requalified?	
TOPIC E:	POROUS/HARD GOODS STERILIZATION PROCESS QUALIFICATION	38
	Should discrete loading patterns be established for all moist heat sterilization processes?	
TOPIC F:	INTEGRITY TEST OF 0.2 MICRON FILTERS	39
	Should 0.2 μ filters, not used for sterilizing purposes (i.e., only for bioload/bioburden reduction), be integrity tested?	

TOPIC G: STERILIZATION — STEAM STERILIZERS.....	40
Are the European Standard EN 285: 1996 and ISO 17665-1:2006 applicable to Pharmaceutical autoclaves and equipment SIP?	
TOPIC H: LYOPHILIZER LEAK QUALIFICATION	42
What is the frequency and the specification for the leak testing of the lyophilizer?	
TOPIC I: STERILIZING GRADE GAS OR VENT FILTER INTEGRITY TESTING	44
How often should sterilizing gas or vent filters be verified for integrity?	
TOPIC K: INTEGRITY TESTING OF STERILIZING FILTERS	45
What is the max number of times that a post-use integrity test of a sterilizing filter should be performed in case of initial failure?	
VII. CRITICAL UTILITIES	46
TOPIC B: REQUIREMENTS FOR WATER FOR INJECTION	47
What are the requirements for preventing microbial contamination of WFI?	