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Recommended Practices for Manual Aseptic Processes

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PDA Recommended Practices for Manual Aseptic Processes Technical Report Team

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1.0 Introduction

The purpose of this technical report is to outline methods and approaches for control and evaluation of aseptic processing operations for drug products/medicinal products which use all or partially manual procedures. The goal of aseptic processing is to prevent the contamination of sterile materials during their processing. The goal of evaluating any aseptic process is to demonstrate that aseptic processing can be achieved and maintained successfully under the specified operational configuration, activities, and conditions. These goals are the same for manual or automated aseptic operations, and for small-scale or large-scale operations.

Manual aseptic processing (MAP) operations differ from automated operations in several ways. These differences pose unique operational and evaluation challenges not generally encountered with automated operations. These challenges must be considered thoroughly when designing the evaluation procedure or protocol for the MAP operation. MAP involves a human operator performing at a minimum, the container and/or closure movements. Some semi-automated equipment may be used, but the process is not fully automated. For this reason MAP relies heavily on individual operator's basic understanding of microbiology proficiency where personnel must be individually qualified.

The greatest source of microbial contamination during MAP is generally recognized to be the operational personnel and their activities. Aseptic processes that rely on manual operations are inherently subject to performance or procedural drift over time. Furthermore, reproducible human performance cannot be assumed, especially where there are significant time gaps between aseptic processing events. The likelihood of human performance deviations or failures is linked to:

- Complex aseptic processing tasks
- The continuous span of time during which an operator carries out repetitive aseptic activities
- The expected rate of activity
- Change in personnel

This technical report has value for hospital and compounding pharmacies where manual aseptic processing may occur. The guidance provided in this report may be applicable to various operations, including: vaccine preparation, cell culture, gene therapy, IND/IMP manufacturing, clinical and commercial manufacturing, and pharmacy formulation and dispensing. When manual aseptic processing of sterile dosage forms is required special consideration must be given to sterility and verification of processing accuracy, as the administration of these products into the vascular and nervous system of human subjects poses the greatest risk of harm. As applicable, the 2004 FDA guidance on aseptic processing, EU GMP–Annex 1, Ph Eur 5. 1. 1, and USP Chapters <797> and <823> provide procedures and the requirements for ***(1-5):***

- Training of personnel involved in sterile preparation processes
- Environmental control and monitoring requirements
- Specifications for sterile and non-sterile ingredients and components
- Release criteria for sterility and pyrogen testing

Compliance with these requirements is paramount to ensure the safety of human recipient.

Some of these processes require aseptic steps subsequent to sterilization but prior to filling, such as volume or pH adjustments, which present their own contamination risks.

This report is not intended to address the brief, relatively infrequent, human interventions into an otherwise automated filling process. Examples include reach-ins to remove a toppled vial from the filling line or to obtain a container for a fill-weight check, aseptic connections made during set-up, corrective activities during line stoppages, and so on. Operator activities and interventions of this nature