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Fundamentals of an Environmental Monitoring Program Annex 1: Environmental Monitoring of Facilities Manufacturing Low Bioburden Products

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Fundamentals of an Environmental Monitoring Program Annex 1: Environmental Monitoring of Facilities Manufacturing Low Bioburden Products Team

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1.0 Introduction

Environmental monitoring (EM) is used to evaluate the effectiveness of contamination controls used in the manufacture of pharmaceutical products. EM programs need to be designed and implemented based on the needs of the specific facility and processes involved. PDA *Technical Report No. 13 (Revised 2014): Fundamentals of an Environmental Monitoring Program* (TR 13) focuses on the environmental requirements for sterile product manufacturing ***(1)***. This addendum will provide elements to consider when designing a risk-based EM program to support the manufacture of low bioburden products using low bioburden processes.

Regulations and guidance are readily available for EM requirements supporting sterile, nonsterile, and advanced therapy medicinal products (ATMP) manufacturing processes ***(2–6)***. Guidance for EM supporting the manufacture of low bioburden products is very limited. Where it is, the documents often cite resources intended for aseptic processes and then recommend establishing a risk-based approach to designing an EM program to support low bioburden processes ***(7, 8)***. This is largely due to the fact that most manufacturing operations where low bioburden control is required combine elements of both sterile and nonsterile processing. However, no specific guidance identifies the elements to which these sterile and nonsterile guidelines should be applied.

This document provides a means of determining the critical aspects, assessing the associated risks, and designing the appropriate EM program for areas where bioburden control of manufacturing processes is required. It can be applied across many types of manufacturing operations used to produce pharmaceutical products including biologics, small molecules, ATMPs, and others. This document should be viewed as technical guidance and is not intended to establish any voluntary or mandatory standards.

1.1 Purpose

This addendum complements the existing PDA TR-13 and is not meant to change or modify its content. The addendum provides recommendations for the development of an environmental control and monitoring program for classified areas and the associated GMP processes used for manufacturing operations requiring bioburden control in the biotechnology and pharmaceutical industries. The content includes a review of regulatory requirements and the development of risk assessments based on the criticality and complexity of processes, as well as industry examples of these risk-based approaches.

Risk assessment tools such as Failure Mode Effects Analysis (FMEA), Hazard Analysis and Critical Control Points (HACCP), or hybrid approaches can be used for these evaluations. This addendum presents a hybrid approach that is intended to help analyze operational risk in order to develop appropriate levels of EM required to monitor operations. When implementing these tools in the design of any EM program, the resulting program should fit the intended purpose. It should not unnecessarily impede the operation or introduce additional risk to the process.

1.2 Scope

TR-13-2 focuses on environmental controls and monitoring programs for classified areas where manufacturing processes are required to ensure a low bioburden level of the material being produced. Although a comprehensive EM program addresses both viable and nonviable aspects of the facility, this addendum concentrates primarily on the viable aspects as these parameters have a greater potential to impact product and process quality related to bioburden. This document is not intended to address EM programs for traditional aseptic or sterile manufacturing, which are covered in TR-13, nor does it address traditional nonsterile dosage forms.

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