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Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Methods

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PDA Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Methods Technical Report Team

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Table of Contents

FIGURES AND TABLES INDEX

1.0 Introduction

Microbiological testing plays an ever-increasing role in the pharmaceutical laboratory. In response to this, a variety of alternative and rapid methodologies that automate existing methods, make use of surrogate markers, or are based on wholly new technologies have emerged in recent years. These alternative methodologies offer significant improvements in terms of speed, accuracy, precision, and specificity over traditional, or classical, microbiology test methodologies.

The majority of testing performed today relies on century-old, conventional methods based on the recovery and growth of microorganisms using solid or liquid microbiological growth media. This is true in part because these methods can be appropriate for their intended use and have a long history of application in both industrial and clinical settings. They often are limited, however, by slow microbial growth rates, the unintended selectivity of microbiological culture, and the inherent variability of microorganisms in their response to culture methods. In spite of the limitations of classical culture methods, acceptance of alternative and potentially superior methods has only started to gain momentum within the pharmaceutical, biotechnology, and medical device industries. The Technical Report Team believes that the lack of clear guidance both on how to demonstrate the equivalence of alternative/rapid methods to existing methods in a manner acceptable to regulatory agencies and on how to validate the equipment associated with alternative/rapid methods is one impediment to the widespread adoption of these methods.

Considerable guidance can be found regarding the validation of chemical methods. Examples include USP General Informational Chapter <1225> *Validation of Compendial Method*s and the International Conference on Harmonisation (ICH) guideline *Validation of Analytical Methods* ***(1,2).*** These publications provide very specific instruction regarding the demonstration of alternative analytical chemistry methods and their equivalence to existing methods. Chapters introduced by the compendia, including USP General Information Chapter <1223> *Validation of Alternative Microbiological Methods,* and Ph. Eur. Informational Chapter 5.1.6 *Alternative Methods for Control of Microbiological Quality*, provide guidance on the steps needed to validate an alternative microbiological method ***(3,4).*** However, additional guidance is needed, as an understandable and holistic approach to the qualification and implementation of novel alternate microbiological methods, including rapid microbiological methods, still does not exist that would satisfy all regulatory agencies.

The original PDA Technical Report No. *33* was published in 2000 to fill this void. Industry, compendial, and regulatory developments since then, however, have necessitated this update to the guidance. The team believes that this revision is timely and will provide additional guidance to assist with the evaluation, validation, and implementation of the alternative microbiological methods.

This Technical Report was developed as a collaborative effort amongst representatives from alternative method suppliers and vendors, the pharmaceutical, biopharmaceutical and medical device industries, and regulatory agencies. It is intended to provide a comprehensive approach to the introduction of alternative microbiology methods in a government-regulated environment. It is anticipated that by providing agreed upon performance standards, the development, qualification and implementation of alternative microbiological methods will be greatly accelerated.

1.1 Scope and Purpose of the Technical Report

This Technical Report is intended to provide guidance for the successful evaluation, validation, and implementation of alternative and rapid microbiological methods needed by the pharmaceutical, biotechnology and medical device industries to assure product quality. Applications for these methods include, but are not limited to, the testing of microbial limits, sterility, and antimicrobial effectiveness; microbiological monitoring of clean rooms and other controlled environments and

water for pharmaceutical purposes; microbial characterization and identification; and microbiological in-process control testing.

The Technical Report Team authored this document for microbiologists responsible for the validation of the microbiological test methods used in the routine microbiology testing laboratory; the document also should be of interest to suppliers of testing equipment, microbiology managers and supervisors, validation specialists, quality control personnel responsible for the approval of validation protocols and the release of product and regulatory agencies.

1.2 Overview of Technical Report Structure

This Technical Report was written to establish industry-wide criteria on what constitutes an acceptable alternative/rapid microbiology test to the compendial or classical method and how to prove it to the satisfaction of quality organizations and regulatory agencies.

The Technical Report Team arranged the guidance in such a way as to describe the technical, quality, regulatory, and business attributes of alternative and rapid microbiological methods, the scientific basis for available technologies, and an efficient process for the validation and implementation of such methods.

