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Exclusion of Objectionable Microorganisms from Nonsterile Pharmaceuticals, Medical Devices, and Cosmetics

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PDA Exclusion of Objectionable Microorganisms from Nonsterile Pharmaceuticals, Medical Devices, and Cosmetics Technical Report Team

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The content of this technical report represents a consensus and not necessarily the views of the organizations that employ the team members.

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1.0 Introduction

The exclusion of objectionable microorganisms from nonsterile healthcare products is a challenge for companies because it can be viewed as an undefined critical quality attribute. All other chemical, physical and microbiological attributes (e.g. potency, content variability, microbial count) are defined by test methods and product specifications, whereas the exclusion of objectionable microorganisms is poorly defined. This consensus industry document was developed by representatives of the pharmaceutical, medical device and cosmetic industries, academia and regulatory agencies and provides guidance to stakeholders, including industry representatives and regulators, to address these issues.

1.1 Purpose

The purpose of this technical report is to provide guidance to the nonsterile product manufacturing industry on how to manage the microbial risks associated with manufacturing and storage and how to determine what isolates would be deemed an objectionable microorganism in nonsterile products that is in alignment with the microbial limits requirements for releasing these products into the marketplace. Nonsterile products exceeding the microbial count limit and/or containing specified microorganisms for their product type would be expected to be rejected. Specified microorganisms include microorganisms with compendial requirements to be absent in a particular dosage form, and/or required by a national board of health to be excluded from a registered non-sterile product.

The contamination of marketed products by potentially objectionable microorganisms continues to be an infrequent but chronic problem. A U.S. survey of reported microbiologically related recalls between 2004 and 2011 found that 72% of recalls of nonsterile products were associated with objectionable microorganisms rather than exceeding microbial enumeration limits ***(1)***. Of the 144 recalls for nonsterile products, 5% involved nonsterile pharmaceutical drug products, 42% were for OTC drug products, 31% were for cosmetics, 14% were for medical devices and 8% were for dietary supplements. The average rate of reported recalls is 20 per year.

1.2 Scope

The scope of this technical report is the exclusion of objectionable microorganisms from nonsterile pharmaceutical drug products, over-the-counter (OTC) drug products; medical devices; cosmetics; and personal care products in the pharmaceutical, medical device, cosmetics and consumer healthcare industries (referred to as "our industry" in the remainder of this report). Objectionable microorganisms for nonsterile products, as cited in the U.S. Code of Federal Regulations (CFR) Title 21, Part 211.113, are microorganisms whose growth or persistence in nonsterile products can cause harm to users of those products and degrade the physicochemical, functional and/or therapeutic attributes of the products ***(2)***.

Since all viable microorganisms are excluded from sterile products, the term "objectionable microorganism" is used to refer only to nonsterile products. Some discussion of microorganisms contaminating sterile products and food may be included in this report for informational purposes, but, in general, such discussion is out of scope for the technical report.

This report provides the following information:

- References to literature on microbial contamination of nonsterile products
- Product types and their formulations as these relate to microbial contamination
- Manufacturing and packaging design and control
- Microbial enumeration, detection and identification
- Clinical aspects of objectionable microorganisms
- Risk assessment and mitigation