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Standard Guide for Evaluation of Cleanroom Disinfectants[1]

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1. Scope

1.1 This guide identifies important factors to consider when selecting a disinfectant for use in a cleanroom or similar controlled environment and recommends test methods suitable for evaluating disinfectants. The proper selection of disinfecting agent combined with qualification testing is a key element of a successful disinfection program. Regulatory guidance such as United States Pharmacopoeia Chapter <1072>, "Disinfectants and Antiseptics" and the FDA Guidance for Industry, "Sterile Drug Products Produced by Aseptic Processing–Current Good Manufacturing Practice" address the necessity of disinfectant effectiveness testing but do not clearly define acceptable test methods.

1.2 An understanding of microbiology and microbiological techniques is essential. Knowledge in the following areas is recommended: microorganisms, antimicrobial products (disinfectants, sporicides, and decontamination agents), the chemistry of disinfection, mechanism of activity of disinfectants on cells, application procedures, cleanroom surfaces, and environmental conditions within a cleanroom. This information is available in several published texts listed in the bibliography.

1.3 The theoretical basis for disinfectant activity is not addressed in this guide. An understanding of the effect of disinfectant concentration on microbial reduction (concentration exponent) and kinetics is desirable in determining the use-dilution of different disinfectants and in using dilution to neutralize a disinfectant for efficacy testing. USP chapter <1072> provides further information on this topic.

1.4 This guide is written for the cleanroom environment, although many of the principles outlined in this standard are applicable to manufacturing and processing environments outside of the cleanroom.

1.5 Evaluation of disinfectants for biofilm control is outside the scope of this document.

2. Referenced Documents

2.1 *ASTM Standards:*[2]

E2111 Quantitative Carrier Test Method to Evaluate the Bactericidal, Fungicidal, Mycobactericidal, and Sporicidal Potencies of Liquid Chemicals

E2197 Quantitative Disk Carrier Test Method for Determining Bactericidal, Virucidal, Fungicidal, Mycobactericidal, and Sporicidal Activities of Chemicals

E2315 Guide for Assessment of Antimicrobial Activity Using a Time-Kill Procedure

2.2 *BSI Standards:*[3]

BS EN 1040 Chemical disinfectants and antiseptics. Quantitative suspension test for the evaluation of basic bactericidal activity of chemical disinfectants and antiseptics. Test method and requirements (phase 1)

BS EN 1276 Chemical disinfectants and antiseptics. Quantitative suspension test for the evaluation of bactericidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic and institutional areas. Test method and requirements (phase 2, step 1)

BS EN 1650 Chemical disinfectants and antiseptics. Quantitative suspension test for the evaluation of fungicidal or yeasticidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic and institutional areas. Test method and requirements (phase 2, step 1)

BS EN 13704 Chemical disinfectants. Quantitative suspension test for the evaluation of sporicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas. Test method and requirements (phase 2, step 1)

BS EN 13697 Chemical disinfectants and antiseptics. Quantitative non-porous surface test for the evaluation of bactericidal and/or fungicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas. Test method and requirements without mechanical action (phase 2, step 2)

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[3] Available from British Standards Institute (BSI), 389 Chiswick High Rd., London W4 4AL, U.K., http://www.bsi-global.com.

2.3 *Other Standards:*

AOAC International, Official Methods of Analysis, Chapter 6—Disinfectants, 18th Edition, 2005[4]

ISO 14644-1 Cleanrooms and associated controlled environments -- Part 1: Classification of air cleanliness[5]

United States Pharmacopeia 38, Chapter <1072> Disinfectants and Antiseptics, May 1, 2015[6]

3. Terminology

3.1 *Definitions:*

3.1.1 *antimicrobial, n*—describes an agent that kills bacteria or suppresses their growth or reproduction.

3.1.2 *bioburden, n*—the number and type of viable microorganisms that can be estimated using prescribed recovery procedures.

3.1.3 *biocide, n*—a physical or chemical agent that kills organisms.

3.1.4 *carrier, n*—a surrogate surface or matrix that facilitates the interaction of test microorganisms and treatment.

3.1.5 *cleanroom, n*—an area that establishes and maintains the level of microbial control necessary for the intended manipulations.

3.1.6 *contact time, n*—predetermined time that a test microorganism is exposed to the activity of a test material.

3.1.7 *disinfectant, n*—a physical or chemical agent or process that destroys pathogenic or potentially pathogenic microorganisms on inanimate surfaces or objects.

3.1.8 *efficacy, n*—the proven performance of a product established under defined conditions.

3.1.9 *effectiveness, n*—a measure of the performance of a product.

3.1.10 *inoculum, n*—the viable microorganisms used to contaminate a sample, device, or surface, often expressed as to number and type.

3.1.11 *neutralization, n*—the process for inactivating or quenching the activity of a microbiocide, often achieved through physical (for example, filtration or dilution) or chemical means.

3.1.12 *qualification, n*—to determine effectiveness in the context of a given process.

3.1.13 *sanitizer, n*—chemical or physical agent(s) used to reduce the number of microorganisms to a level judged to be appropriate for a defined purpose and/or claim.

3.1.14 *soil load, n*—a chemical or physical material(s) included in a test procedure to simulate conditions or use.

3.1.15 *sporicide, n*—a chemical or physical agent(s) that kill spores.

3.1.16 *substrate, n*—surface on which an organism can grow.

3.1.17 *surfactant, n*—an agent that reduces the surface tension of water or the tension at a water-liquid interface

3.2 *Acronyms:*

SDS = Safety Data Sheet
GMP = Good Manufacturing Practice
IPA = Isopropyl Alcohol
USP = United States Pharmacopeia

4. Summary of Guide

4.1 Selecting and qualifying the appropriate disinfection agents is an integral factor in developing a compliant cleaning and disinfection program for a cleanroom. Significant factors to consider when selecting disinfectant for use in cleanrooms and controlled environments are discussed in this guide. A summary of the most common test methods used to determine disinfectant effectiveness is also presented.

5. Significance and Use

5.1 Requirements for aseptic processing areas include readily cleanable floors, walls, and ceilings that have smooth, non-porous surfaces; particle, temperature, and humidity controls; and cleaning and disinfecting procedures to produce and maintain aseptic conditions. These controls, combined with careful and thorough evaluation of the chemical agents used for the cleaning and disinfection program, should lead to achieving the specified cleanliness standards and control of microbial contamination of products. Qualification of disinfectants in pharmaceutical, biotechnology, medical device facilities, and associated controlled environments, along with validation of the cleaning and disinfection process, is subject to scrutiny by regulatory agencies.

5.2 An effective cleaning and disinfection program in aseptic processing areas of a Good Manufacturing Practice (GMP) - regulated facility is critical to assure product quality. Manufacturers are held to a high standard when it comes to product sterility, and regulatory agencies increasingly request validation data to support sanitization and disinfection procedures. Regulatory authorities expect evidence of the effectiveness of disinfection agents against environmental microorganisms isolated from the facility. The FDA Guideline for Aseptic Processing states, "The suitability, efficacy, and limitations of disinfecting agents and procedures should be assessed. The effectiveness of these disinfectants and procedures should be measured by their ability to ensure that potential contaminants are adequately removed from surfaces."[7]

5.3 Basic knowledge regarding the effectiveness of different chemical agents against vegetative bacteria, fungi, and spores will aid in selecting chemical agents.

5.4 An understanding of test methods used to assess disinfectant effectiveness is important. Most methods are adaptable, allowing the user to customize the methods to their specific requirements.

[4] Available from AOAC International, 481 North Frederick Ave., Suite 500, Gaithersburg, Maryland 20877-2417, http://www.aoac.org.

[5] Available from International Organization for Standardization (ISO), Chemin de Blandonnet 8, CP 401, 1214 Vernier, Geneva, Switzerland, http://www.iso.org.

[6] Available from U.S. Pharmacopeia (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, http://www.usp.org.

[7] FDA Guideline for Industry: Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Process, September 2004. Available at http://www.fda.gov/cder/guidance/index.htm