

INSTITUTE OF ENVIRONMENTAL SCIENCES AND TECHNOLOGY

Contamination Control Division Recommended Practice CC023.2

IEST-RP-CC023.2

Microorganisms in Cleanrooms

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1 SCOPE AND LIMITATIONS

1.1 Scope

This Recommended Practice (RP) provides guidelines for the control and quantitative measurement of viable contamination in the air and on surfaces in environments that require control of such contamination. This includes areas designated as aseptic and those considered nonsterile. The procedures and techniques employed to achieve the desired level of microbial control are dependent on the level of bioburden that can be tolerated. This RP presents an introduction to the currently accepted methods for bioburden control and environmental monitoring as well as the devices available for the quantification of airborne and surface viable contamination.

This document also describes disinfectants, their lethality spectrum, and techniques for their application.

1.2 Limitations

Any controlled area designated for the manufacture or storage of a medical device, pharmaceutical product, or food product is subject to regulations imposed by agencies that govern each industry. This document is not intended to supersede or substitute for these regulations. It is intended to provide a framework for meeting the regulatory requirements and to achieve the highest level of bioburden control required for other types of environments.

In selecting a disinfectant, it is the responsibility of the user to consider all factors related to but not necessarily limited to personnel safety, application devices, methods, surface compatibility, residues, and bactericidal or bacteriostatic efficiency.

The selection of testing and disinfection methods varies with the desired level of airborne and surface bioburden.

2 REFERENCES

The cited editions of the following documents are incorporated into this RP to the extent specified herein. Users are encouraged to investigate the possibility of applying the most recent editions of the references.

2.1 Documents

ANSI/AAMI/ISO 11137—1994 Sterilization of health care products—Requirements for validation and routine control—Radiation sterilization

ANSI/AAMI/ISO 11737-1—1995 Sterilization of medical devices—Microbiological methods—Part 1: Estimation of population of microorganisms on products

Association of Official Analytical Chemists. *The Official Methods of Analysis of AOAC International* 18th Ed., Chapter 6, pp. 4, 7, 8.

Guidance for Industry Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice. September 2004. US Food and Drug Administration.

IENT-RP-CC003: Garment System Considerations For Cleanrooms and Other Controlled Environments

IENT-RP-CC018: Cleanroom Housekeeping: Operating and Monitoring Procedures

IENT-RP-CC034: HEPA and ULPA Filter Leak Tests

ISO 14644-1 Cleanrooms and associated controlled environments—Part 1: Classification of air cleanliness

ISO 14644-4 Cleanrooms and associated controlled environments—Part 4: Design, construction and start-up

ISO 14698-1 Cleanrooms and associated controlled environments—Biocontamination control—Part 1: General principles and methods

ISO/DTR 14698-3 Cleanrooms and associated controlled environments—Biocontamination control—Part 3: Measurement of the efficiency of processes of

cleaning and/or disinfection of inert surfaces bearing biocontaminated wet soiling or biofilms

Parenteral Drug Association Task Force on Decontaminating Agents. 1986. Decontaminated Agents. *Journal of Parenteral Science and Technology* 40 (3): 104-109

Parenteral Drug Association. *Technical Report #13—Fundamentals of an Environmental Monitoring Program*

US Air Force. December 1, 1972. *Technical Order 00-25-203 Contamination Control of Aerospace Facilities*, (www.robins.af.mil/logistics/LGEDA/Documents/00series.htm)

USP 29–NF 24 United States Pharmacopeia–National Formulary January 1, 2006

2.2 Sources and Addresses

ANSI

American National Standards Institute
25 West 43rd Street
New York, NY 10036, USA
Phone: 212-642-4900
Fax: 212-398-0023
www.ansi.org

AAMI

Association for the Advancement of
Medical Instrumentation
1110 North Glebe Road, Suite 220
Arlington, VA 22201-4795
Phone: 703-525-4890
Fax: 703-276-0793
www.aami.org

AOAC

Association of Official Analytical Chemists
481 North Frederick Avenue
Suite 500
Gaithersburg, MD 20877-2417, USA
Phone: 301-924-7077
Fax: 301-924-7089
www.aoac.org

FDA

US Food and Drug Administration
Division of Manufacturing and Product Quality
Office of Compliance
5600 Fishers Lane
Rockville, MD 20857, USA
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ISO

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www.iest.org
Outside the US: Documents available from representative ISO member body organization

PDA

Parenteral Drug Association
3 Bethesda Metro Center, Suite 1500
Bethesda, MD 20814 USA
Phone: 301-656-5900
Fax: 301-986-0296
www.pda.org

USAF Robins Air Force Base

WR-ALC/LKCB
Robins AFB, GA 31098, USA
Phone: 478-926-1110
www.robins.af.mil

USP

US Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852-1790, USA
Phone: 800-227-8772
www.usp.org

3 TERMS AND DEFINITIONS

anion

A negatively charged atom or group of atoms.

antimicrobial

A compound or formulation used to retard the growth of or to kill microorganisms.

antiseptic

A substance that prevents or inhibits the growth of microorganisms without necessarily killing them. The term antiseptic is usually associated with substances used on humans or animals.

antistatic compound

A chemical substance that is capable of neutralizing a surface charge.

NOTE: Most antistatic compounds function via one of the following two properties:

- Electrostatic charge neutralization, in which the surface charge of one polarity is dissipated by applying charged materials of the opposite polarity to the surface. The most effective antistatic compounds in this category are quaternary ammonium chlorides.

- b) Film formation, in which moisture from the air absorbs onto a film of (nonionic) antistatic compound, thereby dissipating the buildup of charge.

In the microelectronics industry, and wherever else there is concern regarding the presence of ion species, reduction of static through the use of nonionic formulations is preferred.

aseptic

The state of having eliminated all detectable viable microorganisms.

bacteria

One-celled, microscopic organisms lacking chlorophyll that multiply by fission. Bacteria typically measure from 0.2 to 50 μm in diameter.

bacterial spore

A resistant body produced by a vegetative bacterial cell. These spores may be resistant to heat, ultraviolet light, and desiccation, and may remain dormant for extended periods of time.

bactericide

A substance or formulation capable of destroying bacteria.

bacteriostat

A compound or formulation that retards or prevents the growth of bacteria. Bacteriostats act reversibly; when they are removed, cells resume their normal growth patterns.

bioburden

A measure of the number of microorganisms resident on or within products and inanimate objects. A common synonym is microcount.

cation

A positively charged atom or group of atoms.

CFU (colony-forming unit)

Either one or an aggregate of microbial cells which, when cultivated on solid media, will develop into a single visual colony.

cleanroom

A room in which the concentration of airborne particles is controlled and which contains one or more clean zones.

controlled

A term used to describe a process or environment in which parameters such as temperature, pressure, humidity, contaminate level and so forth are maintained within specified limits.

critical

A term used to describe a parameter whose impact on a product or process renders that product or process useless if the parameter is out of the controlled limits.

decontamination

The removal of microorganisms, chemical residue, or particulate from liquids, surfaces, air, or other gases.

dedicated shoes

Footwear or shoes compatible with an environment or process that are maintained solely within that environment. Typically these will only leave the environment for cleaning or replacement.

degowning or doffing

The act of removing cleanroom garments in a controlled manner to prevent damage and unnecessary contamination of the garments.

deodorant

A compound or formulation with the ability to counteract undesirable odors. The ability of a formulation to counteract odor is directly related to its antimicrobial function, provided that the odor arises from the waste products of the microorganism's cell metabolism. Odors vary according to the food source utilized by the microorganism.

disinfectant

An agent or chemical that destroys vegetative forms of harmful microorganisms, especially on inanimate objects. NOTE: A disinfectant may be less effective in destroying bacterial spores. Disinfection does not necessarily sterilize a surface.

flora

The types of microbiological organisms found in an environment.

fogging

A process of decontamination in which the decontaminant is administered by means of its conversion to an aerosol.

fumigation

A process of decontamination in which the decontaminant is administered in gaseous form at ambient pressure.

fungi

Any of a major group of saprophytic and parasitic lower plants that lack chlorophyll and include molds, rusts, MucS, mushrooms and yeasts.

fungicide

A substance or formulation that is capable of destroying fungi.

fungistat

A compound or formulation that retards or prevents the growth of fungi. Fungistats act reversibly; when the fungistats are removed, the cells resume their normal growth patterns.

Gram-negative bacteria

Bacteria that do not retain the purple color of the crystal violet dye when treated with Gram's staining

technique. Therefore, the saffranin is visible, giving a red or pink color.

Gram-positive bacteria

Bacteria that retain the purple color of the crystal violet dye when treated with Gram's staining technique.

Gram's staining technique

A method for staining and classifying bacteria, developed by Dr. Hans C.J. Gram.

HEPA (high-efficiency particulate air) filter

An extended-medium, dry-type filter in a rigid frame when tested at rated airflow having a minimum particle collection efficiency of 99.97% for 0.3- μm mass median diameter particles of DOP when tested in accordance with MIL-STD-282.

ionic contamination

Contamination in the form of atoms having electrical charge. Common examples include singly charged atoms (ions) from Group IA (such as sodium and potassium) and Group VIIA (such as fluorine and chlorine) of the periodic table.

isokinetic sampling

The condition of isoaxial sampling in which the mean velocity of the air entering the sampling probe inlet is the same as the mean velocity of the unidirectional airflow at that location.

kGy (kilogray)

1000 grays; a standard unit used to measure the absorbed dose of radiation.

microbiological clean area

A defined space with a filtered air supply that is designed to accommodate the performance of activities for which the control of viable particles is essential.

morphology

The characteristic shape, color and consistency of a microbial colony when cultivated on various solid media.

noncorrosive, nonstaining

Terms applied to formulations to indicate that they should have a minimal effect on the integrity or appearance of surfaces with which they come in contact.

nonionic

A term used to describe compounds and formulations that do not possess charged materials.

pathogen

A microorganism capable of causing disease.

pyrogen

A substance capable of producing fevers. The most common pyrogens are endotoxins, a class of lipopolysaccharides that comprise the outer wall of Gram-negative bacteria and are themselves byproducts of cell metabolism.

residual activity

Residue that retains its active properties and remains on surfaces after treatment with an antimicrobial substance.

sanitizer

A substance that reduces the number of microbial contaminants to a level that is considered safe.

shelf life

The estimated length of time that a formulation can be stored before it loses its effectiveness.

sporicide

A substance or formulation capable of destroying bacterial spores.

sterile

The condition of lacking all forms of microbial life.

sterilization

A physical or chemical process that completely destroys or eliminates all forms of microbial life.

toxic

Poisonous, causing an adverse reaction.

ULPA (ultra-low-penetration air) filter

A throwaway, extended-medium, dry-type filter in a rigid frame, having a minimum particle-collection efficiency of 99.999% (that is, a maximum particle penetration of 0.001%) when tested in accordance with the methods of IEST-RP-CC007.

vegetative organisms

Microbial cells that are metabolically active.

viable particle

A particle that is capable of reproduction; an organism.

viricide

A substance or formulation capable of destroying viruses.

virus

An obligate intracellular parasite that can infect and cause disease in humans, animals, plants, insects, and so forth. Viruses usually range in size from 0.01 to 0.1 μm .

4 BACKGROUND AND PURPOSE

Technology advancements in the electronics, medical device, and pharmaceutical/biotech industries consistently produce more capable and complex products that improve the quality of life and health for those who use them. As technology becomes more complex it is more vulnerable to contamination that can cause the product to fail or perform poorly. Contamination can occur in many forms, including: