Status: Currently Official on 12-Feb-2025
Official Date: Official as of 01-May-2024
Document Type: General Chapter
DocId: GUID-404E2D53-B1E9-462A-BD96-14AD0A34DFA7_2_en-US
DOI: https://doi.org/10.31003/USPNF_M17297_02_01
DOI Ref: fspt1

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▲⟨1117.1⟩ MICROBIOLOGICAL CHAPTERS—GLOSSARY

INTRODUCTION

Several chapters interface: linking together on topics and necessarily using a set of terms specific to microbiology and endotoxin analysis. An artificer of microbiology seeking clarity and understanding of the meaning of a particular term requires a single source glossary, including associated definitions of terms. The terms and their definitions are listed in this chapter. For simplicity, all definitions are as concise as feasible and aligned as far as possible with other standard and industry group definitions. However, each definition necessarily fulfills the meaning of the term as used in the USP microbiological chapters. Some critical definitions of terms are accompanied with additional explanatory notes.

GLOSSARY

Aerobe: A microorganism that requires oxygen for growth.

Alternative microbiological methods:

Any non-USP microbiological method.

[Note—1. A USP microbiological method is a microbiological test method specified in a general chapter less than 1000.]

Anaerobe: A microorganism that has the capability to grow in the absence of oxygen.

Antimicrobial:

The ability to kill or suppress the growth of microorganisms.

Antiseptic:

An agent that inhibits or destroys microorganisms on or in living tissue, including skin, oral cavities, and open wounds.

Aseptic: Conditions that minimize viable microbial population.

Aseptic manipulation: Handling of materials in a manner that prevents microbial contamination.

Aseptic processing: An operation in which the product is assembled or filled into its primary package in an ISO 5 or better environment and under conditions that minimize the risk of microbial contamination.

Aseptic process simulation: A means of assessing the efficacy of an aseptic process using microbiological media, also known as media fill.

Aseptic process validation: Establishing documented evidence from the process design stage through commercial production, which provides a high degree of assurance that an aseptic process will consistently produce a product meeting its predetermined microbiological specifications and quality attributes.

Aseptic technique: A reference to actions taken to prevent microbial contamination.

Assurance of sterility: Qualitative concept comprising all activities that provide confidence that product is sterile.

[Note—1. Aligns with ISO 11139:2018 (*1*).]

Bactericidal: An ability to kill vegetative bacteria.

Bacteriostatic: Prevention of bacterial reproduction.

Bioburden: The total number of microorganisms associated with a specific item such as personnel, manufacturing environments (air and surfaces), equipment, product packaging, raw materials (including water), in-process materials, or finished products.

Bioburden test: A test that quantifies the bioburden in a sample.

[Note—1. The term has sometimes been erroneously presumed to be synonymous with the compendial test method *Microbial Enumeration Tests* ⟨61⟩.]

Biocide: A substance that destroys microorganisms.

Biofilm: A population of microorganisms attached to a surface, protected within an extracellular matrix.

Biological indicator (BI)**:** Test system containing viable microorganisms used to evaluate a sterilization, decontamination, or disinfection process.

[Note—1. Adapted from ISO 11139:2018 (*1*) to accommodate BIs where their exact resistance is unknown or indeterminate, allowing for use in explicit demonstrations of process lethality. For example, see *Vapor Phase Sterilization* ⟨1229.11⟩.]

Bracketing approach: A validation strategy in which pairs of process variables are used to establish a proven acceptable range.

Chemical indicator (CI)**:** Test system that reveals change in one or more prespecified process variables based on a chemical or physical change resulting from exposure to a process.

[Note—1. Aligned with ISO 11139:2018 (*1*).]

Cleanroom: A room within which the number and concentration of airborne particles is controlled and classified, and which is designed, constructed, and operated in a manner to control the introduction, generation, and retention of particles inside the room.

[Note—1. Aligned with ISO 14644-1:2015 (2).]

Colony-forming unit (cfu)**:** A viable cell or number of closely associated cells that multiply and form a single detectable entity on solid culture media.

[Note—1. As written, the definition permits the use in context of both compendial and alternative microbiological methods. The term "detectable entity" is most usually the very structured cell mass (colony) generally visible.]

Contaminant: Anything not intended to be part of a product or process.

[Note—1. As written, the definition is inclusive of microorganisms or their associated biomolecules that are undesirable and intolerable. This distinguishes from bioburden that may access or ingress into a facility or process and that must be controlled but is not automatically regarded as adverse to process and product quality.]

Contamination (verb)**:** The introduction of anything by nature or quantity not intended to be part of a product or process.

Contamination control: A holistic and integrated set of controls, planned actions, and conditions designed to prevent, limit, or reduce contamination.

Corrective intervention (aseptic process)**:** An activity (manual or automated) performed to correct malfunctions.

***D*-value:** The time under defined conditions required to reduce a specified pure microbial population by 1 log base 10.

Death rate curve (also called a survivor curve)**:** Graphical representation of microbial death rate kinetics.

Decontamination: Reduction of contaminants to less than a specified level.

Depyrogenation: Reduction of pyrogens to less than a specified level.

Disinfectant: An agent that reduces the population of microorganisms in a vegetative state but that may not affect spores.

[Note—1. Also known as disinfecting agent.]

Disinfection: Reducing the population of microorganisms in a vegetative state but not necessarily affecting spores.

Dosimeter: A device having a reproducible, measurable response to radiation that can be used to measure the absorbed dose in a given system.

[Note—1. Aligned with ISO 11139:2018 (1).]

Endotoxin: The major constituent of the outer membranes of Gram-negative bacteria composed of lipid A, the core polysaccharide, and the O-antigen polysaccharide; endotoxin is also known as lipopolysaccharide (LPS).

Endotoxin calibration analytes: The USP standard employed to establish a calibration curve for the bacterial endotoxin test as the primary standard.

[Note—1. The primary USP Reference Standard Endotoxin (RSE) is extracted and partially purified lipopolysaccharide derivatives from laboratory grown *Escherichia coli*. Secondary Control Standard Endotoxins (CSE) from Gram-negative bacteria must be calibrated against RSE.]

Endotoxin indicator: A test system containing known levels of endotoxin activity that can be used to evaluate a depyrogenation process.

Environmental control: Application of engineering and/or procedural systems to maintain conditions in a defined space within specified limits.

[Note—1. Aligned with ISO 11139:2018 (1).]

Environmental isolate: Microorganism isolated from processing or manufacturing environments, including water systems.

[Note—1. Aligned with ISO 11139:2018 (1).]

Exotoxin: Toxins produced and secreted from a microorganism.

***F* value:** Measure of lethality delivered by a thermal process expressed in terms of the equivalent time, in minutes, at a specified temperature with reference to microorganisms with a specified *z*-value.

[Note—1. Slightly modified from ISO 11139:2018 (1).]

Fluorochrome: A class of dyes that when excited by light of certain wavelengths emit photons and become fluorescent.

Fluorogenic substrate: A nonfluorescent material that is acted upon by an enzyme to produce a fluorescent compound.

Fractional cycle: An abbreviated cycle in which biological indicator results can be extrapolated to support the cycle duration.

Fumigation: Decontamination by exposure to an antimicrobial aerosol, gas, or vapor.

Fungicidal: An ability to kill fungi and their spores.

Fungistatic: Prevention of fungal reproduction.

Gown: Protective clothing used to reduce the risks of contamination from people entering and working in a defined area.

Gowning or gowning procedure: A specified process for donning contamination control garments.

Growth promotion test: A test intended to confirm the ability of a nutrient medium to support growth of a predetermined type and number of microorganisms.

Hygiene: Conditions and practices that help control the survival and distribution of microorganisms.

Inactivation: Rendering microorganisms nonviable.

Infection: The invasion and multiplication of microorganisms in a host to the extent that clinical symptoms are manifested.

Intervention: Planned activity during an aseptic process that may pose a risk of contamination.

Isolate (microbial)**:** A pure culture obtained from a microbiological test (e.g., bioburden test, sterility test).

Isolator: An enclosure capable of preventing ingress of contaminants by means of physical separation of the interior from the exterior that is capable of interior bio-decontamination, and where personal and exterior environment remain separated from the interior of the enclosure by means of a physical barrier.

Load: The defined product, equipment, or materials to be processed together within an operating, sterilization, or decontamination cycle.

Log reduction: The reduction of a microbial population or endotoxins by 10-fold.

Microbial preservation: Maintaining a culture of organisms in its pure, viable state for an extended period of time.

Microbial resistance: The ability of a microorganism to survive a condition that is intended to kill or control them.

Microbiological media: Nutrient media of a defined set of ingredients purposed for the growth of microorganisms.

Microbiological quality: Quality attributes of a material related to microorganisms listed within specifications.

Microorganism: Microorganisms can be bacteria (including mycoplasma) and fungi.

[Note—1. Does not include viruses and prions.]

Nonpyrogenic: Nonfever producing.

Nonsterile product: A pharmaceutical finished drug product manufactured by a process validated to ensure the control of bioburden, protected to prevent recontamination, and conforming to microbiological quality attributes associated with the dosage form and route of administration per *Microbiological Acceptance Criteria for Nonsterile Pharmaceutical Preparations and Substances for Pharmaceutical Use ⟨1111⟩*.

Objectionable microorganism: Microorganism that under certain conditions unique to a product and the associated manufacturing process poses a significant risk to patient safety or product quality.

Overkill sterilization: A method of sterilization in which the destruction of a high concentration of a resistant microorganism supports the destruction of reasonably anticipated bioburden present in routine processing.

Parametric release: A sterility assurance program where demonstrated control of the sterilization process enables a firm to use defined critical process controls, in lieu of the sterility test.

Pathogen: Disease-causing microorganism.

Physicochemical integrator: A device that responds to a sterilization process critical parameter, which results in a measurable or quantifiable value that can be correlated to some standard of microbial lethality.

Preconditioning: A preparatory step required for some sterilization processes that ensures that materials to be sterilized are in a standardized state that facilitates consistent lethality.

Preservation: Preventing the proliferation of microorganisms.

Preservative: A substance that prevents the proliferation of microorganisms.

Prion: A misfolded proteinaceous infectious agent.

Probability of a nonsterile unit (PNSU)**:** The probability of a single container within a sterilization process being nonsterile. This value is expressed as a negative exponent of 10.

Process challenge device: An item designed to provide a “worst case” resistance to a sterilization process and used to directly confirm its lethality.

Product safety: Product safety has the objective of minimizing patient harm.

[Note—1. The term product safety is preferred to patient safety because it is not always feasible to separate an adverse event that could be due to the product or from the administration of the product.]

Pyrogen: A substance that produces a fever.

Reference microorganism: A microbial strain obtained from a recognized culture collection.

[Note—1. Aligned with ISO 11139:2018 (*1*).]

Resistometer: Test equipment designed to evaluate microbial resistance by creating defined combinations of the physical and/or chemical parameters of a process.

Restricted access barrier system (RABS)**:** An aseptic processing system that provides a rigid-wall enclosed environment meeting ISO 5 conditions utilizing air overspill to separate its interior from the surrounding environment.

Result or test result (specific to alternative microbiological test methods)**:** The final, reportable value that would be compared to the acceptance criterion of a specification.

Sample hold time: The time between sample collection and the start of the analysis.

Sanitization: A validated process used to render product free from viable microorganisms.

[Note—1. Aligned with ISO 11139:2018 (*1*).]

Sanitizer: An agent that reduces the population of microorganisms but may not be fully effective against bacterial or some fungal spores.

Spore: A morphologically distinct, physiologically dormant cellular structure of certain differentiating bacteria and fungi.

Sporicide: An agent that kills microbial spores.

Sterile: The state of an item or material that has been subjected to a process validated to ensure the destruction or removal of the presterilization bioburden and protected to prevent recontamination.

Sterility: The complete absence of viable microorganisms.

[Note—1. Sterility is a state that is unprovable by testing.]

Sterility assurance: The collective contribution of microbial controls permitting product quality.

Sterility test: A test method that has some capability of demonstrating a material is not sterile. The test does not prove a product is sterile.

Sterilization: A validated process used to render product free from viable microorganisms.

[Note—1. Aligned with ISO 11139:2018 (*1*).]

Sterilization cycle: A predetermined set of conditions in a sterilizer designed to achieve a product free of viable microorganisms.

Sterilizing agent: Physical or chemical agent(s), or combination thereof, having microbicidal activity to achieve sterility under defined conditions.

[Note—1. Aligned with ISO 11139:2018 (*1*).]

Sterilizing grade filter: A filter that meets the requirements of ASTM F838, Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration (*3*).

Surface-active substance: A material that changes the surface tension of a fluid.

Terminal sterilization: Process whereby a product is sterilized within its primary final sealed container or sterile barrier system.

[NOTE—1. Slightly modified from ISO 11139:2018 (*1*).]

Unidirectional airflow: Airflow moving in a single direction in a uniform manner and at sufficient speed for particulate control.

Viable microorganism: A microorganism that remains in a metabolically and physiologically active state.

***z*-value:** Change in temperature of a thermal sterilization or disinfection process that produces a tenfold change in *D*-value.

[NOTE—1. Aligned with ISO 11139:2018 (*1*).]

[NOTE—2. The *D*-value and *z*-value will be specific for a particular microorganism type.]

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3. ASTM International. ASTM F838-20. Standard test method for determining bacterial retention of membrane filters utilized for liquid filtration. 2020.

▲ (USP 1-May-2024)

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<1117.1> MICROBIOLOGICAL CHAPTERS – GLOSSARY	Leslie Furr Associate Scientific Liaison	GCM2022 General Chapters - Microbiology 2022

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 48(5)

Current DocID: GUID-404E2D53-B1E9-462A-BD96-14AD0A34DFA7_2_en-US

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