Designation: F3127 – 22

Standard Guide for Validating Cleaning Processes Used During the Manufacture of Medical Devices[1]

This standard is issued under the fixed designation F3127; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide provides considerations for validating cleaning processes for medical devices during initial fabrication and assembly prior to initial use. Validated cleaning processes are important for achieving consistency in function and consistency in biocompatibility. The considerations include but are not limited to: validation approach, equipment design, procedures and documentation, analytical methods, sampling, development of limits, and other issues.

1.2 *Inclusions:*

1.2.1 This guide describes the validation of critical cleaning processes for medical devices to reduce contaminants to acceptable levels prior to packaging.

1.3 *Exclusions*—The following items / medical devices / processes are excluded from the scope of this document:

1.3.1 Reusable medical devices.

1.3.1.1 Validation of cleaning operations for reusable medical devices is not within the scope of this standard guide. Although cleaning of reusable medical devices is beyond the scope of this guide, many of the principles outlined in this guide may be applicable to the validation of cleaning operations for reusable devices.

1.3.2 Cleaning of medical devices in health care facilities.

1.3.2.1 Validation of cleaning processes in patient/health care facilities is not within the scope of this standard guide.

1.4 This standard does not purport to be a replacement for biological safety testing.

1.5 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.6 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D543 Practices for Evaluating the Resistance of Plastics to Chemical Reagents

E1766 Test Method for Determination of Effectiveness of Sterilization Processes for Reusable Medical Devices

E2857 Guide for Validating Analytical Methods

E3106 Guide for Science-Based and Risk-Based Cleaning Process Development and Validation

E3219 Guide for Derivation of Health-Based Exposure Limits (HBELs)

E3263 Practice for Qualification of Visual Inspection of Pharmaceutical Manufacturing Equipment and Medical Devices for Residues

F619 Practice for Extraction of Materials Used in Medical Devices

F2459 Test Method for Extracting Residue from Metallic Medical Components and Quantifying via Gravimetric Analysis

F2847 Practice for Reporting and Assessment of Residues on Single-Use Implants and Single-Use Sterile Instruments

G121 Practice for Preparation of Contaminated Test Coupons for the Evaluation of Cleaning Agents

G122 Test Method for Evaluating the Effectiveness of Cleaning Agents and Processes

G131 Practice for Cleaning of Materials and Components by Ultrasonic Techniques

2.2 *ANSI/AAMI/ISO Standards:*[3]

ISO 10993-5 Biological Evaluation of Medical Devices—Part 5: Tests for Cytotoxicity, In Vitro Methods

[1] This guide is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.15 on Material Test Methods.

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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 American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

ISO 11737-1:2018 Sterilization of Health Care Products—Microbiological Methods—Part 1: Determination of a Population of Microorganisms on Products
ISO 14971 Medical Devices—Application of Risk Management to Medical Devices
ISO 17025 General Requirements for the Competence of Testing and Calibration Laboratories
ISO 19227 Implants for Surgery—Cleanliness of Orthopedic Implants—General Requirements
AAMI ST72 Bacterial Endotoxins—Test Methodologies, Routine Monitoring, and Alternatives to Batch Testing

2.3 *United States Pharmacopoeia (USP) – General Chapters:*[4]

USP <61> Microbiological Examination of Nonsterile Products: Microbial Enumeration Test
USP <62> Microbiological Examination of Nonsterile Products: Test for Specified Microorganisms
USP <85> Bacterial Endotoxins Test
USP <161> Transfusion and Infusion Assemblies and Similar Medical Devices
USP <1225> Validation of Compendial Procedures

2.4 *International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH):*

ICH Q2 Validation of Analytical Procedures: Text and Methodology
ICH Q9 Quality Risk Management

2.5 *FDA Guidance Documents:*[5]

FDA Guidance Pyrogen and Endotoxins Testing: Questions and Answers, issued June 2012

2.6 *European Standards and Pharmacopoeia:*

EN 13018 Non-Destructive Testing—Visual Testing—General Principles
European Pharmacopoeia

3. Terminology

3.1 *Definitions:*

3.1.1 *analyte, n*—a substance (usually a residue) for which an analysis is being performed. The residue determination may be qualitative, quantitative, specific, non-specific, and/or it may involve compositional identification. The analyte may be determined as an extract or directly on the surface of the device or portion (subassembly) of the device.

3.1.2 *blank, n*—an analytical sample taken to establish the background value for an analytical measurement which may be subtracted from an experimental value to determine the "true" value.

3.1.3 *clean, n*—having a level of residues and environmental contaminants which does not exceed a maximum permissible level for the intended application.

3.1.4 *cleaning, v*—removal of potential contaminants from an item to the extent necessary for further processing or for intended use.

3.1.5 *cleaning process, n*—a process that is used to remove any product, process-related material, and environmental contaminant introduced as part of the manufacturing process.

3.1.6 *cleaning validation, n*—the documented evidence providing a high degree of assurance that a cleaning process will result in medical devices consistently meeting their predetermined cleanliness requirements.

3.1.7 *cleaning verification, n*—a one-time sampling and testing to ensure that a medical device has been properly cleaned following a specific cleaning event.

3.1.8 *contaminant, n*—any material that potentially adversely impacts the assembly, the functioning of the device, and/or shows undesirable interaction with the host. A contaminant may be a single component or any combination of components. Examples of possible types of contaminants include: (*1*) biological or non-biological in nature; (*2*) living or dead; (*3*) particles or thin films; (*4*) solid, liquid, or vapor; and (*5*) organic or inorganic.

3.1.9 *first use, n*—the initial contact with biological materials or fluids.

3.1.10 *installation qualification (IQ), n*—establishing by objective evidence that all key aspects of the process equipment and ancillary system installation adhere to the manufacturer's approved specification and the recommendations of the supplier of the equipment are suitably considered.

3.1.11 *monitoring, v*—verification testing at predefined intervals.

3.1.12 *operational qualification (OQ), n*—establishing by objective evidence process control limits and action levels which result in product that meets all predetermined requirements.

3.1.13 *process qualification (PQ), n*—establishing by objective evidence that the process, under anticipated conditions, consistently produces a product which meets all predetermined requirements.

3.1.14 *recovery study, n*—a laboratory study combining the sampling method and analytical method to determine the quantitative recovery of a specific residue for a defined surface.

3.1.15 *residue, n*—a substance present at the surface of an implant or embedded therein that is not explicitly recognized and defined as part of the implant specification. It includes processing-based residues as well as contamination by environmental factors (adsorbates).

4. Summary of Practice

4.1 This guide provides an approach for validating the removal of contaminants and residues introduced during the intermediate process steps so that the terminal cleaning process can result in a consistently clean medical device.

5. Significance and Use

5.1 This guide describes an approach to validate a cleaning system for a medical device. It is based on the manufacturer's accurate and comprehensive understanding of their internal manufacturing and cleaning processes.

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

[5] Available from U.S. Food and Drug Administration (FDA), 10903 New Hampshire Ave., Silver Spring, MD 20993, http://www.fda.gov.