Designation: F3438 – 24

Standard Guide for Detection and Quantification of Cleaning Markers (Analytes) for the Validation of Cleaning Methods for Reusable Medical Devices[1]

This standard is issued under the fixed designation F3438; 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 standard guide provides methods and considerations for detecting and quantifying test soil(s) from reusable medical device(s) that result from simulated-use testing of medical devices during validation of the cleaning procedures as described in the instructions for use (IFU) provided by the medical device manufacturer.

1.2 The methods described are for detecting and measuring markers (analytes) that are components within the most common test soils and are relevant to the clinical use of the device. Appropriate test soils without protein, carbon, or carbohydrates (for example, bone) will require other methods.

1.3 This is a part of a series of ASTM standard guides for validating cleaning instructions. The scope of the first guide in the series is selecting appropriate test soils (Guide F3208). The second in the series (Guide F3293) describes methods for inoculating medical devices with test soil. The third in the series (Guide F3321) describes methods for extracting soils for measuring residual soil on medical devices after the performance of cleaning process. This is the fourth guide in the series and describes the methods of detecting and quantifying residual analytes on the device.

1.4 *Units*—The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

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]

D7573 Test Method for Total Carbon and Organic Carbon in Water by High Temperature Catalytic Combustion and Infrared Detection

E1097 Guide for Determination of Various Elements by Direct Current Plasma Atomic Emission Spectrometry

E2520 Practice for Measuring and Scoring Performance of Trace Explosive Chemical Detectors

F3127 Guide for Validating Cleaning Processes Used During the Manufacture of Medical Devices

F3208 Guide for Selecting Test Soils for Validation of Cleaning Methods for Reusable Medical Devices

F3293 Guide for Application of Test Soils for the Validation of Cleaning Methods for Reusable Medical Devices

F3321 Guide for Methods of Extraction of Test Soils for the Validation of Cleaning Methods for Reusable Medical Devices

2.2 *AAMI Documents:*[3]

AAMI TIR12 Designing, testing, and labeling reusable medical devices for reprocessing in health care facilities: A guide for medical device manufacturers

AAMI ST98 Cleaning validation of health care products—Requirements for development and validation of a cleaning process for medical devices

2.3 *ISO Standard:*[4]

ISO 15883-5 Washer-disinfectors—Part 5: Performance requirements and test method criteria for demonstrating cleaning efficacy

[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 Association for the Advancement of Medical Instrumentation (AAMI), 4301 N. Fairfax Dr., Suite 301, Arlington, VA 22203-1633, http://www.aami.org.

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

2.4 *FDA Guidance Document:*[5]

Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling, Guidance for Industry and Food and Drug Administration Staff

3. Terminology

3.1 *Definitions:*

3.1.1 *limit of detection (LOD), n*—the limit of detection is the lowest quantity of a substance that can be distinguished from the absence of that substance within a stated confidence limit (Practice E2520). LOD is also generally defined as three times the standard deviation of the blank (Guide F3127).

3.1.2 *limit of quantification (LOQ), n*—the limit of quantification is the lowest concentration at which the instrument can measure reliably with a defined error and confidence level (Guide E1097).

3.1.3 *test soil, n*—a single substance or a mixture of substances that reflect the contaminants likely to be encountered during the use of the device for its intended clinical procedure (Guide F3208).

4. Summary of Guide

4.1 This standard guide describes methods for detecting and quantifying cleaning markers (analytes) extracted from soiled medical devices during validation testing of the instructions for medical device reprocessing by a healthcare facility.

5. Significance and Use

5.1 This standard guide may be used by medical device manufacturers as part of their design plan and implementation of the validation of the cleaning instructions of their reusable medical devices.

5.2 This guide helps medical device manufacturers to identify the appropriate method(s) for detecting and quantifying markers for the simulated-use test soil (see Guide F3208), thereby evaluating whether the medical device can be adequately cleaned.

5.3 This guide describes various test methods for the different analytes.

5.4 This guide specifies the validation criteria for analyte detection methods.

6. Analyte Validation

6.1 The sensitivity of the analyte method is specified by the limit of detection (LOD), the lowest amount of analyte that can be detected; and the limit of quantification (LOQ), the lowest amount of an analyte in a sample that can be reliably quantified with acceptable accuracy and precision. To establish these values, perform a robust analytical validation of the method to trust the trueness of the reported value. The validation must contain the following validation elements.

6.1.1 *Linearity/Range*—The linearity is assessed by preparing analyte standards in a concentration curve that spans the range of expected analyte concentration and includes method acceptance criteria. The linearity, measured by the R^2 value of the line, should be greater than 0.9900. For the range, the analyte residual acceptance criteria should be in the portion of the curve that demonstrates the best accuracy and precision with the upper and lower points of the curve being both accurate and precise (**1**).[6]

6.1.2 *Accuracy*—The accuracy is expressed as the closeness of agreement between the reference value and the value found, and is determined by comparing the calculated (actual) concentration from the calibration curve to that of the nominal (theoretical) concentration of the protein standard using the following equation:

$$\text{Accuracy} = 100 - \left(\frac{[\text{Nominal}] - [\text{Calculated}]}{[\text{Nominal}]}\right) * 100 \quad (1)$$

6.1.2.1 To demonstrate accuracy, the calculated protein value should be ±15 % of the nominal value.

6.1.3 *Precision*—Defined as the closeness of agreement between a series of measurements obtained from multiple sampling of the same sample, and is quantified using the relative standard deviation (RSD) of each protein calibration point of low and high concentrations across the range.

$$RSD = \frac{S}{\bar{x}} * 100 \quad (2)$$

$$S = \sqrt{\frac{(x_1 - \bar{x})^2 + (x_2 - \bar{x})^2 + (x_3 - \bar{x})^2 + \ldots + (x_n - \bar{x})^2}{n - 1}} \quad (3)$$

where:

S = standard deviation,
$x_1, x_2, \ldots x_n$ = a given response value, and
$\bar{x}$ = average response value.

6.1.3.1 When validating with a non-homogeneous sample matrix, like a test soil, precision must be evaluated first with the reference protein to establish the capability of the instrumentation, and then again with the test soils used within the method. This comparison of a homogenous protein to a complex protein matrix used in test soils validates the use of the specified reference protein within the assay. Precision should be evaluated by both intermediate precision (that is, system suitability measurement of a minimum of three concentrations with three replicates each) and robustness (that is, interlaboratory trial). Precision is achieved when the RSD value is ≤15 % for the average response determinations.

7. Analytes and Detection/Quantification Methods

7.1 *General Considerations:*

7.1.1 Accurate measurement of analyte concentration is critical in reprocessing validations. This section covers the assay methods that are most frequently employed in cleaning validations. There is no one method that is considered as the best for a particular analyte. Each method has its advantages and disadvantages. The decision on selecting the appropriate assay or test method is mostly based on the compatibility of the

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

[6] The boldface numbers in parentheses refer to a list of references at the end of this standard.