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Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices[1]

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1. Scope

1.1 This guide provides information for developing accelerated aging protocols to rapidly determine the effects, if any, due to the passage of time on the sterile integrity of the sterile barrier system (SBS), as defined in ANSI/AAMI/ISO 11607–1:2006 and the physical properties of their component packaging materials.

1.2 Information obtained using this guide may be used to support expiration date claims for medical device sterile barrier systems.

1.3 The accelerated aging guideline addresses the sterile barrier systems in whole with or without devices. The sterile barrier system material and device interaction compatibility that may be required for new product development or the resulting evaluation is not addressed in this guide.

1.4 Real-time aging protocols are not addressed in this guide; however, it is essential that real-time aging studies be performed to confirm the accelerated aging test results using the same methods of evaluation.

1.5 Methods used for sterile barrier system validation, which include the machine process, the effects of the sterilization process, environmental challenge, distribution, handling, and shipping events, are beyond the scope of this guide.

1.6 This guide does not address environmental challenging that stimulates extreme climactic conditions that may exist in the shipping and handling environment. Refer to Practice D4332 for standard conditions that may be used to challenge the sterile barrier system to realistic extremes in temperature and humidity conditions. See Terminology F1327 for a definition of "environmental challenging."

1.7 *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 and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D4332 Practice for Conditioning Containers, Packages, or Packaging Components for Testing

E337 Test Method for Measuring Humidity with a Psychrometer (the Measurement of Wet- and Dry-Bulb Temperatures)

F17 Terminology Relating to Flexible Barrier Packaging

F1327 Terminology Relating to Barrier Materials for Medical Packaging[3]

F2097 Guide for Design and Evaluation of Primary Flexible Packaging for Medical Products

2.2 *AAMI Standards:*

ANSI/AAMI/ISO 11607–1: 2006, Packaging for Terminally Sterilized Medical Devices[4]

AAMI TIR 22–2007, Guidance for ANSI/AAMI/ISO 11607, Packaging for Terminally Sterilized Medical Devices[4]

3. Terminology

3.1 *Definitions*—For general definitions of packaging for medical devices, see ANSI/AAMI/ISO 11607. For terminology related to barrier materials for medical packaging see Terminology F17.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *accelerated aging (AA), n*—storage of samples at an elevated temperature (T_{AA}) in order to simulate real time aging in a reduced amount of time.

3.2.2 *accelerated aging factor (AAF), n*—an estimated or calculated ratio of the time to achieve the same level of physical property change as a sterile barrier system stored at real time (*RT*) conditions.

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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] Withdrawn. The last approved version of this historical standard is referenced on www.astm.org.

[4] Available from the American National Standards Institute, 25 W. 43rd St., 4th Floor, New York, NY 10036.

3.2.3 *accelerated aging temperature (T_{AA})*, *n*—the elevated temperature at which the aging study is conducted, and it may be based on the estimated storage temperature, estimated usage temperature, or both.

3.2.4 *accelerated aging time (AAT)*, *n*—the length of time the accelerated aging is conducted.

3.2.5 *ambient temperature (T_{RT})*, *n*—storage temperature for real-time aging (*RT*) samples that represents storage conditions.

3.2.6 *sterile barrier system shelf life*, *n*—the amount of real time that a sterile barrier system can be expected to remain in storage at ambient conditions, or under specified conditions of storage, and maintain its critical performance properties.

3.2.7 *real-time aging (RT)*, *n*—storage time of samples at ambient conditions.

3.2.8 *real-time equivalent (RTE)*, *n*—amount of real-time aging to which given accelerated aging conditions are estimated to be equivalent.

3.2.9 *zero time (t_0)*, *n*—the beginning of an aging study.

3.3 *Symbols:*

Q_{10} = an aging factor for 10°C increase or decrease in temperature.
T_m = temperature at which a material melts.
T_g = glass transition temperature.
T_α = alpha temperature; heat distortion temperature.

4. Significance and Use

4.1 The loss of sterile barrier system integrity may occur as a result of physical properties of the materials and adhesive or cohesive bonds degrading over time and by subsequent dynamic events during shipping and handling.

4.2 ISO 11607–1:2006, clause 6, states that "the packaging system shall provide physical protection and maintain integrity of the sterile barrier system. The sterile barrier system shall maintain sterility to the point of use or until the expiry date. Stability testing shall demonstrate that the sterile barrier system maintains integrity over time. Stability testing using accelerated aging protocols shall be regarded as sufficient evidence for claimed expiry date until data from real time aging studies are available."

4.3 Real time aging programs provide the best data to ensure that sterile barrier system materials and sterile barrier system integrity do not degrade over time. However, due to market conditions in which products become obsolete in a short time, and the need to get new products to market in the shortest possible time, real time aging studies do not meet this objective. Accelerated aging studies can provide an alternative means. To ensure that accelerated aging studies do truly represent real time effects, real time aging studies must be conducted in parallel to accelerated studies. Real time studies must be carried out to the claimed shelf life of the product and be performed to their completion.

4.4 Conservative accelerated aging factors (AAFs) must be used if little is known about the sterile barrier system material being evaluated. More aggressive AAFs may be used with documented evidence to show a correlation between real time and accelerated aging.

4.5 When conducting accelerated aging programs for establishing expiry dating claims, it must be recognized that the data obtained from the study is based on conditions that simulate the effects of aging on the materials. The resulting creation of an expiration date or shelf life is based on the use of a conservative estimate of the aging factor (for example, Q_{10}) and is tentative until the results of real time aging studies are completed on the sterile barrier system.

NOTE 1—Determining AAFs are beyond the scope of this guide.

5. Apparatus

5.1 *Room (or Cabinet)* of such size that samples may be individually exposed to circulating air at the temperature and relative humidity chosen.

5.1.1 *Control Apparatus*, capable of maintaining the room at the required atmospheric conditions within the tolerance limits.

5.2 *Hygrometer*—The instrument used to indicate the relative humidity should be accurate to ±2 % relative humidity. A psychrometer may be used either for direct measurement of relative humidity or for checking the hygrometer (see Test Method E337).

5.3 *Thermometer*—Any temperature-measuring device may be used provided it can accurately indicate the temperature to within 0.1°C or 0.2°F and be properly recorded. The dry-bulb thermometer of the psychrometer may be used either for direct measurement or for checking the temperature-indicating device.

6. Accelerated Aging Theory

6.1 Accelerated aging of materials refers to the accelerated variation of their properties over time, the properties of interest being those related to safety and function of the material or sterile barrier system.

6.2 In an aging study, the material or sterile barrier system is subjected to an external stress, which is more severe, or more frequently applied than the normal environmental stress, for a relatively short period of time.

6.3 Accelerated aging techniques are based on the assumption that the chemical reactions involved in the deterioration of materials follow the Arrhenius reaction rate function. This function states that a 10°C increase or decrease in temperature of a homogeneous process results in, approximately, a two times or ½-time change in the rate of a chemical reaction (Q_{10})[5].

6.4 Determining the Q_{10} involves testing materials at various temperatures and defining the differences in reaction rate for a 10° change in temperature. Modeling the kinetics of material deterioration is complex and difficult and is beyond the scope of this guide.[6]

6.5 A humidity factor to calculate the accelerated aging time (AAT) is not applicable for accelerated aging protocols. Unrealistic or extreme temperature and humidity conditions may be

[5] Hemmerich, K. J., "General Aging Theory and Simplified Protocol for Accelerated Aging of Medical Devices," *Medical Plastics and Biomaterials*, July/August 1998, pp. 16–23.

[6] Nelson, W., "Accelerated Testing Statistical Models, Test Plans, and Data Analyses," John Wiley and Sons, New York, 1999.

of interest in overall sterile barrier system performance. However, this must be evaluated in a separate study and is not related to aging of the materials. See Appendix X3 for more details on the use of humidity in accelerated aging protocols.

7. Accelerated Aging Plan

7.1 *Characterization of Materials*—AA theory and its application are directly related to packaging material composition. Material properties that may affect the results of accelerated aging studies include:

7.1.1 Composition,

7.1.2 Morphology (glassy, amorphous, semi-crystalline, highly crystalline, % crystallinity, and so forth),

7.1.3 Thermal transitions (T_m, T_g, T_α), as defined in 3.3,

7.1.4 Additives, processing agents, catalysts, lubricants, residual solvents, corrosive gases, and fillers.

7.2 *Accelerated Aging Plan-Design Guidelines*:

7.2.1 Temperature boundaries, based on the characterization of the device and sterile barrier system materials, must be considered in order to ensure that initial, conservative aging factors are applied appropriately. The temperatures used should be based on the characterization of the packaging materials and the intended storage conditions. Material characterization and composition are factors in establishing the accelerated aging temperature boundaries. Temperature selection should be limited to prevent any physical transition of material.

7.2.2 *Room or Ambient Temperature (T_{RT})*—Select a temperature that represents the actual product storage and use conditions.

NOTE 2—This temperature is typically between 20 to 25°C. A temperature of 25°C is considered a conservative approach.

7.2.3 *Accelerated Aging Temperature (T_{AA})*—Considering the characterization of the materials under investigation, select a temperature for the accelerated aging testing. The higher the accelerated temperature, the greater the AAF and, thus, the shorter the accelerated aging time. Care must be taken not to elevate aging temperatures solely for the shortest possible accelerated aging time. Excessively high temperatures may have an effect on the material that may never occur during real time or at room temperature (see Appendix X1). Guidelines for selecting an aging temperature are as follows:

7.2.3.1 T_{AA} should be below any material transitions or below where the sterile barrier system distorts. Consider the thermal transitions of the materials under investigation. (For more information on this topic, see AAMI TIR 22–2007.)

7.2.3.2 Keep T_{AA} at or below 60°C unless a higher temperature has been demonstrated to be appropriate. Temperatures higher than 60°C are not recommended due to the higher probability in many polymeric systems to experience nonlinear changes, such as percent crystallinity, formation of free radicals, and peroxide degradation. (For more information on this topic, see AAMI TIR 22–2007.)

NOTE 3—If sterile barrier systems containing liquid or other volatile components are tested, lower temperatures may be required for safety reasons.

NOTE 4—Tolerances of ±2°C for the test temperature and ±5 % for the humidity are acceptable. Since the shelf life of the finished sterile barrier system is based on a conservative aging factor (Q_{10}) of 2.0 for the accelerated aging protocol, any long term deviation in the temperature less than the specified temperature in the protocol can be compensated for by increasing the total test duration time without invalidating the intent of the aging protocol.

NOTE 5—Where excursions in the test temperature occur over a long period of time, an assessment on the temperature effects to the packaging materials and/or the test duration adjustments required to achieve the desired estimate of shelf life must be determined.

7.2.3.3 When elevated temperature aging is not feasible due to material characteristics, then real-time aging is the only option.

7.3 *Accelerated Aging Factor (AAF) Determination*:

7.3.1 Using the Arrhenius equation with Q_{10} equal to 2 is a common and conservative means of calculating an aging factor.

NOTE 6—A more aggressive reaction rate coefficient, for example, Q_{10}= 2.2 to 2.5, may be used if the system under investigation is sufficiently well characterized in the literature. The level and nature of damage must be similar to that reported in the literature to ensure that the reaction rate coefficient and accelerated aging temperature are maintained within appropriate boundaries. This is the responsibility of the manufacturer. For more information on this topic see AAMI TIR 22–2007.

7.3.2 An accelerated aging factor (AAF) estimate is calculated by the following equation:

$$AAF \equiv Q_{10}^{[(T_{AA} - T_{RT})/10]} \tag{1}$$

where:

T_{AA} ≡ accelerated aging temperature (°C), and

T_{RT} ≡ ambient temperature (°C).

7.3.3 The accelerated aging time (AAT) needed to establish equivalence to real time aging is determined by dividing the desired (or required) shelf life by the AAF.

$$\text{Accelerated Aging Time (AAT)} \equiv \text{Desired (RT)/AAF} \tag{2}$$

NOTE 7—See Appendix X1 for a graphical representation of the time versus temperature. Also, see Appendix X2 for a sample test plan with examples of the calculations using Eq 1 and 2.

7.3.4 When little information is known about the sterile barrier system under investigation, the guidance above is provided for selecting and verifying an appropriately conservative aging factor for the specific scenario. Risk to the manufacturer may be large since the method may predict an unduly short shelf-life; however, consideration must be given to maximizing patient safety since the necessary information to obtain a more accurate and aggressive shelf-life prediction is not readily available.

7.4 *Accelerated Aging Protocol Steps*:

7.4.1 Select the Q_{10} value.

7.4.2 Define the desired shelf life of the sterile barrier system, such as, marketing needs, product needs, and so forth.

7.4.3 Define aging test time intervals, including time zero.

7.4.4 Define test conditions, room temperature (T_{RT}), and accelerated aging temperature (T_{AA}).

7.4.5 Decide if humidity conditions will be used in the aging study. If used, define the relative humidity (RH) conditions and allowable tolerances to be utilized around a targeted value. (See Appendix X3 and chart in Perry's Chemical Engineering Handbook for realistic absolute humidity conditions.)

7.4.6 Calculate the test duration using the Q_{10}, T_{RT}, and T_{AA}.