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

This standard is issued under the fixed designation F1980; 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 information for developing accelerated aging protocols to model the possible effects of the passage of time on the sterile integrity of the sterile barrier system (SBS), as defined in ANSI/AAMI/ISO 11607–1: 2019 and the physical properties of their component packaging materials. Guidance for developing accelerated aging protocols may also be used for medical devices and medical device materials.

1.2 Information obtained using this guide may be regarded as sufficient evidence for expiration date claims for medical devices and sterile barrier systems until data from real-time aging studies are available.

1.3 The accelerated aging guideline addresses sterile barrier systems as a 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. Real-time aging (stability) is the requirement of ANSI/AAMI/ISO 11607–1: 2019.

1.5 Methods used for sterile barrier system performance validation, which include, environmental challenge, distribution, handling, and shipping events, are used for package performance (event-related loss of integrity) testing and are beyond the scope of this guide.

1.6 This guide does not address environmental challenging that simulates 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 F17 for a definition of "environmental challenging."

1.7 The data obtained from accelerated aging studies is not to be used as a manner of establishing label storage conditions for sterile barrier systems.

1.8 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.9 *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.*

1.10 *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]

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 Primary Barrier Packaging

F2097 Guide for Design and Evaluation of Primary Flexible

[1] This guide is under the jurisdiction of ASTM Committee F02 on Primary Barrier Packaging and is the direct responsibility of Subcommittee F02.50 on Package Design and Development.

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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.

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2.2 *Other Standards:*

ANSI/AAMI/ISO 11607–1: 2019 Packaging for Terminally Sterilized Medical Devices[3]

ASHRAE 170-2017 Ventilation of Health Care Facilities[4]

ISO TS 16775:2014 Packaging for terminally sterilized medical devices — Guidance on the application of ISO 11607-1 and ISO 11607-2[5]

3. Terminology

3.1 *Definitions*—For general definitions of packaging for medical devices, see ANSI/AAMI/ISO 11607–1: 2019. 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.

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 is typical for storage conditions. Also, the temperature used to calculate the accelerated aging duration.

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 or by subsequent dynamic events during shipping and handling, or both. Accelerated and real time aging verifies the time-related aspects of potential integrity loss only.

4.2 ANSI/AAMI/ISO 11607–1: 2019, sub-clause 6.1.3, states that "the packaging system shall provide physical protection in order to maintain integrity of the sterile barrier system." Sub-clause 6.1.6 states that, "A terminally sterilized sterile barrier system with its protective packaging, if included, shall be designed to, maintain sterility through exposure to expected conditions and hazards during the specified processing, storage, handling, and distribution until that SBS is opened at the point of use or until the expiry date." Sub-clause 8.3.1 states, "Stability testing shall demonstrate that the sterile barrier system maintains integrity over time." Sub-clause 8.3.3 states, "Stability testing, using accelerated aging protocols, shall be regarded as sufficient evidence for claimed expiry dates 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/medical device materials and sterile barrier system/medical device integrity do not degrade over time. However, due to market conditions in which products may become obsolete in a short time, and the desire 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 of screening for possible aging-related failure mechanisms in the SBS or medical device. To ensure that accelerated aging studies 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 (that is, 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.[6]

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

[4] Available from American Society of Heating, Refrigerating, and Air-Conditioning Engineers, Inc. (ASHRAE), 1791 Tullie Circle, NE, Atlanta, GA 30329, http://www.ashrae.org.

[5] Available from International Organization for Standardization (ISO), ISO Central Secretariat, Chemin de Blandonnet 8, CP 401, 1214 Vernier, Geneva, Switzerland, https://www.iso.org.

[6] Thor, P., "Humidity as Use Condition for Accelerated Aging of Polymers" *MDDI Online*, 2021.

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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. See 7.4.1 for sample configuration guidance.

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 Aging of materials refers to the study of variation of their properties over time, generally due to various degradation mechanisms (for example, thermo-oxidative or hydrolytic) inherent in the materials. For the purposes of this guide, the properties of interest are those related to the safety and function of the material or sterile barrier system.

6.2 In an accelerated aging study, the material or sterile barrier system is subjected to conditions which accelerate the reaction kinetics of possible degradation pathways.

6.3 Accelerated aging techniques are based on the empirical guidance that chemical reactions (including those involved in the deterioration of materials) follow the Arrhenius reaction rate function, and assume little or no change in reactant concentration(s). This function states that, in general, a 10°C increase in temperature of a homogeneous process results in a two-fold increase in the rate of a chemical reaction (Q_{10}).[7]

6.4 Determining the Q_{10} involves testing materials at various temperatures and defining the differences in reaction rate for a 10°C change in temperature. Modeling the kinetics of material deterioration is complex and difficult and is beyond the scope of this guide.[8]

6.5 Since sterile barrier systems and medical device are stored in environments that comprise varying levels of ambient humidity, and since the properties of some materials may depend on the level of absorbed moisture (for example, polyamides absorb moisture from the environment and may have degradation pathways involving moisture, while polyolefins do not), it is important to consider not only the accelerated aging temperature conditions but also the ambient relative humidly during that accelerated aging. See Appendix X3 for more details on the use of humidity in accelerated aging protocols.

NOTE 2—Degradation mechanisms for most flexible packaging materials used as sterile barrier systems do not involve moisture. However, materials used in medical devices are far more varied, and hydrolytic degradation may be a factor in some of those materials. Knowledge of the materials used in either the SBS or the device, and their relevant degradation mechanisms, is important in the proper design of an accelerated aging protocol.

6.6 It is important to consider that humidity will be part of the long-term storage use condition. Controlling humidity during accelerated aging is intended to compensate for low relative humidity at intentionally elevated temperatures, necessary to accelerate the effect of time. The goal of controlling humidity during accelerated aging is to avoid drying out materials (primarily polymers) to moisture levels lower than typical in the long-term storage use condition. Dry accelerated aging conditions may cause the user of this practice to miss moisture driven degradation that can occur on the shelf in long-term storage. Appropriate control of relative humidity during accelerated aging ensures that potential moisture driven degradation mechanisms will be caught during accelerated aging for moisture sensitive materials. The same relative humidity considerations are not necessary when the temperature is not artificially elevated (for example, real-time aging). Control of relative humidity outside the scope of this standard is left to the discretion of the user.

7. Accelerated Aging Plan

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

7.1.1 Composition (including laminating adhesives, primers, and coatings),

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,

7.1.5 Moisture absorption characteristics, and

7.1.6 Known degradation mechanisms (for example, hydrolysis, metal ion oxidation (MIO), photo-degradation, environmental stress cracking (ESC), corrosion, oxidation). This can be accomplished by reviewing published literature/research.

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] 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.

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

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7.2.2 *Room or Ambient Temperature (T_{RT})*—Select a temperature that represents the product storage and use conditions. Selecting a higher temperature for$_{TRT}$ will yield a longer, more conservative accelerated aging duration and can be useful for creating accelerated aging data that verifies compatibility with a range of storage temperature conditions. For products labeled with a specific long-term storage temperature range, aligning the$_{TRT}$ used for the calculation of the AA duration with the upper limit of the range is recommended.

NOTE 3—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 aging 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 are likely to 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 (excluding those that occur below ambient conditions) or below where the sterile barrier system distorts. Consider the thermal transitions of the materials under investigation. (For more information on this topic, see ISO TS 16775:2014.)

7.2.3.2 Keep T_{AA} at or below 60°C (for example 50°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 ISO TS 16775:2014.)

NOTE 4—If sterile barrier systems containing liquid or other volatile components are tested, lower temperatures are generally required for safety reasons.

NOTE 5—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 6—Where excursions in the test temperature occur over a long period of time, an assessment on the temperature effects to the packaging materials or the test duration adjustments required to achieve the desired estimate of shelf life, or both, 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 7—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 medical device manufacturer. For more information on this topic see ISO TS 16775:2014.

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

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

where:

T_{AA} = accelerated aging temperature (°C), and
T_{RT} = representative ambient temperature (°C).

NOTE 8—As an example, if the ambient storage condition is selected as T_{RT} = 25°C, and accelerated aging temperature as T_{AA} = 50°C, then the accelerated aging factor is AAF = 5.657.

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.

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

NOTE 9—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.

NOTE 10—To continue the example in Note 8, using the above AAF = 5.657, and a desired shelf life of 5 years (or 5 × 365.25 = 1826.25 days) then the accelerated aging time would be 323 days.

7.4 *Accelerated Aging Protocol Steps:*

7.4.1 *Sample Configuration*—The configuration of the test samples should be defined. The requirements apply to the sterile barrier system, however, the sample configuration may include protective packaging as well.

7.4.2 Select the Q_{10} value.

7.4.3 Define the desired shelf life of the sterile barrier system.

7.4.4 Define aging test time intervals, including time zero.

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

7.4.6 Define the humidity conditions in the aging study. If controlled, define the relative humidity (RH) conditions and allowable tolerances to be utilized around a targeted value. Care should be used to ensure appropriate relative humidity levels are selected in order to avoid unnatural material changes. (See Appendix X3.) If relative humidity will not be controlled, the rationale for exclusion should be documented.

7.4.7 Calculate the accelerated aging duration using the Q_{10}, T_{RT}, and T_{AA}.

7.4.8 Define the sterile barrier system or material properties, or both, to be evaluated in the study (such as, seal strength and integrity tests), sample sizes, and acceptance criteria.

7.4.9 Age samples at T_{AA}. In parallel, age samples at real-life aging conditions (T_{RT}). Actual real time aging temperature conditions may differ from the temperature used for T_{RT} in the calculation of the AA duration. For products labeled with a specific long-term storage temperature range, aligning the T_{RT} used for the calculation of the AA duration with the upper limit of the range is recommended.

7.4.10 Evaluate the sterile barrier system after accelerated aging to the predetermined sterile barrier system specification requirements (for example, package seal strength and package integrity).

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7.4.11 Evaluate the sterile barrier system after real time aging against the predetermined sterile barrier system specification requirements. The initial AAF method is a simple and conservative technique for estimating the long-term effects on the materials and seals, however, like all accelerated aging techniques, it must be confirmed by real time aging data.

8. Post-Aging Testing Guidance

8.1 Sterile barrier systems that have been subjected to aging (for example, accelerated and real time) are evaluated for both physical properties and integrity.

8.2 Tests selected for evaluation should challenge the material or package functionality that is most critical or most likely to fail as a result of aging.

8.3 Sterile barrier systems that have been subjected to aging without devices should be evaluated for any degradation of strength properties and the ability to maintain integrity both in the individual materials of the system and any seals or closures. Refer to Guide F2097 for test method guidance and selection.

8.4 Aging or stability testing and performance testing are separate entities. Performance testing evaluates the interaction between the packaging system and the products in response to the stresses imposed by the manufacturing, sterilization processes, and the handling, storage, and shipping environment. Aging of a specific sterile barrier system is independent of the physical configuration or contents; the materials and seals are expected to age the same regardless of their physical configuration or contents as long as the processing of that sterile barrier system is the same, that is, sterilized to the same processes.

NOTE 11—New sealing parameters and equipment do not require a new aging study since the short time exposure of the sealing process does not age the material.

8.5 If known package failure or performance limits, such as seal strength, puncture, or impact resistance, and so forth, have been documented and meet the requirements for the intended packaging system, then physical testing data should be sufficient.

8.6 Package performance testing may be performed on packaging systems after or before aging to evaluate the performance of the aged packaging system during simulated distribution, handling, and storage as well as to gather evidence of the device components aging characteristics. If material response to aging is not well understood, this approach is recommended. Combining aging and performance testing is not required by ANSI/AAMI/ISO 11607–1: 2019. If this is an objective, all aging samples will include the devices, or simulated devices, and all the packaging materials that make up the packaging system.

8.7 Acceptance criteria are established prior to any aging testing (accelerated and real-time). Several different methods of evaluation may be used. One is to use the zero-time performance data as a comparison to final performance data at the end of the shelf life test; another is to trend the data over all periods of evaluation; use only the final period test results. The establishment of those criteria are beyond the scope of this guidance document.

9. Report

9.1 *Accelerated Aging:*

9.1.1 A written test protocol specifying the accelerated aging conditions (test temperature, humidity, cycle, ambient temperature), time frame, sample sizes, sterile barrier system description, time intervals of sampling, and specific tests at each time interval must be developed prior to testing.

9.1.2 Document the temperature and relative humidity of the chamber used and the calibrated instruments used for measuring and monitoring the aging conditions.

9.1.3 Document the test standard references and methods used for the sterile barrier system evaluation.

9.1.4 List the equipment used for physical and microbial testing, including the calibration dates.

9.1.5 Document the post-aging test results, including any statistical methods used to determine whether the sterile barrier system meets the performance specification criteria.

10. Keywords

10.1 accelerated aging; Arrhenius reaction rate; Q_{10}; shelf-life

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APPENDIXES

(Nonmandatory Information)

X1. ACCELERATED AGING OF POLYMERS

X1.1 Accelerated aging (Fig. X1.1) equivalent to one year of room-temperature aging when the sterile barrier system is heat-aged at a selected temperature (°C).