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Standard Guide for

Accelerated Aging of Sterile Barrier Systems for Medical Device [1]

指令: F1980– 07

医疗器械无菌屏障系统加速老化标准指南

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 (e) indicates an editorial change since the last revision or reapproval.

此标准依据固定的指令F1980而发行；指令后的数字表明最初采用的年份或，修订状态，最后修订的年份。插入语后的数字表明最后复核的年份。标在单词右上角的希腊字母(e)表明最后修订或复核时做的更改。

1. Scope 范围

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/ISO11607-1:2006 and the physical properties of their component packaging materials.

此指南为发展中的加速老化方案提供信息以便快速测定其有效性，并且， 适用于ANSI/AAMI/ISO11607-1:2006中定义的无菌屏障系统及其组成成分的物理性质的时间影响。

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

此指南提供的信息可用于支持医疗器械无菌屏障系统的有效期声明。

1.3 The accelerated aging guideline addresses the 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.

加速老化指南指导全部的无菌屏障系统或除设备外的系统。此指南不指导新产品开发或结果评估需要的无菌屏障系统原料和设计的相互作用及其兼容性。

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.

此指南不包括实时老化方案；不过，执行实时老化研究是基本的，用以确定加速老化测试结果使用相同的评估方法。

1.5 Methods used for sterile barrier system process 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.

无菌屏障系统程序验证方法，包括机器制造过程，灭菌过程，环境要求，销售，处理和运输，都在此指南范围内。

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 "environment challenging."

本指南不指导可能存在于运输和环境处理中的挑战性环境激发的极端气候条件。参考D4332标准的实践条件，可以被用来以现有的温度和湿度的极端条件挑战无菌屏障系统。见术语F1327“挑战性环境”的定义。

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.*

此标准没有声称含有所有涉及到的安全性，如需要，可以结合其他标准共同使用。在使用此标准之前，进行适当的安全和健康实践及确定规章的限期适用性，是标准使用者的责任。

2. Referenced Documents 参考文件

2.1 *ASTM Standards:*[2] *美国材料试验协会标准*

D 4332 Practice for Conditioning Containers, Packages, or Packaging Components for Testing 试验用调节容器、包装件或包装元件的标准操作规程

E 337 Test Method for Measuring Humidity with a Psychrometer (The Measurement of

Wet- and Dry-Bulb Temperatures

用干湿球湿度计测定湿度的标准试验方法(湿球和干球温度的测量)

F 17 Terminology Relating to Flexible Barrier Packaging

弹性阻隔包装的相关术语

F 1327 Terminology Relating to Barrier Materials for Medical Packaging

医疗包装用阻隔材料的相关术语

F 2097 Guide for Design and Evaluation of Primary Packaging for Medical Products

医疗产品初步包装的设计和评价指南

2.2 *AAMI Standards:医疗器械促进学会标准*

ANSI/AAMI/ISO 11607-1:2006, Packaging for Terminally Sterilized Medical Devices[3]

终端无菌医疗器械的包装ANSI/AAMI/ISO 11607-1:2006

AAMI TIR 22-2007,Guidance for ANSI/AAMI/ISO11607,Packaging for Terminally Sterilized Medical Devices[3]

终端无菌医疗器械包装ANSI/AAMI/ISO11607的指南

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

此指南隶属ASTM委员会F02弹性阻隔包装和小组委员会 F02.50包装的设计和开发

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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.

查阅ASTM标准，访问ASTM网站www.astm.org，或联系ASTM客服service@astm.org.

ASTM标准量年度资讯，请参阅ASTM网站上标准的文件摘要页

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

来源于美国国家标准局，纽约，25 W. 43rd街., 4th 楼, 邮编 10036

3. Terminology 术语

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 F 17.

3.1 定义—关于医疗器械包装的一般定义见ANSI/AAMI/ISO 11607。关于医疗包装的阻隔材料术语见术语F17。

3.2 *Definitions of Terms Specific to This Standard: 本标准特殊术语的定义：*

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.

加速老化（AA）, n— 为了模拟实时老化时间将样品储存在高温(T_{AA})中以减少老化时间总量。

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.

加速老化因数(AAF), n—估算或计算达到相同水平即存储在实时条件下无菌屏障系统改变物理性能的时间，所需时间的比率。

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.

加速老化温度(TAA), n—进行老化试验时的高温，可能以估计的存储温度、使用温度为基础，或者是两者。

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

加速老化时间(AAT), n—进行加速老化试验所需的时间。

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

环境温度(TRT), n—实时老化(RT)样品的储存温度表示贮存条件。

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.

无菌屏障系统的货架寿命，n—无菌屏障系统的实时性可以被预料，通过保持在常规条件或特殊条件下存储达到，并且维持它的关键性能特性。

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

实时老化(RT), n—样品在周围环境的储存时间。

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

实时等量(RTE),n—给定的加速老化条件的即时老化时间被估计是相等的。

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

零点时间(t_0), n—老化试验开始时间

3.3 *Symbols:*　*符号*

Q_{10} = an aging factor for 10°C increase or decrease in temperature.

Q_{10}= 温度增加或减少10°C的一个老化因数。

T_m = temperature at which a material melts.

Tm= 材料软化温度。

T_g = glass transition temperature.

T_g = 玻璃转化温度。

T_α = alpha temperature; heat distortion temperature.

T_α = 阿尔法温度; 热畸变温度。

4. Significance and Use 重要性及使用

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.

无菌屏障系统完整性的失败可能是由于材料物理性能和粘合性或粘合剂降解随时间或后来的运输及处理过程中的动态事件产生的。

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 maintain 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."

ISO 11607-1：2006，第6条规定"包装系统将提供物理防护和维持无菌屏障系统的完整性。无菌屏障系统应维持使用的无菌性或有效期内的无菌性。做稳定性实验证明无菌屏障系统随时间变化的完整性。稳定性实验使用加速老化协议中的规定，应被认为是规定有效期的充分证据，直到实时老化的数据可以使用为止。

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.

实时老化程序提供最佳的数据以确保无菌屏障系统材料和无菌屏障系统的完整性不随时间而降解。但是，由于在市场条件下产品短时间内就变得过时，所以需要在尽可能短的时间内推出新产品占领市场，实时老化研究不符合这个宗旨。加速老化研究可以提供一个可选择的方法。以确保加速老化研究真实的反映实时的效果，实时老化研究必须和加速研究一起进行。实时研究必须符合产品的使用寿命要求并执行要求到完成。

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.

如果对被评估的无菌屏障系统材料所知甚少，必须使用保守的加速老化因数(AAFs)。比较积极的 AAFs 可和证明性文件一起使用来表示实时和加速老化之间的相关性。

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,Q10) and is tentative until the results of real time aging studies are completed on the sterile barrier system.

为确定产品有效期，因此建立加速老化程序，基于模拟材料老化的影响条件从实验中获得的数据必须经过验证。实验结果得出了产品的有效期或货架期，所得期限是建立在对老化因素（例如，Q10）保守估计基础上，直到无菌屏障系统的实时老化研究完成前，该期限均具有假设性。

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

注意1—测定AAFs不在此指南范围内。

5. Apparatus 仪器

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

室(或柜)这种尺寸的样品在适宜的温度和相对湿度下可单独的暴露在流通的空气中。

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

控制仪器，能保持房间必需的大气条件在公差极限内

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 E 337).

湿度计—此仪器经常用于表明相对湿度应该是准确的±2 % 相对湿度。 干湿计可用来直接测量相对湿度或校验湿度计(参见测试方法E 337) 。

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.

温度计—任何一种温度测量设备都能准确地表明温度在0.1°C或0.2°F之内并准确的记录。干湿球温度表的干球温度计可用于直接测量或校验温度指示装置。

6. Accelerated Aging Theory 加速老化理论

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.

材料的加速老化指加速它们性能随时间的变化，性能的影响存在于那些涉及到安全性和材料功能性或无菌屏障系统中。

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.

在老化研究中，材料或无菌屏障系统将在一个相对短的时期内承受更强列的外应力/外界压力或更加频繁地外界正应力/正常压力。

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 1⁄2-time change in the rate of a chemical reaction (Q_{10})[4].

加速老化技术以假设材料变质的化学反应遵循阿列纽斯反应速率定律为基础。此定律规定，均一性的过程中温度约增加或减少10°C时，化学反应率 (Q_{10})[5]呈二倍或1/2倍改变.

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.[5]

确定Q_{10}在不同的温度中测试材料，并定义在温度变化10°时反应速率的差数。 模拟材料变质动力学是复杂和困难的，不在此指南范围内[5]。

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 of interest in overall sterile barrier system performance. However, this must be evaluated in 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.

计算加速老化时间（AAT）的湿度因素不适合加速老化方案。不切实际或极端的温度和湿度条件可能对全面的无菌屏障系统性能存在影响。然而，这种影响需要在单独的实验中评估，并且不涉及到材料的老化。更多信息见附件X3加速老化方案中湿度的使用。

7. Accelerated Aging Plan 加速老化方案

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:

材料的特性—AA理论及其应用直接和包装材料的构成有关。可能影响加速老化实验

结果的材料特性包括:

7.1.1 Composition, 构成,

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

形态(玻璃状, 无定形, 半晶质的, 高度结晶[性],结晶度%, 等等。)

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

在3.3中定义的热量转换(T_m, T_g, T_α)

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

添加剂, 炮制剂, 催化剂, 润滑剂, 残留溶剂和填充物。

7.2 *Accelerated Aging Plan-Design Guidelines*: **加速老化方案设计指南:**

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.

温度界限, 必须考虑装置和无菌屏障系统材料的特性, 以保证原始的保守的老化因数被适当的应用。根据包装材料的特性和预期的储存条件来设定使用温度。材料的特性及其组成成分是设定加速老化温度界限的主要因素。温度选择应该被限定防止任一材料发生物理变化。

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

室或环境温度(TRT)—选择能体现实际产品存贮和使用条件的温度。

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

注意2—此温度应在20-25°C之间。温度25°C是广泛接受的。

[4] Hemmerich, Karl J., "General Aging Theory and Simplified Protocol for Accelerated Aging of Medical Devices," *Medical Plastics and Biomaterials*, July/August 1998, pp.

16–23.

[4] Hemmerich, 卡尔J., “一般老化理论和医疗器械加速老化简化草案，”《医用塑料和生物材料》, 1998年7月/8月 16-23页。

[5] Nelson, Wayne, “Accelerated Testing Statistical Models, Test Plans, and Data Analyses,” John Wiley and Sons, New York, 1999.

[5]纳尔逊, 韦恩, "加速试验法统计模式, 试验方案及数据分析,"约翰威里及其儿子, 纽约, 1999 年。

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:

加速老化温度(T_{AA})—依据调查考虑材料的特性, 选择加速老化测试的适宜温度。加速的温度越高, AAF值就越大, 因而, 加速老化所用的时间越短。注意不要单独在最短的可能的加速老化时间内提高老化温度。过高的温度可能导致材料产生在实时期间或在室温下从未发生的效应(参见附录X1)。 选择老化温度的指导方针如下:

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.)

T_{AA}值应该低于引起任何材料转化或无菌屏障系统变形的温度，考虑研究中材料的热转化。(关于这个主题的更多信息, 参见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.)

保持T_{AA}等于或低于60°C除非更高的温度被证明是适当的。温度高于60°C不被推荐，因为在高于60°C时会导致在多种聚合物体系之间发生非线性变化的几率升高，譬如结晶百分比, 自由基的形成和过氧化物的降解。(关于这个主题的更多信息, 参见AAMI TIR 22-2007。)

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

注意3—如果无菌屏障系统含有液体或其他的挥发性成分，基于安全原因可能需要低温。

NOTE 4—Tolerances of ±2℃ 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 invalidation the intent of the aging protocol.

注意4—测试温度±2℃的差异和湿度±5%差异是可以接受的。由于成品无菌屏障系统的货架期是基于加速老化方案2.0中保守的老化因素（Q10），任何低于方案中规定的在温度上长时期的背离可以通过增加总的测试持续时间来补偿，以使老化方案的目的没有失效。

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.

注意5—测试温度偏移出现很长时间后，包装材料温度影响的评估和/或要求的测试持续时间的调整，须达到预期的货架有效期的评估，这些必须被确定。

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

由于材料自身特性而不能进行高温老化时，那么实时老化是唯一的选择。

7.3 *Accelerated Aging Factor (AAF) Determination*: 加速老化因数的测定

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

使用阿列纽斯方程式，使Q10等于2是计算老化因数的普遍和保守方法。

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.

注意6—更加活泼的反应速率因数，如, Q10 = 2.2 到2.5，可以被使用，如果研究资料证明可以取上述Q10值（2.2-2.5）损害的级别和性质必须和资料中报道的相似，以确保反应速率因数和加速老化的温度被维持在适当的边界范围内。这是制造商的责任。

关于这个主题的更多信息参见AAMI TIR 22-2007。

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

加速老化因素(AAF) 可由下列等式估算出:

$$AAF = Q_{10}^{[(TAA - TRT)/10]} \quad (1)$$

where:

T_{AA}=accelerated aging temperature (°C), and 加速老化温度

T_{RT} =ambient temperature (°C). 环境温度

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.

加速老化时间(AAT) 应该等于实时老化预期（或要求）的保存期限除以加速老化因素。

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

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.

注意7—参见附录X1时间温度对应图。同样地，参见附录X2样品测试计划中使用Eq 1和2计算示例

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.

当通过调查获得少量的无菌屏障系统信息时，上述指南为具体方案的适宜保守老化因数提供选择和验证。制造商冒的风险是很大的，因为此方法可能过短预计保存期限。*然而，必须给与极大的耐心因为获得预测更精确和更活泼的保存期限的必要信息不是轻易可使用的。*

7.4 *Accelerated Aging Protocol Steps*:加速老化方案步骤

7.4.1 Select the Q_{10} value. 选取Q_{10} 的值

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

定义无菌屏障系统的预期使用寿命，譬如，营销需要，产品需要，等等。

7.4.3 Define aging test time intervals, including time zero.

定义老化测试间隔时间，包括零点时间。

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

定义试验条件，室温(T_{RT})，及加速老化温度(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.)

确定湿度条件是否将被应用于老化实验。如果应用，定义相对湿度条件（RH）和目标值周围可利用的容许公差。（见附录X3和佩里的化学工程手册中现实的绝对湿度条件图表）

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

运用Q_{10}，T_{RT}和T_{AA}计算试验持续时间。

7.4.7 Define sterile barrier system material properties, seal strength and integrity tests, sample sizes, and acceptance criteria.

定义无菌屏障系统材料性能，密封度和完整性试验，样品规格及验收标准。

7.4.8 Age samples at T_{AA}. In parallel, age samples at real-life aging conditions (T_{RT}).

在T_{AA}下取老化样品。两种方法同时使用时，在实时老化条件下取样 (T_{RT}) 。

7.4.9 Evaluate the sterile barrier system performance after accelerated aging relative to the initial sterile barrier system requirements, for example, package seal strength, package integrity.

对照原始无菌屏障系统要求评估加速老化后无菌屏障系统的性能例如，包装密封度，包装完整性。

7.4.10 Evaluate the sterile barrier system, after real time aging relative to their initial design requirements. The initial AAF method is a simple and conservative technique for

evaluating the long-term affects on the materials and seals, however, like all accelerated aging techniques, it must be confirmed by real time aging data.

对照原始设计要求评估实时老化后无菌屏障系统。初始的AAF方法是评估原料和密封性的长期影响的一个简单和保守的技术; 然而, 和所有加速老化技术一样, 它必须由实时老化数据证实。

8. Post-Aging Testing Guidance 加速老化试验指南

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

已进行老化（例如，加速老化和实时老化）的无菌屏障系统，评估其物理性能及完整性。

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.

用于评估的选择试验应针对包装和材料的特性，选择最有挑战性的试验。

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 F 2097 for test method guidance and selection.

除设备外已进行老化的无菌屏障系统，对于任何强度特性的降低和维护完整性的能力都应该被评估，无论是系统的个别材料还是任何密封或关闭。参考指南F2097测试方法选择和指南。

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.

老化或稳定性测试和性能测试是单独的实体。性能测试评估包装系统和产品适应制造业的影响压力，灭菌过程，操作，存储和运输环境之间的相互作用。无菌屏障系统老化的细节不依赖于物理结构或内容；只要无菌屏障系统的过程相同，不论它们的物理结构或内容，材料和密封性同样达到预期的老化，也就是说，以相同的过程灭菌。

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.

如果已知包装失败或性能限制，例如已记录在案的密封强度，穿透性或耐冲击性等等，符合有关包装系统的要求。那么物理测试数据应该足够了。

8.6 On occasion, package performance testing may be performed on packaging systems after 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 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.

有时，关于包装系统的包装性能测试在老化后可能被执行，用于评估老化的包装系统的模拟分布，操作和存储，以及收集设备组分老化性能的证据。如果以此为目的，所有的老化样品必须包括设备或模拟设备，和补充包装系统的所有包装材料。

8.7 Acceptance criteria Are established prior to any aging testing. 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.

在进行任何老化测试前必须建立验收标准。可以应用几个不同的评价方法。其中一个方法是在使用寿命试验结束时，用最终包装性能数据和零点时间性能数据相比较；另一个是评估的所有阶段的趋势数据；只使用最后阶段的测试结果。

9. Report 报告编制

9.1 *Accelerated Aging*: 加速老化

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.

在试验进行前必须有一份书面试验规程详细说明加速老化条件 (试验温度、湿度、周期、环境温度), 时间表, 样本规格, 无菌屏障系统描述, 取样间隔时间, 和每次间隔时间的试验细节。

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.

提供使用的室内温度、相对湿度和已校对的仪器监视和测量老化条件。

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

提供试验标准的参考书目和无菌屏障系统评价方法。

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

列出物理和微生物试验使用的设备及其校准日期。

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.

提供后期老化试验结果，包括，用于测定无菌屏障系统是否符合性能技术标准的所有统计方法。

10. Keywords 关键词

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

加速老化；阿列纽斯反应速率；Q_{10}；货架期

F1980-07

APPENDIXES 附录

(Nonmandatory Information) 强制性信息

X1. ACCELERATED AGING OF POLYMERS 聚合物加速老化

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 (℃).

加速老化（图表X1.1）当包装在选择的温度（℃）加热老化时的常温老化使用寿命等值为一年

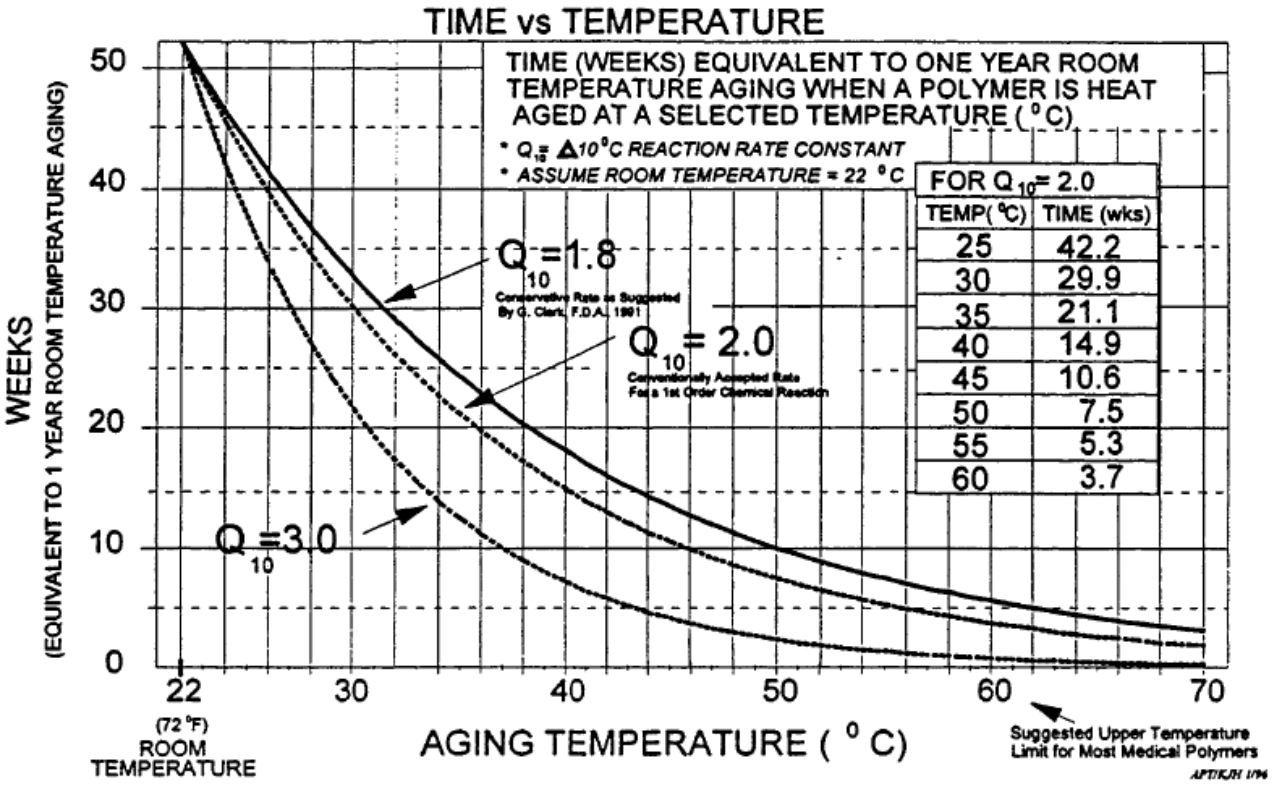

FIG. X1.1 Accelerated Aging of Polymers[5]

X2. EXAMPLE STERILE BARRIER SYSTEM SHELF-LIFE TEST PLAN

无菌屏障系统使用寿命试验计划实例

X2.1 Select a conservative AAF estimate, for example, $Q_{10} = 2$. (See Fig. X1.1.)

选择一个保守的AAF 估计值, 例如，Q10 = 2。(参见图表X1.1.)

X2.2 Define aging time points corresponding to the desired shelf life, for example, two points, such as 2-year and 3-year.

定义老化时间点对应预期使用寿命 / 存储期限, 例如, 二点, 譬如2 年和3 年。

NOTE X2.1—Trending often is helpful when characterizing the aging effects on material and sterile barrier system properties. The number of accelerated aged time points, minimally, is one. The one mandatory time point is at the time equivalent to the desired shelf-life (desired shelf-life divided by aging factor); however, the practice of using only one accelerated time point leaves the risk of failure without prior warning from an earlier accelerated aged time point. At least three time points should be considered when trending.

注意X2.1 —当描述材料和无菌屏障系统性能的老化作用时，趋势是非常有用的。加速老化时间点的数量, 最低限度是一个。这一个必须的时间点等于预期的使用寿命 / 贮藏期限 (老化因素除以预期使用寿命 / 贮藏期限); 但是, 只使用一个加速时间点试验时，不能在初期加速老化时间点预先示警远离风险。 趋向至少需要考虑三个时间点。

X2.3 Build test samples in accordance with a validated production process.

选取试验用样品应符合已验证的生产工序。

NOTE X2.2—Sterile barrier systems used for zero-time, sterilization, and accelerated aging may be produced without actual or simulated product.

注意X2.2 –零点时间使用的无菌屏障系统, 灭菌, 及加速老化可能产生没有实际或被模拟的产品。

X2.4 Sterilize sterile barrier systems using validated sterilization process. The sterilization process may affect the stability of the materials or sterile barrier systems. Materials and sterile barrier systems should be exposed to the maximum process conditions, or number of cycles intended to be used prior to the aging study, or both.

无菌屏障系统灭菌使用已验证的灭菌程序。灭菌过程可能影响材料或无菌屏障系统的稳定性。 材料和无菌屏障系统应该受最大程序条件控制, 或预期的周期数量在老化研究前，或两者。

X2.5 Condition the samples according to Practice D 4332

控制样品根据实践D 4332。

NOTE X2.3—Sterile barrier systems performance testing may be performed as a part of

the aging protocol to determine the long-term effects of distribution, handling, and storage when devices are included in the protective package. Whether performed before aging or after aging will depend on whether the study is to simulate storage on the hospital shelf or on the manufacturer's shelf and then shipped. There may be instances, however, when performance testing may not be necessary. If known sterile barrier systems failure or performance limits, such as seal strength, puncture, or impact resistance, and so forth, have been documented adequately and met for the specific intended product, then physical testing data should be sufficient.

注意X2.3—当设备包括在保护性包装中，无菌屏障系统性能试验可以作为老化草案的一部分执行以测定销售，处理和存贮的长期效果。在老化前或后执行取决于试验是模拟医院存储环境进行或模拟制造商存储环境进行然后运输。仅是建议，性能测试不是必须做的。如果已经知道无菌屏障系统失效或性能限度,如密封度，穿刺力，或冲击阻力等等，关于特殊预期产品已有充分和适宜的证明文件，那么，物理实验数据应该是充足的。

X2.6 Initiate real-time and accelerated aging. Use the defined accelerated aging temperature for the appropriate period of time. The time duration for samples to be placed in the elevated temperature oven can be calculated from Eq 1 and 2 in 7.3.2 and 7.3.3, where AAF is the accelerated aging factor and AAT is the accelerated aging time.

For example, where Q_{10} = 2; ambient temperature = 23°C; test temperature = 55°C;

$AAF = 2.0^{(55-23)/10}$;

$AAF = 2.0^{3.2} = 9.19$;

AAT = 365 days/9.19; and

AAT = 39.7 days = at accelerated aging conditions fror a shelf life of 12 months (real-time equivalent).

开始实时和加速老化。在适当的时期使用被定义的加速老化温度。样品被安置在高温烤箱中的持续时间可以由7.3.2 和7.3.3种的方程式1 和2计算得出，AAF是加速老化因数，AAT是加速老化时间。

例如，当Q_{10} = 2；环境温度= 23°C；试验温度= 55°C

$AAF = 2.0^{(55-23)/10}$;

$AAF = 2.0^{3.2} = 9.19$;

AAT = 365 天/9.19；和

AAT = 39.7 天= 12个月货架期的加速老化条件 (实时等值) 。

NOTE X2.4— Humidity effects can be evaluated as part of the package system design performance qualification testing. See Appendix X3 for more guidance on the use of humidity in aging protocols.

注意 X2.4—湿度影响可作为评估包装系统设计性能条件测试的一部分。见附录 X3 在老化测试中使用湿度的更多指南

X2.7 Evaluate sterile barrier system performance after accelerated aging relative to the sterile barrier system requirements.

对照无菌屏障系统要求评估无菌屏障系统加速老化后的性能。

X2.7.1 If the accelerated aging results meet the acceptance criteria, then the product's shelf-life conditionally is validated depending upon the results of the real-time aging study.

如果加速老化结果符合验收标准，那么产品的贮藏期限/使用寿命条件依据实时老化研究的结果被验证。

X2.7.2 If the accelerated aging results fail to meet the acceptance criteria, then either investigate the production process, redesign the failed medical device or sterile barrier system, attempt to validate a shorter shelf-life, or wait for real time aging results. The shelf-life is validated if real time aging results are acceptable. In this scenario, the accelerated aging program is more rigorous than reality.

如果加速老化结果不符合验收标准，那么调查生产过程，重新设计未通过的医疗器械或无菌屏障系统，尝试验证更短的贮藏期限，或等待实时老化结果。如果实时老化结果确认贮藏期限是可接受的，在这种情况下，加速老化程序应比实际更严谨。

X2.8 Evaluate sterile barrier system performance after real-time aging relative to the sterile barrier system requirements.

评估无菌屏障系统性能在实时老化以后相对于无菌屏障系统的要求。

X2.8.1 If the real-time aging results meet the acceptance criteria, then the sterile barrier system's shelf-life is validated.

如果实时老化结果符合验收标准，那么无菌屏障系统的使用寿命/贮藏期限就是经过验证的。

X2.8.2 If the real-time aging results fail to meet the acceptance criteria, the shelf-life must be reduced to the longest shelf life for which real time testing has been successful. If product has been released to the market at risk based on the accelerated aging data, a careful review must be performed and documented, and the appropriate action taken.

如果实时老化结果不符合验收标准，货架期必须减少至实时老化测试成功的最长的有效期。如果放行到市场上的产品基于加速老化数据存在风险，必须进行细致的评审并备有证明文件，而且应采取适当的措施。

X3. USING RELATIVE HUMIDITY IN AGING PROTOCOLS 老化方案中相对湿度的使用

X3.1 Aging damage for many materials may be exacerbated in the presence of high relative humidity levels. Care should be exercised in using humidity levels, that when combined with temperature produce moisture levels that may not be realistic in nature and may cause unnatural physical changes to materials,(for example ,delamination of water based laminates and coextrusions).

许多材料的老化可能加剧当前的相对湿度水平高度。使用时湿度水平需要特别注意，当与温度结合产生潮湿水平，这种潮湿水平可能不符合实际，也可能导致材料不自然的物理变化（例如，被碾压和混合挤压的水分分层）。

TABLE X3.1 Relationship of Relative Humidity to Constant Moisture Content and Variable Temperature

Elevated Temperature (°C)	Relative Humidity (%)	Water Content (ppm)
23	50.0	13 750
40	19.1	13 750
50	11.4	13 750
55	9.0	13 750
60	7.1	13 750

X3.2 If humidity will be a component of the accelerated aging test then:

如果湿度是加速老化测试的一个部分，那么：

X3.2.1 the relative humidity that is chosen should be equivalent to the moisture content, or

选择的相对湿度应该等同于水分含量，或

X3.2.2 the absolute humidity should be maintained between the test temperature and realistic environments for the sterile barrier system life cycle.

对于无菌屏障系统的寿命周期，应该维持测试温度和实际环境的绝对湿度。

Note X3.1—Table X3.1 provides some examples of the relationship of relative humidity to a constant moisture content and variable temperature.

表格 X3.1 提供了不变的水分含量和可变的温度与相对湿度之间关系的一些例子

Note X3.2—Psychometric calculators are available on the internet for calculating equivalent water vapor at various temperature and relative humidities.

心理测量计算在计算网络上的使用相当于水汽在不同的温度和相对湿度下的使用。

X3.3 Fig. X3.1 can be used to determine the equivalent moisture content in air at various temperatures and relative humidity values.

图 3.1 可以用来确定在不同温度和相对湿度值下空气中相当的水分含量。

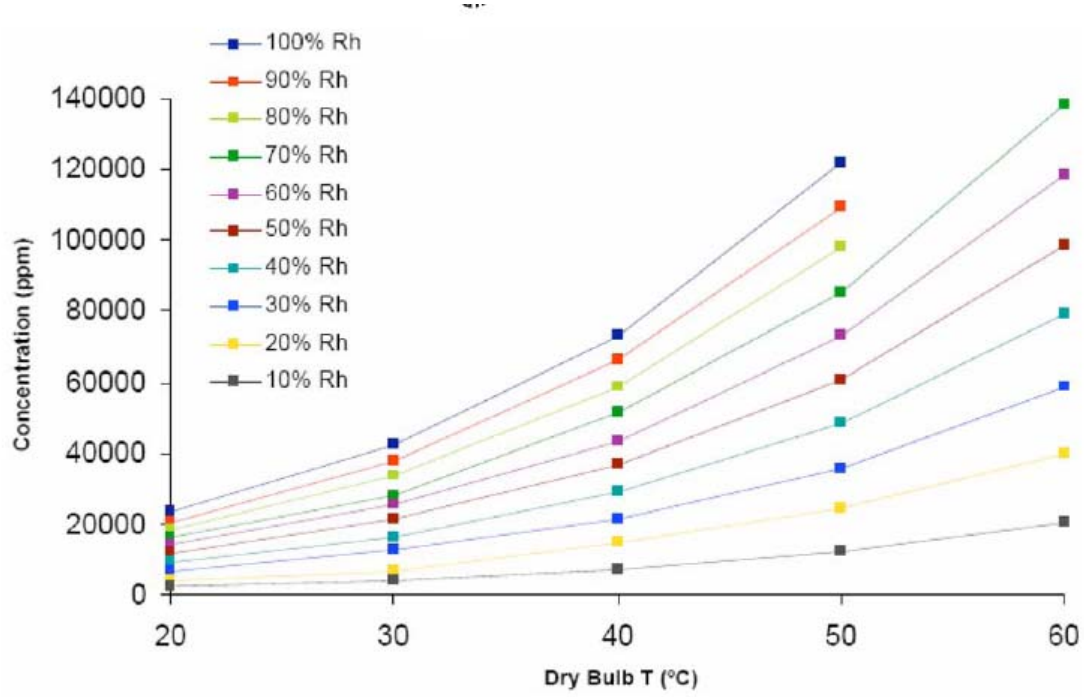

FIG. X3.1 Concentration of Water in Air as a Function of Temperature and Relative Humidity