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Standard Guide for

Accelerated Aging of Sterile Medical Device Packages [1]

指令: F1980– 02

无菌医疗设备包装加速老化标准指南

This standard is issued under the fixed designation; 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 and environmental effects on the sterile integrity of packages and the physical properties of their component packaging materials.

1.1 此指南为发展中的加速老化试验提供信息以便快速测定其有效性,若有的话, 适用于完全灭菌的包装材料及其组成成分的物理性质的时间和环境的影响。

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

1.2 此指南提供的信息可用于支持医疗器械包装的有效期声明。

1.3 The accelerated aging guideline addresses the primary medical package in whole and does not address the package and product interaction or compatibility that may be required for new product development. Package and product compatibility and interactions should be addressed as a material analysis process before package design.

1.3 加速老化指南指导初步的医疗全包装不指导新产品开发需要的包装和产品相互作用及其兼容性。包装和产品相互作用及其兼容性应该在包装设计前的材料分析程

序中指明。

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.

此指南不包括即时老化试验；但是，它是必要的，进行即时老化研究证明加速老化试验结果运用同样的评估方法。

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

包装程序验证方法，包括机器制造过程，灭菌过程，销售，处理和运输，都在此指南范围内。

1.6 *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: 美国材料试验协会标准*

D 3078 Test Method for Determination of Leaks in Flexible Packaging by Bubble Emission[2]

起泡法测定软包装泄漏的标准试验方法

D 4169 Practice for Performance Testing of Shipping Containers and Systems[2]

运输集装箱和设备性能试验的标准实施规范

D 4332 Practice for Conditioning Containers, Packages, or Packaging Components for Testing[2] 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[3]

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 88 Test Method for Seal Strength of Flexible Barrier Materials[2]

弹性阻挡材料密封强度的试验方法

F 1140 Test Methods for Failure Resistance of Unrestrained and Nonrigid Packages for Medical Applications[2]

医疗设备用可伸缩包装箱抗内部增压损坏性的标准试验方法

F 1327 Terminology Relating to Barrier Materials for Medical Packaging[2]

医疗包装用阻隔材料的相关术语

F 1585 Guide for Integrity Testing of Porous Barrier Medical Packages[2]

医用多孔性隔板包装盒完整性试验的标准导则

F 1608 Test Method for Microbial Ranking of Porous Packaging Materials (Exposure Chamber Method) [2]

多孔性包装材料的微生物分等标准试验方法(开放室法)

F 1929 Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration[2]

用染色渗透液检测多孔医疗包装汽封泄漏的标准试验方法

2.2 *AAMI Standards:医疗器械促进学会标准*

ANSI/AAMI/ISO 11607, Packaging for Terminally Sterilized Medical Devices[4]

终端无菌医学设备的包装

AAMI TIR 17-1997, Radiation Sterilization—Material Qualification[4]

AAMI TIR 17-1997, 辐射灭菌—材质限制

[1] This guide is under the jurisdiction of ASTM Committee F02 on Flexible Barrier Materials and is the direct responsibility of Subcommittee F02.60 on Medical Packaging.

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[2] *Annual Book of ASTM Standards*, Vol. 15.09. ASTM年刊标准，卷15.09.

[3] *Annual Book of ASTM Standards*, Vol. 11.03. ASTM年刊标准，卷11.03.

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

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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 1327.

3.1 定义—关于医疗器械包装的一般定义见ANSI/AAMI/ISO 11607 关于绝缘材料的医疗包装术语见术语F1327。

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— 为了模拟真实老化时间将样品储存在高温(TAA)中以减少时间。

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 package 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包装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(T_{AA}), *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 *(T_{RT})*, *n*—实时老化(RT)样品的储存温度表示贮存条件。

3.2.6 *Package shelf life*, *n*—the amount of real time that a package 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.

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 package 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.

包装完整性的损失可能是由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而产生的。

4.2 The ANSI/AAMI/ISO 11607 states that, “the manufacturer shall demonstrate that, under the rigors of distribution, storage, handling, and aging, the integrity of the final package is maintained at least for the claimed shelf-life of the medical device under storage conditions specified by the manufacturer, as long as the package is undamaged or unopened.”

ANSI/AAMI/ISO 11607标准规定：“制造商应该论证，产品的最终包装在销售、贮存、处理及老化全过程，只要包裹是未损坏或未打开的，在制造商指定的储存条件其包装的完整性下至少达到医疗器械要求的贮藏期限。”

4.3 Real time aging programs provide the best data to ensure that package materials and package 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 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.

实时老化程序提供最佳的数据以确保包装材料和包装的完整性不随时间而降解。但是，由于在市场竞争条件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。

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

如果对被评估的包装材料所知甚少，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。

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 sample containers or packages may be individually exposed to circulating air at the temperature and relative humidity chosen.

室(或柜)这种尺寸的样品容器或包装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 62 % relative humidity. A psychrometer may be used either for direct measurement of relative humidity or for checking the hygrometer (see Test Method E 337).

5.2 湿度计—此仪器经常用于表明相对湿度应该是准确的62 % 相对湿度。 干湿球温度表可用来直接测量相对湿度或校验查湿度计(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. The dry-bulb thermometer of the psychrometer may be used either for direct measurement or for checking the temperature-indicating device.

5.3 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° C F 之内。 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 package.

6.1 促进加速老化材料或包装指通过调整时间来影响那些涉及到安全和功能的重要性能.

6.2 In an aging study, the material or package 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.

6.2 在老化研究中, 材料或包装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})[5].

6.3 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 products 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]

6.4 确定Q_{10}在不同的温度中测试产品,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[6].

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. Some areas for consideration are:

7.1 材料的特性-- AA 理论及其应用直接和包装材料的构成有关。 一些需考虑的地方:

7.1.1 Composition, 构成,

7.1.2 Morphology (glassy, amorphous, semi-crystalline, highly crystalline, % crystallinity, etc.),

7.1.2 形态(玻璃状, 无定形, 半晶质的, 高度结晶[性],结晶度%, 等。)

7.1.3 Thermal transitions (T_m, T_g, T_α), 热量转换(T_m, T_g, T_α)

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

7.1.4 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 package 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.

7.2.1 温度界限，必须考虑装置和包装材料的特性，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.

7.2.2 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 20–25°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。

[5] 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.

[5] 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。

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

[6] 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:

7.2.3 加速老化温度(TAA) – 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。注意不要单独提高老化温度在最短的可能的加速老化时间内。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 package distorts. Consider the thermal transitions of the materials under investigation, for example, the choice of T_{AA} should be at least 10°C less than T_g. (For more information on this topic, see AAMI TIR 17-1997.)

7.2.3.1 T_{AA}值应该低于引起任何材料转化或包装变形的温度，考虑研究中材料的热转化，如；选择的T_{AA}至少要比Tg少10°C。(关于这个主题的更多信息，参见AAMI TIR 17-1997 。)

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 17-1997.)
7.2.3.2 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 17-1997 。)

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

注意3 -- 如果包装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。

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

7.2.3.3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.

7.3.1 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 4—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-17-1997.

注意4-- 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-17-1997 。**

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

7.3.2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.

7.3.3 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。

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

See Appendix X1 for a graphical representation of the time versus temperature.

参见附录X1 时间温度对应图。

7.3.4 When little information is known about the package 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包装信息时，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安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*:加速老化草案步骤

7.4.1 Select the value. 选取Q_{10} 的值

7.4.2 Define the desired shelf life of the package, such as, marketing needs, product needs, etc.

7.4.2 定义包装的预期使用寿命，譬如，营销需要，产品需要，等。

7.4.3 Define aging test time intervals, including time zero.

7.4.3 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}).

7.4.4 定义试验条件，室温(T_{RT})，及加速老化温度(T_{AA}) 。

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

7.4.5 运用Q_{10}，T_{RT}和T_{AA}计算试验持续时间。

7.4.6 Define package material properties, seal strength and integrity tests, sample sizes, and acceptance criteria.

7.4.6 定义包装材料性能，密封度和完整性试验，样品规格及验收标准。

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

7.4.7 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}) 。

7.4.8 Evaluate the package performance after accelerated aging relative to the initial package requirements, for example, package seal strength, package integrity.

7.4.8对照原始包装要求评估加速老化后包装的性能例如，包装密封度，包装完整性。

7.4.9 Evaluate package, or package performance, or both, after real time aging relative to the initial package requirements. The estimated AAF method is a simple and conservative technique for evaluating the long-term performance of a package; however, like all accelerated aging techniques, it must be confirmed by real time aging data.

7.4.9 对照原始包装要求评估加速老化后包装，或包装性能，或评估两者。估算AAF方法是评估包装的长期性能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。

7.5 See the example package shelf-life test plan (Appendix X2).

7.5 见实例包装储存期限试验计划(附录X2) 。

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

8.1 Packages and materials that have been subjected to aging, that is, accelerated and real time， must be evaluated for physical properties and integrity.

8.1已进行加速和实时老化的包装及材料，必须评估其物理性能及完整性。

8.2 Tests selected should challenge the material or package functionality that is most critical or most likely to fail due to the stresses resulting from aging. Guide F 1585 may be used as a testing guide for porous barrier medical packaging.

选择试验时应针对包装和材料的特性，选择最有挑战性的试验（此种试验对老化以后的产品最有挑战性）。指南 F 1585 可用于医用多孔性隔板包装盒的试验指导。

8.3 Some of the physical strength properties to be considered for selection are flexure, puncture, tensile and elongation, tear, impact resistance, abrasion resistance, yellowness index, microbial barrier (Test Method F 1608), seal strength (Test Method F 88), and burst strength (Test Methods F 1140).

8.3 选择时应考虑的一些物理性能：弯曲度，穿刺力,拉力和伸张度，撕扯力，冲击阻力，磨损阻力，黄页索引，阻菌性(试验方法F 1608)，密封强度（试验方法 F 88)，和耐破度 （试验方法 F 1140）

8.4 ***Packages may be subjected to whole package integrity testing by using validated physical,*** that is, trace gas detection, dye leak (Test Method F 发1929), bubble leak (Test Method D 3078) or microbial methods (microbial challenge of whole packages). These methods must include documentation showing that the test method has been validated.

8.4***用有效的物理试验证明包装符合全包装完整性，***即染料渗透(试验方法 F 1929)，起泡泄漏(试验方法 D 3078）或微生物的方法(全包装的微生物要求）。

8.5 Acceptance criteria must be established prior to any package shelf-life testing. Zero time performance data may be used as a comparison to final package performance data at the end of the shelf life test.

8.5 在进行任何包装使用寿命试验前必须建立验收标准。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。

9. Documentation 文件编制

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, package description, time intervals of sampling packages, and specific tests at each time interval must be developed prior to testing.

9.1.1 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, 包装描述, 包装采样间隔时间, 和每次间隔时间的试验细节。9.1.2 提供分庭被使用和被校准的仪器的温度被使用为测量和监测老化条件。

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

9.1. 2 提供使用的室内温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 package evaluation.

9.1.3 提供试验标准的参考书目和包装评价方法。

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

9.1.4 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 package meets the performance specification criteria.

9.1.5 提供后期老化试验结果包括,用于测定包装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 of room-temperature aging when the package is heat-aged at a selected temperature

10.1加速老化：阿列纽斯反应速率; Q_{10}; 当包装在选择的温度(°C)加热老化时的常温老化使用寿命

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

X1.1 加速老化（图表X1.1）等值为一年

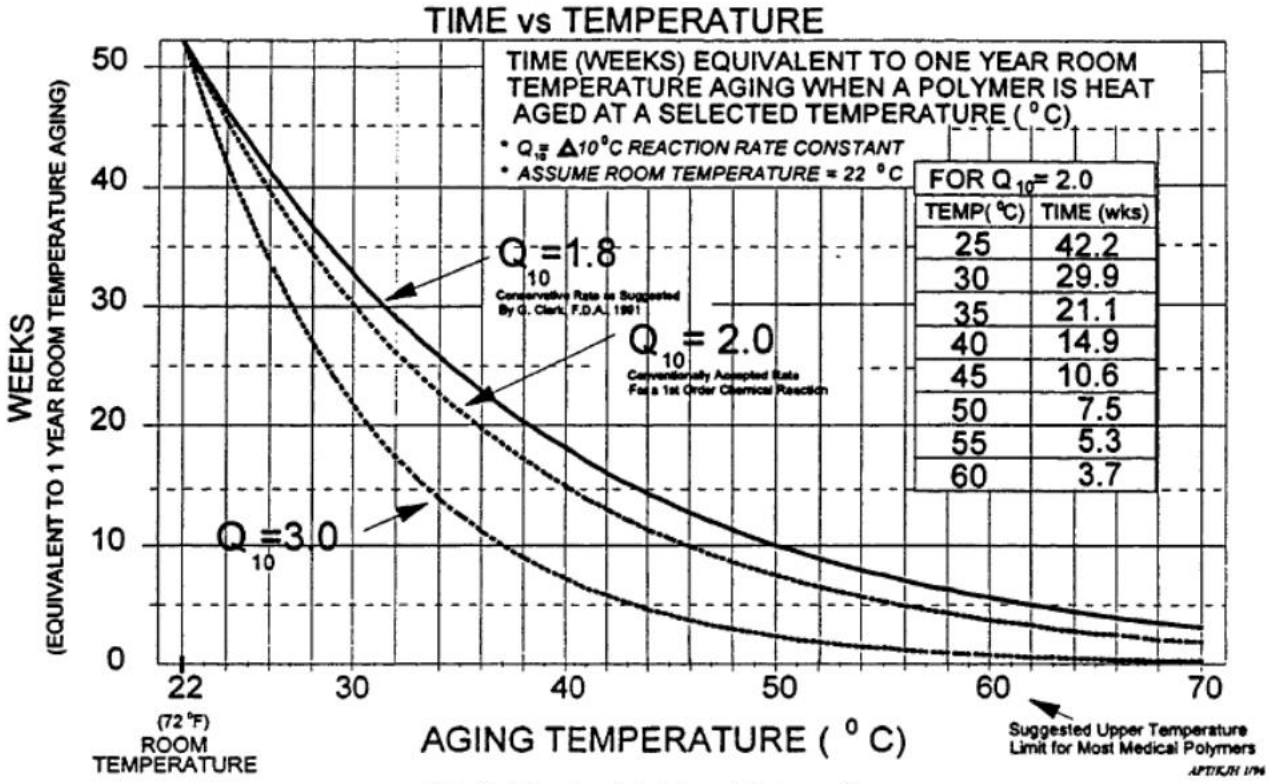


FIG. X1.1 Accelerated Aging of Polymers[5]

X2. EXAMPLE PACKAGE SHELF-LIFE TEST PLAN

包装使用寿命试验计划实例

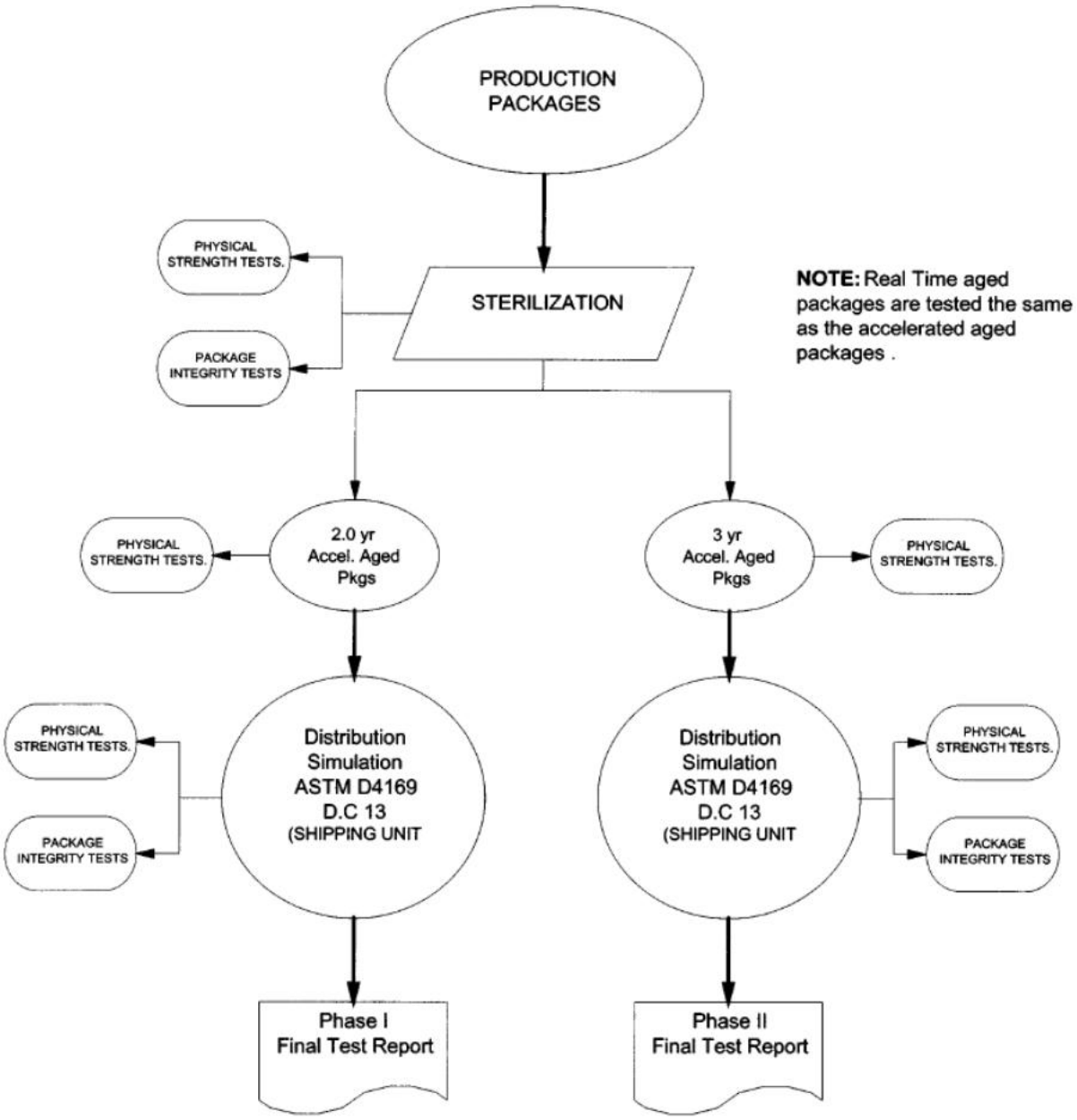
X2.1 Select a conservative AAF estimate, for example, $Q_{10} = 2$. (See Fig. X2.1.)

X2.1 选择一个保守的AAF 估计值, 例如, Q10 = 2 。 (参见图表X2.1.)

NOTE X2.1—Trending often is helpful when characterizing the aging effects on material

and package 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 – 当描绘材料和包装性能的老化作用时，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。 至少三个时间点应该被考虑当趋向。



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

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

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

X2.3 Build test samples in accordance with a validated production process. X2.3选取试验用样品应符合已验证的生产工序。

NOTE X2.3—Package performance testing normally is performed as a part of the aging protocol to determine the long-term effects of distribution, handling, and storage. 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, where this may not be necessary. If known package failure or performance limits, such as seal strength, puncture, or impact resistance, etc., have been documented adequately and met for the specific intended product, then physical testing data should be sufficient.

注意X2.3 -- 包装性能试验通常作为老化草案的一部份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，不是必须做的。如果已经知道包装失效或性能限度,如密封度，穿刺力，或冲击阻力等，关于特殊预期产品已有充分和适宜的证明文件,然后，物理实验数据应该是充足的。

2.4 Sterilize packages using validated sterilization process. The sterilization process may affect the stability of the materials or package. Materials and packages should be exposed to the maximum process conditions, or number of cycles intended to be used prior to the aging study, or both.

X2.4灭菌包装使用已验证的灭菌程序。灭菌过程可能影响材料或包装的稳定性。 材料和包装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。

NOTE X2.4—The effects of humidity may need to be considered in conjunction with temperature and incorporated into a test cycle of high and low humidity duration's. An aging cycle may be designed to account for the effects of humidity.

注意X2.4 -- 湿度的作用可能需要结合温度和测试周期持续时间内的湿度大小值一起考虑。老化周期设计应该说明湿度的影响。

X2.5 Condition the samples according to Practice D 4332, if required; perform distribution simulation according to Practice D 4169, if appropriate. Packages used for this test must contain actual product.

X2.5 控制样品根据实践D 4332, 如果需要; 进行销售模拟根据实践D 4169, 如果适当。 用于做此实验的包装内必须装有实际产品。

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 = 12 months (real-time equivalent).

X2.6 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是加速老化因数和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(实时等值) 。

X2.7 Evaluate package performance after accelerated aging relative to the package requirements.

X2.7 对照包装要求评估包装加速老化后的性能。

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.

X2.7.1 如果加速老化结果符合验收标准，那么产品的贮藏期限/使用寿命条件是被验证的依据实时老化研究的结果。

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 package, 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.

X2.7.2 如果加速老化结果不符合验收标准，那么或者调查生产过程，重新设计未通过的医疗器械或包装，尝试验证更短的贮藏期限，或等实时老化结果。贮藏期限被确认如果实时老化结果是可接受的。在这种情况下，加速老化程序应比实际更严谨。

X2.8 Evaluate package performance after real-time aging relative to the package requirements.

X2.8 评估包裹表现在实时老化以后相对包裹要求。

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

X2.8.1 如果实时老化结果符合验收标准，那么包装的使用寿命/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.

X2.8.2 如果实时老化结果不符合验收标准，贮藏期限必须减少已经成功的实时试验的最长的使用寿命/贮藏期限。如果产品已被放行发往市场根据有风险的加速老化数据,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。