Accelerated Age Testing

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Outline

- Introduction / What is Accelerated Aging?
- Scope of ASTM F1980
- Significance and Use
- Understanding Accelerated Theory & Rationale
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- Cautions Using Accelerated Aging
- The Use of Humidity
- Post Aging Guidance
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- Questions

Introduction

Simply stated…

Accelerated aging is an artificial procedure that allows you to claim expiration dating of materials by utilizing elevated temperatures.

"Shelf Life refers to the period of time a sterilized or disinfected item is safe to use."

"An Expiration Date is the termination of the shelf life."

Introduction

- Standard Guide developed within ASTM Committee F 2.60 on Medical Packaging
- Guide approved on May 10, 1999
- First published document providing guidance on performing accelerated aging of medical device packages for establishing shelf life.

Introduction

- ASTM Standard was developed to provide a guidance for compliance to ANSI/AAMI/ISO 11607-1:2006;

  Section 6.4.3

  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.

Scope of ASTM F 1980

- Provides information for developing accelerated aging protocols.
- Information may be used to support shelf life and expiration date claims.
- Real time aging protocols are not addressed in this guide.

Significance and Use

- Package components and adhesives may breakdown, become brittle, or lose bonding capabilities over time.
- Real time aging is the most valid program.
- Real time aging is not practical.
  - Requires too much time to get to market

Significance and Use

- Conservative aging factors must be used if little information is known about the packaging materials. (Q_{10} of 2)

- Use of accelerated aging protocols involves some risk.

Accelerated Aging Theory

- Materials are subjected to an external stress.
- Techniques are based on the assumption that the chemical reactions involved in deterioration of materials follow the Arrhenius reaction rate function.(Q_{10}).
- Determining Q_{10} requires modeling the kinetics of materials and is very complex and difficult.
- So…a conservative Q_{10} is used in medical device package validation.

Accelerated Aging Rational

European Community Council Directive 93/42/EEC, ANNEX 1, "Essential Requirements" states…

> *"The label must bear the following particulars... where appropriate, an indication of the date by which the device should be used, in safety, expressed as the year and month."*

Accelerated Aging Rational

ISO 11607:2006, section 6.4; *Paraphrased…*

"For medical devices with a defined shelf-life, the manufacturer shall have documented evidence that the performance of the packaging is not adversely affected by storage under specified conditions for a period not less than the shelf-life of the medical device.

This shall be demonstrated by real time aging testing.

ISO 11607:2006, section 6.4; further states…

"If accelerated aging tests are performed, a documented rationale for the accelerated aging conditions and test duration chosen shall be established.

This does not preclude the requirement to perform real-time aging tests."

DOCUMENTED RATIONALE

- The ASTM F 1980, “Standard Guide for Accelerated Aging of Sterile Medical Device Packages” provides the documented rationale for performing accelerated aging to establish shelf life.
- This ASTM ‘Standard’ is recognized by the FDA as a consensus standard.

Most package Shelf Life validation protocols are based on the ASTM Guide and…

Accelerated Aging of Packaging: Considerations, Suggestions, and Use in Expiration Date Verification

Reich, Sharpe, Anderson

MDDI, March 1988

Accelerated Aging test parameters are based on the Q_{10} thermodynamic temperature coefficient (Arrhenius Theory)

Arrhenius Reaction Rate Theory states...

"a rise in temperature of 10°C will roughly double the rate of a chemical reaction"

So...

AAR (Accelerated Aging Rate) $= Q_{10}^{((Te - Ta)/10)}$

Where... Ta = Ambient Temperature

Te = Elevated Temperature

Q_{10} = Reaction Rate = 2

And...

$AATD$ (Accelerated Aging Time Duration) =

$$\frac{\text{Desired Real Time}}{AAR}$$

FOR EXAMPLE

If the desired real time aging or expiration date of the medical device is three years, and the test temperature is chosen to be 55°C, Q_{10} is 2; the AATD is determined as follows...

AAR $(Q_{10}) = 2^{((55-22)/10)} = 9.85$

AATD = 365 days/9.85 = 37.06 days

AATD = 37.06 days/year

Total duration:

1 Year = 37.06 Days

3 Year = 37.06 x 3 = 111.18 Days (Rounded Up: 112 Days)

Accelerated Aging Equivalency Matrix

ACCELERATED AGING EQUIVALENCY TABLE

based on Q10 = 2
ambient Temp. = 22C

DEGREES C	DEGREES F	1 YEAR SHELF LIFE EQUIVALENCY (WKS)
35	95	21.1
40	104	14.9
45	113	10.6
50	122	7.5
55	131	5.3
60	140	3.8
65	149	2.7
70	158	1.9
75	167	1.4

The Use of Humidity

Section: 6.5

A humidity factor to calculate the accelerated aging (AAT) is not applicable for accelerated aging Protocols. Unrealistic or extreme temperature and Conditions may be of interest in overall sterile barrier system performance. However, this must be evaluated in a separate study and is not related to accelerated aging.

The Use of Humidity Cont.

Section: X3.1

- Aging damage for many materials may be exacerbated in the presence of high humidity.
  - Delimitation of water based laminates or coexstrusions.
- The relative humidity that is chosen should be equivalent to the moisture content or the absolute humidity extrapolated from real time aging conditions that will be utilized.

The Use of Humidity Cont.

Table X3.1:

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

The Use of Humidity Cont.

So what does DDL Recommend?

- DDL recommends the use of <20% RH for Accelerated Aging Protocols.
- Aging is a factor of time and temperature.
- Keeping the RH levels low is important to not overstress the packaging materials to a failure that is not observed in the real world.
- Further climatic stressing (Humidity) should take place in performance studies and is more realistic to what transpires in the real world.

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Temperature/Humidity Chambers for Accelerated Aging Studies

TOLERANCES AND PRECISION

Temperature and Humidity Tolerances

- Temp = +/- 2 C
- Humidity = +/-5 %
- Since this is a conservative estimate of shelf life, out of tolerance conditions on the low end for an extended period of time may be corrected with additional test time.

TOLERANCES AND PRECISION

- Out of tolerance conditions on the high end of the required test temperature for an extended period of time may jeopardize the shelf life study due to uncharacteristic damage to packaging materials and/or to actual product.

TOLERANCES AND PRECISION

- Since humidity is not essential to the aging theory, out of tolerance humidity conditions do not invalidate the shelf life study.

TOLERANCES AND PRECISION

- When conducting an accelerated aging program for establishing product and package shelf life or expiration 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.

TOLERANCES AND PRECISION

- The resulting creation of an ‘expiration date’ or shelf life represents a conservative estimate of shelf life and is ***tentative*** until the results of real time aging studies are completed on the product or product/package combination.

TOLERANCES AND PRECISION

- Since the results of the study produce a ***conservative estimate*** of the actual shelf life of the materials, tolerances for the temperature and humidity are only provided to ensure that the chamber operates within a satisfactory range. Accelerated aging is a cumulative effect. The **average** temperature and humidity would be given a higher emphasis because of the thermal lag in bringing product and chamber into equilibrium, when a short term excursion occurs. Therefore, out of tolerance excursions for less than 6 hours in duration for either temperature or humidity are acceptable and do not adversely affect the estimate for shelf life.

TOLERANCES AND PRECISION

- Out of tolerance excursions may be caused by opening doors for sample transfer; inserting moist samples into a dry environment causing spikes in humidity; proximity of monitoring device to temperature and/or humidity source inlets.

Cautions in Using Accelerated Aging Theory

Cautions in Using Accelerated Aging Theory

- Accelerated aging is truly a gift by the FDA and EU to allow MDM's to release products to market faster.
- MDM's push the limits on a daily basis by trying to increase the temperature above the cautioned 60°C to save time.
- This theory is based upon homogeneous materials.

Cautions in Using Accelerated Aging Theory

- Reaction Rates may not be a linear function at temperatures above 60°C.
  - Errors in the theory increase as temperature increases.
- Multi component materials may react at different rates.

Cautions in Using Accelerated Aging Theory

- Elevating the temperature of packaging materials could result in a mode of failure never observed in real life.
  - Melting plastic, warping, crystallization
- The glass-transition temperature of the materials could be reached, drastically altering the characteristics of the package.

Cautions in Using Accelerated Aging Theory

- Ideally, in order for the Q_{10} based accelerated aging program to be utilized, the individual reactions rates of all package components should be identified.
- Accelerated aging studies must be conducted in parallel with real time, ambient packaging studies

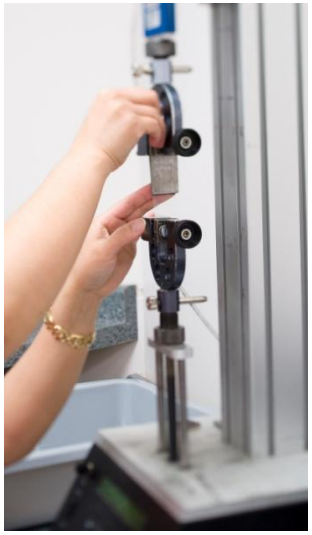
Post Aging Testing Guidance

Aging is a conditioning test and by itself does not evaluate the efficacy of the package system. Therefore…

- Packages must be evaluated for physical properties and integrity.
- Tests should challenge the most critical property.

Post Aging Testing Guidance

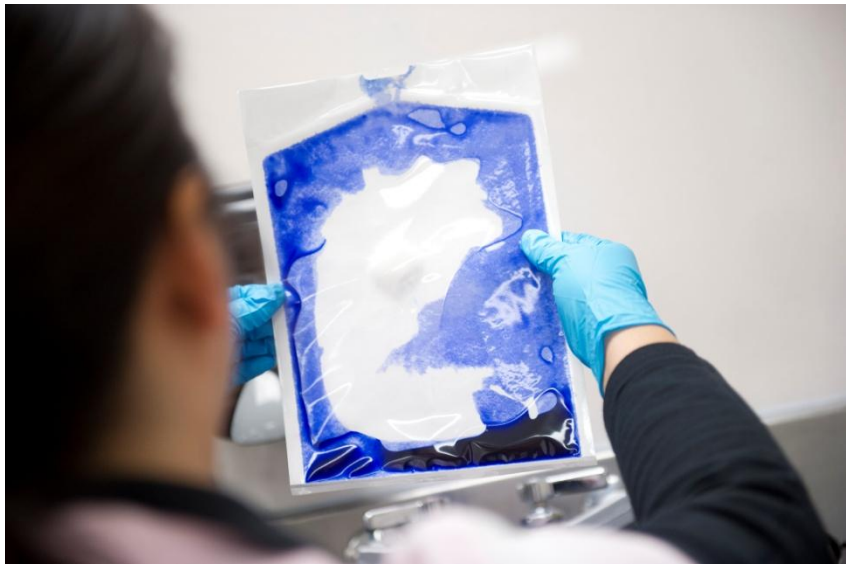
- Strength tests methods include:
  - Peel Strength
  - Burst strength



Seal Strength Testing per ASTM F88

Post Aging Testing Guidance

- Integrity test methods include; bubble leak, dye penetration



Dye Penetration Testing per ASTM F 1929

Bubble Leak Testing per ASTM F 2096

Conclusions

- Accelerated aging theory is complex even for homogeneous materials.
- These theories are all the medical device industry has to use for validating compliance with international and national requirements.
- Results of these tests will be a conservative estimate of shelf life.

Conclusions

- Provide the necessary time to complete an aging study.
- Understand ALL the materials you are utilizing (Product & Package) prior to picking an aging temperature to utilize.
- If you choose to push the aging temperature limits a solid justification above 60° will be needed.

Questions??

Please don’t hesitate to contact Scott with any questions!

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