The Role of Humidity on the Accelerated Aging of Sterilizable Medical Packaging

Understanding the role of time on the efficacy of a sterile medical device is essential for determining shelf life. Devices are generally regarded as sterile so long as package integrity has not been compromised. Using accelerated aging protocols to test package shelf life is generally accepted as valid for new product introductions, provided real time aging is in place to confirm accelerated aging test results. Use of the Arrhenius equation is generally recognized as a valid approach for defining the effect of elevated temperature on a homogeneous first order reaction rate. Phrased more simply, the easier $Q_{10}=2$ calculation developed from this equation assumes that the aging process is approximately doubled for each 10°C rise in temperature[1]. The temperature must be chosen carefully so that materials are not damaged because of conditions that would not be expected to occur in real time or are outside of the recommended range of use for that material. (Further discussion is available in ASTM F1980-02, "Standard Guide for Accelerated Aging of Sterile Medical Device Packages"). While the role of temperature is well documented and understood in this aging process, the impact of humidity is not. While the F1980 standard notes briefly "The effects of humidity may need to be considered…," it is fair to say that the impact of humidity on accelerated aging continues to need more definition.

What is the role of humidity in accelerated aging? Industry practices vary widely. One of the difficulties comes in properly understanding the amount of water suspended in the air *relativ*e to its capacity at that temperature, which defines relative humidity. The warmer the air, the greater potential amount of water load. The water load in air at 25°C at 80% RH equates to about 25,000 ppm. At 55°C, this same 25,000 ppm is less than 21% RH. If the same percent relative humidity (80%) is established at this higher temperature, the amount of water increases to more than 100,000 ppm, a condition that must be created artificially. (See the attached chart for further clarification.[2]) One major medical device manufacturer established a corporate guideline on accelerated aging recommending that a fixed absolute humidity of 27,500 ppm water be maintained, regardless of the temperature chosen for the study. This would be equivalent to over 90% at 25°C and 18% at 55°C. They further recommend that for testing conditions of environmental exposure and/or humidity sensitive materials, 37-40°C at 80% RH (~58,700 ppm water) suitably covers conditions that approximate the temperature/humidity extreme that can be encountered during a product life cycle on the planet Earth. Similarly, hot/cold cycling can be used to mimic seasonal extremes to which packaged medical devices may be subjected.

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[1] 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.

[2] Perry's Chemical Engineering Handbook, Perry, Robert H., ed., McGraw Hill: New York, NY. 1984, pp.20-5 to 20-6.

It may be more helpful to divide these different condition regimens into two categories: accelerated aging, where the effects of time on packaging and its contents are being studied, and environmental challenging, where extremes of temperature and/or humidity are simulated in order to determine the impact of difficult environments on packaging systems. Recently, two new definitions were balloted at ASTM as additions to ASTM F1327, "Terminology Relating to Barrier Materials for Medical Packaging." Clarification of these terms is also intended to be addressed within F1980 in the near future.

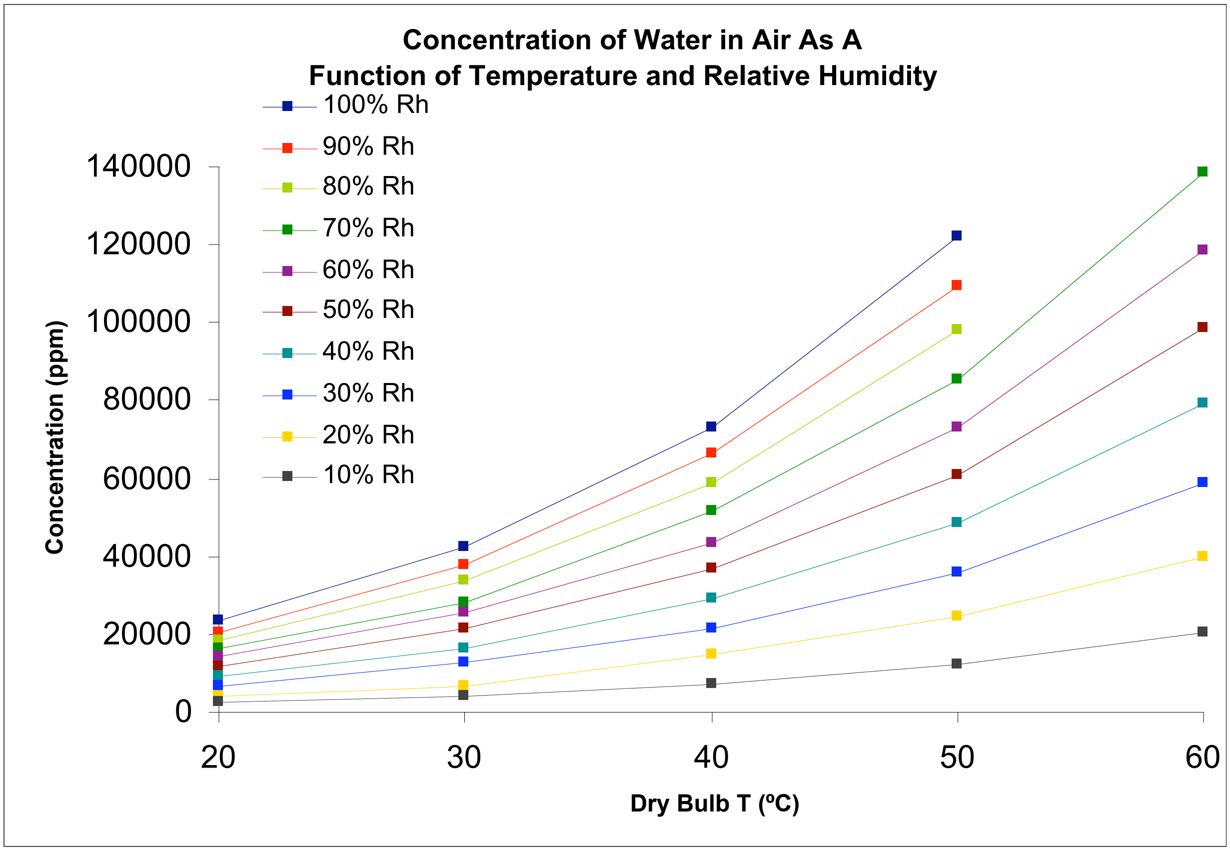
accelerated aging—a technique to simulate the effects of time on a package by subjecting the product/package system to elevated temperatures under conditions otherwise representative of controlled environment storage conditions. The equivalent time is generally estimated by assuming the degradation of packaging materials follows the kinetics described by the Arrhenius reaction rate function, more discussion of which is available in ASTM Standard Guide F1980.

environmental challenging— the process of subjecting a package to extremes of temperature and/or humidity with the goal of determining sensitivities of the package to environmental stress. In contrast to accelerated aging, environmental challenging often includes conditions and/or transitions of temperature/humidity that equal or exceed those that can be encountered in a package life cycle.

In the first case, the humidity level is chosen in accordance with avoiding damage or changes to packaging materials that would not be expected during real time aging. With environmental challenging, the aim is either to assess package performance at the extreme conditions possible in a package life cycle, or (in the case of conditions unattainable except in the laboratory environment as in the example of 55°C at 80% RH) to stress the material near or past its failure point.

This delineation is centered upon the fact that different materials have varying sensitivities to moisture, and conclusions regarding a given material's suitability as a packaging component may not be valid. Paper is particularly sensitive to relative humidity. Excessive drying negatively impacts strength properties, and excessive humidity can lead to mold growth. Some laminates commonly employed in medical packaging, which historically provide excellent protection for medical devices, may fail under extreme conditions. For example, PET extrusion coated with LDPE can be induced to delaminate during environmental challenging, though real time or controlled accelerated aging rarely or never demonstrates such a result.

Obviously, the medical device manufacturer must make the final decision regarding the suitability of a packaging material to ensure efficacy of a sterilized medical device. This FAQ is intended to serve as a guide in choosing the conditions for testing a package so that informed judgments can be made regarding the performance of packaging over time, and to separate shelf life testing from the environmental impact of temperature and humidity.



Concentration of Water in Air As A
Function of Temperature and Relative Humidity
100% Rh
90% Rh
80% Rh
70% Rh
60% Rh
50% Rh
40% Rh
30% Rh
20% Rh
10% Rh
140000
120000
100000
80000
60000
40000
20000
0
Concentration (ppm)
20
30
40
50
60
Dry Bulb T (ºC)