How to Simulate Shelf Life for Ageing Trials

A series of guides to tackling manufacturing problem areas.

Table I: The Arrhenius equation.

Arrhenius' rate equation is an equation giving the rate R of a thermally activated, physical process: $R = Ro \exp(Ea/kT)$ where Ro is a constant, Ea is the activation energy, k is Boltzmann's constant, and T is the absolute temperature.

Source: Hawley's Condensed Chemical Dictionary, 13th Edition, John Wiley and Sons Ltd, Chichester, UK

According to ISO 11607, Packaging for Terminally Sterilised Medical Devices, and United States Food and Drug Administration regulations, medical devices must be given an expiry date, which indicates how long they may be stored prior to use. It is necessary to substantiate any shelf-life claims by verifying product and package performance following ageing. Real-time ageing is the best way to do this, but no organisation can afford to delay its product launch by five years whilst waiting for the results of real-time ageing tests. A method of accelerated ageing is required that realistically recreates what a product may experience during storage.

To limit the range of conditions a product may be subject to, it is common to detail storage recommendations on the packaging and/or in the user instructions. However, it must be assumed that products will be transported by air and road and that perfect conditions cannot be maintained at all times.

The principle

Accelerated ageing is achieved by storing the product at an elevated temperature. Better still, temperature cycling is used because this more closely simulates real life and low temperatures can cause damage. The flexing caused by temperature cycling is much closer to the real stresses experienced by the product and packaging over time than storage at constant elevated temperature. In addition, the effects of humidity can be important in some instances.

The Arrhenius equation is often used to calculate the factor for increased ageing (Table I). This states that a rise in temperature of 10 °C will cause approximately a doubling of the rate of chemical reaction. It is then assumed that doubling the rate of chemical reaction doubles the rate of decay of packaging and product. The accelerated ageing factor is known as Q10. A Q10 figure of 2 is considered conservative. Higher figures may be used if they are shown to be appropriate by testing or if literature information justifies it.

Clearly, there is a limit to the temperature that can be applied to a medical product or package that is made of plastic. Accelerated ageing must be carried out below the glass transition temperature of any of the components of the system. It is generally accepted that 60 °C is the maximum temperature that is suitable for most products (ASTM F1980).

The process

A typical cycling programme would be one year of real-time ageing where Q10 is 2. This is equivalent to 23 days at 55 °C and 70% relative humidity, 3 days at −20 °C, and 23 days at 55 °C and below 20% relative humidity.

As with any scientific testing it is necessary to begin by defining what is being tested and the protocol for testing. There are two things that simulated ageing should address:

- Does the packaging maintain the sterility of the product?
- Does the product still function to specification?

There is likely also to be a marketing requirement that the presentation of the product remains unchanged.

Packaging tests

The following characteristics should be verified before and after accelerated ageing, this ageing and verification taking place after the product has been sterilised:

- Chemical characterisation signature of system components
- Seal strength of pack welds
- Puncture and abrasion resistance
- Porosity of the protective barrier
- Does the product and packaging still look good?

Product tests

The manufacturer should demonstrate that the product performs to specification following ageing. Normally, this requirement is contained within quality assurance procedures, which would have been written during product development.

Summary

Medical device manufacturers are compelled to validate the shelf-life claims of their products. If the materials used in the product and packaging can withstand elevated temperatures, accelerated ageing regimes may be used to simulate real-time ageing. If elevated temperatures are detrimental to the components involved, then real-time ageing is the only option. All testing should be carried out on sterile product when appropriate. mdt

Further reading

■ ASTM F1980 Standard Guide For Accelerated Ageing of Sterile Medical Device Packages.

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