SiO2 MATERIALS SCIENCE℠

Effect of Sterilization Processes on Zeonex 690R: Molecular Weight and Physical Properties Analysis

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ABSTRACT

The effects of sterilization processes on Zeonex 690R COP were assessed by injection molding tensile bars and subjecting them to various sterilization conditions. Steam sterilization, ethylene oxide exposure and e-beam irradiation were utilized individually and in various combinations. There was little to no change in the molecular weight (MW) of the cyclic olefin polymer (COP) caused by these sterilization conditions. The physical properties, as determined by tensile testing, were affected by some of the sterilization conditions. The properties of tensile bars subjected to steam sterilization changed more than did other sterilization modes. The molecular weight of the COP subjected to steam sterilization did not change and thus it is hypothesized that the COP underwent physical aging. The appearance of the COP bars subjected to various sterilization conditions showed no signs of hazing, micro-cracking or etching.

Introduction

Medical products are sterilized by a variety of processes. The sterilization processes commonly used for parenteral containers include steam sterilization, ethylene oxide exposure, gamma irradiation and electron beam irradiation. Glass is generally compatible with these processes and the properties of vials and syringes made from glass are not negatively affected, although glass is inherently brittle. In addition, when exposed to ionizing radiation like electron beam or gamma radiation glass can darken. This discoloration will intensify as dosage increases. This color change can be deleterious to the visual inspection of pharmaceutical dosage forms at various points in the products life cycle. Some plastics, however, can be affected by the sterilization processes, whichdepend on the type of plastic, the specific sterilization process, and the

operating conditions of that process. Medical components, such as syringes and vials can be sterilized prior to filling with a drug, after filling, or both before and after, thus potentially experiencing two (or more) sterilization steps. The steps can be totally different processes. For example, after production of a vial, the manufacturer may sterilize the product with an exposure to ethylene oxide (ETO) and ship the product as a sterile article, ready to be filled by a customer. After filling, the customer may sterilize the filled and sealed vial with steam or irradiation (e-beam/gamma).

The plan for commercial sales by SiO2 Materials Science (SiO2) is to sell and ship sterilized ready-to-use (RTU) products for customers to fill. The two most likely sterilization processes that SiO2 would use before shipment are ETO exposure and e-beam irradiation. It is expected that customers will utilize sterile filtration and/or steam sterilization for their filled products. For temperature sensitive drugs that can withstand irradiation, customers may utilize e-beam or gamma irradiation.

To assess the effects of sterilization processes and combinations of sterilization processes, an experimental plan was designed to test the change in appearance and properties of injection molded tensile bars produced from Zeonex 690R polymer resin. Since it is most likely that SiO2 will utilize either ETO or e-beam sterilization prior to shipping and customers will utilize steam sterilization on most filled products, most tensile bars that were double sterilized to include steam as the second sterilization process.

EXPERIMENTAL

A single lot of Zeonex 690R polymer resin was used for all portions of the study. The COP was injection molded into a large number of tensile bars under molding conditions that were determined to be optimum for the high heat cyclic olefin polymer.

Ethylene Oxide sterilization:

Tensile bars that were exposed to ETO were placed in gas-permeable packages. The sample packages were sent to Sterigenics, Atlanta, GA for exposure. The exposure conditions were those typical of commercial use involving preconditioning, exposure for about 14 hours at 120°F, and aeration.

E-beam sterilization:

Tensile bars exposed to e-beam (EB) irradiation were packaged similar to those exposed to ETO and sent to Synergy Health, Denver, CO. Conditions typical of commercial e-beam sterilization were utilized, exposing samples at either 25 Kgy or 35 Kgy following ISO 11137 conditions.

Steam sterilization:

Tensile bars exposed to steam sterilization were also packaged similar to those exposed to ETO and e-beam. Bars were not removed from the packages when a second sterilization was done, but simply sent to the next operation untouched. Sterilization was conducted at WuXi AppTec, Marietta, GA. Packages were exposed to steam with a target of 121°C for 20 minutes, typical of commercial steam sterilization conditions. The actual temperature was between 121-124°C.

All of the combinations of sterilization conditions listed below were tested for tensile properties and selected samples were analyzed for potential changes in polymer molecular weight (MW). The combination of sterilization conditions were as follows.

Condition #	Sterilization	Molecular Weight Evaluated?
1	None	Yes
2	Ethylene Oxide	No
3	E-Beam (25 kGray Dose)	Yes
4	E-Beam (35 kGray Dose)	Yes
5	Steam (1 Cycle)	Yes
6	Steam (2 Cycles)	Yes
7	Ethylene Oxide + Steam (1 Cycle)	Yes
8	E-Beam (25 kGray Dose) + Steam (1 Cycle)	No
9	E-Beam (35 kGray Dose) + Steam (1 Cycle)	No

PHYSICAL PROPERTY TESTING

The injection molded tensile bars; both sterilized and unsterilized were sent to Intertek Laboratories, Pittsfield, MA. Following ASTM D-638, test specimens were conditioned at 23°C/50% relative humidly for 40 hours before testing. Tensile testing was conducted at 23°C/50% relative humidity at a strain rate of 2.0 inch/minute crosshead speed. Samples were drawn to failure.

MOLECULAR WEIGHT ANALYSIS

Broken pieces of tensile bars were sent to Impact Analytical, Midland, MI for molecular weight analysis by gel permeation chromatography (GPC) using the conditions previously optimized for COP. The analysis utilized cyclohexane solvent, polyisoprene-1, 4 standards, refractive index detector and PLgel mixed-D columns operated at 50°C. A Zeonex 690R standard resin (lot 2Y51101) was also analyzed at the same time to verify reproducibility and consistency. In addition to the molded bars, the starting resin (pellets), lot 2Y50907, used to mold the bars was also analyzed for molecular weight.

RESULTS & DISCUSSION

In this set of samples, the molecular weight (MW) of the molded bar (no sterilization) was slightly higher than that measured for the starting pellets. Only slight differences in MW were observed in the sterilized samples. It can be concluded that none of the sterilization processes significantly affect the MW of Zeonex 690R. This is important because a change in the molecular weight of the polymer can be indicative of several things; 1) Original physical properties may have changed, 2) Original chemical properties may have changed, and 3) New species of chemicals may have been created through the breakdown of the original molecule. This can affect the nature of the extractables and leachables one can expect from the packaging material.

Esthetic Properties:

The samples from the 3 sterilization processes were examined for changes in appearance such as hazing, micro-cracking and yellowing. None of the processes caused any observable changes in clarity, micro-cracking or surface etching. E-beam caused a slight yellowing which increased with increased dosage.

Physical Properties:

The effect of sterilization processes on COP was assessed by determining changes in the tensile properties of injection molded tensile bars. Zeonex 690R, as molded and without sterilization, was very ductile and failed by shear yielding, followed by localized necking and then drawing to high elongation before failing.

When the test specimens that had been sterilized by the various processes were tested for tensile properties, the COP polymer was most affected by steam sterilization. Both a single steam sterilization treatment and steam sterilizing the samples twice resulted in what appears to be physical aging of the polymer. The dimensions of the bars were not affected by the steam sterilization process. This evidence highlights the need to reduce the exposure of this material to high heat conditions whenever possible. Further, drug stability studies and drop testing performed after similar terminal steam sterilization processes have not indicated any negative issues with respect to this mode of sterilization.

SUMMARY

The effect of sterilization processes on the properties, molecular weight, and appearance of test specimens molded from Zeonex 690R were determined. Sterilization has no effect on the molecular weight of the polymer. Physical properties are most affected by steam sterilization and Zeonex 690R physically ages during steam sterilization and becomes more brittle. Ethylene oxide and E-beam sterilization have minimal effect on the physical properties of articles produced with Zeonex 690R. Color changes occur during E-beam sterilization, but none of the sterilization processes caused observable surface defects, micro-cracking or hazing.