MATERIAL COMPATIBILITY WITH VAPORIZED HYDROGEN PEROXIDE (VHP®) STERILIZATION

A New Option for Point-of-Manufacture Sterilization

INTRODUCTION

Various sterilization methods (including gamma irradiation and ethylene oxide) have been widely used for terminal medical device sterilization. No single method offers the perfect sterilization solution for every application. Steam sterilization may be overly aggressive to device components or packaging materials (may form stress cracks in metal components) and cannot be used for heat-sensitive devices. Gamma irradiation or E-beam sterilization are reliable alternatives for low temperature sterilization, but are generally only performed on a contract basis at a limited number of facilities. Contract sterilization can also include the expense of transportation and storage of a product. Ethylene oxide sterilization is an alternative for integration into a manufacturing line, but cycle times are relatively long (particularly post-sterilization aeration) and toxicity/carcinogenicity issues are often a significant concern.

Figure 1 STERIS VHP® MD Series Sterilizer

A newer process is low temperature, Vaporized Hydrogen Peroxide (VHP®) point-of-manufacture sterilization. This method uses hydrogen peroxide vapor under vacuum to sterilize medical devices. In addition to rapid sporicidal activity, VHP sterilization demonstrates low toxicity, and rapidly decomposes into the non-toxic by-products of water vapor and oxygen, offering a safe and rapid alternative for point-of-manufacture sterilization.

STERIS VHP® 1000 Biodecontamination Systems have been widely used and validated in industrial applications for over 10 years. They are used for the biodecontamination of sterility testing environments, production filling lines, biosafety cabinets, rooms, and other enclosed areas.

The VHP process is a dry sterilization process (Malmorg *et al*, 2001; Krause *et al*, 2001). A single mobile or modular system generates, delivers, controls, and removes hydrogen peroxide vapor for an enclosed environment. During the sterilization phase of the cycle, the system maintains hydrogen peroxide in a dry vapor form to optimize efficacy and continually removes and replenishes vapor concentrations throughout the programmed cycle.

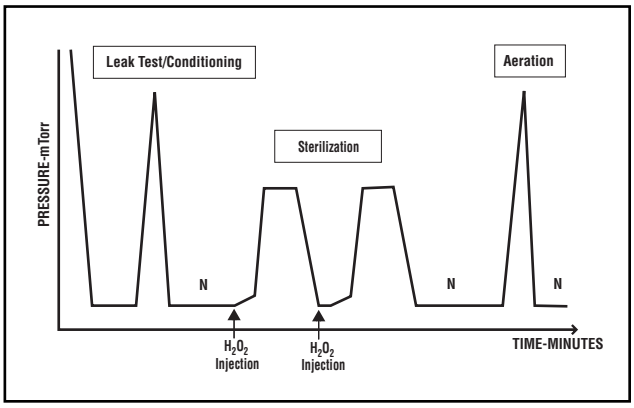
Vacuum applications have also been developed to increase the penetration of the vapor. For example, the mobile VHP® DV1000 Biodecontamination System is utilized for freeze dryer and aseptic filling lines (Klapes & Vesley, 1990; Johnson *et al*, 1992). The STERIS VHP® MD Series Sterilizers (Figure 1) are based on similar vacuum technology and allow for the terminal sterilization of both simple and complex medical devices.

A typical VHP MD sterilization cycle includes a leak test (optional), condition, sterilization, and aeration (Figure 2). The leak test holds the sterilization chamber under vacuum for a preset time and monitors the pressure to detect leaks. The condition (or drying) phase uses the vacuum system to dry the chamber/load and condition the load temperature for sterilization (generally in the range of 25 to 50°C).

The sterilization cycle involves drawing a deep vacuum, injecting and diffusing hydrogen peroxide vapor, and then bleeding dry, sterile air or nitrogen to the sterilization set point pressure (150-700 Torr). Hydrogen peroxide vapor is created by the direct vaporization of Vaprox® 35% Hydrogen Peroxide Sterilant. As in the atmospheric applications, the hydrogen peroxide concentration is kept below the saturation point to prevent condensation on the device surfaces and to maximize the antimicrobial activity and material compatibility of VHP sterilization. The actual number of sterilization pulses for each application will vary depending on device design, load size, and construction and packaging of materials.

During aeration, the vacuum system is used to rapidly remove hydrogen peroxide vapor from the chamber by a series of vacuum/air pulses. Unlike processes such as ethylene oxide sterilization, no further aeration time is required. This minimizes the overall sterilization cycle time and cost, and can improve productivity. Although the cycle time may vary depending on the application, the overall cycle time is generally two hours or less.

Figure 2 Typical VHP® MD Sterilization Cycle



Previous industrial experience has shown that hydrogen peroxide vapor is compatible with, and safe for, a wide range of materials typically used for medical devices, including metals (300 series stainless steel, aluminum, and titanium), plastics (polypropylene, polyethylene, and polycarbonate), and other materials (silicones, glass, electronics etc.). In this report, a detailed analysis of the material compatibility of the most widely used medical device materials has been investigated using a typical sterilization cycle.

MATERIALS AND METHODS

Medical device materials chosen for this study were based on a representative sample of the materials used to manufacture medical devices. A list of the materials follows (all materials were obtained from McMaster Carr; Aurora, Ohio):

Elastomers:

1/32" white FDA Buna-N vinyl rubber 70A
1/8" thick black polyurethane 80A
1/8" thick EPDM rubber sheet 60A
Silicone rubber FDA Grade 1/16" thick

Rigid Plastics:

1/8" thick white nylon 6/6 Sheet
1/8" polypropylene sheet white translucent
1/8" thick high impact polystyrene sheet
1/8" thick ultra-high molecular weight polyethylene sheet
0.118" thick cast acrylic sheet

Sterilization Cycle. All materials were exposed to a single, typical VHP MD sterilization cycle, developed at 30°C. All exposures were conducted in a 5.00 cubic foot (0.14 cubic meter) chamber. Following a successful leak test, two conditioning pulses were performed to equilibrate the chamber and its contents for temperature and humidity. This was accomplished by evacuating the chamber to 2.3 mmHg, holding the vacuum for 30 seconds, and then raising the pressure to ambient by allowing warm, dry air to fill the chamber.

The sterilization phase consisted of evacuating the chamber to 1.0 mmHg and introducing 1.0 grams of 35% hydrogen peroxide converted into vapor. The vapor introduction into the chamber causes a slight pressure rise to ~ 10 mmHg. The initial vapor concentration was 2.0 mg/l, which at the set temperature of 30°C is equivalent to 80% saturation. The vapor was held at this pressure for five minutes and then raised to 538 mmHg by introducing warm, dry air into the chamber. Chamber contents were exposed for an additional five minutes at this pressure, then the chamber was evacuated by pulling the chamber pressure back to 1 mmHg. This pulse sequence was repeated for a total of 6 injection pulses. After the sterilization phase, 6 aeration pulses were used to aerate the chamber. Each of the aeration pulses consisted of evacuating the chamber to 2.3 mmHg and holding for 30 seconds, followed by transitioning to 654 mmHg.

The total cycle time was 90 minutes, and a total weight of 6 grams of 35% hydrogen peroxide was used.

Material compatibility evaluation. All physical tests were conducted at an ASTM certified testing facility. The material was machined into test strips per the guidelines of ASTM D 638 (Standard Test Method for Tensile Properties of Plastics). All exposed materials were compared to unexposed controls. Elastomer materials were tested using the following methods: ASTM D412 standard test methods for rubber and elastomers, ASTM D2240 hardness determination, ASTM D638 tensile properties, ASTM D2457 specular gloss, ASTM D6290 color analysis. In addition, hydrogen peroxide residuals and FTIR surface analyses were conducted. Rigid plastic materials were tested using the following methods: ASTM D256 IZOD impact resistance, ASTM D638 tensile properties, ASTM D2457 specular gloss, ASTM D6290 color analysis, hydrogen peroxide residual analysis, and FTI surface analysis. FTIR analysis, using diamond ATR correction, was performed using a Nicolet Impact 410 infrared spectrophotometer.

RESULTS AND DISCUSSION

Tensile Testing. Tensile testing measured the force required to break a specimen and the extent to which the specimen stretches or elongates to that break point. The data from this testing is useful when specifying a material, to design parts to withstand application forces, and as a quality control check of materials. All rigid and flexible elastomer materials tested maintained between 92% and 113% of their original tensile strength following the VHP cycle, which was within the range observed for unexposed controls (Table 1).

IZOD Impact Resistance. Notched IZOD impact resistance is a single point test that measures a material's resistance to impact from a swinging pendulum. It is also used to determine a material's general toughness to impacts. This test can be used as a quick and easy quality control check to determine if a material meets specific impact properties. Analysis on the rigid plastics showed no significant change from before exposure data (Table 1). Of the materials tested, four of the five retained between 93%-120% of their original values.

The cast acrylic showed an increase in impact resistance after exposure of 300%. It should be noted that the acrylic had an initial impact resistance of 0.1-0.2ft-lbs/in and was increased to 0.6ft-lbs/in, which is not significant. All of the other materials had starting values in the 0.5 to 12.3 ft-lbs/in range. Impact resistance is not an important parameter for this material.

Color Analysis. Color analysis, using the Hunter scale, is the standard three-dimensional color analysis that allows precise definition of the color of a test sample. Color analysis can be used to match adjacent parts or to evaluate color change due to environmental or chemical exposure. The color analysis of the materials showed no significant affect after exposure to hydrogen peroxide vapor (Table 1). The FDA Silicone rubber material showed the greatest change; it had a Delta L of 1.84%, showing a slight darkening of the red material. It should be noted that this change was not perceivable to the naked eye.

Specular Gloss Analysis. Specular gloss is a measure of the light reflected by the surface of a material. Gloss can be inherent to the material, a result of the molding process, or a result of surface texture. Hydrogen peroxide vapor exposure had no impact on surface gloss of the materials tested (Table 1).

Table 1: Result of the Physical Testing Showing Percentage of Original Values Retained

Description	Units	Silicone	Buna-N/Vinyl	EPDM	Polyurethane	Acrylic	Nylon 6/6	UHMW Polyethylene	Poly-propolene	Polystyrene
Flexible Tensile										
Retention of 200%	%	97	101	101	102					
Retention of stress max	%	105	94	100	95					
Retention of strain max	%	106	98	99	96					
Rigid Tensile										
Retention of tensile mod	%					100	100	100	92	99
Retention of stress at break	%					99	113	98	107	100
Retention of stress at yield	%					n/a	100	100	100	100
Retention of strain at break	%					189	100	107	112	104
Retention of strain at yield	%					n/a	100	100	100	100
Durometer, Shore A										
Retention of Immediate	%	100	101	99	100					
Retention of 15 second delay	%	100	100	99	100					
Izod Impact										
Retention of Izod impact	%					300	113	120	93	105
Gloss										
Retention of gloss	%	99	150	99	115	100	107	101	101	100
Color										
Delta L	CIE Lab	-0.69	0.65	-1.46	0.08	-0.03	0.32	0.13	0.14	-0.03
Delta A	CIE Lab	1.05	-0.22	-0.01	0.06	0	0.03	-0.03	0	-0.02
Delta B	CIE Lab	1.35	0.06	-0.1	0.2	0.01	-0.84	0.03	0.03	-0.04
Delta E	CIE Lab	1.84	0.69	1.46	0.22	0.03	0.9	0.14	0.14	0.05

Retained gloss values for most materials ranged from 99% to 115% of the original values.

Durometer Hardness. ASTM D2240 is a testing procedure used to determine the relative hardness of soft materials, usually plastics or rubbers. It is used on elastomeric materials to identify a particular hardness range and as a quality control measure. Following exposure to hydrogen peroxide vapor, all materials retained between 99%-101% of their original values (Table 1).

FTIR Analysis using Diamond ATR Correction. FTIR analysis was used to determine the chemical composition and surface structure of a material. It is a useful technique to determine changes to the surface structure of a material after exposure. This procedure was performed using a Nicolet Impact 410 infrared spectrophotometer. Each material had an infrared analysis of its structure taken before exposure. An additional analysis was taken after cycle exposure and the two spectrums overlaid on a graph for examination. There were no shifts in peak height or wavelength indicating no change in structure or composition that may have occurred due to oxidation during processing.

Hydrogen Peroxide Residual Analysis. Residual analysis was performed on the samples to determine the levels of hydrogen peroxide absorbed by the materials during exposure. Five test coupons from each material were removed from the chamber immediately after the cycle and placed into 10 ml of deionized water at 25°C. Following sonication and vortex mixing, the samples were allowed to stand for 60 minutes. The extract was then analyzed using a Xylenol orange assay to assess the hydrogen peroxide levels. A second extraction procedure was done to ensure complete removal of all hydrogen peroxide from the test piece. Residual levels were then determined in both mg/l and ug/cm2 (Table 2).

Residual levels for most of the materials ranged from 0.09 mg/l to 1.2 mg/l. Of the materials tested, only polyurethane, nylon 6/6, and cast acrylic were considered somewhat absorptive. Results for these materials ranged from 6.61 mg/l to 62 mg/l immediately following exposure. After two hours sitting at room temperature, the levels had been reduced to a range of 4 mg/l to 35 mg/l.

Table 2 Hydrogen Peroxide Residual Levels

Sample	Surface Area (cm2)	Extraction Volume (ML)	H_2O_2 Levels (MG/L)	H_2O_2 Levels (ug/CM2)
Control	4.0145	10	0.069	0.17
FDA Silicone Rubber	4.0175	10	1.32	3.1
Control	3.477	10	0.08	0.23
VINYL-BUNA N Rubber	3.477	10	0.33	0.99
Control	4.9	10	0.08	0.18
EPDM Rubber	4.9	10	0.12	0.27
Control	5.33	10	0.14	0.26
Polyurethane	5.33	10	62.85	117.93
Control	5.097	10	0.11	0.21
Cast Acrylic	5.097	10	6.61	12.98
Control	5.15	10	0.15	0.29
Nylon 6/6	5.15	10	61	119
Control	5.42	10	0.08	0.16
UHMW Polyethylene	5.42	10	0.12	0.22
Control	4.827	10	0.06	0.13
Polypropylene	4.827	10	0.09	0.19
Control	5.11	10	0.15	0.29
Polystyrene	5.11	10	0.37	0.72

Residual testing showed all materials were below the safe and acceptable limit for hydrogen peroxide of 500mg/l. Hydrogen peroxide is approved for use and widely used in toothpaste, mouthwash, and as a food additive in concentrations of 500 mg/l. Further, it is available for household use as a disinfectant/antiseptic at 30,000 mg/l. These safe levels are in contrast to significantly lower safety limits with ethylene oxide. The levels observed in this study were all significantly below hydrogen peroxide safety levels and, in the case of absorptive materials, could be further reduced by adding cycle aeration pulses or storing the materials at room temperature.

CONCLUSIONS

The VHP MD sterilization process was shown to be compatible with all of the materials tested. The physical and chemical properties of the materials showed little to no change following exposure. The process did not affect material's strength or cause embrittlement of any of the elastic materials tested. Chemical results showed no changes observed with the test samples.

Overall, results have proven that VHP sterilization is a safe, rapid, and material-compatible alternative for low temperature, point-of-manufacture, medical device sterilization.

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