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Terminal Sterilization utilizing Vaporized Hydrogen Peroxide (VHP) to minimize the dependency on Ethylene Oxide (EO) sterilization

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Introduction

Ethylene Oxide (EO) sterilized medical devices account for over 50% of the global sterilized medical devices utilized in healthcare. Because of the risks associated with EO, It has been recognized that there is a need for other technologies as an alternative to EO with similar benefits. Although not a complete replacement for EO sterilization, VHP can offer an alternate methodology that can sterilize a significant portion of devices currently sterilized with EO. EO has been utilized for the sterilization process for over half a century, the stigma and potential dangers of its use has been a point of heated discussion amongst governmental health groups and environmental agencies that regulate and monitor its usage both directly and indirectly. This discussion has become a point of contention with these groups and has been a key factor in recent 2019 closures of commercial EO sterilization processing facilities in Willowbrook, IL and Smyrna, GA. With increased concerns about product safety, occupational exposure risks and impact to the environment, EO usage is being challenged by governmental agencies. For these reasons, Stryker's Sustainability Solutions division (Stryker) is beginning the process, of migrating away from EO sterilization and using Vaporized Hydrogen Peroxide (VHP) sterilization.

The use of VHP has grown steadily in industries that require disinfection and the elimination of microorganisms, as its ability to kill spores and sterilize materials has been demonstrated in many studies with a variety of practical applications[1]. Numerous types of benchtop hydrogen peroxide gas delivery systems are in use in the healthcare setting across the globe (STERIS VPro, and ASP Sterrad systems to name a few). Questions have arisen though, about compatibility with different materials used in the healthcare and biomedical industries and efficacy for sterility claims. This paper will address these concerns and demonstrate the advantages of VHP. The conclusion being that VHP is both a safe and effective alternative to EO sterilization.

Background

Vaporized Hydrogen Peroxide technology was developed in the mid-1970's utilizing a patented closed-loop, low concentration "dry" process. The origins of the use of VHP in industrial sterilization may be traced back to the 1977 US patent #4 169 123 which was granted to Francis Moore and Leon Perkinson for their 'Hydrogen Peroxide Vapor Sterilization Method'. The patent describes a 'cold sterilization process' alternative to EO sterilization and radiation sterilization. AMSCO (now part of STERIS) secured rights to use Vaporized Hydrogen Peroxide as a sterilant, and further developments of the equipment and process were refined. The release of the 'VHP 1000' Biodecontamination System that was launched to the pharmaceutical customer base in 1991 was the platform instrumental in securing VHP in a practical process[2]. Early work by Rickloff reported success with sterilization of intravenous sets using a 4·5-h deep vacuum VH2O2 process with **Bacillus subtilis** as an indicator organism.[2] Klapes and Vesley reported: "While aqueous hydrogen peroxide has a long history of use as a sterilant, the concept of vapour phase H2O2 (VPHP) sterilization has been developed within the past decade. VPHP represents a class of nontoxic cold gas sterilant which provides an opportunity to discontinue the use of such toxic or carcinogenic gaseous sterilants as EO and formaldehyde. VPHP technology could have immediate applications for the sterilization of specialty medical products, especially those which would be destroyed by steam sterilization or require lengthy aeration to reduce toxic EO residuals."[3]

Over the last three decades, the application of VHP technology has evolved into atmospheric and vacuum processes: atmospheric pressure conditions, as is the case for VHP room, isolator, vehicle and building decontamination; or vacuum conditions in low-temperature sterilization applications, such as reusable medical device sterilization.[4] Stryker intends to leverage these established technologies to decontaminate and sterilize some of its product offerings that are compatible with VHP.

VHP processing advantages

VHP is a low temperature, highly efficacious process that has relatively short processing exposure times. VHP has excellent material compatibility with device materials and the hydrogen peroxide gas breaks down to oxygen and water as end products with its usage. Further explanation of advantages of decontaminating and sterilizing with Vaporized Hydrogen Peroxide are as follows:

1. Efficacy

Hydrogen peroxide vapor at low concentrations is an effective decontaminant against a wide variety of microorganisms. Not only is it capable of permeating most materials, VHP can kill microorganisms residing in seams and joints. Permeation by a vapor allows effective penetration into these areas. Vapor hydrogen peroxide can also penetrate plastic membranes.

The original patent describes, the efficacy of the process in delivering a minimum of 1×10^{-6} Sterility Assurance Level (SAL), in line with the FDA recommendation for sterile medical and surgical products. Validation and routine processing utilizes biological indicators (BIs) as part of the process validation and verification. The BIs utilized carry a spore forming bacillus known to be the most resistant microorganism (MRO) to this sterilant (**G. stearothermophilus**). Following established ISO guidelines, the VHP process shows consistent repeatability and reproducibility for medical device sterilization in the same fashion as EO.[5]

2. Low temperature processing

Most polymers and adhesives being used to manufacture devices cannot tolerate high temperatures without suffering deleterious effects. Sterilization with VHP can be accomplished efficiently at temperatures as low as 4°C (39°F). Using these low temperatures during processing lessens the chances of damage to the materials which could comprise the load being sterilized. Typical VHP processing cycle temperatures range in temperature of 24-38°C (75-100°F) which is lower than traditional EO cycles. Lower temperature equates to less stress and damage to device materials.

3. Short processing cycles

D-values for vapor hydrogen peroxide sterilization are low, thus allowing for short sterilization cycles. Short cycle times, mean increasing the availability of chambers for additional processing and expedited turn times for reprocessing devices. Extended product residual outgassing associated with EO processing is either substantially decreased or not necessary.

4. Reduced emissions

VHP is considered a "Green" sterilization modality; the active hydrogen peroxide vapor breaks down to oxygen and water vapor as by products to the process. Dangerous emissions associated with EO processing from equipment leaks, normal wear and tear, improper assemble, etc. are non-existent with VHP sterilization. In addition, because of increased efficacy of peroxide vapor, there is low chemical consumption per cycle.

5. Materials compatibility

VHP is known to have excellent compatibility with most device materials of construction with the predominant limitation of cellulosic material. Stryker's Sustainability Solutions division addresses this limitation by processing devices only in their primary sterile barrier that is VHP compatible and composed of non-cellulosic materials (Tyvek, Mylar, various plastic polymers). Following VHP processing, products are packaged in secondary and shipping containers for distribution. In addition, the VHP processing extends the service life of enclosures (as compared to other sterilant systems) by virtue of the low temperature, the low concentrations of peroxide vapor used, and minimal pressure differences.

VHP is compatible with a wide range of metal and polymeric materials, making it an effective sterilization method for healthcare products such as:

- General Surgical Instruments – Both single use and reusable devices
- Surgical endoscopes
- Implants and devices with electronics
- Pharmaceutical containers
- Parenteral drug delivery systems such as pre-filled syringes
- Combination delivery devices
- Single-packaged complex devices
- Complete assemblies or devices with loose components (e.g. needles)
- Temperature sensitive devices

Discussion

Vaporized Hydrogen Peroxide is sporicidal, bactericidal, fungicidal and virucidal. Because of this broad spectrum range, VHP is an excellent modality choice to sterilize medical devices for reprocessing. Like any alternate sterilization modality to EO, VHP has some limitations which need to be considered and addressed. The two primary limitations involve material incompatibility and vapor penetration. In developing a sterilization process, Stryker has addressed both in creating and validating their process.

Material incompatibility

It is well documented in the literature that cellulosic materials are not compatible with VHP.[6] The specific interaction with cellulose degrades the hydrogen peroxide gas and reduces the ability to achieve the same "kill" kinetics in a vapor form.[7] In addition to cellulosic material, certain uncoated reactive metals (Copper and Brass as examples) may react and cause surface reactions which may degrade or discolor the material. As previously stated, the device exposure cycles at Stryker are exposed in primary packaging that does not contain cellulosic materials. This allows for avoidance of the reaction with VHP. Following sterile processing, devices packaged in the primary configuration are then placed into their secondary package and then boxed out into corrugate shippers for distribution to customers. During design and development of VHP Sterile Processing cycles, devices are inspected both from a cosmetic and functional aspect post exposure. Any materials or devices that are found to not pass stringent requirements for functionality and cosmetic appearance are not adopted into the VHP processing cycles.

Effective penetration deficiencies

Difficulties exhibited with sterilization of certain device types in specific load patterns have arisen in past applications.[1] Adsorption and condensation play key roles in these situations. These are most apparent in long lumen devices and densely packed exposure loads. Poor cycle development which does not consider potential dew point changes, gas concentration and saturation levels and exposure environment temperature will exhibit these processing non-conformances. Stryker Sterilization Engineers account for these conditions and parameters during the developmental process of a VHP cycle. Devices are seeded with appropriate biological challenges to challenge the process and achieve the desired sterility assurance levels to avoid these anomalies.

Summary

The medical device market currently relies on sterilization technologies such as irradiation (Gamma, E-Beam and X-Ray), steam or gaseous EO. For some time, it has been recognized that there is a need for other technologies as an alternative to EO. Although not a complete replacement for EO sterilization, VHP can offer an alternate methodology that can sterilize a portion of devices currently sterilized with EO. Vaporized hydrogen peroxide sterilization is a widely adopted method in the hospital setting, but it is still very much in its infancy in the terminal sterilization of medical devices for industry. VHP does have limitations, including cellulosic material compatibility and penetration, which may affect the efficacy of sterilization for established and emerging medical devices that are increasing in complexity. The limitations of VHP can be addressed through avoidance of certain materials during processing, specifically cellulosic packaging materials, and establishing resistance and penetration studies where applicable during cycle development to verify penetration of gas in complex designed products. Vaporized Hydrogen Peroxide provides a safe alternate to Ethylene Oxide sterilization of medical devices when specific limitations of the technology are appropriately addressed during process development.

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