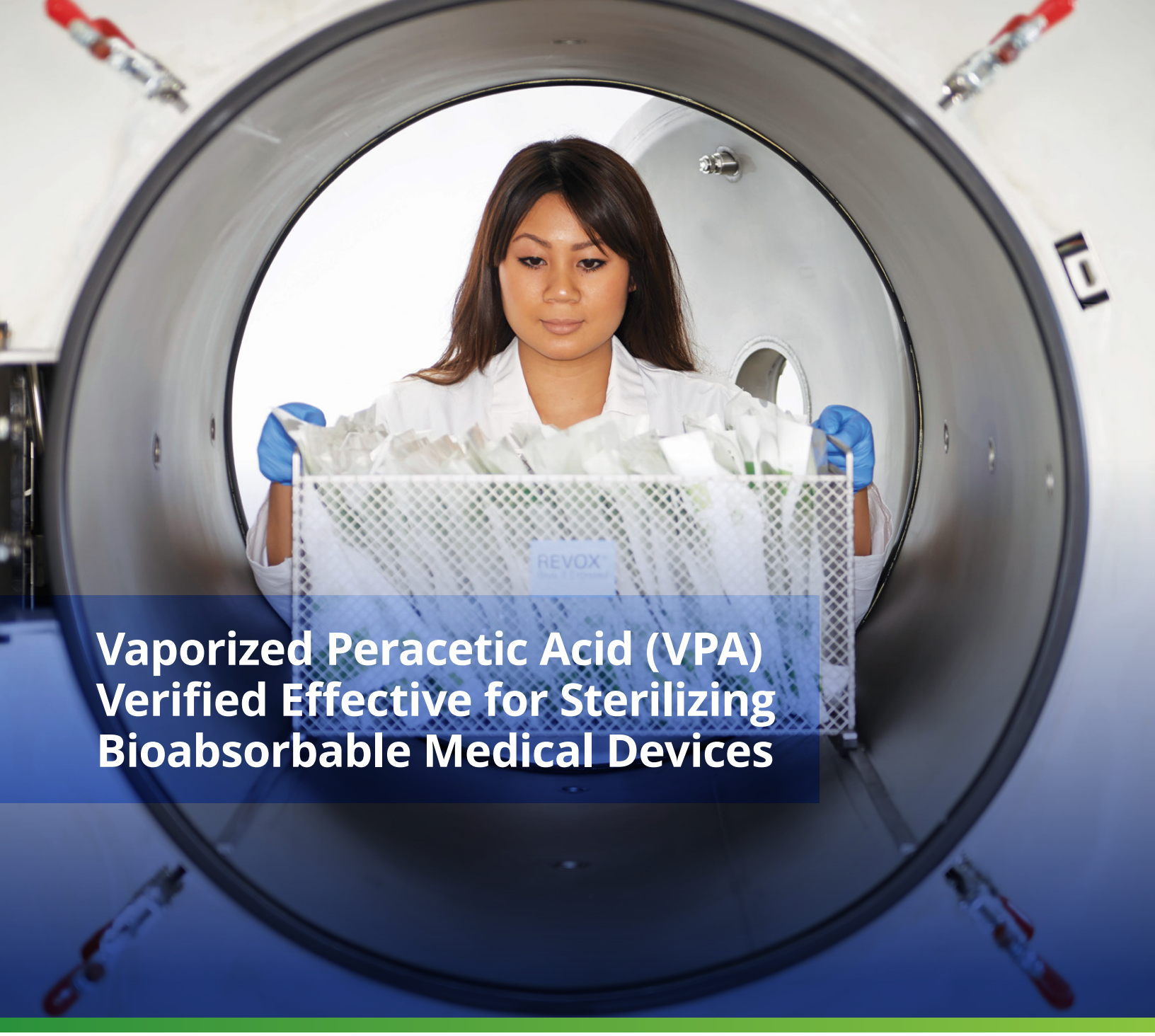


Vaporized Peracetic Acid (VPA) Verified Effective for Sterilizing Bioabsorbable Medical Devices

Contents

REVOX®
Sterilization Solutions
by Cantel Medical

ABSTRACT

This report explains how the innovative usage of vaporized peracetic acid (VPA) provides a safe, reliable, and versatile method for sterilizing bioabsorbable implants.

It describes the thorough testing method used to verify that bioaborbable polymers are fully compatible with the VPA process, and it shows the specific results of these tests using Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) spectroscopy and other measurements. For instance, sterilization methods that operate at high temperatures, such as steam autoclave, can damage, degrade, or even melt the polymer materials used in these implants. Likewise, chemical processes such as ethylene oxide (EO) sterilization can leave behind carcinogenic residuals. VPA offers an alternative sterilization solution that is both safe and effective for these bioabsorbable devices.

THIS STUDY HIGHLIGHTS FOUR KEY BENEFITS OF VPA:

1. It is compatible with materials that have proven challenging for traditional sterilization methods, such as bioabsorbable implants.
2. Unlike traditional methods, the VPA process sterilizes at room temperature.
3. The VPA sterilant breaks down into basic carbon dioxide, oxygen, and water, so there are no harmful chemical residuals that could linger on the surfaces of sterilized items.
4. The ability to sterilize polymer-based bioabsorbable implants and devices expands the innovation potential of future medical device development.

INTRODUCTION

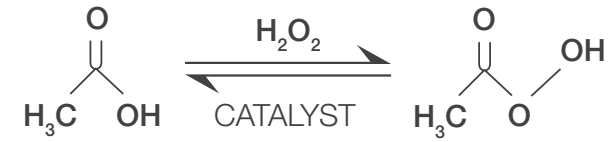
The medical device industry is increasingly relying upon the use of bioabsorbable implants, and that trend will continue to grow. In fact, the bioabsorbable stent market alone is expected to reach $2.4B by 2021, up from $400M in 2016, according to a 2016 *MarketsandMarkets* report. Traditional sterilization methods, however, have typically posed significant problems for implants like bioabsorbable stents and related FDA Class II and Class III medical devices.

*"The bioabsorbable stent market alone is expected to reach **$2.4B by 2021, up from $400M in 2016"***

MarketsandMarkets report 2016

BACKGROUND ON VAPORIZED PERACETIC ACID

Peracetic acid (PAA) (CH_3CO_3H) is an organic compound formed through a reaction that occurs when acetic acid is combined with hydrogen peroxide. Acetic acid is a naturally occurring compound that gives vinegar its sour taste and pungent odor, as well as its natural disinfecting properties. Peracetic acid was first patented in Germany in 1914, and it has been used as a liquid antibacterial agent in a number of commercial applications since the 1950s, particularly in the food industry and in water purification. As a highly biocidal oxidizer, liquid peracetic acid is an effective chemical sterilant.



ACETIC ACID PERACETIC ACID

Chemical formulation of peracetic acid.

Peracetic acid was first used in automated sterilization for medical, surgical, and dental instruments in 1988, and in 2010, REVOX® introduced a room-temperature, vaporized form of peracetic acid sterilization, which is less corrosive than using peracetic acid in its liquid form and has a wider range of materials compatibility. Vaporized peracetic acid (VPA) can safely disinfect products that would normally be damaged by a liquid chemical or by moisture and heat.

Since the development of bioabsorbable medical devices, manufacturers have faced challenges in sterilizing them safely with traditional methods. The polymer materials that comprise these devices can degrade under the high-temperature conditions of steam and hydrogen peroxide sterilization, as well as under gamma irradiation. Additionally, EO sterilization with EtO (Ethylene Oxide), an EPA designated carcinogen, poses the risk for carcinogenic chemical residuals. Fortunately, the VPA sterilization process presents a safe and effective alternative that works at room temperature (20°C).

Vaporized peracetic acid (VPA) can safely disinfect products that would normally be damaged by a liquid chemical or by moisture and heat.

TIMELINE OF STERILIZATION

2014 — FDA clears first Class II medical device (cranial implant) using the REVOX® Sterilization Solutions vaporized peracetic acid process

2008 — The REVOX Sterilization Solutions room-temperature vaporized peracetic acid process is patented

1987 — Patent for low-temp plasma sterilization using hydrogen peroxide is granted

1977 — First patent for vapor hydrogen peroxide sterilization granted

1956 — The commercial use of electron beams (e-beam) in sterilization begins

1950'S — The industrial use of gamma radiation begins with Cobalt-60 as a radiation source

1938 — Ethylene Oxide (EO) sterilization for the preservation of spices is patented

1881 — Sterilization by boiling introduced

1876 — Charles Chamberland, Louis Pasteur's pupil & collaborator, develops the first pressure steam sterilizer

1858 — English physician B.W. Richardson begins using Hydrogen Peroxide as disinfectant

LIQUID VS. VAPORIZED PERACETIC ACID

The pH of PAA in its liquid state is acidic and can be corrosive. To counter this liquid state acidity, buffers are typically used to neutralize it. pH values of a vaporized liquid cannot be measured, so the pH of Vaporized Peracetic Acid (VPA) is unknown, however, the concentration of VPA in contact with materials during sterilization is quite low compared to that of the liquid state, which contributes to its wide-ranging materials compatibility. Formal compatibility studies confirm that VPA has an excellent compatibility profile with over 100 materials tested. Even copper, after being exposed to VPA in 10 repeated four-hour cycles, only showed a slight dulling of the original gloss.

In contrast, liquid PAA exposed to copper results in an immediate reaction, which results in corrosion. The distinct contrast between liquid and vapor PAA interacting with copper, along with other material compatibility test results, illustrates that vapor PAA is far more compatible than liquid PAA. The compatibility study results are supported by the results seen with numerous complex and sensitive devices and device/drug combinations. In addition, VPA breaks down into three simple compounds—carbon dioxide, oxygen, and water—leaving no harmful chemical residuals behind.

BACKGROUND ON BIOABSORBABLES

Bioabsorbable medical devices are specialized products designed for the implantation into living tissue without negatively affecting the patient and to eventually dissolve and be absorbed in the bloodstream. They include internal drug delivery mechanisms, stents, vascular grafts, and scaffolds for tissue engineering, and they fall under either Class II or III of commercially distributed medical devices, according to section 513(a)(1) of the federal Food, Drug, and Cosmetic (FD&C) Act (21 U.S.C. § 360c(a)(1)).

Technological advancements, an increasing number of clinical trials, and patient safety have been the driving forces of the emergence of bioabsorbable medical devices. Bioabsorbable implants are growing more popular because they require no removal operations, reduce medical costs and the risk of infection, and increase patient comfort. As advancements in medical technologies develop and further uses for bioabsorbable materials are developed, demand for these types of medical devices will only increase.

Sterilization needs to keep pace with the production requirements of these sophisticated biomaterials, and also serve the needs of future device innovation. VPA meets the challenges of sterilizing bioabsorbable polymers—it kills microbes at room temperature, degrades rapidly, leaves little residue, and decomposes into relatively harmless naturally occurring substances: water, oxygen, and carbon dioxide.

Formal compatibility studies confirm that VPA has an excellent compatibility profile with ***more than 100 materials tested****.*

DEFINING CLASS II AND III

CLASS II categorizes "devices for which general controls, by themselves, are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance."

CLASS III is defined similarly, although these devices do not have sufficient information to establish special controls, and they require pre-market FDA approval. Circulatory blood contact devices are considered Class III, as are combination products that have separate types of components (drug/device/biologic) that are combined as a single entity, packaged together, or intended for use with another specific required product.

THE VPA PROCESSING CYCLE

The REVOX® Sterilization Solutions VPA system achieves sterilization and/or bioburden reduction by vaporizing a chemical sterilant in a vacuum environment. The chemical sterilant used in this process includes two active ingredients: hydrogen peroxide (~22%), and peracetic acid (~4%).

THE MACHINE CYCLE CONSISTS OF THE FOLLOWING PHASES:

1. **Chamber Evacuation:** The air is removed from the chamber and the primary packaging of the product being sterilized.
2. **Chemical Injection and Hold Time:** The peracetic acid sterilant is atomized while pressure within the chamber is raised. The hold time is the time remaining after the chemical injection has completed, which allows the chemical to remain in contact with the product for a period of time.
3. **Chamber Dehumidification:** The chemical is removed from the chamber in between each chemical injection.
4. **Chamber Ventilation:** Any chemical residuals are removed from the chamber.

REVOX Sterilization Solutions by Cantel Medical

STANDARD VPA CYCLE

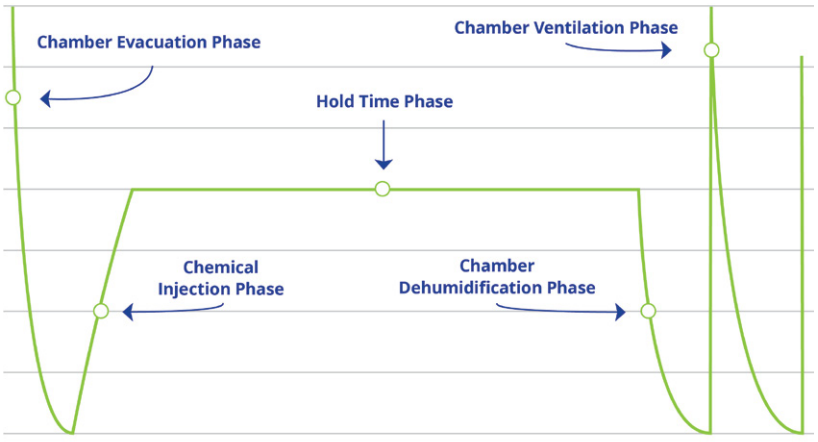
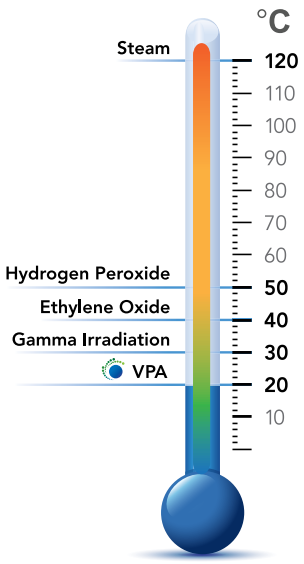


fig. 1



The VPA process offers true room temperature sterilization (18–30°C) and aseptic processing capabilities throughout all phases.

TESTING METHOD

REVOX® Sterilization Solutions chemists thoroughly tested the VPA sterilization* process on three polymer materials commonly used in bioabsorbable medical devices. These bioabsorbable polymers included polylactic acid (PLA), poly lactic-co-glycolic acid (PLGA), and polyglycolic acid (PGA). Measurements were conducted before and after the VPA processing so that the results could be compared.

Materials compatibility analysis included weight and dimensions measurements, visual and hardness tests, and using Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) spectroscopy. This method uses light spectra to provide information on a material's molecular functional groups and chemical bonds.

**Tyvek®-Mylar, Mylar only, or Tyvek® only pouches or equivalent must be used to allow for optimal REVOX sterilization of materials.*

ACCEPTANCE CRITERIA

Upon VPA-processing, materials are evaluated holistically in order to determine their compatibility with the REVOX Sterilization Solutions process. Weight, dimensions, or visual changes, including alterations in color and brittleness or hardness are recorded. Analysis of the pre- and post-processed material ATR-FTIR spectra are crucial. Any change in chemical structure (gain or loss of peaks) as observed by ATR-FTIR spectra indicates a change in chemical structure. Thus, the material is incompatible regardless of whether the other measured material properties remained unchanged. The material compatibility acceptance criteria are summarized in the table (Fig. 2) below.

COMPATIBILITY	Δ, (% REFLECTANCE)	ATR-FTIR INDICATORS
Excellent	≤1% change	No observable change in spectra pre- and post-exposure.
Good	1% to ≤ 3% change	
Fair	3% to ≤ 5% change	Peak addition(s) and/or deletion(s) following ten VPA cycles.
Poor	> 5% change	Peak addition(s) and/or deletion(s) following both single and ten VPA cycles.

fig. 2

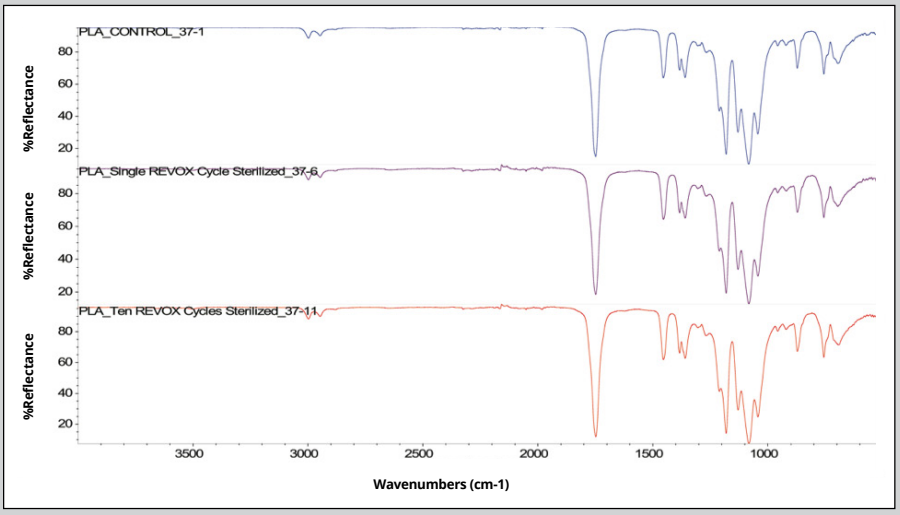
The customer may establish acceptance criteria, depending on pre-established product tolerances. The acceptance criteria above are guidelines, which are subject to change, depending on the material.

VPA can achieve an industry-leading SAL of 10^{-6}, meaning there is a one in a million chance of retaining any trace microbes.

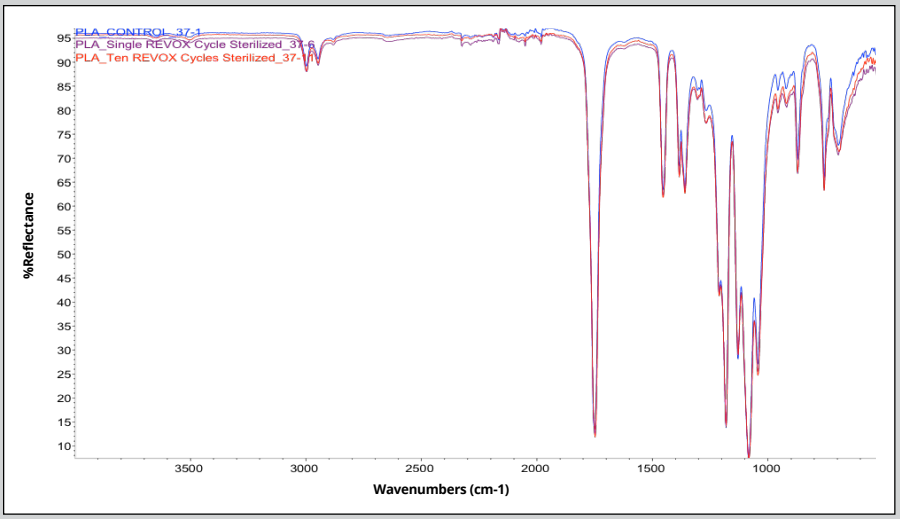
TEST RESULTS FOR BIOABSORBABLE POLYMERS

The following are the specific recorded measurements for the three bioabsorbable polymers tested, along with a chart graphing the ATR-FTIR spectral analyses of the control baseline, a single cycle of VPA sterilization, and ten cycles of VPA sterilization at ambient temperatures (18–30°C) for each material:

Polylactic Acid (PLA): The processed materials showed no observable change in appearance. Weight and dimensions analysis was not achievable because the material was in a very fine powder form with negligible mass. ATR-FTIR spectral analysis showed no observable change in chemical structure.



ATR-FTIR spectra of PLA control, single cycle (37-6), and ten cycles (37-11) of the REVOX® Sterilization Solutions VPA process.



ATR-FTIR spectra of PLA control, single cycle (37-6), and ten cycles (37-11) of the REVOX Sterilization Solutions VPA process, overlaid.

POLYLACTIC ACID (PLA)

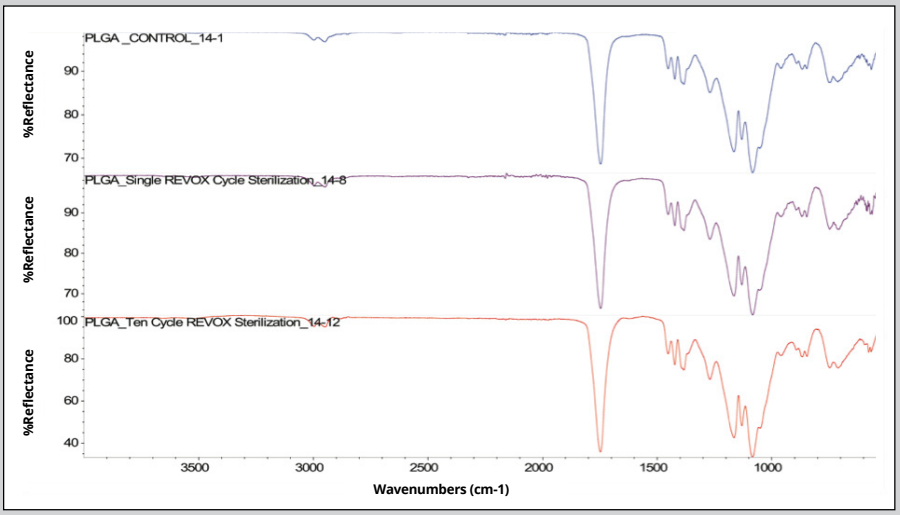
Biodegradable and bioactive thermoplastic aliphatic polyester derived from renewable resources

Common uses:

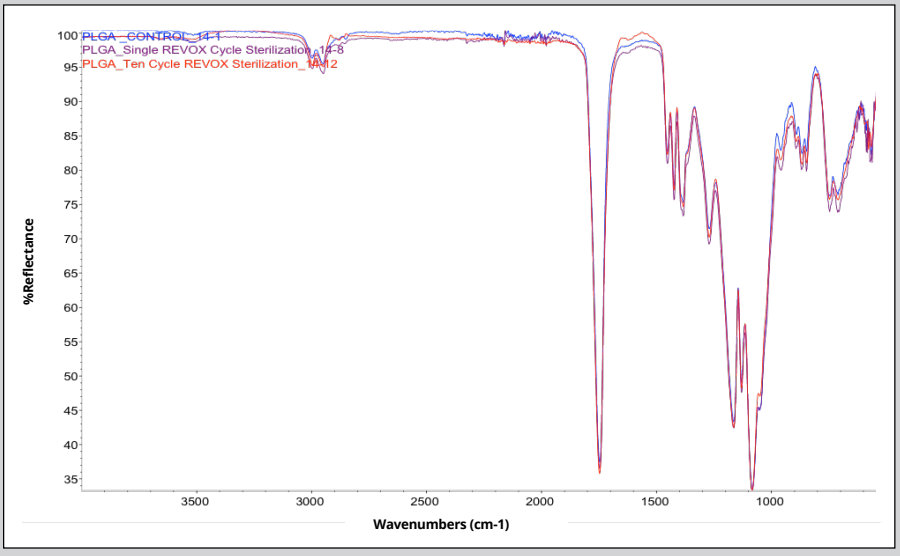
- 3D printer filament
- Biodegradable medical devices (screws, pins, rods, etc.)

TEST RESULTS FOR BIOABSORBABLE POLYMERS

Poly lactic-co-glycolic acid (PLGA): The processed materials showed no observable changes in appearance, and less than or equal to an average of a three percent change in mass. The weight of the samples tested were 0.003 grams each, thus the three percent change in weight falls within accuracy of the balance. Dimensions analysis was not achievable because this material was in crystalline form. ATR-FTIR spectral analysis showed no observable change in chemical structure.



ATR-FTIR spectra of PLGA (control), single cycle (14-8), and ten cycles (14-12) of the REVOX® Sterilization Solutions VPA process.



ATR-FTIR spectra of PLGA (control), single cycle (14-8), and ten cycles (14-12) of the REVOX Sterilization Solutions VPA process, overlaid.

POLY LACTIC-CO-GLYCOLIC ACID (PLGA)

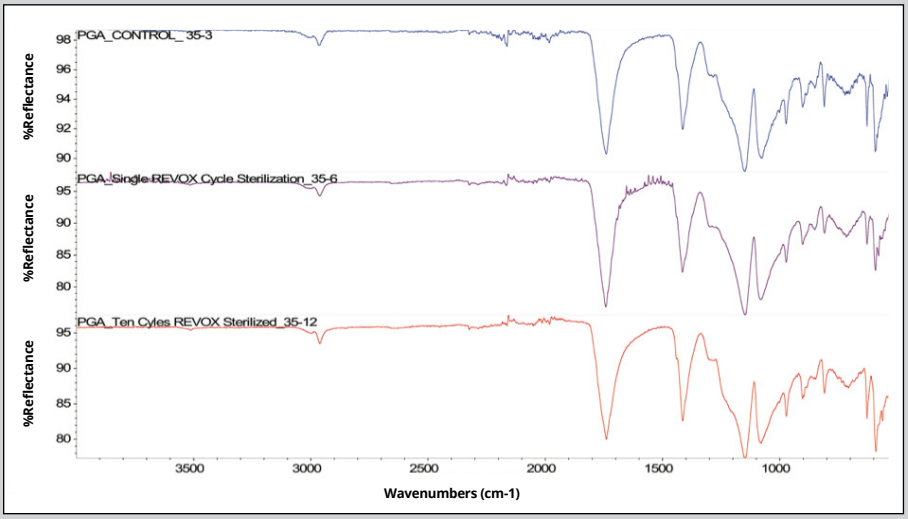
Biodegradable copopolymer used in a wide range of medical applications

Common uses:

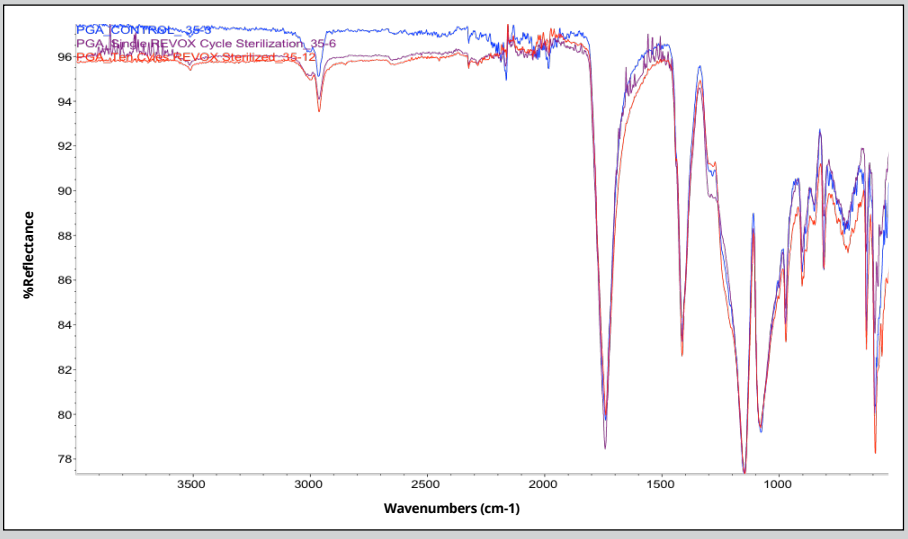
- Grafts, sutures, implants
- Prosthetic devices, surgical sealant films

TEST RESULTS FOR BIOABSORBABLE POLYMERS

Polyglycolic acid (PGA): The processed materials showed no observable change in appearance, and less than a one percent change in mass. Dimension analysis was not achievable because this material was in pellet form. ATR-FTIR spectral analysis showed no observable change in chemical structure.



ATR-FTIR spectra of PGA control (35-3), single cycle (35-6), and ten cycles (35-12) of the REVOX® Sterilization Solutions VPA process.



ATR-FTIR spectra of PGA control (35-3), single cycle (35-6), and ten cycles (35-12) of the REVOX Sterilization Solutions VPA process, overlaid.

MATERIALS COMPATIBILITY

Bioabsorbable materials are considered compatible with VPA sterilization because, as shown in the preceding test results, the process does not cause statistically significant changes to their composition, appearance, or mass.

POLYGLYCOLIC ACID (PGA)

Biodegradable, thermoplastic polymer and the simplest linear, aliphatic polyester

Common uses:

- Biodegradable sutures
- Implantable pins, rods, and screws

CONCLUSION

As these test results indicate, the vaporized peracetic acid (VPA) sterilization system provides excellent materials compatibility for bioabsorbable polymers PLA, PLGA, and PGA. VPA sterilization makes it possible for manufacturers to safely disinfect polymer-based implants without exposing them to high temperatures, moisture, radiation, or hazardous chemical byproducts.

The REVOX® Sterilization Solutions patented, room-temperature, VPA sterilant achieves exceptionally low chemical residuals and compatibility with over 100 materials. This technology eliminates safety risks associated with traditional sterilization methods and the inefficiencies of pre-conditioning and lengthy post-sterilization wait times. Many materials that may otherwise be ideal for optimal product design are simply not suitable with common sterilization methods. VPA changes that. Chemical and heat-sensitive materials that were once off-limits to innovative product development are now available.

VPA opens the door for bioabsorbable product developers who are able to design implants and other medical devices using materials that they could not have sterilized safely with conventional methods.

ABOUT REVOX STERILIZATION SOLUTIONS

REVOX Sterilization Solutions and Mar Cor Purification are subsidiaries of Cantel Medical (NYSE:CMD) and share the same campus in Plymouth, Minnesota. Cantel Medical is a leading provider of infection prevention products and services in the healthcare market, specializing in endoscopy, water purification and filtration, and health care disposables. Cantel Medical patented the novel VPA sterilization system used by REVOX Sterilization Solutions. REVOX Sterilization Solutions provides room-temperature sterilization in the medical device, biologic, implantable, and combination device industries.

To see if VPA Sterilization is your sterilization solution, visit our website at **www.revoxsterilization.com** or call 1-855-473-8690 for a free consultation.

REVOX® Sterilization Solutions by Cantel Medical

RevoxSterilization.com

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