# Compatibility of Medical Devices and Materials with Low-Temperature Hydrogen Peroxide Gas Plasma

A new sterilization technique safely treated about 95% of the materials tested in an average of 75 minutes.

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Manufacturers can draw from a broad spectrum of techniques to sterilize and disinfect medical devices, and new physical and chemical processes continue to be developed. A leading reason for this continued search for new methods is to meet the needs of an increasing number of cost-conscious, managed-care hospital and clinical environments, which are forgoing the use of single-use, disposable devices in favor of devices that can be used more than once.
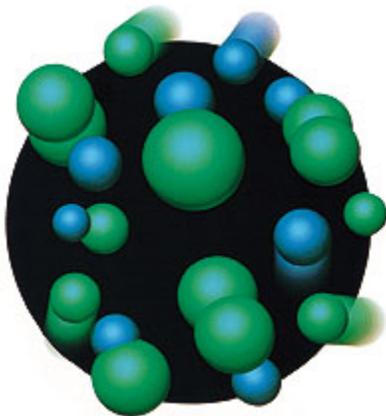
Radio-frequency energy generates plasma from vaporized hydrogen peroxide. Illustration by Advanced Sterilization Products (Irvine, CA)

While traditional methods of sterilization, like steam and ethylene oxide (EtO), successfully treat many devices, new techniques can sterilize a broader range of materials in a single system. Some of the newer sterilization techniques currently on the market or under development include low-temperature hydrogen peroxide gas plasma (Sterrad system, Advanced Sterilization Products, Div. of Johnson & Johnson Medical, Inc., Irvine, CA), low-temperature peracetic acid gas plasma (Plazlyte system, Abtox, Inc., Mundelein, IL), vapor-phase hydrogen peroxide (Steris, Mentor, OH), chlorine dioxide (Johnson & Johnson, New Brunswick, NJ), and high-intensity visible light (PureBright, PurePulse Technologies, San Diego).

Very little information has been published to date on materials compatibility with these processes; therefore, recently more than 600 individual resterilizable devices from more than 125 medical device manufacturers were tested for compatibility and

functionality with the Sterrad system. Overall, approximately 95% of the devices tested could safely be sterilized by low-temperature hydrogen peroxide gas plasma.

TRADITIONAL PROCESSES

Various sterilization processes have different characteristics and will also have different effects on materials and devices. For example, contrasts can be seen between applications for the newer low-temperature gas plasma technique and those for the older, established processes of steam and EtO gas sterilization. Sterilant type and concentration, cycle time, temperature, and pressure parameters will differ among the various processes, and these parameters will determine in part the types of devices and materials that each process can sterilize.

For example, materials and devices that cannot tolerate high temperature and humidity, such as some plastics, electrical devices, and corrosion-susceptible metal alloys, may not be recommended for steam sterilization. Some materials, like certain plastics, such as plastic optical fibers, cannot withstand radiation. EtO is not recommended for use with materials that absorb or react with it. Liquids and some devices that can be physically damaged or changed by exposure to vacuum cannot be processed by EtO and low-temperature gas plasma.
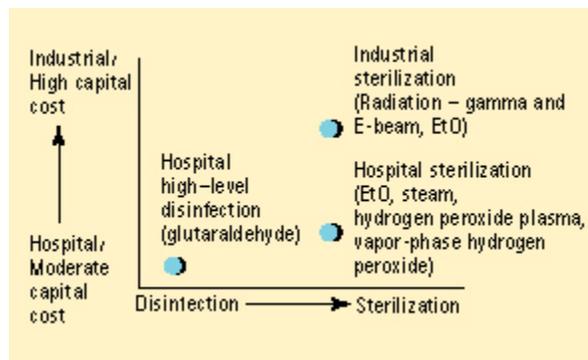

Figure 1. Sterilization and disinfection processes afford different degrees of protection at varying costs.

The relationships among some of these processes are illustrated in Figure 1, which plots various methods as points on a two-dimensional map of relative cost and degree of disinfection or sterilization. Some techniques, such as liquid immersion methods, can be considered disinfecting or sterilizing, depending on the length of the cycle.[1] Relative costs vary, depending on facility requirements (e.g., shielding in the case of radiation, or space and exhaust vapor handling in the case of EtO), cycle time (which can affect the number of duplicate instrument sets needed), materials compatibility (which can determine the types of instruments sterilized), packaging, and so forth.

COMPARATIVE ADVANTAGES AND DISADVANTAGES OF STERILIZATION PROCESSES

Steam. Steam is the oldest and most common method for hospital sterilization of medical devices. Some of its advantages include speed, low cost, and low environmental impact; however, the high temperatures associated with steam may cause damage and lead to safety concerns, and steam can corrode surgical alloys and cutting edges. Chrome stainless-steel surgical blades and other related devices

have developed pitting and dulling of the cutting edges after multiple steam sterilization cycles, while low-temperature gas plasma has shown no detrimental effects.[2] Also, most plastics cannot withstand high temperatures.

EtO. A long-established and widely used method, EtO provides a low-temperature environment (enabling many heat-sensitive devices, such as modern electronic instruments, to be processed), widespread availability, a long track record, and a wide range of compatible materials. Its disadvantages include toxicity, environmental threat from hydrochlorofluorocarbons, long aeration and total processing time, high costs, custom facilities requirements, and residual EtO in materials.

Hydrogen Peroxide Gas Plasma. The Sterrad system offers a short cycle (averaging 75 minutes), low temperature and humidity, no aeration requirement, no chemical residues, negligible environmental impact, and wide compatibility with materials. Its drawback is an inability to process liquids, powders, or strong absorbers (e.g., cellulosics).

Some lumen restrictions also apply. For long and narrow lumens, the time it takes for the vapor to travel through the lumen can exceed the length of the diffusion cycle. Thus, guidelines have been developed for lumen diameter and length to ensure adequate penetration and efficacy for the given cycle parameters. Care must also be taken to ensure that the walls of the restricted area are not composed of materials that may absorb or decompose vapor and thus decrease sterilization efficacy.

Other Low-Temperature Processes. Published information on the compatibility of materials with vapor-phase hydrogen peroxide (VHP), low-temperature peracetic acid vapor gas plasma sterilization (Plazlyte), and other new processes is limited.[3] However, one common theme is a shift toward processes that are more oxidizing.[4] Thus, oxidation effects on materials may be similar for both low-temperature hydrogen peroxide gas plasma and other new processes.

THE HYDROGEN PEROXIDE GAS PLASMA CYCLE

The new low-temperature hydrogen peroxide plasma technology system sterilizes in five phases: vacuum, injection, diffusion, plasma, and vent cycles.

During the vacuum stage, the chamber is evacuated to 0.3 mmHg pressure. Items to be sterilized, which are typically placed into the chamber in a tray covered with a double layer of nonwoven polypropylene fabric wrap or a Tyvek pouch, must be thoroughly dried first. Excess moisture in the instrument load will prolong the evacuation phase because of continued evaporation of the moisture and can lead to cancellation of the cycle.

A dose of liquid peroxide is then injected into the evacuated chamber through a heated injector nozzle, which both evaporates the aqueous hydrogen peroxide solution and disperses it into the chamber. The chamber temperature is controlled at a point somewhat warmer than room temperature, not exceeding 40°—45°C, to reduce the chance of condensation. The chamber pressure rises slightly during the injection phase as the hydrogen peroxide evaporates. The process can be considered fairly dry, since the relative humidity stays between 6 and 14%, and the equilibrium vapor pressure of water at 40°C is about 60 mmHg.[5]

During the diffusion phase (approximately 50 minutes in duration), the hydrogen peroxide vapor is allowed to permeate the chamber and completely expose all surfaces of the load to the sterilant. At the completion of the diffusion phase, the chamber pressure is reduced to 0.5 torr, and the radio-frequency plasma discharge is initiated, which lasts for 15 minutes. In the plasma state, the hydrogen peroxide vapor breaks apart into reactive species that include free radicals. The combined use of hydrogen peroxide vapor and plasma safely and rapidly sterilizes most medical instruments and materials without leaving toxic residues. Following the reaction, the activated components lose their high energy and recombine to form primarily oxygen, water, and other nontoxic by-products.[6]

In the final phase, the chamber is vented to atmosphere through a high-efficiency particulate air (HEPA) filter, reevacuated, and vented again. The vapor purged from the chamber is vented to the atmosphere through a catalytic filter to decompose all remaining traces of hydrogen peroxide into water and oxygen vapor.

FUNCTIONALITY AND COMPATIBILITY TESTING

The Association for the Advancement of Medical Instrumentation has developed a guideline for evaluating resterilization of reusable medical devices,[1] and a testing program that adheres to this guideline is under way at ASP for evaluating material compatibility of medical devices with the Sterrad system. The functionality and compatibility testing program subjects devices to a preestablished number of reprocessing cycles—typically, up to 100—and includes visual and microscopic evaluation of the effects of processing, functionality assessment by the device manufacturer, and a final report. Functionality testing may include evaluation of electrical function, optical function, mechanical function (i.e., changes in strength, fit, or dimensions), and appearance.

A wide range of different device types have been tested, including flexible and rigid endoscopes, fiber-optic light cables, laser handpieces, power drills and saws, and ophthalmic devices. As mentioned previously, approximately 95% of the devices tested could safely be sterilized by low-temperature hydrogen peroxide gas plasma. Those devices that appear incompatible exhibited cosmetic changes such as fading of dyed anodized aluminum components and of some colored plastic identification rings (which are not required for device functionality), and some chipping of paint coatings. Embrittlement of some adhesives has been noted, as well as chemical changes in some organic and polymeric sulfides.

Materials to Consider for Medical Devices (except Trays)

Metals

Stainless steel 300 series, aluminum 6000 series, titanium

Nonmetals

Glass, silica, ceramic

Plastics and Elastomers

Polyethylene (LDPE, HDPE, UHMPE), polypropylene copolymer, polymethylpentene, Tefzel, chlorinated polyvinyl chloride, polystyrene, polyethersulfone, polyvinylidene fluoride, polyetherketone, Viton, trifluorochloroethylene resins, fluoroelastomer, polypropylene, polyphenylene oxide, Teflon (PTFE, PFA, FEP), polyvinyl chloride, polycarbonate, polysulfone, acrylonitrile butadiene styrene, polyetherimide, most silicones and fluorinated silicones, ethylene-propylene rubber

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MATERIALS COMPATIBILITY ISSUES

Fading of Anodized Aluminum. To address the issue of fading with some anodized aluminum products, electrocoloring techniques were evaluated. Electrocoloring differs from conventional type II anodization processes in that instead of dyeing the component and then sealing the dye in the porous anodized oxide layer that is electrochemically grown on the aluminum, the part is immersed in a second electrolysis tank following initial clear anodization. The second electrolysis tank typically contains specific metal salts, such as stannous sulfate, for coloring.[7] The coloring effect is believed to be due to the deposit of extremely small crystals or particles, such as metal or oxides, in the pores of the electrolytic oxide film. Such deposits can lead to coloring or shading due to the optical effects of absorption. In repeated testing this type of electrocoloring resists oxidation and bleaching for a minimum of 500 cycles.[8]

Adhesives. Many types and categories of adhesives are used in fabricating medical devices, and the hydrogen peroxide gas plasma system was tested with a variety of adhesives. Many compatible adhesives were identified, as were some mechanisms and guidelines for predicting incompatibility of certain adhesives. A partial list of adhesives that were tested for stability after 500 cycles is shown in Table I.

Adhesive	Type	Rating	Rank
Loctite 363	Modified acrylic; USP VI, medical grade	Excellent compatibility	1
Dymaas 128-M	Urethane acrylate; USP VI, medical grade	Excellent compatibility	1
Dymax 20288 (625-M)	Urethane acrylate; USP VI, medical grade	Excellent compatibility	1
Dymax 136-M	Urethane acrylate; USP VI, medical grade	Excellent compatibility	1
Dymax 197-M	Urethane acrylate; USP VI, medical grade	Excellent compatibility	1
Dymax 186 UV	One-part solid	Excellent compatibility	1

Epotek 353ND	Epoxy (two-part)	Excellent compatibility	1
Epotek 320[a]	Epoxy	Excellent compatibility	1
7520 A/B Urethane,	A/B urethane	Excellent compatibility	1
Dow Corning	Silicone	Good compatibility	2
Devcon 14270	Epoxy	Good compatibility	2
TyRite	Urethane (two-part)	Good compatibility	2
Tra-Con FDA 2T	Epoxy	Good compatibility	2
B2086 Nusil	Silicone (two-part)	Good compatibility	2
Sylgard 186	Silicone (two-part)	Good compatibility	2
GE #103	Silicone, medical grade	Good compatibility	2
DP 105, Clear Epoxy,[a] 3M	Clear epoxy	Good compatibility	2
Araldite PY 302-2[b]	Epoxy (two-part)	Compatible	3
Araldite PY 302-6[b]	Epoxy (two-part)	Compatible	3
Epotek 354[c]	Epoxy (two-part)	Compatible	3
Epotek 314	Epoxy (two-part)	Compatible	3
Epotek 377	Epoxy (two-part)	Compatible	3
Hysol 9340	Epoxy	Compatible	3
Castall 343 A/B	Epoxy (coating)	Compatible	3
Eccobond UV 1190	UV acrylate	Compatible	3
Eccobond 1962-31	Epoxy (one-part)	Compatible	3
Electrolite ELC4M31	UV, medical grade	Compatible	3
Master Bond EP42HT	Epoxy	Compatible	3
Epotek 301	Epoxy (two-part)	Fair compatibility	4
Epotek 302	Epoxy (two-part)	Fair compatibility	4

Epotek 305	Epoxy (two-part)	Fair compatibility	4
Epotek 310	Epoxy (two-part)	Fair compatibility	4
Master Bond EP30HT	Epoxy	Fair compatibility	4
Eccobond 45/15	Epoxy (two-part)	Least compatible	5
Eccobond 45LV	Epoxy (two-part)	Least compatible	5
Stycast 2651	Epoxy (two-part)	Least compatible	5
PRC PR 1422	Polysulfide	Least compatible	5
3M EC 301	Polysulfide	Least compatible	5
Rank 1: No material damage after 200 cycles; no leakage on the fixture after 500 cycles.			
Rank 2: No material damage after 200 cycles; not leak tested; samples received fully cured.			
Rank 3: Minor material changes after 200 cycles; leakage after 100 cycles.			
Rank 4: Material damage after 100 cycles; leakage after 200 cycles.			
Rank 5: Material damage after 60 cycles; leakage after 100 cycles.			
[a] Exception: Adhesives were tested for only 100 cycles, without leak test.			
[b] Exception: Araldite adhesives showed material damage after 200 cycles; no leakage after 500 cycles.			
[c] Epotek 354 was totally debonded; no material deterioration after 200 cycles; no leakage after 500 cycles.			

Table I. A partial list of adhesive compatibility for up to 500 cycles of hydrogen peroxide gas plasma sterilization.

Adhesives that use large proportions of amines as curing or cross-linking agents tended to be incompatible. It was previously reported in the literature that the epoxy matrix of a graphite-epoxy composite deteriorated after lengthy immersion in liquid hydrogen peroxide because of the breaking of amine cross-links securing the polymer network, a breaking that resulted from an attack on secondary and tertiary amine linkages by hydrogen peroxide.[9] This theory was supported by infrared spectroscopy analysis of the epoxy before and after immersion as well as by other work that indicated hydrogen peroxide reacts with secondary and tertiary amines.[10]

ASP's finding that some epoxies were more adversely affected than others in the low-temperature hydrogen peroxide gas plasma system is consistent with these

data. For example, most room temperaturecuring epoxies with approximately a 1:1 ratio of resin- and amine-type curing agents exhibited low compatibility. These epoxies are cross-linked mainly by amine groups.

In contrast, some high-temperature-curing epoxies that use small amounts of catalytic curing agents showed better compatibility. An example was imidazole-cured resins (such as Epotek 353ND or Shell 828 resin with EMI-24 catalyst). Imidazole curing agents cure largely by homopolymerization, with relatively low proportions of curing agent to resin, leading to relatively low levels of amine cross-linkages. Homopolymerization operates through catalytic opening of the epoxy group of the uncured resin, leading to formation of an OH group, which can then react and form a cross-link with an unreacted epoxy group.[11]

Sulfides. Because of the tendency of sulfur-sulfur linkages to react with hydrogen peroxide, some materials containing these linkages—such as certain metal sulfides and organic sulfides—are susceptible to degradation. Some adhesives, such as polysulfides, also degrade due to oxidative attack by sulfur-sulfur linkage, leading to depolymerization and deterioration.[12]

DESIRABLE CHARACTERISTICS FOR COMPATIBILITY WITH HYDROGEN PEROXIDE GAS PLASMA

Considerations and issues for designing devices compatible with sterilization and reuse include materials choice and packaging, component design, application purpose, manufacturing processes, and the user environment.

The primary materials guideline for designing reusable devices is to select materials that are compatible with various sterilization processes. Materials that are good candidates for low-temperature hydrogen peroxide gas plasma sterilization possess hydrophobic character, are chemically stable, and resist oxidation and moisture.

If devices will be sterilized in trays, special design considerations are required because of the trays' large surface area. Devices are typically loaded into trays that have been validated for the process. These trays have been tested to confirm that good sterilization efficacy is achieved through optimal choice of the tray material and design. For example, the hydrogen peroxide gas plasma process, like many other processes, depends heavily on adequate diffusion of sterilant through the load. Therefore, the trays must be designed with sufficient open area and gas pathways to permit unimpeded diffusion. The trays can also be double-wrapped in a nonwoven polypropylene to provide a sterile barrier, allowing the sterilization load, which is completely dry after processing, to remain sterile until use.

For industrial or terminal sterilization, as well as for hospital applications, individual devices can also be separately pouched in heat-sealed Tyvek-mylar pouches, which allow adequate diffusion around the device. Large amounts of paper products or cellulosics cannot be used because they can absorb and immobilize excessive quantities of hydrogen peroxide.

The relative compatibility of various materials with liquid hydrogen peroxide and EtO are tabulated in several reference sources.[13-15] These sources can be used as guides to gaseous hydrogen peroxide compatibility as well, since published information in this area is rather limited.

Component design can also influence materials compatibility. Materials that may not be compatible with the process may remain undamaged if contained within or shielded by another component. However, materials that decompose or catalyze decomposition of hydrogen peroxide, including certain transition elements such as copper, silver, and manganese, should be avoided within sealed areas. If a small amount of hydrogen peroxide is diffused into the enclosed area, high internal pressures may be generated, possibly damaging components.

Similarly, using materials that decompose or absorb hydrogen peroxide is not recommended in diffusion-restricted areas such as lumens or deeply recessed, blind openings due to localized hydrogen peroxide depletion or efficacy considerations. When designing such features for devices, it is best to avoid decomposers—such as silver, copper, and copper alloys—and absorbers, such as polyurethane, nylon, and cellulosics. Noncatalytic, nonabsorbing materials such as PTFE, polyethylene, stainless steel, or low-copper/aluminum alloys are recommended.

Application purpose is another important aspect in designing devices. For example, some materials with only moderate compatibility may be completely adequate in devices intended for a limited number of resterilization cycles.

Material compatibility also can be significantly affected by the manufacturing process, particularly bonding. Selecting compatible adhesives is critical; adhesives such as epoxies, cyanoacrylates, UV curables, and silicones can all be used, although specific formulations can vary in their compatibility.

Joint design influences bond longevity as well, particularly the amount of exposed surface area of the bond relative to the amount of bond material shielded between the adherends. A greater amount of exposed material may shorten the bond life, while more shielded material will extend the life of the joint through multiple cycles.

Proper thermal processing may be another issue. Adhesives that require elevated-temperature cure conditions must be chosen carefully so that other materials used in the device will not be damaged by heat during manufacturing. Thermal annealing and stress relieving can play a major role. For example, some grades of plastics, such as polymethylmethacrylate, acrylonitrile butadiene styrene, and polycarbonate, may be subject to stress cracking after multiple cycles, causing fine surface microcracking, which can affect mechanical strength and optical clarity. However, proper stress relief by thermal annealing can reduce the incidence of these changes.

Other processes may use dry solid lubricants, such as molybdenum disulfide, during component assembly. These lubricants remain in the device and can lead to eventual deterioration. A two-stage mechanism may occur where, in the first stage, small amounts of hydrogen peroxide may diffuse into the part and reach the lubricant. The lubricant reacts with the hydrogen peroxide, oxidizing the sulfur and leading to sulfuric or sulfurous acidic residue formation. The second stage occurs when the acidic residues attack materials, such as plastics and adhesives, from within the device, leading to eventual weakening and leakage.

In addition to purely materials issues, effects on appearance should be considered. As mentioned previously, type II anodized aluminum with a black organic dye is often used in medical devices. Typically the dye oxidizes or bleaches within a few cycles, fading the black anodized coating almost colorless. Fading can be prevented

by using an electrocoloring or two-step anodization process, which resists bleaching because the dark color is obtained from internal metal oxide deposits in the anodization layer and not from an organic dye. This type of process is most commonly used in architectural applications on the exterior of buildings, where it resists fading and bleaching from oxidation and UV exposure.

CONCLUSION

New sterilization processes such as low-temperature hydrogen peroxide gas plasma are generally compatible with most of the materials used in medical devices. However, many of these new sterilization techniques use oxidizing agents like hydrogen peroxide, ozone, peracetic acid, and chlorine dioxide, which can damage cell walls and membranes as well as affect genetic material and other systems.[16] As always, manufacturers should use care in selecting materials and designing components and devices, remaining aware of how materials may interact with various sterilizing processes. This concern with compatibility will, in turn, ensure longer life cycles and better cost-effectiveness for users in today's managed-care market.

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