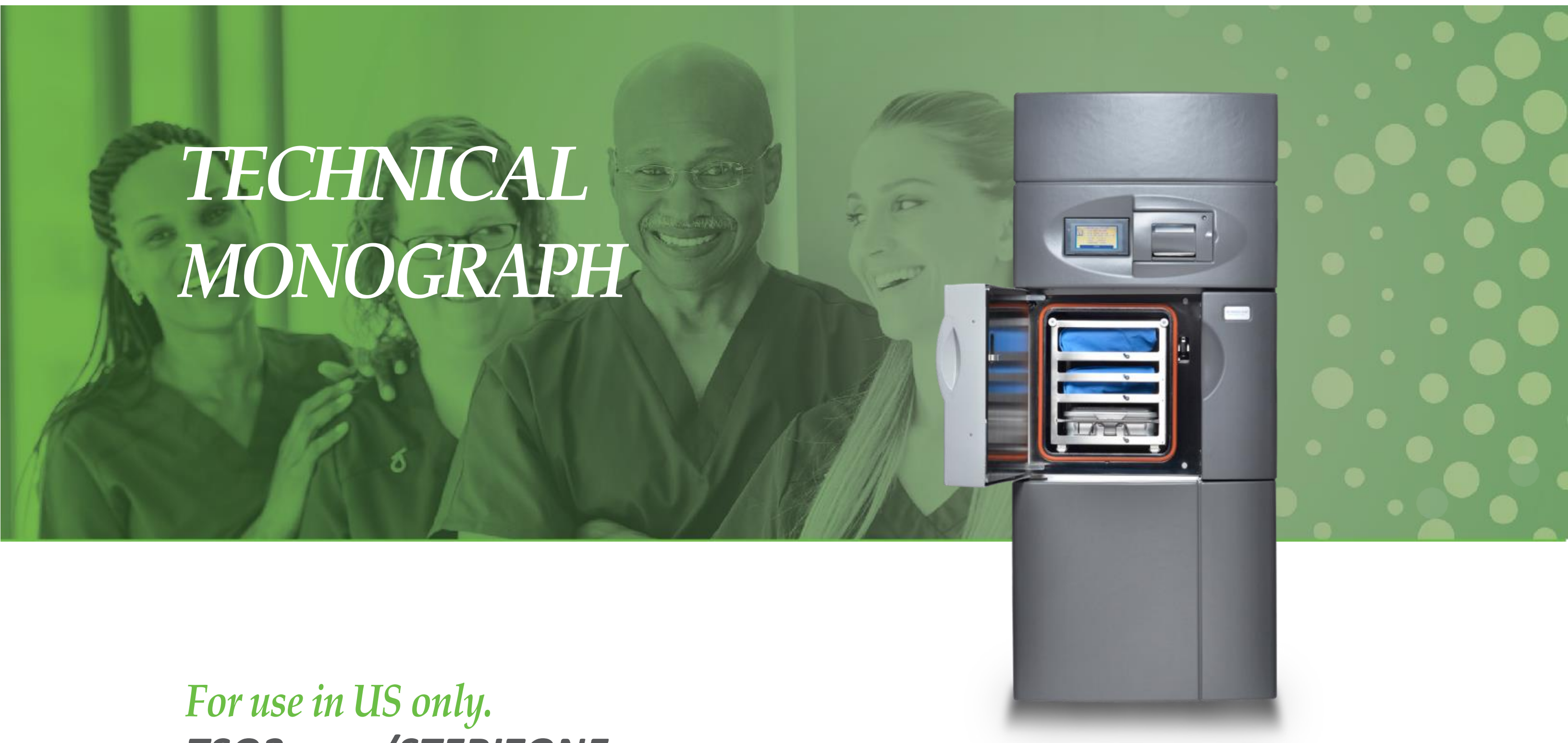
TECHNICAL MONOGRAPH



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OUR MISSION: A STERILE DEVICE FOR EVERY PATIENT.

The STERIZONE VP4 Sterilizer is patented in the US under US Pat. 9,101,679; 9,474,815; 9,480,763; 9,480,765 and 9,814,795. Other patent applications pending. Corresponding patents granted or pending in other countries.

This monograph references device claims only approved for use in the United States of America as of the date of the publication (April 2018).

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1.0 INTRODUCTION

The STERIZONE VP4 Sterilizer currently offers a single preset sterilization cycle (Cycle 1) designed for the sterilization of a wide variety of loads consisting of general instruments, single, double or multi-channel flexible endoscopes, and rigid and semi-rigid channeled devices including single channel and double channel rigid endoscopes.

The STERIZONE VP4 Sterilizer uses dual sterilants, vaporized hydrogen peroxide (H_2O_2) and ozone (O_3), in a multiphase process, and is the only dual-sterilant sterilizer cleared for use in the United States.

After a preconditioning step, the first cycle phase is initiated with the Dynamic H_2O_2 exposure step. During this step, a 50 weight-percent hydrogen peroxide solution (referred to as *125-280 Solution*™) is injected at a fixed injection rate in vapor form into the sterilization chamber. The patented micro-pulsed injection (referred to as *Dynamic Sterilant Injection System*™) continues until a differential pressure set point of 19 Torr is reached. The total amount of hydrogen peroxide introduced into the sterilization chamber, and thus the duration of the injection, varies depending on load composition, weight and temperature. Thus, the STERIZONE VP4 Sterilizer is the first sterilizer to automatically vary the amount of sterilant based on the load, which is why a single-cycle can be used to sterilize a wide variety of different loads.

The ozone used in the process is generated within the sterilizer using oxygen (e.g. 94% O_2 or greater). Oxygen required by the sterilizer can be supplied by connecting directly to the hospital's existing oxygen network, an oxygen concentrator or a portable oxygen cylinder.

After injection of hydrogen peroxide into the chamber, a set concentration of ozone is injected, which reacts with residual hydrogen peroxide to form hydroxyl radicals. The formation of hydroxyl radicals further enhances the overall lethality of the process.

The STERIZONE VP4 Sterilizer produces no toxic residues, thereby reducing risks to workers and potential patient health concerns. A user manual is provided and users must read, understand and follow the instructions provided in the manual.

This Technical Monograph illustrates the principles of operation and demonstrates the safety and efficacy of the STERIZONE VP4 Sterilizer. The summary of the test data for microbicidal efficacy, material compatibility, and biocompatibility testing performed on the STERIZONE VP4 Sterilizer is included.

1.1. Single Sterilization Cycle

The single pre-set cycle of the STERIZONE VP4 Sterilizer (Cycle 1) uses dual sterilants: hydrogen peroxide and ozone. The injection of vaporized hydrogen peroxide is followed by the injection of ozone, which reacts with residual hydrogen peroxide to form hydroxyl radicals, which adds to the overall lethality of the process.

Sterilization efficacy was demonstrated using a representative sample of one or more device types and packaging, in nine separate validation loads, as described in Table 1. The load to be processed should be maintained between 20°C to 26°C (68°F to 78°F). The total load weight shall not exceed 75 lb, inclusive of the containers/packaging weight but excluding the 25 lb loading rack.

Table 1. Description of the nine validation loads

Validation load #	Load description	Load weight[1]
1	Validation load #1 consisted of general medical instruments, representing the following geometries: • Clamp • Serrated surface • Box-lock • Handle • Button • Pivot hinge • Stopcock Type of packaging used: wrapped plastic tray, including silicone mats and brackets, and Pouch General medical instruments were spread out over three trays, six pouches and one wrapped instrument.	11 lb
2	Validation load #2 consisted of general medical instruments, representing the following geometries: • Gliding mechanism • Hinges and screws • Serrated surface • Luer-Lok™ • Spring • Rigid nonlumen scopes Type of packaging used: wrapped plastic and aluminum tray, including silicone mats and brackets, rigid aluminum container and pouch. General medical instruments were spread out over one container, three trays, and six pouches.	20 lb
3	Validation load #3 consisted of **three** single channel flexible endoscopes (ureteroscope) with inside diameter of 1.0 mm and length of 850 mm, packaged individually in wrapped trays or containers, including appropriate silicone brackets or mats. Eight general medical instruments, each packaged in a pouch, were added.	23 lb

Validation load #	Load description	Load weight[1]
4	Validation load #4 consisted of up to **15** rigid or semi-rigid channeled instruments in the presence of other packaged medical devices. Three double channel semi-rigid endoscopes (ureteroscope – 0.7 mm × 500 mm and 1.1 mm × 500 mm) were packaged individually in wrapped trays or containers including appropriate silicone brackets or mats. Additional rigid channeled instruments or stainless steel rigid lumens were added to each package. Two additional general medical instruments, each packaged in a pouch, were added.	19 lb
5	Validation load #5 consisted in **two** single channel flexible endoscopes; one ureteroscope with inside diameter of 1.0 mm and length of 850 mm, and a bronchoscope with inside diameter of 1.8 mm and length of 830 mm, and **one** double channel semi- rigid endoscope (ureteroscope – 0.7 mm × 500 mm and 1.1 mm × 500 mm), packaged individually in wrapped trays or containers including appropriate silicone brackets or mats. No additional item was added.	21 lb
6	Validation load #6 consisted of general medical instruments, representing the following geometries: • Distal end (swivel parts) • Hinge with screw • Cannula General medical instruments packaged in one aluminum sterilization container.	9 lb
7	Validation load #7 consisted of general medical instruments, representing the following geometries: • Box-lock hinge • Pivot hinge • Luer-Lok™ General medical instruments, spread out over three aluminum sterilization containers, each weighting 25 lb.	75 lb
8	Validation load #8 consisted of **two double channel** flexible endoscopes (ureteroscope) with inside diameter of 1 mm and lengths of 850 and 989 mm; and **one single channel** flexible endoscope (ureteroscope) with inside diameter of 1 mm and length of 850 mm, packaged individually in wrapped plastic sterilization trays, including appropriate silicone brackets or mats.	16 lb
9	Validation load #9 consisted of **one multi-channel** flexible endoscope (Video colonoscope), with no more than 4 channels (such as working, air, water, etc.,) excluding umbilical tubes, with inside diameters of 1.2 or more and lengths of 1955 mm or less, or 1.45 or more and lengths of 3500 mm or less; packaged in aluminium sterilization container.	17 lb

[1]Excluding the 25 lb loading rack

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1.2. Components

The following components are part of the STERIZONE VP4 Sterilizer system:

- STERIZONE VP4 Sterilizer
- STERIZONE Loading Rack
- 125-280 Solution
- STERIZONE BI+ Self-contained Biological Indicator
- STERIZONE CI+ Chemical Indicator
- STERIZONE VP4 Test Pack

2.0 STERIZONE VP4 STERILIZER MODE OF OPERATION

Prior to sterilization, cleaned and dried instruments are packaged using either aluminum containers compatible with hydrogen peroxide in combination with disposable polypropylene filters, and either wrapped trays or heat-sealable nonwoven, polyethylene sterilization pouches.

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The STERIZONE VP4 Sterilizer uses dual sterilants, vaporized hydrogen peroxide (H_2O_2) and ozone (O_3), in a multiphase process.

Upon loading the medical devices into the sterilization chamber and closure of the door, the chamber is subjected to a vacuum of 1 Torr (referred to as preconditioning step). The first cycle phase (Phase 1) is initiated with the Dynamic H_2O_2 exposure step. During this step, a 50 weight-percent hydrogen peroxide solution (referred to as 125-280 Solution) is injected at a fixed injection rate in vapor form into the sterilization chamber through a continuous micro-pulsed injection until a differential pressure set point of 19 Torr is reached (i.e., the actual chamber pressure is 20 Torr, less the initial vacuum of 1 Torr, which is equivalent to a "differential pressure" or "ΔP" of 19 Torr). The total amount of hydrogen peroxide introduced into the sterilization chamber and thus the duration of the injection varies depending on load composition (e.g. surface area), weight and temperature.

The second step of the cycle phase is the H_2O_2 Reduction Step. During this step, a set concentration of ozone is injected into the chamber, which reacts with residual hydrogen peroxide to form hydroxyl radicals, further enhancing lethality.

During the second cycle phase (Phase 2), the same sequence is repeated, including the Dynamic H_2O_2 exposure and H_2O_2 reduction steps. The full cycle (Figure 1) is then completed with an evacuation and ventilation, through a catalytic converter, to the atmosphere, at which point the chamber door can be safely opened.

The cycle process parameters are summarized in Table 2.

Table 2. STERIZONE VP4 Sterilizer – Cycle process parameters

Hydrogen peroxide exposure					Ozone exposure		Nb of phases
Hydrogen peroxide solution	Chamber differential pressure set point	Time	Sterilant injected	Vaporizer / Chamber temperature	O_3 injection	O_3 dwell	
125-280 Solution (H_2O_2 50 wt%)	19 Torr	210-600 sec*	8.4-24 g*	120°C / 41 ± 3°C	2 mg/L	5 min	2

* Vaporized hydrogen peroxide injection/exposure time (Dynamic H_2O_2 exposure step) varies with load composition and conditions. The quantity of vaporized hydrogen peroxide injected is directly related to the time required to reach a pressure differential of 19 Torr in the chamber, for load temperature ranging from 20°C to 26°C. If the H_2O_2 injection time is less than 210 seconds, or greater than 600 seconds, the cycle will abort.

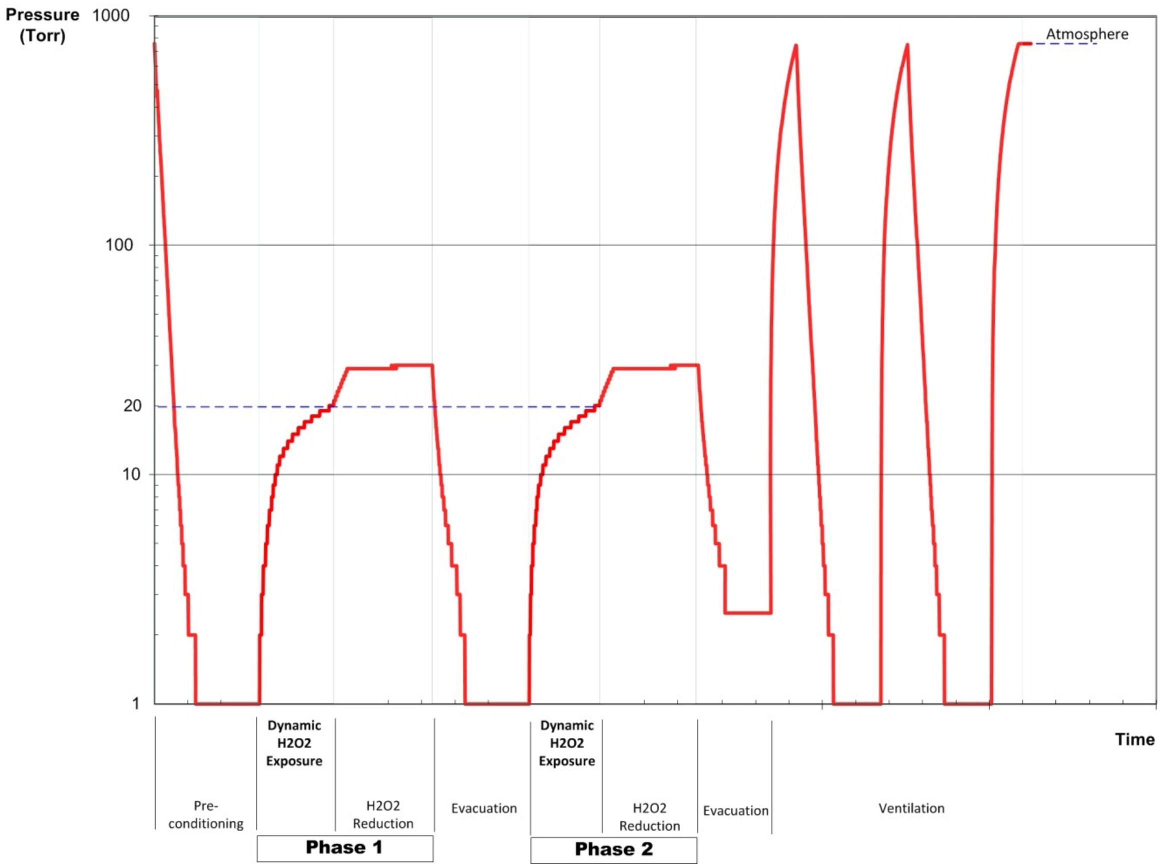


Figure 1. Cycle 1 graph

3.0 MONITORING OF THE PROCESS

3.1. Sterilizer Control

The STERIZONE VP4 Sterilizer is fully controlled by a programmable logic controller (PLC). The software has been developed to monitor the critical performance parameters of the sterilization process and to confirm that the equipment is functioning correctly.

All critical process parameters are monitored during the cycle. At the end of each cycle step, the process parameters are printed on the screen of the sterilizer. At the end of the overall cycle, the screen will indicate "Cycle Completed" and a paper printout will be produced. During the sterilization cycle, if one of the critical process parameters is not reached, the cycle will abort and the reason for the interruption will be displayed on the screen and on the printout.

3.2. Load Control

The STERIZONE VP4 Sterilizer provides cycle printouts for verification of critical performance parameters. The user can enter a load and an identification number prior to starting a cycle. At the end of the printout, space is provided for the user's initials or signature.

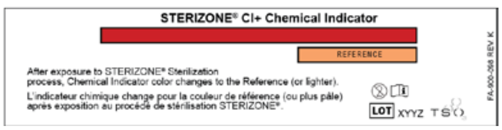
The STERIZONE VP4 Test Pack uses a biological indicator (the STERIZONE BI+ Self-contained Biological Indicator) inserted into a diffusion-restricted container (Figure 2). It is recommended to be used at least once a day or in every sterilization load, to monitor and release loads.

Figure 2. STERIZONE VP4 Test Pack

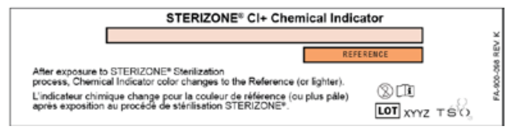
The STERIZONE VP4 Test Pack has equivalent to or greater resistance than the worst-case devices and loads in any load configuration, and is designed to be more resistant than the half-cycle, including exposure to hydrogen peroxide and ozone.

3.3. Packaging Control

The STERIZONE CI+ Chemical Indicator is a Class 1 process indicator intended to distinguish between processed and unprocessed packaged medical devices to be sterilized using the STERIZONE VP4 Sterilizer (Figure 3). The indicator strips are designed to be easily inserted into the sterilization pouches or trays. The indicator works by means of a chemical reaction, which results in a recognizable color change from red to peach (or lighter).



Unprocessed Chemical Indicator



Processed Chemical Indicator

Figure 3. STERIZONE CI+ Chemical Indicator

4.0 MICROBIAL EFFECTIVENESS

The microbial efficacy of the STERIZONE VP4 Sterilizer is established by demonstrating that the process can:

1. Provide, by established validation methods, a Sterility Assurance Level (SAL) of 10^{-6} with *G. stearothermophilus* spores.
2. Pass the AOAC Sporicidal Test, as defined by the American Association of Official Analytical Chemists.
3. Sterilize medical instruments under simulated-use conditions.
4. Sterilize medical instruments that were used and reprocessed in a hospital (referred to as "in-use tests").
5. Sterilize devices with long, narrow lumens.

4.1. Demonstration of 10^{-6} Sterility Assurance Level (SAL)

A half-cycle approach (commonly referred to as "overkill"), described in ISO 14937:2009, was used to demonstrate a SAL of 10^{-6} for the STERIZONE VP4 Sterilizer. Tests were performed by inoculating actual medical devices with an initial concentration of at least 10^{6} CFU (Colony Forming Units) of the most resistant microorganism.

4.1.1. Selection of the most resistant microorganism

Geobacillus stearothermophilus spore has been recognized as the most resistant microorganism to oxidative sterilization processes such as hydrogen peroxide and ozone, and is recommended to be used as the strain for the biological indicator (Chaunet, 2007; Smith, 2008; STERIS®, 2008). It was demonstrated that *G. stearothermophilus* spores are far more resistant to sterilization processes than viruses (lipid and nonlipid), fungi or mycobacteria, and other vegetative spores and spores forming bacteria.

In addition, the US Food and Drug Administration (FDA) recommends the use of *G. stearothermophilus* as a biological indicator for a hydrogen peroxide process in their 2007 “Guidance for Industry and FDA Staff - Biological Indicator Premarket Notification 510(k) Submission,” and that same microorganism was cleared as the appropriate species to be used for the biological monitoring of ozone sterilization. Thus, *G. stearothermophilus* spores were identified as the most resistant organism and therefore, were used to perform the SAL^{-6} demonstration and the other microbial efficacy tests.

4.1.2. Load composition

The SAL^{-6} demonstration was performed using a series of validation loads, with a wide variety of different devices requiring sterilization. Representative devices were then selected to represent a challenge in terms of configuration and construction materials.

Validation loads were selected based on the maximum load consistent with the capacity of the chamber. Furthermore, each validation load represented a variety of different devices (i.e., mixed loads) using typical packaging (pouches, containers, and wrapping).

Nine validation loads were assembled to include devices as described in Table 1:

- Two loads of general instruments representing the most challenging device configurations such as gliding mechanisms, hinges and screws, stopcocks, clamps, serrated surfaces, Luer-Lok™, and springs were assembled. Each load was composed of at least 10 packages: containers, wrapped trays and/or pouches for a total weight of 11 lb and 20 lb respectively.
- Three loads for flexible endoscopes: One load composed of three individually packaged single channel flexible endoscopes, with eight additional instruments in pouches, for a total weight of 23 lb. One load composed of two double channel flexible endoscopes and one single channel flexible endoscope packaged individually in wrapped plastic sterilization trays, including appropriate silicone brackets or mats for a total weight of 16 lb. And one load composed of one multi-channel endoscope containing a maximum of four channels (such as working, suction, air, water, etc., excluding the umbilical cord tubes) packaged in a container for a total weight of 17 lb.
- One load composed of three packages containing each one double channel semi-rigid endoscopes and several other larger rigid channel instruments. In addition, two stainless steel lumens were packaged in pouches for a total of 15 channels per load and a total weight of 19 lb.
- One mixed load composed of one double channel rigid ureteroscope and two flexible endoscopes, packaged individually, for a total weight of 21 lb.
- Two loads representing the maximum weight range: a light weight load of 9 lb and a heavy weight load of 75 lb. The heavy weight load was composed of three containers of 25 lb each.

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The type and quantity of instruments included in the validation loads highlights the utility of the STERIZONE VP4 Sterilizer. It is the only sterilization process using hydrogen peroxide that can sterilize three flexible endoscopes in a single load, particularly with additional medical devices (Figure 4), or sterilize semi-rigid endoscopes and flexible endoscopes in the same load. The STERIZONE VP4 Sterilizer is also the only low temperature sterilizer using hydrogen peroxide capable of processing load weights of up to 75 lb.

Figure 4. Validation load #3: three single channel flexible endoscopes with additional general medical devices

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4.1.3. Exposure conditions (Half-cycle definition)

Tests were performed by inoculating actual medical instruments with an initial concentration of at least 10^6 CFU of the *G. stearothermophilus* spores and left to dry overnight. The inoculated medical instruments were placed in the validation loads.

The required load temperature to be processed in the STERIZONE VP4 Sterilizer is 20°C to 26°C. All validation loads were preconditioned at 26°C prior to be processed in the sterilizer, since this temperature was determined as the worst load condition for sterile efficacy testing (shortest Dynamic H_2O_2 exposure step duration and lowest injected mass of 125-280 Solution™).

For half-cycle sterility testing of loads #1 to #8, the half-cycle was defined as the exposure to the Dynamic H_2O_2 exposure step of Phase 1 only (i.e., without the addition of ozone). For load #9, the half-cycle was defined as the complete Phase 1 (Dynamic H_2O_2 exposure and H_2O_2 reduction steps i.e. with the addition of ozone). Each validation load was tested in triplicate.

After exposure, each inoculated site was sampled and tested for sterility. A summary of the results is presented in Table 3 to Table 10. The number of sterile instruments or inoculated sites has been determined and compared to the number of instruments or sites tested. All medical instruments were sterile under half-cycle testing.

Table 3. Half-cycle validation results for general instruments (loads #1 and #2)

Instrument name	Inoculation site	Number sterile/ Number tested
Camera (head)	Handle	3/3
	ON/OFF button	3/3
Battery pack	One side	3/3
Kelly hemostats A (Open position)	Clamp (both sides)	3/3
Kelly hemostats B (Open position)	Serrated surface (both sides)	3/3
Mayo scissors (Open position)	Pivot hinge	3/3
Crile hemostats (Open position)	Box-lock hinge	3/3
Electrophysiology cable	Patient lead connector	3/3
Cystoscope stopcock	Pivot mechanism	3/3
Defibrillator handles	Handle	3/3
Internal defibrillator paddles (2)	One black side of the paddle spoon	3/3
Reuter tip deflecting handle	Open screw	3/3
	Closed screw	3/3
Stryker System 6 (drill)	Cannula (5.0 mm x 12 cm)	3/3
Stryker System 6 (drill attachment)	Drill bit mechanism (jaws)	3/3
Stryker System 6 (wire collet)	Cannula (0.7/1.8 mm × 9.0 cm)	3/3
Bulldog clamp	Spring (basis of the spring)	3/3
Forceps micro cup end	Distal end only (cup)	3/3
Rongeur punch A (Kerrison)	Hinge with screw	3/3
Rongeur punch B (Kerrison)	Gliding mechanism	3/3
Resectoscope sheath	Locking bridge mechanism	3/3
Haemorrhoidal ligator	Distal end (swivel parts)	3/3
Fiberoptic lightcable	10 cm^2 of cord	3/3
Rigid telescope (no lumen)	Distal end (lens + 2 cm^2 distal tip)	3/3
	Proximal lens (lens only)	3/3
	Eyepiece (surface)	3/3
Syringe (unlock)	Luer-Lok™	3/3

Table 4. Half-cycle validation results for short single channel flexible endoscopes (load #3)

Instrument name	Inoculation site	Number sterile/ Number tested
Flexible ureteroscope	Channel: 1 mm × 850 mm	9/9

Table 5. Half-cycle validation results for semi-rigid or rigid endoscope (load #4)

Instrument name	Inoculation site	Number sterile/ Number tested
Semi-rigid ureteroscope	Channel: 0.7 mm × 500 mm	9/9
	Channel: 1.0 mm × 500 mm	9/9
Stainless steel tubing	Channel: 2.0 mm × 575 mm	6/6
Resectoscope (working element)	Channel: 2.2 mm × 173 mm	3/3
	Channel: 4.7 mm × 270 mm	3/3
Rotary resectoscope with irrigation	Channel: 7.0 mm × 227 mm	3/3
	Channel: 7.8 mm × 198 mm	3/3
Thoracoscope	Channel: 4.0 mm × 370 mm	3/3
Trocar	Channel: 5.5 mm × 166 mm	3/3
	Channel: 7.0 mm × 105 mm	3/3
Cystourethroscope short bridge double-horn	Pivot mechanism	3/3

Table 6. Half-cycle validation results for the mixed load (load #5)

Instrument name	Inoculation site	Number sterile/ Number tested
Flexible ureteroscope	Channel: 1 mm × 850 mm	3/3
Semi-rigid ureteroscope	Channel: 0.7 mm × 500 mm	3/3
	Channel: 1.0 mm × 500 mm	3/3
Flexible bronchoscope	Channel:1.8 mm × 830 mm	3/3

Table 7. Half-cycle validation results for the light weight load evaluation (Load #6)

Instrument name	Inoculation site	Number sterile/ Number tested
Haemorrhoidal ligator	Distal end (swivel parts)	3/3
Rongeur punch A (Kerrison)	Hinge with screw	3/3
Stryker System 6 (wire collet)	Cannula (0.7/1.8 mm × 9.0 cm)	3/3

Table 8. Half-cycle validation results for the heavy weight load evaluation (load #7)

Instrument name	Inoculation site	Number sterile/ Number tested
Mayo scissors	Pivot hinge	9/9
Crile hemostats	Box-lock hinge	9/9
Syringe (unlock)	Luer-lock	9/9

Table 9. Half-cycle validation results for short single and double channel flexible endoscopes (load #8)

Instrument name	Inoculation site	Number sterile/ Number tested
Flexible single channel ureteroscope	Channel: 1 mm × 850 mm	3/3
Flexible double channel ureteroscope	Channel: 1 mm × 850 mm	6/6
	Channel: 1 mm × 989 mm	6/6

Table 10. Half-cycle validation results for multi-channel flexible endoscope (load #9)

Channel name	channel dimension	Number sterile/ Number tested
Working (distal end to instrument channel inlet)	3.8 mm × 1840 mm	3/3
Working (instrument channel inlet to suction valve)	3.8 mm × 130 mm	3/3
Suction	3.9 mm × 1580 mm	3/3
Air: distal end to the air/water valve	1.2 mm × 1955 mm	3/3
Air: umbilical	2.35 mm × 1580 mm	3/3
Water: distal end to the air/water valve	1.2 mm × 1955 mm	3/3
Water: umbilical	2.35 mm × 1580 mm	3/3
Water jet channel	1.45 mm × 3500 mm	3/3

No positives were obtained after device exposure to the first half-cycle, which is consistent with a 6-log reduction in microorganisms. Devices tested included general instruments with challenging configurations including serrated surfaces, clamps, stopcocks, hinges and screws, gliding mechanisms, Luer-Lok™, springs, instruments with rigid lumens, and rigid nonlumen scopes.

This demonstration has also been achieved for single, double, and multi-channels flexible endoscopes as well as single and double channel rigid endoscopes as summarized in Table 11.

Table 11. Summary of the extended claims for flexible and rigid endoscopes that can be processed in Cycle 1 of the STERIZONE VP4 Sterilizer

		Inside diameter	Length
Cycle 1	Single and double channel flexible endoscopes [1]	≥ 1 mm	≤ 989 mm
	Multi-channel flexible endoscopes [2]	≥ 1.2 mm	≤ 1955 mm
		≥ 1.45 mm	≤ 3500 mm
	Rigid channel devices including single channel and double rigid channel endoscopes [3]	≥ 0.7 mm	≤ 500 mm
		≥ 2.0 mm	≤ 575 mm

[1] Sterilization efficacy of Cycle 1 was demonstrated for a load comprising of up to three packaged single channel flexible endoscopes or two double channels and one single channel flexible endoscope per load, for a total of five channels.

[2] Sterilization efficacy of Cycle 1 was demonstrated for a load comprising of one multi-channel flexible endoscope packaged in a compatible container placed on the lower shelf of the loading rack without any additional load, up to four channels per endoscope (such as working, air, water, etc. excluding the umbilical cord tubes). A single channel is defined as any lumen in between two openings; for example, the air channel from the distal end to the air/water valve is one channel.

[3] Sterilization efficacy of Cycle 1 was demonstrated for a load comprising of up to 15 rigid channels in the presence of other packaged medical devices.

4.2. AOAC Sporicidal Test

The AOAC Sporicidal Screening Test, as defined by the American Association of Official Analytical Chemists, was conducted to confirm the sporicidal effectiveness of the chemical sterilant to sterilize different types of porous carriers contaminated with resistant aerobic and anaerobic spores in the presence of organic soil and inorganic salts. The test stipulates that no failures can be tolerated over 720 inoculated carriers.

The results of this study, as shown in Table 12, show that no growth was obtained for all AOAC inoculated carriers exposed to a complete cycle in the STERIZONE VP4 Sterilizer for more than three sterilant lots.

Table 12. AOAC Sporicidal Screening Test Results with the STERIZONE VP4 Sterilizer

Carriers	Number of positive/Number tested	
	B. subtilis	***C. sporogenes***
Validation test		
Penicylinders	0/180	0/180
Dacron suture loops	0/180	0/180
Confirmatory test		
Penicylinders	0/30	0/30
Dacron suture loops	0/30	0/30

Based on the results obtained during the validation and testing of the AOAC sporicidal activity, the conditions found in the STERIZONE VP4 Sterilizer meet the requirements of the Official Methods of Analysis of AOAC International to qualify as a sterilant.

4.3. Simulated-use Tests

Once the process parameters were established to achieve an SAL of 10^{-6}, the effectiveness of the process was confirmed by simulated-use tests. The same medical instruments used for determining the effectiveness of the SAL^{-6} (half-cycle study) were tested under worst-case, simulated-use conditions.

Tests were performed by directly inoculating actual medical instruments with an initial concentration of at least 10^6 CFU of the *G. stearothermophilus* spores mixed with 5% foetal bovine serum and 300 to 400 ppm hard water and left to dry overnight. The inoculated medical instruments were placed in the validation loads and exposed to Cycle 1. Each validation load was tested in triplicate.

After exposure, each inoculated site was sampled and tested for sterility. A summary of the results is presented in Table 13 to Table 20. The number of sterile instruments or inoculated sites compared to the number of instruments or sites tested was determined. All instruments were sterile under worst-case simulated-use conditions.

Table 13. Simulated-use validation results for general instruments (loads #1 and #2)

Instrument name	Inoculation site	Number sterile/ Number tested
Camera (head)	Handle	3/3
	ON/OFF button	3/3
Battery pack	One side	3/3
Kelly hemostats A (Open position)	Clamp (both sides)	3/3
Kelly hemostats B (Open position)	Serrated surface (both sides)	3/3
Mayo scissors (Open position)	Pivot hinge	3/3
Crile hemostats (Open position)	Box-lock hinge	3/3
Electrophysiology cable	Patient lead connector	3/3
Cystoscope stopcock	Pivot mechanism	3/3
Defibrillator handles	Handle	3/3
Internal defibrillator paddles (2)	One black side of the paddle spoon	3/3
Reuter tip deflecting handle	Open screw	3/3
	Closed screw	3/3
Stryker System 6 (drill)	Cannula (5.0 mm x 12 cm)	3/3
Stryker System 6 (drill attachment)	Drill bit mechanism (jaws)	3/3
Stryker System 6 (wire collet)	Cannula (0.7/1.8 mm × 9.0 cm)	3/3
Bulldog clamp	Spring (basis of the spring)	3/3
Forceps micro cup end	Distal end only (cup)	3/3
Rongeur punch A (Kerrison)	Hinge with screw	3/3
Rongeur punch B (Kerrison)	Gliding mechanism	3/3
Resectoscope sheath	Locking bridge mechanism	3/3
Haemorrhoidal ligator	Distal end (swivel parts)	3/3
Fiberoptic lightcable	10 cm^2 of cord	3/3
Rigid telescope (no lumen)	Distal end (lens + 2 cm^2 distal tip)	3/3
	Proximal lens (lens only)	3/3
	Eyepiece (surface)	3/3
Syringe (unlock)	Luer-Lok™	3/3

Table 14. Simulated-use validation results for short single channel flexible endoscopes (load #3)

Instrument name	Inoculation site	Number sterile/ Number tested
Flexible ureteroscope	Channel: 1 mm × 850 mm	9/9

Table 15. Simulated-use validation results for semi-rigid or rigid endoscope (load #4)

Instrument name	Inoculation site	Number sterile/ Number tested
Semi-rigid ureteroscope	Channel: 0.7 mm × 500 mm	9/9
	Channel: 1.0 mm × 500 mm	9/9
Stainless steel tubing	Channel: 2.0 mm × 575 mm	6/6
Resectoscope (working element)	Channel: 2.2 mm × 173 mm	3/3
	Channel: 4.7 mm × 270 mm	3/3
Rotary resectoscope with irrigation	Channel: 7.0 mm × 227 mm	3/3
	Channel: 7.8 mm × 198 mm	3/3
Thoracoscope	Channel: 4.0 mm × 370 mm	3/3
Trocar	Channel: 5.5 mm × 166 mm	3/3
	Channel: 7.0 mm × 105 mm	3/3
Cystourethroscope short bridge double-horn	Pivot mechanism	3/3

Table 16. Simulated-use validation results for the mixed load (load #5)

Instrument name	Inoculation site	Number sterile/ Number tested
Flexible ureteroscope	Channel: 1 mm × 850 mm	3/3
Semi-rigid ureteroscope	Channel: 0.7 mm × 500 mm	3/3
	Channel: 1.0 mm × 500 mm	3/3
Flexible bronchoscope	Channel:1.8 mm × 830 mm	3/3

Table 17. Simulated-use validation results for the light weight load evaluation (Load #6)

Instrument name	Inoculation site	Number sterile/ Number tested
Haemorrhoidal ligator	Distal end (swivel parts)	3/3
Rongeur punch A (Kerrison)	Hinge with screw	3/3
Stryker System 6 (wire collet)	Cannula (0.7/1.8 mm × 9.0 cm)	3/3

Table 18. Simulated-use validation results for the heavy weight load evaluation (Load #7)

Instrument name	Inoculation site	Number sterile/ Number tested
Mayo scissors	Pivot hinge	9/9
Crile hemostats	Box-lock hinge	9/9
Syringe (unlock)	Luer-Lok™	9/9

Table 19. Simulated-use validation results for short single and double channel flexible endoscopes (load #8)

Instrument name	Inoculation site	Number sterile/ Number tested
Flexible single channel ureteroscope	Channel: 1 mm × 850 mm	3/3
Flexible double channel ureteroscope	Channel: 1 mm × 850 mm	6/6
	Channel: 1 mm × 989 mm	6/6

Table 20. Simulated-use validation results for multi-channel flexible endoscopes (colonoscope) (load #9)

Channel name	Channel dimension	Number sterile/ Number tested
Working (distal end to instrument channel inlet)	3.8 mm × 1840 mm	3/3
Working (instrument channel inlet to suction valve)	3.8 mm × 130 mm	3/3
Suction	3.9 mm × 1580 mm	3/3
Air: distal end to the air/water valve	1.2 mm × 1955 mm	3/3
Air: umbilical	2.35 mm × 1580 mm	3/3
Water: distal end to the air/water valve	1.2 mm × 1955 mm	3/3
Water: umbilical	2.35 mm × 1580 mm	3/3
Water jet channel	1.45 mm × 3500 mm	3/3

Data confirm that the STERIZONE VP4 Sterilizer reproducibly and repeatedly sterilizes challenging medical instruments under worst-case simulated-use conditions.

4.3.1. Material study

The goal of the Material study was to verify that common materials used in medical devices could be sterilized in the STERIZONE VP4 Sterilizer. To do so, material samples (coupons) were inoculated with at least 10^6 CFU of the *G. stearothermophilus* spores mixed with 5% foetal bovine serum and 300 ppm hard water and left to dry overnight. The inoculated and dried material coupons were placed inside packaging of a validation load and exposed to the sterilization cycle in triplicate.

Simulated-use tests performed on inoculated material samples have demonstrated the ability of the STERIZONE VP4 Sterilizer to sterilize a wide range of materials (Table 21).

Table 21. Test results for the simulated-use on material coupons

Materials	Number sterile/Number tested
Anodized aluminum	3/3
Brass	3/3
Fluoroelastomer	3/3
Liquid crystal polymer	3/3
Polyamide	3/3
Polycarbonate	3/3
Polydimethylsiloxane	3/3
Polyetheretherketone	3/3
Polyetherimide	3/3
Polyethylene	3/3
Polymethylmethacrylate	3/3
Polyoxymethylene	3/3
Polyphenyleneoxide	3/3
Polyphenylsulfone	3/3
Polypropylene	3/3
Polystyrene	3/3
Polytetrafluoroethylene	3/3
Polyurethane	3/3
Polyvinylchloride	3/3
Stainless steel	3/3
Titanium	3/3

Simulated-use tests performed on inoculated material samples demonstrate the ability of the STERIZONE VP4 Sterilizer to successfully sterilize all materials commonly used to manufacture reusable medical devices.

4.4. In-use tests (Hospital study)

Instrument sterilization plays a key role in the reduction of transmission of nosocomial infection. Understanding the factors that can interfere with the sterilization process and device reprocessing is crucial to prevent infection. Consequently, in-use tests were performed on previously used medical instruments, then cleaned and lubricated by hospital personnel in accordance with standardized protocols. Instruments were selected on the basis of materials and overall sterilization challenge. All devices were packaged and sterilized in the STERIZONE VP4 Sterilizer in accordance with each manufacturer guidelines.

After sterilization, sterility testing on one or two sites on each instrument was performed. Hinges, lock mechanisms, handles, distal ends (serrated surfaces), sliding systems, and lumens are some examples of the site selections. Survival of aerobic and anaerobic bacteria, yeast and fungi was evaluated.

No surviving organisms were found on the instruments listed in Table 22.

Table 22. STERIZONE VP4 Sterilizer Cycle 1 in-use validation results

Medical instruments	Selected site	Number sterile/ Number tested
Surgical scissors	Hinge	3/3
Towel forceps	Clamp	3/3
Trocar	Stopcock	3/3
	6 mm ID × 65 mm length lumen	3/3
Fiberoptic light cable	Cord	3/3
Telescope	Ocular	3/3
	Distal Lens	3/3
Suction	3 mm ID × 140 mm length lumen	3/3
Flexible ureteroscope	1.0 mm ID × 850 mm length lumen	3/3
Flexible cystoscope	2.2 mm ID × 510 mm length lumen	3/3
Flexible bronchoscope	1.8 mm ID × 830 mm length lumen	3/3
Flexible uretoroscope	1 mm ID × 850 mm length lumen 1 mm ID × 989 mm length lumen	12/12
Flexible colonoscope	3.8 mm ID × 1840 mm length lumen 3.8 mm ID × 130 mm length lumen 3.9 mm ID × 1580 mm length lumen 1.2 mm ID × 1955 mm length lumen 2.35 mm ID × 1580 mm length lumen 1.2 mm ID × 1955 mm length lumen 2.35 mm ID × 1580 mm length lumen 1.45 mm ID × 3500 mm length lumen	24/24
Dual channel semi-rigid ureterorenoscope	0.8 mm ID x 430 mm length 1.3 mm ID x 430 mm length	6/6

In-use studies confirm that devices used in actual surgical procedures are sterilized to the same degree as inoculated devices in a controlled environment.

5.0 MATERIAL COMPATIBILITY

Material and device compatibility testing is an integral and fundamental part of the verification and validation of the STERIZONE VP4 Sterilizer. Exhaustive testing ensures that the material and devices are compatible with the sterilization process, and that the reusable medical devices remain safe, sterile, and work as designed.

Compatibility testing ensures that the devices can be safely and repeatedly processed, and continue to meet performance specifications as determined by the manufacturer. TSO_3 Inc. performs testing, as part of its Compatibility Testing Services (CTS), in an ongoing and rigorous program, with the cooperation of the device manufacturers. This testing is based on the intended use and manufacturer's instructions for reprocessing.

Functionality is determined by the manufacturer and is based on the number of cycles selected for testing of a device. It is dependent on many factors, determined by the manufacturer, such as:

- Industry standards
- Historical data
- Intended use
- Device criticality
- Warranty
- Expected life of device

Device compatibility is assessed after the predetermined number of sterilization cycles to ensure that the device is not adversely affected by exposure to repeated STERIZONE VP4 Sterilizer cycles. The compatibility is assessed based on visual and mechanical criteria for a specific device, and is based on functional and cosmetic characteristics such as:

- Overall appearance and integrity
- Optics
- Mechanical properties and proper function of moving parts
- Visual observations

Table 23 shows the categories of medical devices whose compatibility has been tested. All devices were found to be compatible with Cycle 1 of the STERIZONE VP4 Sterilizer.

Table 23. Compatible device categories for the STERIZONE VP4 Sterilizer Cycle 1

Medical Instruments Category
Battery
Bipolar cord
Bipolar forceps
Bridge
Camera
Defibrillator paddles and handles
Doppler probe
Electrocautery instrument
Electrode
Electrophysiology cable
Electrosurgical cable
Fiberoptic light cable
ENT flexible endoscope
Flexible bronchoscope
Flexible cystoscope
Flexible hysteroscope
Flexible nephroscope
Flexible ureteroscope
Forceps
Laryngoscope blade
High frequency cable
Lacrimal probe
Laser fiber
Lighted retractor
Ophthalmic surgical instrument (without channel)
Resectoscope and resectoscope sheath
Rigid endoscope (without channel)
Rigid hysteroscope
Scalpel handle
Semi-rigid and rigid endoscope
Speculum
Stopcock
Temperature probe
Thoracoscope
Trocar and trocar sheath

Extensive material and compatibility testing demonstrates that commonly used materials found in common medical devices can be safely and repeatedly processed with the STERIZONE VP4 Sterilizer.

6.0 SAFETY

The toxicity of hydrogen peroxide (H_2O_2) and ozone are well documented in the scientific literature, with relevant standards having been established by the United States Occupational Safety and Health Administration (OSHA).

The by-products from reaction of hydrogen peroxide with ozone are oxygen and hydroxyl radicals. Hydroxyl radicals, in turn, can react with ozone or hydrogen peroxide to produce either oxygen or water (nontoxic by-products).

Both hydrogen peroxide and ozone decompose with the formation of water (H_2O) and oxygen gas (O_2).

$$2\ H_2O_2 \longrightarrow 2\ H_2O + O_2$$

$$2\ O_3 \longrightarrow 3\ O_2$$

6.1. Hydrogen peroxide

In accordance with OSHA (Occupational Safety and Health Administration) standards (29 CFR 1910.1000, Table Z-1), an individual must not be exposed to a concentration of hydrogen peroxide higher than:

- One part per million (ppm) parts of air (1.4 milligrams per cubic meter (mg/m^3)) over a time-weighted-average (TWA) of eight hours.

Verify with local regulation if additional exposure limit apply to your location.

6.2. Ozone

In accordance with OSHA (Occupational Safety and Health Administration) standards (29 CFR part 1910.1000, Table Z-1), an individual must not be exposed to a concentration of ozone higher than:

- An average of 0.1 ppm (0.2 mg ozone/m^3 air) over a time-weighted-average (TWA) of eight hours.

Verify with local regulation if additional exposure limit apply to your location.

6.3. Emission of hydrogen peroxide and ozone at the outlet of the catalytic converter

The STERIZONE VP4 Sterilizer is equipped with a catalytic converter to decompose residual hydrogen peroxide and ozone to oxygen and water vapor before they are returned to the room.

A study was conducted to demonstrate the efficiency of the catalytic converter to catalyze the destruction (decomposition) of hydrogen peroxide and maintain its efficiency against ozone destruction (decomposition). Ozone and hydrogen peroxide concentrations were monitored at the outlet of the catalytic converter for a period equivalent to more than two years of use (3300 cycles). The results demonstrate that emissions of hydrogen peroxide and ozone were below OSHA limits (Table 24).

Table 24. H_2O_2 and O_3 concentration at the outlet of the catalytic converter after every 100 cycles*

Cycle number	H_2O_2 Concentration (ppm)	O_3 Concentration (ppm)
0	0.00	0.003
100	0.00	0.010
200	0.00	0.000
300	0.01	0.013
400	0.02	0.015
500	0.00	0.001
600	0.00	0.013
700	0.00	0.011
800	0.00	0.010
900	0.00	0.014
1000	0.00	0.020
1100	0.06	0.017
1200	0.02	0.008
1300	0.02	0.004
1400	0.00	0.012
1500	0.07	0.012
1600	0.08	0.011
1700	0.05	0.015
1800	0.04	0.017
1900	0.06	0.027
2000	0.10	0.012
2100	0.00	0.014
2900	0.00	0.024
3000	0.03	0.022
3100	0.00	0.019
3200	0.00	0.021
3300	0.02	0.009

* The data of seven points are missing, the monitors were in calibration

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6.4. Determination of hydrogen peroxide and ozone in the breathing zone

The STERIZONE VP4 Sterilizer uses two sterilants, hydrogen peroxide and ozone, which are potential contaminants in the immediate environment surrounding the sterilizer. As such, the operator may be exposed to residual chemicals when opening the sterilizer chamber door, manipulating loads and packaging materials, or opening the packaging that contains sterilized instruments. A study designed to assess the ventilation system incorporated as part of the sterilization cycle and in particular its effectiveness in removing chemical residues below OSHA breathing zone limits, was conducted.

The results presented in Table 25 and Table 26 show that the 15-minute average concentration is lower than the STEL and also lower than the 8-hour TWA limits for both hydrogen peroxide and ozone, as required by OSHA.

Table 25. Hydrogen peroxide average exposure (15 min) value in mg/m^3 in the breathing zone of the operator from the opening of the door to the end of the load manipulation (minimum 15 minutes)

Description of the load	Hydrogen peroxide average exposure (15 min) value (mg/m^3)
STERIZONE VP4 Test Pack	0.00
One small wrapped tray	0.32
One large wrapped tray	0.40
One full-length container	0.18
Two large wrapped trays	0.99
Three full-length containers	0.53
Pouches	0.03

Table 26. Ozone peak reached from the opening of the door to the end of the load manipulation (minimum 15 minutes) in mg/m^3

Description of the load	Ozone peak (15 min) value in mg/m^3
STERIZONE VP4 Test Pack	0.04
One small wrapped tray	0.04
One large wrapped tray	0.04
One full-length container	0.00
Two large wrapped trays	0.02
Three full-length containers	0.00
Pouches	0.04

The airborne concentration of residual hydrogen peroxide and ozone levels remaining in the breathing zone of the STERIZONE VP4 operator immediately after sterilization of different loads of medical instruments satisfy all current regulatory standards.

6.5. Safety of medical instruments (Biocompatibility)

Biocompatibility testing of commonly used medical device materials after their reprocessing in the STERIZONE VP4 Sterilizer sterilization process was conducted in accordance with ISO EN 10993 standards series (*Biological evaluation of medical devices).* Six biocompatibility tests were selected based on ISO 10993-1:2009 standards for reusable medical devices with body contact for less than 24 hours.

- *in vitro* testing: cytotoxicity and hemocompatibility
- *in vivo* testing: sensitization, intracutaneous reactivity, ocular irritation testing and systemic toxicity.

Hydrogen peroxide solution is known to cause cytotoxic reactivity at very low concentrations (Ikarashi, Tsuchiya *et al.* 1995). Nevertheless, hydrogen peroxide is commonly and widely used for such purposes as disinfection of eye contact lenses, disinfection of wounds, and mouth washing. These products contain a sufficient amount of hydrogen peroxide to show a cytotoxic reactivity. However, these levels of hydrogen peroxide are considered safe to be used since they pass the *in vivo* tests (European Commission, 2005).

Therefore, results of the cytotoxicity tests on materials processed in the STERIZONE VP4 Sterilizer were analyzed in combination with the *in vivo* tests results. All materials tested passed the four *in vivo* tests performed (Table 27). Based on the results of the *in vivo* biocompatibility testing performed using worst-case conditions, the chemicals used in the STERIZONE VP4 Sterilizer sterilization process are shown to be safe for users and patients.

Table 27. *In vivo* test results of materials processed in STERIZONE VP4 Sterilizer

Material	Irritation - Intracutaneous Reactivity	Systemic Toxicity	Irritation - Ocular	Sensitization
Anodized aluminium	Pass	Pass	Pass	Pass
Brass	Pass	Pass	Pass	Pass
Fluoroelastomer	Pass	Pass	Pass	Pass
Liquid crystal polymer	Pass	Pass	Pass	Pass
Polyamide	Pass	Pass	Pass	Pass
Polycarbonate	Pass	Pass	Pass	Pass
Polydimethylsiloxane	Pass	Pass	Pass	Pass
Polyetheretherketone	Pass	Pass	Pass	Pass
Polyetherimide	Pass	Pass	Pass	Pass
Polyethylene (high density)	Pass	Pass	Pass	Pass
Polymethylmethacrylate	Pass	Pass	Pass	Pass
Polyoxymethylene	Pass	Pass	Pass	Pass
Polyphenyleneoxide	Pass	Pass	Pass	Pass
Polyphenylsulfone	Pass	Pass	Pass	Pass
Polypropylene	Pass	Pass	Pass	Pass
Polystyrene	Pass	Pass	Pass	Pass
Polytetrafluoroethylene	Pass	Pass	Pass	Pass
Polyurethane	Pass	Pass	Pass	Pass
Polyvinylchloride	Pass	Pass	Pass	Pass
Stainless steel	Pass	Pass	Pass	Pass
Titanium	Pass	Pass	Pass	Pass

The exhaustive material evaluation testing performed demonstrates that most medical devices commonly reprocessed using low-temperature sterilization technologies can safely be reprocessed in the STERIZONE VP4 Sterilizer.

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