STERRAD® NX

STERRAD® NX Sterilization System

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ADVANCED STERILIZATION PRODUCTS®
a Johnson & Johnson company

1.0 Abstract

The STERRAD® NX System, developed by Advanced Sterilization Products (ASP), a Johnson & Johnson company, uses a combination of hydrogen peroxide vapor and low-temperature gas plasma to rapidly sterilize most medical instruments and materials without leaving any toxic residues. The technology can be used to sterilize a wide range of medical devices currently sterilized in steam, ethylene oxide, formaldehyde, or peracetic acid. Since the load temperatures do not exceed 55 °C and sterilization occurs in a low moisture environment, the STERRAD® NX System is particularly suited to the sterilization of heat and moisture-sensitive instruments. There are two cycles available on the STERRAD® NX System. The Standard cycle time is approximately 28 minutes. The Advanced cycle time is approximately 38 minutes. The efficacy of the process has been established by demonstrating a sterility assurance level (SAL) of at least 10^{-6} with G. stearothermophilus spores, an organism that has been shown to be highly resistant to the process. The system has also passed the AOAC Sporicidal Test, as outlined in the Official Methods of Analysis of the Association of Official Analytical Chemists (AOAC), and has demonstrated the ability to terminally sterilize medical devices containing diffusion-restricted areas such as lumens and mated surfaces.

2.0 Introduction

The STERRAD® NX System, a new low-temperature sterilizer developed by ASP, a Johnson & Johnson company, represents the next generation of low-temperature hydrogen peroxide gas plasma sterilizers. This product utilizes hydrogen peroxide vapor gas plasma technology (1) as in previous generations of STERRAD Sterilizers but with a smaller rectangular sterilization chamber. The STERRAD® NX System has the following distinct features:

1. The STERRAD® NX System has two cycles. The Standard cycle is used for processing most medical instruments. The Standard cycle time is approximately 28 minutes. An Advanced cycle is also available to process instruments with longer lumens and flexible endoscopes. The Advanced cycle time is approximately 38 minutes.
2. The STERRAD® NX System has a new vaporization system that removes most water from the hydrogen peroxide solution before the peroxide is transferred to the sterilization chamber. This new feature allows for reduced cycle times and processing of longer-lumened devices without the use of a booster.
3. The STERRAD® NX System has a usable volume of about 30 liters (1.06 cu. ft).
4. The STERRAD® NX System has an optional Independent Monitoring System (IMS) to support compliance with the international sterilization standard, ANSI/AAMI/ISO 14937.
5. A fully integrated hydrogen peroxide monitor for direct measurement of chamber sterilant concentration.
6. Network connectivity package.
7. Optional bar code scanner for reliable instrument tracking.
8. Self-diagnostics capability for optimizing system up time.

The STERRAD® NX Sterilization Process consists of two consecutive and equal sterilization phases. The events of the process are as follows: items to be sterilized are placed in the sterilization chamber, the chamber is closed, aqueous hydrogen peroxide is delivered to the vaporizer/condenser, and evacuation begins. As pressure is reduced, water is removed from the peroxide solution until the solution concentration is approximately 90 %. The chamber pressure is then further reduced in preparation for the transfer step. The hydrogen peroxide solution is vaporized and transferred to the sterilization chamber. The hydrogen peroxide diffuses throughout the chamber surrounding the items to be sterilized and initiates the inactivation of microorganisms. The pressure in the system is first increased and then, following a subsequent pressure reduction, a low-temperature plasma is generated by applying energy to create an electric field, which in turn initiates the generation of the plasma. In the plasma step, the hydrogen peroxide vapor is broken apart into reactive species known as free radicals. The plasma power is then terminated, causing the free radicals to lose their high energy and recombine to form oxygen, water vapor and other nontoxic by-products. This constitutes one-half of the total sterilization process. The cycle is completed by repeating the above steps a second time. The sterilization process, therefore, consists of two consecutive, equal, and distinct half cycles. At the completion of the second half cycle, the plasma power is turned off. The chamber is brought to atmospheric pressure by the introduction of HEPA-filtered air.

The STERRAD® NX System is designed for sterilization of both metal and nonmetal medical devices at low temperatures. Because the cycle operates within a dry environment and at low temperatures, it is especially suitable for instruments sensitive to heat and moisture. The STERRAD® NX System can sterilize instruments that have diffusion-restricted spaces, such as the hinged portion of forceps and scissors. The STERRAD® NX System is designed to process most medical items currently sterilized by steam, ethylene oxide, formaldehyde, and peracetic acid, with the exception of linens, other cellulosic materials, powders, liquids, and devices containing long, narrow, dead-end lumens. Items are sterilized and ready for use in either 28 or 38 minutes after starting the sterilizer, depending on the cycle selected. The process requires no aeration, and there are no toxic residues or emissions. Preparation of instruments for sterilization is similar to current practices: cleaning and drying the instruments, reassembly, and wrapping in porous material.

The system requires the use of nonwoven polypropylene wraps or Tyvek® Pouches with STERRAD Chemical Indicator and specially designed trays available from ASP.*

Long, narrow, dead-end lumens are not common in reusable medical devices, since they present a special challenge for cleaning and reprocessing and may not be processed in STERRAD Sterilizers.

ASP offers chemical indicators, chemical indicator tape, self-contained biological indicators, a biological indicator challenge pack, trays and pouches that were specially developed for use with STERRAD Sterilizers.

2.1 Mode of action

The STERRAD® NX System involves the combined use of hydrogen peroxide and low-temperature gas plasma to safely and rapidly sterilize medical devices and materials without leaving any toxic residues. Hydrogen peroxide is an oxidizing agent that affects sterilization by oxidation of key cellular components. Plasma is a state of matter distinguishable from a solid, liquid, or gas. Gas plasmas are highly ionized gases, composed of ions, electrons, and neutral particles that produce a visible glow. A solution of hydrogen peroxide and water (59 % nominal peroxide by weight) is delivered to the sterilizer, concentrated to approximately 90 %, vaporized and allowed to surround and interact with the devices to be sterilized. Hydrogen peroxide is a bactericidal, virucidal, sporicidal, and fungicidal agent, even at low concentration and temperature. Applying a strong electrical field then creates plasma. The plasma breaks down the peroxide into a "cloud" of highly energized species that recombine, turning the hydrogen peroxide into water and oxygen. Literature references indicate that, in a highly simplified form, the reactions in plasma, for which H_2O_2 serves as a precursor, may be summarized as follows:

H_2O_2 → HO o + HO o_1
HO o + H_2O_2 → H_2O + H_2O_2
H_2O_2 → H_2O_2#$_3$
H_2O_2# → H_2O_2 + Visible and/or UV radiation

- HO o refers to the hydroxyl free radical.
- HO_2o refers to the hydroproxyl free radical.
- H_2O_2# refers to an electronically excited hydrogen peroxide molecule in which an electron has been elevated to a higher energy level. When the molecule spontaneously drops to the stable ground state, ultraviolet or visible radiation is given off as shown in the next equation.

The STERRAD® NX System produces a biocidal environment that is capable of inactivating microorganisms by chemical interactions at multiple biologically important reaction sites.(1)

Some of the active species formed in the hydrogen peroxide plasma are similar to those formed when γ-radiation is used to sterilize medical devices. For example, both hydroxyl free radicals and hydroperoxyl free radicals are formed from the interaction of γ-radiation with water molecules in the presence of oxygen. In addition, the recombination of radicals present in γ-radiation also produces hydrogen peroxide. Although similar reactive species are present in both processes, the effect of the two processes on the physical properties of some nonmetallic devices can be dramatically different. The high-energy γ-radiation is capable of passing through nonmetallic materials, used in medical devices, and generating secondary reactions that can detrimentally affect the bulk properties of the materials. Low-temperature plasmas are known to affect only a thin layer, a few atoms in depth, on the surface of nonmetallic materials and do not affect the bulk properties of these materials. In addition, the STERRAD® NX System utilizes a secondary plasma that minimizes surface modification since the item in the sterilizer is not exposed to the direct or primary plasma discharge.

3.0 Efficacy

By definition, a sterilization process must have the ability to inactivate a broad spectrum of microorganisms, including resistant bacterial spores. Previous studies conducted with the STERRAD® 100 Sterilizer, which also utilizes hydrogen peroxide vapor gas plasma technology, have demonstrated the broad spectrum of activity of this process. These activity studies were conducted against vegetative bacteria (including mycobacteria), bacterial spores, yeasts, fungi, and viruses. The reasons for the selection of each organism, as well as the results of these tests, are presented in Table I. All of the organisms shown in Table I were found to be readily inactivated by an abbreviated STERRAD System cycle consisting of 20 minutes of diffusion with 2 mg/liter of hydrogen peroxide and 5 minutes of plasma at a power of 300 watts. By comparison, the two Standard STERRAD® NX Sterilization cycles utilize a minimum of about 14 mg/liter of hydrogen peroxide and a plasma power of 500 watts. As the STERRAD System cycle conditions were further reduced (using abbreviated cycles), bacterial spores were found to be the most resistant organism to the process and the most resistant bacterial spore was found to be G. stearothermophilus.

The two viruses tested, Poliovirus Type 1 and Herpesvirus Type 1, are representative of the two major classes of viruses, hydrophilic and lipophilic viruses, respectively. Of these two classes, the hydrophilic group normally exhibits the greater resistance to chemical sterilants, and poliovirus is known to be a highly resistant hydrophilic virus. The log10 virus titers of 3.98, 3.20, and 2.84 represent the minimum concentration of viruses in these tests. Due to the nature of the virucidal test, a minimum virus concentration is determined but the actual concentration is not. In all virucidal tests there was no infectivity obtained after exposure to the highly abbreviated STERRAD System cycle. This shows that even an abbreviated STERRAD System cycle is capable of inactivating both hydrophilic and lipophilic viruses.

Table I

Vegetative Bacteria, Spores and Fungi

Microorganism	Type	Interest in testing	Control*	Results**
Geobacillus stearothermophilus	Bacterial Spore	H_2O_2 Resistance; Stream Indicator Organism	2.04×10^6	0/9
Bacillus subtilis var. niger (globigii)	Bacterial Spore	H_2O_2 Resistance; EtO Indicator Organism	2.69×10^6	0/9
Bacillus pumilus	Bacterial Spore	Ionizing Radiation Resistance; Indicator Organism	1.82×10^6	0/9
Staphylococcus aureus	Gram Positive	H_2O_2 Resistance; Clinical Significance	2.82×10^6	0/9
Deinococcus radiodurans	Gram Positive	Ionizing Radiation Resistance	3.10×10^6	0/9
Pseudomonas aeruginosa	Gram Negative	Clinical Significance	1.32×10^6	0/9
Escherichia coli	Gram Negative	Clinical Significance	9.23×10^6	0/9
Serratia marcescens	Gram Negative	H_2O_2 Resistance; Clinical Significance	1.85×10^6	0/9
Moroxelia osloensis	Gram Negative	Ionizing Radiation Resistance EtO Indicator Organism	3.14×10^6	0/9
Mycobacterium bovis	Acid Fast	Chemical Resistance; Clinical Resistance	4.20×10^6	0/9
Candida albicans	Yeast	H_2O_2 Resistance	3.95×10^6	0/9
Candida parapsilosis	Yeast	H_2O_2 Resistance; Clinical Significance	1.07×10^6	0/9
Trichophyton mentagrophytes	Filamentous Fungus	Clinical Significance	1.25×10^6	0/9
Aspergillus niger	Filamentous Fungus	H_2O_2 Resistance; Clinical Significance	1.46×10^6	0/9

* Average titer recovered from nine samples.
** # Positive/ # Tested.

Viruses

Mikroorganism	Type	Interest in testing	Virus Titer log10	Infectivity
Poliovirus Type 1 (Brunhilde)	Hydrophil	Chemical Resistance: Clinical Significance	Test 1 ≥ 3.98 Test 2 ≥ 3.98	Not detected Not detected
Herpesvirus Type 1	Lipophil	Clinical Significance	Test 1 ≥ 3.20 Test 2 ≥ 2.84	Not detected Not detected

To further establish the broad spectrum of activity of the STERRAD® Sterilizer, tests were conducted with actual hospital pathogens. In one study, clinical isolates of a wide variety of clinically significant organisms were tested after an abbreviated STERRAD System cycle consisting of 40 minutes of diffusion with 3 mg/liter of hydrogen peroxide and 10 minutes of plasma at a power of 300 watts. In these tests, conducted in a hospital, approximately 2.5×10^6 organisms in the presence of either 5% or 10% serum were inoculated onto a paper strip and sealed in Tyvek®/Mylar envelopes. For each test, one-half the samples were in 5% serum and one-half were in 10% serum. The results of these tests, which are presented in Table II, show that total kill was obtained with all clinical isolates tested.

Based on the spectrum of activity studies conducted, it has been established that G. stearothermophilus spores are the most resistant to the process. Therefore, the tests conducted to validate the efficacy of the STERRAD NX System were all conducted with this organism.

The efficacy of the STERRAD® NX System was established by demonstrating the ability of the system to: (1) provide by established validation methods an SAL of 10^{-6} with G. stearothermophilus spores, (2) kill over 10^6 G. stearothermophilus spores on a mated surface, (3) pass the AOAC Sporicidal test, and (4) sterilize devices with long, narrow lumens.

Table II **Clinical Isolates***

Microorganism	# positive/# tested
Pseudomonas aeruginosa	0/10
Pseudomonas cepacia	0/10
Xanthomonas maltophilia	0/10
Serratia marcescens	0/10
Klebsiella (encapsulated)	0/10
Methicillin-resistant Staphylococcus aureus	0/10
Slime-producing Staphylococcus epidermidis	0/10
Listeria monocytogenes	0/10
Enterococcus faecalis	0/10
Acinetobacter calcoaceticus	0/10
Salmonella sp.	0/10
Shigella sp.	0/10
Campylobacter sp.	0/10
Aeromonas sp.	0/10
Clostridium perfringens	0/10
Clostridium tetani	0/10
Clostridium difficile	0/10
Bacillus subtilis spores	0/10
Micrococcus sp.	0/10
Mycobacterium tuberculosis	0/10
Mycobacterium chelonei	0/10
Bacteroides fragilis	0/10
Furobacterium sp.	0/10
Anaereobic cocci	0/10
Candida albicans	0/10

3.1 Validation Method to Demonstrate 10^{-6} Sterility Assurance Level (SAL)

Well-established and universally accepted methods exist for the validation of sterilization processes. Two well recognized standards detail requirements and methods for validation of sterilization processes:

1. The Association for the Advancement of Medical Instrumentation (AAMI), Standards and Recommended Practices, (2)
2. ANSI/AAMI/ISO 14937:2000, Sterilization of medical devices – General requirements for characterization of sterilizing agent and the development, validation and routine control of a sterilization process(4)

Implicit in these test methods is the demonstration of at least a 10^{-6} sterility assurance level (SAL) for the sterilization process. Sterilization is a probability function and a minimum SAL of 10^{-6} means that the probability of a bioburden microorganism surviving after exposure to the sterilization process is no greater than 10^{-6}. It can also be stated in terms of the probability of having a nonsterile device after processing as being less than one in one million. This definition for sterility of terminally sterilized products is well accepted in the scientific community.

* Clinical Isolates tested in an abbreviated STERRAD® System Cycle. Abbreviated cycle consisted of 40 minutes of diffusion with 3 mg/liter of hydrogen peroxide and 10 minutes of plasma at a power of 300 watts.
** Five tests were conducted in the presence of 5% serum and five tests were conducted in the presence of 10% serum.

Critical to the demonstration of the 10^{-6} SAL is the use of a consistent and reproducible biological monitor for evaluating the efficacy of the sterilization process. The organism used in the biological challenge should represent a widely recognized test microorganism that has been found appropriate for the sterilization process being monitored. (2, 3) The recommended biological challenge organisms for steam and ethylene oxide sterilization processes are G. stearothermophilus and B. subtilis var. niger, respectively. It is recommended in the AAMI guidelines that G. stearothermophilus be used at a population of 10^3 to 10^6, and that B. subtilis be used at a population of at least 10^3 and that it is typically used at a population of 10^6 (2).It has become customary to use 106 microorganisms as the bioload for biological challenges utilized to validate sterilization processes; (3) a biological challenge of at least 10^6 G. stearothermophilus spores were used in all validation testing conducted with the STERRAD® NX System.

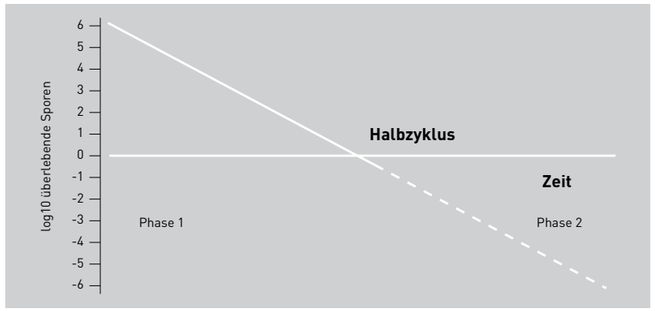
The nature of the spore suspension and the substrate on which the spore suspension is inoculated are critical to the preparation of a consistent, reproducible biological challenge. Inoculation of spores on solid surfaces can produce a high concentration of spores in a small area. This can result in clumping and occlusion of spores, especially on nonwetting hydrophobic materials. Occlusion of spores can also occur if inoculations are made on cracked or irregular hard surfaces. Occlusion of spores, either in clumps or on irregular surfaces, will delay the penetration of the sterilizing conditions to the spores and result in extended survival times. Since the degree of clumping or occlusion is not reproducible, a consistent endpoint will not be obtained for the characterization of a sterilization process. The presence of organic or inorganic debris in spore suspensions can also result in occluded spores and a nonreproducible sterilization result. For this reason, relatively clean suspensions of spores need to be uniformly deposited on appropriate substrates for consistent biological test results, and to create a biological indicator that is acceptable for the validation of a sterilization process.

One of the most commonly used methods for sterilizer validation is the half-cycle overkill method. Using the half-cycle method, a sterilization process is challenged with a biological challenge, usually containing 10^6 spores per carrier, at a sterilization time that is equal to one-half of the full process time. As can be seen in Figure 1, an extrapolation of the kill curve, which provided 6 logs of kill at the half-cycle condition, provides a 10^{-6} SAL for the total process. This method requires the demonstration of linear semilogarithmic kill kinetics in the first half cycle and an understanding that the same linear kill kinetics occur during the second half cycle.

For rapid, synergistic sterilization technologies that contain several dynamic stages, such as occurs in the STERRAD® NX System process, the demonstration of straight-line, time-based semilogarithmic microbial destruction kinetics can be difficult. For this reason, the validation of the STERRAD® NX System double injection system was conducted utilizing a variation of the half-cycle method. Using this method, the entire sterilization process is split into two consecutive, equal phases. The critical process parameters in each phase are identical. A 6 log reduction of the resistant bacterial spore utilized to validate the process is demonstrated with the first phase. Since the second injection cycle is equal to the first, i.e., all of the critical process parameters are identical, an additional 6 log reduction will be obtained at the end of the second phase, and the total process will provide an SAL of 10^{-6}. The graphical presentation of the two-phase method can be seen in Figure 2, and a description of this method can be found in the September 1996 printing of the eighth edition of Microbiology and Engineering of Sterilization Processes. (3)

Figure 1

Graphical Presentation of Half-Cycle Method of Sterilizer (2,3)



3.1.1 Validation Testing with Lumen Devices

Advances in the sterilizer control system and test methodology allowed measurement of the reduction in organisms as a function of both time and peroxide concentration. Testing was conducted utilizing the plate count (enumeration) method as well as the fraction-negative analyses (sterility test method).

The STERRAD® NX System is designed for sterilization of both metal and nonmetal medical devices at low temperatures. Because the cycle operates within a dry environment and at low temperatures, it is especially suitable for instruments sensitive to heat and moisture.

The STERRAD® NX System can sterilize instruments which have diffusion-restricted spaces, such as the hinged portion of forceps and scissors.

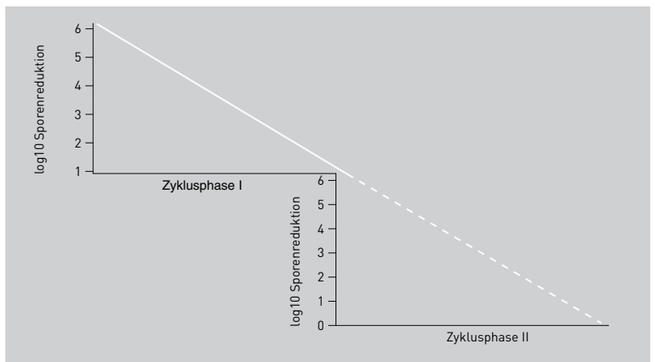
Medical devices with the following materials and dimensions can be processed in the STERRAD® NX System Standard cycle:

Single channel stainless steel lumens with:
- An inside diameter of 1 mm or larger and a length of 150 mm or shorter
- An inside diameter of 2 mm or larger and a length of 400 mm or shorter

Single channel polyethylene and Teflon (PTFE) lumen instruments (excluding flexible endoscopes) with:
- An inside diameter of 1 mm or larger and length of 350 mm or shorter

Figure 2

Graphical Presentation of the Two-Phase Cycle



Medical devices, including most flexible endoscopes, with the following materials and dimensions can be processed in the STERRAD NX System Advanced cycle:

Single channel stainless steel lumens with:
- An inside diameter of 1 mm or larger and a length of 500 mm or shorter

Single Polyethylene/Teflon (PTFE) lumen tubing (excluding flexible endoscopes) with:
- An inside diameter of 1 mm or larger and length of 1000 mm or shorter
(Up to 10 pieces of tubing may be sterilized at one time with no additional load.)

Single channel flexible endoscope with a polyethylene or Teflon (PTFE) lumen with:
- An inside diameter of 1 mm or larger and length of 850 mm or shorter
(only one endoscope per tray per cycle with no additional load)

The most difficult-to-sterilize configuration was determined to be the 1 mm × 350 mm Teflon (PTFE) lumens for the Standard cycle and the 1 mm × 500 mm stainless steel lumens for the Advanced cycle. Sterility assurance level for these worst case (biological models) lumens, were demonstrated by placing inoculated carriers containing at least 1×10^6 G. stearothermophilus spores at the midpoint of these lumens. The lumens with spore carriers are termed biological test units.

Ten biological test units were placed in a standardized hospital tray containing medical devices. The tray was then double wrapped with Kimguard® KC 400 Sterilization Wrap and placed in the STERRAD® NX System. This provided a total of at least ten biological test units per test. The replicate biological test units were exposed to STERRAD® NX System half-cycle processes at reduced concentrations of hydrogen peroxide. After exposure, the carriers were enumerated or placed in broth media, as appropriate. Enumeration plates were incubated 48 hours at 55°C and then the plates counted. Sterility test samples were transferred to Tryptic soy broth, incubated for 21 days at 55°C, and scored for growth (positive) or no growth (negative). The results of these tests, which are presented in Table IIIa and Table IIIb, demonstrate that the microbial kill obtained is dependent on the concentration of hydrogen peroxide injected into the chamber and that no spores survived the nominal first half-cycle process conditions. In fact, surviving organisms were only found when the amount of hydrogen peroxide utilized in the half cycle test was about fifty percent (50%) or less of the nominal hydrogen peroxide concentration. Since at least a 6 log reduction was obtained at the end of the first half cycle, and the second half cycle is identical to the first, the total STERRAD® NX Sterilization process provides an SAL of at least 10^{-6}.

Table IIIa

Half-Cycle Validation Test with 1.37×10^6 G. stearothermophilus Spores on Stainless Steel Carrier in 1 mm by 350 mm Teflon (PTFE) Lumens in a Standardized Validation Load with Reduced Concentrations of Hydrogen Peroxide.

STERRAD® NX System Standard Cycle

Half-Cycle Number	ml of H_2O_2 Injected 53%	Enumeration Test Spore Log Reduction	Biological Results # nonsterile/# tested
1	0.19	1.40	–
2	0.28	3.15	–
3	0.37	–	2/10
4	0.75	–	0/10
5	0.94	–	0/10
6	1.12	–	0/10
7	1.31	–	0/10
8	1.50	–	0/10

* Kimguard is a registered trademark of Kimberly Clark Corporation.

Table IIIb

Half-Cycle Validation Test with 1.63×10^6 G. stearothermophilus Spores on Stainless Steel Carrier in 1 mm by 500 mm Stainless Steel Lumens in a Standardized Validation Load with Reduced Concentrations of Hydrogen Peroxide.

STERRAD® NX System Advanced Cycle

Mg H_2O_2/Liter of Chamber Volume	% of Nominal[1] H_2O_2 Concentration Utilized	1 mm × 125 mm	2 mm × 250 mm
1	0.19	0.82	–
2	0.28	1.49	10/10
3	0.37	–	0/10
4	0.75	–	0/10
5	0.94	–	0/10
6	1.12	–	0/10
7	1.31	–	0/10
8	1.50	–	–

3.1.2 Validation Test with Mated Surfaces

The sterilization of devices containing mated surfaces represents a special challenge for sterilization processes. Stainless steel, titanium, and three plastic materials used in the construction of medical device mated surfaces have been validated. The ability of the STERRAD® NX System to sterilize mated surfaces to an SAL of 10^{-6} was demonstrated by exposing a double-wrapped tray containing the mated surfaces and a standardized load of medical devices to half-cycle conditions. The mated surface biological challenge consisted of a material sample inoculated with 10^6 G. stearothermophilus spores mated with an identical material sample, such that the inoculum was sandwiched between the two mated surfaces. One tray was used per test and the results of these tests, which contained a total of four mated surface biological challenges that were repeated three times, are presented in Table IV. All samples exposed to one half Standard cycle showed no growth after incubating for 21 days at 55 °C in tryptic soy broth, while all positive control samples consisting of the unprocessed mated surface biological challenge were positive. The results of these tests demonstrate the ability of the complete STERRAD® NX Process that consists of two consecutive half cycles to provide an SAL of 10^{-6} with mated surfaces of these materials. These tests were conducted in the Standard cycle as the Advanced cycle presents increased lethal conditions.

Table IV

G. stearothermophilus Spores Between Mated Surfaces in a Standardized Validation Load at Half-Cycle Conditions

Material	Test 1 #Positive/ #Tested	Test 2 #Positive/ #Tested	Test 3 #Positive/ #Tested
Stainless Steel Blades	0/4	0/4	0/4
Titanium	0/4	0/4	0/4
Polyacetal (Delrin)	0/4	0/4	0/4
Polyetherimide (ULTEM*)	0/4	0/4	0/4
Polyarylsulfone (RADEL**)	0/4	0/4	0/4

3.1.3 Validation Test with Flexible Endoscopes

The dimensions of the polyethylene (PE) and (PTFE) lumen claim for the processing of single channel flexible endoscopes through the STERRAD® NX Advanced sterilization cycle are: (1) inner diameters (ID) equal to or greater than 1 mm; and (2) with lengths equal to or less than 850 mm. Typical instruments such as choledochoscopes, bronchovideoscopes or ureterorenofiberscopes are representative of this claim. The devices were processed as individual loads under Advanced

* Ultem is a trademark of GE Plastics.
** Radel is a trademark of Amoco.

half-cycle conditions. A biological indicator (BI) was inserted and positioned at the center of the channel of each device. The load, a tray containing one device, was processed through an Advanced half-cycle with reduced hydrogen peroxide concentration. The results of these tests, a total of nine data points, three replicates for each device, demonstrated sterility of all BIs throughout the 21-day, 55 °C incubation period. The results, presented in Table V, confirm that a sterility assurance level (SAL) of 10^{-6} was achieved in the devices when processed through the STERRAD® NX Advanced sterilization cycle.

Table V

Half-Cycle Validation Test with 1.63×10^6 G. stearothermophilus Spores on Stainless Steel Carrier in 1 mm by 850 mm Flexible Endoscope with Reduced Concentrations of Hydrogen Peroxide.

STERRAD® NX System Advanced Cycle

Cycle # (per device)	Biological Results: # nonsterile/# tested		
	Choledochoscope	Bronchovideoscope	Ureterorenofiberscope
1	0/1	0/1	0/1
2	0/1	0/1	0/1
3	0/1	0/1	0/1

3.2 AOAC Sporicidal Test

The AOAC Sporicidal Test is a test listed in the United States Food and Drug Administration (FDA) Guidance Document for the evaluation of sterilization systems. AOAC tests were conducted with B. subtilis ATCC 19659 spores and Clostridium sporogenes ATCC 3584 spores on porcelain penicylinders and polyester* suture loops according to Official Methods of Analysis 966.04 of the Association of Official Analytical Chemists. The tests stipulate that large numbers of carriers, contaminated with high numbers of spores of aerobic and anaerobic bacteria, must be sterilized without failure. These tests include a significant organic challenge due to the presence of dried, spent growth media with the spores. Additionally, the sterilizing agent must be able to penetrate into small crevices to kill spores on the porous porcelain penicylinders and in the knotted portion of the polyester suture loops. The results of this study, in Table VI, showed that no growth was obtained in three separate tests containing a total of 720 carriers, when exposed to a full STERRAD® NX Standard Cycle Sterilization process. By passing the AOAC sporicidal test, the STERRAD® NX System has met a fundamental FDA requirement for sterilization systems and has demonstrated that it is capable of sterilizing large numbers of porous carriers inoculated with resistant aerobic and anaerobic spores in the presence of organic soil and inorganic salts. Testing was repeated for the STERRAD® NX System advanced sterilization process with identical results.

Table VI

AOAC Sporicidal Test with STERRAD® NX System

Test #	Carrier	# of Failures/# Tested	
		B. subtilis	C. sporogenes
1	Suture Porcelain	0/60 0/60	0/60 0/60
2	Suture Porcelain	0/60 0/60	0/60 0/60
3	Suture Porcelain	0/60 0/60	0/60 0/60

* Polyester suture loops have been recognized as viable alternative carriers for the oxidizer sterilant by AOAC and FDA Office of Science and Technology. Polyester suture loops are low hydrogen peroxide absorbers and are more suitable carriers for hydrogen peroxide concentrating technology.

4.0 Monitoring of STERRAD® NX System

4.1 Process Control

The STERRAD® NX Standard Cycle time is approximately 28 minutes and the STERRAD® NX Advanced Cycle time is approximately 38 minutes.

The STERRAD® NX System cycle is controlled by a microprocessor. All critical process parameters are monitored during the operation of the sterilizer. At the end of each cycle, a printed record of the process parameters is obtained. If any process parameter exceeds its acceptable limits, which were established by statistical analysis of microbiological efficacy testing, the sterilization cycle will be canceled and the printed record for the cycle will state the reason for the malfunction. Operating within these process limits, the STERRAD® NX System has been demonstrated to provide consistently a minimum SAL of 10^{-6}. The STERRAD® NX System is the first healthcare model of STERRAD Sterilizer to feature a control system having a fully integrated hydrogen peroxide monitor as standard equipment. The hydrogen peroxide monitor provides the data to the process controller. The process controller can then utilize this data to make decisions regarding the acceptability of each cycle.

Additional new features available with the STERRAD® NX System include barcode reading capability and a communications package that will allow the STERRAD® NX System to be connected to an external computer network for data tracking and storage.

An optional independent monitoring system (IMS) is also available. The IMS provides backup sensors to monitor temperatures, pressures, and plasma power in order to provide independent confirmation that process specifications were achieved. The IMS system supports compliance with ANSI/AAMI/ISO 14937.

4.2 Biological Monitoring

A self-contained biological indicator, the STERRAD® CycleSure® Biological Indicator, developed for use with the STERRAD 100S and STERRAD 50 Sterilizers, can also be used with the STERRAD® NX System. This biological indicator (BI) contains 106 G. stearothermophilus spores on a glass fiber disc located at the end of a dead-end plastic tube that contains Tyvek® as a microbial barrier on the open end. In use, the self-contained BI should be packaged consistent with the items being sterilized. The self-contained CycleSure Biological Indicator utilizes the same spores with equivalent resistance to the STERRAD® NX Process as the G. stearothermophilus spores in the validation load that were used to validate the STERRAD Sterilizer to an SAL of 10^{-6}. The CycleSure Self-Contained Biological Indicator also has a chemical indicator disc mounted in the cap. The chemical indicator indicates that hydrogen peroxide, an essential part of the STERRAD Sterilization cycle, has been introduced into the sterilization chamber.

A newly designed STERRAD NX Challenge Pack is available for use in the STERRAD® NX System. The challenge pack utilizes the CycleSure Biological Indicator and is designed to provide a challenge equivalent to or greater than the most difficult-to-sterilize biological models discussed in section 3.1.1 above. The STERRAD NX Challenge Pack consists of a plastic vial with a small hole in the cap. A CycleSure Biological Indicator is placed within the vial, the cap tightened, and then the vial is pouched. The chemical indicator disc on top of the CycleSure Biological Indicator indicates that hydrogen peroxide has been introduced into the sterilization chamber. The biological indicator consists of a glass fiber disc containing 10^{6} G. stearothermophilus spores within the self-contained BI.

5.0 Safety of Sterilization Instruments

5.1 Functionality of Medical Products

In order to function and be of value as a sterilizer, any sterilization system, no matter how efficacious it may be in killing organisms, must not impair or negatively affect the functional properties of medical devices. The effect of the STERRAD® NX Process on the functional properties of medical devices has been studied in a laboratory setting. Laboratory tests were conducted on specific medical devices to quantify the effect of exposure to repeated STERRAD® NX Sterilization Cycles on the functional properties of the devices.

Table VII Representative Medical Devices Evaluated for Compatibility with the STERRAD® NX Sterilization System After Repetitive Sterilizations

Device	Property Measured	Total Cycles
Resectoscope	Power Output	50
Forceps	Mechanical Properties	50
Defibrillator Handle and Internal Electrodes	Power Output Compared to Charge Taken	50
Microsurgical Instruments	Subjective Evaluation of Instrument Appearance and Sharpness by Visual Observation, and Mechanical Functioning of Moving Parts	50
Fiberoptic Hysteroscope	Optics, Mechanical Properties, Subjective Evaluation of Instrument Appearance	50
Rigid Hysteroscope	Optics, Mechanical Properties, Subjective Evaluation of Instrument Appearance	50

5.1.1 Laboratory Functionality Tests

The laboratory functionality tests were conducted on devices that represent a wide range of materials including metals, plastics, rubber, and optical surfaces that must retain properties such as sharpness, flexibility, optical clarity, electrical discharge, etc., after being repeatedly sterilized. The list of devices evaluated is presented in Table VII. The table also describes the property measured and the total number of sterilization cycles to which the devices were exposed. In all tests, the devices were manipulated between sterilization cycles to simulate actual use of the product. The total number of 50 cycles was chosen for devices that normally undergo repeated sterilization and use. If no effect is seen in 50 cycles, it is unlikely that unusual adverse effects would occur as a result of additional exposures. Functionality tests were conducted according to the device manufacturer's protocol, when available, or by a quantifiable test procedure developed by ASP. After exposure to the specified number of STERRAD® NX Sterilization cycles, all test devices passed the manufacturer's functionality test and showed no statistically significant change in the functional property measured. These test results demonstrate that the functional properties of the test devices were not adversely affected by exposure to repeated STERRAD® NX Sterilization cycles.

ASP has an extensive materials compatibility testing program. Over 309 manufacturers of medical devices partnered to establish the materials compatibility of their devices with the STERRAD Process. Over 2073 resterilizable medical devices have been tested and more than 95% of those devices are compatible. Less than 5% of the devices tested are incompatible and there is only a short list of materials, such as some sulfides and some nylons (polyamides), that are not compatible. Materials compatibility assessments from these companies documenting the compatibility of their devices with the STERRAD Sterilization System are currently available to users of the STERRAD System and this list is constantly being updated and expanded. The goal of this ongoing program is to provide the user of the STERRAD Sterilizer with the most complete material compatibility information possible and to ensure that future medical devices have the optimum compatibility with the STERRAD Process.

5.2 Safety for Patient Use

Medical devices and commonly used medical materials sterilized by the STERRAD® Sterilization System were subjected to an extensive battery of toxicological tests as part of the original biocompatibility studies conducted on the STERRAD 100 Sterilization System.

These tests included:

- Cytotoxicity: Cytotoxicity testing is valuable as a method to screen for biocompatibility of materials intended for use in medical devices. Because cytotoxicity tests are so sensitive, some materials with a history of safe clinical use in medical devices can produce positive cytotoxic responses.
- Medical devices and materials were tested by the extraction/minimal essential medium (MEM) elution tissue culture response cytotoxicity method. In all these tests, the bioreactivity of devices and materials, after processing in the STERRAD Sterilizer, was comparable to the bioreactivity of materials and devices before sterilization.
- Acute Systemic Toxicity: Acute systemic toxicity tests demonstrate the symptomatology and lethality caused by a substance. No toxic responses were seen in mice injected with extracts of materials sterilized in the STERRAD Sterilization System.
- Ocular Irritation: Ocular irritation tests are a sensitive means of identifying substances that can cause local surface irritation or mucosal irritation. Extracts of materials sterilized by the STERRAD Sterilization System were non-irritating in this test.
- Intracutaneous Test: The intracutaneous test is used to determine the irritant effect of any leachables present in extracts of test materials. No irritation was observed in rabbits injected intracutaneously with extracts of materials sterilized in the STERRAD Sterilization System.
- Blood Compatibility: Tests for hemolysis and complement activation were conducted to establish the compatibility of STERRAD Sterilization System processed materials with blood. These tests are designed, respectively, to detect the potential of materials to cause blood cells to lyse and to initiate certain inflammatory responses. Test results demonstrated that the STERRAD Sterilization System process did not cause safe materials to become unsafe with regard to blood compatibility.

Additionally, the STERRAD 50 and 100S Sterilizers were tested for material biocompatibility and found to be safe. The extensive biocompatibility data available for STERRAD Sterilizers provides historical perspective and confidence that devices processed in the STERRAD® NX System will also be safe. To confirm this, a battery of materials was processed in the STERRAD® NX System and evaluated for biocompatibility. Cytotoxicity, acute systemic toxicity, intraocular irritation, and intracutaneous tests conducted on this battery of materials sterilized in the STERRAD® NX System demonstrated that it has a biocompatibility equivalent to that observed with earlier STERRAD Sterilizer models. The medical devices processed in the STERRAD® NX System do not pose a risk to the health of patients or personnel handling the devices.

* Material compatibility studies in the STERRAD 100, STERRAD 100S, and STERRAD 50 Systems have been conducted in which material samples were sterilized 100 times and evaluated for damage. Comparative laboratory tests with selected material samples have been conducted that show equivalent or better results can be expected in the STERRAD® NX System.

6.0 Worker Safety

6.1 Exposure to Hydrogen Peroxide

The STERRAD® NX Sterilization System has been designed to prevent hospital personnel from contacting hydrogen peroxide in either the liquid or vapor phase. To prevent worker exposure to liquid hydrogen peroxide, the 59% nominal hydrogen peroxide solution required for the sterilization process is packaged in a sealed cassette. The patented cassette contains a chemical leak indicator on each side of the package that changes from yellow to red when exposed to liquid or vapor hydrogen peroxide. This chemical indicator is visible through a clear plastic overwrap that will protect personnel handling the cassette from the hydrogen peroxide solution in the event of even a small leak. If the indicator has changed color, the plastic overwrap should not be removed from the cassette. Once the cassette has been placed in the sterilizer, it is automatically advanced by the machine, eliminating any danger of exposure to liquid hydrogen peroxide through handling of the cassette. After five sterilization cycles, the used cassette is automatically discarded into a collection box for disposal.

The sterilizer injects the hydrogen peroxide into the sterilization chamber where it is concentrated and vaporized in the reduced pressure that exists during the sterilization cycle. During the pump down prior to plasma treatment, or at pump down after a cycle has been completed, all vapor removed from the chamber passes through a filter that is specially designed to decompose hydrogen peroxide into nonhazardous water and oxygen. Monitoring of the area around the STERRAD® NX System during operation has demonstrated that the concentration of hydrogen peroxide in the atmosphere is less than the OSHA-established limit of 1.0 ppm (8 hour time weighted average). The normal use of the STERRAD® NX System is, therefore, not associated with concerns about emissions of harmful, toxic chemicals into the atmosphere.

6.2 Toxicity of Hydrogen Peroxide

Concentrated hydrogen peroxide liquid will irritate skin and, like other oxidants, can cause severe damage to eyes if direct contact occurs. The safeguards built into the STERRAD® NX Sterilization System make any direct contact with hydrogen peroxide unlikely. In the vapor phase, concentrated hydrogen peroxide is irritating to the eyes, nose, throat, and lungs. Generally, this irritation subsides soon after exposure to the vapor ceases. Because hydrogen peroxide has a low vapor pressure, the concentration of hydrogen peroxide vapor above a hydrogen peroxide solution at atmospheric conditions is very low and presents no special safety hazard. A significant concentration of hydrogen peroxide vapor occurs only at the reduced pressure conditions that exist inside the sterilization chamber in the STERRAD® NX Process. This means that hydrogen peroxide vapor would not leak out of the chamber under normal operating conditions.

It should be noted that hydrogen peroxide has been commonly used as a general disinfectant for many years. In spite of the widespread use of hydrogen peroxide by the general public, there has been no epidemiological evidence suggesting that hydrogen peroxide is a potential carcinogen.

6.3 Electronic Emission

The plasma power supply used to generate the low-temperature gas plasma in the STERRAD® NX System can only be turned on when the sterilization chamber door is closed and the chamber is under vacuum. The power supply operates at a frequency of 49 to 54 kHz. The STERRAD® NX System complies with the following standards:

- CAN/CSA-C22.2 No. 1010.1B: 1997; Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use.
- UL 61010A-1: 2002; Standard for Safety for Electrical Equipment for Laboratory Use.
- EN 61010-1: 2001; Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use.
- EN 60601-1-2: 2001; Medical Electrical Equipment, Part 1: General Requirements for Safety, Section 2: Collateral Standard: Electromagnetic Compatibility
- EN 55011, Group I Class A limits, based on CISPR 11:1997, Group I Class A limits.

7.0 Summation

The development of the STERRAD® NX Sterilization System is a continuation of Johnson & Johnson's tradition of leadership in the development and validation of sterilization processes. Johnson & Johnson developed the first commercial steam sterilization system for medical products in 1889 and has since played a leading role in the commercialization of such sterilization technologies as ethylene oxide and gamma irradiation. In keeping with that tradition, in 1992, ASP introduced the STERRAD 100 Sterilizer, the first commercial sterilization process that utilizes hydrogen peroxide and low-temperature plasma to rapidly sterilize medical devices and provide products that are free of toxic residues and are ready for use immediately after sterilization. In 1996, ASP introduced two additional models, the STERRAD 50 Sterilizer and the STERRAD 100S Sterilizers continuing ASP's product line expansion. In 2000, ASP introduced a larger model, the STERRAD 200 Sterilizer, and now, in 2004, ASP is introducing the STERRAD® NX System as a demonstration of ASP's commitment to continually provide "better medicine" to health care workers and patients. The discussions of the scientific aspects of the characterization and validation of the STERRAD® NX Sterilization System is also reflective of ASP's commitment to help bring better understanding of sterilization science to the users of our products.

Refer to the STERRAD® NX User's Guide for a complete description of the operation of this sterilizer. See the instructions for use for the STERRAD® NX Challenge Pack, STERRAD CycleSure® Biological Indicator, and Tyvek® Pouches with STERRAD Chemical Indicator for complete information regarding the use of those products.

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