STERIS®

Technical Data Monograph

SYSTEM 1E™
Liquid Chemical Sterilant Processing System

REF **T6530 Rev B**

56401-970

SYSTEM
E
TM

SYSTEM 1E LIQUID CHEMICAL STERILANT PROCESSING SYSTEM
TECHNICAL DATA EXECUTIVE SUMMARY:
MICROBIAL EFFICACY AND WATER TREATMENT SYSTEM VALIDATION

MICROBIAL EFFICACY VALIDATION

The technical data generated demonstrate effective and reproducible liquid chemical sterilization through a three tier testing system, including standardized potency tests, laboratory simulated-use tests and clinical in-use tests for the SYSTEM 1E™ Liquid Chemical Sterilant Processing System. [1]

Potency Tests

The standard potency test battery listed in the January 2000 FDA Guidance for Liquid Chemical Sterilants/High Level Disinfectants under worst case conditions as summarized in **(Table 1)**, passed when using S40™ Sterilant Concentrate.

Table 1: Summary of Potency Tests conducted for S40 Sterilant Concentrate

Test	Replicates	Test Result
AOAC Sporicidal Test Official Method 966.04	960	Free of Viable Microorganisms
Quantitative Suspension Test against Mycobacterium	8	Average Kill Rate for a 1 log Reduction in Population = 2 Seconds
Fungicidal Activity of Disinfectants AOAC Method 955.17	10	Free of Viable Microorganisms
Bactericidal Activity, Use-Dilution AOAC Methods 955.14, 955.15, 964.02	180	Free of Viable Microorganisms
Virucidal Tests DIS/TSS-7	12	Complete Inactivation

Simulated-Use Tests

Laboratory simulated-use tests were conducted for S40 Sterilant Concentrate in a manual soak application as well as in the SYSTEM 1E™ Processor. Medical devices were contaminated with the most resistant organism, *Geobacillus stearothermophilus* spores, at greater than a 10^6 challenge level. The medical devices were processed under worst case use conditions and then harvested to determine if there were any surviving organisms. **(Table 2)** lists the seven evaluated devices which were reproducibly liquid chemically sterilized after exposure to sterilant use dilution* either during manual soak or in the SYSTEM 1E Processor, i.e., no viable organisms were recovered after exposure to use dilution.

**** Throughout this publication sterilant use dilution refers to the dilution created when the SYSTEM 1E Liquid Chemical Sterilant Processing System dilutes the S40 Sterilant Concentrate within the processing chamber.***

In-Use Test

Clinical in-use tests were conducted at the Cleveland Clinic Foundation (Cleveland, OH) and University Hospitals of Cleveland, Geauga Medical Center (Chardon, OH) to show that patient soiled devices were successfully processed in the SYSTEM 1E Liquid Chemical Sterilant Processing System. **(Table 2)** lists the evaluated device types which were reproducibly liquid chemically sterilized after the completion of a sterilization cycle in the SYSTEM 1E Processor.

[1] References to **SYSTEM 1E Liquid Chemical Sterilant Processing System** refer to the **SYSTEM 1E Processor** and the **S40 Sterilant Concentrate**. References to the **SYSTEM 1E Processor** refer to the Processor alone and not to the Sterilant Concentrate.

Table 2. Summary of Simulated-Use and Clinical In-Use Tests for S40 Sterilant Concentrate and SYSTEM 1E Processor

Device Type	# Free of Viable Microorganisms /# Conducted		
	Simulated-Use		In Use
	Manual Soak	In Processor	
Colonoscope	6/6	6/6	3/3
Bronchoscope	6/6	6/6	3/3
Duodenoscope/Gastroscope	6/6	6/6	3/3
Choledochofiberscope/Cystoscope/ Hysteroscope	6/6	6/6	3/3
Ureteroscope/Telescope	6/6	6/6	6/6
Camera	6/6	6/6	3/3
Light Cord	6/6	6/6	3/3

Conclusion
S40 Sterilant Concentrate is microbially effective against a wide variety of organisms and under worst case conditions achieves a 6 log reduction of the most resistant organism. Under clinical conditions the devices evaluated were liquid chemically sterilized.

WATER TREATMENT SYSTEM VALIDATION

The water treatment system of the SYSTEM 1E Processor prepares the rinse water by extensively treating US EPA potable water through three stages: (1) Pre-filtration through two pre-filters that removes particles/contaminants > 0.1 micron (2) UV Irradiation with a UV dose sufficient to achieve a > 6 log reduction of MS2 virus (3) 0.1 micron filtration that is achieved by redundant, 0.1-micron (absolute rated) membranes to remove bacteria, fungi and protozoa > 0.1 micron through the MaxPure™ Filter. The UV treatment and filtration efficacy were validated under worst case conditions of operation.

UV Treatment

Viral inactivation by the UV lamp was validated using MS2 phage as a surrogate organism because it has been widely used in the past as a surrogate for human enteric viruses due to its similarity in physical structure, composition and morphology. As an RNA coliphage it is also similar to the most common enteric viruses (poliovirus, hepatitis A, and noroviruses). MS2 is a good model for this work because it is also capable of being detected and quantified by simple and reliable methods. MS2 is relatively easy to propagate and to grow to the required titers. Results obtained using MS2 are more reproducible than other potential surrogates and it is not a human pathogen. MS2 is a virus that is recommended by the US EPA for validation of water treatment using UV irradiation systems. MS2 is more resistant to UV irradiation (harder to kill) than are most waterborne pathogenic viruses. Because of its resistance, STERIS selected this organism for the UV water treatment system validation studies in the SYSTEM 1E Processor. Through a series of preliminary tests, the UV intensity that was predicted to achieve at least a 6 log reduction of MS2 virus was determined. A stand alone UV water treatment system was then validated by challenging three UV lamps with an incoming MS2 virus challenge of ~8 log/mL. The system challenge occurred under worst case operating conditions of maximum flow rate through the system at the UV monitor abort level. Testing demonstrated that the UV irradiation reproducibly provided > 6 log reduction of MS2 virus. The test was conducted at full power output (100%) and at 80% output to simulated end of lamp life. The UV lamp reproducibly achieved > a 6 log reduction of MS2 virus as shown in **(Table 3)**.

Table 3. MS2 Virus Inactivation by the Isolated UV Lamp

Lamp Power	Log Reduction MS2 Virus		
	Lamp 1	Lamp 2	Lamp 3
100%	6.7	6.9	6.8
80%	7.3	6.7	6.6

Testing was also conducted using MS2 as the challenge organism in a SYSTEM 1E Processor operated under normal conditions, but slightly above the abort level UV intensity (so that the cycle did not abort) and at or slightly under the maximum flow rate. **(Table 4)** shows that in the context of the entire system the UV lamp reproducibly achieved a > 6 log reduction of MS2 virus in the SYSTEM 1E Processor.

Table 4. MS2 Virus Inactivation by the Integrated UV Water Treatment System of the SYSTEM 1E Processor

SYSTEM 1E Processor	Log Reduction MS2 Virus		
	Trial 1	Trial 2	Trial 3
1	>7.7	>7.6	>8.5
2	8.2	>7.8	>8.5
3	7.9	>7.8	>8.5

The published scientific literature [2] reports that calicivirus (canine, bovine, and feline), hepatitis A, poliovirus type 1, coxsackievirus B3, B4, and B5, echovirus 1, 2, 12 and rotavirus SA-11 are all less resistant than the MS2 virus to the type of UV irradiation used by the SYSTEM 1E Processor. MS2 has been demonstrated to be less resistant than adenovirus ST2, 15, 40 and 41. The data generated for the UV light validation demonstrate that at least a 4 log reduction of adenovirus is achieved (as defined by EPA water treatment standards). [3] Adenovirus is more sensitive to chlorine in water than are waterborne pathogenic viruses such as coxsackievirus and echovirus. [4]

Conclusion

The UV Water Treatment achieves a > 6 log reduction of MS2 virus under worst case conditions of use. Waterborne pathogenic viruses less resistant to UV irradiation than MS2 virus (e.g. poliovirus type 1) will similarly be inactivated by > 6 logs. According to EPA, the UV radiation output generated by the SYSTEM 1E Processor will result in at least a 4 log inactivation of adenovirus. See US EPA (US Environmental Protection Agency), 2006. National Primary Drinking Water Regulation, Long-Term 2 Enhanced Surface Water Treatment Rule. Fed. Reg., 71:2:653, Jan 5, 2006.

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[2] W.A.M. Hijnen, E.F. Beerendonk, and G.J. Medema; Inactivation credit of UV radiation for viruses, bacteria and protozoan (oo)cysts in water: A review. Water Research 40 (2006) 3-22.
C.P. Gerba Environmental Microbiology second edition, 2009. Elsevier Inc. Chapter 26 Disinfection pages 539-552.

[3] US EPA (US Environmental Protection Agency), 2006. National Primary Drinking Water Regulation, Long-Term 2 Enhanced Surface Water Treatment Rule. Fed. Reg., 71:2:653, Jan 5, 2006.

[4] Cromeans TL *et al*., Inactivation of Adenovirus, Enteroviruses and Murine Norovirus in Water by Free Chlorine and Monochloramine. Appl. Environ. Microbiol., 2010, 76(4) 1028 - 1033.

WATER FILTRATION

After pre-filtration and UV irradiation, the potable water is filtered through two pharmaceutical sterilizing-grade 0.1 micron filter membranes to remove bacteria, fungi and protozoa > 0.1 micron from the rinse water. The effectiveness of the filter membranes was validated following ASTM F838-05 using the challenge organism identified in the test method *Brevundimonas diminuta*. A smaller challenge organism, *Ralstonia pickettii*, which can pass through a standard 0.2 micron pharmaceutical sterilizing-grade filter, was also evaluated. Prior to the challenge to validate a filter life of 90 days, the MaxPure Filters had been exposed to > 470 liquid chemical sterilization cycles in the SYSTEM 1E Processor. The filters were able to remove all of the challenge bacteria at a challenge level > 1×10^7 colony forming units (CFU) per cm^2 of effective filtration area, see **(Table 5)**.

Table 5. Validation Challenge of the MaxPure Filter

Challenge Organism	Filter Number	Challenge Level (CFU*/cm^2)	Organism Recovered
Brevundimonas diminuta	1	4.9×10^7	0
	2	5.2×10^7	0
	3	4.6×10^7	0
Ralstonia pickettii	1	3.6×10^7	0
	2	3.8×10^7	0
	3	3.3×10^7	0

* CFU = Colony Forming Units

Conclusion

All bacteria, fungi and protozoa > 0.1 micron are retained at the end of filter use life by the MaxPure Filter.

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INTRODUCTION

This Technical Data Monograph illustrates the principles of operation, outlines the processor cycle, and provides data to support performance claims of the SYSTEM 1E Liquid Chemical Sterilant Processing System. Performance data are presented supporting microbial efficacy, material compatibility, non-toxicity, safe residual levels, and hemocompatibility testing achieved with the SYSTEM 1E Processor.

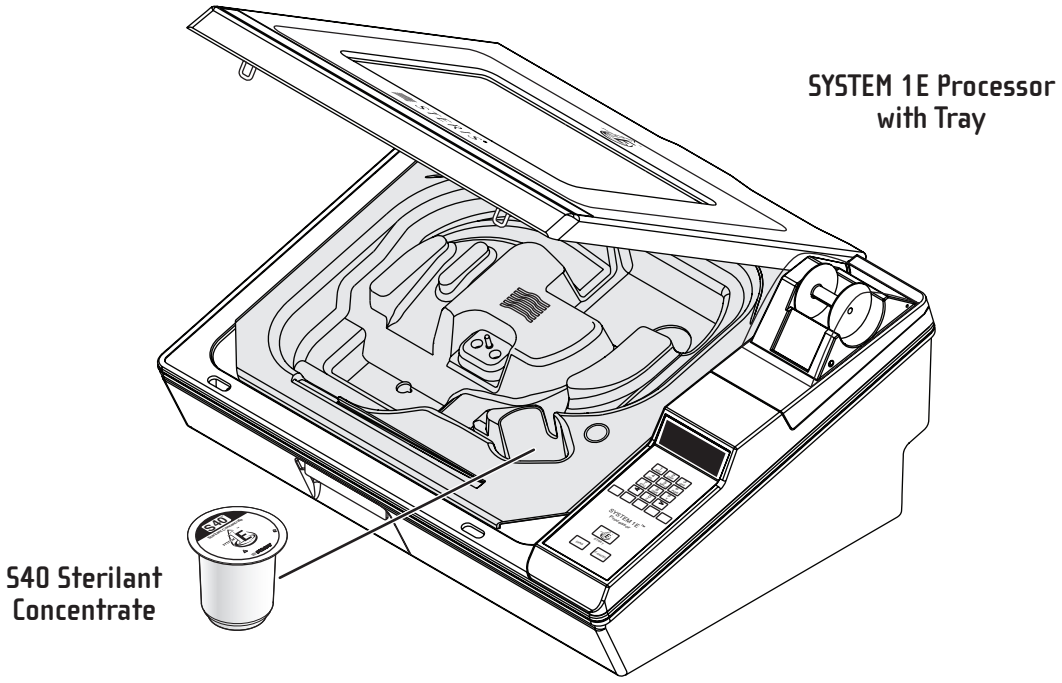
The SYSTEM 1E Liquid Chemical Sterilant Processing System is intended for liquid chemical sterilization of cleaned, totally immersible, and reusable critical and semi-critical heat sensitive medical devices, such as rigid surgical and gastrointestinal (GI) flexible endoscopes, bronchoscopes, and their accessories, used in healthcare facilities. Some specific examples are: arthroscopes, colonoscopes, cystoscopes, gastroscopes, laparoscopes, and sigmoidoscopes.

The principal features of the SYSTEM 1E Processor include:

- Automated, easy-to-use, microprocessor control panel with unalterable, standardized processing and diagnostic cycles
- Liquid chemical sterilization using low temperature, liquid immersion
- Proprietary, single use, chemical formulation of germicide sealed in its own delivery system
- Automated delivery and dilution of the sterilant concentrate
- Two rinses following liquid chemical sterilization with water that has been extensively treated by:
  - Filtration through 3/2.5 µm and 0.6/0.1 µm layered filters to remove particulates
  - Ultra-violet (UV) irradiation for viral inactivation
  - Filtration through a 0.8/0.1/0.1 µm layered filter to remove bacteria, fungi, and protozoa > 0.1 micron in size
- Air entering the processor chamber during draining of the liquid is passed through a 0.2 micron membrane filter to remove air-borne contaminants
- Process monitoring and load documentation
- Technology to accommodate a broad spectrum of heat sensitive endoscopes and their accessories
- System features and functions designed for the safety of patients, healthcare workers, medical devices, and the environment
- System designed for ease of maintenance

The **(Figure A)** shows components of the SYSTEM 1E Liquid Chemical Sterilant Processing System. These components include the SYSTEM 1E Processor (including the tray inside of the chamber) and S40 Sterilant Concentrate.

Figure A: S40 Sterilant Concentrate and Processor Tray used in the SYSTEM 1E Liquid Sterilant Processing System

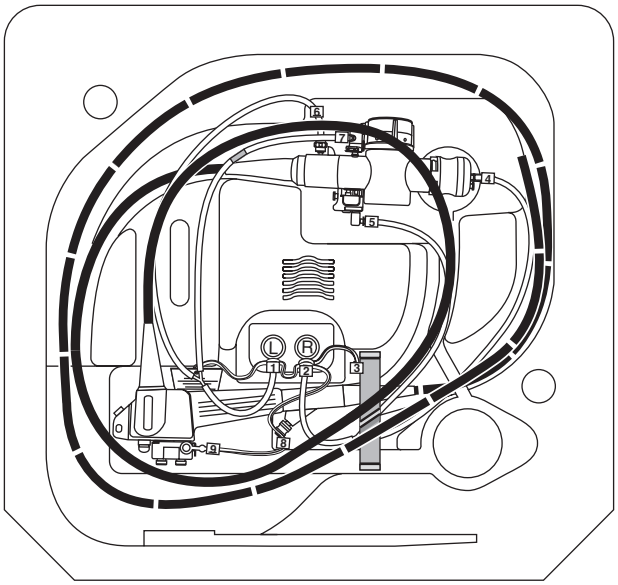


PRINCIPLES OF OPERATION

The interchangeable processor trays and associated Quick Connects (QCs) (see **(Figure B)** for example) provide for effective delivery of the sterilant use dilution, and the extensively treated rinse water removes residuals from endoscopes and their accessories when used in the SYSTEM 1E Processor.

Cleaned, heat sensitive critical and semi-critical endoscopes are loaded into the appropriate processing tray. There are four different processor tray configurations for use in the SYSTEM 1E Processor. Each tray has unique features that are designed to maintain instruments in the appropriate positions for optimal liquid chemical sterilization of the different manufacturer's endoscope design features or for procedure-specific sets of devices. Assistance in selecting the specific tray to use can be found by consulting the STERIS device matrix (available online at www.steris.com). This online device matrix also identifies the appropiate Quick Connect to attach the lumens of the specified device to the tray/container ports.

Figure B: Drawing of tray with a loaded endoscope, attached QC, and container well for S40 Sterilant Concentrate.



The container well of the processor tray is the insertion location for S40 Sterilant Concentrate. An aspirator probe, attached to the tray, is inserted into the container at the + mark located on the lid of the container.

Once the lid is closed the [START] button is pressed. When the processor is filled with water, the pump activates dissolving the dry powder Builders and mixing the peracetic acid. The endoscopes are completely submerged in liquid during the processor cycle. The Quick Connects direct fluid flow through all lumens of rigid or flexible endoscopes (see detailed discussion of the Quick Connects). The sterilant use dilution is circulated throughout the chamber, liquid chemically sterilizing the load.

At the conclusion of the Exposure Phase, the processor contents and chamber are drained and then rinsed two times with extensively treated potable hot water.

A filter integrity test is performed after every cycle to verify the integrity of the pharmaceutical sterilizing-grade 0.1 micron MaxPure Filter.

At the conclusion of a successful integrity test the cycle is complete. The processor can be opened and the liquid chemically sterilized device is ready for immediate use.

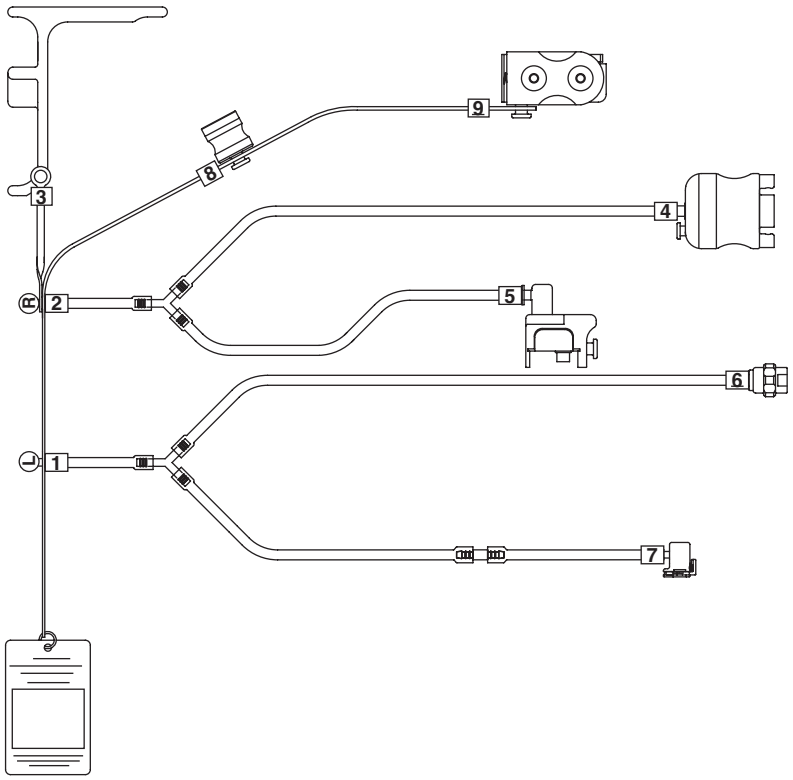
Extensively treated water used for dissolution and dilution of S40 Sterilant Concentrate and for effective rinsing of the processed endoscopes and accessories is delivered by the SYSTEM 1E Processor.

- EPA potable water is pre-filtered through a dual filter set to remove particulates as small as 2.5 microns in size with the A pre-filter, and as small as 0.1 microns with the B pre-filter.
- The pre-filtered water is then exposed to a dose of UV light for a ≥ 6 log reduction of most, but not all viruses; in the unlikely event they may be present in EPA potable water.
- The treated water is then passed through a pharmaceutical sterilizing-grade tri-layered filter (0.8/0.1/0.1 microns) to remove bacteria, fungi, and protozoa > 0.1 micron in size before being used to fill the processor.

QUICK CONNECTS

The unique design of the processor trays permits a wide variety of heat sensitive devices to be loaded into the SYSTEM 1E Processor. Quick Connects (see **(Figure C)**) are available and have been validated by STERIS for those devices identified in the STERIS device matrix available online at www.steris.com. Each Quick Connect includes processing instructions for the devices included in the STERIS device matrix. When properly attached, the sterilant use dilution is flowed through all channels simultaneously. Some devices can be processed through the SYSTEM 1E Liquid Chemical Sterilant Processing System without the use of Quick Connects. Before using the SYSTEM 1E Liquid Chemical Sterilant Processing System, check the STERIS device matrix (available online at www.steris.com) to determine whether or not a Quick Connect is required for processing in the system, and if so, determine the appropriate Quick Connect model.

Figure C: Example of a Quick Connect flow unit showing endoscope connections, tubing, device support, and reference card.



CONSUMABLES

S40 Sterilant Concentrate

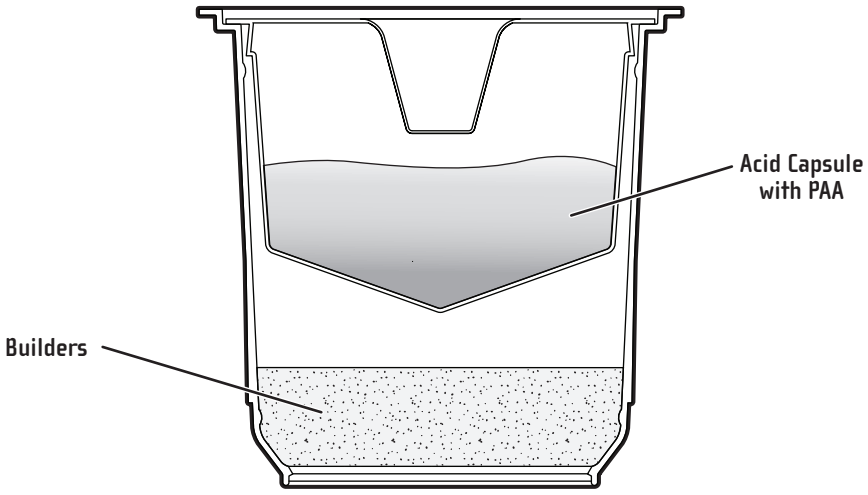
S40 Sterilant Concentrate is a proprietary, two-part formulation that was developed exclusively for use in the SYSTEM 1E Liquid Chemical Sterilant Processing System. It delivers the pre-measured components from a single-use container. A proprietary formulation of dry powder Builders, the inert ingredients, is in the lower compartment of the container. When packaged, the upper compartment contains the active ingredient, a nominally 35.5% solution of peracetic acid (PAA). The two components are mixed with water during the automated cycle providing a sterilant use dilution capable of:

- Liquid chemical sterilization of processed endoscopes
- Inhibiting corrosion of metals, polymers, and other materials

The container of S40 Sterilant Concentrate **(Figure D)** has been engineered to provide a safe and easy-to-use product for healthcare workers. The single use carton allows for convenient storage of the liquid chemical sterilant container. It can only be loaded into the tray container well in one orientation. The concentration and volume of the PAA in the container is sufficient to provide a 6-month shelf life from date of manufacture of S40 Sterilant Concentrate.

The liquid compartment of the container allows gases generated from the normal degradation of the PAA to escape and not build-up pressure during transportation and storage of S40 Sterilant Concentrate. A room with standard ventilation and temperature control are the only requirements needed for storage of S40 Sterilant Concentrate. An empty container is safe for disposal without special treatment by the healthcare worker when removed from the SYSTEM 1E Processor.

Figure D: Cut away figure showing labeled components and orientation for the assembled container of S40 Sterilant Concentrate.



PROCESSING CYCLE

The SYSTEM 1E Processor provides a fully automated and validated processing cycle. It is a self-contained system which creates and maintains the conditions necessary for liquid chemical sterilization. The processing cycle of the SYSTEM 1E Processor consists of a:

1. Fill Phase

2. Warm/Mix Phase

3. Exposure Phase

4. Two Rinse Phases

5. Air Purge Phase

6. On-board Filter Integrity Test

The critical process parameters are:

- Contact Time
- Use Dilution Temperature
- Peracetic Acid Concentration
- Multi-layered 0.1 micron Filter Integrity
- UV Radiation Dose

Prior to the start of each new cycle, a new container of S40 Sterilant Concentrate is placed within the sterilant well of the installed interchangeable tray.

In the Fill Phase, when the supply water reaches a minimum of 43°C (109°F), it enters the processing chamber to dissolve and mix the dry powder components. During the Warm/Mix Phase, the pump activates and siphons the concentrated PAA solution into the processing chamber. To ensure a suitable sterilant use dilution temperature and uniform concentration of the active ingredient, the components are mixed for the next 1.6 to 5 minutes (depending on in-coming water temperature) within the SYSTEM 1E Processor.

The liquid chemical sterilization occurs during the 6 minute Exposure Phase. The PAA concentration will be $\geq$ 1820 mg/L. The use dilution is continuously circulated throughout the processing chamber, including circulation over every surface and through the lumens of the endoscopes. The water is heated to a controlled temperature and will be between 46-55°C (115-131°F) during exposure.

After the liquid chemical sterilization at the end of the Exposure Phase, the use dilution drains and the tray empties while 0.2 micron filtered air enters the chamber. Two Rinse Phases follow using extensively treated potable hot water which is filtered through two pre-filters, passed through a UV light path, and filtered again through a 0.8/0.1/0.1 µm multi-laminate bacteria retentive MaxPure Filter. After rinsing, an Air Purge Phase follows in which air is pulled through a 0.2 micron HEPA filter and circulated through the endoscope channels to help remove excess water.

After the air purge, an integrity test is performed on the MaxPure Filter. The filter housing is pressurized and then monitored to verify the integrity of the MaxPure Filter.

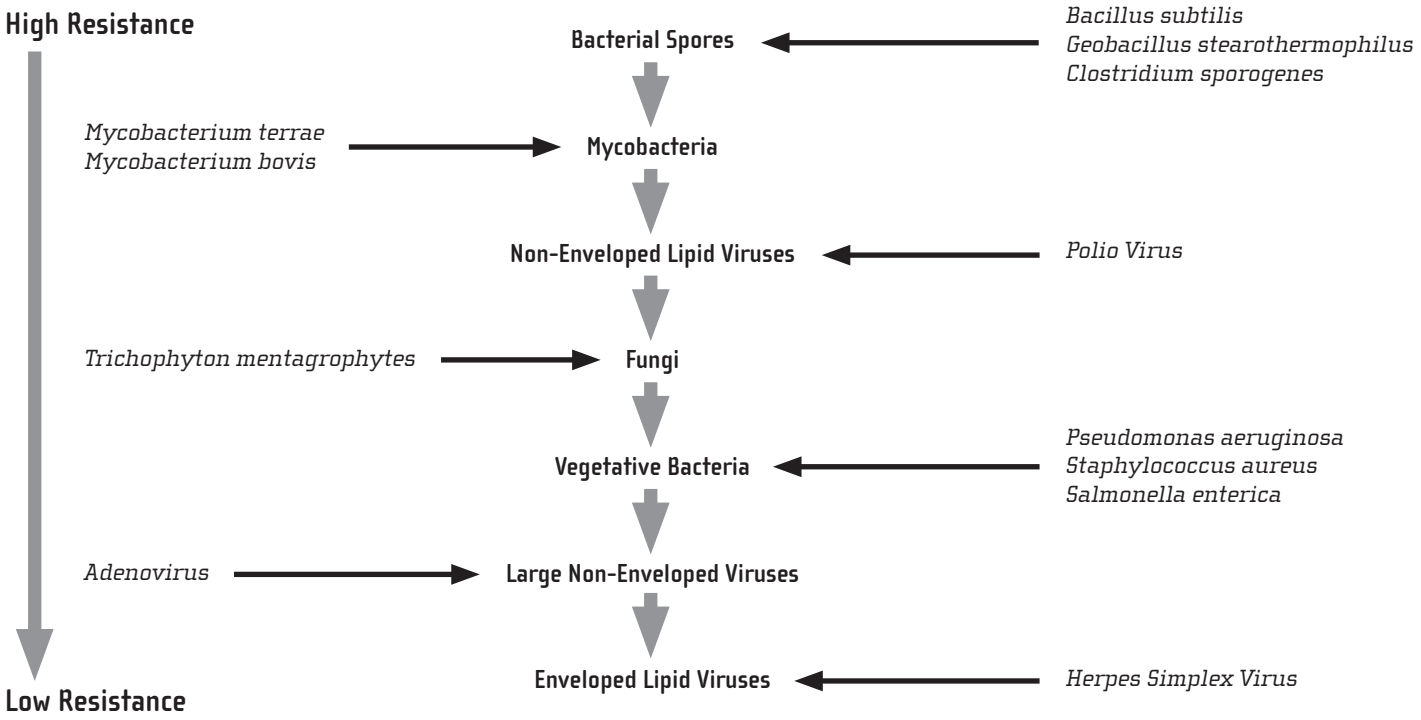
The processor cycle time is approximately 23 minutes.

PERFORMANCE EVALUATIONS

Microbial Efficacy Testing

Microbial efficacy testing was conducted using standard *in vitro* methods with various organisms to confirm the efficacy of the liquid chemical sterilization solution provided by S40 Sterilant Concentrate. As depicted in **(Figure E)**, an assortment of organisms, from those with low resistance to most germicides (vegetative bacteria), to those with the highest known resistance to most germicides (bacterial spores), were tested after exposure to sterilant use dilution.

Figure E: Classes of Microorganism Ranked from Least to Most Susceptible to Chemical Disinfectants (S. Block, 4th Edition, 1991)



Potency Testing

Potency testing was performed with a variety of organisms to challenge S40 Sterilant Concentrate. Testing was conducted using the following parameters:

- PAA concentration of < 1820 mg/L (minimum recommended concentration)
- Temperature of ≤ 43°C
- Exposure time of six minutes or less (for testing purposes)
- Hard water concentration of ~140 ppm
- All testing was performed *in vitro*
- All testing was performed with End of Shelf Life (EOSL) S40 Sterilant Concentrate
- Methods allowing organic (5% serum) and inorganic (hard water) challenge present in the inocula (Tuberculocidal, Virucidal, and Fungicidal) incorporated these challenges.

Test methodologies, number of product lots tested, and replicates performed were compliant with the document "Guidance for Industry and FDA Reviewers: Content and Format of Premarket Notification [510(k)] Submissions for Liquid Chemical Sterilants/High Level Disinfectants", 01/03/00. Results are summarized in **(Table 1)**.

Table 1: Summary of Potency Testing

Testing	Method(s)	Test Organism	Lots Tested	Replicates	Outcome Following Exposure	Result
Bacterial Spores	AOAC 966.04	*Bacillus subtilis*	3	720	No Growth	Pass
		Clostridium sporogenes				
	AOAC 966.04 Confirmatory Test	*Bacillus subtilis*	1	240	No Growth	Pass
		Clostridium sporogenes				
Mycobacteria	Tuberculocidal Activity Ascenzi Quantitative Suspension Test	*Mycobacterium terrae*	2	8	Average Kill Rate = 2.0 seconds	Pass
Virus	EPS Virucidal Testing (DIS/TSS-7, 11/81)	Poliovirus Type 1	1	4	Complete Inactivation	Pass
		Adenovirus Type 5	1	4	Complete Inactivation	Pass
		Herpes simplex virus Type 1	1	4	Complete Inactivation	Pass
Fungus	AOAC 955.17	*Trichophyton mentagrophytes*	1	10	No Growth	Pass
Vegitative Bacteria	AOAC 955.14	*Salmonella enterica*	1	60	No Growth	Pass
	AOAC 955.15	*Staphylococcus aureus*	1	60	No Growth	Pass
	AOAC 962.02	*Pseudomonas aeruginosa*	1	60	No Growth	Pass

Conclusion for Potency Testing

All potency requirements for a liquid chemical sterilant are met by S40 Sterilant Concentrate.

Microbial Lethality Kinetics

Kill kinetics testing was performed to identify the most resistant organism to PAA, as well as to characterize the kill rate for the sterilant use dilution.

Previous unpublished data compared the kill rates of various organisms exposed to PAA with a focus on bacterial spores. Results from this testing determined that *Geobacillus stearothermophilus* was identified to be the most resistant organism (MRO) to PAA.

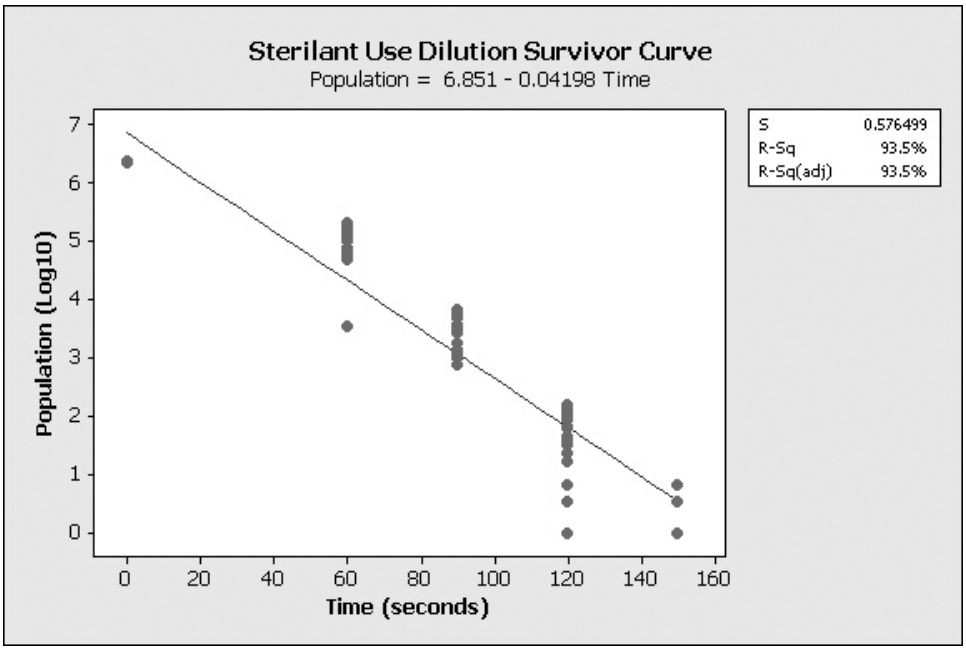
Kill kinetics testing was then performed using the most resistant organism to characterize the efficacy for the use dilution. Testing was performed using the following parameters:

- PAA concentration was ≤ 1820 mg/L
- Temperature was ≤ 43°C
- Inorganic burden amongst the trials was equally distributed to include:
  - DI water
  - 140 ppm hard water
  - 140 ppm hard water with heavy metals
- Organic burden amongst the trials was equally distributed to include:
  - With 1% serum
  - Without 1% serum
- Each inorganic/organic burden combination was performed in triplicate (18 total trials)

Testing was performed by preparing a volume of use dilution using specified amounts of the S40 Sterilant Concentrate. The use dilution was inoculated with *G. stearothermophilus* at ~10^6 CFU/mL. Aliquots of the inoculated use dilution were sampled at designated time intervals, neutralized, serially diluted, plated on growth media, and incubated to determine the resulting population present at a given time point.

A statistical analysis of the data from all 18 trials determined that the kill kinetics did not vary significantly between trials. Therefore, results from all 18 trials were pooled together and a survivor curve was plotted **(Figure F)**. Linear regression analysis of the data was performed. The resulting analysis determined that the kill kinetics, time to kill one log of the MRO, under the test conditions was ~24 seconds with an adjusted R-squared value of 93.5%. The high R-squared value indicates good linearity in the data. All controls (positive, negative, neutralization) performed as required.

Figure F: Survivor Curve for Sterilant Use Dilution



Conclusion for Microbial Lethality Kinetics

Under the test conditions and time range evaluated, kill kinetics of ~24 seconds has been measured for S40 Sterilant Concentrate.

MEDICAL DEVICE TESTING

Manual Soak Testing

STERIS conducted manual static soak testing, of representative challenging, heat sensitive medical devices with respect to size and features that are difficult to liquid chemically sterilize, to demonstrate the effectiveness for liquid chemical sterilization of medical devices with the sterilant use dilution.

[*Manual soak testing was performed for validation purposes only and is not a recommended practice, nor is it practical, for the end use of S40 Sterilant Concentrate. This product is intended for use only in an integrated, software controlled SYSTEM 1E Processor.*]

Four flexible endoscopes and a device set were used to verify that liquid chemical sterilization was reproducibly achieved with sterilant use dilution. The device set consisted of a Gyrus ACMI Semi-Rigid Ureteroscope, a Karl Storz or Dyonics Camera and a Karl Storz Light Cord.

Testing was performed using the following parameters:

- Spores of the most resistant organism, *Geobacillus stearothermophilus*, were suspended in an organic (5% serum) and inorganic (400 ppm hard water) challenge
- Devices were air dried for ≥ 30 minutes prior to processing
- PAA concentration of < 1820 mg/L
- Temperature of ≤ 43°C
- Exposure time was six minutes
- Hard water concentration was ~140 ppm

The test organism was inoculated into all internal channels. Selected external sites were also inoculated. Three replicate trials were performed for each endoscope or device set. Three additional trials were also performed with use dilution of End of Shelf Life (EOSL) S40 Sterilant Concentrate.

Exposure of the devices was performed in a basin filled with use dilution, at a concentration less than the minimum recommended concentration of PAA (1820 mg/L). Following exposure, devices were sequentially rinsed twice with sterile water. Selected external surface sites and all internal channels were harvested following sterile rinsing.

Acceptable performance was demonstrated when each trial resulted in complete elimination of viable test organism. Results from this testing are presented in **(Table 2)**. All controls (positive, negative, recovery and neutralization) performed as required.

Table 2: Manual Soak Testing with Sterilant Use Dilution

Medical Device		Recoverable Challenge (CFU/device)	Test Organism Recovered					
			Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Trial 6
Olympus Colonoscope		$> 10^6$	0	0	0	0	0	0
Fujinon Bronchoscope		$> 10^6$	0	0	0	0	0	0
Olympus Duodenoscope		$> 10^6$	0	0	0	0	0	0
Pentax Peroral Choledochofiberscope		$> 10^6$	0	0	0	0	0	0
Device Set	Gyrus ACMI Semi-Rigid Ureteroscope	$> 10^6$	0	0	0	0	0	0
	Dyonics Camera	$> 10^6$	0	0	0			
	Karl Storz Camera	$> 10^6$				0	0	0
	Karl Storz Light Cord	$> 10^6$	0	0	0	0	0	0

Shaded portions of Table 2 indicate that a specific device was not used in the test performed.

Conclusion for Manual Soak Testing

Reproducible liquid chemical sterilization of medical devices has been demonstrated by the ability to eliminate $> 10^6$ CFU/device of the most resistant organism, *Geobacillus stearothermophilus* spores with sterilant use dilution.

Simulated-Use Testing

To demonstrate the effectiveness of the processor for liquid chemical sterilization of medical devices, STERIS conducted simulated-use testing, with the same devices used for manual soak testing, in the SYSTEM 1E Processor.

Testing was performed using the same parameters as in Manual Soak:

- The most resistant organism, *Geobacillus stearothermophilus* spores, were suspended in an organic (5% serum) and inorganic (400 ppm hard water) challenge
- Devices were air dried for ≥ 30 minutes prior to processing
- PAA concentration of < 1820 mg/L
- Exposure time of six minutes
- Hard water concentration of ~140 ppm

Additional parameters instituted for the use of the SYSTEM 1E Processor included:

- Exposure temperature of ≥ 45.5°C
- Setting of the high pressure pump to the worst case fluid flow rate
- Use of MaxPure Filters with > 470 standard cycles in the SYSTEM 1E Processor
- The UV system was set to the minimum specified UV intensity

The test organism was inoculated into all internal channels. Selected external sites were also inoculated. Three replicate test trials were performed for each endoscope or device set. Three additional trials were also performed with EOSL S40 Sterilant Concentrate.

Exposure of the device(s) was performed by placing the inoculated and dried device(s) in the SYSTEM 1E Processor. PAA concentrations at less than the minimum recommended concentration of 1820 mg/L were prepared in special containers of S40 Sterilant Concentrate. A processing cycle was initiated consisting of a 6-minute Exposure Phase and two rinses. All internal channels and selected external surface sites were harvested following completion of the cycle in the SYSTEM 1E Processor.

Acceptable test performance required that each trial resulted in complete elimination of viable test organism. Results from this testing are presented in **(Table 3)**. All controls (positive, negative, recovery, and neutralization) performed as expected.

Table 3: Simulated-Use Testing in the SYSTEM 1E Processor

Medical Device		Recoverable Challenge (CFU/device)	Test Organism Recovered					
			Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Trial 6
Olympus Colonoscope		$> 10^6$	0	0	0	0	0	0
Fujinon Bronchoscope		$> 10^6$	0	0	0	0	0	0
Olympus Duodenoscope		$> 10^6$	0	0	0	0	0	0
Pentax Peroral Choledochofiberscope		$> 10^6$	0	0	0	0	0	0
Device Set	Gyrus ACMI Semi-Rigid Ureteroscope	$> 10^6$	0	0	0	0	0	0
	Dyonics Camera	$> 10^6$	0	0	0			
	Karl Storz Camera	$> 10^6$				0	0	0
	Karl Storz Light Cord	$> 10^6$	0	0	0	0	0	0

Shaded portions of Table 3 indicate that a specific device was not used in the test performed.

Conclusion for Simulated-Use Testing

The S40 Sterilant Concentrate reproducibly liquid chemically sterilized medical devices as demonstrated by the ability to eliminate > 10^6 CFU/device of the most resistant organism, *Geobacillus stearothermophilus* spores when used in the SYSTEM 1E Processor.

In-Use Testing

In a hospital setting, clinically used medical devices with patient soil were evaluated using the SYSTEM 1E Processor. Devices were selected to represent the range of device designs likely to be encountered in a clinical setting.

- Bronchoscope (pulmonary, bronchial)
- Duodenoscope/Gastroscope (upper GI, esophageal)
- Colonoscope (lower GI, bowel)
- Cystoscope/Hysteroscope (urology/gynecological)
- Device Set (rigid endoscope, light cord, camera and telescope)

After patient use, clinical personnel manually cleaned each device per the manufacturer's instructions. The cleaned devices and a container of S40 Sterilant Concentrate were placed in the processor and the processor cycle was initiated. After processing, each device's external surfaces and internal channels were harvested. Multiple trials were performed for each device type.

Positive control recovery sampling was performed before and after manual cleaning, demonstrating that some reduction (but not elimination) of clinical microbiological loads by manual cleaning occurred, as expected.

No remaining clinical isolates were recovered from any of the devices after all trials in the clinical setting as shown in **(Table 4)** and **(Table 5)**. **(Table 4)** identifies both external and internal test sites of the individual devices that were cycled in the SYSTEM 1E Processor. **(Table 5)** presents data for a device set, or a group of devices processed together and having only external test sites.

Table 4: In-Use Testing with SYSTEM 1E Processor

Test Site		Post Processing Recovery (CFU)											
		Bronchoscope			Duodenoscope/ Gastroscope			Colonoscope			Cystoscope/ Hysteroscope		
		Trials			Trials			Trials			Trials		
		1	2	3	1	2	3	1	2	3	1	2	3
External	Bending Rubber	0	0	0	0	0	0	0	0	0	0	0	0
	Actuation Lever	0	0	0	0	0	0	0	0	0	0	0	0
	Biopsy/Suction	0	0	0	0	0	0	0	0	0			
	Air/Water				0	0	0	0	0	0			
Internal	Elevator Guide Wire				0	0							
	Auxiliary Water									0			
	Working Channel										0	0	0
	Irrigation Channel										0	0	0

Shaded portions of Table 4 indicate that a specific test site was not present on the device tested.

Table 5: In-Use Testing of Device Set with SYSTEM 1E Processor

Test Site	Post Processing Recovery (CFU)											
	Rigid Endoscope			Light Cord			Camera			Telescope		
	Trials			Trials			Trials			Trials		
	1	2	3	1	2	3	1	2	3	1	2	3
External (7 per device)	0	0	0									
External (2 per device)				0	0	0	0	0	0	0	0	0

Shaded portions of Table 5 indicate that a specific test site was not present on the device tested.

Conclusion for In-Use Testing

In-use testing confirmed the effectiveness observed in simulated-use testing by demonstrating that all devices were reproducibly liquid chemically sterilized since no organisms were recovered from device surfaces or channels following a standard cycle of the SYSTEM 1E Processor using S40 Sterilant Concentrate.

Water Treatment System

Public water treatment facilities are required by the EPA to treat source water to a level that achieves at least a 4 log (10,000 fold) reduction or removal of virus before the water leaves their facility. This potable (drinking) water is the input water source for the SYSTEM 1E Processor. That water is then further treated extensively by the processor's water treatment system prior to its use for all water fills including the Rinse Phases.

The additional steps provided by the water treatment system of the SYSTEM 1E Processor consist of the following:

1. Pre-filtration through two pre-filters:

- Pre-filter A is a gross depth filter that removes approximately 2.5 micron or larger particles/contaminants
- Pre-filter B is a surface filter that removes particles/contaminants > 0.1 micron

2. UV irradiation:

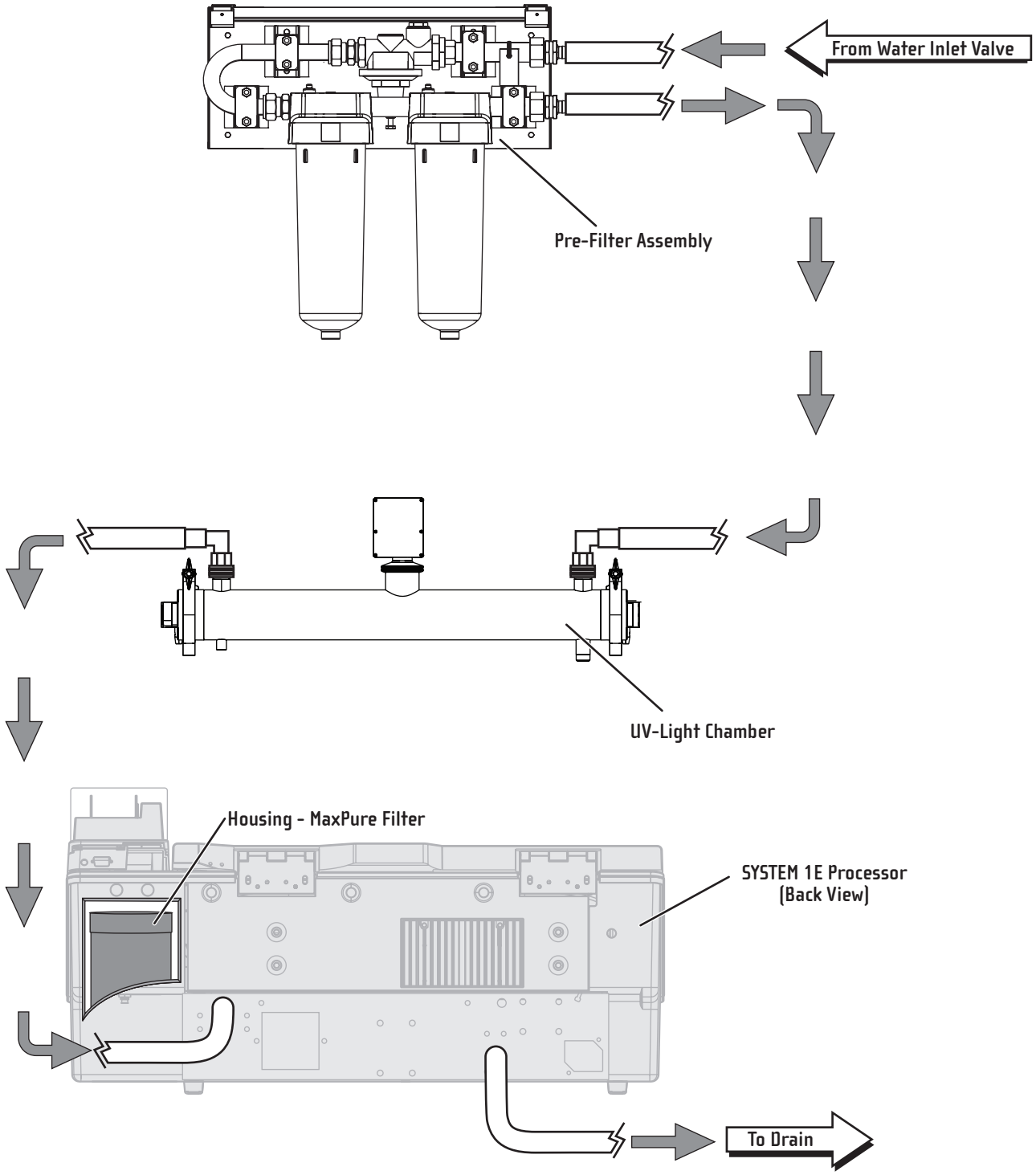
- The pre-filtered water is passed through the UV Water Treatment Chamber, where a UV dose sufficient to achieve a $\geq$ 6 log reduction of MS2 virus is delivered to the water

3. 0.1 micron filtration:

- The water prepared by pre-filtration and UV irradiation is filtered through redundant, 0.1 micron (absolute rated) membranes to remove bacteria, fungi and protozoa > 0.1 micron

After this extensive, validated, controlled and monitored treatment, the water is used to rinse the liquid chemically sterilized devices. All water passes through this treatment process before entering the SYSTEM 1E Processor.

Figure G: Components of the Water Treatment System used in the SYSTEM 1E Processor



Pre-filtration

The pre-filters are designed to remove the particulates that are released and carried in the potable water between the supply source and the demand location, i.e. from the supply plumbing, heater systems, water softeners.

UV Irradiation

An ultraviolet irradiation system was incorporated into the SYSTEM 1E Processor to inactivate viral particles in incoming water (in the unlikely event that viral particles would be present in EPA potable tap water). The UV irradiation system is located just after the two pre-filters in the water treatment system of the SYSTEM 1E Processor. The UV irradiation system is a cylindrical tube through which all incoming water flows. The inside of the cylindrical tube and the UV lamp are designed to optimize contact of the UV light with the flowing water. This design delivers a specified dose of UV light. The UV irradiation system also consists of a UV monitor that interfaces with microprocessor controls of the SYSTEM 1E Processor. The monitor ensures that the UV lamp is delivering a sufficient intensity of UV light. If the UV light intensity ever falls below the specified minimum threshold, the processor will abort the cycle. To operate properly, the UV irradiation system requires that the incoming water have a UV transmission capacity of $\geq$ 88% at 254 nm and a water hardness of $\leq$ 140 ppm.

Validation of the UV Irradiation System

The UV irradiation system was validated using MS2 virus. MS2 is a virus that is recommended by the US EPA for validation of water UV irradiation systems. It is more resistant to UV irradiation (harder to kill) than are most waterborne pathogenic viruses. The published scientific literature [5] reports that calicivirus (canine, bovine, and feline), hepatitis A, poliovirus type 1, coxsackievirus B3, B4, and B5, echovirus 1, 2, and 12 and rotavirus SA-11 are all less resistant than is MS2 virus to the type of UV irradiation used by the SYSTEM 1E Processor. However, MS2 has been demonstrated to be less resistant than adenovirus ST2, 15, 40, and 41 to the type of UV irradiation used in the SYSTEM 1E Processor. Adenovirus is more sensitive to chlorine in water than are waterborne pathogenic viruses such as coxsackievirus and echovirus. [6]

All validation testing was performed by an independent laboratory. Range finding was performed to determine at what water quality and UV intensity the UV irradiation system achieved the required 6 log reduction of MS2 virus. Following determination of the point at which the required 6 log reduction was achieved, testing was performed to validate the UV irradiation system. For this testing, the following parameters were employed:

- Worst case UV lamps were used (~80% intensity)
- Three replicate UV irradiation systems configured to function at the minimum specified UV intensity were evaluated
- A UV monitor on each system monitored the UV intensity during the test
- Dechlorinated potable tap water at ambient temperature was inoculated with MS2 and flowed through the UV irradiation system
- Aliquots of effluent from the UV irradiation system were analyzed to determine the log inactivation for MS2
- A collimated dose response test was performed with the MS2 to ensure that the virus was within inactivation bounds required by the EPA for valid testing

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[5] W.A.M. Hijnen, E.F. Beerendonk, and G.J. Medema; Inactivation credit of UV radiation for viruses, bacteria and protozoan (oo)cysts in water: A review. Water Research 40 (2006) 3-22.
C.P. Gerba Environmental Microbiology second edition, 2009. Elsevier Inc. Chapter 26 Disinfection pages 539-552.

[6] Cromeans TL *et al*., Inactivation of Adenovirus, Enteroviruses and Murine Norovirus in Water by Free Chlorine and Monochloramine. Appl. Environ. Microbiol., 2010, 76(4) 1028 - 1033.

(Table 6) Details the viral log inactivation during the evaluation of only the UV irradiation system. Viral log inactivation of > 6 logs was observed for all trials performed.

Table 6: MS2 Virus Inactivation by the Isolated UV Lamp

Lamp Power	Log Reduction MS2 Virus		
	Lamp 1	Lamp 2	Lamp 3
100%	6.7	6.9	6.8
80%	7.3	6.7	6.6

Following completion of the validation of the UV irradiation system itself, an independent laboratory tested the UV irradiation system incorporated into the SYSTEM 1E Processor. For this testing, the following was employed:

- UV systems configured to function at the minimum specified UV intensity were evaluated on three replicate SYSTEM 1E Processors
- A UV monitor on each system monitored the UV intensity during the test
- Dechlorinated potable tap water at ~50°C was inoculated with MS2 and flowed through the SYSTEM 1E Processor
- New filters were used for each trial of the SYSTEM 1E Processor
- The log inactivation for MS2 was determined for aliquots of rinse water from each SYSTEM 1E Processor
- A collimated dose response test was performed with the MS2 to ensure that the virus was within inactivation bounds required by the EPA for valid testing
- Trials were also performed with the UV irradiation system deactivated (No UV Control) to determine the impact of any residual stresses upon the test organism independent of the UV irradiation system

(Table 7) details the viral log inactivation observed in these studies for the SYSTEM 1E Processor. In all test cycles, inactivation was demonstrated to be at least 7.6 log, and in some instances greater than 8.5 log. Inactivation for the No UV Control resulted in minimal inactivation, 0.3 – 0.4 log.

Table 7: MS2 Log Reduction for SYSTEM 1E Processor

Trial	Viral Log Inactivation		
	Processor A	Processor B	Processor C
1	>7.7	>7.6	>8.5
2	8.2	>7.8	>8.5
3	7.9	>7.8	>8.5
No UV Control	0.3	0.4	0.3

Conclusion for UV Irradiation

At least a 6 log reduction in MS2 virus was observed when the UV irradiation treatment was incorporated into the SYSTEM 1E Processor.

Filtration

The 0.1 micron filtration system is located just after the UV irradiation system as part of the water treatment system of the SYSTEM 1E Processor. The filtration system is a 0.8/0.1/0.1 µm layered pharmaceutical sterilizing-grade filter that removes bacteria, fungi, and protozoa > 0.1 micron in size identified as the MaxPure Filter. To validate the effectiveness of this filter, testing was performed with various organisms per test method ASTM F838-05, "*Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration.*"

Using the test organism specifically identified in ASTM F838-05, *Brevundimonas diminuta*, validation was performed on the MaxPure Filters. *B. diminuta* is also recommended in the FDA guidance document "*Guidance for Industry, Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Process*", 09/04. *B. diminuta* is a gram-negative, environmental organism that, when grown as outlined in ASTM F838-05, is > 0.2 µm in size, but smaller than 0.45 µm. Testing was performed as follows:

- Three MaxPure Filters were cycled for ≥ 470 standard, full cycles in the SYSTEM 1E Processor with S40 Sterilant Concentrate.
- A forward flow diffusion test was used to confirm filter integrity prior to bacterial challenge of the three cycled MaxPure Filters.
- Filters and the test apparatus were sterilized via steam.
- Prior to testing, the ability of the challenge organism to pass through a 0.45 µm filter, but be retained by a 0.2 µm filter was confirmed.
- Challenge solution was passed through each filter and the downstream effluent was passed through a 0.2 µm filter. Filters were incubated and scored to confirm the absence of viable microorganisms in the test system prior to microbial challenge.
- Each individual cycled filter was challenged with *B. diminuta*. The *B. diminuta* was at a concentration of ≥ 10^7 CFU/cm^2 of effective filter area as stipulated in ASTM F838-05.
- Downstream effluent from each challenge test was passed through a 0.2 µm filter. Filters were transferred to growth media and incubated to determine if organism was present in the effluent.
- In addition to the cycled MaxPure Filters, three non-cycled MaxPure Filters were also challenged.

The bacterial challenge was carried out with a system free of viable microorganisms and an appropriate challenge level. All cycled and non-cycled filters were fully retentive of *B. diminuta*. Nondestructive integrity tests (diffusional flow tests) confirmed that cycled filters were integral prior to testing. All controls performed as expected. Results from the *B. diminuta* challenged filters are presented in **(Table 8)**.

Table 8: Challenge with *B. diminuta* of the MaxPure Filters

Filter	Negative Microbial Control	Challenge Organism Concentration (CFU/cm^2)	Number of Organisms Recovered	Microbial Challenge Test Result (Pass/Fail)
Cycled Filter #1	Yes	4.9×10^7	0	Pass
Cycled Filter #2	Yes	5.2×10^7	0	Pass
Cycled Filter #3	Yes	4.6×10^7	0	Pass
Non-cycled Filter #1	Yes	1.5×10^7	0	Pass
Non-cycled Filter #2	Yes	1.1×10^7	0	Pass
Non-cycled Filter #3	Yes	1.2×10^7	0	Pass

Conclusion for *B. diminuta* filter challenge testing

This testing validates the ability of the MaxPure filter to deliver an effluent that is free of viable organisms, including fungi, protozoa and bacteria > 0.2 microns even after being cycled through a minimum of 470 cycles in the SYSTEM 1E Liquid Chemical Sterilant Processing System.

Validation was also performed using the test organism *Ralstonia pickettii* on the MaxPure Filters. Testing was performed as outlined in ASTM F838-05. *R. pickettii* is a gram-negative environmental organism that is > 0.1 µm in size, but smaller than 0.2 µm. Testing was performed following the same steps as described above using *R. pickettii*.

- Three MaxPure Filters were cycled for ≥ 470 standard, full cycles in the SYSTEM 1E Processor with S40 Sterilant Concentrate.
- A forward flow diffusion test was used to confirm filter integrity prior to bacterial challenge of the three cycled MaxPure Filters.
- Filters and the test apparatus were sterilized via steam-in-place.
- Prior to testing, the ability of the challenge organism to pass through a 0.2 µm filter, but be retained by a 0.1 µm filter was confirmed.
- Challenge solution was passed through each filter and the downstream effluent was passed through a 0.1 µm filter. Filters were incubated and scored to confirm the absence of viable microorganisms in the test system prior to microbial challenge.
- Each individual cycled filter was challenged with *R. pickettii*. The *R. pickettii* was at a concentration of ≥ 10^7 CFU/cm^2 of effective filter area as stipulated in ASTM F838-05.
- Downstream effluent from each challenge test was passed through a 0.1 µm filter. Filters were transferred to growth media and incubated to determine if organism was present in the effluent.
- In addition to the cycled MaxPure Filters, three non-cycled MaxPure Filters were also challenged.

The bacterial challenge was carried out with a system free of viable microorganisms and an appropriate challenge level. All cycled and non-cycled filters were fully retentive of *R. pickettii*. Nondestructive integrity tests (diffusional flow tests) confirmed that two of the cycled filters were integral prior to testing. The third cycled filter failed the diffusional flow test, but fully retained the test organism, indicating the filter was still intact. The fact that the filter maintained integrity above the diffusional flow "pass" limit shows that a sufficient safety factor is built into the specified value. All controls performed as expected. Results from the *R. pickettii* challenged filters are presented in **(Table 9)**.

Table 9: Challenge with *R. pickettii* of the MaxPure Filters

Filter	Negative Microbial Control	Challenge Organism Concentration (CFU/cm^2)	Number of Organisms Recovered	Microbial Challenge Test Result (Pass/Fail)
Cycled Filter #1	Yes	3.6×10^7	0	Pass
Cycled Filter #2	Yes	3.8×10^7	0	Pass
Cycled Filter #3	Yes	3.3×10^7	0	Pass
Non-cycled Filter #1	Yes	3.9×10^7	0	Pass
Non-cycled Filter #2	Yes	4.7×10^7	0	Pass
Non-cycled Filter #3	Yes	4.0×10^7	0	Pass

Conclusion for *R. pickettii* filter challenge testing

This testing validates the ability of the MaxPure filter to deliver an effluent that is free of viable organisms, including fungi, protozoa and bacteria > 0.1 microns even after being cycled through a minimum of 470 cycles in the SYSTEM 1E Liquid Chemical Sterilant Processing System.

MATERIALS COMPATIBILITY

Extensive device materials compatibility evaluations were performed to ensure that processing in the SYSTEM 1E Liquid Chemical Sterilant Processing System is safe for representative medical devices, accessories, and components exposed to sterilant use dilution in the SYSTEM 1E Processor. Original equipment manufactured (OEM) devices and accessories were used in this evaluation. Prior to being processed, the test articles were examined visually and for functionality, and again after 100, 200, and 300 processor cycles, for evidence of the following:

- Corrosion of metal components
- Degradation in light transmission of optics
- Degradation in device performance
- Changes in mechanical resistance
- Cosmetic changes (i.e. discoloration)
- Loss of tubing and o-ring flexibility (where appropriate)
- Degradation in lens adhesive

The appropriate endoscope Quick Connects (needed to flow use dilution through the lumens) and the processor trays (used to provide optimal placement of the device in the processor chamber) were examined at the same time points to evaluate for physical or performance changes such as:

- Corrosion of metal components or cracking of polymeric components
- Changes in mechanical resistance
- Cosmetic changes (i.e. discoloration)
- Loss of tubing and o-ring flexibility (where appropriate)

Five representative endoscopes, their associated Quick Connects, and two accessories (see **(Table 10)**)were evaluated after multiple exposure cycles to use dilution in the SYSTEM 1E Processor. The complete cycle consisted of the following phases: fill, warm/mix, the 6-minute exposure, two rinses, an air purge phase, and the filter integrity test. The test articles were manually cleaned with a neutral enzymatic cleaner prior to each day of testing.

At intervals of 100 cycles, the devices were evaluated for evidence of changes in functionality or cosmetic appearance, as listed above. A change in device performance or physical appearance could act as an indicator of material incompatibility. An acceptable result (Pass) was determined when device functionality or appearance was not adversely affected by repeated exposure to use dilution.

At the evaluation intervals, some cosmetic changes, (i.e. color changes and normal wear) were observed in the devices, Quick Connects, and trays, but these changes did not affect the functionality of the endoscopes, connectors, or trays.

Table 10: Materials Compatibility Testing with Sterilant Use Dilution in the SYSTEM1E Processor

Filter	Number of Cycles Processed	Result
Pentax FI-10P2	300	Pass
Fujinon EC-450 HL5	300	Pass
GYRUS/ACMI MR-6LA	300	Pass
Karl Storz Camera 22220150-3	300	Pass
Richard Wolf 8708.518	300	Pass
Karl Storz Telescope 27005AA	300	Pass
Karl Storz Light Guide Cable 495NE	300	Pass

The seven test articles selected had critical design features found in all flexible or rigid endoscopes and accessories:

- Insertion Tube
- Bending Section or Bending Rubber
- Control Body
- Control Knobs
- Umbilical Cable
- Light Guide End
- Soaking Cap
- Metal Ports or Connectors

Each of these design features are manufactured with the same basic materials:

- Polyurethane
- Rubber
- Glass
- Anodized Aluminum
- Polytetrafluoroethylene
- Polyethylene
- Stainless Steel
- Polycarbonate
- Brass
- Adhesives

In addition, some of these scopes contained critical endoscope features and systems needed for functionality:

- Angulation System
- Light Guide Fibers
- Suction Control
- Air/Water Delivery System

The materials of construction for the Quick Connects and device trays used in this study are representative of all connectors and trays available for use in the SYSTEM 1E Processor. They are:

- Stainless Steel
- Acrylonitrile Butadiene Styrene (ABS)
- 20% Glass-filled ABS
- Polyvinyl Chloride
- Acetyl Copolymer
- Polypropylene
- Polycarbonate
- Silicone and Rubber Tubing
- Polyethylene

Exposure to the use dilution showed no functional or performance change for representative endoscopes, connectors or trays after 300 cycles in a SYSTEM 1E Processor. There were some cosmetic changes, (i.e. normal wear as well as progressive loss of black anodized aluminum coloration without underlying damage to the base metal) that occurred, but these did not adversely affect the functionality of the test articles.

Materials compatibility testing has shown that *in situ* cycling of representative flexible or rigid endoscopes, accessories, adapters, and trays is safe for OEM devices as a result of exposure to use dilution in the SYSTEM 1E Processor.

TOXICITY TESTING

Toxicology Assessment

Under normal conditions of use the operator is not exposed to the contents of the container of S40 Sterilant Concentrate, the processor sterilant use dilution or processor rinse water of the SYSTEM 1E Processor. Nevertheless, a variety of toxicological evaluations were performed on the components of the S40 Sterilant Concentrate and use dilution to determine what, if any, safety risks are associated with inadvertent exposure. The toxicological evaluations were commissioned or undertaken by STERIS to evaluate effects from potential exposure to processed device extracts, liquid chemical sterilant use dilution or components in the container of S40 Sterilant Concentrate.

An alkaline dust which may irritate the eyes and respiratory system may form from the dry powder components in the container of S40 Sterilant Concentrate. Repeated contact with the skin is likely to cause drying. Ingestion of large amounts of powder may irritate the gastrointestinal tract as one of the components can exhibit a laxative effect.

The peracetic acid solution has a pH of 2.5 and has a corrosive effect on human tissues. It is the liquid component in the container of S40 Sterilant Concentrate. The target organs are the eyes, skin and respiratory tract due to the potential for severe irritation for corrosion of tissues at those sites.

The use dilution is practically nontoxic if ingested, mildly irritating to the eyes, non-mutagenic, non-sensitizing and would not be expected to cause significant adverse effect if contact or other exposure occurs. It will have a slight vinegar-like odor; however, there should be no operator exposure to the use dilution during normal operation of the processor. The use dilution has a near neutral pH of 6.5.

A literature review was conducted for known toxicological hazards of all raw materials used in the manufacture of S40 Sterilant Concentrate. The search identified one of the components of the inert powder portion of the concentrate as a potential health hazard due to oral toxicity. This component was evaluated in the rinsing studies. The liquid active ingredient also has a cytotoxic effect thus making it suitable as a germicide.

See **(Table 11)** for a summary of toxicity and hazard classifications.

Table 11: Acute Toxicity Test Results, Derived Toxicity Values and Hazard Classification for Sterilant Use Dilution and S40 Sterilant Concentrate

Acute Toxicity of S40 Sterilant Concentrate and Use Dilution						
	Oral LD_{50} mg/kg Rat	Dermal LD_{50} mg/kg Rabbit	Inhalation LC_{50} Rat 4hr	Skin Irritation Rabbit	Eye Irritation Rabbit	Skin Sensitization
PAA Concentrate Solution (liquid)						
Toxicity Test Results	50-500	> 200	0.450 mg/L			
Classification	GHS Category 3	GHS Category 3	GHS Category 1	Corrosive	Corrosive	Not a sensitizer
Builders (dry powder)						
Derived Effect Level	> 5000	> 5000	N/A			
Classification	Not classified hazardous	Not classified hazardous	Not classified hazardous Dust may be irritating	Not an irritant	Slight irritant	Not a sensitizer
Use Dilution						
Derived Effect Level	> 5000	> 5000	N/A			
Classification	Not classified hazardous	Not classified hazardous	Not classified hazardous May cause irritation	Not an irritant	Minimal irritant	Not a sensitizer

* The Globally Harmonized System (GHS) is an international standardized system for classifying chemicals and communicating their health and environmental hazards to consumers, workers, transport workers and emergency responders.

Cytotoxicity

Exhaustive extractions to remove chemical residuals from processed devices were performed. The extraction times were longer than the worst case procedure length for the device being extracted. The extract solutions were placed over confluent monolayers of L-929 mouse fibroblast cells and examined for degree of lysis according to ISO 10993, Part 5. The extracts were found to be non-cytotoxic.

RESIDUAL TESTING

Representative medical devices were evaluated after exposure to 10 cycles in a SYSTEM 1E Processor. The containers of S40 Sterilant Concentrate were prepared at the highest weight tolerances of Builders and peracetic used in the assembly of S40 Sterilant Concentrate. This results in the worst case exposure to the chemical components of the sterilant use dilution. The exposed devices were extracted in deionized water at 37°C on both interior and exterior surfaces to remove any residue that might be present. The extracted samples were assayed for the components of the Builders solution. One of these is known to have a potential for toxic effects in humans.

Results of these evaluations show that the level of the potentially toxic component (measured following 10 consecutive processor cycles) is present at less than 0.02% on rigid endoscopes and less than 4.2% of the upper residue limit for flexible endoscopes. Exhaustive extraction of the medical devices showed that the residual levels for all components were well below the established levels making the process devices safe for patient use.

HEMOCOMPATIBILITY TESTING

A hemocompatibility evaluation was conducted on operating room medical devices after processing through multiple cycles in the SYSTEM 1E Liquid Chemical Sterilant Processing System using S40 Sterilant Concentrate. The evaluations were performed on six representative endoscopes. Three devices were evaluated by extraction and three devices were evaluated by direct contact. The devices that were tested according to ASTM F756 and ISO 10993-4 Part 4 guidelines were exposed to 10 cycles in the SYSTEM 1E Processor using worst case weight of sterilant components as described above.

A hemolytic index of less than 2% is considered to be non-hemolytic. A hemolytic grade for the devices tested was assigned based on the following scoring scheme:

Hemolytic Index	Hemolytic Grade
0 - < 2%	Non-Hemolytic
2 - 5%	Slightly Hemolytic
> 5%	Hemolytic

The mean hemolytic index for the test articles in direct contact with blood was 0.3% and the mean hemolytic index for the device extracts were 0.0%. This indicates that any residues remaining on medical devices are non-hemolytic following a normal processing cycle in the SYSTEM 1E Processor using S40 Sterilant Concentrate.

PERFORMANCE EVALUATION – SUMMARY OF TEST RESULTS

The SYSTEM 1E Liquid Chemical Sterilant Processing System is intended for liquid chemical sterilization of cleaned, immersible, and reusable critical and semi-critical heat sensitive medical devices.

System features and functions are designed for the safety of patients, healthcare workers, medical devices, and the environment. The principal technical features of the SYSTEM 1E Processor include:

- Automated, easy-to-use, microprocessor control panel with unalterable, standardized processing and diagnostic cycles
- Proprietary, single use, chemical formulation which is automatically delivered and diluted
- Liquid chemical sterilization of processed medical devices
- Two rinses following liquid chemical sterilization with water that has been extensively treated by:
  - Filtration of particulates down to 0.1 µm through layered filters
  - UV irradiation for viral inactivation
  - Another filtration to remove bacteria, fungi, and protozoa > 0.1 micron in size is through a 0.8/0.1/0.1 µm layered MaxPure Filter
- Air filtered through 0.2 micron membrane

These technical features ensure:

- Nominal processor cycle of < 23 minutes
- Sterilant use dilution temperature maintained between 46-55°C and is in contact with devices for 6 minutes
- Integrity of the on-board MaxPure Filter
- The easy to load sterilant container provides the ≥ 1820 mg/L peracetic acid (PAA) concentration needed for efficacious results
- Incoming EPA potable water is extensively treated, making it suitable for rinsing liquid chemically sterilized devices
- Filtered air used to purge rinse water from the Quick Connects and lumens of the processed device maintains the post processing environment

The interchangeable processing trays and associated Quick Connects used in the SYSTEM 1E Processor provide flexibility of use for a wide variety of heat sensitive medical devices and effective delivery of the use dilution.

Water Treatment

Extensively treated, EPA potable water is used in the SYSTEM 1E Processor. The water treatment system of the SYSTEM 1E Processor ensures that all water prior to entering the processor is exposed to the following:

- Filtration through two pre-filters that removes particles/contaminants > 0.1 micron
- A UV dose sufficient to achieve a ≥ 6 log reduction of MS2 virus
- Filtration through redundant, 0.1 micron membranes to remove bacteria, fungi and protozoa > 0.1 micron
- After this extensive, validated, controlled and monitored treatment, the water is used to both fill the processor and rinse the liquid chemically sterilized devices.

UV Irradiation

The UV irradiation system monitors light intensity insuring that a specified dose of UV light is delivered. The system was validated:

- By achieving a > 6 log reduction of MS2 virus, since MS2 is more resistant to UV irradiation (harder to kill) than most waterborne pathogenic viruses
- With UV lamps set to approximately 80% intensity

The UV irradiation treatment results in at least a 6 log reduction in MS2 virus in the SYSTEM 1E Processor.

Filtration

There are two externally mounted pre-filters that deliver filtered water to the UV light system. Pre-filter A is a gross depth filter and removes approximately 2.5 micron and larger particles or contaminants. Pre-filter B is a surface filter that removes particles or contaminants > 0.1 micron.

The UV treated water is passed through a 0.8/0.1/0.1 µm layered pharmaceutical sterilizing-grade MaxPure Filter. This filter removes bacteria, fungi, and protozoa > 0.1 micron in size. It is installed internally in the SYSTEM 1E Processor. This filter was validated:

- By achieving a $\geq 10^7$ CFU/cm^2 reduction of *Brevundimonas diminuta* through filters that were new and filters that were exposed to ≥ 470 full cycles with S40 Sterilant Concentrate in the SYSTEM 1E Processor
- By achieving a $\geq 10^7$ CFU/cm^2 reduction of *Ralstonia pickettii* through filters that were new and filters that were exposed to ≥ 470 full cycles with S40 Sterilant Concentrate in the SYSTEM 1E Processor

B. diminuta is a gram-negative, environmental organism that, when grown as outlined in ASTM F838-05, is > 0.2 µm in size, but smaller than 0.45 µm.

R. pickettii is a gram-negative, environmental organism that is > 0.1 µm in size, but smaller than 0.2 µm.

The MaxPure Filter cartridge cycled through a minimum of 470 cycles in the SYSTEM 1E Processor with S40 Sterilant Concentrate can deliver water that is free of bacteria, fungi and protozoa >0.1 µm in size.

Microbial Efficacy Testing

Microbial efficacy testing was conducted using standard *in vitro* and *in situ* methods with different organisms to confirm the efficacy of the liquid chemical sterilization solution provided by S40 Sterilant Concentrate.

Potency Testing

A variety of organisms were used to challenge the sterilant use dilution. Testing was conducted using the following parameters:

- PAA amounts at less than or equal to the minimum recommended concentration of 1820 mg/L, using end of shelf life chemistry components
- Temperature of ≤ 43°C during the six minutes or less exposure time
- Water for testing at approximately 140 ppm hardness

Methods allowing organic (5% serum) and inorganic (hard water) challenge present in the inocula (Tuberculocidal, Virucidal, and Fungicidal) were incorporated in these challenges.

All potency requirements for a liquid chemical sterilant were met by S40 Sterilant Concentrate.

Microbial Lethality Kinetics

Kill kinetics testing was performed on *Geobacillus stearothermophilus* spores, the most resistant organism to PAA, to characterize the kill rate of the sterilant use dilution. Testing in 18 trials was conducted using the following parameters:

- Use dilution with an average concentration of 1581 mg/L PAA
- Use dilution was inoculated at approximately 10^6 CFU/mL
- Temperature of ≤ 43°C during the six minutes or less exposure time
- Inorganic burden evaluation included:
  - DI water, 140 ppm hard water, 140 ppm hard water with heavy metals
- Organic burden evaluation included each of the above:
  - With and without 1% serum

All controls (positive, negative, neutralization) performed as required.

Microbial lethality for the most resistant organism is achieved in approximately 24 seconds with use dilution.

Manual Soak Testing

Testing of eight representative medical devices was evaluated to verify that liquid chemical sterilization was reproducibly achieved with sterilant use dilution. Testing was performed using the following parameters:

- A challenge of *Geobacillus stearothermophilus* spores at a concentration of approximately 10^6 CFU/mL and, suspended in an organic (5% serum) and inorganic (400 ppm hard water) solution, were applied to each device and air dried for ≥ 30 minutes
- Use dilution at ≤ 1820 mg/L PAA in water of approximately 140 ppm hardness
- Exposure time was six minutes at temperature of ≤ 43°C

The test organism was inoculated into all internal channels and selected external sites. In each of the 6 trials, complete elimination of viable test organism was observed. All controls (positive, negative, recovery and neutralization) performed as required.

Medical devices were reproducibly liquid chemically sterilized in sterilant use dilution.

Simulated-Use Testing

The effectiveness of the liquid chemical sterilization of eight representative/worst case medical devices, with respect to size and features, was conducted using S40 Sterilant Concentrate in the SYSTEM 1E Processor. Testing was performed using the following parameters:

- A challenge of *Geobacillus stearothermophilus* spores at a concentration of approximately 10^6 CFU/mL and suspended in an organic (5% serum) and inorganic (400 ppm hard water) solution, were applied to each device and air dried for ≥ 30 minutes
- Use dilution at ≤ 1820 mg/L PAA in water of approximately 140 ppm hardness
- Exposure time was six minutes at temperature of ≥ 45.5°C
- High pressure pump set to deliver the worst case fluid flow rate
- Use of MaxPure Filters having > 470 cycles accumulated in the SYSTEM 1E Processor
- The UV system set for exposure at the minimum UV intensity specification

The test organism was inoculated into all internal channels and selected external sites. In each of the 6 trials, complete elimination of viable test organism was observed. All controls (positive, negative, recovery and neutralization) performed as required.

In these tests, medical devices were reproducibly liquid chemically sterilized in use dilution when used in the SYSTEM 1E Processor.

In-Use Testing

The SYSTEM 1E Processor was evaluated with clinically used medical devices and patient soil. Three trials were performed on each of the eight devices selected to represent the range of designs likely to be encountered when using this system. No clinical isolates were recovered from any of the devices for all clinical setting trials.

S40 Sterilant Concentrate demonstrated liquid chemical sterilization of clinically used medical devices showing no organism recovery from device surfaces or channels following cycles in the SYSTEM 1E Processor.

Materials Compatibility

Extensive device evaluations over the course of 300 processor cycle exposures were performed on five representative endoscopes and two accessories to verify that processed articles are undamaged upon repeated exposures to sterilant use dilution. Exposure to the processor cycles showed no functional or performance change for representative endoscopes, connectors or trays after 300 cycles. There were some cosmetic changes that occurred which did not adversely affect the functionality of the test articles. The appropriate processor trays and endoscope Quick Connects were also evaluated and found to be compatible with the use dilution.

The sterilant use dilution is safe for flexible or rigid endoscopes, accessories, adapters, and trays, when used in the SYSTEM 1E Processor.

Toxicity Testing

Toxicology Assessment

Under normal conditions of use, the processor operator is not exposed to the container contents, the processor sterilant use dilution or processor rinse water. If an exposure should occur:

- Dry powder components may form an alkaline dust which may irritate the eyes and respiratory system. Repeated contact with the skin may cause drying. Ingestion of large amounts of powder may irritate the gastrointestinal tract.
- The peracetic acid solution has a pH of 2.5 and has a corrosive effect on human tissues. The most sensitive organs are the eyes, skin and respiratory tract and may cause severe irritation or corrosion of tissues at those sites.
- The use dilution has a pH of 6.5 and is practically nontoxic if ingested, mildly irritating to the eyes, non-mutagenic, non-sensitizing and would not be expected to cause significant adverse effects. It has a slight vinegar-like odor.

Cytotoxicity

Exhaustive extractions, longer than the worst case procedure length, were performed to collect chemical residuals from processed devices. The extracts were found to be non-cytotoxic.

There are some toxic and irritant characteristics of S40 Sterilant Concentrate; however the use dilution is essentially non-hazardous. Under normal processor use the operator is not exposed to these hazards. Any residue remaining on a processed device following normal operation will be non-toxic to the patient.

Residual Testing

Representative medical devices were exposed to cycles in the SYSTEM 1E Processor with S40 Sterilant Concentrate. Both interior and exterior surfaces of the devices were extracted and assayed for the components of the Builders solution. One of these components is known to have a potentially toxic effect in humans.

Results of these exhaustive extraction evaluations show that the level of the potentially toxic component is present at less than 0.02% of the limit on rigid endoscopes and less than 4.2% of the limit for flexible endoscopes, making them safe for use.

Residue levels on a processed medical device are well below the established safety levels for use dilution components of S40 Sterilant Concentrate. Therefore, the processed devices are safe for patient use.

Hemocompatibility Testing

A hemocompatibility evaluation was performed on six representative endoscopes or their extracts. Three devices were evaluated by extraction and three devices were evaluated by direct contact. The mean hemolytic index for the test articles in direct contact with blood was 0.3% and the mean hemolytic index for the device extracts were 0.0%.

Residues remaining on medical devices following a normal processing cycle are non-hemolytic making the devices safe for patient use after being processed in the SYSTEM 1E Processor using S40 Sterilant Concentrate.

CONCLUSION

The test data summarized in this Technical Data Monograph demonstrate the microbiological efficacy, materials compatibility, and non-toxicity of residuals of the SYSTEM 1E Liquid Chemical Sterilant Processing System.

The data provide confirmation that the S40 Sterilant Concentrate is safe for the patient, safe for the user, and safe for the processing of heat sensitive critical and semi-critical devices, when used in the SYSTEM 1E Processor.

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