World Journal of Clinical Infectious Diseases

Online Submissions: http://www.wjgnet.com/2220-3176office
wjcid@wjgnet.com
doi:10.5495/wjcid.v2.i2.13

*World J Clin Infect Dis* 2012 April 25; 2(2): 13-27
ISSN 2220-3176 (online)


EDITORIAL

# Medical errors, infection-control breaches and the use of adulterated and misbranded medical devices

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Received: July 12, 2011 Revised: February 25, 2012
Accepted: March 10, 2012
Published online: April 25, 2012

**Key words:** Infection control; Sterilization; Disinfection; Disease notification; Infectious disease transmission; Communicable disease control; Decontamination; Medical errors; Government regulation; Equipment and supplies, hospital; Aseptic technique; Liquid chemical sterilization

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Muscarella LF. Medical errors, infection-control breaches and the use of adulterated and misbranded medical devices. *World J Clin Infect Dis* 2012; 2(2): 13-27 Available from: URL: http://www.wjgnet.com/2220-3176/full/v2/i2/13.htm DOI: http://dx.doi.org/10.5495/wjcid.v2.i2.13

## Abstract

Several well-publicized cases of improper cleaning, disinfection or sterilization of contaminated reusable medical equipment that posed an increased risk of patient-to-patient disease transmission were reported within the past few years, resulting in the notification of approximately 20 000 patients. These medical errors, the specific infection-control standards they breached, and assessments of the risk of infection associated with each are discussed. Other topics discussed include the Food and Drug Administration's (FDA) regulation of medical devices and infection-control products; the use of adulterated, misbranded, and investigational devices; consent decrees and associated Certificates of Medical Necessity; and informed patient consent. Focus is placed on liquid chemical sterilization, its history, and the FDA's recent censure and discontinuation of a medical device labeled with this claim, namely, the STERIS System 1 processor. Recommendations are provided for healthcare facilities, regulatory agencies, manufacturers of reusable medical devices, and professional healthcare organizations and administrations to improve public health and prevent healthcare-associated infections.



## INTRODUCTION

Several cases of improper cleaning, disinfection or sterilization of contaminated reusable medical equipment have been identified in the U.S. during the past decade[1-7]. These cases reportedly posed an increased risk of patient exposure to infectious agents, including HIV and the hepatitis B (HBV) and C (HCV) viruses. In one instance in 2004, a healthcare system in North Carolina notified more than 3500 patients of its inadvertent use of hydraulic fluid, in lieu of detergent, to "clean" soiled surgical instruments prior to terminal sterilization[4,5]. Similarly, in 2008 and 2009 three Veterans Affairs medical centers (VAMCs) in Tennessee, Georgia and Florida notified more than 10 000 patients of the increased risk of infection associated with the improper reprocessing of reusable medical instruments[2,6]. Several of the breaches identified at these three VAMCs, along with each breach's assessed risk of infection, are listed in Table 1. This VAMC in Georgia notified 1069 affected patients of its improper reprocessing of flexible laryngoscopes, and one of these patients sued the VAMC for $10 million, claiming this breach infected her with the HCV[1,2,6]. More recently, 6800 affected patients of a clinic in Ottawa,

Canada, were notified in 2011 of the potential for infection due to the improper reprocessing of reusable medical equipment used during both upper and lower gastrointestinal (GI) endoscopy[7].

Receiving as much media attention as any of these medical errors, the VAMC in Tennessee inadvertently fitted and used the Olympus MAJ-855 auxiliary water tube with a two-way connector[2,8-10]. [A "medical error" is defined in this article as any lapse, breach, faulty procedure or other adverse event in a healthcare setting that caused (or posed the potential to cause) harm to one or more patients or healthcare practitioners. The improper reprocessing of reusable medical equipment is an example of a medical error.] According to its manufacturer, this reusable water tube is to be exclusively used with the similarly looking, but differently designed and functioning, one-way valve with which this tube is packaged and shipped[2,8,9]. This one-way valve's primary purpose is to prevent this reusable water tube's contamination with patient materials during colonoscopy[2,8-10].

Briefly, the Olympus MAJ-855 tube connects the colonoscope's auxiliary water channel to an irrigation system that includes a pump. The clinician's activation of this pump during the procedure provides a stream of pressurized water that flushes the colon's mucosa (*via* this auxiliary water channel) to enhance visibility[2,8,9]. The unwitting use of this water tube, improperly fitted with this two-way connector, reportedly facilitated this tube's contamination, due to the unrestricted backflow of potentially infectious debris (e.g., feces) from the lower GI tracts of patients[2,8,9]. Because this contaminated water tube was not reprocessed after each procedure (as its manufacturer requires), its reuse posed an increased risk of patient-to-patient disease transmission, requiring the notification of 6387 affected patients[2,8,9].

Whether the improper use of the Olympus MAJ-855 auxiliary water tube resulted in instances of patient infection is unclear. According to the VA tests performed on affected patients of these three VAMCs in Tennessee, Florida, and Georgia [as well as on affected patients of two VAMCs in St Louis (MO) and Dayton (OH), where other instrument-reprocessing lapses had been identified] revealed "eight HIV-positive results and 61 confirmed cases of hepatitis B or C" infection, although it is unknown how many of these cases were due to the infection-control breaches identified at these VAMCs[11]. Recommendations for the proper reprocessing of both the MAJ-855 auxiliary water tube and the GI endoscope's auxiliary water channel have been previously published[10].

### *A "negligible" risk of infection*

Although these five medical facilities in North Carolina, Tennessee, Georgia, Florida and Ottawa (Canada) informed affected patients of the potential for their respective infection-control breaches to have resulted in disease transmission, patient disclosure of a potentially significant instrument-reprocessing breach or other type of medical error is not a foregone conclusion[1,12,13]. For example, while performing on-site inspections during the summer of 2009, officials of the VA's Office of the Inspector General (VAOIG) confirmed several infection-control breaches at a number of U.S. medical facilities in the Caribbean, including a VAMC in San Juan (Puerto Rico)[1,3,10,12]. Several of these breaches, along with this author's assessed risk of infection for each of these breaches, are listed in Table 2. These breaches included: (1) the improper disinfection of transvaginal ultrasound transducers (or probes); (2) the improper leak-testing of colonoscopes; and (3) the use of misbranded, damaged, and improperly reprocessed flexible laryngoscopes.

Nevertheless, the VAOIG issued a report in 2010 concluding, based on the Veterans Health Administration's (VHA) risk assessments, that each of these breaches posed a "negligible" risk of infection and, therefore, the VHA did not notify affected patients, estimated to be in the thousands[12], of these breaches - this author's risk assessments and the VHA's policies and directives addressing the consistency of patient notification with the VHA's core values of "trust, respect, excellence, commitment, and compassion" notwithstanding[1,3,10,14]. The VHA's risk assessments associated with these breaches identified in the Caribbean, along with eight other, unrelated risk assessments, are listed in Table 3. (An apparent display of inconsistent standards of care and different thresholds for patient notification, the risk assessments listed in Table 3 demonstrate that whereas one medical facility may notify patients of a breach assessed to pose a "extremely remote" risk of infection, another may not notify patients of a breach assessed to pose a comparably "negligible" risk of infection.)

## STERIS SYSTEM 1

### *Liquid chemical sterilization*

A study of these several well-publicized breaches investigated at these medical facilities in North Carolina, Tennessee, Georgia, Florida, Ottawa (Canada), and the Caribbean, along with Tables 1-3, can assist a healthcare facility's optimization of the quality and effectiveness of its infection-control practices. This study also places renewed focus on: (1) openness, honesty, and trust in health care, including patient notification and informed patient consent[9]; (2) the Food and Drug Administration's (FDA) regulation of the safety, effectiveness, substantial equivalence and labeling claims of medical devices and infection-control products; (3) the clinical use of medical devices that are without a legal clearance or approval (or exemption); (4) enhanced efforts to prevent infection-control breaches and healthcare-associated infections (or, HAIs); and (5) the oversight of infection-control practices by healthcare and accrediting organizations.

An examination of the claim of liquid chemical sterilization provides an ideal and rare opportunity to address all of these topics and evaluate the quality of health care. A common fixture used for many years in operating room settings to process many different types of reusable medical equipment, including rigid endoscopes

**Table 1 Several of the infection-control breaches identified at three Veterans Affairs Medical Centers in Murfreesboro (TN), Augusta (GA) and Miami (FL)**

| Breach | Details of breach | Guidelines, manufacturers' instructions | Infection risk |
|---|---|---|---|
| Improper reprocessing of irrigation tubing used during colonoscopy (Murfreesboro, TN)[1,2] | For as many as 5 yr, the VAMC in Murfreesboro (TN) had been using the Olympus MAJ-855 auxiliary water tube that was: (1) fitted with an improper "two-way" connector; and (2) reprocessed once at the end of the day, not after each patient procedure, as required[2]. Further, the short "irrigation tube" that connects the MAJ-855 tube to a flushing pump was not discarded at the end of the day, also as required[2,8] | According to its manufacturer: (1) the MAJ-855 tube is to be used only with the "one-way" valve with which it is manufactured and shipped (the removal of this valve and its replacement with the two-way connector used by the Olympus MH-974 "washing tube" is contraindicated); (2) the MAJ-855 tube is to be reprocessed after each procedure; and (3) the short irrigation tube is to be discarded at the end of each day[2,9] | Use of the MAJ-855 tube fitted with the MH-974's two-way connector (instead of the correct one-way valve) can result in: the auxiliary water tube's malfunction, its contamination due to the "back-flow" of potentially infectious debris from the patient's colon, and patient-to-patient disease transmission[2]. Further, failure to clean and high-level disinfect (or sterilize) the MAJ-855 tube after each patient procedure, or to discard the short irrigation tube at the end of each day, also poses an increased risk of infection[2,9] |
| Improper reprocessing of colonoscopes (Miami, FL)[1,2] | For as many as 5 yr, the VAMC in Miami (FL): (1) failed to reprocess the MAJ-855 tube after each procedure, instead merely flushing or rinsing it with (sterile) water; (2) often connected the MAJ-855 tube to the colonoscope while the procedure was already in progress; and (3) did not discard the short irrigation tube (that connects the MAJ-855 tube to a flushing pump) at the end of the day[2]. In addition, "debris" had been identified in the auxiliary water channel of "reprocessed" colonoscopes[2] | According to its manufacturer: (1) the MAJ-855 tube is to be cleaned and high-level disinfected (or sterilized) after each procedure; (2) the MAJ-855 tube is to be connected to the colonoscope, with the auxiliary water system primed, prior to the procedure; and (3) the short irrigation tube is to be discarded at the end of the day[2,9]. The use of an endoscope whose channels are soiled with patient debris is contraindicated[1,2,63,74-77] | Indeed, (1) The failure to clean and high-level disinfect the colonoscope, including its auxiliary water channel, or to discard the short irrigation tube at the end of each day; or, (2) the practice of neither cleaning and high-level disinfecting (or sterilizing) the MAJ-855 tube after each patient procedure nor connecting the MAJ-855 tube to the colonoscope, with the auxiliary water system primed, prior to the procedure, poses an increased risk of disease transmission[2] |
| Improper cleaning and high-level disinfection of flexible laryngoscopes (Augusta, GA)[1,2] | For almost a year, the VAMC in Augusta (GA) had been improperly reprocessing flexible laryngoscopes after each procedure, namely, by merely wiping them down with a disposable "sanitizing" cloth[2] | Guidelines and manufacturers' instructions require cleaning and high-level disinfection (or sterilization) of flexible endoscopes and other semi-critical items after each use[49,61,75,78]. The use of an improperly cleaned or disinfected flexible laryngoscope is contraindicated[1-3,75,78] | The improper cleaning and/or high-level disinfection of flexible endoscopes have been causally associated with disease transmission[61,74-80] |

The Veterans Health Administration (VHA) concluded that each of these infection-control breaches posed an increased risk of infection[2]. Consequently, in accordance with the VHA's relevant directives[14], patients were notified of these breaches and of their potential for infection. Several recommendations to prevent infections associated with each of these breaches are provided in Table 6. VAMC: Veterans Affairs Medical Center.

and other types of surgical instruments[15-21], the STERIS System 1 Sterile Processing System ("SS1") is the first device (and as of April, 2010, only one of two devices) cleared by the FDA with this anomalous label claim. The FDA cleared the SS1 for marketing in 1988. [Parenthetically, at the time of this device's clearance, however, no substantially equivalent, legally-marketed predicate device with the same intended use as the SS1's to achieve "liquid chemical sterilization" (and to produce "sterile" rinse water from a tap) were available, as seemingly would have been required for the SS1 to receive a 510(k) clearance with this specific claim. That a premarket approval (PMA), instead of a 510(k) clearance, was the appropriate regulatory avenue for this device to be marketed in 1988 is debatable.]

Unlike traditional sterilizers that typically expose surgical instruments to heat or a lethal gas or plasma, the SS1 (as its unique claim indicates) instead processes instruments using a liquid chemical sterilant[16,18-22]. A tabletop automated device with a relatively small footprint, the SS1 features two primary phases. During its first phase, the SS1 fully immerses manually cleaned, unwrapped instruments in a unique single-use sterilant, known as the Steris 20, which is packaged as a liquid concentrate, but is diluted with filtered water (to a use-concentration of 0.2% peracetic acid)[18-21]. During its second and last phase, the SS1 terminally rinses these instruments with filtered water to remove residues of the Steris 20 sterilant from the processed instruments' surfaces[16,18-33]. According to the manufacturer, the SS1 "sterilizes" its rinse water by filtering the medical facility's tap water through the SS1's water filtration system[18,19,22]. While it features a 0.2 μ bacterial membrane, this water filtration system is not associated with a sterility assurance level (SAL)[18,19,21-27]. The quality of its rinse water is the Achilles' heel of any liquid-based automated reprocessor, especially those labeled to achieve liquid chemical sterilization. Indeed, the "sterility" of the SS1's processed instruments requires that its rinse water be assuredly sterile[16,18-25,30].

### *Sterility assurance levels*

Surgical instruments that are processed by traditional sterilizers are wrapped and remain dry in storage prior to reuse, to prevent their re-contamination with potentially

**Table 2 Several of the infection-control breaches identified within the VA Caribbean Healthcare System, in Puerto Rico**

| Breach | Details of breach | Guidelines, manufacturers' instructions | FDA regulations | Infection risk |
|---|---|---|---|---|
| Improper high-level disinfection of transvaginal ultrasound transducers[1,3,12] | For approximately 2 yr, the VAMC (in San Juan) and an outpatient clinic (in Mayaguez) did not high-level disinfect transvaginal ultrasound transducers after each use[3]. Instead, staff sprayed these instruments with an ineffective disinfectant (and then, at least at this clinic in Mayaguez, covered them with two latex sheaths before use). Whether these transducers were properly cleaned prior to being sprayed is unclear | Transvaginal ultrasound transducers are semi-critical devices for which high-level disinfection (or sterilization) is recommended after each use[75,81], whether or not these transducers are covered with a protective sheath[1,75,82] | | Failure to clean and/or to high-level disinfect these semi-critical devices poses an increased risk of patient infection[75,81]. Further, improperly reprocessed transvaginal ultrasound transducers, even when covered with a protective sheath during the procedure, may pose an increased risk of transmission of infectious agents, including HPV[75,82] |
| Failure to leak-test colonoscopes[1,3,12] | Colonoscopes used in this VAMC's operating room were not leak-tested for (at least) 9 mo[3] | Leak testing of the colonoscope is required after each procedure, just prior to cleaning[3,79,83]. This test detects leaks that can permit fluids to invade and damage the endoscope's internal structures[3]. Manufacturers' instructions contraindicate the use of a colonoscope (or flexible laryngoscope) that fails this crucial test[83] | | Leak testing of the colonoscope is also critical to infection control[3]. Reports causally associate use of a torn or damaged flexible endoscope, with a leak, to disease transmission[3,75,79] |
| Failure to leak-test flexible laryngoscopes; and the use of a damaged laryngoscope[1,3,12] | Having not leak-tested these instruments for 9 mo, this VAMC (namely, its radiotherapy department) routinely used a damaged flexible laryngoscope, with a leak. Similarly, an outpatient clinic (in Ponce) did not leak-test its flexible laryngoscopes for 3 yr[3] | Leak testing of the laryngoscope is required after each procedure, just prior to cleaning[3,78]. Manufacturers' instructions contraindicate the use of a laryngoscope that is damaged and/or fails the leak test[3,83] | | Both the use of damaged flexible endoscopes and the failure to leak test them have been causally associated with disease transmission[79,80] |
| Improper cleaning (and high-level disinfection) of flexible laryngoscopes[1,3,12] | For possibly as many as 9 mo, this VAMC (namely, its radiotherapy department) was not properly cleaning a flexible laryngoscope after each procedure using a detergent[3]. Instead, it was rinsed with running water (followed by drying with a clean gauze pad). Further, for 3 yr an outpatient clinic (in Ponce) was not properly cleaning (nor leak testing; see above) its flexible laryngoscope after each use, and this clinic, too, may not have been properly high-level disinfecting the laryngoscope[3] | Guidelines and manufacturers' instructions require the cleaning (using a detergent) and high-level disinfection of flexible endoscopes after each use[2,3,63,74-78]. The use of an improperly cleaned or high-level disinfected laryngoscope is contraindicated[2,3,75] | | Because the laryngoscope was not properly cleaned, this VAOIG report acknowledges that "adequate (high-level) disinfection cannot be ensured"[3]. The improper cleaning and/or high-level disinfection of flexible endoscopes have been causally associated with disease transmission[64,74,76,77,79] |
| Use of a misbranded flexible laryngoscope[1,3,12] | For possibly as many as 3 yr, an outpatient clinic (in Ponce) used a misbranded flexible laryngoscope[3] | | A misbranded device lacks the necessary clearance to be legally marketed in the US[17,43,56]. The use of a misbranded (or adulterated) device is expressly prohibited by the Food, Drug and Cosmetic Act, unless the "unapproved" device has received, for example, an approved "investigational device exemption" (or, IDE), which, among other considerations, requires for its use informed patient consent[17,56] | The safety and effectiveness of a misbranded medical device cannot be assured, and its use could pose an increased risk of patient harm including infection[41,42,45] |

The Veterans Health Administration (VHA) concluded that each of these five listed breaches posed a "negligible" risk of infection[1,3,10]. Consequently, patients were not notified of the potential for their exposure to infectious agents, including HIV and other blood-borne pathogens[12]. Several recommendations to prevent infections associated with each of these breaches are provided in Table 6. VAMC: Veterans Affairs Medical Center.

**Table 3 Assessed risk of infection associated with nine different confirmed infection-control breaches, the number of patients notified of the breach, and the reference discussing the breach**

| Assessed risk of infection[1] | No. of patients notified | Ref. |
|---|---|---|
| Negligible[2] | No patients notified | [1,3,12] |
| Extremely low | 1812 | [84] |
| Small but not zero[3] | > 10 000 | [2,6] |
| Extremely low | > 500 | [85] |
| Extremely remote | 9000 | [86] |
| Minimal to non-existent | 360 | [87] |
| Extremely low risk | 38 | [88] |
| No increased risk | > 3500 | [4,5] |
| Very low risk | 6800 | [7,89] |

[1]Although this table's nine risk assessments are seemingly without significant clinical differences, the actions associated with each assessment were, at times, notably dissimilar. Whereas breaches assessed to have a "negligible" infection risk did not result in patient notification (Table 3's first row), other breaches assessed either to have similar infection risks, including "extremely low" and "extremely remote" infection risks, nevertheless resulted in patient notification; [2]Some researchers who have studied these breaches have instead concluded that each posed an increased risk of infection warranting the notification of affected patients[1,10,12]. Among other considerations, including to be consistent with the VHA's policies and procedures[14,15], patient notification is important to transparency and quality improvement; [3]These breaches were also assessed to have a "low but significant risk"[2] of infection and a risk of infection that is "substantially less than 1 in 10 000"[2]. The table's sign ">" denotes "more than".

infectious agents including (but not limited to) *Pseudomonas aeruginosa* (*P. aeruginosa*) and other microorganisms[24]. Moreover, a traditional sterilizer's lethality, or likelihood of success, is described by its SAL, which is both typically equal to $10^{-6}$ and inversely proportional to the sterilizer's effectiveness. As its SAL increases (say, from $10^{-6}$ to $10^{-3}$), the probability that the processor did not successfully sterilize the instrument also increases[24]. For background, healthcare staff routinely monitor the effectiveness of sterilizers using biological indicators (BIs)[24-26]. Medical devices themselves, BIs may vary in physical design and type, but each contains a high number of viable (alive yet dormant) bacterial endospores that are resistant to the sterilizer's specific biocidal agent. Published concerns that the SS1's sterilant might "wash off" the endospores from the SS1's (compromised) BI and not destroy them notwithstanding, the FDA cleared a BI in 1996 for exclusive use with the SS1 (8 years after the SS1's clearance, in 1988)[19,25]. According to its labeling, however, this BI is limited in function, exposed (not sealed), and designed to monitor only the SS1's Steris 20 sterilant - not the effectiveness of the SS1's complete process, which includes the production of "sterile" filtered water *via* the SS1's water filtration system. (In general, the claim of "liquid chemical sterilization" requires that surgical instruments and flexible endoscopes be immersed in a liquid chemical sterilant followed by their terminal rinsing with "sterile" water[18-30].) Due to the SS1's design, however, this water filtration system cannot be routinely monitored microbiologically, and, therefore, the "sterility" of the SS1's filtered rinse water cannot be confirmed and documented[21-27]. Because the SS1's filtered rinse water during this processor's second phase: (1) contacts the processed instruments after their immersion in its Steris 20 sterilant; and (2) is not microbiologically monitored (i.e., is of an unknown microbial quality and may be contaminated with potentially pathogenic microorganisms)[21-23,34-37], the "sterility" of the SS1's wet, processed instruments is in doubt[16,21,22,25,28,29].

This conclusion raises a number of questions about not only the effectiveness of liquid chemical sterilization, but also the FDA's regulation of medical devices. As early as 1993, the validity of this claim, in general, and of the SS1's claim, in particular, to "sterilize" instruments and to produce "sterile" filtered rinse water from tap water was questioned[21-25,29]. Also questioned were both the SS1's "guarantee"[30] to achieve sterilization (sterilization being a probability, not a certainty, notwithstanding[24]) and the SS1's intended use, which promotes the clinical use of wet, processed surgical instruments[16,18,19,21-29,31-37]. (The SS1 and its water filtration system are not associated with a SAL[24,27,33].) Moisture or water on a surgical instrument presages its microbial contamination[28,31], and the clinical use of wet medical instruments - for example, the introduction of wet bronchoscopes into a patient's lungs - has been associated with patient infection[16,21-23,25,28,31-37]. Indeed, the Centers for Disease Control and Prevention (CDC) wrote a report in 1999 that linked the SS1's use to the transmission of waterborne bacteria[34] (and also the causative agent of respiratory tuberculosis), with associated patient morbidity[34,35]. Expressing similar concerns, the FDA wrote a letter 2 years later, in April, 2001, that suggested the SS1 may be mislabeled[32]. This letter questioned the effectiveness of the SS1 and the "sterility" of its processed instruments, concluding (as had been previously published by others[24,25,33,34,36,38-40]) that the SS1's association "with patient infections usually caused by waterborne organisms" has led the Agency "to question the ability of the (SS1) to provide a sterile water rinse"[21,32,37].

### FDA warning letter

Other reports through the years have also linked the SS1's use to patient injury, typically to infections of waterborne bacteria following bronchoscopy[21,23,32,37]. In once instance in 2003, officials of a hospital in Pittsburgh (PA) linked an outbreak of *P. aeruginosa* to the SS1's processing of bronchoscopes, finding the SS1's water filtration system to be "defective" and at fault[21]. (Five years earlier in 1998, a published report concluded that 0.2 μ bacterial water filters, such as the SS1's, could fail and pose an increased risk of patient infection due to opportunistic waterborne bacteria[33].) The investigation of this outbreak in Pittsburgh, which was discussed in an article on the front page of *The Wall Street Journal*[21], echoed the FDA's earlier concerns published in 2001[32], namely, that the SS1 may not be producing sterile rinse water as both its labeling and aseptic technique require[21-25]. A federal investigation of the SS1 was initiated circa 2004 in response, in part, to these re-

ports questioning this device's safety and effectiveness[21].

Seven years after it wrote its letter of April, 2001, suggesting that the SS1 may be mislabeled[32], the FDA, in May, 2008, published a warning letter concluding that both the SS1 and Steris 20 sterilant were "adulterated" and "misbranded"[41-43]. More specifically, the FDA wrote in this letter that the SS1 and Steris 20 sterilant had undergone several "changes or modifications" that could "significantly affect (their) safety or effectiveness"[43]. According to this warning letter, these changes, which the FDA determined to include the manufacturer's re-formulation of the Steris 20's chemical ingredients, had not been submitted to and reviewed by the FDA as required by federal regulations[43]. In addition to concluding that the SS1 (and Steris 20 sterilant) is an "unapproved device that violates federal law"[43], this warning letter once again expressed the FDA's concerns - like those that the FDA had previously presented in its aforementioned letter of April, 2001[32] (and like those, too, that others had previously published[21-25,28,29,33,36-40]) - about the SS1's safety, effectiveness, and "ability to sterilize" instruments[43]. A timeline of these and other events relevant to the SS1's history, 510(k) clearance, regulation and recent censure is provided in Table 4.

### Adulterated and misbranded device

In response to the FDA's warning letter of May, 2008, the SS1's manufacturer issued a letter to its customers on January 20, 2009[44]. This letter disclosed that its manufacturer, first, had discontinued the marketing of the SS1; and, second, had submitted a 510(k) clearance application to the FDA just days earlier requesting to market this "altered" SS1[43,44], which the manufacturer named the STERIS System 1E Liquid Sterilant Processing System[20]. This new device features the System 1E Processor ("SS1E") and the S40 sterilant, which is a single-use, peracetic-acid concentrate that is not unlike the Steris 20 sterilant[20]. Cognizant of the popularity and potential revenue that a device with this coveted claim could garner, especially from its use in operating-room settings, the manufacturer's submitted 510(k) application, like the SS1's[19], requested to market the SS1E to achieve liquid chemical sterilization. Almost 10 mo later, on both December 3 and 10, 2009, the FDA formally and publicly censured the SS1, stressing not only that it was "adulterated and misbranded," but also that the SS1's safety and effectiveness were of a sufficient concern to require the discontinuation of its marketing (Table 4)[41,42,45].

According to the FDA, every manufactured SS1 since its clearance in 1988 was subject to this regulatory declaration and *de facto* recall[41,42,45]. Nevertheless, presumably to mitigate the potential inconvenience and expense that the immediate termination of the SS1's use might cause them, the FDA granted healthcare facilities a grace, or "transition," period of 3 to 6 mo to replace the censured SS1 with a legally marketed alternative[41,42,45]. Two months later, on February 2, 2010, however, the FDA extended this transition period for the first of three times, sanctioning the censured SS1's continued use (in the operating-room and other settings) for more than 18 mo, until August 2, 2011[46]. (Raising fair questions about the regulation of medical devices, this date in 2011 is notable because, it is almost a decade after the FDA first published its concerns about the SS1's safety and effectiveness, in 2001[32], and is more than 3 years after the FDA wrote of the SS1's adulteration and misbranding in a warning letter, in 2008[43].) Specifically, pursuant to the terms of this extended deadline, the FDA would permit the Steris 20 sterilant and other parts, components, and accessories required for the SS1's operation to continue to be sold and used in the U.S. for another year and a half[47] (the FDA's censure of the SS1 notwithstanding). Interestingly, a conclusion that a researcher had previously published[16], the FDA concluded on February 22, 2010, that rigid endoscopes and other reusable medical instruments whose labeling lists the SS1 as an appropriate, acceptable, or recommended reprocessing method are, as a consequence of the SS1's censure, themselves misbranded[15,48].

### STERIS System 1E

On April 5, 2010, the FDA cleared for marketing (by way of a letter) the SS1E, along with its S40 sterilant and an accompanying chemical indicator (CI), both for use only with the SS1E[20]. Although it cleared the SS1E with the claim of liquid chemical sterilization, the FDA (possibly, in acknowledgment of questions that researchers had previously raised about this claim's validity[21-26,33,36-40]) did not originally clear a BI for use with the SS1E (although almost two years later, on March 30, 2012, the FDA cleared a spore strip, or BI, for use with the SS1E). Nor did the FDA clear the SS1E with a "sterile" rinse water claim, which raises questions about this device's both clearance and effectiveness[45]. Rather, the FDA cleared the SS1E's rinse water with the significantly more limiting (although more scientifically sound) claim of "extensively treated potable water"[20]. [This quality of water (as opposed to sterile water) might be acceptable for reprocessing and terminally rinsing semi-critical (and non-critical) devices, but its use in the operating-room setting for reprocessing and rinsing critical instruments may be questioned[16,21,25,32].]

On April 6, 2010, one day after the SS1E's clearance, the FDA issued a clarifying statement emphasizing that the SS1E's rinse water and processed instruments are "not sterile"[49-51]. The FDA added in its statement that "the SS1E should not be used on devices that must be sterile"[51] (the SS1E's cleared claim of liquid chemical sterilization notwithstanding). Three days later, on April 9, 2010, the FDA again reiterated that the SS1E's rinse water is not sterile[50]. That confusion and inconsistencies associated with the cleared claim of liquid chemical sterilization might typify some of the tension between a manufacturer's marketing goals and the FDA's public-health mission is a possibility[49].

### Certificate of medical necessity

The conclusions of the FDA's letter written in April, 2001, notwithstanding[32], it was not until December

**Table 4 A timeline of significant events associated with the STERIS System 1 and System 1E**

| Year | Events |
|---|---|
| 1988 | The Food and Drug Administration (FDA) grants the STERIS System 1 ("SS1") and its accompanying Steris 20 sterilant a 510(k) clearance (reference No. K875280)[19] |
| 1992-1998 | Several articles questioning the safety and effectiveness of the SS1 are published[21,29,33,38-40] |
| 1996 | The FDA grants a 510(k) clearance for a biological indicator (BI) to be used exclusively with the SS1[25] |
| 1999 | A hospital in New York City (NY) links patient injury to the SS1[34,35] |
| 1999 | The CDC writes a report that links the SS1 to patient injury[34] |
| February 2000 | The safety and effectiveness of the SS1 is questioned in the newspaper *Investors Business Daily*[25] |
| October 2000 | Another article questioning the safety of the SS1 is published[36] |
| April 2001 | The FDA raises doubts about the "sterility" of the SS1's filtered rinse water and, therefore, about the SS1's effectiveness[32] |
| 2002-2004 | Two articles questioning the labeling claims, effectiveness and safety of devices (like the SS1) labeled to achieve liquid chemical sterilization are published[23,31,36,37] |
| 2003, 2004 | A hospital in Pittsburgh (PA) links patient injuries to the SS1's rinse water and "defective" water filters[21,90,91] |
| 2003 | An ex-employee of STERIS asserts that the SS1 "poses a public health risk"[21,90] |
| Circa 2004 | The federal government investigates whether the SS1 may have been "adulterated"[21,90,91] |
| December, 2004 | The safety and effectiveness of the SS1 is questioned in the newspaper *The Wall Street Journal*[21] |
| April, 2008 | The safety of the SS1, namely, the validity of its labeling claim that the SS1's filtered rinse water is "sterile," is again questioned[22] |
| May, 2008 | On May 15, 2008, the FDA issues a warning letter concluding that the SS1 is adulterated and misbranded pursuant to the Food, Drug and Cosmetic (FD&C) Act[43]. The FDA states in this letter that changes made to the SS1 by its manufacturer could significantly affect the device's safety and effectiveness |
| January, 2009 | Steris "discontinues" marketing of the SS1 and its Steris 20 sterilant[44] |
| January, 2009 | Steris submits a 510(k) application to the FDA requesting to market this censured and "updated" model of the SS1 known as the STERIS System 1E[44] |
| July-August, 2009 | An article about the SS1 concludes that reusable medical instruments including rigid endoscopes whose labeling lists the (censured) SS1 as a reprocessing method may themselves be misbranded[16] |
| December 3, 2009 | The FDA notifies healthcare facilities that the SS1 has been without a legal approval or clearance (as required for its marketing and sale) since 1988. Facilities are provided a period of 3-6 mo to transition to a legally marketed alternative[41,42,45] |
| January 5, 2010 | While acknowledging that the SS1 is an "unapproved" device that "violates US federal law," a Canadian health agency writes that it has "no objection" to this device's continued sale and use[58] |
| February 2, 2010 | The FDA extends for 18 mo (through August 2, 2011) the time period for healthcare providers to stop using the unapproved SS1 and transition to a legally marketed alternative[46] |
| February 22, 2010 | The FDA writes a letter stating that reusable medical instruments including rigid endoscopes listing in their labeling the (censured) SS1 as a reprocessing method are themselves be misbranded[15,48] |
| April 5, 2010 | The FDA grants the "updated" SS1, known as the STERIS System 1E, or SS1E, a 510(k) clearance. Unlike the SS1's clearance in 1988, however, the SS1E is cleared without a BI or a "sterile water" claim[20] |
| April 6, 2010 | The FDA clarifies the SS1E's 510(k) clearance, stating that this device's filtered rinse water "is not sterile" and, therefore, its "final processed devices (or instruments) are not sterile"[51] |
| April 9, 2010 | The FDA again writes about the SS1E's clearance, adding that "because the rinse water is not sterile, devices processed using liquid chemical sterilization cannot be assured to be sterile"[50] |
| April-July, 2010 | On April 20, 2010, the FDA obtains a Consent Decree of Permanent Injunction, requiring its manufacturer to stop selling the unapproved SS1[52]. Pursuant to this Injunction, each healthcare provider continuing to use the SS1 (and to receive service, parts, consumables, accessories, including purchase and use of the Steris 20 sterilant) are required to complete and return to the SS1's manufacturer a signed Certificate of Medical Necessity (CN) by July 2, 2010[53,54] |
| March, 2011 | The FDA extends the use of the unapproved SS1 for 6 more months, until February 2, 2012[55] |
| December, 2011 | The FDA again extends the use of the unapproved SS1 (and both the sale and use of its Steris 20 sterilant) for 6 more months, until August 2, 2012[47]. This time, however, the FDA requires healthcare providers continuing to use the SS1 (and to receive service, parts, consumables, accessories, including purchase and use of the Steris 20 sterilant) to sign, complete, and comply with a Certificate of Transition, which is to be returned to the SS1's manufacturer by February 2, 2012[47] |
| February 2, 2012 | Healthcare providers who have not completed and returned to its manufacturer a signed Certificate of Transition by February 2, 2012, will be prohibited from using the unapproved SS1 and from purchasing its accompanying Steris 20 sterilant[47,52-54] |
| March 30, 2012 | The FDA grants a 510(k) clearance for a spore test strip (i.e., a BI) to be used exclusively with the SS1E |
| August 2, 2012 | According to the FDA, healthcare providers (who had returned a signed Certificate of Transition to the SS1's manufacturer by February 2, 2012) can no longer use the unapproved SS1 after August 2, 2012[47] |

3, 2009, as previously noted, that the Agency formally censured the SS1, declaring that every one of SS1's models and serial numbers manufactured since 1988 were adulterated and misbranded[41-48,52]. No matter the primary impetus for the SS1's ultimate censure (Was this censure due more to the SS1's questionable "sterile" rinse water claim[16,21-25,32,36-40] than to its manufacturer's cited design changes?[43]) or for this regulatory action's delay of more than 20 years, the FDA obtained on April, 20, 2010, a consent decree of permanent injunction that legally prohibited the sale and distribution of the SS1, but not of its accompanying Steris 20 sterilant (Table 4)[52]. One of this decree's primary provisions required that any healthcare facility continuing to use the SS1 (and to receive and purchase parts, components, accessories, and "consumables," including its Steris 20 sterilant) have an authorized official - for example, the healthcare facility's chief medical officer, or the chairman of the Institutional Review Board (IRB) - sign a certificate of medical necessity (CN) issued by the SS1's manufacturer[53]. This CN,

which was to be returned to the SS1's manufacturer by July 2, 2010, would certify that the healthcare facility's continued use of the unapproved SS1, during the time its "transitions" to a legally marked alternative, is "an immediate and continued medical necessity"[53,54].

Although this CN states that this transition period ends on August 2, 2011[53], the manufacturer notified the SS1's customers in March, 2011, that the FDA had pushed back (for the second time in as many years) the date that they would have to stop using the SS1 (and stop purchasing the Steris 20 sterilant), from August, 2, 2011, to February 2, 2012 (Table 4)[55]. Then, in late December, 2011, the FDA published a notice entitled "Second 6 Month Extension for Health Care Facilities to Replace STERIS System 1 with a Legally-Marketed Alternative" that again extended the time for healthcare facilities to continue using the SS1 (and to continue purchasing and using the Steris 20 sterilant) until August 2, 2012 (Table 4)[47]. (While the title of this FDA notice is technically correct, it can be misunderstood. Indeed, the FDA twice extended the use of the SS1, each for 6 mo. But, on February 3, 2010, the FDA also extended the SS1's use for 18 mo, so that, in total, the FDA extended the SS1's use for 30 mo after the SS1's formal censure in December, 2009.) Among other criteria, this notice required users of the SS1 to complete and return to the SS1's manufacturer a signed certificate of transition (CT) by February 2, 2012[47]. Though a different document, this CT, issued by the SS1's manufacturer, is similar in focus and format to the SS1's CN[53]. (Whether the manufacturers of those reusable rigid endoscopes and surgical instruments that were the subject of the FDA's aforementioned letter of February 22, 2010, would also have had to issue a similar CN and a CT has not been published by the FDA and is unclear[48].)

## DISCUSSION

### *A faulty risk assessment?*

The threshold for notification of affected patients of a medical error, including of an infection-control breach, is a topic of debate[5]. Due in part to a number of considerations, a healthcare facility or network can be affected by unrecognized biases that may cause it to underestimate a breach's true risk of infection (e.g., publication bias), concluding that a substantive breach with the potential to have infected patients posed instead a negligible risk not warranting patient notification[1,3,12]. The lack of a universally-adopted standard instructing a medical facility to inform affected patients of a confirmed breach (unless, debatably, a compelling, evidence-based rationale for not doing so can be provided) can engender poor quality, a mistrust of health care, and inconsistent patient care. Based primarily on utilitarian and duty-oriented principles, Dudzinski *et al*[5] (2010) recommend notification of patients "even when the probability of physical harm to patients is very low" (Table 3). This recommendation is well-taken and consistent with one of the VHA's own directives[14], which states that: "VHA facilities and individual VHA providers have an ethical and legal obligation to disclose to patients adverse events that have been sustained in the course of their care, including cases where the adverse event may not be obvious or severe, or where the harm may only be evident in the future." So, a fair question may be asked: why did the VHA not notify affected patients of the infection-control breaches it identified in the Caribbean in 2009 (Table 2)?

Adopting a standard like Dudzinski *et al*'s (2010)[5] and ironically, like this directive by the VHA[14], some researchers (with whom the VAOIG consulted prior to the publication of its report[3,12]) concluded that these breaches confirmed in the Caribbean - like those confirmed at the three VAMCs in Tennessee, Georgia, and Florida about which more than 10 000 affected patients were notified (Table 1) - similarly posed an "increased" risk of infection warranting patient notification[1,10,12,14]. The VHA's decision, to date, not to notify the patients affected by these breaches identified in the Caribbean is further critiqued because - in addition to this decision by the VHA not being consistent with the VHA's own directives, which also state that: (1) "disclosure of adverse events to patients or their personal representatives is consistent with VHA core values of trust, respect, excellence, commitment, and compassion"; and (2) "honestly discussing the difficult truth that an adverse event has occurred demonstrates respect for the patient, professionalism, and a commitment to improving care"[14] - one of these confirmed breaches, namely, the improper reprocessing of flexible laryngoscopes at the VAMC in San Juan, PR (Table 2), had also been confirmed at the aforementioned VAMC in Georgia, previously causing the VHA to notify the 1069 affected patients (Table 1)[1-3,5,6].

### *Investigational devices*

Adoption of a policy that notifies patients of a potentially significant medical error or infection-control breach may not only improve the quality and trust of health care but also, in addition to minimizing potential conflicts of interest, is the patient's expectation. In some circumstances, however, patient notification may be less of a dilemma than a federal mandate. For example, consider a "significant risk" medical device whose design has been modified, but that may be used lawfully in the clinical setting without a regulatory approval or clearance[56]. This modified device - like those unapproved devices that may be the subject of a clinical study conducted by a manufacturer or sponsor to demonstrate the device's safety and effectiveness (as required of a PMA) or its substantially equivalence to a legally marketed predicate device [as required of a 510(k)] - is referred to as "investigational"[56,57], and it may be lawfully used in the US provided a number of criteria are satisfied[56,57]. These criteria are detailed in the Code of Federal Regulations and include, among others: (1) obtaining for the device an investigational device exemption ("IDE") approved by an IRB (and, possibly, by the FDA); (2) labeling the device "caution - investiga-

tional"; and (3) having the IRB additionally monitor the device's clinical use. This third criterion is a check and balance designed to ensure that the unapproved device's use does not inadvertently overlook or unduly compromise the patient's "rights, safety and welfare"[16,17,56,57]. From the FDA's perspective, the safety and effectiveness of a modified, unapproved device (or the device's substantial equivalence to a legally marketed predicate device) have not been demonstrated and, therefore, the device's clinical use manifestly poses the potential for patient harm[43,45,48,52,53,57]. Without an approved IDE, the manufacturer's shipment and introduction into interstate commerce of this unapproved device, as required for its clinical use, would violate federal law[55,56].

Federal rules and regulations governing the clinical and lawful use of medical devices that are without a regulatory clearance or approval also mandate a fourth criterion: that all affected patients be informed of, and consent to, the device's use[16,17,56,57]. Nevertheless, applying this discussion to both the claim of liquid chemical sterilization and the federal oversight of infection-control products, the censured SS1 and Steris 20 sterilant, which are "significant risk," modified devices, not only remain in use (and the Steris 20 will continue to be sold through August 2, 2012) almost 4 years after the FDA declared in May, 2008, the SS1 to be adulterated and misbranded, but also do so apparently without reasonable assurance that these four criteria have been satisfied[41-48,52,54]. Namely, the SS1's consent decree, CN and CT - like the FDA's statements, notices, and letters discussing the SS1's censure and discontinued marketing - do not formally address or clarify whether the SS1 and Steris 20 sterilant are investigational devices[16,41-48,52-55]. To be sure, the concordance of, on the one hand, the FDA's countenanced use of the SS1 (and both use and sale of the Steris 20 sterilant) through August 2, 2012, in the US[47] (and possibly for longer in at least one other country[58]) with, on the other hand, the clear intent and provisions of both the Food, Drug and Cosmetic (FD&C) Act and the Code of Federal Regulations (and with Medicare's reimbursement rules[59]) prohibiting the shipment and clinical use of unapproved devices without an approved IDE is not self-evident.

### A conflict of interest?

Both the SS1's consent decree[52] (and associated CN, which are not entirely unlike those associated with some other censured medical devices[60]) and the FDA's approbation of the unapproved SS1's continued use (through August 2, 2012[47]) are arguably as notable for their apparent tension with federal rules and regulations as for their lack of clarity and completeness. In summary, the FDA in 2001 expressed concern about the SS1's safety and labeling claims[21,32]; concluded in 2008 that this device's safety and effectiveness cannot be assured[43]; and wrote in December, 2009, that the SS1 and Steris 20 sterilant are adulterated and misbranded (i.e., unapproved) devices (Table 4)[41,42,45]. Moreover, the FDA wrote in December, 2009, that the Agency is "acting now (against the SS1) to limit the risk of harm to patients and users"[41,42,45]. Nevertheless, in the spring of 2012, both the SS1 and Steris 20 sterilant remain in use, apparently lawfully. Whether the SS1 has been classified by the FDA (pursuant to the terms of the SS1's consent decree) as an investigational device, however, requiring (but not limited to) informed patient consent remains nebulous[16,41-48,52-55].

This confusion brings into focus an interesting, but (at least for the patient) unfavorable, dynamic. Specifically, the SS1's consent decree, CN and CT (possibly, like those of other devices, too) define the terms of the established and financial relationship between the device's manufacturer (who sells and ships the unapproved device) and the healthcare provider (who purchased the device and uses it to treat patients during the course of business). These terms, however, do not appear to expressly consider or address the rights, safety, and welfare of the patient, even though the patient could, according to the FDA[41,42,45], be harmed by the use of this (or of any other) unapproved device. Therefore, by not requiring that the patient be informed of the SS1's clinical use, the regulation of this unapproved device (e.g., the SS1's oversight pursuant to its consent decree, CN and CT) becomes party to a potential conflict of interest, because the patient's knowledge of, and potential objections to, this censured device's clinical use could adversely affect this financial relationship between the manufacturer and healthcare provider (as well as raise questions about the FDA's regulation of medical devices like the SS1). Interestingly, not only were the FD&C Act and its provisions for informed patient consent designed to redress this potential conflict of interest, but the formal classification of the SS1 and Steris 20 sterilant as investigational devices would reasonably have corrected and abrogated it.

Additionally conflicting, if a patient, not informed or aware of the SS1's use (pursuant to the apparent terms of the SS1's consent decree, CN and CT), were harmed by this unapproved device, the healthcare provider and manufacturer - both of whom as a consequence could face allegations of negligence and a lack of due diligence, baseless or not - might further be incentivized not to disclose the SS1's use. It is acknowledged that physicians and other healthcare providers cannot be expected or required to disclose to their patients every detail of treatment. But, a consent decree's establishment of a financial relationship between a manufacturer and a healthcare provider without the expressed requirement that both the patient be informed and other necessary checks and balances be in place to ensure the patient's safety raises questions not only about this established relationship's fairness, objectivity, and impartiality, but also about its consistency with the intent of those provisions of the FD&C Act and Code of Federal Regulations that address the use of unapproved medical devices. Therefore, that the SS1's consent decree and associated CN and CT, although seemingly consistent with federal regulations, may not be adequately transparent or complete could be argued.

### FDA's definition of liquid chemical sterilization

Confusion and ambiguity have surrounded the anomalous and controversial claim of liquid chemical sterilization for more than two decades, when it was first introduced in 1988[19-22,24,25,32,49-51,61]. Briefly, quality incorporated into a device's labeling claims and instructions for use (IFUs) reduces the potential for the device's misuse and patient harm. As if want of this quality, however, liquid chemical sterilization not only is an oxymoronic claim, but also is defined, at times, less in terms of what it actually achieves than by what this claim does *not* achieve[20,49,51]. Namely, the FDA cleared the SS1E to achieve liquid chemical sterilization while also incongruously concluding that instruments processed in the SS1E "are not sterile"[20,51] (which is in part due to the FDA's clearance of the SS1E without a "sterile" filtered rinse water claim). Indeed, published reports suggest that processes labeled with the claim of liquid chemical sterilization achieve an outcome that may be more akin to disinfection. For instance, a document that the FDA recently published equates liquid chemical sterilization with high-level disinfection, as if these two processes might be comparable and interchangable[49,62]. Whether confusion about the claim and regulation of liquid chemical sterilization [How can a processor be cleared to achieve (liquid chemical) sterilization with the acknowledgment that the processed instruments are not sterile? Can the outcome of instruments exposed to liquid chemical sterilization instead be expected to be one of the three levels of disinfection?] might have confounded healthcare providers about, if not have also downplayed, the importance of instrument reprocessing and aseptic technique, posing an increased risk of HAIs, is unclear, although possible.

## POSITION STATEMENT

### Lack of guidance

Lacking is published guidance advising medical facilities whether the continued use of the unapproved SS1 (or of any censured device) through August 2, 2012, in the US[47] (or longer in other countries[58]) might be prejudicial and pose legal and safety risks; require an approved IDE; or warrant the implementation of specific corrective or preventative actions ("CAPAs") designed to minimize the risk of patient (and healthcare staff) injuries - for example, to dry the SS1's wet, processed instruments before their reuse (and before their storage)[25,36,37]. Nor have any published papers, sentinel alerts, or guidance documents discussed the significance, accrediting implications, or potential compromise of aseptic technique (Would affected patients have to be informed?) associated with the unapproved SS1's use since 1988 (the year the FDA concluded the SS1 first became adulterated and misbranded[43,45,52]). The paucity of such guidance is surprising, in part because healthcare organizations, state departments of health, and other agencies, when faced with similar circumstances, have published reports, "position statements", and sentinel alerts addressing concerns about infection control, reprocessing practices and the safety and effectiveness of medical devices, including, for example, of infusion pumps, arthroscopic shaver handpieces, and an automated reprocessor (although not about the SS1)[63-71]. Guidance evaluating the impact on patient safety of reusing single-use devices has also been published[65-67]. And partly in response to publicized infection-control lapses, guidelines providing recommendations to prevent disease transmission during GI endoscopy have been published and endorsed by several societies and organizations[64].

### A circumspective approach

Circumspection applies to the clinical use of an adulterated, misbranded or federally censured medical device[17]. Before using such a device, it is recommended that the healthcare facility: (1) assess the risks and benefits associated with the device's continued use (by reviewing the published literature and the FDA's databases for more insight into the device's safety and effectiveness); (2) determine, when applicable, whether signing and returning a CN and CT is appropriate; and (3) obtain a letter of indemnification from the device's manufacturer discussing the device's safety and its support of the device's effectiveness. The healthcare facility may also consider receiving written clarification from a supervisory healthcare, accrediting, or certification organization, or a state or federal agency, advising whether the device's continued use: (1) is medically unsound; (2) requires an approved IDE (including informed patient consent); (3) might jeopardize the healthcare facility's accreditation, certification, or state licensing (and, too, is consistent with Medicare's reimbursement and billing regulations and does not adversely affect the healthcare facility's insurance premiums or malpractice coverage[59]); and (4) requires any corrective actions to reduce the risk of injury to patients (and, possibly, to staff members[41,42,45]). Otherwise, the continued use of the unapproved or censured medical device could be problematic and subject the healthcare facility to claims of negligence and a failure of due diligence[59], especially if the device's continued use were associated with an injury.

## CONCLUSION

In 2008 and 2009 the FDA concluded that the SS1 and Steris 20 sterilant have been adulterated and misbranded since 1988. This federal censure is not academic, and, arguing for consideration of the SS1's labeling, design, and use as a bona fide "medical error," several reports have linked this censured device's use to the injury of patients (and staff members[21,25,32,34-37,41,42,45]). The history and circumstances of the SS1, its regulation, marketing and ultimate censure are as fascinating as they are educational, although they suggest that evidence-based and consistent oversight of infection-control products (by federal and state agencies, and by private organizations) is lacking.

Several questions remain unanswered, including the factors that contributed to both the SS1 and Steris 20 sterilant being on the U.S. market for almost two decades,

**Table 5 Recommendations that are provided for healthcare facilities, federal agencies, medical device manufacturers, and healthcare organizations and administrations, to minimize the risk of injury to patients and of legal exposure to healthcare facilities**

To healthcare facilities:

- Review a previously published set of instructions for reprocessing the Olympus MAJ-855 auxiliary water tube, along with the colonoscope's auxiliary water channel[10]. Also, review Table 6
- Before using an adulterated or misbranded device, or a censured medical device subject to a consent decree and/or CN: (1) consider whether describing it as investigational subject to an approved IDE, the oversight by an IRB and informed patient consent is warranted; and (2) ensure that its use does not contravene the healthcare facility's policies and procedures (or other documents, including its insurance policies[59])
- Ensure that the certification of a censured device's continued use pursuant to a signed CN (or CT) is lawful and based on sound medical considerations and patient safety
- To maintain a consistent standard of patient care, quality, and transparency, consider patient disclosure of a medical error to be the norm, no matter whether the error is an infection-control breach associated with a low risk of infection (Table 3)[1,5,12]
- The use of a wet flexible endoscope or surgical instrument to treat patients is not recommended. Prior to their use (and storage), wet, processed flexible endoscopes, such as those processed by the SS1 (or SS1E), may be dried using 70% alcohol followed by forced air
- Consider periodically monitoring the microbial quality of the water used to rinse flexible (and rigid) endoscopes following their high-level disinfection or liquid chemical sterilization. Contaminated rinse water will yield contaminated, processed instruments. Failure to monitor the rinse water microbiologically precludes assurances that it does not contain potentially pathogenic microorganisms
- Review the history of the SS1's use, regulation, and discontinuation (Table 4). Also, review the risk assessments provided in Tables 1-3
- Review all infection-control product's labeling claims. Question any processor's labeling that "guarantees" sterilization (or high-level disinfection)

To regulatory agencies:

- Continued attention to the scientifically-sound, active regulation of medical devices with infection-control applications is appreciated. One important aspect of this oversight is the frequent and/or detailed auditing of medical device manufacturers, to ensure, among other considerations, the proper control and documentation of any changes to a medical device's labeling and design. Also recommended are more frequent and thorough audits by international standard organizations that certify the quality of manufacturers
- Continued efforts to ensure that the wording of 510(k) clearances describing a device's intended use is clear and consistent are encouraged. Cleared labeling claims that detail what the device does achieve, rather than what it does not achieve (e.g., the SS1E's FDA-cleared liquid chemical sterilization claim), are important to quality and to reducing the risk of confusion, user error, and patient harms
- Consider eliminating the oxymoronic and anomalous claim of liquid chemical sterilization and replacing it with a more scientific and consistent claim (e.g., enhanced, ultra, or rapidly sporicidal high-level disinfection)
- Also recommended are: (1) the enhanced attention of consent decrees, CNs and CTs to transparency, and patient safety; (2) the definitive clarification by the FDA whether the continued use of an unapproved or otherwise censured device requires an approved IDE; and (3) improved efforts to ensure that the patient's rights, safety and welfare are protected whenever an unapproved or otherwise censured device is used

To manufacturers:

- Adopt more rigorous quality and regulatory standards that prevent the design, manufacture, sale and marketing of potentially unsafe, mislabeled, ineffective, or unapproved medical devices [e.g., those without a 510(k) clearance or PMA]. Do not change or modify the designs (including the labeling and intended uses) of medical devices (e.g., the re-formulation of a high-level disinfectant's labeling and chemical ingredients) without adequate documentation and control (per the FDA's Quality System Regulation). Submit to the FDA for its review and clearance substantively modified devices prior to their marketing and sale. Whenever in doubt, conclude that a design change requires a new 510(k) submission
- Use caution before including in a reusable surgical instrument's instructions for use (IFUs) a reprocessing device (e.g., the SS1), that is adulterated, misbranded, or lacks adequate design control, documentation and/or data validating its labeling claims, safety, and compatibility with the surgical instrument's materials. Otherwise, the FDA may consider the surgical instrument to be itself misbranded

To healthcare organizations:

- Consider a more proactive role in the oversight of the safety and effectiveness of infection-control products and of the validity of their labeling claims
- Consider publishing guidance to advise a medical facility evaluating whether the continued use of a censured medical device subject to a CN (e.g., the SS1) is legally and medically sound; warrants an approved IDE including informed patient consent; could adversely impact a healthcare facility's accreditation, certification, or licensing; and requires any corrective or preventative actions or changes in clinical practice

To the VHA:

- Notification of patients affected by the infection-control breaches confirmed within the Caribbean in 2009 (Table 2) is recommended[1,3,12], to ensure compliance and consistency with the VHA's relevant directives and policies vis-a-vis patient notification[14]; a consistent standard of patient care; and a commitment to transparency and quality. In general, consider patient notification to be the norm[5,14]

To patients:

- While formal recommendations for patients are not, per se, the focus of this article, some guidance is provided
  - If an infection is contracted (or other type of patient harm is encountered) during or following a medical procedure, among other considerations:
    - Verify that the healthcare facility did not use (without the patient's knowledge) a medical device that had been censured, adulterated, misbranded, described as investigational, or subject to a signed CN and/or CT (e.g., the SS1)
    - Investigate whether, at the time the patient received medical care or treatment, any known or undisclosed infection-control breaches, lapses, or medical errors were identified by the healthcare facility
  - Consider contacting the healthcare facility prior to a procedure and ask for the facility to certify its relative risk of infections and other adverse events, compared to other facilities. Ensure that this risk is based on internal data that have been independently validated for accuracy and completeness
  - Patients potentially affected by one or more of the breaches confirmed within the Caribbean and listed in Table 2 might consider contacting the VHA and requesting being tested to ensure they were not infected with a transmissible disease due to any of these confirmed breaches
    - These patients may also consider asking the VHA for evidence-based justification for having not notified them of any of these breaches listed in Table 2. The medical literature suggests that these breaches may have posed an increased risk of infection
  - Consider having a blood test taken before the procedure to demonstrate a negative blood-borne pathogen result. A positive result promptly after the procedure might implicate the procedure as the infection's cause

**Table 6 Several recommendations to prevent patient infections associated with the breaches described in Tables 1 and 2**

Olympus MAJ-855 auxiliary water tube:
- Clean and high-level disinfect (or steam sterilize) the MAJ-855 auxiliary water tube (in accordance with its manufacturer's instructions)[9]. Recommendations for reprocessing this MAJ-855 tube and the colonoscope's auxiliary water tube have been previously published[10]
  - Improper reprocessing, or the misuse, of the MAJ-855 tube may pose an increased risk of infection warranting patient notification[2]

Colonoscope:
- After each clinical case, clean and high-level disinfect (at a minimum) the colonoscope (and all other types of GI endoscopes)[64]. Refer to the colonoscope's operator's manual for detailed reprocessing instructions[83]
  - In addition to its other channels and surfaces, including the suction and air/water valves, reprocess the auxiliary water channel regardless of whether this channel was used or flushed with water during the clinical case[76,77]. Do not use the GI endoscope if assurances that this channel (or any other surface) was properly reprocessed cannot be provided
  - Soil dripping from a "reprocessed" colonoscope may indicate improper cleaning of the auxiliary water channel. Do not use a visibly soiled or improperly reprocessed GI endoscope rather, reprocess it again before its reuse
  - Improper reprocessing of the colonoscope and its auxiliary water channel may pose an increased risk of infection warranting patient notification[2]
  - Prior to its reprocessing, visually inspect (for damage) and leak-test the colonoscope, in accordance with its manufacturer's instructions. Do not use a colonoscope that has not been leak-tested, has a leak and fails this test, is torn, and/or is otherwise damaged. Return the damaged colonoscope to its manufacturer, in accordance with its operator's manual

Flexible laryngoscope:
- After each clinical case, clean and high-level disinfect (at a minimum) the flexible laryngoscope, including, if featured, its suction channel, suction valve, and biopsy inlet or port[2,78]
  - A unique set of step-by-step instructions for reprocessing laryngoscopes is provided in reference 78, to which the reader is referred
  - Prior to its reprocessing, visually inspect (for damage) and leak-test the flexible laryngoscope, in accordance with its manufacturer's instructions. Do not use a flexible laryngoscope that has not been leak-tested, has a leak and fails this test, is torn, and/or is otherwise damaged. Instead, return the flexible laryngoscope to its manufacturer, in accordance with its operator's manual
  - Improper reprocessing of the flexible laryngoscope-for example, failing to use a detergent to clean it; or "cleaning" and "disinfecting" its surfaces by wiping them with a sanitizing cloth or a gauze soaked with a disinfectant, such as 70% alcohol or a quaternary ammonium product-may pose an increased risk of infection warranting patient notification[1,2,6]
  - Service and maintain the flexible laryngoscope, like all types of flexible endoscopes, including colonoscopes, as recommended by its manufacturer[80]

Transvaginal ultrasound transducer (or probe):
- After each clinical case, clean and high-level disinfect (at a minimum) the transvaginal ultrasound transducer regardless of whether this reusable probe was covered with one or two protective sheaths[75,82]. Refer to this transducer's reprocessing manual for more detailed instructions
  - Improper reprocessing of this transducer-for example, "cleaning and disinfecting" its surfaces by spraying them with a disinfectant; wiping them with a disposable sanitizing cloth; or using running tap water (without detergent)-may pose an increased risk of infection warranting patient notification[1,12,81]

since 1988, without the adulteration and misbranding of either being detected during internal and external audits, including those performed by the FDA, until May, 2008[43]. Whether more rigorous scrutiny and vetting by regulatory agencies (and accrediting organizations, among others), of the SS1's labeling and its claim "guaranteeing"[30] sterilization might have both prevented patient harms linked to this device's use and reduced the financial burden and health care costs[72] associated with the SS1's use, censure, consent decree, CN, CT, discontinuation, and replacement is debatable, although possible. According to a non-profit healthcare organization - which in 1994 demurred when availed the opportunity to publish identified concerns about the SS1's safety, effectiveness and labeling claims[16,21,29] - the cost to replace the censured SS1 with legal marketed alternatives (presumably including the SS1E) in the U.S. could exceed $500M[72].

Two other questions remain unanswered: first, whether the FDA's clearance of the SS1E in 2010 to achieve liquid chemical sterilization, but without the claim of "sterile" filtered rinse water, coupled with the FDA's censure of every SS1 device manufactured since its clearance in 1988, indicates that the SS1's censure was due more to the SS1's questionable labeling claims - namely, to "guarantee" to achieve a "sterile", even though wet, processed surgical instrument - than to a rebuke of its manufacturer's unapproved changes and design modifications; and, second, whether the FDA might have hesitated less and initiated a more prompt and aggressive recall, had the SS1 been less ubiquitous and used by considerably fewer healthcare facilities, instead of sanctioning the SS1's continued use until August 2, 2012, more than 4 years after the FDA published its warning letter. The Abtox Plazlyte Sterilization System, for example, was used more than a decade ago in a limited number of medical facilities to "sterilize" instruments, like the SS1, using a low-temperature, peracetic acid-based sterilizing agent[73]. This device was abruptly recalled from the market shortly after the FDA determined that its manufacturer had modified, adulterated and misbranded the device without affording the FDA the opportunity to review these changes as federal rules and regulations require[73]. Indeed, Abtox's Plazlyte Sterilization System did not remain on the market subject to a CN and CT, and, unlike the SS1, its continued use was not sanctioned by the FDA.

To be sure, the changes in the management of instrument reprocessing, if not in health care, that the SS1's omnipresence in operating-room settings the past 20 years prompted (e.g., reprocessing surgical instruments and endoscopes "just in time"[30] at the point of their use) are as much a credit to the SS1's marketing and advertising as they are a mandate to study not only this processor's history, regulation, and labeling claims, but also its impact on public health and aseptic technique since 1988.

A number of recommendations are provided in Tables 5 and 6, to minimize the risk of injury to patients and of legal exposure to healthcare facilities. Those provided in Table 6 address the infection-control breaches discussed in Tables 1 and 2.

In closing, of the many lessons that the SS1 and its regulation by the FDA has taught the infection control community about the causes and prevention of HAIs, this unapproved device's countenanced use (through August, 2012) begets the precipiced conclusion that, contrary to the public's general understanding and expectation, a medical device without a regulatory approval, clearance, or approved IDE may be clinically used and sold in the U.S. (e.g., the Steris 20 sterilant), pursuant to the terms of a consent decree, CT, and CN, without the patient's knowledge or informed consent. This is an unexpected finding that, like other conclusions presented herein, suggests the regulation and oversight of medical devices could be significantly improved.

## REFERENCES


1 **Muscarella LF**. Patient safety concerns in Puerto Rico. *The Q-Net Monthly* 2010; **16**: 7-12
2 **Veterans Administration Office of Inspector General**. Healthcare Inspection: Use and reprocessing of flexible fiberoptic endoscopes at VA medical facilities. Report No. 09-01784-146. Issued: June 16, 2009. Pages 1-45
3 **Veterans Administration Office of Inspector General**. Health Inspection. Patient safety issues: VA Caribbean Healthcare System. Report No. 09-03055-103. Issued: March 16, 2010. San Juan, Puerto Rico. Pages 1-13. Available from: URL: http://www.va.gov/oig/54/reports/VAOIG-09-03055-103.pdf
4 **Dzau VJ**. Letter to physicians and hospital staff of Duke University Health System. Re: Update on Hydraulic Fluid Issue. Date: June 15, 2005. Available from: URL: http://www.dukehealth.org/health_library/news/9091
5 **Dudzinski DM**, Hébert PC, Foglia MB, Gallagher TH. The disclosure dilemma--large-scale adverse events. *N Engl J Med* 2010; **363**: 978-986
6 **Corwin T**. Woman sues Augusta VA. Patient says she contracted hepatitis C. Available from: URL: http://chronicle.augusta.com/news/health/2010-07-06/woman-sues-augusta-va
7 **Willing J**. Ottawa's public health names clinic at heart of infection scare. Available from: URL: http://www.torontosun.com/2011/10/17/ottawas-public-health-names-clinic-at-heart-of-infection-scare
8 **Olympus Canada**. Important safety notice. February 11, 2009. Available from: URL: http://www.olympusamerica.com/files/MAJ-855_CustomerLetter_2112009.pdf
9 **Veterans Health Administration Warning System**. Improper set-up and reprocessing of flexible endoscope tubing and accessories. Patient safety ale rt. AL09-07 December 22, 2008. Available from: URL: http://www.patientsafety.gov/alerts/OlympusScopesAlertAL09-07-WWW.pdf
10 **Muscarella LF**. Recommendations to prevent healthcare-acquired infections. *The Q-Net Monthly* 2011; **17**: 1-8
11 **Associated Press**. Scares at VAs warn 13,000 to get blood tested. Augusta Chronicle Sunday, May 29, 2011. Available from: URL: http://chronicle.augusta.com/news/health/2011-05-29/scares-vas-warn-13000-get-blood-tested
12 **Rios J**. Infection control breaches unveiled at Veterans Medical Center. The San Juan Weekly June 24-30, 2010. Available from: URL: http://www.myendosite.com/articles/SanJuanWeekly.pdf
13 **Associated Press**. VA defends limited Ohio infection testing. April 22, 2011. Available from: URL: http://dailymail.com/ap/ApSports/201104250420
14 **Veterans Health Administration**. VHA Directive 2008-002. Disclosure of adverse events to patients. Dated: January 18, 2008. Department of Veterans Affairs. Washington, DC. Available from: URL: http://www.ethics.va.gov/docs/policy/VHA_Directive_2008-002_Disclosure_of_Adverse_Events_20080118.pdf
15 **Karl Storz**. Indications for use of STERIS SYSTEM 1® Sterile Processing System. Actuality: August 20, 2008
16 **Muscarella LF**. The STERIS System 1. *The Q-Net Monthly* 2009; **15**: 13-18S2
17 **Muscarella LF**. Adulterated and misbranded devices: A position statement. *The Q-Net Monthly* 2009; **15**: 19-22S1
18 **Alfa M**. System 1 Sterile Processing System. Liquid Chemical Sterilization Anthology. 2004. Available from: URL: http://www.quirurgil.com/espanol/notas/Sistema 1.pdf
19 **FDA clearance letter**. Steris System 1 K875280. Cleared September 13, 1988. Available from: URL: http://www.accessdata.fda.gov/cdrh_docs/pdf9/K090036.pdf
20 **FDA clearance letter**. Steris System 1E K090036. Cleared April 5, 2010. Available from: URL: http://www.accessdata.fda.gov/cdrh_docs/pdf9/K090036.pdf
21 **Davies P**. Germ watch: clinic infections put a sterilizer of lab devices under microscope. The Wall Street Journal December 24, 2004. Page A1. Available from: URL: http://www.myendosite.com/articles/wsj122404.pdf
22 **Muscarella LF**. 'Sterile' filtered rinse water? *The Q-Net Monthly* 2008; **14**: 7-8
23 **Muscarella LF**. Contribution of tap water and environmental surfaces to nosocomial transmission of antibiotic-resistant Pseudomonas aeruginosa. *Infect Control Hosp Epidemiol* 2004; **25**: 342-345
24 **Muscarella LF**. Are all sterilization processes alike? *AORN J* 1998; **67**: 966-970, 973-976
25 **Berlau J**. A new risk for high-tech surgery? Investors Business Daily February 14, 2000. Page A1. Available from: URL: http://www.myendosite.com/articles/ibd021400.pdf
26 **Muscarella LF**. Boplogical indicators for monitoring water? *The Q-Net Monthly* 2008; **14**: 13-16S
27 **Advanced Sterilization Products**. Maintaining device sterility. AD-100228-01-US_B. (Advertisement) 2010. Available from: URL: http://www.aspjj.com/us/sites/default/files/pdf/AD-100228-01-US_SS1ERinseWater.pdf
28 **Muscarella LF**. Double standards. *The Q-Net Monthly* 2006; **12**: 9-12
29 **Muscarella LF**. Let sleeping dogs lie? *The Q-Net Monthly* 2008; **14**: 17-20
30 **Steris Corporation**. The Steris Process Sterilization Guarantee. Publication ID: No. M1016EN. 2006-02, Rev. H.
31 **Muscarella LF**. The importance of bronchoscope reprocessing guidelines: raising the standard of care. *Chest* 2004; **126**: 1001-1002; author reply 1002-1003
32 **Food and Drug Administration**. Letter to Steris Corporation. April 23, 2001. Page 1-6
33 **Muscarella LF**. Anticipated reliability of liquid chemical sterilants. *Am J Infect Control* 1998; **26**: 155-156
34 **Centers for Disease Control and Prevention (CDC)**. Bronchoscopy-related infections and pseudoinfections--New York, 1996 and 1998. *MMWR Morb Mortal Wkly Rep* 1999; **48**: 557-560
35 **Sorin M**, Segal-Maurer S, Mariano N, Urban C, Combest A, Rahal JJ. Nosocomial transmission of imipenem-resistant Pseudomonas aeruginosa following bronchoscopy associated with improper connection to the Steris System 1 processor. *Infect Control Hosp Epidemiol* 2001; **22**: 409-413
36 **Muscarella LF**. Déjà Vu...all over again? The importance of instrument drying. *Infect Control Hosp Epidemiol* 2000; **21**: 628-629

37 **Muscarella LF**. Leading a horse to water: are crucial lessons in endoscopy and outbreak investigations being learned? *Infect Control Hosp Epidemiol* 2002; **23**: 358-360; author reply 360
38 **Bond WW**. Biological indicators for a liquid chemical sterilizer: a solution to the instrument reprocessing problem? *Infect Control Hosp Epidemiol* 1993; **14**: 309-312
39 **Daschner F**, Rüden H. Does Steris sterilize? *Infect Control Hosp Epidemiol* 1998; **19**: 740
40 **Daschner F**. STERIS SYSTEM 1 in Germany. *Infect Control Hosp Epidemiol* 1994; **15**: 294, 296
41 **Food and Drug Administration**. Questions and Answers About the Steris System 1 Processor For Healthcare Facilities. Available from: URL: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm192685.htm
42 **Food and Drug Administration**. FDA Notice: Concerns About the Steris System 1 Processor, Components, and Accessories, and FDA Recommendations. Issued: December 3, 2009. Available from: URL: http://www.fda.gov/medicaldevices/safety/alertsandnotices/ucm191585.htm
43 **Food and Drug Administration**. Steris warning letter. May 15, 2008. Available from: URL: http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2008/ucm1048303.htm
44 **Steris Corporation**. Important notice. January 20, 2009. Available from: URL: http://www.steris.com/media/pdf/products/SYSTEM1CustomerNotice2009JAN.pdf
45 **Food and Drug Administration**. Transcript of teleconference. Moderator: Heidi Marchand. December 10, 2009. Pages 1-37. Available from: URL: http://www.fda.gov/downloads/MedicalDevices/Safety/AlertsandNotices/UCM194981.pdf
46 **Food and Drug Administration**. STERIS System 1 Processor: 6 Month Extension for Healthcare Facilities to Transition to Legally-Marketed Alternative. February 2, 2010. Available from: URL: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm199567.htm
47 **Food and Drug Administration**. STERIS System 1 (SS1) Processor: Second 6 Month Extension for Health Care Facilities to Replace STERIS System 1 with a Legally-Marketed Alternative. December 22, 2011. Available from: URL: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm284779.htm
48 **Food and Drug Administration**. Letter to Endoscope Manufacturers: Possible Misbranding of Reusable Devices Labeled for Reprocessing by the STERIS System 1 Processor. February 22, 2010. Available from: URL: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm201497.htm
49 **Muscarella LF**. Federal Register: Reprocessing Reusable Medical Instruments. *The Q-Net Monthly* 2011; **17**: 15-20
50 **Food and Drug Administration**. Steris System 1E (SS1E) Liquid Chemical Sterilant - K090036. April 9, 2010. Available from: URL: http://www.organizedwisdom.com/steris-system-1e-ss1e-liquid-chemical-sterilant-k090036/711830/nxi/med
51 **Food and Drug Administration**. Steris System 1E (SS1E) Liquid Chemical Sterilant - K090036. April 6, 2010
52 **Food and Drug Administration**. FDA Obtains Consent Decree to Stop Marketing of Unapproved Sterilization System. FDA news release. April 20, 2010. Available from: URL: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm209164.htm
53 **Steris Corporation**. Certificate of medical necessity (CN): System 1 and accessories. April 20, 2010. Publication ID: 4436. Available from: URL: http://www.faqs.org/secfilings/100420/STERIS-CORP_8-K/dex992.htm
54 **Food and Drug Administration**. STERIS System 1 Update: FDA Grants Extension for Healthcare Providers Using STERIS System 1 to Submit a Certificate of Medical Necessity. June 23, 2010. Available from: URL: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm216931.htm
55 **Steris Corporation**. Customer letter. March 25, 2011. Available from: URL: http://www.steris.com/media/PDF/system1/Customer_Extension_Letter_-_FINAL_-_25MAR20111.pdf
56 **Food and Drug Administration**. Device Advice: Investigational Device Exemption (IDE). Available from: URL: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/default.htm
57 **Kaufman HH**, Lewin JL, eds. The physician's perspective on medical law, volume II. American Association of Neurological Surgeons. Illinois: Park Ridge, 1997. Available from: URL: http://books.google.com.hk/books/about/The_physician_s_perspective_on_medical_l.html?id=BYhqAAAAMAAJ
58 **Canadian Health Agency**. Re: STERIS System 1 Steris Processing System (License No. 8206). January 5, 2010. Available from: URL: http://www.myendosite.com/htmlsite/2010/refs0710.pdf
59 **Vernaglia LW**, Beaver NA, Lacktman NM, Sorensen HA, Waltz JA. Health Care Professionals and Certificates of Medical Necessity Under FDA Consent Decrees. Legal News Alert: Healthcare. April 19, 2011. Available from: URL: http://www.foley.com/intelligence/detail.aspx?int=8049
60 **Baxter Healthcare Corporation**. Certificate of medical necessity (CN): Colleague volumetric infusion pumps. July 13, 2010
61 **Muscarella LF**. High-level disinfection or "sterilization" of endoscopes? *Infect Control Hosp Epidemiol* 1996; **17**: 183-187
62 **Food and Drug Administration**. Public Workshop - Reprocessing of reusbale medical devices. 2011. Available from: URL: http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm252205.htm
63 **American Society for Gastrointestinal Endoscopy (ASGE)**. ASGE emphasizes steps in endoscope reprocessing. July 2007. Available from: URL: http://www.olympusamerica.com/msg_section/files/Evotech_July2007_final_ASGEnews.pdf
64 **American Society for Gastrointestinal Endoscopy**. Multisociety guideline for reprocessing flexible gastrointestinal endoscopes. *Gastrointest Endosc* 2003; **58**: 1-8
65 **Association of periOperative Registered Nurses (AORN)**. Guidance statement: Reuse of single-use devices. 2006 Standards, Recommended Practices, and Guidelines. 309-315
66 **Association for Professionals in Infection Control and Epidemiology (APIC)**. Reprocessing of Single Use Medical Devices. August 31, 2007. Available from: URL: http://amdr.org/documents/APICsingleusedevicepositionChangesIncluded-Final8_31_07-r.pdf
67 **Emergency Care Research Institute (ECRI)**. FDA Issues Statement on Reuse of Single-Use Devices. Health Devices Alerts May 12, 2008. Available from: URL: https://www.ecri.org/Documents/Device_Reuse/single_use_hda_alert_10_06.pdf
68 **Tosh PK**, Disbot M, Duffy JM, Boom ML, Heseltine G, Srinivasan A, Gould CV, Berríos-Torres SI. Outbreak of Pseudomonas aeruginosa surgical site infections after arthroscopic procedures: Texas, 2009. *Infect Control Hosp Epidemiol* 2011; **32**: 1179-1186
69 **Department of Veterans Affairs**. Patient safety alert. Medtronic SynchroMed II Implantable Drug Infusion Pump; Models: 8637-20 and 8637-40. AL09-24. August 6, 2009. Available from: URL: http://www.patientsafety.gov/alerts/AL09-24MedtronicImplantablePump.pdf
70 **Joint Commission (JCAHO)**. Sentinel event alert. Infusion Pumps: Preventing Future Adverse Events Issue 15 - November 30, 2000. Available from: URL: http://www.jointcommission.org/assets/1/18/SEA_15.pdf
71 **ECRI Institute**. JCAHO's 2003 National Patient Safety Goal for Infusion Pump Free-Flow Protection: Assessing General-Purpose and Patient-Controlled Analgesic (PCA) Pumps. Health Devices Alerts No. SR0018, March 2003. Available from: URL: https://www.premierinc.com/safety/safety-share/05-03_full_txt.htm

72 **ECRI Institute**. Perspectives from ECRI Institute. STERIS System 1 and FDA. January 22, 2010. Available from: URL: https://www.ecri.org/Documents/Esource/HT_Winter_2010/Perspectives_Steris_FDA_JK.pdf

73 **Food and Drug Administration**. FDA Safety Alert: Warning Regarding the Use of the AbTox Plazlyte™ Sterilization System. April 13, 1998. Available from: URL: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/ucm062297.htm

74 **Bronowicki JP**, Venard V, Botté C, Monhoven N, Gastin I, Choné L, Hudziak H, Rihn B, Delanoë C, LeFaou A, Bigard MA, Gaucher P. Patient-to-patient transmission of hepatitis C virus during colonoscopy. *N Engl J Med* 1997; **337**: 237-240

75 **Centers for Disease Control and Prevention (CDC)**. Guideline for disinfection and sterilization in healthcare facilities, 2008. Available from: URL: http://www.cdc.gov/hicpac/pdf/guidelines/Disinfection_Nov_2008.pdf

76 **Muscarella LF**. The study of a contaminated colonoscope. *Clin Gastroenterol Hepatol* 2010; **8**: 577-580.e1

77 **Muscarella LF**. Dear Los Angeles Times: the risk of disease transmission during gastrointestinal endoscopy. *Gastroenterol Nurs* 2004; **27**: 271-278

78 **Muscarella LF**. Prevention of disease transmission during flexible laryngoscopy. *Am J Infect Control* 2007; **35**: 536-544

79 **Ramsey AH**, Oemig TV, Davis JP, Massey JP, Török TJ. An outbreak of bronchoscopy-related Mycobacterium tuberculosis infections due to lack of bronchoscope leak testing. *Chest* 2002; **121**: 976-981

80 **DiazGranados CA**, Jones MY, Kongphet-Tran T, White N, Shapiro M, Wang YF, Ray SM, Blumberg HM. Outbreak of Pseudomonas aeruginosa infection associated with contamination of a flexible bronchoscope. *Infect Control Hosp Epidemiol* 2009; **30**: 550-555

81 **Kac G**, Podglajen I, Si-Mohamed A, Rodi A, Grataloup C, Meyer G. Evaluation of ultraviolet C for disinfection of endocavitary ultrasound transducers persistently contaminated despite probe covers. *Infect Control Hosp Epidemiol* 2010; **31**: 165-170

82 **Muscarella LF**. Recommendations to resolve inconsistent guidelines for the reprocessing of sheathed and unsheathed rigid laryngoscopes. *Infect Control Hosp Epidemiol* 2007; **28**: 504-507

83 **Olympus Corporation**. Olympus EVIS EXERA II GIF/CF/PCF Type 180 Series Reprocessing Manual. Available from: URL: http://www.myendosite.com/manuals/180_Olympus_Reprocessing_manual.pdf

84 **Lambrecht B**. VA patients get letter of warning on dental work. St. Louis Post-Dispatch, June 30, 2010. Available from: URL: http://www.stltoday.com/lifestyles/health-med-fit/fitness/article_2729bf3f-d947-5708-9b89-a0d7a1bc5e32.html

85 **Veterans Administration Office of Inspector General**. Health Inspection: Oversight review of dental clinic issues. Dayton VA Medical Center, Dayton, OH. Report No. 10-03330-148. Issued: April 25, 2011. Pages 1-24. Available from: URL: http://www.va.gov/oig/54/reports/VAOIG-10-03330-148.pdf

86 **Anonymous**. No increase in infections despite sterilization problem, officials say. Vancouver Sun December 10, 2010

87 **Barrow B**. Tulane Medical Center alerts patients after medical gear improperly sterilized. The Times-Picayune March 10, 2011. Available from: URL: http://www.nola.com/health/index.ssf/2011/03/tulane_medical_center_alerts_p.html

88 Health News. Hospital surgery puts dozens of patients at risk of CJD. Telegraph March 29, 2011. Available from: URL: http://www.telegraph.co.uk/health/healthnews/8413797/Hospital-surgery-puts-dozens-of-patients-at-risk-of-CJD.html

89 **Ottawa Public Health**. Patient notification letter. [Letter] October 17, 2011. Pages 1-3. Available from: URL: http://ottawa.ca/cs/groups/content/@webottawa/documents/pdf/mdaw/mdy5/~edisp/con064398.pdf

90 **Febregas L**. Suit: Maker of sterilization equipment ignored flaws. Pittsburgh Tribune-Review, May 13, 2003. Available from: URL: http://www.pittsburghlive.com/x/pittsburghtrib/s_134155.html

91 **Snowbeck C**. AGH blames bronchoscope cleaning machine. Pittsburgh Post Gazette, January 21, 2003. Available from: URL: http://www.yourlawyer.com/articles/title/agh-blames-bronchoscope-cleaning-machine


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