



Efficacy of High-Level Disinfection with CIDEX® OPA Solution

OPA Solution

Hospital-acquired infections (HAIs) pose a serious threat to patient safety, affecting more than 2 million patients every year in the United States and many more worldwide.¹ As a result, they have received increasing attention from healthcare professionals, as well as state and federal regulatory agencies, hospital administrators, payors, the media, and patients. A number of campaigns are underway to reduce the incidence of HAIs, focusing on prevention practices and changes in reimbursement. The Joint Commission has added preventable infections as one of its National Patient Safety Goals,² and the Association for Professionals in Infection Control and Epidemiology (APIC) has launched a campaign emphasizing prevention of HAIs and other adverse events.³ In addition, the Centers for Medicare and Medicaid Services will no longer provide reimbursement for the added cost of care of patients with several types of HAIs.⁴ The implications of these initiatives are far-reaching for hospitals and infection prevention professionals.

“CIDEX® OPA Solution...is proven effective against a broad range of viruses, fungi, and mycobacteria.”

With more than 10 million gastrointestinal endoscopic and 500,000 flexible bronchoscopic procedures performed every year in the United States,^{5,6} reusable flexible endoscopes have the potential to play a role in HAIs. During clinical use, endoscopes are contaminated by multiple microorganisms, and failure to appropriately

clean, disinfect, or sterilize endoscopes has resulted in nosocomial outbreaks and serious infections.^{7,8} As a result, proper cleaning and disinfection of expensive, delicate endoscopes are crucial to ensure patient safety and maintain optimal function.^{7,9} The clinically established efficacy of detergents and disinfectants clearly plays a key part in instrument processing, and their selection is an important clinical and risk management decision.

High-Level Disinfection

Endoscopes and other devices that contact mucous membranes but normally do not cross the blood barrier are, by definition, semi-critical devices and must undergo high-level disinfection. According to APIC, this means elimination of many or all pathogenic organisms, except bacterial spores.¹⁰ High-level disinfectants cleared for use with semi-critical medical devices must demonstrate 100% kill of 10⁵ to 10⁶ mycobacteria in the presence of 2% horse serum in quantitative tests and pass the sporicidal

test of AOAC International, the Association of Analytical Communities.¹¹

Liquid chemical germicides that are high-level disinfectants ideally should offer effectiveness, speed, and ease of use and be compatible with a variety of materials used in medical devices. These chemicals also should not be noxious or toxic to personnel.⁷ The high-level disinfectant CIDEX® OPA Solution (0.55% *ortho*-phthalaldehyde) (Advanced Sterilization Products [ASP], Division of Ethicon, Inc.) meets these criteria and, in nearly 10 years of clinical use and efficacy testing, is proven effective against a broad range of viruses, fungi, and mycobacteria.

CIDEX® OPA Solution

CIDEX® OPA Solution was introduced by ASP in 1999 to meet the need for effective, fast, easy-to-use high-level disinfection and to address staff concerns about the safety of glutaraldehyde. CIDEX OPA Solution is bactericidal, sporicidal, virucidal, fungicidal, and tuberculocidal. It achieves high-level disinfection in 12 minutes at room temperature and also has been cleared for marketing in the United States for use in automatic endoscope reprocessors (high-level disinfection in 5 minutes at 25°C). Extensive testing has shown that the high-level disinfectant is non-corrosive and is compatible with a wide variety of materials commonly found in endoscopes and other medical devices. (See Table 1) It also is gentler on flexible endoscopes than peracetic acid.¹²

Table 1: Materials Shown To Be Compatible with CIDEX® OPA Solution*

Metals	
<ul style="list-style-type: none"> Aluminum Brass Chrome-plated brass/steel Nickel-plated brass Stainless-steel/titanium 	<ul style="list-style-type: none"> Anodized aluminum Carbon steel Copper Nickel-silver alloy Tungsten carbide/vanadium steel
Plastics & Elastomers	
<ul style="list-style-type: none"> Acetal Nylon Polycarbonate Polypropylene Polysulfone PTFE Natural rubber latex Polyurethane Polyethylene terephthalate (polyester) 	<ul style="list-style-type: none"> Acrylonitrile-butadiene-styrene (ABS) Polyamide Polyethylene Polystyrene Polyvinyl chloride (PVC) Kraton G Polychloroprene (Neoprene) Silicone rubber Polymethylmethacrylate (acrylic)
Adhesives	
<ul style="list-style-type: none"> Cyanoacrylate EPO-TEK 353 epoxy 	<ul style="list-style-type: none"> EPO-TEK 301 epoxy
Dental Materials	
<ul style="list-style-type: none"> Addition silicone Polysulphide 	<ul style="list-style-type: none"> Polyether

*Data on file at ASP.

CIDEX® OPA Solution has no offensive odor. In contrast to glutaraldehyde, the Occupational Safety & Health Administration has not set permissible exposure limits for CIDEX OPA Solution and does not require special venting or air monitoring in areas where the solution is used or monitoring of staff who work with it. Local regulations may vary, but generally the solution can be discarded with running water into an ordinary drain.

CIDEX® OPA Solution is ready to use from the bottle and requires no mixing or activation. Test strips are used to verify that the germicide has maintained the minimum effective concentration (MEC) of 0.3% CIDEX OPA Solution. Tests have shown that even reused, stressed solution diluted to the MEC remains bactericidal, sporicidal, virucidal, fungicidal, and tuberculocidal at room temperature.¹³⁻¹⁷ CIDEX OPA Solution has a 14-day reuse life and an open-bottle shelf life of 75 days. Unopened bottles have a shelf life of two years when stored at 15–30°C. Although provided at a near-neutral pH of 7.5, the solution is stable for use over a wide range of pH (3-9).

Efficacy

The efficacy of CIDEX® OPA Solution as a high-level disinfectant has been established through extensive evaluation by ASP over the past 10 years. A summary of key efficacy testing follows.

Methodology

Two types of quantitative tests have been used predominantly to evaluate the efficacy of CIDEX® OPA Solution. The first type utilized suspensions of microorganisms diluted 1:10 into the solution at a specified concentration and temperature. After a specified period (usually minutes), a neutralizer was added or the microorganisms were removed from the suspension by vacuum filtration and then rinsed. The number of viable organisms remaining after exposure to the solution then was determined by quantitative assay and compared quantitatively with organisms that had no exposure to the solution. The reduction in viable microorganisms is expressed as a log of the number of organisms.

A second, more stringent test type evaluated the efficacy of CIDEX® OPA Solution in inactivating microorganisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecalis* (VRE), and viruses that had dried onto a flat solid surface. After exposure to CIDEX OPA Solution, the microbes were recovered, rinsed, and quantitatively assayed.

CIDEX® OPA Solution has been cleared for marketing in the United States as a high-level disinfectant for reusable medical and dental equipment processed at

20°C (12 minutes) and at 25°C (5 minutes).^{*} Because the solution is used around the world and claims vary by country, evaluations also have been done based on other times and temperatures. Testing shows that CIDEX OPA Solution is bactericidal when instruments are processed at 20°C for five minutes.

Mycobacteria

Effective control of mycobacteria is crucial in preventing the transmission of disease by contaminated medical devices. Mycobacteria demonstrating resistance to aldehyde-based disinfectants (i.e., glutaraldehyde and formaldehyde) have caused nosocomial infections in the United States and elsewhere, and glutaraldehyde-resistant mycobacteria have been isolated from flexible endoscope reprocessing machines.^{18,19} To address this problem, the efficacy of reused CIDEX® OPA Solution was tested against glutaraldehyde-resistant *Mycobacterium chelonae*. The test was based on a protocol determined by the Environmental Protection Agency (EPA) to simulate clinically reused disinfectants. Suspensions of *M. chelonae* were exposed to reused 0.5% OPA at 20°C. The result: 5-log reduction after 5 minutes and complete kill (of 10⁶ colony-forming units/mL) after 15 minutes. By comparison, a solution of reused 2.0% glutaraldehyde showed a 4-log reduction in 20 minutes at 20°C.¹³

Similar assays with *Mycobacterium bovis* (BCG) were done with 0.2% OPA. Results showed a complete kill (>5 log₁₀) of viable mycobacteria after 5 minutes at 20°C. In contrast, although this mycobacterium was not resistant to glutaraldehyde, 2.0% glutaraldehyde gave a 2-log reduction after 10 minutes at the same temperature.¹³

Subsequent studies have provided more information about the efficacy of CIDEX® OPA Solution. For example, a 2001 comparison of the mycobactericidal activity of *ortho*-phthalaldehyde (OPA), glutaraldehyde, and other dialdehydes by quantitative suspension testing found

Table 2: Bactericidal Efficacy Test with CIDEX® OPA Solution, 5 Minutes at 20°C

Organism Tested	Result
<i>Staphylococcus aureus</i> (ATCC 6538)	No growth
<i>Salmonella choleraesuis</i> (ATCC 10708)	No growth
<i>Pseudomonas aeruginosa</i> (ATCC 15442)	No growth
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) (ATCC 33592)	No growth
Vancomycin-resistant <i>Enterococcus faecalis</i> (VRE) (ATCC 51299)	No growth
<i>Staphylococcus aureus</i> (CIP 4.83)	>5 log reduction
<i>Enterococcus hirae</i> (CIP 58.55)	>5 log reduction
<i>Pseudomonas aeruginosa</i> (ATCC 103467)	>5 log reduction

^{*}When used or reused in a legally marketed AER that can be set to a minimum of 25C.

that a 0.5% OPA was rapidly mycobactericidal under both “clean” and “dirty” conditions.¹⁹ In particular, the solution was active against glutaraldehyde-resistant strains of mycobacteria.¹⁹ Another study using a quantitative suspension protocol found that OPA is effective as a tuberculocidal disinfectant: at MEC levels, OPA achieved a 6-log₁₀ reduction of *Mycobacterium bovis* in nearly one-sixth the time required with glutaraldehyde (5.5 minutes versus 32 minutes).²⁰ In a study of the mechanisms of the mycobacterial action of *ortho*-phthalaldehyde, glutaraldehyde, and chlorhexidine diacetate, Fraud and colleagues concluded that, “The rapid micobactericidal effect of OPA probably arises from its more efficient penetration across biological membranes.”²¹

Antibiotic-Resistant Bacteria

Drug-resistant bacterial infection is a widespread health concern, and some controversy exists as to whether resistance to antibiotics is somehow related to resistance to disinfectants. Two common drug-resistant organisms, MRSA (ATCC® #33592) and VRE (ATCC® #51299), have been tested with CIDEX® OPA Solution.

As in the efficacy tests with mycobacteria, these assays evaluated reused CIDEX® OPA Solution in conformance with EPA specifications. Stainless steel carriers coated with bacteria were submerged in reused solution diluted to 0.3% at 20°C. After a 10-minute exposure, carriers were placed into individual containers of culture medium containing an agent that neutralizes *ortho*-phthalaldehyde. Each strain was used in triplicate tests involving 10 carriers each. No organisms survived exposure to the dilute solution, illustrating that the antibiotic-resistant strains of *S. aureus* and *E. faecalis* demonstrate no increased resistance to dilute CIDEX OPA Solution.¹⁷

Clostridium Difficile

Clostridium difficile, a spore-forming, gram-positive anaerobic bacillus, is the leading cause of antibiotic-associated diarrhea in hospitalized patients. The serious health effects of *C. difficile* include diarrhea, colitis, blood poisoning, and even death. This, combined with an increasing prevalence and incidence, make *C. difficile* a significant healthcare issue.²²

A recent study, results of which were presented at the APIC 2008 Annual Conference, evaluated the biocidal activity of an *ortho*-phthalaldehyde solution (prepared from CIDEX® OPA Solution) against *C. difficile*. Results showed that OPA is efficacious against the vegetative

form and achieves a significant reduction of the spore form of *C. difficile*. (See Figure 1) In particular, there were no surviving *C. difficile* vegetative cells observed after a 2-minute exposure in 0.3% OPA at 20° C. With the spore form of *C. difficile*, a 2.4 log₁₀ reduction was demonstrated with 0.3% OPA and at least 4.9 log₁₀ reduction with 0.5% OPA after a five-minute exposure.²³

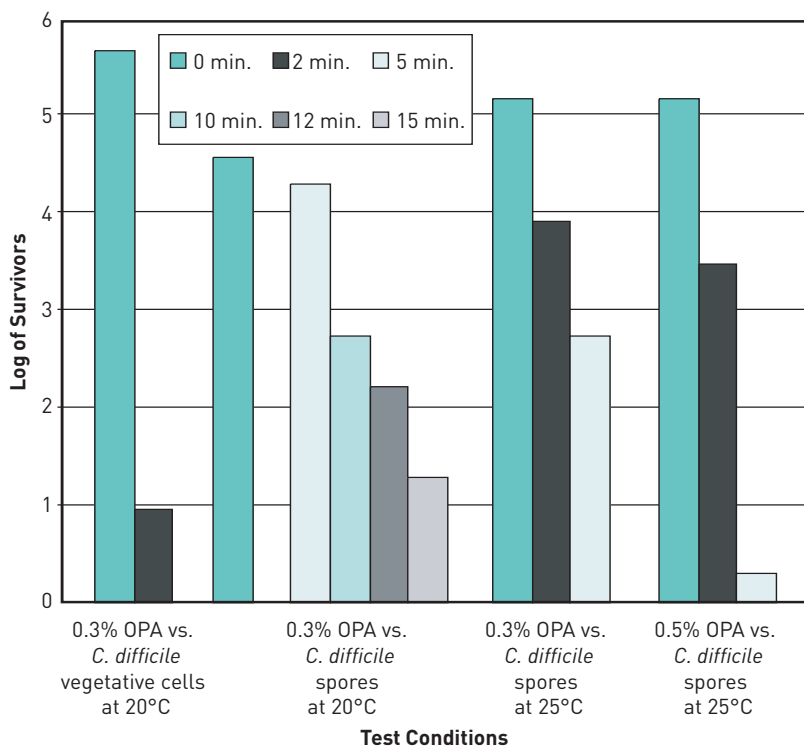
Viruses

Hepatitis B and C viruses (HBV and HCV)—the most prevalent blood-borne viruses²⁴—are parenterally transmitted infectious agents that are a major cause of acute hepatitis and chronic liver disease, including cirrhosis and cancer. Disinfection of HBV is assayed with an *in vitro* test using duck hepatitis B virus as a surrogate for HBV.

To test the efficacy of CIDEX® OPA Solution against the HBV surrogate, a suspension of duck hepatitis B virus was dried on a Petri dish, then exposed to 0.3% *ortho*-phthalaldehyde for 5 minutes at 20°C. The bottom of the dish was scraped, and the resulting suspension was passed through a filtration column to remove the CIDEX OPA Solution. In the immunofluorescence assay, the number of viable virus particles was reduced by more than 4 logs after exposure to 0.3% CIDEX OPA Solution.¹⁵

Similar tests were done with bovine viral diarrhea virus, a surrogate for HCV. For these tests, virus suspensions also contained 5% horse serum as organic soil. This

Figure 1. OPA Solution Versus *Clostridium Difficile* at Various Study Conditions.



mixture was dried on Petri dishes and recovered as described above. Exposure to 0.5% CIDEX® OPA Solution for 5 minutes at 20°C caused a >4-log reduction in the number of viable virus particles.¹⁵ (See Table 3)

Table 3: Virucidal Test with CIDEX® OPA Solution, 5 Minutes at 20°C (Pass Test= >3-log Reduction)

Virus Tested	Result
Adenovirus Type 5	Pass test
Herpes Simplex Type 1 (HSV1)	Pass test
HSV 2	Pass test
Influenza A (Hong Kong)	Pass test
Coxsackievirus Type B3	Pass test
Polio Type 1 (Brunhilde strain)	Pass test
Rhinovirus Type 37	Pass test
Vaccinia	Pass test
HIV Type 1	Pass test
Cytomegalovirus	Pass test
Human Coronavirus	Pass test
Rotavirus (Strain WA)	Pass test
Duck Hepatitis B Virus (surrogate for Hepatitis B)	Pass test
Bovine viral diarrhea virus (surrogate for Hepatitis C)	Pass test
Rotavirus (Strain WA)	Pass test
Feline calicivirus as (surrogate for Norovirus)	Pass test
Avian influenza A (H5N1) virus	Pass test
Canine Parvovirus	Pass test
Hepatitis A virus	Pass test

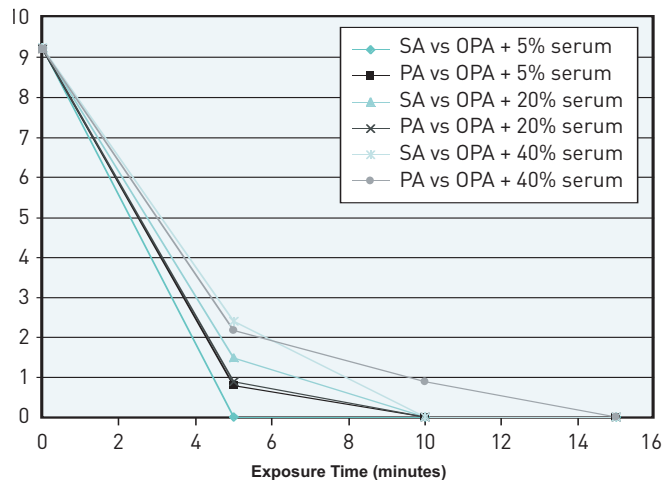
Temperature

The effect of temperature on biocidal activity was further assessed in quantitative tests of *Bacillus subtilis* spores (ATCC #19659). Suspensions of spores were diluted into various concentrations of CIDEX® OPA Solution and tested at 35°C, 40°C, 45°C, and 50°C. Results showed that the solution is sporicidal and that, within defined parameters, study temperature has a bigger influence on the degree of sporicidal activity than the concentration of the solution. For example, a ≥6-log reduction in the number of viable spores occurred with 2-hour exposure to 0.05% disinfectant at 50°C, and a 3-log reduction was observed in the more concentrated solution of 0.3% OPA at 35°C.¹⁶

Organic Soil

Cleaning of instruments before disinfection is the first step in removing bioburden from instruments. However, manual cleaning is known to have variable results,²⁵ potentially reducing the effectiveness of disinfection. To assess the impact of an organic load on bactericidal activity of 0.3% CIDEX® OPA Solution, suspensions of *S. aureus* and *Pseudomonas aeruginosa* were exposed to 0.3% CIDEX OPA Solution at room temperature (20°C) in the presence of 0%, 5%, 20%, and 40% horse serum. For exposure times of up to 5 minutes, bactericidal activity decreased with increasing concentration of horse serum. However, when exposure to 0.3% CIDEX OPA Solution was 10 minutes or longer, these concentrations of horse serum did not prevent >7-log reduction of viable bacteria.¹⁷

Figure 2. Biocidal Activity of 0.3% CIDEX® OPA Solution.



Biocidal activity of 0.3% CIDEX® OPA Solution was evaluated in the presence of variable amounts of horse serum. Suspensions of *Staphylococcus aureus* (SA) or *Pseudomonas aeruginosa* (PA) were diluted 1:10 into 0.3% OPA+horse serum. After exposure to disinfectant, viable organisms were assayed quantitatively.¹⁷

Summary

For more than 10 years, CIDEX® OPA Solution has been successfully utilized by healthcare facilities worldwide to high-level disinfect reusable medical and dental devices. As part of its commitment to infection prevention, ASP has conducted extensive tests to evaluate the efficacy of CIDEX OPA Solution. Results show that CIDEX OPA Solution is bactericidal—including for MRSA and VRE—mycobactericidal, sporicidal, and virucidal—including for surrogates for HBV and HCV.

CIDEX® OPA Solution is currently used to disinfect a wide variety of devices, including delicate and costly flexible gastroenterology endoscopes. This range of applications is possible because of the solution's broad materials compatibility. An important benefit of broad materials compatibility is simple standardization of processing protocols—a single protocol can be developed for disinfection of many items.

The fast processing time and ease of use of CIDEX® OPA Solution also contribute to rapid turnaround time, allowing smaller inventories of instruments and potential cost savings. Cost savings also might be realized by eliminating the monitoring of air and personnel exposure required with glutaraldehyde.

Combined, these factors demonstrate why CIDEX® OPA Solution makes both clinical and economic sense for facilities seeking an effective, more cost-efficient option for instrument reprocessing. Furthermore, the efficacy testing and quality assurance measures applied by ASP should be an important consideration for healthcare personnel as they work toward the control and prevention of HAIs. ■

References

1. Centers for Disease Control and Prevention. Public health focus: Surveillance, prevention and control of nosocomial infections. *Morbidity and Mortality Weekly Report*. 1992;41(42):783–787.
2. *Joint Commission 2009 National Patient Safety Goals—Hospital 2008*.
3. *APIC Vision 2012*. Washington, D.C.: Association for Professionals in Infection Control and Epidemiology.
4. Mitka M. Public, private insurers refusing to pay hospitals for costs of avoidable errors. *JAMA*. 2008;299:2495–2496.
5. Mehta A, Prakash U, Garland R, et al. Prevention of flexible bronchoscopy-associated infection. *Chest*. 2005;128:1742–1755.
6. Nelson D, Jarvis W, Rutala W, et al. Multi-society guideline for reprocessing flexible gastrointestinal endoscopes. *Infect Control Hosp Epidemiol*. 2003;24:532–537.
7. Rutala W, Weber D. Disinfection of Endoscopes: Review of new chemical sterilants used for high-level disinfection. *Infect Control Hosp Epidemiol*. 1999;20:69–76.
8. Spach D, Silverstein F, Stamm W. Transmission of infection by gastrointestinal endoscopy and bronchoscopy. *Ann Intern Med*. 1993;118:117–128.
9. Miller M. ICRE-1108: Instrument processing overview: cleaning, disinfection, sterilization. <http://www.iceinstitute.com/>. Accessed Nov. 11, 2008.
10. Association for Professionals in Infection Control and Epidemiology (APIC). *Disinfection and sterilization principles*; 2002.
11. Committee on Antimicrobial Efficacy Testing. Methods Committee Report. *J AOAC Int*. 2008;91:68B–72B.
12. Abraham J, Abdelshehid C, Lee H, et al. Effects of Steris 1™ sterilization and Cidex® *ortho*-phthalaldehyde high-level disinfection on durability of new-generation flexible ureteroscopes. *J Endourol*. 2007;21:985–992.
13. Roberts C, Chan-Myers H. Efficacy of dilute *ortho*-phthalaldehyde solutions with glutaraldehyde-resistant mycobacteria. *American Society for Microbiology*; 1998; Atlanta.
14. Roberts C, Chan-Myers H, Ascenzi J. Activity of dilute *ortho*-phthalaldehyde solutions against drug-resistant bacteria. *American Society for Microbiology*; 2001; Olando.
15. Roberts C, Chan-Myers H, Favero M. Virucidal activity of *ortho*-phthalaldehyde solutions against hepatitis B and C viruses. *Am J Infect Control*. 2008;36:223–226.
16. Chan-Myers H, Roberts C. The role of temperature and concentration on the sporicidal activity of *ortho*-phthalaldehyde. *Society for Healthcare Epidemiologists of America*; 2001; Baltimore.
17. Chan-Myers H, Roberts C. Effect of temperature and organic soil concentration on biocidal activity of *ortho*-phthalaldehyde solution. *Association for Professionals in Infection Control and Epidemiology (APIC)*; 2000.
18. van Klingeren B, Pullen W. Glutaraldehyde resistant mycobacteria from endoscope washers. *Hosp Infect*. 1993;25:147–149.
19. Fraud S, Maillard J, Russell A. Comparison of the mycobactericidal activity of *ortho*-phthalaldehyde, glutaraldehyde and other dialdehydes by a quantitative suspension test. *J Hosp Infect*. 2001;48:214–221.
20. Gregory A, Schaalje G, Smart J, Robison R. The mycobactericidal efficacy of *ortho*-phthalaldehyde and the comparative resistance of *Mycobacterium bovis*, *Mycobacterium terrae*, and *Mycobacterium chelonae*. *Infect Control Hosp Epidemiol*. 1999;20:324–330.
21. Fraud S, Hann A, Maillard J, Russell A. Effects of *ortho*-phthalaldehyde, glutaraldehyde and chlorhexidine diacetate on *Mycobacterium chelonae* and *Mycobacterium abscessus* strains with modified permeability. *JAC*. 2003;51:575–584.
22. Agency for Healthcare Research and Quality. Potentially deadly infection doubles among hospital patients over last 5 years. *Statistical Brief #50*; 2008.
23. Chan-Myers H, Roberts C. Evaluation of the biocidal efficacy of *ortho*-phthalaldehyde solution with vegetative and spore forms of *Clostridium difficile*. Association for Professionals in Infection Control and Epidemiology (APIC); June 15–19, 2008; Denver.
24. Sattar S, Tetro J, Springthorpe V, Guilivi A. Preventing the spread of hepatitis B and C viruses: where are germicides relevant? *Am J Infect Control*. 2001;29:187–197.
25. Alfa M, Olson N, Degagne P, Jackson M. A survey of reprocessing methods, residual viable bioburden, and soil levels in patient-ready endoscopic retrograde cholangiopancreatography duodenoscopes used in Canadian centers. *Infect Control Hosp Epidemiol*. 2002;23:198–206.

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