Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008

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This guideline discusses use of products by healthcare personnel in healthcare settings such as hospitals, ambulatory care and home care; the recommendations are not intended for consumer use of the products discussed.

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EXECUTIVE SUMMARY

The Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008, presents evidence-based recommendations on the preferred methods for cleaning, disinfection and sterilization of patient-care medical devices and for cleaning and disinfecting the healthcare environment. This document supercedes the relevant sections contained in the 1985 Centers for Disease Control (CDC) Guideline for Handwashing and Environmental Control.[1] Because maximum effectiveness from disinfection and sterilization results from first cleaning and removing organic and inorganic materials, this document also reviews cleaning methods. The chemical disinfectants discussed for patient-care equipment include alcohols, glutaraldehyde, formaldehyde, hydrogen peroxide, iodophors, *ortho*-phthalaldehyde, peracetic acid, phenolics, quaternary ammonium compounds, and chlorine. The choice of disinfectant, concentration, and exposure time is based on the risk for infection associated with use of the equipment and other factors discussed in this guideline. The sterilization methods discussed include steam sterilization, ethylene oxide (ETO), hydrogen peroxide gas plasma, and liquid peracetic acid. When properly used, these cleaning, disinfection, and sterilization processes can reduce the risk for infection associated with use of invasive and noninvasive medical and surgical devices. However, for these processes to be effective, health-care workers should adhere strictly to the cleaning, disinfection, and sterilization recommendations in this document and to instructions on product labels.

In addition to updated recommendations, new topics addressed in this guideline include 1) inactivation of antibiotic-resistant bacteria, bioterrorist agents, emerging pathogens, and bloodborne pathogens; 2) toxicologic, environmental, and occupational concerns associated with disinfection and sterilization practices; 3) disinfection of patient-care equipment used in ambulatory settings and home care; 4) new sterilization processes, such as hydrogen peroxide gas plasma and liquid peracetic acid; and 5) disinfection of complex medical instruments (e.g., endoscopes).

INTRODUCTION

In the United States, approximately 46.5 million surgical procedures and even more invasive medical procedures—including approximately 5 million gastrointestinal endoscopies—are performed each year. [2] Each procedure involves contact by a medical device or surgical instrument with a patient's sterile tissue or mucous membranes. A major risk of all such procedures is the introduction of pathogens that can lead to infection. Failure to properly disinfect or sterilize equipment carries not only risk associated with breach of host barriers but also risk for person-to-person transmission (e.g., hepatitis B virus) and transmission of environmental pathogens (e.g., *Pseudomonas aeruginosa*).

Disinfection and sterilization are essential for ensuring that medical and surgical instruments do not transmit infectious pathogens to patients. Because sterilization of all patient-care items is not necessary, health-care policies must identify, primarily on the basis of the items' intended use, whether cleaning, disinfection, or sterilization is indicated.

Multiple studies in many countries have documented lack of compliance with established guidelines for disinfection and sterilization. [3-6] Failure to comply with scientifically-based guidelines has led to numerous outbreaks. [6-12] This guideline presents a pragmatic approach to the judicious selection and proper use of disinfection and sterilization processes; the approach is based on well-designed studies assessing the efficacy (through laboratory investigations) and effectiveness (through clinical studies) of disinfection and sterilization procedures.

METHODS

This guideline resulted from a review of all MEDLINE articles in English listed under the MeSH headings of *disinfection* or *sterilization* (focusing on health-care equipment and supplies) from January 1980 through August 2006. References listed in these articles also were reviewed. Selected articles published before 1980 were reviewed and, if still relevant, included in the guideline. The three major peer-reviewed journals in infection control—*American Journal of Infection Control, Infection Control and Hospital Epidemiology,* and *Journal of Hospital Infection*—were searched for relevant articles published from January 1990 through August 2006. Abstracts presented at the annual meetings of the Society for Healthcare Epidemiology of America and Association for professionals in Infection Control and Epidemiology, Inc. during 1997–2006 also were reviewed; however, abstracts were not used to support the recommendations.

DEFINITION OF TERMS

Sterilization describes a process that destroys or eliminates all forms of microbial life and is carried out in health-care facilities by physical or chemical methods. Steam under pressure, dry heat, EtO gas, hydrogen peroxide gas plasma, and liquid chemicals are the principal sterilizing agents used in health-care facilities. Sterilization is intended to convey an absolute meaning; unfortunately, however, some health professionals and the technical and commercial literature refer to "disinfection" as "sterilization" and items as "partially sterile." When chemicals are used to destroy all forms of microbiologic life, they can be called chemical sterilants. These same germicides used for shorter exposure periods also can be part of the disinfection process (i.e., high-level disinfection).

Disinfection describes a process that eliminates many or all pathogenic microorganisms, except bacterial spores, on inanimate objects (Tables 1 and 2). In health-care settings, objects usually are disinfected by liquid chemicals or wet pasteurization. Each of the various factors that affect the efficacy of

disinfection can nullify or limit the efficacy of the process.

Factors that affect the efficacy of both disinfection and sterilization include prior cleaning of the object; organic and inorganic load present; type and level of microbial contamination; concentration of and exposure time to the germicide; physical nature of the object (e.g., crevices, hinges, and lumens); presence of biofilms; temperature and pH of the disinfection process; and in some cases, relative humidity of the sterilization process (e.g., ethylene oxide).

Unlike sterilization, disinfection is not sporicidal. A few disinfectants will kill spores with prolonged exposure times (3–12 hours); these are called *chemical sterilants*. At similar concentrations but with shorter exposure periods (e.g., 20 minutes for 2% glutaraldehyde), these same disinfectants will kill all microorganisms except large numbers of bacterial spores; they are called *high-level disinfectants*. *Low-level disinfectants* can kill most vegetative bacteria, some fungi, and some viruses in a practical period of time (≤10 minutes). *Intermediate-level disinfectants* might be cidal for mycobacteria, vegetative bacteria, most viruses, and most fungi but do not necessarily kill bacterial spores. Germicides differ markedly, primarily in their antimicrobial spectrum and rapidity of action.

Cleaning is the removal of visible soil (e.g., organic and inorganic material) from objects and surfaces and normally is accomplished manually or mechanically using water with detergents or enzymatic products. Thorough cleaning is essential before high-level disinfection and sterilization because inorganic and organic materials that remain on the surfaces of instruments interfere with the effectiveness of these processes. *Decontamination* removes pathogenic microorganisms from objects so they are safe to handle, use, or discard.

Terms with the suffix *cide* or *cidal* for killing action also are commonly used. For example, a germicide is an agent that can kill microorganisms, particularly pathogenic organisms ("germs"). The term *germicide* includes both antiseptics and disinfectants. *Antiseptics* are germicides applied to living tissue and skin; *disinfectants* are antimicrobials applied only to inanimate objects. In general, antiseptics are used only on the skin and not for surface disinfection, and disinfectants are not used for skin antisepsis because they can injure skin and other tissues. Virucide, fungicide, bactericide, sporicide, and tuberculocide can kill the type of microorganism identified by the prefix. For example, a bactericide is an agent that kills bacteria. [13-18]

A RATIONAL APPROACH TO DISINFECTION AND STERILIZATION

More than 30 years ago, Earle H. Spaulding devised a rational approach to disinfection and sterilization of patient-care items and equipment.[14] This classification scheme is so clear and logical that it has been retained, refined, and successfully used by infection control professionals and others when planning methods for disinfection or sterilization.[1, 13, 15, 17, 19, 20] Spaulding believed the nature of disinfection could be understood readily if instruments and items for patient care were categorized as critical, semicritical, and noncritical according to the degree of risk for infection involved in use of the items. The CDC *Guideline for Handwashing and Hospital Environmental Control*[21], *Guidelines for the Prevention of Transmission of Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV) to Health-Care and Public-Safety Workers*[22], and *Guideline for Environmental Infection Control in Health-Care Facilities*[23] employ this terminology.

Critical Items

Critical items confer a high risk for infection if they are contaminated with any microorganism. Thus, objects that enter sterile tissue or the vascular system must be sterile because any microbial contamination could transmit disease. This category includes surgical instruments, cardiac and urinary catheters, implants, and ultrasound probes used in sterile body cavities. Most of the items in this category should be purchased as sterile or be sterilized with steam if possible. Heat-sensitive objects can be treated with EtO, hydrogen peroxide gas plasma; or if other methods are unsuitable, by liquid chemical sterilants. Germicides categorized as chemical sterilants include ≥2.4% glutaraldehyde-based formulations, 0.95% glutaraldehyde with 1.64% phenol/phenate, 7.5% stabilized hydrogen peroxide, 7.35% hydrogen peroxide with 0.23% peracetic acid, 0.2% peracetic acid, and 0.08% peracetic acid with 1.0% hydrogen peroxide. Liquid chemical sterilants reliably produce sterility only if cleaning precedes treatment and if proper guidelines are followed regarding concentration, contact time, temperature, and pH.

Semicritical Items

Semicritical items contact mucous membranes or nonintact skin. This category includes respiratory therapy and anesthesia equipment, some endoscopes, laryngoscope blades[24], esophageal manometry probes, cystoscopes[25], anorectal manometry catheters, and diaphragm fitting rings. These medical devices should be free from all microorganisms; however, small numbers of bacterial spores are permissible. Intact mucous membranes, such as those of the lungs and the gastrointestinal tract, generally are resistant to infection by common bacterial spores but susceptible to other organisms, such as bacteria, mycobacteria, and viruses. Semicritical items minimally require high-level disinfection using chemical disinfectants. Glutaraldehyde, hydrogen peroxide, *ortho*-phthalaldehyde, and peracetic acid with hydrogen peroxide are cleared by the Food and Drug Administration (FDA) and are dependable high-level disinfectants provided the factors influencing germicidal procedures are met (Table 1). When a disinfectant is selected for use with certain patient-care items, the chemical compatibility after extended use with the items to be disinfected also must be considered.

High-level disinfection traditionally is defined as complete elimination of all microorganisms in or on an instrument, except for small numbers of bacterial spores. The FDA definition of high-level disinfection is a sterilant used for a shorter contact time to achieve a 6-$\log_{10}$ kill of an appropriate *Mycobacterium* species. Cleaning followed by high-level disinfection should eliminate enough pathogens to prevent transmission of infection.[26, 27]

Laparoscopes and arthroscopes entering sterile tissue ideally should be sterilized between patients. However, in the United States, this equipment sometimes undergoes only high-level disinfection between patients.[28-30] As with flexible endoscopes, these devices can be difficult to clean and high-level disinfect or sterilize because of intricate device design (e.g., long narrow lumens, hinges). Meticulous

cleaning must precede any high-level disinfection or sterilization process. Although sterilization is preferred, no reports have been published of outbreaks resulting from high-level disinfection of these scopes when they are properly cleaned and high-level disinfected. Newer models of these instruments can withstand steam sterilization that for critical items would be preferable to high-level disinfection.

Rinsing endoscopes and flushing channels with sterile water, filtered water, or tap water will prevent adverse effects associated with disinfectant retained in the endoscope (e.g., disinfectant-induced colitis). Items can be rinsed and flushed using sterile water after high-level disinfection to prevent contamination with organisms in tap water, such as nontuberculous mycobacteria, [10, 31, 32] *Legionella*, [33-35] or gram-negative bacilli such as *Pseudomonas*. [1, 17, 36-38] Alternatively, a tapwater or filtered water (0.2μ filter) rinse should be followed by an alcohol rinse and forced air drying. [28, 38-40] Forced-air drying markedly reduces bacterial contamination of stored endoscopes, most likely by removing the wet environment favorable for bacterial growth. [39] After rinsing, items should be dried and stored (e.g., packaged) in a manner that protects them from recontamination.

Some items that may come in contact with nonintact skin for a brief period of time (i.e., hydrotherapy tanks, bed side rails) are usually considered noncritical surfaces and are disinfected with intermediate-level disinfectants (i.e., phenolic, iodophor, alcohol, chlorine) [23]. Since hydrotherapy tanks have been associated with spread of infection, some facilities have chosen to disinfect them with recommended levels of chlorine [23, 41].

In the past, high-level disinfection was recommended for mouthpieces and spirometry tubing (e.g., glutaraldehyde) but cleaning the interior surfaces of the spirometers was considered unnecessary. [42] This was based on a study that showed that mouthpieces and spirometry tubing become contaminated with microorganisms but there was no bacterial contamination of the surfaces inside the spirometers. Filters have been used to prevent contamination of this equipment distal to the filter; such filters and the proximal mouthpiece are changed between patients.

Noncritical Items

Noncritical items are those that come in contact with intact skin but not mucous membranes. Intact skin acts as an effective barrier to most microorganisms; therefore, the sterility of items coming in contact with intact skin is "not critical." In this guideline, noncritical items are divided into noncritical patient care items and noncritical environmental surfaces [43, 44]. Examples of noncritical patient-care items are bedpans, blood pressure cuffs, crutches and computers [45]. In contrast to critical and some semicritical items, most noncritical reusable items may be decontaminated where they are used and do not need to be transported to a central processing area. Virtually no risk has been documented for transmission of infectious agents to patients through noncritical items [37] when they are used as noncritical items and do not contact non-intact skin and/or mucous membranes. Table 1 lists several low-level disinfectants that may be used for noncritical items. Most Environmental Protection Agency (EPA)-registered disinfectants have a 10-minute label claim. However, multiple investigators have demonstrated the effectiveness of these disinfectants against vegetative bacteria (e.g., *Listeria*, *Escherichia coli*, *Salmonella*, vancomycin-resistant Enterococci, methicillin-resistant *Staphylococcus aureus*), yeasts (e.g., *Candida*), mycobacteria (e.g., *Mycobacterium tuberculosis*), and viruses (e.g. poliovirus) at exposure times of 30–60 seconds[46-64] Federal law requires all applicable label instructions on EPA-registered products to be followed (e.g., use-dilution, shelf life, storage, material compatibility, safe use, and disposal). If the user selects exposure conditions (e.g., exposure time) that differ from those on the EPA-registered products label, the user assumes liability for any injuries resulting from off-label use and is potentially subject to enforcement action under Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) [65].

Noncritcal environmental surfaces include bed rails, some food utensils, bedside tables, patient furniture and floors. Noncritical environmental surfaces frequently touched by hand (e.g., bedside tables,

bed rails) potentially could contribute to secondary transmission by contaminating hands of health-care workers or by contacting medical equipment that subsequently contacts patients [13, 46-48, 51, 66, 67]. Mops and reusable cleaning cloths are regularly used to achieve low-level disinfection on environmental surfaces. However, they often are not adequately cleaned and disinfected, and if the water-disinfectant mixture is not changed regularly (e.g., after every three to four rooms, at no longer than 60-minute intervals), the mopping procedure actually can spread heavy microbial contamination throughout the health-care facility [68]. In one study, standard laundering provided acceptable decontamination of heavily contaminated mopheads but chemical disinfection with a phenolic was less effective. [68] Frequent laundering of mops (e.g., daily), therefore, is recommended. Single-use disposable towels impregnated with a disinfectant also can be used for low-level disinfection when spot-cleaning of noncritical surfaces is needed[45].

Changes in Disinfection and Sterilization Since 1981

The Table in the CDC *Guideline for Environmental Control* prepared in 1981 as a guide to the appropriate selection and use of disinfectants has undergone several important changes (Table 1). [15] First, formaldehyde-alcohol has been deleted as a recommended chemical sterilant or high-level disinfectant because it is irritating and toxic and not commonly used. Second, several new chemical sterilants have been added, including hydrogen peroxide, peracetic acid [58, 69, 70], and peracetic acid and hydrogen peroxide in combination. Third, 3% phenolics and iodophors have been deleted as high-level disinfectants because of their unproven efficacy against bacterial spores, *M. tuberculosis,* and/or some fungi. [55, 71] Fourth, isopropyl alcohol and ethyl alcohol have been excluded as high-level disinfectants [15] because of their inability to inactivate bacterial spores and because of the inability of isopropyl alcohol to inactivate hydrophilic viruses (i.e., poliovirus, coxsackie virus). [72] Fifth, a 1:16 dilution of 2.0% glutaraldehyde-7.05% phenol-1.20% sodium phenate (which contained 0.125% glutaraldehyde, 0.440% phenol, and 0.075% sodium phenate when diluted) has been deleted as a high-level disinfectant because this product was removed from the marketplace in December 1991 because of a lack of bactericidal activity in the presence of organic matter; a lack of fungicidal, tuberculocidal and sporicidal activity; and reduced virucidal activity. [49, 55, 56, 71, 73-79] Sixth, the exposure time required to achieve high-level disinfection has been changed from 10-30 minutes to 12 minutes or more depending on the FDA-cleared label claim and the scientific literature. [27, 55, 69, 76, 80-84] A glutaraldehyde and an ortho-phthalaldehyde have an FDA-cleared label claim of 5 minutes when used at 35°C and 25°C, respectively, in an automated endoscope reprocessor with FDA-cleared capability to maintain the solution at the appropriate temperature. [85]

In addition, many new subjects have been added to the guideline. These include inactivation of emerging pathogens, bioterrorist agents, and bloodborne pathogens; toxicologic, environmental, and occupational concerns associated with disinfection and sterilization practices; disinfection of patient-care equipment used in ambulatory and home care; inactivation of antibiotic-resistant bacteria; new sterilization processes, such as hydrogen peroxide gas plasma and liquid peracetic acid; and disinfection of complex medical instruments (e.g., endoscopes).

DISINFECTION OF HEALTHCARE EQUIPMENT

Concerns about Implementing the Spaulding Scheme

One problem with implementing the aforementioned scheme is oversimplification. For example, the scheme does not consider problems with reprocessing of complicated medical equipment that often is heat-sensitive or problems of inactivating certain types of infectious agents (e.g., prions, such as Creutzfeldt-Jakob disease [CJD] agent). Thus, in some situations, choosing a method of disinfection remains difficult, even after consideration of the categories of risk to patients. This is true particularly for a few medical devices (e.g., arthroscopes, laparoscopes) in the critical category because of controversy about whether they should be sterilized or high-level disinfected. [28, 86] Heat-stable scopes (e.g., many rigid scopes) should be steam sterilized. Some of these items cannot be steam sterilized because they are heat-sensitive; additionally, sterilization using ethylene oxide (EtO) can be too time-consuming for routine use between patients (new technologies, such as hydrogen peroxide gas plasma and peracetic acid reprocessor, provide faster cycle times). However, evidence that sterilization of these items improves patient care by reducing the infection risk is lacking[29, 87-91]. Many newer models of these instruments can withstand steam sterilization, which for critical items is the preferred method.

Another problem with implementing the Spaulding scheme is processing of an instrument in the semicritical category (e.g., endoscope) that would be used in conjunction with a critical instrument that contacts sterile body tissues. For example, is an endoscope used for upper gastrointestinal tract investigation still a semicritical item when used with sterile biopsy forceps or in a patient who is bleeding heavily from esophageal varices? Provided that high-level disinfection is achieved, and all microorganisms except bacterial spores have been removed from the endoscope, the device should not represent an infection risk and should remain in the semicritical category [92-94]. Infection with spore-forming bacteria has not been reported from appropriately high-level disinfected endoscopes.

An additional problem with implementation of the Spaulding system is that the optimal contact time for high-level disinfection has not been defined or varies among professional organizations, resulting in different strategies for disinfecting different types of semicritical items (e.g., endoscopes, applanation tonometers, endocavitary transducers, cryosurgical instruments, and diaphragm fitting rings). Until simpler and effective alternatives are identified for device disinfection in clinical settings, following this guideline, other CDC guidelines [1, 22, 95, 96] and FDA-cleared instructions for the liquid chemical sterilants/high-level disinfectants would be prudent.

Reprocessing of Endoscopes

Physicians use endoscopes to diagnose and treat numerous medical disorders. Even though endoscopes represent a valuable diagnostic and therapeutic tool in modern medicine and the incidence of infection associated with their use reportedly is very low (about 1 in 1.8 million procedures) [97], more healthcare–associated outbreaks have been linked to contaminated endoscopes than to any other medical device [6-8, 12, 98]. To prevent the spread of health-care–associated infections, all heat-sensitive endoscopes (e.g., gastrointestinal endoscopes, bronchoscopes, nasopharygoscopes) must be properly cleaned and, at a minimum, subjected to high-level disinfection after each use. High-level disinfection can be expected to destroy all microorganisms, although when high numbers of bacterial spores are present, a few spores might survive.

Because of the types of body cavities they enter, flexible endoscopes acquire high levels of microbial contamination (bioburden) during each use [99]. For example, the bioburden found on flexible gastrointestinal endoscopes after use has ranged from 10^5 colony forming units (CFU)/mL to 10^{10} CFU/mL, with the highest levels found in the suction channels [99-102]. The average load on bronchoscopes before cleaning was 6.4×10^4 CFU/mL. Cleaning reduces the level of microbial contamination by 4–6 $\log_{10}$ [83, 103]. Using human immunovirus (HIV)-contaminated endoscopes, several investigators have shown that cleaning completely eliminates the microbial contamination on the scopes [104, 105]. Similarly, other investigators found that EtO sterilization or soaking in 2% glutaraldehyde for 20 minutes was effective only when the device first was properly cleaned [106].

FDA maintains a list of cleared liquid chemical sterilants and high-level disinfectants that can be used to reprocess heat-sensitive medical devices, such as flexible endoscopes (http://www.fda.gov/cdrh/ode/germlab.html). At this time, the FDA-cleared and marketed formulations include: ≥2.4% glutaraldehyde, 0.55% *ortho*-phthalaldehyde (OPA), 0.95% glutaraldehyde with 1.64% phenol/phenate, 7.35% hydrogen peroxide with 0.23% peracetic acid, 1.0% hydrogen peroxide with 0.08% peracetic acid, and 7.5% hydrogen peroxide [85]. These products have excellent antimicrobial activity; however, some oxidizing chemicals (e.g., 7.5% hydrogen peroxide, and 1.0% hydrogen peroxide with 0.08% peracetic acid [latter product is no longer marketed]) reportedly have caused cosmetic and functional damage to endoscopes [69]. Users should check with device manufacturers for information about germicide compatibility with their device. If the germicide is FDA-cleared, then it is safe when used according to label directions; however, professionals should review the scientific literature for newly available data regarding human safety or materials compatibility. EtO sterilization of flexible endoscopes is infrequent because it requires a lengthy processing and aeration time (e.g., 12 hours) and is a potential hazard to staff and patients. The two products most commonly used for reprocessing endoscopes in the United States are glutaraldehyde and an automated, liquid chemical sterilization process that uses peracetic acid [107]. The American Society for Gastrointestinal Endoscopy (ASGE) recommends glutaraldehyde solutions that do not contain surfactants because the soapy residues of surfactants are difficult to remove during rinsing [108]. *ortho*-phthalaldehyde has begun to replace glutaraldehyde in many health-care facilities because it has several potential advantages over glutaraldehyde: is not known to irritate the eyes and nasal passages, does not require activation or exposure monitoring, and has a 12-minute high-level disinfection claim in the United States [69]. Disinfectants that are not FDA-cleared and should not be used for reprocessing endoscopes include iodophors, chlorine solutions, alcohols, quaternary ammonium compounds, and phenolics. These solutions might still be in use outside the United States, but their use should be strongly discouraged because of lack of proven efficacy against all microorganisms or materials incompatibility.

FDA clearance of the contact conditions listed on germicide labeling is based on the manufacturer's test results (http://www.fda.gov/cdrh/ode/germlab.html). Manufacturers test the product under worst-case conditions for germicide formulation (i.e., minimum recommended concentration of the active ingredient), and include organic soil. Typically manufacturers use 5% serum as the organic soil and hard water as examples of organic and inorganic challenges. The soil represents the organic loading to which the device is exposed during actual use and that would remain on the device in the absence of cleaning. This method ensures that the contact conditions completely eliminate the test mycobacteria (e.g., 10^5 to 10^6 *Mycobacteria tuberculosis* in organic soil and dried on a scope) if inoculated in the most difficult areas for the disinfectant to penetrate and contact in the absence of cleaning and thus provides a margin of safety [109]. For 2.4% glutaraldehyde that requires a 45-minute immersion at 25°C to achieve high-level disinfection (i.e., 100% kill of *M. tuberculosis*). FDA itself does not conduct testing but relies solely on the disinfectant manufacturer's data. Data suggest that *M. tuberculosis* levels can be reduced by at least 8 $\log_{10}$ with cleaning (4 $\log_{10}$) [83, 101, 102, 110], followed by chemical disinfection for 20 minutes at 20°C (4 to 6 $\log_{10}$) [83, 93, 111, 112]. On the basis of these data, APIC [113], the Society of Gastroenterology Nurses and Associates (SGNA) [38, 114, 115], the ASGE [108], American College of Chest Physicians [12], and a multi-society guideline [116] recommend alternative contact conditions with 2% glutaraldehyde to achieve high-level disinfection (e.g., that equipment be immersed in 2% glutaraldehyde at 20°C for at least 20 minutes for high-level disinfection). Federal regulations are to follow the FDA-cleared label claim for high-level disinfectants. The FDA-cleared labels for high-level disinfection with >2% glutaraldehyde at 25°C range from 20-90 minutes, depending upon the product based on three tier testing which includes AOAC sporicidal tests, simulated use testing with mycobacterial and in-use testing. The studies supporting the efficacy of >2% glutaraldehyde for 20 minutes at 20°C assume adequate cleaning prior to disinfection, whereas the FDA-cleared label claim incorporates an added margin of safety to accommodate possible lapses in cleaning practices. Facilities that have chosen to apply the 20 minute duration at 20°C have done so based on the IA recommendation in the July 2003 SHEA position paper, "Multi-society Guideline for Reprocessing Flexible Gastrointestinal Endoscopes" [19, 57, 83, 94, 108, 111, 116-121].

Flexible endoscopes are particularly difficult to disinfect [122] and easy to damage because of their intricate design and delicate materials. [123] Meticulous cleaning must precede any sterilization or high-level disinfection of these instruments. Failure to perform good cleaning can result in sterilization or disinfection failure, and outbreaks of infection can occur. Several studies have demonstrated the importance of cleaning in experimental studies with the duck hepatitis B virus (HBV) [106, 124], HIV [125] and *Helicobacter pylori*. [126]

An examination of health-care–associated infections related only to endoscopes through July 1992 found 281 infections transmitted by gastrointestinal endoscopy and 96 transmitted by bronchoscopy. The clinical spectrum ranged from asymptomatic colonization to death. *Salmonella* species and *Pseudomonas aeruginosa* repeatedly were identified as causative agents of infections transmitted by gastrointestinal endoscopy, and *M. tuberculosis*, atypical mycobacteria, and *P. aeruginosa* were the most common causes of infections transmitted by bronchoscopy [12]. Major reasons for transmission were inadequate cleaning, improper selection of a disinfecting agent, and failure to follow recommended cleaning and disinfection procedures [6, 8, 37, 98], and flaws in endoscope design [127, 128] or automated endoscope reprocessors. [7, 98] Failure to follow established guidelines has continued to result in infections associated with gastrointestinal endoscopes [8] and bronchoscopes [7, 12]. Potential device-associated problems should be reported to the FDA Center for Devices and Radiologic Health. One multistate investigation found that 23.9% of the bacterial cultures from the internal channels of 71 gastrointestinal endoscopes grew ≥100,000 colonies of bacteria after completion of all disinfection and sterilization procedures (nine of 25 facilities were using a product that has been removed from the marketplace [six facilities using 1:16 glutaraldehyde phenate], is not FDA-cleared as a high-level disinfectant [an iodophor] or no disinfecting agent) and before use on the next patient[129]. The incidence of postendoscopic procedure infections from an improperly processed endoscope has not been rigorously assessed.

Automated endoscope reprocessors (AER) offer several advantages over manual reprocessing: they automate and standardize several important reprocessing steps[130-132], reduce the likelihood that an essential reprocessing step will be skipped, and reduce personnel exposure to high-level disinfectants or chemical sterilants. Failure of AERs has been linked to outbreaks of infections [133] or colonization [7, 134], and the AER water filtration system might not be able to reliably provide "sterile" or bacteria-free rinse water[135, 136]. Establishment of correct connectors between the AER and the device is critical to ensure complete flow of disinfectants and rinse water [7, 137]. In addition, some endoscopes such as the duodenoscopes (e.g., endoscopic retrograde cholangiopancreatography [ERCP]) contain features (e.g., elevator-wire channel) that require a flushing pressure that is not achieved by most AERs and must be reprocessed manually using a 2- to 5-mL syringe, until new duodenoscopes equipped with a wider elevator-channel that AERs can reliably reprocess become available [132]. Outbreaks involving removable endoscope parts [138, 139] such as suction valves and endoscopic accessories designed to be inserted through flexible endoscopes such as biopsy forceps emphasize the importance of cleaning to remove all foreign matter before high-level disinfection or sterilization. [140] Some types of valves are now available as single-use, disposable products (e.g., bronchoscope valves) or steam sterilizable products (e.g., gastrointestinal endoscope valves).

AERs need further development and redesign [7, 141], as do endoscopes [123, 142], so that they do not represent a potential source of infectious agents. Endoscopes employing disposable components (e.g., protective barrier devices or sheaths) might provide an alternative to conventional liquid chemical high-level disinfection/sterilization[143, 144]. Another new technology is a swallowable camera-in-a-capsule that travels through the digestive tract and transmits color pictures of the small intestine to a receiver worn outside the body. This capsule currently does not replace colonoscopies.

Published recommendations for cleaning and disinfecting endoscopic equipment should be strictly followed [12, 38, 108, 113-116, 145-148]. Unfortunately, audits have shown that personnel do not consistently adhere to guidelines on reprocessing [149-151] and outbreaks of infection continue to occur. [152-154] To ensure

reprocessing personnel are properly trained, each person who reprocesses endoscopic instruments should receive initial and annual competency testing [38, 155].

In general, endoscope disinfection or sterilization with a liquid chemical sterilant involves five steps after leak testing:

1. Clean: mechanically clean internal and external surfaces, including brushing internal channels and flushing each internal channel with water and a detergent or enzymatic cleaners (leak testing is recommended for endoscopes before immersion).
2. Disinfect: immerse endoscope in high-level disinfectant (or chemical sterilant) and perfuse (eliminates air pockets and ensures contact of the germicide with the internal channels) disinfectant into all accessible channels, such as the suction/biopsy channel and air/water channel and expose for a time recommended for specific products.
3. Rinse: rinse the endoscope and all channels with sterile water, filtered water (commonly used with AERs) or tap water (i.e., high-quality potable water that meets federal clean water standards at the point of use).
4. Dry: rinse the insertion tube and inner channels with alcohol, and dry with forced air after disinfection and before storage.

Store: store the endoscope in a way that prevents recontamination and promotes drying (e.g., hung vertically). Drying the endoscope (steps 3 and 4) is essential to greatly reduce the chance of recontamination of the endoscope by microorganisms that can be present in the rinse water [116, 156]. One study demonstrated that reprocessed endoscopes (i.e., air/water channel, suction/biopsy channel) generally were negative (100% after 24 hours; 90% after 7 days [1 CFU of coagulase-negative *Staphylococcus* in one channel]) for bacterial growth when stored by hanging vertically in a ventilated cabinet[157]. Other investigators found all endoscopes were bacteria-free immediately after high-level disinfection, and only four of 135 scopes were positive during the subsequent 5-day assessment (skin bacteria cultured from endoscope surfaces). All flush-through samples remained sterile [158]. Because tapwater can contain low levels of microorganisms[159], some researchers have suggested that only sterile water (which can be prohibitively expensive) [160] or AER filtered water be used. The suggestion to use only sterile water or filtered water is not consistent with published guidelines that allow tapwater with an alcohol rinse and forced air-drying [38, 108, 113] or the scientific literature. [39, 93] In addition, no evidence of disease transmission has been found when a tap water rinse is followed by an alcohol rinse and forced-air drying. AERs produce filtered water by passage through a bacterial filter (e.g., 0.2 μ). Filtered rinse water was identified as a source of bacterial contamination in a study that cultured the accessory and suction channels of endoscopes and the internal chambers of AERs during 1996–2001 and reported 8.7% of samples collected during 1996–1998 had bacterial growth, with 54% being *Pseudomonas* species. After a system of hot water flushing of the piping (60°C for 60 minutes daily) was introduced, the frequency of positive cultures fell to approximately 2% with only rare isolation of >10 CFU/mL [161]. In addition to the endoscope reprocessing steps, a protocol should be developed that ensures the user knows whether an endoscope has been appropriately cleaned and disinfected (e.g., using a room or cabinet for processed endoscopes only) or has not been reprocessed. When users leave endoscopes on movable carts, confusion can result about whether the endoscope has been processed. Although one guideline recommended endoscopes (e.g., duodenoscopes) be reprocessed immediately before use [147], other guidelines do not require this activity [38, 108, 115] and except for the Association of periOperative Registered Nurses (AORN), professional organizations do not recommended that reprocessing be repeated as long as the original processing is done correctly. As part of a quality assurance program, healthcare facility personnel can consider random bacterial surveillance cultures of processed endoscopes to ensure high-level disinfection or sterilization[7, 162-164]. Reprocessed endoscopes should be free of microbial pathogens except for small numbers of relatively avirulent microbes that represent exogenous environmental contamination (e.g., coagulase-negative *Staphylococcus*, *Bacillus* species, diphtheroids). Although recommendations exist for the final rinse water used during endoscope reprocessing to be microbiologically cultured at least monthly [165], a microbiologic standard has not been

set, and the value of routine endoscope cultures has not been shown [166]. In addition, neither the routine culture of reprocessed endoscopes nor the final rinse water has been validated by correlating viable counts on an endoscope to infection after an endoscopic procedure. If reprocessed endoscopes were cultured, sampling the endoscope would assess water quality and other important steps (e.g., disinfectant effectiveness, exposure time, cleaning) in the reprocessing procedure. A number of methods for sampling endoscopes and water have been described [23, 157, 161, 163, 167, 168]. Novel approaches (e.g., detection of adenosine triphosphate [ATP]) to evaluate the effectiveness of endoscope cleaning [169, 170] or endoscope reprocessing [171] also have been evaluated, but no method has been established as a standard for assessing the outcome of endoscope reprocessing.

The carrying case used to transport clean and reprocessed endoscopes outside the health-care environment should not be used to store an endoscope or to transport the instrument within the health-care facility. A contaminated endoscope should never be placed in the carrying case because the case can also become contaminated. When the endoscope is removed from the case, properly reprocessed, and put back in the case, the case could recontaminate the endoscope. A contaminated carrying case should be discarded (Olympus America, June 2002, written communication).

Infection-control professionals should ensure that institutional policies are consistent with national guidelines and conduct infection-control rounds periodically (e.g., at least annually) in areas where endoscopes are reprocessed to ensure policy compliance. Breaches in policy should be documented and corrective action instituted. In incidents in which endoscopes were not exposed to a high-level disinfection process, patients exposed to potentially contaminated endoscopes have been assessed for possible acquisition of HIV, HBV, and hepatitis C virus (HCV). A 14-step method for managing a failure incident associated with high-level disinfection or sterilization has been described [Rutala WA, 2006 #12512]. The possible transmission of bloodborne and other infectious agents highlights the importance of rigorous infection control[172, 173].

Laparoscopes and Arthroscopes

Although high-level disinfection appears to be the minimum standard for processing laparoscopes and arthroscopes between patients [28, 86, 174, 175], this practice continues to be debated [89, 90, 176]. However, neither side in the high-level disinfection versus sterilization debate has sufficient data on which to base its conclusions. Proponents of high-level disinfection refer to membership surveys [29] or institutional experiences [87] involving more than 117,000 and 10,000 laparoscopic procedures, respectively, that cite a low risk for infection (<0.3%) when high-level disinfection is used for gynecologic laparoscopic equipment. Only one infection in the membership survey was linked to spores. In addition, growth of common skin microorganisms (e.g., *Staphylococcus epidermidis*, diphtheroids) has been documented from the umbilical area even after skin preparation with povidone-iodine and ethyl alcohol. Similar organisms were recovered in some instances from the pelvic serosal surfaces or from the laparoscopic telescopes, suggesting that the microorganisms probably were carried from the skin into the peritoneal cavity [177, 178]. Proponents of sterilization focus on the possibility of transmitting infection by spore-forming organisms. Researchers have proposed several reasons why sterility was not necessary for all laparoscopic equipment: only a limited number of organisms (usually $\leq$10) are introduced into the peritoneal cavity during laparoscopy; minimal damage is done to inner abdominal structures with little devitalized tissue; the peritoneal cavity tolerates small numbers of spore-forming bacteria; equipment is simple to clean and disinfect; surgical sterility is relative; the natural bioburden on rigid lumened devices is low[179]; and no evidence exists that high-level disinfection instead of sterilization increases the risk for infection [87, 89, 90]. With the advent of laparoscopic cholecystectomy, concern about high-level disinfection is justifiable because the degree of tissue damage and bacterial contamination is greater than with laparoscopic procedures in gynecology. Failure to completely dissemble, clean, and high-level disinfect laparoscope parts has led to infections in patients[180]. Data from one study suggested that disassembly, cleaning, and proper reassembly of laparoscopic equipment used in gynecologic procedures before steam sterilization presents no risk for infection[181].

As with laparoscopes and other equipment that enter sterile body sites, arthroscopes ideally should be sterilized before used. Older studies demonstrated that these instruments were commonly (57%) only high-level disinfected in the United States [28, 86]. A later survey (with a response rate of only 5%) reported that high-level disinfection was used by 31% and a sterilization process in the remainder of the health-care facilities[30] High-level disinfection rather than sterilization presumably has been used because the incidence of infection is low and the few infections identified probably are unrelated to the use of high-level disinfection rather than sterilization. A retrospective study of 12,505 arthroscopic procedures found an infection rate of 0.04% (five infections) when arthroscopes were soaked in 2% glutaraldehyde for 15–20 minutes. Four infections were caused by *S. aureus*; the fifth was an anaerobic streptococcal infection [88]. Because these organisms are very susceptible to high-level disinfectants, such as 2% glutaraldehyde, the infections most likely originated from the patient's skin. Two cases of *Clostridium perfringens* arthritis have been reported when the arthroscope was disinfected with glutaraldehyde for an exposure time that is not effective against spores [182, 183].

Although only limited data are available, the evidence does not demonstrate that high-level disinfection of arthroscopes and laparoscopes poses an infection risk to the patient. For example, a prospective study that compared the reprocessing of arthroscopes and laparoscopes (per 1,000 procedures) with EtO sterilization to high-level disinfection with glutaraldehyde found no statistically significant difference in infection risk between the two methods (i.e., EtO, 7.5/1,000 procedures; glutaraldehyde, 2.5/1,000 procedures)[89]. Although the debate for high-level disinfection versus sterilization of laparoscopes and arthroscopes will go unsettled until well-designed, randomized clinical trials are published, this guideline should be followed [1, 17]. That is, laparoscopes, arthroscopes, and other scopes that enter normally sterile tissue should be sterilized before each use; if this is not feasible, they should receive at least high-level disinfection.

Tonometers, Cervical Diaphragm Fitting Rings, Cryosurgical Instruments, and Endocavitary Probes

Disinfection strategies vary widely for other semicritical items (e.g., applanation tonometers, rectal/vaginal probes, cryosurgical instruments, and diaphragm fitting rings). FDA requests that device manufacturers include at least one validated cleaning and disinfection/sterilization protocol in the labeling for their devices. As with all medications and devices, users should be familiar with the label instructions. One study revealed that no uniform technique was in use for disinfection of applanation tonometers, with disinfectant contact times varying from <15 sec to 20 minutes [28]. In view of the potential for transmission of viruses (e.g., herpes simplex virus [HSV], adenovirus 8, or HIV) [184] by tonometer tips, CDC recommended that the tonometer tips be wiped clean and disinfected for 5-10 minutes with either 3% hydrogen peroxide, 5000 ppm chlorine, 70% ethyl alcohol, or 70% isopropyl alcohol [95]. However, more recent data suggest that 3% hydrogen peroxide and 70% isopropyl alcohol are not effective against adenovirus capable of causing epidemic keratoconjunctivitis and similar viruses and should not be used for disinfecting applanation tonometers [49, 185, 186]. Structural damage to Schiotz tonometers has been observed with a 1:10 sodium hypochlorite (5,000 ppm chlorine) and 3% hydrogen peroxide[187]. After disinfection, the tonometer should be thoroughly rinsed in tapwater and air dried before use. Although these disinfectants and exposure times should kill pathogens that can infect the eyes, no studies directly support this [188, 189]. The guidelines of the American Academy of Ophthalmology for preventing infections in ophthalmology focus on only one potential pathogen: HIV. [190] Because a short and simple decontamination procedure is desirable in the clinical setting, swabbing the tonometer tip with a 70% isopropyl alcohol wipe sometimes is practiced. [189] Preliminary reports suggest that wiping the tonometer tip with an alcohol swab and then allowing the alcohol to evaporate might be effective in eliminating HSV, HIV, and adenovirus[189, 191, 192]. However, because these studies involved only a few replicates and were conducted in a controlled laboratory setting, further studies are needed before this technique can be recommended. In addition, two reports have found that disinfection of pneumotonometer tips between uses with a 70% isopropyl alcohol wipe contributed to outbreaks of epidemic keratoconjunctivitis caused

by adenovirus type 8[193, 194].

Limited studies have evaluated disinfection techniques for other items that contact mucous membranes, such as diaphragm fitting rings, cryosurgical probes, transesophageal echocardiography probes [195], flexible cystoscopes [196] or vaginal/rectal probes used in sonographic scanning. Lettau, Bond, and McDougal of CDC supported the recommendation of a diaphragm fitting ring manufacturer that involved using a soap-and-water wash followed by a 15-minute immersion in 70% alcohol[96]. This disinfection method should be adequate to inactivate HIV, HBV, and HSV even though alcohols are not classified as high-level disinfectants because their activity against picornaviruses is somewhat limited[72]. No data are available regarding inactivation of human papillomavirus (HPV) by alcohol or other disinfectants because in vitro replication of complete virions has not been achieved. Thus, even though alcohol for 15 minutes should kill pathogens of relevance in gynecology, no clinical studies directly support this practice.

Vaginal probes are used in sonographic scanning. A vaginal probe and all endocavitary probes without a probe cover are semicritical devices because they have direct contact with mucous membranes (e.g., vagina, rectum, pharynx). While use of the probe cover could be considered as changing the category, this guideline proposes use of a new condom/probe cover for the probe for each patient, and because condoms/probe covers can fail [195, 197-199], the probe also should be high-level disinfected. The relevance of this recommendation is reinforced with the findings that sterile transvaginal ultrasound probe covers have a very high rate of perforations even before use (0%, 25%, and 65% perforations from three suppliers). [199] One study found, after oocyte retrieval use, a very high rate of perforations in used endovaginal probe covers from two suppliers (75% and 81%) [199], other studies demonstrated a lower rate of perforations after use of condoms (2.0% and 0.9%) [197 200]. Condoms have been found superior to commercially available probe covers for covering the ultrasound probe (1.7% for condoms versus 8.3% leakage for probe covers)[201]. These studies underscore the need for routine probe disinfection between examinations. Although most ultrasound manufacturers recommend use of 2% glutaraldehyde for high-level disinfection of contaminated transvaginal transducers, the this agent has been questioned [202] because it might shorten the life of the transducer and might have toxic effects on the gametes and embryos [203]. An alternative procedure for disinfecting the vaginal transducer involves the mechanical removal of the gel from the transducer, cleaning the transducer in soap and water, wiping the transducer with 70% alcohol or soaking it for 2 minutes in 500 ppm chlorine, and rinsing with tap water and air drying[204]. The effectiveness of this and other methods [200] has not been validated in either rigorous laboratory experiments or in clinical use. High-level disinfection with a product (e.g., hydrogen peroxide) that is not toxic to staff, patients, probes, and retrieved cells should be used until the effectiveness of alternative procedures against microbes of importance at the cavitary site is demonstrated by well-designed experimental scientific studies. Other probes such as rectal, cryosurgical, and transesophageal probes or devices also should be high-level disinfected between patients.

Ultrasound probes used during surgical procedures also can contact sterile body sites. These probes can be covered with a sterile sheath to reduce the level of contamination on the probe and reduce the risk for infection. However, because the sheath does not completely protect the probe, the probes should be sterilized between each patient use as with other critical items. If this is not possible, at a minimum the probe should be high-level disinfected and covered with a sterile probe cover.

Some cryosurgical probes are not fully immersible. During reprocessing, the tip of the probe should be immersed in a high-level disinfectant for the appropriate time; any other portion of the probe that could have mucous membrane contact can be disinfected by immersion or by wrapping with a cloth soaked in a high-level disinfectant to allow the recommended contact time. After disinfection, the probe should be rinsed with tap water and dried before use. Health-care facilities that use nonimmersible probes should replace them as soon as possible with fully immersible probes.

As with other high-level disinfection procedures, proper cleaning of probes is necessary to ensure the success of the subsequent disinfection [205]. One study demonstrated that vegetative bacteria

inoculated on vaginal ultrasound probes decreased when the probes were cleaned with a towel [206]. No information is available about either the level of contamination of such probes by potential viral pathogens such as HBV and HPV or their removal by cleaning (such as with a towel). Because these pathogens might be present in vaginal and rectal secretions and contaminate probes during use, high-level disinfection of the probes after such use is recommended.

Dental Instruments

Scientific articles and increased publicity about the potential for transmitting infectious agents in dentistry have focused attention on dental instruments as possible agents for pathogen transmission[207, 208]. The American Dental Association recommends that surgical and other instruments that normally penetrate soft tissue or bone (e.g., extraction forceps, scalpel blades, bone chisels, periodontal scalers, and surgical burs) be classified as critical devices that should be sterilized after each use or discarded. Instruments not intended to penetrate oral soft tissues or bone (e.g., amalgam condensers, and air/water syringes) but that could contact oral tissues are classified as semicritical, but sterilization after each use is recommended if the instruments are heat-tolerant [43, 209]. If a semicritical item is heat–sensitive, it should, at a minimum, be processed with high-level disinfection [43, 210]. Handpieces can be contaminated internally with patient material and should be heat sterilized after each patient. Handpieces that cannot be heat sterilized should not be used. [211] Methods of sterilization that can be used for critical or semicritical dental instruments and materials that are heat-stable include steam under pressure (autoclave), chemical (formaldehyde) vapor, and dry heat (e.g., 320°F for 2 hours). Dental professionals most commonly use the steam sterilizer [212]. All three sterilization procedures can damage some dental instruments, including steam-sterilized hand pieces [213]. Heat-tolerant alternatives are available for most clinical dental applications and are preferred[43].

CDC has divided noncritical surfaces in dental offices into clinical contact and housekeeping surfaces[43]. Clinical contact surfaces are surfaces that might be touched frequently with gloved hands during patient care or that might become contaminated with blood or other potentially infectious material and subsequently contact instruments, hands, gloves, or devices (e.g., light handles, switches, dental X-ray equipment, chair-side computers). Barrier protective coverings (e.g., clear plastic wraps) can be used for these surfaces, particularly those that are difficult to clean (e.g., light handles, chair switches). The coverings should be changed when visibly soiled or damaged and routinely (e.g., between patients). Protected surfaces should be disinfected at the end of each day or if contamination is evident. If not barrier-protected, these surfaces should be disinfected between patients with an intermediate-disinfectant (i.e., EPA-registered hospital disinfectant with tuberculocidal claim) or low-level disinfectant (i.e., EPA-registered hospital disinfectant with an HBV and HIV label claim) [43, 214, 215].

Most housekeeping surfaces need to be cleaned only with a detergent and water or an EPA-registered hospital disinfectant, depending of the nature of the surface and the type and degree of contamination. When housekeeping surfaces are visibly contaminated by blood or body substances, however, prompt removal and surface disinfection is a sound infection control practice and required by the Occupational Safety and Health Administration (OSHA) [43, 214].

Several studies have demonstrated variability among dental practices while trying to meet these recommendations[216, 217]. For example, 68% of respondents believed they were sterilizing their instruments but did not use appropriate chemical sterilants or exposure times and 49% of respondents did not challenge autoclaves with biological indicators[216]. Other investigators using biologic indicators have found a high proportion (15%–65%) of positive spore tests after assessing the efficacy of sterilizers used in dental offices. In one study of Minnesota dental offices, operator error, rather than mechanical malfunction[218], caused 87% of sterilization failures. Common factors in the improper use of sterilizers include chamber overload, low temperature setting, inadequate exposure time, failure to preheat the sterilizer, and interruption of the cycle.

Mail-return sterilization monitoring services use spore strips to test sterilizers in dental clinics, but

delay caused by mailing to the test laboratory could potentially cause false-negatives results. Studies revealed, however, that the post-sterilization time and temperature after a 7-day delay had no influence on the test results[219]. Delays (7 days at 27°C and 37°C, 3-day mail delay) did not cause any predictable pattern of inaccurate spore tests [220].

Disinfection of HBV-, HCV-, HIV- or TB-Contaminated Devices

The CDC recommendation for high-level disinfection of HBV-, HCV-, HIV- or TB-contaminated devices is appropriate because experiments have demonstrated the effectiveness of high-level disinfectants to inactivate these and other pathogens that might contaminate semicritical devices [61, 62, 73, 81, 105, 121, 125, 221-238]. Nonetheless, some healthcare facilities have modified their disinfection procedures when endoscopes are used with a patient known or suspected to be infected with HBV, HIV, or *M. tuberculosis* [28, 239]. This is inconsistent with the concept of Standard Precautions that presumes all patients are potentially infected with bloodborne pathogens[228]. Several studies have highlighted the inability to distinguish HBV- or HIV-infected patients from noninfected patients on clinical grounds[240-242]. In addition, mycobacterial infection is unlikely to be clinically apparent in many patients. In most instances, hospitals that altered their disinfection procedure used EtO sterilization on the endoscopic instruments because they believed this practice reduced the risk for infection [28, 239]. EtO is not routinely used for endoscope sterilization because of the lengthy processing time. Endoscopes and other semicritical devices should be managed the same way regardless of whether the patient is known to be infected with HBV, HCV, HIV or *M. tuberculosis*.

An evaluation of a manual disinfection procedure to eliminate HCV from experimentally contaminated endoscopes provided some evidence that cleaning and 2% glutaraldehyde for 20 minutes should prevent transmission [236]. A study that used experimentally contaminated hysteroscopes detected HCV by polymerase chain reaction (PCR) in one (3%) of 34 samples after cleaning with a detergent, but no samples were positive after treatment with a 2% glutaraldehyde solution for 20 minutes [120]. Another study demonstrated complete elimination of HCV (as detected by PCR) from endoscopes used on chronically infected patients after cleaning and disinfection for 3–5 minutes in glutaraldehyde [118]. Similarly, PCR was used to demonstrate complete elimination of HCV after standard disinfection of experimentally contaminated endoscopes [236] and endoscopes used on HCV-antibody–positive patients had no detectable HCV RNA after high-level disinfection [243]. The inhibitory activity of a phenolic and a chlorine compound on HCV showed that the phenolic inhibited the binding and replication of HCV, but the chlorine was ineffective, probably because of its low concentration and its neutralization in the presence of organic matter [244].

Disinfection in the Hemodialysis Unit

Hemodialysis systems include hemodialysis machines, water supply, water-treatment systems, and distribution systems. During hemodialysis, patients have acquired bloodborne viruses and pathogenic bacteria [245-247]. Cleaning and disinfection are important components of infection control in a hemodialysis center. EPA and FDA regulate disinfectants used to reprocess hemodialyzers, hemodialysis machines, and water-treatment systems.

Noncritical surfaces (e.g., dialysis bed or chair, countertops, external surfaces of dialysis machines, and equipment [scissors, hemostats, clamps, blood pressure cuffs, stethoscopes]) should be disinfected with an EPA-registered disinfectant unless the item is visibly contaminated with blood; in that case a tuberculocidal agent (or a disinfectant with specific label claims for HBV and HIV) or a 1:100 dilution of a hypochlorite solution (500–600 ppm free chlorine) should be used [248, 248]. This procedure accomplishes two goals: it removes soil on a regular basis and maintains an environment that is consistent with good patient care. Hemodialyzers are disinfected with peracetic acid, formaldehyde, glutaraldehyde, heat pasteurization with citric acid, and chlorine-containing compounds [249]. Hemodialysis systems usually are disinfected by chlorine-based disinfectants (e.g., sodium hypochlorite), aqueous

formaldehyde, heat pasteurization, ozone, or peracetic acid [250, 251]. All products must be used according to the manufacturers' recommendations. Some dialysis systems use hot-water disinfection to control microbial contamination.

At its high point, 82% of U.S. chronic hemodialysis centers were reprocessing (i.e., reusing) dialyzers for the same patient using high-level disinfection [249]. However, one of the large dialysis organizations has decided to phase out reuse and, by 2002 the percentage of dialysis facilities reprocessing hemodialyzers had decreased to 63% [252]. The two commonly used disinfectants to reprocess dialyzers were peracetic acid and formaldehyde; 72% used peracetic acid and 20% used formaldehyde to disinfect hemodialyzers. Another 4% of the facilities used either glutaraldehyde or heat pasteurization in combination with citric acid [252]. Infection-control recommendations, including disinfection and sterilization and the use of dedicated machines for hepatitis B surface antigen (HBsAg)-positive patients, in the hemodialysis setting were detailed in two reviews [245, 246]. The Association for the Advancement of Medical Instrumentation(AAMI) has published recommendations for the reuse of hemodialyzers[253].

Inactivation of *Clostridium difficile*

The source of health-care–associated acquisition of *Clostridium difficile* in nonepidemic settings has not been determined. The environment and carriage on the hands of health-care personnel have been considered possible sources of infection [66, 254]. Carpeted rooms occupied by a patient with *C. difficile* were more heavily contaminated with *C. difficile* than were noncarpeted rooms [255]. Because *C. difficile* spore-production can increase when exposed to nonchlorine-based cleaning agents and the spores are more resistant than vegetative cells to commonly used surface disinfectants[256], some investigators have recommended use of dilute solutions of hypochlorite (1,600 ppm available chlorine) for routine environmental disinfection of rooms of patients with *C. difficile*-associated diarrhea or colitis [257], to reduce the incidence of *C. difficile* diarrhea [258], or in units with high *C. difficile* rates. [259] Stool samples of patients with symptomatic *C. difficile* colitis contain spores of the organism, as demonstrated by ethanol treatment of the stool to reduce the overgrowth of fecal flora when isolating *C. difficile* in the laboratory[260, 261]. *C. difficile*-associated diarrhea rates were shown to have decreased markedly in a bone-marrow transplant unit (from 8.6 to 3.3 cases per 1,000 patient-days) during a period of bleach disinfection (1:10 dilution) of environmental surfaces compared with cleaning with a quaternary ammonium compound. Because no EPA-registered products exist that are specific for inactivating *C. difficile* spores, use of diluted hypochlorite should be considered in units with high *C. difficile* rates. Acidified bleach and regular bleach (5000 ppm chlorine) can inactivate 10^6 *C. difficile* spores in $\leq$10 minutes [262]. However, studies have shown that asymptomatic patients constitute an important reservoir within the health-care facility and that person-to-person transmission is the principal means of transmission between patients. Thus, combined use of hand washing, barrier precautions, and meticulous environmental cleaning with an EPA-registered disinfectant (e.g., germicidal detergent) should effectively prevent spread of the organism [263].

Contaminated medical devices, such as colonoscopes and thermometers,can be vehicles for transmission of *C. difficile* spores [264]. For this reason, investigators have studied commonly used disinfectants and exposure times to assess whether current practices can place patients at risk. Data demonstrate that 2% glutaraldehyde [79, 265-267] and peracetic acid [267, 268] reliably kill *C. difficile* spores using exposure times of 5–20 minutes. *ortho*-Phthalaldehyde and $\geq$0.2% peracetic acid (WA Rutala, personal communication, April 2006) also can inactivate $\geq 10^4$ *C. difficile* spores in 10–12 minutes at 20°C [268]. Sodium dichloroisocyanurate at a concentration of 1000 ppm available chlorine achieved lower $\log_{10}$ reduction factors against *C. difficile* spores at 10 min, ranging from 0.7 to 1.5, than 0.26% peracetic acid with $\log_{10}$ reduction factors ranging from 2.7 to 6.0[268].

OSHA Bloodborne Pathogen Standard

In December 1991, OSHA promulgated a standard entitled "Occupational Exposure to

Bloodborne Pathogens" to eliminate or minimize occupational exposure to bloodborne pathogens [214]. One component of this requirement is that all equipment and environmental and working surfaces be cleaned and decontaminated with an appropriate disinfectant after contact with blood or other potentially infectious materials. Even though the OSHA standard does not specify the type of disinfectant or procedure, the OSHA original compliance document [269] suggested that a germicide must be tuberculocidal to kill the HBV. To follow the OSHA compliance document a tuberculocidal disinfectant (e.g., phenolic, and chlorine) would be needed to clean a blood spill. However, in February 1997, OSHA amended its policy and stated that EPA-registered disinfectants labeled as effective against HIV and HBV would be considered as appropriate disinfectants ". . . provided such surfaces have not become contaminated with agent(s) or volumes of or concentrations of agent(s) for which higher level disinfection is recommended." When bloodborne pathogens other than HBV or HIV are of concern, OSHA continues to require use of EPA-registered tuberculocidal disinfectants or hypochlorite solution (diluted 1:10 or 1:100 with water) [215, 228]. Studies demonstrate that, in the presence of large blood spills, a 1:10 final dilution of EPA-registered hypochlorite solution initially should be used to inactivate bloodborne viruses [63, 235] to minimize risk for infection to health-care personnel from percutaneous injury during cleanup.

Emerging Pathogens (*Cryptosporidium, Helicobacter pylori, Escherichia coli* O157:H7, Rotavirus, Human Papilloma Virus, Norovirus, Severe Acute Respiratory Syndrome [SARS] Coronavirus)

Emerging pathogens are of growing concern to the general public and infection-control professionals. Relevant pathogens include *Cryptosporidium parvum, Helicobacter pylori, E. coli* O157:H7, HIV, HCV, rotavirus, norovirus, severe acute respiratory syndrome (SARS) coronavirus, multidrug-resistant *M. tuberculosis*, and nontuberculous mycobacteria (e.g., *M. chelonae*). The susceptibility of each of these pathogens to chemical disinfectants and sterilants has been studied. With the exceptions discussed below, all of these emerging pathogens are susceptible to currently available chemical disinfectants and sterilants [270].

Cryptosporidium is resistant to chlorine at concentrations used in potable water. *C. parvum* is not completely inactivated by most disinfectants used in healthcare including ethyl alcohol [271], glutaraldehyde [271, 272], 5.25% hypochlorite [271], peracetic acid [271], ortho-phthalaldehyde [271], phenol [271, 272], povidone-iodine [271, 272], and quaternary ammonium compounds[271]. The only chemical disinfectants and sterilants able to inactivate greater than 3 $\log_{10}$ of *C. parvum* were 6% and 7.5% hydrogen peroxide [271]. Sterilization methods will fully inactivate *C. parvum*, including steam [271], EtO [271, 273], and hydrogen peroxide gas plasma[271]. Although most disinfectants are ineffective against *C. parvum*, current cleaning and disinfection practices appear satisfactory to prevent healthcare-associated transmission. For example, endoscopes are unlikely to be an important vehicle for transmitting *C. parvum* because the results of bacterial studies indicate mechanical cleaning will remove approximately 10^4 organisms, and drying results in rapid loss of *C. parvum* viability (e.g., 30 minutes, 2.9 $\log_{10}$ decrease; and 60 minutes, 3.8 $\log_{10}$ decrease) [271].

Chlorine at ~1 ppm has been found capable of eliminating approximately 4 $\log_{10}$ of *E. coli* O157:H7 within 1 minute in a suspension test[64]. Electrolyzed oxidizing water at 23°C was effective in 10 minutes in producing a 5-$\log_{10}$ decrease in *E. coli* O157:H7 inoculated onto kitchen cutting boards[274]. The following disinfectants eliminated >5 $\log_{10}$ of *E. coli* O157:H7 within 30 seconds: a quaternary ammonium compound, a phenolic, a hypochlorite (1:10 dilution of 5.25% bleach), and ethanol[53]. Disinfectants including chlorine compounds can reduce *E. coli* O157:H7 experimentally inoculated onto alfalfa seeds or sprouts [275, 276] or beef carcass surfaces[277].

Data are limited on the susceptibility of *H. pylori* to disinfectants. Using a suspension test, one study assessed the effectiveness of a variety of disinfectants against nine strains of *H. pylori* [60]. Ethanol (80%) and glutaraldehyde (0.5%) killed all strains within 15 seconds; chlorhexidine gluconate (0.05%, 1.0%), benzalkonium chloride (0.025%, 0.1%), alkyldiaminoethylglycine hydrochloride (0.1%), povidone-iodine (0.1%), and sodium hypochlorite (150 ppm) killed all strains within 30 seconds. Both ethanol

(80%) and glutaraldehyde (0.5%) retained similar bactericidal activity in the presence of organic matter; the other disinfectants showed reduced bactericidal activity. In particular, the bactericidal activity of povidone-iodine (0.1%) and sodium hypochlorite (150 ppm) markedly decreased in the presence of dried yeast solution with killing times increased to 5 - 10 minutes and 5 - 30 minutes, respectively.

Immersing biopsy forceps in formalin before obtaining a specimen does not affect the ability to culture *H. pylori* from the biopsy specimen [278]. The following methods are ineffective for eliminating *H. pylori* from endoscopes: cleaning with soap and water [119, 279], immersion in 70% ethanol for 3 minutes[280], instillation of 70% ethanol[126], instillation of 30 ml of 83% methanol[279], and instillation of 0.2% Hyamine solution[281]. The differing results with regard to the efficacy of ethyl alcohol against *Helicobacter* are unexplained. Cleaning followed by use of 2% alkaline glutaraldehyde (or automated peracetic acid) has been demonstrated by culture to be effective in eliminating *H. pylori* [119, 279, 282]. Epidemiologic investigations of patients who had undergone endoscopy with endoscopes mechanically washed and disinfected with 2.0%–2.3% glutaraldehyde have revealed no evidence of person-to-person transmission of *H. pylori* [126, 283]. Disinfection of experimentally contaminated endoscopes using 2% glutaraldehyde (10-minute, 20-minute, 45-minute exposure times) or the peracetic acid system (with and without active peracetic acid) has been demonstrated to be effective in eliminating *H. pylori* [119]. *H. pylori* DNA has been detected by PCR in fluid flushed from endoscope channels after cleaning and disinfection with 2% glutaraldehyde [284]. The clinical significance of this finding is unclear. *In vitro* experiments have demonstrated a >3.5-$\log_{10}$ reduction in *H. pylori* after exposure to 0.5 mg/L of free chlorine for 80 seconds[285].

An outbreak of healthcare-associated rotavirus gastroenteritis on a pediatric unit has been reported [286]. Person to person through the hands of health-care workers was proposed as the mechanism of transmission. Prolonged survival of rotavirus on environmental surfaces (90 minutes to >10 days at room temperature) and hands (>4 hours) has been demonstrated. Rotavirus suspended in feces can survive longer [287, 288]. Vectors have included hands, fomites, air, water, and food [288, 289]. Products with demonstrated efficacy (>3 $\log_{10}$ reduction in virus) against rotavirus within 1 minute include: 95% ethanol, 70% isopropanol, some phenolics, 2% glutaraldehyde, 0.35% peracetic acid, and some quaternary ammonium compounds [59, 290-293]. In a human challenge study, a disinfectant spray (0.1% ortho-phenylphenol and 79% ethanol), sodium hypochlorite (800 ppm free chlorine), and a phenol-based product (14.7% phenol diluted 1:256 in tapwater) when sprayed onto contaminated stainless steel disks, were effective in interrupting transfer of a human rotavirus from stainless steel disk to fingerpads of volunteers after an exposure time of 3- 10 minutes. A quaternary ammonium product (7.05% quaternary ammonium compound diluted 1:128 in tapwater) and tapwater allowed transfer of virus [52].

No data exist on the inactivation of HPV by alcohol or other disinfectants because in vitro replication of complete virions has not been achieved. Similarly, little is known about inactivation of noroviruses (members of the family *Caliciviridae* and important causes of gastroenteritis in humans) because they cannot be grown in tissue culture. Improper disinfection of environmental surfaces contaminated by feces or vomitus of infected patients is believed to play a role in the spread of noroviruses in some settings [294-296]. Prolonged survival of a norovirus surrogate (i.e., feline calicivirus virus [FCV], a closely related cultivable virus) has been demonstrated (e.g., at room temperature, FCV in a dried state survived for 21–18 days) [297]. Inactivation studies with FCV have shown the effectiveness of chlorine, glutaraldehyde, and iodine-based products whereas the quaternary ammonium compound, detergent, and ethanol failed to inactivate the virus completely. [297] An evaluation of the effectiveness of several disinfectants against the feline calicivirus found that bleach diluted to 1000 ppm of available chlorine reduced infectivity of FCV by 4.5 logs in 1 minute. Other effective ($\log_{10}$ reduction factor of >4 in virus) disinfectants included accelerated hydrogen peroxide, 5,000 ppm (3 min); chlorine dioxide, 1,000 ppm chlorine (1 min); a mixture of four quaternary ammonium compounds, 2,470 ppm (10 min); 79% ethanol with 0.1% quaternary ammonium compound (3 min); and 75% ethanol (10 min) [298]. A quaternary ammonium compound exhibited activity against feline calicivirus supensions dried on hard surface carriers in 10 minutes [299]. Seventy percent ethanol and 70% 1-propanol reduced FCV by a 3–4-$\log_{10}$

reduction in 30 seconds [300].

CDC announced that a previously unrecognized human virus from the coronavirus family is the leading hypothesis for the cause of a described syndrome of SARS [301]. Two coronaviruses that are known to infect humans cause one third of common colds and can cause gastroenteritis. The virucidal efficacy of chemical germicides against coronavirus has been investigated. A study of disinfectants against coronavirus 229E found several that were effective after a 1-minute contact time; these included sodium hypochlorite (at a free chlorine concentration of 1,000 ppm and 5,000 ppm), 70% ethyl alcohol, and povidone-iodine (1% iodine) [186]. In another study, 70% ethanol, 50% isopropanol, 0.05% benzalkonium chloride, 50 ppm iodine in iodophor, 0.23% sodium chlorite, 1% cresol soap and 0.7% formaldehyde inactivated >3 logs of two animal coronaviruses (mouse hepatitis virus, canine coronavirus) after a 10-minute exposure time [302]. The activity of povidone-iodine has been demonstrated against human coronaviruses 229E and OC43 [303]. A study also showed complete inactivation of the SARS coronavirus by 70% ethanol and povidone-iodine with an exposure times of 1 minute and 2.5% glutaraldehyde with an exposure time of 5 minute [304]. Because the SARS coronavirus is stable in feces and urine at room temperature for at least 1–2 days (WHO, 2003; http://www.who.int/csr/sars/survival_2003_05_04/en/index.html), surfaces might be a possible source of contamination and lead to infection with the SARS coronavirus and should be disinfected. Until more precise information is available, environments in which SARS patients are housed should be considered heavily contaminated, and rooms and equipment should be thoroughly disinfected daily and after the patient is discharged. EPA-registered disinfectants or 1:100 dilution of household bleach and water should be used for surface disinfection and disinfection on noncritical patient-care equipment. High-level disinfection and sterilization of semicritical and critical medical devices, respectively, does not need to be altered for patients with known or suspected SARS.

Free-living amoeba can be pathogenic and can harbor agents of pneumonia such as *Legionella pneumophila*. Limited studies have shown that 2% glutaraldehyde and peracetic acid do not completely inactivate *Acanthamoeba polyphaga* in a 20-minute exposure time for high-level disinfection. If amoeba are found to contaminate instruments and facilitate infection, longer immersion times or other disinfectants may need to be considered [305].

Inactivation of Bioterrorist Agents

Publications have highlighted concerns about the potential for biological terrorism[306, 307]. CDC has categorized several agents as "high priority" because they can be easily disseminated or transmitted from person to person, cause high mortality, and are likely to cause public panic and social disruption [308]. These agents include *Bacillus anthracis* (the cause of anthrax), *Yersinia pestis* (plague), variola major (smallpox), *Clostridium botulinum* toxin (botulism), *Francisella tularensis* (tularemia), filoviruses (Ebola hemorrhagic fever, Marburg hemorrhagic fever); and arenaviruses (Lassa [Lassa fever], Junin [Argentine hemorrhagic fever]), and related viruses[308].

A few comments can be made regarding the role of sterilization and disinfection of potential agents of bioterrorism[309]. First, the susceptibility of these agents to germicides *in vitro* is similar to that of other related pathogens. For example, variola is similar to vaccinia [72, 310, 311] and *B. anthracis* is similar to *B. atrophaeus* (formerly *B. subtilis*)[312, 313]. *B. subtilis* spores, for instance, proved as resistant as, if not more resistant than, *B. anthracis* spores (>6 $\log_{10}$ reduction of *B. anthracis* spores in 5 minutes with acidified bleach [5,250 ppm chlorine])[313]. Thus, one can extrapolate from the larger database available on the susceptibility of genetically similar organisms[314]. Second, many of the potential bioterrorist agents are stable enough in the environment that contaminated environmental surfaces or fomites could lead to transmission of agents such as *B. anthracis*, *F. tularensis*, variola major, *C. botulinum* toxin, and *C. burnetti* [315]. Third, data suggest that current disinfection and sterilization practices are appropriate for managing patient-care equipment and environmental surfaces when potentially contaminated patients are evaluated and/or admitted in a health-care facility after exposure to a bioterrorist agent. For example,

sodium hypochlorite can be used for surface disinfection (see http://www.epa.gov/pesticides/factsheets/chemicals/bleachfactsheet.htm). In instances where the health-care facility is the site of a bioterrorist attack, environmental decontamination might require special decontamination procedures (e.g., chlorine dioxide gas for *B. anthracis* spores). Because no antimicrobial products are registered for decontamination of biologic agents after a bioterrorist attack, EPA has granted a crises exemption for each product (see http://www.epa.gov/pesticides/factsheets/chemicals/bleachfactsheet.htm). Of only theoretical concern is the possibility that a bioterrorist agent could be engineered to be less susceptible to disinfection and sterilization processes [309].

Toxicological, Environmental and Occupational Concerns

Health hazards associated with the use of germicides in healthcare vary from mucous membrane irritation to death, with the latter involving accidental injection by mentally disturbed patients[316]. Although their degrees of toxicity vary [317-320], all disinfectants should be used with the proper safety precautions [321] and only for the intended purpose.

Key factors associated with assessing the health risk of a chemical exposure include the duration, intensity (i.e., how much chemical is involved), and route (e.g., skin, mucous membranes, and inhalation) of exposure. Toxicity can be acute or chronic. Acute toxicity usually results from an accidental spill of a chemical substance. Exposure is sudden and often produces an emergency situation. Chronic toxicity results from repeated exposure to low levels of the chemical over a prolonged period. Employers are responsible for informing workers about the chemical hazards in the workplace and implementing control measures. The OSHA Hazard Communication Standard (29 CFR 1910.1200, 1915.99, 1917.28, 1918.90, 1926.59, and 1928.21) requires manufacturers and importers of hazardous chemicals to develop Material Safety Data Sheets (MSDS) for each chemical or mixture of chemicals. Employers must have these data sheets readily available to employees who work with the products to which they could be exposed.

Exposure limits have been published for many chemicals used in health care to help provide a safe environment and, as relevant, are discussed in each section of this guideline. Only the exposure limits published by OSHA carry the legal force of regulations. OSHA publishes a limit as a time-weighted average (TWA), that is, the average concentration for a normal 8-hour work day and a 40-hour work week to which nearly all workers can be repeatedly exposed to a chemical without adverse health effects. For example, the permissible exposure limit (PEL) for EtO is 1.0 ppm, 8 hour TWA. The CDC National Institute for Occupational Safety and Health (NIOSH) develops recommended exposure limits (RELs). RELs are occupational exposure limits recommended by NIOSH as being protective of worker health and safety over a working lifetime. This limit is frequently expressed as a 40-hour TWA exposure for up to 10 hours per day during a 40-hour work week. These exposure limits are designed for inhalation exposures. Irritant and allergic effects can occur below the exposure limits, and skin contact can result in dermal effects or systemic absorption without inhalation. The American Conference on Governmental Industrial Hygienists (ACGIN) also provides guidelines on exposure limits [322]. Information about workplace exposures and methods to reduce them (e.g., work practices, engineering controls, PPE) is available on the OSHA (http://www.osha.gov) and NIOSH (http://www.cdc.gov/niosh) websites.

Some states have excluded or limited concentrations of certain chemical germicides (e.g., glutaraldehyde, formaldehyde, and some phenols) from disposal through the sewer system. These rules are intended to minimize environmental harm. If health-care facilities exceed the maximum allowable concentration of a chemical (e.g., $\geq$5.0 mg/L), they have three options. First, they can switch to alternative products; for example, they can change from glutaraldehyde to another disinfectant for high-level disinfection or from phenolics to quaternary ammonium compounds for low-level disinfection. Second, the health-care facility can collect the disinfectant and dispose of it as a hazardous chemical. Third, the

facility can use a commercially available small-scale treatment method (e.g., neutralize glutaraldehyde with glycine).

Safe disposal of regulated chemicals is important throughout the medical community. For disposal of large volumes of spent solutions, users might decide to neutralize the microbicidal activity before disposal (e.g., glutaraldehyde). Solutions can be neutralized by reaction with chemicals such as sodium bisulfite [323, 324] or glycine [325].

European authors have suggested that instruments and ventilation therapy equipment should be disinfected by heat rather than by chemicals. The concerns for chemical disinfection include toxic side effects for the patient caused by chemical residues on the instrument or object, occupational exposure to toxic chemicals, and recontamination by rinsing the disinfectant with microbially contaminated tap water [326].

Disinfection in Ambulatory Care, Home Care, and the Home

With the advent of managed healthcare, increasing numbers of patients are now being cared for in ambulatory-care and home settings. Many patients in these settings might have communicable diseases, immunocompromising conditions, or invasive devices. Therefore, adequate disinfection in these settings is necessary to provide a safe patient environment. Because the ambulatory-care setting (i.e., outpatient facility) provides the same risk for infection as the hospital, the Spaulding classification scheme described in this guideline should be followed (Table 1) [17].

The home environment should be much safer than hospitals or ambulatory care. Epidemics should not be a problem, and cross-infection should be rare. The healthcare provider is responsible for providing the responsible family member information about infection-control procedures to follow in the home, including hand hygiene, proper cleaning and disinfection of equipment, and safe storage of cleaned and disinfected devices. Among the products recommended for home disinfection of reusable objects are bleach, alcohol, and hydrogen peroxide. APIC recommends that reusable objects (e.g., tracheostomy tubes) that touch mucous membranes be disinfected by immersion in 70% isopropyl alcohol for 5 minutes or in 3% hydrogen peroxide for 30 minutes. Additionally, a 1:50 dilution of 5.25%–6.15% sodium hypochlorite (household bleach) for 5 minutes should be effective [327-329]. Noncritical items (e.g., blood pressure cuffs, crutches) can be cleaned with a detergent. Blood spills should be handled according to OSHA regulations as previously described (see section on OSHA Bloodborne Pathogen Standard). In general, sterilization of critical items is not practical in homes but theoretically could be accomplished by chemical sterilants or boiling. Single-use disposable items can be used or reusable items sterilized in a hospital [330, 331].

Some environmental groups advocate "environmentally safe" products as alternatives to commercial germicides in the home-care setting. These alternatives (e.g., ammonia, baking soda, vinegar, Borax, liquid detergent) are not registered with EPA and should not be used for disinfecting because they are ineffective against *S. aureus*. Borax, baking soda, and detergents also are ineffective against *Salmonella* Typhi and *E.coli*; however, undiluted vinegar and ammonia are effective against *S.* Typhi and *E.coli* [53, 332, 333]. Common commercial disinfectants designed for home use also are effective against selected antibiotic-resistant bacteria [53].

Public concerns have been raised that the use of antimicrobials in the home can promote development of antibiotic-resistant bacteria [334, 335]. This issue is unresolved and needs to be considered further through scientific and clinical investigations. The public health benefits of using disinfectants in the home are unknown. However, some facts are known: many sites in the home kitchen and bathroom are microbially contaminated [336], use of hypochlorites markedly reduces bacteria [337], and good standards of hygiene (e.g., food hygiene, hand hygiene) can help reduce infections in the home [338, 339]. In addition, laboratory studies indicate that many commercially prepared household disinfectants are effective against common pathogens [53] and can interrupt surface-to-human transmission of pathogens [48]. The "targeted

hygiene concept"—which means identifying situations and areas (e.g., food-preparation surfaces and bathroom) where risk exists for transmission of pathogens—may be a reasonable way to identify when disinfection might be appropriate [340].

Susceptibility of Antibiotic-Resistant Bacteria to Disinfectants

As with antibiotics, reduced susceptibility (or acquired "resistance") of bacteria to disinfectants can arise by either chromosomal gene mutation or acquisition of genetic material in the form of plasmids or transposons [338, 341-343, 344, 345, 346]. When changes occur in bacterial susceptibility that renders an antibiotic ineffective against an infection previously treatable by that antibiotic, the bacteria are referred to as "resistant." In contrast, reduced susceptibility to disinfectants does not correlate with failure of the disinfectant because concentrations used in disinfection still greatly exceed the cidal level. Thus, the word "resistance" when applied to these changes is incorrect, and the preferred term is "reduced susceptibility" or "increased tolerance"[344, 347]. No data are available that show that antibiotic-resistant bacteria are less sensitive to the liquid chemical germicides than antibiotic-sensitive bacteria at currently used germicide contact conditions and concentrations.

MRSA and vancomycin-resistant *Enterococcus* (VRE) are important health-care–associated agents. Some antiseptics and disinfectants have been known for years to be, because of MICs, somewhat less inhibitory to *S. aureus* strains that contain a plasmid-carrying gene encoding resistance to the antibiotic gentamicin [344]. For example, gentamicin resistance has been shown to also encode reduced susceptibility to propamidine, quaternary ammonium compounds, and ethidium bromide [348], and MRSA strains have been found to be less susceptible than methicillin-sensitive *S. aureus* (MSSA) strains to chlorhexidine, propamidine, and the quaternary ammonium compound cetrimide [349]. In other studies, MRSA and MSSA strains have been equally sensitive to phenols and chlorhexidine, but MRSA strains were slightly more tolerant to quaternary ammonium compounds [350]. Two gene families (*qac*CD [now referred to as *smr*] and *qac*AB) are involved in providing protection against agents that are components of disinfectant formulations such as quaternary ammonium compounds. Staphylococci have been proposed to evade destruction because the protein specified by the *qac*A determinant is a cytoplasmic-membrane–associated protein involved in an efflux system that actively reduces intracellular accumulation of toxicants, such as quaternary ammonium compounds, to intracellular targets [351].

Other studies demonstrated that plasmid-mediated formaldehyde tolerance is transferable from *Serratia marcescens* to *E. coli* [352] and plasmid-mediated quaternary ammonium tolerance is transferable from *S. aureus* to *E. coli*.[353]. Tolerance to mercury and silver also is plasmid borne [341, 343-346].

Because the concentrations of disinfectants used in practice are much higher than the MICs observed, even for the more tolerant strains, the clinical relevance of these observations is questionable. Several studies have found antibiotic-resistant hospital strains of common healthcare-associated pathogens (i.e., *Enterococcus, P. aeruginosa, Klebsiella pneumoniae, E. coli, S. aureus,* and *S. epidermidis*) to be equally susceptible to disinfectants as antibiotic-sensitive strains [53, 354-356]. The susceptibility of glycopeptide-intermediate *S. aureus* was similar to vancomycin-susceptible, MRSA [357]. On the basis of these data, routine disinfection and housekeeping protocols do not need to be altered because of antibiotic resistance provided the disinfection method is effective [358, 359]. A study that evaluated the efficacy of selected cleaning methods (e.g., QUAT-sprayed cloth, and QUAT-immersed cloth) for eliminating VRE found that currently used disinfection processes most likely are highly effective in eliminating VRE. However, surface disinfection must involve contact with all contaminated surfaces [358]. A new method using an invisible flurorescent marker to objectively evaluate the thoroughness of cleaning activities in patient rooms might lead to improvement in cleaning of all objects and surfaces but needs further evaluation [360].

Lastly, does the use of antiseptics or disinfectants facilitate the development of disinfectant-tolerant organisms? Evidence and reviews indicate enhanced tolerance to disinfectants can be

developed in response to disinfectant exposure [334, 335, 346, 347, 361]. However, the level of tolerance is not important in clinical terms because it is low and unlikely to compromise the effectiveness of disinfectants of which much higher concentrations are used [347, 362].

The issue of whether low-level tolerance to germicides selects for antibiotic-resistant strains is unsettled but might depend on the mechanism by which tolerance is attained. For example, changes in the permeability barrier or efflux mechanisms might affect susceptibility to both antibiotics and germicides, but specific changes to a target site might not. Some researchers have suggested that use of disinfectants or antiseptics (e.g., triclosan) could facilitate development of antibiotic-resistant microorganisms [334, 335, 363]. Although evidence in laboratory studies indicates low-level resistance to triclosan, the concentrations of triclosan in these studies were low (generally <1 µg/mL) and dissimilar from the higher levels used in antimicrobial products (2,000–20,000 µg/mL) [364, 365]. Thus, researchers can create laboratory-derived mutants that demonstrate reduced susceptibility to antiseptics or disinfectants. In some experiments, such bacteria have demonstrated reduced susceptibility to certain antibiotics [335]. There is no evidence that using antiseptics or disinfectants selects for antibiotic-resistant organisms in nature or that such mutants survive in nature[366].). In addition, the action of antibiotics and the action of disinfectants differ fundamentally. Antibiotics are selectively toxic and generally have a single target site in bacteria, thereby inhibiting a specific biosynthetic process. Germicides generally are considered nonspecific antimicrobials because of a multiplicity of toxic-effect mechanisms or target sites and are broader spectrum in the types of microorganisms against which they are effective [344, 347].

The rotational use of disinfectants in some environments (e.g., pharmacy production units) has been recommended and practiced in an attempt to prevent development of resistant microbes [367, 368]. There have been only rare case reports that appropriately used disinfectants have resulted in a clinical problem arising from the selection or development of nonsusceptible microorganisms [369].

Surface Disinfection

Is Surface Disinfection Necessary?

The effective use of disinfectants is part of a multibarrier strategy to prevent health-care–associated infections. Surfaces are considered noncritical items because they contact intact skin. Use of noncritical items or contact with noncritical surfaces carries little risk of causing an infection in patients or staff. Thus, the routine use of germicidal chemicals to disinfect hospital floors and other noncritical items is controversial [370-375]. A 1991 study expanded the Spaulding scheme by dividing the noncritical environmental surfaces into housekeeping surfaces and medical equipment surfaces [376]. The classes of disinfectants used on housekeeping and medical equipment surfaces can be similar. However, the frequency of decontaminating can vary (see Recommendations). Medical equipment surfaces (e.g., blood pressure cuffs, stethoscopes, hemodialysis machines, and X-ray machines) can become contaminated with infectious agents and contribute to the spread of health-care–associated infections [248, 375]. For this reason, noncritical medical equipment surfaces should be disinfected with an EPA-registered low- or intermediate-level disinfectant. Use of a disinfectant will provide antimicrobial activity that is likely to be achieved with minimal additional cost or work.

Environmental surfaces (e.g., bedside table) also could potentially contribute to cross-transmission by contamination of health-care personnel from hand contact with contaminated surfaces, medical equipment, or patients [50, 375, 377]. A paper reviews the epidemiologic and microbiologic data (Table 3) regarding the use of disinfectants on noncritical surfaces [378].

Of the seven reasons to usie a disinfectant on noncritical surfaces, five are particularly noteworthy and support the use of a germicidal detergent. First, hospital floors become contaminated with microorganisms from settling airborne bacteria: by contact with shoes, wheels, and other objects; and occasionally by spills. The removal of microbes is a component in controling health-care–associated infections. In an investigation of the cleaning of hospital floors, the use of soap and water (80% reduction) was less effective in reducing the numbers of bacteria than was a phenolic disinfectant (94%–99.9%

reduction) [379]. However, a few hours after floor disinfection, the bacterial count was nearly back to the pretreatment level. Second, detergents become contaminated and result in seeding the patient's environment with bacteria. Investigators have shown that mop water becomes increasingly dirty during cleaning and becomes contaminated if soap and water is used rather than a disinfectant. For example, in one study, bacterial contamination in soap and water without a disinfectant increased from 10 CFU/mL to 34,000 CFU/mL after cleaning a ward, whereas contamination in a disinfectant solution did not change (20 CFU/mL) [380]. Contamination of surfaces close to the patient that are frequently touched by the patient or staff (e.g., bed rails) could result in patient exposures0 [381]. In a study, using of detergents on floors and patient room furniture, increased bacterial contamination of the patients' environmental surfaces was found after cleaning (average increase = 103.6 CFU/24cm^2) [382]. In addition, a *P. aeruginosa* outbreak was reported in a hematology-oncology unit associated with contamination of the surface cleaning equipment when nongermicidal cleaning solutions instead of disinfectants were used to decontaminate the patients' environment [383] and another study demonstrated the role of environmental cleaning in controlling an outbreak of *Acinetobacter baumannii* [384]. Studies also have shown that, in situations where the cleaning procedure failed to eliminate contamination from the surface and the cloth is used to wipe another surface, the contamination is transferred to that surface and the hands of the person holding the cloth[381, 385]. Third, the CDC Isolation Guideline recommends that noncritical equipment contaminated with blood, body fluids, secretions, or excretions be cleaned and disinfected after use. The same guideline recommends that, in addition to cleaning, disinfection of the bedside equipment and environmental surfaces (e.g., bedrails, bedside tables, carts, commodes, door-knobs, and faucet handles) is indicated for certain pathogens, e.g., enterococci, which can survive in the inanimate environment for prolonged periods [386]. Fourth, OSHA requires that surfaces contaminated with blood and other potentially infectious materials (e.g., amniotic, pleural fluid) be disinfected. Fifth, using a single product throughout the facility can simplify both training and appropriate practice.

Reasons also exist for using a detergent alone on floors because noncritical surfaces contribute minimally to endemic health-care–associated infections [387], and no differences have been found in healthcare–associated infections rates when floors are cleaned with detergent rather than disinfectant [382, 388, 389]. However, these studies have been small and of short duration and suffer from low statistical power because the outcome—healthcare–associated infections—is of low frequency. The low rate of infections makes the efficacy of an intervention statistically difficult to demonstrate. Because housekeeping surfaces are associated with the lowest risk for disease transmission, some researchers have suggested that either detergents or a disinfectant/detergent could be used [376]. No data exist that show reduced healthcare–associated infection rates with use of surface disinfection of floors, but some data demonstrate reduced microbial load associated with the use of disinfectants. Given this information; other information showing that environmental surfaces (e.g., bedside table, bed rails) close to the patient and in outpatient settings [390] can be contaminated with epidemiologically important microbes (such as VRE and MRSA)[47, 390-394]; and data showing these organisms survive on various hospital surfaces [395, 396], some researchers have suggested that such surfaces should be disinfected on a regular schedule [378]. Spot decontamination on fabrics that remain in hospitals or clinic rooms while patients move in and out (e.g., privacy curtains) also should be considered. One study demonstrated the effectiveness of spraying the fabric with 3% hydrogen peroxide [397]. Future studies should evaluate the level of contamination on noncritical environmental surfaces as a function of high and low hand contact and whether some surfaces (e.g., bed rails) near the patient with high contact frequencies require more frequent disinfection. Regardless of whether a detergent or disinfectant is used on surfaces in a health-care facility, surfaces should be cleaned routinely and when dirty or soiled to provide an aesthetically pleasing environment and to prevent potentially contaminated objects from serving as a source for health-care–associated infections [398]. The value of designing surfaces (e.g. hexyl-polyvinylpyridine) that kill bacteria on contact [399]or have sustained antimicrobial activity [400] should be further evaluated.

Several investigators have recognized heavy microbial contamination of wet mops and cleaning cloths and the potential for spread of such contamination [68, 401]. They have shown that wiping hard surfaces with contaminated cloths can contaminate hands, equipment, and other surfaces [68, 402]. Data

have been published that can be used to formulate effective policies for decontamination and maintenance of reusable cleaning cloths. For example, heat was the most reliable treatment of cleaning cloths as a detergent washing followed by drying at 80°C for 2 hours produced elimination of contamination. However, the dry heating process might be a fire hazard if the mop head contains petroleum-based products or lint builds up within the equipment or vent hose (American Health Care Association, personal communication, March 2003). Alternatively, immersing the cloth in hypochlorite (4,000 ppm) for 2 minutes produced no detectable surviving organisms in 10 of 13 cloths [403]. If reusable cleaning cloths or mops are used, they should be decontaminated regularly to prevent surface contamination during cleaning with subsequent transfer of organisms from these surfaces to patients or equipment by the hands of health-care workers. Some hospitals have begun using a new mopping technique involving microfiber materials to clean floors. Microfibers are densely constructed, polyester and polyamide (nylon) fibers, that are approximately 1/16 the thickness of a human hair. The positively charged microfibers attract dust (which has a negative charge) and are more absorbent than a conventional, cotton-loop mop. Microfiber materials also can be wet with disinfectants, such as quaternary ammonium compounds. In one study, the microfiber system tested demonstrated superior microbial removal compared with conventional string mops when used with a detergent cleaner (94% vs 68%). The use of a disinfectant did not improve the microbial elimination demonstrated by the microfiber system (95% vs 94%). However, use of disinfectant significantly improved microbial removal when a conventional string mop was used (95% vs 68%)(WA Rutala, unpublished data, August 2006). The microfiber system also prevents the possibility of transferring microbes from room to room because a new microfiber pad is used in each room.

Contact Times for Surface Disinfectants

An important issue concerning use of disinfectants for noncritical surfaces in health-care settings is that the contact time specified on the label of the product is often too long to be practically followed. The labels of most products registered by EPA for use against HBV, HIV, or *M. tuberculosis* specify a contact time of 10 minutes. Such a long contact time is not practical for disinfection of environmental surfaces in a health-care setting because most health-care facilities apply a disinfectant and allow it to dry (~1 minute). Multiple scientific papers have demonstrated significant microbial reduction with contact times of 30 to 60 seconds[46-56, 58-64]. In addition, EPA will approve a shortened contact time for any product for which the manufacturers will submit confirmatory efficacy data.

Currently, some EPA-registered disinfectants have contact times of one to three minutes. By law, users must follow all applicable label instructions for EPA-registered products. Ideally, product users should consider and use products that have the shortened contact time. However, disinfectant manufacturers also need to obtain EPA approval for shortened contact times so these products will be used correctly and effectively in the health-care environment.

Air Disinfection

Disinfectant spray-fog techniques for antimicrobial control in hospital rooms has been used. This technique of spraying of disinfectants is an unsatisfactory method of decontaminating air and surfaces and is not recommended for general infection control in routine patient-care areas[386]. Disinfectant fogging is rarely, if ever, used in U.S. healthcare facilities for air and surface disinfection in patient-care areas. Methods (e.g., filtration, ultraviolet germicidal irradiation, chlorine dioxide) to reduce air contamination in the healthcare setting are discussed in another guideline [23].

Microbial Contamination of Disinfectants

Contaminated disinfectants and antiseptics have been occasional vehicles of health-care infections and pseudoepidemics for more than 50 years. Published reports describing contaminated disinfectants and antiseptic solutions leading to health-care-associated infections have been summarized

[404]. Since this summary additional reports have been published [405-408]. An examination of reports of disinfectants contaminated with microorganisms revealed noteworthy observations. Perhaps most importantly, high-level disinfectants/liquid chemical sterilants have not been associated with outbreaks due to intrinsic or extrinsic contamination.Members of the genus *Pseudomonas* (e.g., *P. aeruginosa*) are the most frequent isolates from contaminated disinfectants—recovered from 80% of contaminated products. Their ability to remain viable or grow in use-dilutions of disinfectants is unparalleled. This survival advantage for *Pseudomonas* results presumably from their nutritional versatility, their unique outer membrane that constitutes an effective barrier to the passage of germicides, and/or efflux systems [409]. Although the concentrated solutions of the disinfectants have not been demonstrated to be contaminated at the point of manufacture, an undiluted phenolic can be contaminated by a *Pseudomonas* sp. during use [410]. In most of the reports that describe illness associated with contaminated disinfectants, the product was used to disinfect patient-care equipment, such as cystoscopes, cardiac catheters, and thermometers. Germicides used as disinfectants that were reported to have been contaminated include chlorhexidine, quaternary ammonium compounds, phenolics, and pine oil.

The following control measures should be instituted to reduce the frequency of bacterial growth in disinfectants and the threat of serious healthcare–associated infections from the use of such contaminated products [404]. First, some disinfectants should not be diluted; those that are diluted must be prepared correctly to achieve the manufacturers' recommended use-dilution. Second, infection-control professionals must learn from the literature what inappropriate activities result in extrinsic contamination (i.e., at the point of use) of germicides and train users to prevent recurrence. Common sources of extrinsic contamination of germicides in the reviewed literature are the water to make working dilutions, contaminated containers, and general contamination of the hospital areas where the germicides are prepared and/or used. Third, stock solutions of germicides must be stored as indicated on the product label. EPA verifies manufacturers' efficacy claims against microorganisms. These measures should provide assurance that products meeting the EPA registration requirements can achieve a certain level of antimicrobial activity when used as directed.

FACTORS AFFECTING THE EFFICACY OF DISINFECTION AND STERILIZATION

The activity of germicides against microorganisms depends on a number of factors, some of which are intrinsic qualities of the organism, others of which are the chemical and external physical environment. Awareness of these factors should lead to better use of disinfection and sterilization processes and will be briefly reviewed. More extensive consideration of these and other factors is available elsewhere [13, 14, 16, 411-413].

Number and Location of Microorganisms

All other conditions remaining constant, the larger the number of microbes, the more time a germicide needs to destroy all of them. Spaulding illustrated this relation when he employed identical test conditions and demonstrated that it took 30 minutes to kill 10 *B. atrophaeus* (formerly *Bacillus subtilis*) spores but 3 hours to kill 100,000 *Bacillus atrophaeus* spores. This reinforces the need for scrupulous cleaning of medical instruments before disinfection and sterilization. Reducing the number of microorganisms that must be inactivated through meticulous cleaning, increases the margin of safety when the germicide is used according to the labeling and shortens the exposure time required to kill the entire microbial load. Researchers also have shown that aggregated or clumped cells are more difficult to inactivate than monodispersed cells [414].

The location of microorganisms also must be considered when factors affecting the efficacy of germicides are assessed. Medical instruments with multiple pieces must be disassembled and equipment such as endoscopes that have crevices, joints, and channels are more difficult to disinfect than are flat-surface equipment because penetration of the disinfectant of all parts of the equipment is more difficult. Only surfaces that directly contact the germicide will be disinfected, so there must be no air pockets and the equipment must be completely immersed for the entire exposure period. Manufacturers should be encouraged to produce equipment engineered for ease of cleaning and disinfection.

Innate Resistance of Microorganisms

Microorganisms vary greatly in their resistance to chemical germicides and sterilization processes (Figure 1) [342] Intrinsic resistance mechanisms in microorganisms to disinfectants vary. For example, spores are resistant to disinfectants because the spore coat and cortex act as a barrier, mycobacteria have a waxy cell wall that prevents disinfectant entry, and gram-negative bacteria possess an outer membrane that acts as a barrier to the uptake of disinfectants [341, 343-345]. Implicit in all disinfection strategies is the consideration that the most resistant microbial subpopulation controls the sterilization or disinfection time. That is, to destroy the most resistant types of microorganisms (i.e., bacterial spores), the user needs to employ exposure times and a concentration of germicide needed to achieve complete destruction. Except for prions, bacterial spores possess the highest innate resistance to chemical germicides, followed by coccidia (e.g., *Cryptosporidium*), mycobacteria (e.g., *M. tuberculosis*), nonlipid or small viruses (e.g., poliovirus, and coxsackievirus), fungi (e.g., *Aspergillus,* and *Candida*), vegetative bacteria (e.g., *Staphylococcus,* and *Pseudomonas*) and lipid or medium-size viruses (e.g., herpes, and HIV). The germicidal resistance exhibited by the gram-positive and gram-negative bacteria is similar with some exceptions (e.g., *P. aeruginosa* which shows greater resistance to some disinfectants) [369, 415, 416]. *P. aeruginosa* also is significantly more resistant to a variety of disinfectants in its "naturally occurring" state than are cells subcultured on laboratory media [415, 417]. *Rickettsiae*, *Chlamydiae*, and mycoplasma cannot be placed in this scale of relative resistance because information about the efficacy of germicides against these agents is limited [418]. Because these microorganisms contain lipid and are similar in structure and composition to other bacteria, they can be predicted to be inactivated by the same germicides that destroy lipid viruses and vegetative bacteria. A known exception to this supposition is *Coxiella burnetti*, which has demonstrated resistance to disinfectants [419].

Concentration and Potency of Disinfectants

With other variables constant, and with one exception (iodophors), the more concentrated the

disinfectant, the greater its efficacy and the shorter the time necessary to achieve microbial kill. Generally not recognized, however, is that all disinfectants are not similarly affected by concentration adjustments. For example, quaternary ammonium compounds and phenol have a concentration exponent of 1 and 6, respectively; thus, halving the concentration of a quaternary ammonium compound requires doubling its disinfecting time, but halving the concentration of a phenol solution requires a 64-fold (i.e., 2^6) increase in its disinfecting time [365, 413, 420].

Considering the length of the disinfection time, which depends on the potency of the germicide, also is important. This was illustrated by Spaulding who demonstrated using the mucin-loop test that 70% isopropyl alcohol destroyed 10^4 *M. tuberculosis* in 5 minutes, whereas a simultaneous test with 3% phenolic required 2–3 hours to achieve the same level of microbial kill [14].

Physical and Chemical Factors

Several physical and chemical factors also influence disinfectant procedures: temperature, pH, relative humidity, and water hardness. For example, the activity of most disinfectants increases as the temperature increases, but some exceptions exist. Furthermore, too great an increase in temperature causes the disinfectant to degrade and weakens its germicidal activity and thus might produce a potential health hazard.

An increase in pH improves the antimicrobial activity of some disinfectants (e.g., glutaraldehyde, quaternary ammonium compounds) but decreases the antimicrobial activity of others (e.g., phenols, hypochlorites, and iodine). The pH influences the antimicrobial activity by altering the disinfectant molecule or the cell surface [413].

Relative humidity is the single most important factor influencing the activity of gaseous disinfectants/sterilants, such as EtO, chlorine dioxide, and formaldehyde.

Water hardness (i.e., high concentration of divalent cations) reduces the rate of kill of certain disinfectants because divalent cations (e.g., magnesium, calcium) in the hard water interact with the disinfectant to form insoluble precipitates [13, 421].

Organic and Inorganic Matter

Organic matter in the form of serum, blood, pus, or fecal or lubricant material can interfere with the antimicrobial activity of disinfectants in at least two ways. Most commonly, interference occurs by a chemical reaction between the germicide and the organic matter resulting in a complex that is less germicidal or nongermicidal, leaving less of the active germicide available for attacking microorganisms. Chlorine and iodine disinfectants, in particular, are prone to such interaction. Alternatively, organic material can protect microorganisms from attack by acting as a physical barrier [422, 423].

The effects of inorganic contaminants on the sterilization process were studied during the 1950s and 1960s [424, 425]. These and other studies show the protection by inorganic contaminants of microorganisms to all sterilization processes results from occlusion in salt crystals [426, 427]. This further emphasizes the importance of meticulous cleaning of medical devices before any sterilization or disinfection procedure because both organic and inorganic soils are easily removed by washing [428].

Duration of Exposure

Items must be exposed to the germicide for the appropriate minimum contact time. Multiple investigators have demonstrated the effectiveness of low-level disinfectants against vegetative bacteria (e.g., *Listeria*, *E. coli*, *Salmonella*, VRE, MRSA), yeasts (e.g., *Candida*), mycobacteria (e.g., *M. tuberculosis*), and viruses (e.g., poliovirus) at exposure times of 30–60 seconds [46-64]. By law, all applicable label instructions on EPA-registered products must be followed. If the user selects exposure conditions that differ from those on the EPA-registered product label, the user assumes liability for any injuries resulting from off-label use and is potentially subject to enforcement action under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)

All lumens and channels of endoscopic instruments must contact the disinfectant. Air pockets interfere with the disinfection process, and items that float on the disinfectant will not be disinfected. The disinfectant must be introduced reliably into the internal channels of the device. The exact times for disinfecting medical items are somewhat elusive because of the effect of the aforementioned factors on disinfection efficacy. Certain contact times have proved reliable (Table 1), but, in general, longer contact times are more effective than shorter contact times.

Biofilms

Microorganisms may be protected from disinfectants by production of thick masses of cells [428] and extracellular materials, or biofilms [429-435]. Biofilms are microbial communities that are tightly attached to surfaces and cannot be easly removed. Once these masses form, microbes within them can be resistant to disinfectants by multiple mechanisms, including physical characteristics of older biofilms, genotypic variation of the bacteria, microbial production of neutralizing enzymes, and physiologic gradients within the biofilm (e.g., pH). Bacteria within biofilms are up to 1,000 times more resistant to antimicrobials than are the same bacteria in suspension [436]. Although new decontamination methods [437] are being investigated for removing biofilms, chlorine and monochloramines can effectively inactivate biofilm bacteria [431, 436]. Investigators have hypothesized that the glycocalyx-like cellular masses on the interior walls of polyvinyl chloride pipe would protect embedded organisms from some disinfectants and be a reservoir for continuous contamination [429, 430, 439]. Biofilms have been found in whirlpools [440], dental unit waterlines[441], and numerous medical devices (e.g., contact lenses, pacemakers, hemodialysis systems, urinary catheters, central venous catheters, endoscopes) [434, 436, 438, 442]. Their presence can have serious implications for immunocompromised patients and patients who have indwelling medical devices. Some enzymes [436, 443, 444] and detergents [436] can degrade biofilms or reduce numbers of viable bacteria within a biofilm, but no products are EPA-registered or FDA-cleared for this purpose.

CLEANING

Cleaning is the removal of foreign material (e.g., soil, and organic material) from objects and is normally accomplished using water with detergents or enzymatic products. Thorough cleaning is required before high-level disinfection and sterilization because inorganic and organic materials that remain on the surfaces of instruments interfere with the effectiveness of these processes. Also, if soiled materials dry or bake onto the instruments, the removal process becomes more difficult and the disinfection or sterilization process less effective or ineffective. Surgical instruments should be presoaked or rinsed to prevent drying of blood and to soften or remove blood from the instruments.

Cleaning is done manually in use areas without mechanical units (e.g., ultrasonic cleaners or washer-disinfectors) or for fragile or difficult-to-clean instruments. With manual cleaning, the two essential components are friction and fluidics. Friction (e.g., rubbing/scrubbing the soiled area with a brush) is an old and dependable method. Fluidics (i.e., fluids under pressure) is used to remove soil and debris from internal channels after brushing and when the design does not allow passage of a brush through a channel [445]. When a washer-disinfector is used, care should be taken in loading instruments: hinged instruments should be opened fully to allow adequate contact with the detergent solution; stacking of instruments in washers should be avoided; and instruments should be disassembled as much as possible.

The most common types of mechanical or automatic cleaners are ultrasonic cleaners, washer-decontaminators, washer-disinfectors, and washer-sterilizers. Ultrasonic cleaning removes soil by cavitation and implosion in which waves of acoustic energy are propagated in aqueous solutions to disrupt the bonds that hold particulate matter to surfaces. Bacterial contamination can be present in used ultrasonic cleaning solutions (and other used detergent solutions) because these solutions generally do not make antibacterial label claims [446]. Even though ultrasound alone does not significantly inactivate bacteria, sonication can act synergistically to increase the cidal efficacy of a disinfectant [447]. Users of ultrasonic cleaners should be aware that the cleaning fluid could result in endotoxin contamination of surgical instruments, which could cause severe inflammatory reactions [448]. Washer-sterilizers are modified steam sterilizers that clean by filling the chamber with water and detergent through which steam passes to provide agitation. Instruments are subsequently rinsed and subjected to a short steam-sterilization cycle. Another washer-sterilizer employs rotating spray arms for a wash cycle followed by a steam sterilization cycle at 285°F [449, 450]. Washer-decontaminators/disinfectors act like a dishwasher that uses a combination of water circulation and detergents to remove soil. These units sometimes have a cycle that subjects the instruments to a heat process (e.g., 93°C for 10 minutes) [451]. Washer-disinfectors are generally computer-controlled units for cleaning, disinfecting, and drying solid and hollow surgical and medical equipment. In one study, cleaning (measured as 5–6 $\log_{10}$ reduction) was achieved on surfaces that had adequate contact with the water flow in the machine [452]. Detailed information about cleaning and preparing supplies for terminal sterilization is provided by professional organizations [453, 454] and books [455]. Studies have shown that manual and mechanical cleaning of endoscopes achieves approximately a 4-$\log_{10}$ reduction of contaminating organisms [83, 104, 456, 457]. Thus, cleaning alone effectively reduces the number of microorganisms on contaminated equipment. In a quantitative analysis of residual protein contamination of reprocessed surgical instruments, median levels of residual protein contamination per instrument for five trays were 267, 260, 163, 456, and 756 µg [458]. In another study, the median amount of protein from reprocessed surgical instruments from different hospitals ranged from 8 µg to 91 µg [459]. When manual methods were compared with automated methods for cleaning reusable accessory devices used for minimally invasive surgical procedures, the automated method was more efficient for cleaning biopsy forceps and ported and nonported laparoscopic devices and achieved a >99% reduction in soil parameters (i.e., protein, carbohydrate, hemoglobin) in the ported and nonported laparoscopic devices [460, 461]

For instrument cleaning, a neutral or near-neutral pH detergent solution commonly is used because such solutions generally provide the best material compatibility profile and good soil removal.

Enzymes, usually proteases, sometimes are added to neutral pH solutions to assist in removing organic material. Enzymes in these formulations attack proteins that make up a large portion of common soil (e.g., blood, pus). Cleaning solutions also can contain lipases (enzymes active on fats) and amylases (enzymes active on starches). Enzymatic cleaners are not disinfectants, and proteinaceous enzymes can be inactivated by germicides. As with all chemicals, enzymes must be rinsed from the equipment or adverse reactions (e.g., fever, residual amounts of high-level disinfectants, proteinaceous residue) could result [462, 463]. Enzyme solutions should be used in accordance with manufacturer's instructions, which include proper dilution of the enzymatic detergent and contact with equipment for the amount of time specified on the label [463]. Detergent enzymes can result in asthma or other allergic effects in users. Neutral pH detergent solutions that contain enzymes are compatible with metals and other materials used in medical instruments and are the best choice for cleaning delicate medical instruments, especially flexible endoscopes [457]. Alkaline-based cleaning agents are used for processing medical devices because they efficiently dissolve protein and fat residues [464]; however, they can be corrosive [457]. Some data demonstrate that enzymatic cleaners are more effective than neutral detergents [465, 466] in removing microorganisms from surfaces but two more recent studies found no difference in cleaning efficiency between enzymatic and alkaline-based cleaners [443, 464]. Another study found no significant difference between enzymatic and non-enzymatic cleaners in terms of microbial cleaning efficacy [467]. A new non-enzyme, hydrogen peroxide-based formulation (not FDA-cleared) was as effective as enzymatic cleaners in removing protein, blood, carbohydrate, and endotoxin from surface test carriers[468] In addition, this product effected a 5-$\log_{10}$ reduction in microbial loads with a 3-minute exposure at room temperature [468].

Although the effectiveness of high-level disinfection and sterilization mandates effective cleaning, no "real-time" tests exist that can be employed in a clinical setting to verify cleaning. If such tests were commercially available they could be used to ensure an adequate level of cleaning [469-472].). The only way to ensure adequate cleaning is to conduct a reprocessing verification test (e.g., microbiologic sampling), but this is not routinely recommended [473]. Validation of the cleaning processes in a laboratory-testing program is possible by microorganism detection, chemical detection for organic contaminants, radionuclide tagging, and chemical detection for specific ions [426, 471]. During the past few years, data have been published describing use of an artificial soil, protein, endotoxin, X-ray contrast medium, or blood to verify the manual or automated cleaning process [169, 452, 474-478] and adenosine triphosphate bioluminescence and microbiologic sampling to evaluate the effectiveness of environmental surface cleaning[170, 479]. At a minimum, all instruments should be individually inspected and be visibly clean.

DISINFECTION

Many disinfectants are used alone or in combinations (e.g., hydrogen peroxide and peracetic acid) in the health-care setting. These include alcohols, chlorine and chlorine compounds, formaldehyde, glutaraldehyde, *ortho*-phthalaldehyde, hydrogen peroxide, iodophors, peracetic acid, phenolics, and quaternary ammonium compounds. Commercial formulations based on these chemicals are considered unique products and must be registered with EPA or cleared by FDA. In most instances, a given product is designed for a specific purpose and is to be used in a certain manner. Therefore, users should read labels carefully to ensure the correct product is selected for the intended use and applied efficiently.

Disinfectants are not interchangeable, and incorrect concentrations and inappropriate disinfectants can result in excessive costs. Because occupational diseases among cleaning personnel have been associated with use of several disinfectants (e.g., formaldehyde, glutaraldehyde, and chlorine), precautions (e.g., gloves and proper ventilation) should be used to minimize exposure [318, 480, 481]. Asthma and reactive airway disease can occur in sensitized persons exposed to any airborne chemical, including germicides. Clinically important asthma can occur at levels below ceiling levels regulated by OSHA or recommended by NIOSH. The preferred method of control is elimination of the chemical (through engineering controls or substitution) or relocation of the worker.

The following overview of the performance characteristics of each provides users with sufficient information to select an appropriate disinfectant for any item and use it in the most efficient way.

Chemical Disinfectants

Alcohol

Overview. In the healthcare setting, "alcohol" refers to two water-soluble chemical compounds—ethyl alcohol and isopropyl alcohol—that have generally underrated germicidal characteristics [482]. FDA has not cleared any liquid chemical sterilant or high-level disinfectant with alcohol as the main active ingredient. These alcohols are rapidly bactericidal rather than bacteriostatic against vegetative forms of bacteria; they also are tuberculocidal, fungicidal, and virucidal but do not destroy bacterial spores. Their cidal activity drops sharply when diluted below 50% concentration, and the optimum bactericidal concentration is 60%–90% solutions in water (volume/volume) [483, 484].

Mode of Action. The most feasible explanation for the antimicrobial action of alcohol is denaturation of proteins. This mechanism is supported by the observation that absolute ethyl alcohol, a dehydrating agent, is less bactericidal than mixtures of alcohol and water because proteins are denatured more quickly in the presence of water [484, 485]. Protein denaturation also is consistent with observations that alcohol destroys the dehydrogenases of *Escherichia coli* [486], and that ethyl alcohol increases the lag phase of *Enterobacter aerogenes* [487] and that the lag phase effect could be reversed by adding certain amino acids. The bacteriostatic action was believed caused by inhibition of the production of metabolites essential for rapid cell division.

Microbicidal Activity. Methyl alcohol (methanol) has the weakest bactericidal action of the alcohols and thus seldom is used in healthcare [488]. The bactericidal activity of various concentrations of ethyl alcohol (ethanol) was examined against a variety of microorganisms in exposure periods ranging from 10 seconds to 1 hour [483]. *Pseudomonas aeruginosa* was killed in 10 seconds by all concentrations of ethanol from 30% to 100% (v/v), and *Serratia marcescens, E, coli* and *Salmonella typhosa* were killed in 10 seconds by all concentrations of ethanol from 40% to 100%. The gram-positive organisms *Staphylococcus aureus* and *Streptococcus pyogenes* were slightly more resistant, being killed in 10 seconds by ethyl alcohol concentrations of 60%–95%. Isopropyl alcohol (isopropanol) was slightly more bactericidal than ethyl alcohol for *E. coli* and *S. aureus* [489].

Ethyl alcohol, at concentrations of 60%–80%, is a potent virucidal agent inactivating all of the lipophilic viruses (e.g., herpes, vaccinia, and influenza virus) and many hydrophilic viruses (e.g.,

adenovirus, enterovirus, rhinovirus, and rotaviruses but not hepatitis A virus (HAV) [58] or poliovirus) [49]. Isopropyl alcohol is not active against the nonlipid enteroviruses but is fully active against the lipid viruses [72]. Studies also have demonstrated the ability of ethyl and isopropyl alcohol to inactivate the hepatitis B virus(HBV) [224, 225] and the herpes virus, [490] and ethyl alcohol to inactivate human immunodeficiency virus (HIV) [227], rotavirus, echovirus, and astrovirus [491].

In tests of the effect of ethyl alcohol against *M. tuberculosis*, 95% ethanol killed the tubercle bacilli in sputum or water suspension within 15 seconds [492]. In 1964, Spaulding stated that alcohols were the germicide of choice for tuberculocidal activity, and they should be the standard by which all other tuberculocides are compared. For example, he compared the tuberculocidal activity of iodophor (450 ppm), a substituted phenol (3%), and isopropanol (70%/volume) using the mucin-loop test (10^6 *M. tuberculosis* per loop) and determined the contact times needed for complete destruction were 120–180 minutes, 45–60 minutes, and 5 minutes, respectively. The mucin-loop test is a severe test developed to produce long survival times. Thus, these figures should not be extrapolated to the exposure times needed when these germicides are used on medical or surgical material [482].

Ethyl alcohol (70%) was the most effective concentration for killing the tissue phase of *Cryptococcus neoformans*, *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Histoplasma capsulatum* and the culture phases of the latter three organisms aerosolized onto various surfaces. The culture phase was more resistant to the action of ethyl alcohol and required about 20 minutes to disinfect the contaminated surface, compared with <1 minute for the tissue phase [493, 494].

Isopropyl alcohol (20%) is effective in killing the cysts of *Acanthamoeba culbertsoni* (*560*) as are chlorhexidine, hydrogen peroxide, and thimerosal [496].

Uses. Alcohols are not recommended for sterilizing medical and surgical materials principally because they lack sporicidal action and they cannot penetrate protein-rich materials. Fatal postoperative wound infections with *Clostridium* have occurred when alcohols were used to sterilize surgical instruments contaminated with bacterial spores [497]. Alcohols have been used effectively to disinfect oral and rectal thermometers[498, 499], hospital pagers [500], scissors [501], and stethoscopes [502]. Alcohols have been used to disinfect fiberoptic endoscopes [503, 504] but failure of this disinfectant have lead to infection [280, 505]. Alcohol towelettes have been used for years to disinfect small surfaces such as rubber stoppers of multiple-dose medication vials or vaccine bottles. Furthermore, alcohol occasionally is used to disinfect external surfaces of equipment (e.g., stethoscopes, ventilators, manual ventilation bags) [506], CPR manikins [507], ultrasound instruments [508] or medication preparation areas. Two studies demonstrated the effectiveness of 70% isopropyl alcohol to disinfect reusable transducer heads in a controlled environment [509, 510]. In contrast, three bloodstream infection outbreaks have been described when alcohol was used to disinfect transducer heads in an intensive-care setting [511].

The documented shortcomings of alcohols on equipment are that they damage the shellac mountings of lensed instruments, tend to swell and harden rubber and certain plastic tubing after prolonged and repeated use, bleach rubber and plastic tiles [482] and damage tonometer tips (by deterioration of the glue) after the equivalent of 1 working year of routine use [512]. Tonometer biprisms soaked in alcohol for 4 days developed rough front surfaces that potentially could cause corneal damage; this appeared to be caused by weakening of the cementing substances used to fabricate the biprisms [513]. Corneal opacification has been reported when tonometer tips were swabbed with alcohol immediately before measurement of intraocular pressure [514]. Alcohols are flammable and consequently must be stored in a cool, well-ventilated area. They also evaporate rapidly, making extended exposure time difficult to achieve unless the items are immersed.

Chlorine and Chlorine Compounds

Overview. Hypochlorites, the most widely used of the chlorine disinfectants, are available as liquid (e.g., sodium hypochlorite) or solid (e.g., calcium hypochlorite). The most prevalent chlorine

products in the United States are aqueous solutions of 5.25%–6.15% sodium hypochlorite (see glossary), usually called household bleach. They have a broad spectrum of antimicrobial activity, do not leave toxic residues, are unaffected by water hardness, are inexpensive and fast acting [328], remove dried or fixed organisms and biofilms from surfaces[465], and have a low incidence of serious toxicity [515-517]. Sodium hypochlorite at the concentration used in household bleach (5.25-6.15%) can produce ocular irritation or oropharyngeal, esophageal, and gastric burns [318, 518-522]. Other disadvantages of hypochlorites include corrosiveness to metals in high concentrations (>500 ppm), inactivation by organic matter, discoloring or "bleaching" of fabrics, release of toxic chlorine gas when mixed with ammonia or acid (e.g., household cleaning agents) [523-525], and relative stability [327]. The microbicidal activity of chlorine is attributed largely to undissociated hypochlorous acid (HOCl). The dissociation of HOCl to the less microbicidal form (hypochlorite ion OCl^-) depends on pH. The disinfecting efficacy of chlorine decreases with an increase in pH that parallels the conversion of undissociated HOCl to OCl^- [329, 526]. A potential hazard is production of the carcinogen bis(chloromethyl) ether when hypochlorite solutions contact formaldehyde [527] and the production of the animal carcinogen trihalomethane when hot water is hyperchlorinated [528]. After reviewing environmental fate and ecologic data, EPA has determined the currently registered uses of hypochlorites will not result in unreasonable adverse effects to the environment [529].

Alternative compounds that release chlorine and are used in the health-care setting include demand-release chlorine dioxide, sodium dichloroisocyanurate, and chloramine-T. The advantage of these compounds over the hypochlorites is that they retain chlorine longer and so exert a more prolonged bactericidal effect. Sodium dichloroisocyanurate tablets are stable, and for two reasons, the microbicidal activity of solutions prepared from sodium dichloroisocyanurate tablets might be greater than that of sodium hypochlorite solutions containing the same total available chlorine. First, with sodium dichloroisocyanurate, only 50% of the total available chlorine is free (HOCl and OCl^-), whereas the remainder is combined (monochloroisocyanurate or dichloroisocyanurate), and as free available chlorine is used up, the latter is released to restore the equilibrium. Second, solutions of sodium dichloroisocyanurate are acidic, whereas sodium hypochlorite solutions are alkaline, and the more microbicidal type of chlorine (HOCl) is believed to predominate [530-533]. Chlorine dioxide-based disinfectants are prepared fresh as required by mixing the two components (base solution [citric acid with preservatives and corrosion inhibitors] and the activator solution [sodium chlorite]). In vitro suspension tests showed that solutions containing about 140 ppm chlorine dioxide achieved a reduction factor exceeding 10^6 of *S. aureus* in 1 minute and of *Bacillus atrophaeus* spores in 2.5 minutes in the presence of 3 g/L bovine albumin. The potential for damaging equipment requires consideration because long-term use can damage the outer plastic coat of the insertion tube [534]. In another study, chlorine dioxide solutions at either 600 ppm or 30 ppm killed *Mycobacterium avium-intracellulare* within 60 seconds after contact but contamination by organic material significantly affected the microbicidal properties[535].

The microbicidal activity of a new disinfectant, "superoxidized water," has been examined The concept of electrolyzing saline to create a disinfectant or antiseptics is appealing because the basic materials of saline and electricity are inexpensive and the end product (i.e., water) does not damage the environment. The main products of this water are hypochlorous acid (e.g., at a concentration of about 144 mg/L) and chlorine. As with any germicide, the antimicrobial activity of superoxidized water is strongly affected by the concentration of the active ingredient (available free chlorine) [536]. One manufacturer generates the disinfectant at the point of use by passing a saline solution over coated titanium electrodes at 9 amps. The product generated has a pH of 5.0–6.5 and an oxidation-reduction potential (redox) of >950 mV. Although superoxidized water is intended to be generated fresh at the point of use, when tested under clean conditions the disinfectant was effective within 5 minutes when 48 hours old [537]. Unfortunately, the equipment required to produce the product can be expensive because parameters such as pH, current, and redox potential must be closely monitored. The solution is nontoxic to biologic tissues. Although the United Kingdom manufacturer claims the solution is noncorrosive and nondamaging to endoscopes and processing equipment, one flexible endoscope manufacturer (Olympus Key-Med, United Kingdom) has voided the warranty on the endoscopes if superoxidized water is used to disinfect them [538]. As with any germicide formulation, the user should check with the device manufacturer for

compatibility with the germicide. Additional studies are needed to determine whether this solution could be used as an alternative to other disinfectants or antiseptics for hand washing, skin antisepsis, room cleaning, or equipment disinfection (e.g., endoscopes, dialyzers) [400, 539, 540]. In October 2002, the FDA cleared superoxidized water as a high-level disinfectant (FDA, personal communication, September 18, 2002).

Mode of Action. The exact mechanism by which free chlorine destroys microorganisms has not been elucidated. Inactivation by chlorine can result from a number of factors: oxidation of sulfhydryl enzymes and amino acids; ring chlorination of amino acids; loss of intracellular contents; decreased uptake of nutrients; inhibition of protein synthesis; decreased oxygen uptake; oxidation of respiratory components; decreased adenosine triphosphate production; breaks in DNA; and depressed DNA synthesis [329, 347]. The actual microbicidal mechanism of chlorine might involve a combination of these factors or the effect of chlorine on critical sites [347].

Microbicidal Activity. Low concentrations of free available chlorine (e.g., HOCl, OCl^-, and elemental chlorine-Cl_2) have a biocidal effect on mycoplasma (25 ppm) and vegetative bacteria (<5 ppm) in seconds in the absence of an organic load [329, 418]. Higher concentrations (1,000 ppm) of chlorine are required to kill *M. tuberculosis* using the Association of Official Analytical Chemists (AOAC) tuberculocidal test [73]. A concentration of 100 ppm will kill ≥99.9% of *B. atrophaeus* spores within 5 minutes [541, 542] and destroy mycotic agents in <1 hour [329]. Acidified bleach and regular bleach (5,000 ppm chlorine) can inactivate 10^6 *Clostridium difficile* spores in ≤10 minutes [262]. One study reported that 25 different viruses were inactivated in 10 minutes with 200 ppm available chlorine [72]. Several studies have demonstrated the effectiveness of diluted sodium hypochlorite and other disinfectants to inactivate HIV [61]. Chlorine (500 ppm) showed inhibition of *Candida* after 30 seconds of exposure [54]. In experiments using the AOAC Use-Dilution Method, 100 ppm of free chlorine killed 10^6–10^7 *S. aureus*, *Salmonella choleraesuis*, and *P. aeruginosa* in <10 minutes [327]. Because household bleach contains 5.25%–6.15% sodium hypochlorite, or 52,500–61,500 ppm available chlorine, a 1:1,000 dilution provides about 53–62 ppm available chlorine, and a 1:10 dilution of household bleach provides about 5250–6150 ppm.

Data are available for chlorine dioxide that support manufacturers' bactericidal, fungicidal, sporicidal, tuberculocidal, and virucidal label claims [543-546]. A chlorine dioxide generator has been shown effective for decontaminating flexible endoscopes [534] but it is not currently FDA-cleared for use as a high-level disinfectant [85]. Chlorine dioxide can be produced by mixing solutions, such as a solution of chlorine with a solution of sodium chlorite [329]. In 1986, a chlorine dioxide product was voluntarily removed from the market when its use caused leakage of cellulose-based dialyzer membranes, which allowed bacteria to migrate from the dialysis fluid side of the dialyzer to the blood side [547].

Sodium dichloroisocyanurate at 2,500 ppm available chlorine is effective against bacteria in the presence of up to 20% plasma, compared with 10% plasma for sodium hypochlorite at 2,500 ppm [548].

"Superoxidized water" has been tested against bacteria, mycobacteria, viruses, fungi, and spores [537, 539, 549]. Freshly generated superoxidized water is rapidly effective (<2 minutes) in achieving a 5-$\log_{10}$ reduction of pathogenic microorganisms (i.e., *M. tuberculosis*, *M. chelonae*, poliovirus, HIV, multidrug-resistant *S. aureus*, *E. coli*, *Candida albicans*, *Enterococcus faecalis*, *P. aeruginosa*) in the absence of organic loading. However, the biocidal activity of this disinfectant decreased substantially in the presence of organic material (e.g., 5% horse serum) [537, 549, 550]. No bacteria or viruses were detected on artificially contaminated endoscopes after a 5-minute exposure to superoxidized water [551] and HBV-DNA was not detected from any endoscope experimentally contaminated with HBV-positive mixed sera after a disinfectant exposure time of 7 minutes[552].

Uses. Hypochlorites are widely used in healthcare facilities in a variety of settings. [328] Inorganic chlorine solution is used for disinfecting tonometer heads [188] and for spot-disinfection of countertops and floors. A 1:10–1:100 dilution of 5.25%–6.15% sodium hypochlorite (i.e., household bleach) [22, 228, 553, 554] or

an EPA-registered tuberculocidal disinfectant [17] has been recommended for decontaminating blood spills. For small spills of blood (i.e., drops of blood) on noncritical surfaces, the area can be disinfected with a 1:100 dilution of 5.25%-6.15% sodium hypochlorite or an EPA-registered tuberculocidal disinfectant. Because hypochlorites and other germicides are substantially inactivated in the presence of blood [63, 548, 555, 556], large spills of blood require that the surface be cleaned before an EPA-registered disinfectant or a 1:10 (final concentration) solution of household bleach is applied [557]. If a sharps injury is possible, the surface initially should be decontaminated [69, 318], then cleaned and disinfected (1:10 final concentration) [63]. Extreme care always should be taken to prevent percutaneous injury. At least 500 ppm available chlorine for 10 minutes is recommended for decontaminating CPR training manikins [558]. Full-strength bleach has been recommended for self-disinfection of needles and syringes used for illicit-drug injection when needle-exchange programs are not available. The difference in the recommended concentrations of bleach reflects the difficulty of cleaning the interior of needles and syringes and the use of needles and syringes for parenteral injection [559]. Clinicians should not alter their use of chlorine on environmental surfaces on the basis of testing methodologies that do not simulate actual disinfection practices [560, 561]. Other uses in healthcare include as an irrigating agent in endodontic treatment [562] and as a disinfectant for manikins, laundry, dental appliances, hydrotherapy tanks [23, 41], regulated medical waste before disposal [328], and the water distribution system in hemodialysis centers and hemodialysis machines [563].

Chlorine long has been used as the disinfectant in water treatment. Hyperchlorination of a *Legionella*-contaminated hospital water system [23] resulted in a dramatic decrease (from 30% to 1.5%) in the isolation of *L. pneumophila* from water outlets and a cessation of healthcare-associated Legionnaires' disease in an affected unit [528, 564]. Water disinfection with monochloramine by municipal water-treatment plants substantially reduced the risk for healthcare–associated Legionnaires disease [565, 566]. Chlorine dioxide also has been used to control *Legionella* in a hospital water supply. [567] Chloramine T [568] and hypochlorites [41] have been used to disinfect hydrotherapy equipment.

Hypochlorite solutions in tap water at a pH >8 stored at room temperature (23°C) in closed, opaque plastic containers can lose up to 40%–50% of their free available chlorine level over 1 month. Thus, if a user wished to have a solution containing 500 ppm of available chlorine at day 30, he or she should prepare a solution containing 1,000 ppm of chlorine at time 0. Sodium hypochlorite solution does not decompose after 30 days when stored in a closed brown bottle [327].

The use of powders, composed of a mixture of a chlorine-releasing agent with highly absorbent resin, for disinfecting spills of body fluids has been evaluated by laboratory tests and hospital ward trials. The inclusion of acrylic resin particles in formulations markedly increases the volume of fluid that can be soaked up because the resin can absorb 200–300 times its own weight of fluid, depending on the fluid consistency. When experimental formulations containing 1%, 5%, and 10% available chlorine were evaluated by a standardized surface test, those containing 10% demonstrated bactericidal activity. One problem with chlorine-releasing granules is that they can generate chlorine fumes when applied to urine [569].

Formaldehyde

Overview. Formaldehyde is used as a disinfectant and sterilant in both its liquid and gaseous states. Liquid formaldehyde will be considered briefly in this section, and the gaseous form is reviewed elsewhere [570]. Formaldehyde is sold and used principally as a water-based solution called formalin, which is 37% formaldehyde by weight. The aqueous solution is a bactericide, tuberculocide, fungicide, virucide and sporicide [72, 82, 571-573]. OSHA indicated that formaldehyde should be handled in the workplace as a potential carcinogen and set an employee exposure standard for formaldehyde that limits an 8-hour time-weighted average exposure concentration of 0.75 ppm [574, 575]. The standard includes a second permissible exposure limit in the form of a short-term exposure limit (STEL) of 2 ppm that is the maximum exposure allowed during a 15-minute period [576]. Ingestion of formaldehyde can be fatal, and long-term exposure to low levels in the air or on the skin can cause asthma-like respiratory problems and skin irritation, such as dermatitis and itching. For these reasons, employees should have limited direct contact

with formaldehyde, and these considerations limit its role in sterilization and disinfection processes. Key provisions of the OSHA standard that protects workers from exposure to formaldehyde appear in Title 29 of the Code of Federal Regulations (CFR) Part 1910.1048 (and equivalent regulations in states with OSHA-approved state plans) [577].

Mode of Action. Formaldehyde inactivates microorganisms by alkylating the amino and sulfhydral groups of proteins and ring nitrogen atoms of purine bases [376].

Microbicidal Activity. Varying concentrations of aqueous formaldehyde solutions destroy a wide range of microorganisms. Inactivation of poliovirus in 10 minutes required an 8% concentration of formalin, but all other viruses tested were inactivated with 2% formalin [72]. Four percent formaldehyde is a tuberculocidal agent, inactivating 10^4 *M. tuberculosis* in 2 minutes [82], and 2.5% formaldehyde inactivated about 10^7 *Salmonella* Typhi in 10 minutes in the presence of organic matter [572]. The sporicidal action of formaldehyde was slower than that of glutaraldehyde in comparative tests with 4% aqueous formaldehyde and 2% glutaraldehyde against the spores of *B. anthracis* [82]. The formaldehyde solution required 2 hours of contact to achieve an inactivation factor of 10^4, whereas glutaraldehyde required only 15 minutes.

Uses. Although formaldehyde-alcohol is a chemical sterilant and formaldehyde is a high-level disinfectant, the health-care uses of formaldehyde are limited by its irritating fumes and its pungent odor even at very low levels (<1 ppm). For these reasons and others—such as its role as a suspected human carcinogen linked to nasal cancer and lung cancer [578], this germicide is excluded from Table 1. When it is used, , direct exposure to employees generally is limited; however, excessive exposures to formaldehyde have been documented for employees of renal transplant units [574, 579], and students in a gross anatomy laboratory [580]. Formaldehyde is used in the health-care setting to prepare viral vaccines (e.g., poliovirus and influenza); as an embalming agent; and to preserve anatomic specimens; and historically has been used to sterilize surgical instruments, especially when mixed with ethanol. A 1997 survey found that formaldehyde was used for reprocessing hemodialyzers by 34% of U.S. hemodialysis centers—a 60% decrease from 1983 [249, 581]. If used at room temperature, a concentration of 4% with a minimum exposure of 24 hours is required to disinfect disposable hemodialyzers reused on the same patient [582, 583]. Aqueous formaldehyde solutions (1%–2%) also have been used to disinfect the internal fluid pathways of dialysis machines [583]. To minimize a potential health hazard to dialysis patients, the dialysis equipment must be thoroughly rinsed and tested for residual formaldehyde before use.

Paraformaldehyde, a solid polymer of formaldehyde, can be vaporized by heat for the gaseous decontamination of laminar flow biologic safety cabinets when maintenance work or filter changes require access to the sealed portion of the cabinet.

Glutaraldehyde

Overview. Glutaraldehyde is a saturated dialdehyde that has gained wide acceptance as a high-level disinfectant and chemical sterilant [107]. Aqueous solutions of glutaraldehyde are acidic and generally in this state are not sporicidal. Only when the solution is "activated" (made alkaline) by use of alkalinating agents to pH 7.5–8.5 does the solution become sporicidal. Once activated, these solutions have a shelf-life of minimally 14 days because of the polymerization of the glutaraldehyde molecules at alkaline pH levels. This polymerization blocks the active sites (aldehyde groups) of the glutaraldehyde molecules that are responsible for its biocidal activity.

Novel glutaraldehyde formulations (e.g., glutaraldehyde-phenol-sodium phenate, potentiated acid glutaraldehyde, stabilized alkaline glutaraldehyde) produced in the past 30 years have overcome the problem of rapid loss of activity (e.g., use-life 28–30 days) while generally maintaining excellent microbicidal activity [584-588]. However, antimicrobial activity depends not only on age but also on use conditions, such as dilution and organic stress. Manufacturers' literature for these preparations suggests the neutral or alkaline glutaraldehydes possess microbicidal and anticorrosion properties superior to

those of acid glutaraldehydes, and a few published reports substantiate these claims [542, 589, 590]. However, two studies found no difference in the microbicidal activity of alkaline and acid glutaraldehydes [73, 591]. The use of glutaraldehyde-based solutions in health-care facilities is widespread because of their advantages, including excellent biocidal properties; activity in the presence of organic matter (20% bovine serum); and noncorrosive action to endoscopic equipment, thermometers, rubber, or plastic equipment (Tables 4 and 5).

Mode of Action. The biocidal activity of glutaraldehyde results from its alkylation of sulfhydryl, hydroxyl, carboxyl, and amino groups of microorganisms, which alters RNA, DNA, and protein synthesis. The mechanism of action of glutaraldehydes are reviewed extensively elsewhere [592, 593].

Microbicidal Activity. The in vitro inactivation of microorganisms by glutaraldehydes has been extensively investigated and reviewed [592, 593]. Several investigators showed that ≥2% aqueous solutions of glutaraldehyde, buffered to pH 7.5–8.5 with sodium bicarbonate effectively killed vegetative bacteria in <2 minutes; *M. tuberculosis*, fungi, and viruses in <10 minutes; and spores of *Bacillus* and *Clostridium* species in 3 hours [542, 592-597]. Spores of *C. difficile* are more rapidly killed by 2% glutaraldehyde than are spores of other species of *Clostridium* and *Bacillus* [79, 265, 266]. Microorganisms with substantial resistance to glutaraldehyde have been reported, including some mycobacteria (*M. chelonae*, *Mycobacterium avium-intracellulare*, *M. xenopi*) [598-601], *Methylobacterium mesophilicum* [602], *Trichosporon*, fungal ascospores (e.g., *Microascus cinereus*, *Cheatomium globosum*), and *Cryptosporidium*[271, 603]. *M. chelonae* persisted in a 0.2% glutaraldehyde solution used to store porcine prosthetic heart valves [604].

Two percent alkaline glutaraldehyde solution inactivated 10^5 *M. tuberculosis* cells on the surface of penicylinders within 5 minutes at 18°C [589]. However, subsequent studies[82] questioned the mycobactericidal prowess of glutaraldehydes. Two percent alkaline glutaraldehyde has slow action (20 to >30 minutes) against *M. tuberculosis* and compares unfavorably with alcohols, formaldehydes, iodine, and phenol [82]. Suspensions of *M. avium*, *M. intracellulare*, and *M. gordonae* were more resistant to inactivation by a 2% alkaline glutaraldehyde (estimated time to complete inactivation: ~60 minutes) than were virulent *M. tuberculosis* (estimated time to complete inactivation ~25 minutes) [605]. The rate of kill was directly proportional to the temperature, and a standardized suspension of *M. tuberculosis* could not be sterilized within 10 minutes [84]. An FDA-cleared chemical sterilant containing 2.5% glutaraldehyde uses increased temperature (35°C) to reduce the time required to achieve high-level disinfection (5 minutes) [85, 606], but its use is limited to automatic endoscope reprocessors equipped with a heater. In another study employing membrane filters for measurement of mycobactericidal activity of 2% alkaline glutaraldehyde, complete inactivation was achieved within 20 minutes at 20°C when the test inoculum was 10^6 *M. tuberculosis* per membrane [81]. Several investigators [55, 57, 73, 76, 80, 81, 84, 605] have demonstrated that glutaraldehyde solutions inactivate 2.4 to >5.0 $\log_{10}$ of *M. tuberculosis* in 10 minutes (including multidrug-resistant *M. tuberculosis*) and 4.0–6.4 $\log_{10}$ of *M. tuberculosis* in 20 minutes. On the basis of these data and other studies, 20 minutes at room temperature is considered the minimum exposure time needed to reliably kill *Mycobacteria* and other vegetative bacteria with ≥2% glutaraldehyde [17, 19, 27, 57, 83, 94, 108, 111, 117-121, 607].

Glutaraldehyde is commonly diluted during use, and studies showed a glutaraldehyde concentration decline after a few days of use in an automatic endoscope washer [608, 609]. The decline occurs because instruments are not thoroughly dried and water is carried in with the instrument, which increases the solution's volume and dilutes its effective concentration [610]. This emphasizes the need to ensure that semicritical equipment is disinfected with an acceptable concentration of glutaraldehyde. Data suggest that 1.0%–1.5% glutaraldehyde is the minimum effective concentration for >2% glutaraldehyde solutions when used as a high-level disinfectant [76, 589, 590, 609]. Chemical test strips or liquid chemical monitors [610, 611] are available for determining whether an effective concentration of glutaraldehyde is present despite repeated use and dilution. The frequency of testing should be based on how frequently the solutions are used (e.g., used daily, test daily; used weekly, test before use; used 30 times per day, test each 10th use), but the strips should not be used to extend the use life beyond the expiration date. Data suggest the chemicals in the test strip deteriorate with time [612] and a

manufacturer's expiration date should be placed on the bottles. The bottle of test strips should be dated when opened and used for the period of time indicated on the bottle (e.g., 120 days). The results of test strip monitoring should be documented. The glutaraldehyde test kits have been preliminarily evaluated for accuracy and range [612] but the reliability has been questioned [613]. To ensure the presence of minimum effective concentration of the high-level disinfectant, manufacturers of some chemical test strips recommend the use of quality-control procedures to ensure the strips perform properly. If the manufacturer of the chemical test strip recommends a quality-control procedure, users should comply with the manufacturer's recommendations. The concentration should be considered unacceptable or unsafe when the test indicates a dilution below the product's minimum effective concentration (MEC) (generally to ≤1.0%–1.5% glutaraldehyde) by the indicator not changing color.

A 2.0% glutaraldehyde–7.05% phenol–1.20% sodium phenate product that contained 0.125% glutaraldehyde–0.44% phenol–0.075% sodium phenate when diluted 1:16 is not recommended as a high-level disinfectant because it lacks bactericidal activity in the presence of organic matter and lacks tuberculocidal, fungicidal, virucidal, and sporicidal activity [49, 55, 56, 71, 73-79, 614]. In December 1991, EPA issued an order to stop the sale of all batches of this product because of efficacy data showing the product is not effective against spores and possibly other microorganisms or inanimate objects as claimed on the label [615]. FDA has cleared a glutaraldehyde–phenol/phenate concentrate as a high-level disinfectant that contains 1.12% glutaraldehyde with 1.93% phenol/phenate at its use concentration. Other FDA cleared glutaraldehyde sterilants that contain 2.4%–3.4% glutaraldehyde are used undiluted [606].

Uses. Glutaraldehyde is used most commonly as a high-level disinfectant for medical equipment such as endoscopes [89, 107, 504], spirometry tubing, dialyzers [616], transducers, anesthesia and respiratory therapy equipment [617], hemodialysis proportioning and dialysate delivery systems [249, 618], and reuse of laparoscopic disposable plastic trocars [619]. Glutaraldehyde is noncorrosive to metal and does not damage lensed instruments, rubber, or plastics. Glutaraldehyde should not be used for cleaning noncritical surfaces because it is too toxic and expensive.

Colitis believed caused by glutaraldehyde exposure from residual disinfecting solution in endoscope solution channels has been reported and is preventable by careful endoscope rinsing [318, 620-630]. One study found that residual glutaraldehyde levels were higher and more variable after manual disinfection (<0.2 mg/L to 159.5 mg/L) than after automatic disinfection (0.2–6.3 mg/L)[631]. Similarly, keratopathy and corneal decompensation were caused by ophthalmic instruments that were inadequately rinsed after soaking in 2% glutaraldehyde [632, 633].

Healthcare personnel can be exposed to elevated levels of glutaraldehyde vapor when equipment is processed in poorly ventilated rooms, when spills occur, when glutaraldehyde solutions are activated or changed,[634], or when open immersion baths are used. Acute or chronic exposure can result in skin irritation or dermatitis, mucous membrane irritation (eye, nose, mouth), or pulmonary symptoms [318, 635-639]. Epistaxis, allergic contact dermatitis, asthma, and rhinitis also have been reported in healthcare workers exposed to glutaraldehyde [636, 640-647].

Glutaraldehyde exposure should be monitored to ensure a safe work environment. Testing can be done by four techniques: a silica gel tube/gas chromatography with a flame ionization detector, dinitrophenylhydrazine (DNPH)-impregnated filter cassette/high-performance liquid chromatography (HPLC) with an ultraviolet (UV) detector, a passive badge/HPLC, or a handheld glutaraldehyde air monitor [648]. The silica gel tube and the DNPH-impregnated cassette are suitable for monitoring the 0.05 ppm ceiling limit. The passive badge, with a 0.02 ppm limit of detection, is considered marginal at the Americal Council of Governmental Industrial Hygienists (ACGIH) ceiling level. The ceiling level is considered too close to the glutaraldehyde meter's 0.03 ppm limit of detection to provide confidence in the readings [648]. ACGIH does not require a specific monitoring schedule for glutaraldehyde; however, a monitoring schedule is needed to ensure the level is less than the ceiling limit. For example, monitoring

should be done initially to determine glutaraldehyde levels, after procedural or equipment changes, and in response to worker complaints [649]. In the absence of an OSHA permissible exposure limit, if the glutaraldehyde level is higher than the ACGIH ceiling limit of 0.05 ppm, corrective action and repeat monitoring would be prudent [649].

Engineering and work-practice controls that can be used to resolve these problems include ducted exhaust hoods, air systems that provide 7–15 air exchanges per hour, ductless fume hoods with absorbents for the glutaraldehyde vapor, tight-fitting lids on immersion baths, personal protection (e.g., nitrile or butyl rubber gloves but not natural latex gloves, goggles) to minimize skin or mucous membrane contact, and automated endoscope processors [7, 650]. If engineering controls fail to maintain levels below the ceiling limit, institutions can consider the use of respirators (e.g., a half-face respirator with organic vapor cartridge [640] or a type "C" supplied air respirator with a full facepiece operated in a positive pressure mode) [651]. In general, engineering controls are preferred over work-practice and administrative controls because they do not require active participation by the health-care worker. Even though enforcement of the OSHA ceiling limit was suspended in 1993 by the U.S. Court of Appeals [577], limiting employee exposure to 0.05 ppm (according to ACGIH) is prudent because, at this level, glutaraldehyde can irritate the eyes, throat, and nose [318, 577, 639, 652]. If glutaraldehyde disposal through the sanitary sewer system is restricted, sodium bisulfate can be used to neutralize the glutaraldehyde and make it safe for disposal.

Hydrogen Peroxide

Overview. The literature contains several accounts of the properties, germicidal effectiveness, and potential uses for stabilized hydrogen peroxide in the health-care setting. Published reports ascribe good germicidal activity to hydrogen peroxide and attest to its bactericidal, virucidal, sporicidal, and fungicidal properties [653-655]. (Tables 4 and 5) The FDA website lists cleared liquid chemical sterilants and high-level disinfectants containing hydrogen peroxide and their cleared contact conditions.

Mode of Action. Hydrogen peroxide works by producing destructive hydroxyl free radicals that can attack membrane lipids, DNA, and other essential cell components. Catalase, produced by aerobic organisms and facultative anaerobes that possess cytochrome systems, can protect cells from metabolically produced hydrogen peroxide by degrading hydrogen peroxide to water and oxygen. This defense is overwhelmed by the concentrations used for disinfection [653, 654].

Microbicidal Activity. Hydrogen peroxide is active against a wide range of microorganisms, including bacteria, yeasts, fungi, viruses, and spores [78, 654]. A 0.5% accelerated hydrogen peroxide demonstrated bactericidal and virucidal activity in 1 minute and mycobactericidal and fungicidal activity in 5 minutes [656]. Bactericidal effectiveness and stability of hydrogen peroxide in urine has been demonstrated against a variety of health-care–associated pathogens; organisms with high cellular catalase activity (e.g., *S. aureus*, *S. marcescens*, and *Proteus mirabilis*) required 30–60 minutes of exposure to 0.6% hydrogen peroxide for a 10^8 reduction in cell counts, whereas organisms with lower catalase activity (e.g., *E. coli*, *Streptococcus* species, and *Pseudomonas* species) required only 15 minutes' exposure [657]. In an investigation of 3%, 10%, and 15% hydrogen peroxide for reducing spacecraft bacterial populations, a complete kill of 10^6 spores (i.e., *Bacillus* species) occurred with a 10% concentration and a 60-minute exposure time. A 3% concentration for 150 minutes killed 10^6 spores in six of seven exposure trials [658]. A 10% hydrogen peroxide solution resulted in a 10^3 decrease in *B. atrophaeus* spores, and a $\geq 10^5$ decrease when tested against 13 other pathogens in 30 minutes at 20°C [659, 660]. A 3.0% hydrogen peroxide solution was ineffective against VRE after 3 and 10 minutes exposure times [661] and caused only a 2-$\log_{10}$ reduction in the number of *Acanthamoeba* cysts in approximately 2 hours [662]. A 7% stabilized hydrogen peroxide proved to be sporicidal (6 hours of exposure), mycobactericidal (20 minutes), fungicidal (5 minutes) at full strength, virucidal (5 minutes) and bactericidal (3 minutes) at a 1:16 dilution when a quantitative carrier test was used [655]. The 7% solution of hydrogen peroxide, tested after 14 days of stress (in the form of germ-loaded carriers and respiratory therapy equipment), was sporicidal (>7 $\log_{10}$ reduction in 6 hours), mycobactericidal (>6.5 $\log_{10}$ reduction in 25

minutes), fungicidal (>5 $\log_{10}$ reduction in 20 minutes), bactericidal (>6 $\log_{10}$ reduction in 5 minutes) and virucidal (5 $\log_{10}$ reduction in 5 minutes) [663]. Synergistic sporicidal effects were observed when spores were exposed to a combination of hydrogen peroxide (5.9%–23.6%) and peracetic acid [664]. Other studies demonstrated the antiviral activity of hydrogen peroxide against rhinovirus [665]. The time required for inactivating three serotypes of rhinovirus using a 3% hydrogen peroxide solution was 6–8 minutes; this time increased with decreasing concentrations (18-20 minutes at 1.5%, 50–60 minutes at 0.75%).

Concentrations of hydrogen peroxide from 6% to 25% show promise as chemical sterilants. The product marketed as a sterilant is a premixed, ready-to-use chemical that contains 7.5% hydrogen peroxide and 0.85% phosphoric acid (to maintain a low pH) [69]. The mycobactericidal activity of 7.5% hydrogen peroxide has been corroborated in a study showing the inactivation of >10^5 multidrug-resistant *M. tuberculosis* after a 10-minute exposure [666]. Thirty minutes were required for >99.9% inactivation of poliovirus and HAV [667]. Three percent and 6% hydrogen peroxide were unable to inactivate HAV in 1 minute in a carrier test [58]. When the effectiveness of 7.5% hydrogen peroxide at 10 minutes was compared with 2% alkaline glutaraldehyde at 20 minutes in manual disinfection of endoscopes, no significant difference in germicidal activity was observed [668].). No complaints were received from the nursing or medical staff regarding odor or toxicity. In one study, 6% hydrogen peroxide (unused product was 7.5%) was more effective in the high-level disinfection of flexible endoscopes than was the 2% glutaraldehyde solution [456]. A new, rapid-acting 13.4% hydrogen peroxide formulation (that is not yet FDA-cleared) has demonstrated sporicidal, mycobactericidal, fungicidal, and virucidal efficacy. Manufacturer data demonstrate that this solution sterilizes in 30 minutes and provides high-level disinfection in 5 minutes[669]. This product has not been used long enough to evaluate material compatibility to endoscopes and other semicritical devices, and further assessment by instrument manufacturers is needed.

Under normal conditions, hydrogen peroxide is extremely stable when properly stored (e.g., in dark containers). The decomposition or loss of potency in small containers is less than 2% per year at ambient temperatures [670].

Uses. Commercially available 3% hydrogen peroxide is a stable and effective disinfectant when used on inanimate surfaces. It has been used in concentrations from 3% to 6% for disinfecting soft contact lenses (e.g., 3% for 2–3 hrs) [653, 671, 672], tonometer biprisms [513], ventilators [673], fabrics [397], and endoscopes [456]. Hydrogen peroxide was effective in spot-disinfecting fabrics in patients' rooms [397]. Corneal damage from a hydrogen peroxide-soaked tonometer tip that was not properly rinsed has been reported [674]. Hydrogen peroxide also has been instilled into urinary drainage bags in an attempt to eliminate the bag as a source of bladder bacteriuria and environmental contamination [675]. Although the instillation of hydrogen peroxide into the bag reduced microbial contamination of the bag, this procedure did not reduce the incidence of catheter-associated bacteriuria [675].

A chemical irritation resembling pseudomembranous colitis caused by either 3% hydrogen peroxide or a 2% glutaraldehyde has been reported [621]. An epidemic of pseudomembrane-like enteritis and colitis in seven patients in a gastrointestinal endoscopy unit also has been associated with inadequate rinsing of 3% hydrogen peroxide from the endoscope [676].

As with other chemical sterilants, dilution of the hydrogen peroxide must be monitored by regularly testing the minimum effective concentration (i.e., 7.5%–6.0%). Compatibility testing by Olympus America of the 7.5% hydrogen peroxide found both cosmetic changes (e.g., discoloration of black anodized metal finishes) [69] and functional changes with the tested endoscopes (Olympus, written communication, October 15, 1999).

Iodophors

Overview. Iodine solutions or tinctures long have been used by health professionals primarily as antiseptics on skin or tissue. Iodophors, on the other hand, have been used both as antiseptics and

disinfectants. FDA has not cleared any liquid chemical sterilant or high-level disinfectants with iodophors as the main active ingredient. An iodophor is a combination of iodine and a solubilizing agent or carrier; the resulting complex provides a sustained-release reservoir of iodine and releases small amounts of free iodine in aqueous solution. The best-known and most widely used iodophor is povidone-iodine, a compound of polyvinylpyrrolidone with iodine. This product and other iodophors retain the germicidal efficacy of iodine but unlike iodine generally are nonstaining and relatively free of toxicity and irritancy [677, 678].

Several reports that documented intrinsic microbial contamination of antiseptic formulations of povidone-iodine and poloxamer-iodine [679-681] caused a reappraisal of the chemistry and use of iodophors[682]. "Free" iodine (I_2) contributes to the bactericidal activity of iodophors and dilutions of iodophors demonstrate more rapid bactericidal action than does a full-strength povidone-iodine solution. The reason for the observation that dilution increases bactericidal activity is unclear, but dilution of povidone-iodine might weaken the iodine linkage to the carrier polymer with an accompanying increase of free iodine in solution [680]. Therefore, iodophors must be diluted according to the manufacturers' directions to achieve antimicrobial activity.

Mode of Action. Iodine can penetrate the cell wall of microorganisms quickly, and the lethal effects are believed to result from disruption of protein and nucleic acid structure and synthesis.

Microbicidal Activity. Published reports on the in vitro antimicrobial efficacy of iodophors demonstrate that iodophors are bactericidal, mycobactericidal, and virucidal but can require prolonged contact times to kill certain fungi and bacterial spores [14, 71-73, 290, 683-686]. Three brands of povidone-iodine solution have demonstrated more rapid kill (seconds to minutes) of *S. aureus* and *M. chelonae* at a 1:100 dilution than did the stock solution [683]. The virucidal activity of 75–150 ppm available iodine was demonstrated against seven viruses [72]. Other investigators have questioned the efficacy of iodophors against poliovirus in the presence of organic matter [685]and rotavirus SA-11 in distilled or tapwater [290]. Manufacturers' data demonstrate that commercial iodophors are not sporicidal, but they are tuberculocidal, fungicidal, virucidal, and bactericidal at their recommended use-dilution.

Uses. Besides their use as an antiseptic, iodophors have been used for disinfecting blood culture bottles and medical equipment, such as hydrotherapy tanks, thermometers, and endoscopes. Antiseptic iodophors are not suitable for use as hard-surface disinfectants because of concentration differences. Iodophors formulated as antiseptics contain less free iodine than do those formulated as disinfectants [376]. Iodine or iodine-based antiseptics should not be used on silicone catheters because they can adversely affect the silicone tubing [687].

Ortho-phthalaldehyde (OPA)

Overview. Ortho-phthalaldehyde is a high-level disinfectant that received FDA clearance in October 1999. It contains 0.55% 1,2-benzenedicarboxaldehyde (OPA). OPA solution is a clear, pale-blue liquid with a pH of 7.5. (Tables 4 and 5)

Mode of Action. Preliminary studies on the mode of action of OPA suggest that both OPA and glutaraldehyde interact with amino acids, proteins, and microorganisms. However, OPA is a less potent cross-linking agent. This is compensated for by the lipophilic aromatic nature of OPA that is likely to assist its uptake through the outer layers of mycobacteria and gram-negative bacteria [688-690]. OPA appears to kill spores by blocking the spore germination process [691].

Microbicidal Activity. Studies have demonstrated excellent microbicidal activity in vitro [69, 100, 271, 400, 692-703]. For example, OPA has superior mycobactericidal activity (5-$\log_{10}$ reduction in 5 minutes) to glutaraldehyde. The mean times required to produce a 6-$\log_{10}$ reduction for *M. bovis* using 0.21% OPA was 6 minutes, compared with 32 minutes using 1.5% glutaraldehyde [693]. OPA showed good activity against the mycobacteria tested, including the glutaraldehyde-resistant strains, but 0.5% OPA was not sporicidal with 270 minutes of exposure. Increasing the pH from its unadjusted level (about 6.5) to pH 8 improved the sporicidal activity of OPA [694]. The level of biocidal activity was directly related to the

temperature. A greater than 5-$\log_{10}$ reduction of *B. atrophaeus* spores was observed in 3 hours at 35°C, than in 24 hours at 20°C. Also, with an exposure time ≤5 minutes, biocidal activity decreased with increasing serum concentration. However, efficacy did not differ when the exposure time was ≥10 minutes [697]. In addition, OPA is effective (>5-$\log_{10}$ reduction) against a wide range of microorganisms, including glutaraldehyde-resistant mycobacteria and *B. atrophaeus* spores [694].

The influence of laboratory adaptation of test strains, such as *P. aeruginosa*, to 0.55% OPA has been evaluated. Resistant and multiresistant strains increased substantially in susceptibility to OPA after laboratory adaptation ($\log_{10}$ reduction factors increased by 0.54 and 0.91 for resistant and multiresistant strains, respectively) [704]. Other studies have found naturally occurring cells of *P. aeurginosa* were more resistant to a variety of disinfectants than were subcultured cells [705].

Uses. OPA has several potential advantages over glutaraldehyde. It has excellent stability over a wide pH range (pH 3–9), is not a known irritant to the eyes and nasal passages [706], does not require exposure monitoring, has a barely perceptible odor, and requires no activation. OPA, like glutaraldehyde, has excellent material compatibility. A potential disadvantage of OPA is that it stains proteins gray (including unprotected skin) and thus must be handled with caution [69]. However, skin staining would indicate improper handling that requires additional training and/or personal protective equipment (e.g., gloves, eye and mouth protection, and fluid-resistant gowns). OPA residues remaining on inadequately water-rinsed transesophageal echo probes can stain the patient's mouth [707]. Meticulous cleaning, using the correct OPA exposure time (e.g., 12 minutes) and copious rinsing of the probe with water should eliminate this problem. The results of one study provided a basis for a recommendation that rinsing of instruments disinfected with OPA will require at least 250 mL of water per channel to reduce the chemical residue to a level that will not compromise patient or staff safety (<1 ppm) [708]. Personal protective equipment should be worn when contaminated instruments, equipment, and chemicals are handled [400]. In addition, equipment must be thoroughly rinsed to prevent discoloration of a patient's skin or mucous membrane.

In April 2004, the manufacturer of OPA disseminated information to users about patients who reportedly experienced an anaphylaxis-like reaction after cystoscopy where the scope had been reprocessed using OPA. Of approximately 1 million urologic procedures performed using instruments reprocessed using OPA, 24 cases (17 cases in the United States, six in Japan, one in the United Kingdom) of anaphylaxis-like reactions have been reported after repeated cystoscopy (typically after four to nine treatments). Preventive measures include removal of OPA residues by thorough rinsing and not using OPA for reprocessing urologic instrumentation used to treat patients with a history of bladder cancer (Nevine Erian, personal communication, June 4, 2004; Product Notification, Advanced Sterilization Products, April 23, 2004) [709].

A few OPA clinical studies are available. In a clinical-use study, OPA exposure of 100 endoscopes for 5 minutes resulted in a >5-$\log_{10}$ reduction in bacterial load. Furthermore, OPA was effective over a 14-day use cycle [100]. Manufacturer data show that OPA will last longer in an automatic endoscope reprocessor before reaching its MEC limit (MEC after 82 cycles) than will glutaraldehyde (MEC after 40 cycles) [400]. High-pressure liquid chromatography confirmed that OPA levels are maintained above 0.3% for at least 50 cycles [706, 710]. OPA must be disposed in accordance with local and state regulations. If OPA disposal through the sanitary sewer system is restricted, glycine (25 grams/gallon) can be used to neutralize the OPA and make it safe for disposal.

The high-level disinfectant label claims for OPA solution at 20°C vary worldwide (e.g., 5 minutes in Europe, Asia, and Latin America; 10 minutes in Canada and Australia; and 12 minutes in the United States). These label claims differ worldwide because of differences in the test methodology and requirements for licensure. In an automated endoscope reprocessor with an FDA-cleared capability to maintain solution temperatures at 25°C, the contact time for OPA is 5 minutes.

Peracetic Acid

Overview. Peracetic, or peroxyacetic, acid is characterized by rapid action against all microorganisms. Special advantages of peracetic acid are that it lacks harmful decomposition products (i.e., acetic acid, water, oxygen, hydrogen peroxide), enhances removal of organic material [711], and leaves no residue. It remains effective in the presence of organic matter and is sporicidal even at low temperatures (Tables 4 and 5). Peracetic acid can corrode copper, brass, bronze, plain steel, and galvanized iron but these effects can be reduced by additives and pH modifications. It is considered unstable, particularly when diluted; for example, a 1% solution loses half its strength through hydrolysis in 6 days, whereas 40% peracetic acid loses 1%–2% of its active ingredients per month [654].

Mode of Action. Little is known about the mechanism of action of peracetic acid, but it is believed to function similarly to other oxidizing agents—that is, it denatures proteins, disrupts the cell wall permeability, and oxidizes sulfhydryl and sulfur bonds in proteins, enzymes, and other metabolites [654].

Microbicidal Activity. Peracetic acid will inactivate gram-positive and gram-negative bacteria, fungi, and yeasts in ≤5 minutes at <100 ppm. In the presence of organic matter, 200–500 ppm is required. For viruses, the dosage range is wide (12–2250 ppm), with poliovirus inactivated in yeast extract in 15 minutes with 1,500–2,250 ppm. In one study, 3.5% peracetic acid was ineffective against HAV after 1-minute exposure using a carrier test [58]. Peracetic acid (0.26%) was effective ($\log_{10}$ reduction factor >5) against all test strains of mycobacteria (*M. tuberculosis, M. avium-intracellulare, M. chelonae, and M. fortuitum*) within 20–30 minutes in the presence or absence of an organic load [607, 712]. With bacterial spores, 500–10,000 ppm (0.05%–1%) inactivates spores in 15 seconds to 30 minutes using a spore suspension test [654, 659, 713-715].

Uses. An automated machine using peracetic acid to chemically sterilize medical (e.g., endoscopes, arthroscopes), surgical, and dental instruments is used in the United States[716-718]. As previously noted, dental handpieces should be steam sterilized. The sterilant, 35% peracetic acid, is diluted to 0.2% with filtered water at 50°C. Simulated-use trials have demonstrated excellent microbicidal activity [111, 718-722], and three clinical trials have demonstrated both excellent microbial killing and no clinical failures leading to infection[90, 723, 724]. The high efficacy of the system was demonstrated in a comparison of the efficacies of the system with that of ethylene oxide. Only the peracetic acid system completely killed 6 $\log_{10}$ of *M. chelonae, E. faecalis,* and *B. atrophaeus* spores with both an organic and inorganic challenge[722]. An investigation that compared the costs, performance, and maintenance of urologic endoscopic equipment processed by high-level disinfection (with glutaraldehyde) with those of the peracetic acid system reported no clinical differences between the two systems. However, the use of this system led to higher costs than the high-level disinfection, including costs for processing ($6.11 vs. $0.45 per cycle), purchasing and training ($24,845 vs. $16), installation ($5,800 vs. $0), and endoscope repairs ($6,037 vs. $445) [90]. Furthermore, three clusters of infection using the peracetic acid automated endoscope reprocessor were linked to inadequately processed bronchoscopes when inappropriate channel connectors were used with the system [725]. These clusters highlight the importance of training, proper model-specific endoscope connector systems, and quality-control procedures to ensure compliance with endoscope manufacturer recommendations and professional organization guidelines. An alternative high-level disinfectant available in the United Kingdom contains 0.35% peracetic acid. Although this product is rapidly effective against a broad range of microorganisms [466, 726, 727], it tarnishes the metal of endoscopes and is unstable, resulting in only a 24-hour use life [727].

Peracetic Acid and Hydrogen Peroxide

Overview. Two chemical sterilants are available that contain peracetic acid plus hydrogen peroxide (i.e., 0.08% peracetic acid plus 1.0% hydrogen peroxide [no longer marketed]; and 0.23% peracetic acid plus 7.35% hydrogen peroxide (Tables 4 and 5).

Microbicidal Activity. The bactericidal properties of peracetic acid and hydrogen peroxide have been demonstrated [728]. Manufacturer data demonstrated this combination of peracetic acid and

hydrogen peroxide inactivated all microorganisms except bacterial spores within 20 minutes. The 0.08% peracetic acid plus 1.0% hydrogen peroxide product effectively inactivated glutaraldehyde-resistant mycobacteria[729].

Uses. The combination of peracetic acid and hydrogen peroxide has been used for disinfecting hemodialyzers [730]. The percentage of dialysis centers using a peracetic acid-hydrogen peroxide-based disinfectant for reprocessing dialyzers increased from 5% in 1983 to 56% in 1997[249]. Olympus America does not endorse use of 0.08% peracetic acid plus 1.0% hydrogen peroxide (Olympus America, personal communication, April 15, 1998) on any Olympus endoscope because of cosmetic and functional damage and will not assume liability for chemical damage resulting from use of this product. This product is not currently available. FDA has cleared a newer chemical sterilant with 0.23% peracetic acid and 7.35% hydrogen peroxide (Tables 4 and 5). After testing the 7.35% hydrogen peroxide and 0.23% peracetic acid product, Olympus America concluded it was not compatible with the company's flexible gastrointestinal endoscopes; this conclusion was based on immersion studies where the test insertion tubes had failed because of swelling and loosening of the black polymer layer of the tube (Olympus America, personal communication, September 13, 2000).

Phenolics

Overview. Phenol has occupied a prominent place in the field of hospital disinfection since its initial use as a germicide by Lister in his pioneering work on antiseptic surgery. In the past 30 years, however, work has concentrated on the numerous phenol derivatives or phenolics and their antimicrobial properties. Phenol derivatives originate when a functional group (e.g., alkyl, phenyl, benzyl, halogen) replaces one of the hydrogen atoms on the aromatic ring. Two phenol derivatives commonly found as constituents of hospital disinfectants are *ortho*-phenylphenol and *ortho*-benzyl-*para*-chlorophenol. The antimicrobial properties of these compounds and many other phenol derivatives are much improved over those of the parent chemical. Phenolics are absorbed by porous materials, and the residual disinfectant can irritate tissue. In 1970, depigmentation of the skin was reported to be caused by phenolic germicidal detergents containing *para*-tertiary butylphenol and *para*-tertiary amylphenol [731].

Mode of Action. In high concentrations, phenol acts as a gross protoplasmic poison, penetrating and disrupting the cell wall and precipitating the cell proteins. Low concentrations of phenol and higher molecular-weight phenol derivatives cause bacterial death by inactivation of essential enzyme systems and leakage of essential metabolites from the cell wall [732].

Microbicidal Activity. Published reports on the antimicrobial efficacy of commonly used phenolics showed they were bactericidal, fungicidal, virucidal, and tuberculocidal [14, 61, 71, 73, 227, 416, 573, 732-738]. One study demonstrated little or no virucidal effect of a phenolic against coxsackie B4, echovirus 11, and poliovirus 1 [736]. Similarly, 12% *ortho*-phenylphenol failed to inactivate any of the three hydrophilic viruses after a 10-minute exposure time, although 5% phenol was lethal for these viruses [72]. A 0.5% dilution of a phenolic (2.8% *ortho*-phenylphenol and 2.7% *ortho*-benzyl-*para*-chlorophenol) inactivated HIV [227] and a 2% solution of a phenolic (15% ortho-phenylphenol and 6.3% para-tertiary-amylphenol) inactivated all but one of 11 fungi tested [71].

Manufacturers' data using the standardized AOAC methods demonstrate that commercial phenolics are not sporicidal but are tuberculocidal, fungicidal, virucidal, and bactericidal at their recommended use-dilution. Attempts to substantiate the bactericidal label claims of phenolics using the AOAC Use-Dilution Method occasionally have failed [416, 737]. However, results from these same studies have varied dramatically among laboratories testing identical products.

Uses. Many phenolic germicides are EPA-registered as disinfectants for use on environmental surfaces (e.g., bedside tables, bedrails, and laboratory surfaces) and noncritical medical devices. Phenolics are not FDA-cleared as high-level disinfectants for use with semicritical items but could be used to preclean or decontaminate critical and semicritical devices before terminal sterilization or high-

level disinfection.

The use of phenolics in nurseries has been questioned because of hyperbilirubinemia in infants placed in bassinets where phenolic detergents were used [739]. In addition, bilirubin levels were reported to increase in phenolic-exposed infants, compared with nonphenolic-exposed infants, when the phenolic was prepared according to the manufacturers' recommended dilution [740]. If phenolics are used to clean nursery floors, they must be diluted as recommended on the product label. Phenolics (and other disinfectants) should not be used to clean infant bassinets and incubators while occupied. If phenolics are used to terminally clean infant bassinets and incubators, the surfaces should be rinsed thoroughly with water and dried before reuse of infant bassinets and incubators [17].

Quaternary Ammonium Compounds

Overview. The quaternary ammonium compounds are widely used as disinfectants. Health-care–associated infections have been reported from contaminated quaternary ammonium compounds used to disinfect patient-care supplies or equipment, such as cystoscopes or cardiac catheters [741, 742]. The quaternaries are good cleaning agents, but high water hardness [743] and materials such as cotton and gauze pads can make them less microbicidal because of insoluble precipitates or cotton and gauze pads absorb the active ingredients, respectively. One study showed a significant decline (~40%–50% lower at 1 hour) in the concentration of quaternaries released when cotton rags or cellulose-based wipers were used in the open-bucket system, compared with the nonwoven spunlace wipers in the closed-bucket system [744] As with several other disinfectants (e.g., phenolics, iodophors) gram-negative bacteria can survive or grow in them [404].

Chemically, the quaternaries are organically substituted ammonium compounds in which the nitrogen atom has a valence of 5, four of the substituent radicals (R1-R4) are alkyl or heterocyclic radicals of a given size or chain length, and the fifth (X^-) is a halide, sulfate, or similar radical [745]. Each compound exhibits its own antimicrobial characteristics, hence the search for one compound with outstanding antimicrobial properties. Some of the chemical names of quaternary ammonium compounds used in healthcare are alkyl dimethyl benzyl ammonium chloride, alkyl didecyl dimethyl ammonium chloride, and dialkyl dimethyl ammonium chloride. The newer quaternary ammonium compounds (i.e., fourth generation), referred to as twin-chain or dialkyl quaternaries (e.g. didecyl dimethyl ammonium bromide and dioctyl dimethyl ammonium bromide), purportedly remain active in hard water and are tolerant of anionic residues [746].

A few case reports have documented occupational asthma as a result of exposure to benzalkonium chloride [747].

Mode of Action. The bactericidal action of the quaternaries has been attributed to the inactivation of energy-producing enzymes, denaturation of essential cell proteins, and disruption of the cell membrane[746]. Evidence exists that supports these and other possibilities [745 748].

Microbicidal Activity. Results from manufacturers' data sheets and from published scientific literature indicate that the quaternaries sold as hospital disinfectants are generally fungicidal, bactericidal, and virucidal against lipophilic (enveloped) viruses; they are not sporicidal and generally not tuberculocidal or virucidal against hydrophilic (nonenveloped) viruses [14, 54-56, 58, 59, 61, 71, 73, 186, 297, 748, 749]. The poor mycobactericidal activities of quaternary ammonium compounds have been demonstrated [55, 73]. Quaternary ammonium compounds (as well as 70% isopropyl alcohol, phenolic, and a chlorine-containing wipe [80 ppm]) effectively (>95%) remove and/or inactivate contaminants (i.e., multidrug-resistant *S. aureus*, vancomycin-resistant *Enterococcus*, *P. aeruginosa*) from computer keyboards with a 5-second application time. No functional damage or cosmetic changes occurred to the computer keyboards after 300 applications of the disinfectants [45].

Attempts to reproduce the manufacturers' bactericidal and tuberculocidal claims using the AOAC

tests with a limited number of quaternary ammonium compounds occasionally have failed [73, 416, 737]. However, test results have varied extensively among laboratories testing identical products [416, 737].

Uses. The quaternaries commonly are used in ordinary environmental sanitation of noncritical surfaces, such as floors, furniture, and walls. EPA-registered quaternary ammonium compounds are appropriate to use for disinfecting medical equipment that contacts intact skin (e.g., blood pressure cuffs).

MISCELLANEOUS INACTIVATING AGENTS

Other Germicides

Several compounds have antimicrobial activity but for various reasons have not been incorporated into the armamentarium of health-care disinfectants. These include mercurials, sodium hydroxide, β-propiolactone, chlorhexidine gluconate, cetrimide-chlorhexidine, glycols (triethylene and propylene), and the Tego disinfectants. Two authoritative references examine these agents in detail [16, 412].

A peroxygen-containing formulation had marked bactericidal action when used as a 1% weight/volume solution and virucidal activity at 3% [49], but did not have mycobactericidal activity at concentrations of 2.3% and 4% and exposure times ranging from 30 to 120 minutes [750]. It also required 20 hours to kill *B. atrophaeus* spores [751]. A powder-based peroxygen compound for disinfecting contaminated spill was strongly and rapidly bactericidal [752].

In preliminary studies, nanoemulsions (composed of detergents and lipids in water) showed activity against vegetative bacteria, enveloped viruses and *Candida*. This product represents a potential agent for use as a topical biocidal agent. [753-755].

New disinfectants that require further evaluation include glucoprotamin[756], tertiary amines [703], and a light-activated antimicrobial coating [757]. Several other disinfection technologies might have potential applications in the healthcare setting [758].

Metals as Microbicides

Comprehensive reviews of antisepsis [759], disinfection[421], and anti-infective chemotherapy [760] barely mention the antimicrobial activity of heavy metals[761, 762]. Nevertheless, the anti-infective activity of some heavy metals has been known since antiquity. Heavy metals such as silver have been used for prophylaxis of conjunctivitis of the newborn, topical therapy for burn wounds, and bonding to indwelling catheters, and the use of heavy metals as antiseptics or disinfectants is again being explored [763]. Inactivation of bacteria on stainless steel surfaces by zeolite ceramic coatings containing silver and zinc ions has also been demonstrated [764, 765].

Metals such as silver, iron, and copper could be used for environmental control, disinfection of water, or reusable medical devices or incorporated into medical devices (e.g., intravascular catheters) [400, 761-763, 766-770]. A comparative evaluation of six disinfectant formulations for residual antimicrobial activity demonstrated that only the silver disinfectant demonstrated significant residual activity against *S. aureus* and *P. aeruginosa* [763]. Preliminary data suggest metals are effective against a wide variety of microorganisms.

Clinical uses of other heavy metals include copper-8-quinolinolate as a fungicide against *Aspergillus*, copper-silver ionization for *Legionella* disinfection [771-774], organic mercurials as an antiseptic (e.g., mercurochrome) and preservative/disinfectant (e.g., thimerosal [currently being removed from vaccines]) in pharmaceuticals and cosmetics [762].

Ultraviolet Radiation (UV)

The wavelength of UV radiation ranges from 328 nm to 210 nm (3280 A to 2100 A). Its maximum bactericidal effect occurs at 240–280 nm. Mercury vapor lamps emit more than 90% of their radiation at 253.7 nm, which is near the maximum microbicidal activity [775]. Inactivation of microorganisms results from destruction of nucleic acid through induction of thymine dimers. UV radiation has been employed in the disinfection of drinking water [776], air [775], titanium implants [777], and contact lenses[778]. Bacteria and viruses are more easily killed by UV light than are bacterial spores [775]. UV radiation has several potential applications, but unfortunately its germicidal effectiveness and use is influenced by organic matter; wavelength; type of suspension; temperature; type of microorganism; and UV intensity, which is affected by distance and dirty tubes[779]. The application of UV radiation in the health-care environment (i.e.,

operating rooms, isolation rooms, and biologic safety cabinets) is limited to destruction of airborne organisms or inactivation of microorganisms on surfaces. The effect of UV radiation on postoperative wound infections was investigated in a double-blind, randomized study in five university medical centers. After following 14,854 patients over a 2-year period, the investigators reported the overall wound infection rate was unaffected by UV radiation, although postoperative infection in the "refined clean" surgical procedures decreased significantly (3.8%–2.9%) [780]. No data support the use of UV lamps in isolation rooms, and this practice has caused at least one epidemic of UV-induced skin erythema and keratoconjunctivitis in hospital patients and visitors [781].

Pasteurization

Pasteurization is not a sterilization process; its purpose is to destroy all pathogenic microorganisms. However, pasteurization does not destroy bacterial spores. The time-temperature relation for hot-water pasteurization is generally ~70°C (158°F) for 30 minutes. The water temperature and time should be monitored as part of a quality-assurance program [782]. Pasteurization of respiratory therapy [783, 784] and anesthesia equipment [785] is a recognized alternative to chemical disinfection. The efficacy of this process has been tested using an inoculum that the authors believed might simulate contamination by an infected patient. Use of a large inoculum (10^7) of *P. aeruginosa* or *Acinetobacter calcoaceticus* in sets of respiratory tubing before processing demonstrated that machine-assisted chemical processing was more efficient than machine-assisted pasteurization with a disinfection failure rate of 6% and 83%, respectively [783]. Other investigators found hot water disinfection to be effective (inactivation factor >5 $\log_{10}$) against multiple bacteria, including multidrug-resistant bacteria, for disinfecting reusable anesthesia or respiratory therapy equipment [784-786].

Flushing- and Washer-Disinfectors

Flushing- and washer-disinfectors are automated and closed equipment that clean and disinfect objects from bedpans and washbowls to surgical instruments and anesthesia tubes. Items such as bedpans and urinals can be cleaned and disinfected in flushing-disinfectors. They have a short cycle of a few minutes. They clean by flushing with warm water, possibly with a detergent, and then disinfect by flushing the items with hot water or with steam. Because this machine empties, cleans, and disinfects, manual cleaning is eliminated, fewer disposable items are needed, and fewer chemical germicides are used. A microbiologic evaluation of one washer/disinfector demonstrated complete inactivation of suspensions of *E. faecalis* or poliovirus [787]. Other studies have shown that strains of *Enterococcus faecium* can survive the British Standard for heat disinfection of bedpans (80°C for 1 minute). The significance of this finding with reference to the potential for enterococci to survive and disseminate in the health-care environment is debatable [788-790]. These machines are available and used in many European countries.

Surgical instruments and anesthesia equipment are more difficult to clean. They are run in washer-disinfectors on a longer cycle of approximately 20–30 minutes with a detergent. These machines also disinfect by hot water at approximately 90°C [791].

THE REGULATORY FRAMEWORK FOR DISINFECTANTS AND STERILANTS

Before using the guidance provided in this document, health-care workers should be aware of the federal laws and regulations that govern the sale, distribution, and use of disinfectants and sterilants. In particular, health-care workers need to know what requirements pertain to them when they apply these products. Finally, they should understand the relative roles of EPA, FDA, and CDC so the context for the guidance provided in this document is clear.

EPA and FDA

In the United States, chemical germicides formulated as sanitizers, disinfectants, or sterilants are regulated in interstate commerce by the Antimicrobials Division, Office of Pesticides Program, EPA, under the authority of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) of 1947, as amended [792]. Under FIFRA, any substance or mixture of substances intended to prevent, destroy, repel, or mitigate any pest (including microorganisms but excluding those in or on living humans or animals) must be registered before sale or distribution. To obtain a registration, a manufacturer must submit specific data about the safety and effectiveness of each product. For example, EPA requires manufacturers of sanitizers, disinfectants, or chemical sterilants to test formulations by using accepted methods for microbiocidal activity, stability, and toxicity to animals and humans. The manufacturers submit these data to EPA along with proposed labeling. If EPA concludes the product can be used without causing "unreasonable adverse effects," then the product and its labeling are registered, and the manufacturer can sell and distribute the product in the United States.

FIFRA also requires users of products to follow explicitly the labeling directions on each product. The following standard statement appears on all labels under the "Directions for Use" heading: "It is a violation of federal law to use this product in a manner inconsistent with its labeling." This statement means a health-care worker must follow the safety precautions and use directions on the labeling of each registered product. Failure to follow the specified use-dilution, contact time, method of application, or any other condition of use is considered a misuse of the product and potentially subject to enforcement action under FIFRA.

In general, EPA regulates disinfectants and sterilants used on environmental surfaces, and not those used on critical or semicritical medical devices; the latter are regulated by FDA. In June 1993, FDA and EPA issued a "Memorandum of Understanding" that divided responsibility for review and surveillance of chemical germicides between the two agencies. Under the agreement, FDA regulates liquid chemical sterilants used on critical and semicritical devices, and EPA regulates disinfectants used on noncritical surfaces and gaseous sterilants [793]. In 1996, Congress passed the Food Quality Protection Act (FQPA). This act amended FIFRA in regard to several types of products regulated by both EPA and FDA. One provision of FQPA removed regulation of liquid chemical sterilants used on critical and semicritical medical devices from EPA's jurisdiction, and it now rests solely with FDA [792, 794]. EPA continues to register nonmedical chemical sterilants. FDA and EPA have considered the impact of FQPA, and in January 2000, FDA published its final guidance document on product submissions and labeling. Antiseptics are considered antimicrobial drugs used on living tissue and thus are regulated by FDA under the Food, Drug and Cosmetic Act. FDA regulates liquid chemical sterilants and high-level disinfectants intended to process critical and semicritical devices. FDA has published recommendations on the types of test methods that manufacturers should submit to FDA for 510[k] clearance for such agents.

CDC

At CDC, the mission of the Coordinating Center for Infections Diseases is to guide the public on how to prevent and respond to infectious diseases in both health-care settings and at home. With respect to disinfectants and sterilants, part of CDC's role is to inform the public (in this case healthcare personnel) of current scientific evidence pertaining to these products, to comment about their safety and efficacy, and to recommend which chemicals might be most appropriate or effective for specific microorganisms and settings.

Test Methods

The methods EPA has used for registration are standardized by the AOAC International; however, a survey of scientific literature reveals a number of problems with these tests that were reported during 1987–1990 [58, 76, 80, 428, 736, 737, 795-800] that cause them to be neither accurate nor reproducible [416, 737]. As part of their regulatory authority, EPA and FDA support development and validation of methods for assessing disinfection claims [801-803]. For example, EPA has supported the work of Dr. Syed Sattar and coworkers who have developed a two-tier quantitative carrier test to assess sporicidal, mycobactericidal, bactericidal, fungicidal, virucidal, and protozoacidal activity of chemical germicides [701, 803]. EPA is accepting label claims against hepatitis B virus (HBV) using a surrogate organism, the duck HBV, to quantify disinfectant activity [124, 804]. EPA also is accepting labeling claims against hepatitis C virus using the bovine viral diarrhea virus as a surrogate.

For nearly 30 years, EPA also performed intramural preregistration and postregistration efficacy testing of some chemical disinfectants in its own laboratories. In 1982, this was stopped, reportedly for budgetary reasons. At that time, manufacturers did not need to have microbiologic activity claims verified by EPA or an independent testing laboratory when registering a disinfectant or chemical sterilant [805]. This occurred when the frequency of contaminated germicides and infections secondary to their use had increased [404]. Investigations demonstrating that interlaboratory reproducibility of test results was poor and manufacturers' label claims were not verifiable [416, 737] and symposia sponsored by the American Society for Microbiology [800] heightened awareness of these problems and reconfirmed the need to improve the AOAC methods and reinstate a microbiologic activity verification program. A General Accounting Office report entitled *Disinfectants: EPA Lacks Assurance They Work* [806] seemed to provide the necessary impetus for EPA to initiate corrective measures, including cooperative agreements to improve the AOAC methods and independent verification testing for all products labeled as sporicidal and disinfectants labeled as tuberculocidal. For example, of 26 sterilant products tested by EPA, 15 were canceled because of product failure. A list of products registered with EPA and labeled for use as sterilants or tuberculocides or against HIV and/or HBV is available through EPA's website at http://www.epa.gov/oppad001/chemregindex.htm. Organizations (e.g., Organization for Economic Cooperation and Development) are working to standardize requirements for germicide testing and registration.

Neutralization of Germicides

One of the difficulties associated with evaluating the bactericidal activity of disinfectants is prevention of bacteriostasis from disinfectant residues carried over into the subculture media. Likewise, small amounts of disinfectants on environmental surfaces can make an accurate bacterial count difficult to get when sampling of the health-care environment as part of an epidemiologic or research investigation. One way these problems may be overcome is by employing neutralizers that inactivate residual disinfectants [807-809]. Two commonly used neutralizing media for chemical disinfectants are Letheen Media and D/E Neutralizing Media. The former contains lecithin to neutralize quaternaries and polysorbate 80 (Tween 80) to neutralize phenolics, hexachlorophene, formalin, and, with lecithin, ethanol. The D/E Neutralizing media will neutralize a broad spectrum of antiseptic and disinfectant chemicals, including quaternary ammonium compounds, phenols, iodine and chlorine compounds, mercurials, formaldehyde, and glutaraldehyde [810]. A review of neutralizers used in germicide testing has been published[808].

STERILIZATION

Most medical and surgical devices used in healthcare facilities are made of materials that are heat stable and therefore undergo heat, primarily steam, sterilization. However, since 1950, there has been an increase in medical devices and instruments made of materials (e.g., plastics) that require low-temperature sterilization. Ethylene oxide gas has been used since the 1950s for heat- and moisture-sensitive medical devices. Within the past 15 years, a number of new, low-temperature sterilization systems (e.g., hydrogen peroxide gas plasma, peracetic acid immersion, ozone) have been developed and are being used to sterilize medical devices. This section reviews sterilization technologies used in healthcare and makes recommendations for their optimum performance in the processing of medical devices [1, 18, 811-820].

Sterilization destroys all microorganisms on the surface of an article or in a fluid to prevent disease transmission associated with the use of that item. While the use of inadequately sterilized critical items represents a high risk of transmitting pathogens, documented transmission of pathogens associated with an inadequately sterilized critical item is exceedingly rare [821, 822]. This is likely due to the wide margin of safety associated with the sterilization processes used in healthcare facilities. The concept of what constitutes "sterile" is measured as a probability of sterility for each item to be sterilized. This probability is commonly referred to as the sterility assurance level (SAL) of the product and is defined as the probability of a single viable microorganism occurring on a product after sterilization. SAL is normally expressed a 10^{-n}. For example, if the probability of a spore surviving were one in one million, the SAL would be 10^{-6} [823, 824]. In short, a SAL is an estimate of lethality of the entire sterilization process and is a conservative calculation. Dual SALs (e.g., 10^{-3} SAL for blood culture tubes, drainage bags; 10^{-6} SAL for scalpels, implants) have been used in the United States for many years and the choice of a 10^{-6} SAL was strictly arbitrary and not associated with any adverse outcomes (e.g., patient infections) [823].

Medical devices that have contact with sterile body tissues or fluids are considered critical items. These items should be sterile when used because any microbial contamination could result in disease transmission. Such items include surgical instruments, biopsy forceps, and implanted medical devices. If these items are heat resistant, the recommended sterilization process is steam sterilization, because it has the largest margin of safety due to its reliability, consistency, and lethality. However, reprocessing heat- and moisture-sensitive items requires use of a low-temperature sterilization technology (e.g., ethylene oxide, hydrogen peroxide gas plasma, peracetic acid) [825]. A summary of the advantages and disadvantages for commonly used sterilization technologies is presented in Table 6.

Steam Sterilization

Overview. Of all the methods available for sterilization, moist heat in the form of saturated steam under pressure is the most widely used and the most dependable. Steam sterilization is nontoxic, inexpensive [826], rapidly microbicidal, sporicidal, and rapidly heats and penetrates fabrics (Table 6) [827]. Like all sterilization processes, steam sterilization has some deleterious effects on some materials, including corrosion and combustion of lubricants associated with dental handpieces[212]; reduction in ability to transmit light associated with laryngoscopes[828]; and increased hardening time (5.6 fold) with plaster-cast [829].

The basic principle of steam sterilization, as accomplished in an autoclave, is to expose each item to direct steam contact at the required temperature and pressure for the specified time. Thus, there are four parameters of steam sterilization: steam, pressure, temperature, and time. The ideal steam for sterilization is dry saturated steam and entrained water (dryness fraction ≥97%)[813, 819]. Pressure serves as a means to obtain the high temperatures necessary to quickly kill microorganisms. Specific temperatures must be obtained to ensure the microbicidal activity. The two common steam-sterilizing temperatures are 121°C (250°F) and 132°C (270°F). These temperatures (and other high temperatures) [830] must be maintained for a minimal time to kill microorganisms. Recognized minimum exposure periods for sterilization of wrapped healthcare supplies are 30 minutes at 121°C (250°F) in a gravity displacement

sterilizer or 4 minutes at 132°C (270°C) in a prevacuum sterilizer (Table 7). At constant temperatures, sterilization times vary depending on the type of item (e.g., metal versus rubber, plastic, items with lumens), whether the item is wrapped or unwrapped, and the sterilizer type.

The two basic types of steam sterilizers (autoclaves) are the gravity displacement autoclave and the high-speed prevacuum sterilizer. In the former, steam is admitted at the top or the sides of the sterilizing chamber and, because the steam is lighter than air, forces air out the bottom of the chamber through the drain vent. The gravity displacement autoclaves are primarily used to process laboratory media, water, pharmaceutical products, regulated medical waste, and nonporous articles whose surfaces have direct steam contact. For gravity displacement sterilizers the penetration time into porous items is prolonged because of incomplete air elimination. This point is illustrated with the decontamination of 10 lbs of microbiological waste, which requires at least 45 minutes at 121°C because the entrapped air remaining in a load of waste greatly retards steam permeation and heating efficiency[831, 832]. The high-speed prevacuum sterilizers are similar to the gravity displacement sterilizers except they are fitted with a vacuum pump (or ejector) to ensure air removal from the sterilizing chamber and load before the steam is admitted. The advantage of using a vacuum pump is that there is nearly instantaneous steam penetration even into porous loads. The Bowie-Dick test is used to detect air leaks and inadequate air removal and consists of folded 100% cotton surgical towels that are clean and preconditioned. A commercially available Bowie-Dick-type test sheet should be placed in the center of the pack. The test pack should be placed horizontally in the front, bottom section of the sterilizer rack, near the door and over the drain, in an otherwise empty chamber and run at 134°C for 3.5 minutes[813, 819]. The test is used each day the vacuum-type steam sterilizer is used, before the first processed load. Air that is not removed from the chamber will interfere with steam contact. Smaller disposable test packs (or process challenge devices) have been devised to replace the stack of folded surgical towels for testing the efficacy of the vacuum system in a prevacuum sterilizer. [833] These devices are "designed to simulate product to be sterilized and to constitute a defined challenge to the sterilization process"[819, 834]. They should be representative of the load and simulate the greatest challenge to the load[835]. Sterilizer vacuum performance is acceptable if the sheet inside the test pack shows a uniform color change. Entrapped air will cause a spot to appear on the test sheet, due to the inability of the steam to reach the chemical indicator. If the sterilizer fails the Bowie-Dick test, do not use the sterilizer until it is inspected by the sterilizer maintenance personnel and passes the Bowie-Dick test[813, 819, 836].

Another design in steam sterilization is a steam flush-pressure pulsing process, which removes air rapidly by repeatedly alternating a steam flush and a pressure pulse above atmospheric pressure. Air is rapidly removed from the load as with the prevacuum sterilizer, but air leaks do not affect this process because the steam in the sterilizing chamber is always above atmospheric pressure. Typical sterilization temperatures and times are 132°C to 135°C with 3 to 4 minutes exposure time for porous loads and instruments[827, 837].

Like other sterilization systems, the steam cycle is monitored by mechanical, chemical, and biological monitors. Steam sterilizers usually are monitored using a printout (or graphically) by measuring temperature, the time at the temperature, and pressure. Typically, chemical indicators are affixed to the outside and incorporated into the pack to monitor the temperature or time and temperature. The effectiveness of steam sterilization is monitored with a biological indicator containing spores of *Geobacillus stearothermophilus* (formerly *Bacillus stearothermophilus*). Positive spore test results are a relatively rare event [838] and can be attributed to operator error, inadequate steam delivery[839], or equipment malfunction.

Portable (table-top) steam sterilizers are used in outpatient, dental, and rural clinics[840]. These sterilizers are designed for small instruments, such as hypodermic syringes and needles and dental instruments. The ability of the sterilizer to reach physical parameters necessary to achieve sterilization should be monitored by mechanical, chemical, and biological indicators.

Microbicidal Activity. The oldest and most recognized agent for inactivation of microorganisms is heat. D-values (time to reduce the surviving population by 90% or 1 $\log_{10}$) allow a direct comparison of the heat resistance of microorganisms. Because a D-value can be determined at various temperatures, a subscript is used to designate the exposure temperature (i.e., D_{121C}). D_{121C}-values for *Geobacillus stearothermophilus* used to monitor the steam sterilization process range from 1 to 2 minutes. Heat-resistant nonspore-forming bacteria, yeasts, and fungi have such low D_{121C} values that they cannot be experimentally measured[841].

Mode of Action. Moist heat destroys microorganisms by the irreversible coagulation and denaturation of enzymes and structural proteins. In support of this fact, it has been found that the presence of moisture significantly affects the coagulation temperature of proteins and the temperature at which microorganisms are destroyed.

Uses. Steam sterilization should be used whenever possible on all critical and semicritical items that are heat and moisture resistant (e.g., steam sterilizable respiratory therapy and anesthesia equipment), even when not essential to prevent pathogen transmission. Steam sterilizers also are used in healthcare facilities to decontaminate microbiological waste and sharps containers [831, 832, 842] but additional exposure time is required in the gravity displacement sterilizer for these items.

Flash Sterilization

Overview. "Flash" steam sterilization was originally defined by Underwood and Perkins as sterilization of an unwrapped object at 132°C for 3 minutes at 27-28 lbs. of pressure in a gravity displacement sterilizer[843]. Currently, the time required for flash sterilization depends on the type of sterilizer and the type of item (i.e., porous vs non-porous items)(see Table 8). Although the wrapped method of sterilization is preferred for the reasons listed below, correctly performed flash sterilization is an effective process for the sterilization of critical medical devices[844, 845]. Flash sterilization is a modification of conventional steam sterilization (either gravity, prevacuum, or steam-flush pressure-pulse) in which the flashed item is placed in an open tray or is placed in a specially designed, covered, rigid container to allow for rapid penetration of steam. Historically, it is not recommended as a routine sterilization method because of the lack of timely biological indicators to monitor performance, absence of protective packaging following sterilization, possibility for contamination of processed items during transportation to the operating rooms, and the sterilization cycle parameters (i.e., time, temperature, pressure) are minimal. To address some of these concerns, many healthcare facilities have done the following: placed equipment for flash sterilization in close proximity to operating rooms to facilitate aseptic delivery to the point of use (usually the sterile field in an ongoing surgical procedure); extended the exposure time to ensure lethality comparable to sterilized wrapped items (e.g., 4 minutes at 132°C)[846, 847]; used biological indicators that provide results in 1 hour for flash-sterilized items[846, 847]; and used protective packaging that permits steam penetration[812, 817-819, 845, 848]. Further, some rigid, reusable sterilization container systems have been designed and validated by the container manufacturer for use with flash cycles. When sterile items are open to air, they will eventually become contaminated. Thus, the longer a sterile item is exposed to air, the greater the number of microorganisms that will settle on it. Sterilization cycle parameters for flash sterilization are shown in Table 8.

A few adverse events have been associated with flash sterilization. When evaluating an increased incidence of neurosurgical infections, the investigators noted that surgical instruments were flash sterilized between cases and 2 of 3 craniotomy infections involved plate implants that were flash sterilized[849]. A report of two patients who received burns during surgery from instruments that had been flash sterilized reinforced the need to develop policies and educate staff to prevent the use of instruments hot enough to cause clinical burns[850]. Staff should use precautions to prevent burns with potentially hot instruments (e.g., transport tray using heat-protective gloves). Patient burns may be prevented by either air-cooling the instruments or immersion in sterile liquid (e.g., saline).

Uses. Flash sterilization is considered acceptable for processing cleaned patient-care items that

cannot be packaged, sterilized, and stored before use. It also is used when there is insufficient time to sterilize an item by the preferred package method. Flash sterilization should not be used for reasons of convenience, as an alternative to purchasing additional instrument sets, or to save time[817]. Because of the potential for serious infections, flash sterilization is not recommended for implantable devices (i.e., devices placed into a surgically or naturally formed cavity of the human body); however, flash sterilization may be unavoidable for some devices (e.g., orthopedic screw, plates). If flash sterilization of an implantable device is unavoidable, recordkeeping (i.e., load identification, patient's name/hospital identifier, and biological indicator result) is essential for epidemiological tracking (e.g., of surgical site infection, tracing results of biological indicators to patients who received the item to document sterility), and for an assessment of the reliability of the sterilization process (e.g., evaluation of biological monitoring records and sterilization maintenance records noting preventive maintenance and repairs with dates).

Low-Temperature Sterilization Technologies

Ethylene oxide (ETO) has been widely used as a low-temperature sterilant since the 1950s. It has been the most commonly used process for sterilizing temperature- and moisture-sensitive medical devices and supplies in healthcare institutions in the United States. Two types of ETO sterilizers are available, mixed gas and 100% ETO. Until 1995, ethylene oxide sterilizers combined ETO with a chloroflourocarbon (CFC) stabilizing agent, most commonly in a ratio of 12% ETO mixed with 88% CFC (referred to as 12/88 ETO).

For several reasons, healthcare personnel have been exploring the use of new low-temperature sterilization technologies[825, 851]. First, CFCs were phased out in December 1995 under provisions of the Clean Air Act [852]. CFCs were classified as a Class I substance under the Clean Air Act because of scientific evidence linking them to destruction of the earth's ozone layer. Second, some states (e.g., California, New York, Michigan) require the use of ETO abatement technology to reduce the amount of ETO being released into ambient air from 90 to 99.9% depending on the state. Third, OSHA regulates the acceptable vapor levels of ETO (i.e., 1 ppm averaged over 8 hours) due to concerns that ETO exposure represents an occupational hazard[318]. These constraints have led to the development of alternative technologies for low-temperature sterilization in the healthcare setting.

Alternative technologies to ETO with chlorofluorocarbon that are currently available and cleared by the FDA for medical equipment include 100% ETO; ETO with a different stabilizing gas, such as carbon dioxide or hydrochlorofluorocarbons (HCFC); immersion in peracetic acid; hydrogen peroxide gas plasma; and ozone. Technologies under development for use in healthcare facilities, but not cleared by the FDA, include vaporized hydrogen peroxide, vapor phase peracetic acid, gaseous chlorine dioxide, ionizing radiation, or pulsed light [400, 758, 853]. However, there is no guarantee that these new sterilization technologies will receive FDA clearance for use in healthcare facilities.

These new technologies should be compared against the characteristics of an ideal low-temperature (<60°C) sterilant (Table 9). [851] While it is apparent that all technologies will have limitations (Table 9), understanding the limitations imposed by restrictive device designs (e.g., long, narrow lumens) is critical for proper application of new sterilization technology[854]. For example, the development of increasingly small and complex endoscopes presents a difficult challenge for current sterilization processes. This occurs because microorganisms must be in direct contact with the sterilant for inactivation to occur. Several peer-reviewed scientific publications have data demonstrating concerns about the efficacy of several of the low-temperature sterilization processes (i.e., gas plasma, vaporized hydrogen peroxide, ETO, peracetic acid), particularly when the test organisms are challenged in the presence of serum and salt and a narrow lumen vehicle[469, 721, 825, 855, 856]. Factors shown to affect the efficacy of sterilization are shown in Table 10.

Ethylene Oxide "Gas" Sterilization

Overview. ETO is a colorless gas that is flammable and explosive. The four essential

parameters (operational ranges) are: gas concentration (450 to 1200 mg/l); temperature (37 to 63°C); relative humidity (40 to 80%)(water molecules carry ETO to reactive sites); and exposure time (1 to 6 hours). These influence the effectiveness of ETO sterilization[814, 857, 858]. Within certain limitations, an increase in gas concentration and temperature may shorten the time necessary for achieving sterilization.

The main disadvantages associated with ETO are the lengthy cycle time, the cost, and its potential hazards to patients and staff; the main advantage is that it can sterilize heat- or moisture-sensitive medical equipment without deleterious effects on the material used in the medical devices (Table 6). Acute exposure to ETO may result in irritation (e.g., to skin, eyes, gastrointestinal or respiratory tracts) and central nervous system depression[859-862]. Chronic inhalation has been linked to the formation of cataracts, cognitive impairment, neurologic dysfunction, and disabling polyneuropathies[860, 861, 863-866]. Occupational exposure in healthcare facilities has been linked to hematologic changes [867] and an increased risk of spontaneous abortions and various cancers[318, 868-870]. ETO should be considered a known human carcinogen[871].

The basic ETO sterilization cycle consists of five stages (i.e., preconditioning and humidification, gas introduction, exposure, evacuation, and air washes) and takes approximately 2 1/2 hrs excluding aeration time. Mechanical aeration for 8 to 12 hours at 50 to 60°C allows desorption of the toxic ETO residual contained in exposed absorbent materials. Most modern ETO sterilizers combine sterilization and aeration in the same chamber as a continuous process. These ETO models minimize potential ETO exposure during door opening and load transfer to the aerator. Ambient room aeration also will achieve desorption of the toxic ETO but requires 7 days at 20°C. There are no federal regulations for ETO sterilizer emission; however, many states have promulgated emission-control regulations[814].

The use of ETO evolved when few alternatives existed for sterilizing heat- and moisture-sensitive medical devices; however, favorable properties (Table 6) account for its continued widespread use[872]. Two ETO gas mixtures are available to replace ETO-chlorofluorocarbon (CFC) mixtures for large capacity, tank-supplied sterilizers. The ETO-carbon dioxide (CO_2) mixture consists of 8.5% ETO and 91.5% CO_2. This mixture is less expensive than ETO-hydrochlorofluorocarbons (HCFC), but a disadvantage is the need for pressure vessels rated for steam sterilization, because higher pressures (28-psi gauge) are required. The other mixture, which is a drop-in CFC replacement, is ETO mixed with HCFC. HCFCs are approximately 50-fold less damaging to the earth's ozone layer than are CFCs. The EPA will begin regulation of HCFC in the year 2015 and will terminate production in the year 2030. Two companies provide ETO-HCFC mixtures as drop-in replacement for CFC-12; one mixture consists of 8.6% ETO and 91.4% HCFC, and the other mixture is composed of 10% ETO and 90% HCFC[872]. An alternative to the pressurized mixed gas ETO systems is 100% ETO. The 100% ETO sterilizers using unit-dose cartridges eliminate the need for external tanks.

ETO is absorbed by many materials. For this reason, following sterilization the item must undergo aeration to remove residual ETO. Guidelines have been promulgated regarding allowable ETO limits for devices that depend on how the device is used, how often, and how long in order to pose a minimal risk to patients in normal product use[814].

ETO toxicity has been established in a variety of animals. Exposure to ETO can cause eye pain, sore throat, difficulty breathing and blurred vision. Exposure can also cause dizziness, nausea, headache, convulsions, blisters and vomiting and coughing[873]. In a variety of *in vitro* and animal studies, ETO has been demonstrated to be carcinogenic. ETO has been linked to spontaneous abortion, genetic damage, nerve damage, peripheral paralysis, muscle weakness, and impaired thinking and memory[873]. Occupational exposure in healthcare facilities has been linked to an increased risk of spontaneous abortions and various cancers[318]. Injuries (e.g., tissue burns) to patients have been associated with ETO residues in implants used in surgical procedures[874]. Residual ETO in capillary flow dialysis membranes has been shown to be neurotoxic in vitro[875]. OSHA has established a PEL of 1 ppm airborne ETO in the workplace, expressed as a TWA for an 8-hour work shift in a 40-hour work week. The "action level" for ETO is 0.5 ppm, expressed as an 8-hour TWA, and the short-term excursion limit is 5 ppm, expressed as

a 15-minute TWA[814]. For details of the requirements in OSHA's ETO standard for occupational exposures, see Title 29 of the Code of Federal Regulations (CFR) Part 1910.1047[873]. Several personnel monitoring methods (e.g., charcoal tubes and passive sampling devices) are in use[814]. OSHA has established a PEL of 5 ppm for ethylene chlorohydrin (a toxic by-product of ETO) in the workplace[876]. Additional information regarding use of ETO in health care facilities is available from NIOSH.

Mode of Action. The microbicidal activity of ETO is considered to be the result of alkylation of protein, DNA, and RNA. Alkylation, or the replacement of a hydrogen atom with an alkyl group, within cells prevents normal cellular metabolism and replication[877].

Microbicidal Activity. The excellent microbicidal activity of ETO has been demonstrated in several studies [469, 721, 722, 856, 878, 879] and summarized in published reports[877]. ETO inactivates all microorganisms although bacterial spores (especially *B. atrophaeus*) are more resistant than other microorganisms. For this reason *B. atrophaeus* is the recommended biological indicator.

Like all sterilization processes, the effectiveness of ETO sterilization can be altered by lumen length, lumen diameter, inorganic salts, and organic materials[469, 721, 722, 855, 856, 879]. For example, although ETO is not used commonly for reprocessing endoscopes[28], several studies have shown failure of ETO in inactivating contaminating spores in endoscope channels [855]or lumen test units [469, 721, 879] and residual ETO levels averaging 66.2 ppm even after the standard degassing time[456]. Failure of ETO also has been observed when dental handpieces were contaminated with *Streptococcus mutans* and exposed to ETO[880]. It is recommended that dental handpieces be steam sterilized.

Uses. ETO is used in healthcare facilities to sterilize critical items (and sometimes semicritical items) that are moisture or heat sensitive and cannot be sterilized by steam sterilization.

Hydrogen Peroxide Gas Plasma

Overview. New sterilization technology based on plasma was patented in 1987 and marketed in the United States in 1993. Gas plasmas have been referred to as the fourth state of matter (i.e., liquids, solids, gases, and gas plasmas). Gas plasmas are generated in an enclosed chamber under deep vacuum using radio frequency or microwave energy to excite the gas molecules and produce charged particles, many of which are in the form of free radicals. A free radical is an atom with an unpaired electron and is a highly reactive species. The proposed mechanism of action of this device is the production of free radicals within a plasma field that are capable of interacting with essential cell components (e.g., enzymes, nucleic acids) and thereby disrupt the metabolism of microorganisms. The type of seed gas used and the depth of the vacuum are two important variables that can determine the effectiveness of this process.

In the late 1980s the first hydrogen peroxide gas plasma system for sterilization of medical and surgical devices was field-tested. According to the manufacturer, the sterilization chamber is evacuated and hydrogen peroxide solution is injected from a cassette and is vaporized in the sterilization chamber to a concentration of 6 mg/l. The hydrogen peroxide vapor diffuses through the chamber (50 minutes), exposes all surfaces of the load to the sterilant, and initiates the inactivation of microorganisms. An electrical field created by a radio frequency is applied to the chamber to create a gas plasma. Microbicidal free radicals (e.g., hydroxyl and hydroperoxyl) are generated in the plasma. The excess gas is removed and in the final stage (i.e., vent) of the process the sterilization chamber is returned to atmospheric pressure by introduction of high-efficiency filtered air. The by-products of the cycle (e.g., water vapor, oxygen) are nontoxic and eliminate the need for aeration. Thus, the sterilized materials can be handled safely, either for immediate use or storage. The process operates in the range of 37-44°C and has a cycle time of 75 minutes. If any moisture is present on the objects the vacuum will not be achieved and the cycle aborts[856, 881-883].

A newer version of the unit improves sterilizer efficacy by using two cycles with a hydrogen

peroxide diffusion stage and a plasma stage per sterilization cycle. This revision, which is achieved by a software modification, reduces total processing time from 73 to 52 minutes. The manufacturer believes that the enhanced activity obtained with this system is due in part to the pressure changes that occur during the injection and diffusion phases of the process and to the fact that the process consists of two equal and consecutive half cycles, each with a separate injection of hydrogen peroxide.[856, 884, 885] This system and a smaller version [400, 882] have received FDA 510[k] clearance with limited application for sterilization of medical devices (Table 6). The biological indicator used with this system is *Bacillus atrophaeus* spores[851]. The newest version of the unit, which employs a new vaporization system that removes most of the water from the hydrogen peroxide, has a cycle time from 28-38 minutes (see manufacturer's literature for device dimension restrictions).

Penetration of hydrogen peroxide vapor into long or narrow lumens has been addressed outside the United States by the use of a diffusion enhancer. This is a small, breakable glass ampoule of concentrated hydrogen peroxide (50%) with an elastic connector that is inserted into the device lumen and crushed immediately before sterilization[470, 885]. The diffusion enhancer has been shown to sterilize bronchoscopes contaminated with *Mycobacteria tuberculosis*[886]. At the present time, the diffusion enhancer is not FDA cleared.

Another gas plasma system, which differs from the above in several important ways, including the use of peracetic acid-acetic acid-hydrogen peroxide vapor, was removed from the marketplace because of reports of corneal destruction to patients when ophthalmic surgery instruments had been processed in the sterilizer[887, 888]. In this investigation, exposure of potentially wet ophthalmologic surgical instruments with small bores and brass components to the plasma gas led to degradation of the brass to copper and zinc[888, 889]. The experimenters showed that when rabbit eyes were exposed to the rinsates of the gas plasma-sterilized instruments, corneal decompensation was documented. This toxicity is highly unlikely with the hydrogen peroxide gas plasma process since a toxic, soluble form of copper would not form (LA Feldman, written communication, April 1998).

Mode of Action. This process inactivates microorganisms primarily by the combined use of hydrogen peroxide gas and the generation of free radicals (hydroxyl and hydroproxyl free radicals) during the plasma phase of the cycle.

Microbicidal Activity. This process has the ability to inactivate a broad range of microorganisms, including resistant bacterial spores. Studies have been conducted against vegetative bacteria (including mycobacteria), yeasts, fungi, viruses, and bacterial spores[469, 721, 856, 881-883, 890-893]. Like all sterilization processes, the effectiveness can be altered by lumen length, lumen diameter, inorganic salts, and organic materials[469, 721, 855, 856, 890, 891, 893].

Uses. Materials and devices that cannot tolerate high temperatures and humidity, such as some plastics, electrical devices, and corrosion-susceptible metal alloys, can be sterilized by hydrogen peroxide gas plasma. This method has been compatible with most (>95%) medical devices and materials tested[884, 894, 895].

Peracetic Acid Sterilization

Overview. Peracetic acid is a highly biocidal oxidizer that maintains its efficacy in the presence of organic soil. Peracetic acid removes surface contaminants (primarily protein) on endoscopic tubing[711, 717]. An automated machine using peracetic acid to sterilize medical, surgical, and dental instruments chemically (e.g., endoscopes, arthroscopes) was introduced in 1988. This microprocessor-controlled, low-temperature sterilization method is commonly used in the United States[107]. The sterilant, 35% peracetic acid, and an anticorrosive agent are supplied in a single-dose container. The container is punctured at the time of use, immediately prior to closing the lid and initiating the cycle. The concentrated peracetic acid is diluted to 0.2% with filtered water (0.2 μm) at a temperature of approximately 50°C. The diluted peracetic acid is circulated within the chamber of the machine and

pumped through the channels of the endoscope for 12 minutes, decontaminating exterior surfaces, lumens, and accessories. Interchangeable trays are available to permit the processing of up to three rigid endoscopes or one flexible endoscope. Connectors are available for most types of flexible endoscopes for the irrigation of all channels by directed flow. Rigid endoscopes are placed within a lidded container, and the sterilant fills the lumens either by immersion in the circulating sterilant or by use of channel connectors to direct flow into the lumen(s) (see below for the importance of channel connectors). The peracetic acid is discarded via the sewer and the instrument rinsed four times with filtered water. Concern has been raised that filtered water may be inadequate to maintain sterility[896]. Limited data have shown that low-level bacterial contamination may follow the use of filtered water in an AER but no data has been published on AERs using the peracetic acid system[161]. Clean filtered air is passed through the chamber of the machine and endoscope channels to remove excess water[719]. As with any sterilization process, the system can only sterilize surfaces that can be contacted by the sterilant. For example, bronchoscopy-related infections occurred when bronchoscopes were processed using the wrong connector[155, 725]. Investigation of these incidents revealed that bronchoscopes were inadequately reprocessed when inappropriate channel connectors were used and when there were inconsistencies between the reprocessing instructions provided by the manufacturer of the bronchoscope and the manufacturer of the automatic endoscope reprocessor[155]. The importance of channel connectors to achieve sterilization was also shown for rigid lumen devices[137, 856].

The manufacturers suggest the use of biological monitors (*G. stearothermophilus* spore strips) both at the time of installation and routinely to ensure effectiveness of the process. The manufacturer's clip must be used to hold the strip in the designated spot in the machine as a broader clamp will not allow the sterilant to reach the spores trapped under it[897]. One investigator reported a 3% failure rate when the appropriate clips were used to hold the spore strip within the machine[718]. The use of biological monitors designed to monitor either steam sterilization or ETO for a liquid chemical sterilizer has been questioned for several reasons including spore wash-off from the filter paper strips which may cause less valid monitoring[898-901]. The processor is equipped with a conductivity probe that will automatically abort the cycle if the buffer system is not detected in a fresh container of the peracetic acid solution. A chemical monitoring strip that detects that the active ingredient is >1500 ppm is available for routine use as an additional process control.

Mode of Action. Only limited information is available regarding the mechanism of action of peracetic acid, but it is thought to function as other oxidizing agents, i.e., it denatures proteins, disrupts cell wall permeability, and oxidizes sulfhydral and sulfur bonds in proteins, enzymes, and other metabolites[654, 726].

Microbicidal Activity. Peracetic acid will inactivate gram-positive and gram-negative bacteria, fungi, and yeasts in <5 minutes at <100 ppm. In the presence of organic matter, 200-500 ppm is required. For viruses, the dosage range is wide (12-2250 ppm), with poliovirus inactivated in yeast extract in 15 minutes with 1500 to 2250 ppm. Bacterial spores in suspension are inactivated in 15 seconds to 30 minutes with 500 to 10,000 ppm (0.05 to 1%)[654].

Simulated-use trials have demonstrated microbicidal activity [111, 718-722] and three clinical trials have demonstrated both microbial killing and no clinical failures leading to infection[90, 723, 724]. Alfa and co-workers, who compared the peracetic acid system with ETO, demonstrated the high efficacy of the system. Only the peracetic acid system was able to completely kill 6-$\log_{10}$ of *Mycobacterium chelonae*, *Enterococcus faecalis*, and *B. atrophaeus* spores with both an organic and inorganic challenge[722]. Like other sterilization processes, the efficacy of the process can be diminished by soil challenges [902] and test conditions[856].

Uses. This automated machine is used to chemically sterilize medical (e.g., GI endoscopes) and surgical (e.g., flexible endoscopes) instruments in the United States. Lumened endoscopes must be connected to an appropriate channel connector to ensure that the sterilant has direct contact with the contaminated lumen. [137, 856, 903] Olympus America has not listed this system as a compatible product for

use in reprocessing Olympus bronchoscopes and gastrointestinal endoscopes (Olympus America, January 30, 2002, written communication).

Microbicidal Activity of Low-Temperature Sterilization Technologies

Sterilization processes used in the United States must be cleared by FDA, and they require that sterilizer microbicidal performance be tested under simulated-use conditions[904]. FDA requires that the test article be inoculated with 10^6 colony-forming units of the most resistant test organism and prepared with organic and inorganic test loads as would occur after actual use. FDA requires manufacturers to use organic soil (e.g., 5% fetal calf serum), dried onto the device with the inoculum, to represent soil remaining on the device following marginal cleaning. However, 5% fetal calf serum as a measure of marginal cleaning has not been validated by measurements of protein load on devices following use and the level of protein removal by various cleaning methods. The inocula must be placed in various locations of the test articles, including those least favorable to penetration and contact with the sterilant (e.g., lumens). Cleaning before sterilization is not allowed in the demonstration of sterilization efficacy[904]. Several studies have evaluated the relative microbicidal efficacy of these low-temperature sterilization technologies (Table 11). These studies have either tested the activity of a sterilization process against specific microorganisms[892, 905, 906], evaluated the microbicidal activity of a singular technology [711, 719, 724, 855, 879, 882-884, 890, 891, 907] or evaluated the comparative effectiveness of several sterilization technologies[271, 426, 469, 721, 722, 856, 908, 909]. Several test methodologies use stainless steel or porcelain carriers that are inoculated with a test organism. Commonly used test organisms include vegetative bacteria, mycobacteria, and spores of *Bacillus* species. The available data demonstrate that low-temperature sterilization technologies are able to provide a 6-$\log_{10}$ reduction of microbes when inoculated onto carriers in the absence of salt and serum. However, tests can be constructed such that all of the available sterilization technologies are unable to reliably achieve complete inactivation of a microbial load.[425, 426, 469, 721, 856, 909] For example, almost all of the sterilization processes will fail to reliably inactivate the microbial load in the presence of salt and serum[469, 721, 909].

The effect of salts and serums on the sterilization process were studied initially in the 1950s and 1960s[424, 910]. These studies showed that a high concentration of crystalline-type materials and a low protein content provided greater protection to spores than did serum with a high protein content[426]. A study by Doyle and Ernst demonstrated resistance of spores by crystalline material applied not only to low-temperature sterilization technology but also to steam and dry heat[425]. These studies showed that occlusion of *Bacillus atrophaeus* spores in calcium carbonate crystals dramatically increased the time required for inactivation as follows: 10 seconds to 150 minutes for steam (121°C), 3.5 hours to 50 hours for dry heat (121°C), 30 seconds to >2 weeks for ETO (54°C). Investigators have corroborated and extended these findings[469, 470, 721, 855, 908, 909]. While soils containing both organic and inorganic materials impair microbial killing, soils that contain a high inorganic salt-to-protein ratio favor crystal formation and impair sterilization by occlusion of organisms[425, 426, 881].

Alfa and colleagues demonstrated a 6-$\log_{10}$ reduction of the microbial inoculum of porcelain penicylinders using a variety of vegetative and spore-forming organisms (Table 11)[469]. However, if the bacterial inoculum was in tissue-culture medium supplemented with 10% serum, only the ETO 12/88 and ETO-HCFC sterilization mixtures could sterilize 95% to 97% of the penicylinder carriers. The plasma and 100% ETO sterilizer demonstrated significantly reduced activity (Table 11). For all sterilizers evaluated using penicylinder carriers (i.e., ETO 12/88, 100% ETO, hydrogen peroxide gas plasma), there was a 3- to 6-$\log_{10}$ reduction of inoculated bacteria even in the presence of serum and salt. For each sterilizer evaluated, the ability to inactivate microorganisms in the presence of salt and serum was reduced even further when the inoculum was placed in a narrow-lumen test object (3 mm diameter by 125 cm long). Although there was a 2- to 4-$\log_{10}$ reduction in microbial kill, less than 50% of the lumen test objects were sterile when processed using any of the sterilization methods evaluated except the peracetic acid immersion system (Table 11)[721]. Complete killing (or removal) of 6-$\log_{10}$ of *Enterococcus faecalis*, *Mycobacterium chelonei*, and *Bacillus atrophaeus* spores in the presence of salt and serum and lumen test objects was observed only for the peracetic acid immersion system.

With respect to the results by Alfa and coworkers[469], Jacobs showed that the use of the tissue culture media created a technique-induced sterilization failure[426]. Jacobs et al. showed that microorganisms mixed with tissue culture media, used as a surrogate body fluid, formed physical crystals that protected the microorganisms used as a challenge. If the carriers were exposed for 60 sec to nonflowing water, the salts dissolved and the protective effect disappeared. Since any device would be exposed to water for a short period of time during the washing procedure, these protective effects would have little clinical relevance[426].

Narrow lumens provide a challenge to some low-temperature sterilization processes. For example, Rutala and colleagues showed that, as lumen size decreased, increased failures occurred with some low-temperature sterilization technologies. However, some low-temperature processes such as ETO-HCFC and the hydrogen peroxide gas plasma process remained effective even when challenged by a lumen as small as 1 mm in the absence of salt and serum[856].

The importance of allowing the sterilant to come into contact with the inoculated carrier is demonstrated by comparing the results of two investigators who studied the peracetic acid immersion system. Alfa and coworkers demonstrated excellent activity of the peracetic acid immersion system against three test organisms using a narrow-lumen device. In these experiments, the lumen test object was connected to channel irrigators, which ensured that the sterilant had direct contact with the contaminated carriers[722]. This effectiveness was achieved through a combination of organism wash-off and peracetic acid sterilant killing the test organisms[722]. The data reported by Rutala et al. demonstrated failure of the peracetic acid immersion system to eliminate *Geobacillus stearothermophilus* spores from a carrier placed in a lumen test object. In these experiments, the lumen test unit was not connected to channel irrigators. The authors attributed the failure of the peracetic acid immersion system to eliminate the high levels of spores from the center of the test unit to the inability of the peracetic acid to diffuse into the center of 40-cm long, 3-mm diameter tubes. This may be caused by an air lock or air bubbles formed in the lumen, impeding the flow of the sterilant through the long and narrow lumen and limiting complete access to the *Bacillus* spores[137, 856]. Experiments using a channel connector specifically designed for 1-, 2-, and 3-mm lumen test units with the peracetic acid immersion system were completely effective in eliminating an inoculum of 10^6 *Geobacillus stearothermophilus* spores[7]. The restricted diffusion environment that exists in the test conditions would not exist with flexible scopes processed in the peracetic acid immersion system, because the scopes are connected to channel irrigators to ensure that the sterilant has direct contact with contaminated surfaces. Alfa and associates attributed the efficacy of the peracetic acid immersion system to the ability of the liquid chemical process to dissolve salts and remove protein and bacteria due to the flushing action of the fluid[722].

Bioburden of Surgical Devices

In general, used medical devices are contaminated with a relatively low bioburden of organisms[179, 911, 912]. Nystrom evaluated medical instruments used in general surgical, gynecological, orthopedic, and ear-nose-throat operations and found that 62% of the instruments were contaminated with $<10^1$ organisms after use, 82% with $<10^2$, and 91% with $<10^3$. After being washed in an instrument washer, more than 98% of the instruments had $<10^1$ organisms, and none $>10^2$ organisms[911]. Other investigators have published similar findings[179, 912]. For example, after a standard cleaning procedure, 72% of 50 surgical instruments contained $<10^1$ organisms, 86% $<10^2$, and only 6% had $>3 \times 10^2$[912]. In another study of rigid-lumen medical devices, the bioburden on both the inner and outer surface of the lumen ranged from 10^1 to 10^4 organisms per device. After cleaning, 83% of the devices had a bioburden $\leq 10^2$ organisms[179]. In all of these studies, the contaminating microflora consisted mainly of vegetative bacteria, usually of low pathogenicity (e.g., coagulase-negative *Staphylococcus*)[179, 911, 912].

An evaluation of the microbial load on used critical medical devices such as spinal anesthesia needles and angiographic catheters and sheaths demonstrated that mesophilic microorganisms were detected at levels of 10^1 to 10^2 in only two of five needles. The bioburden on used angiographic

catheters and sheath introducers exceeded 10^3 CFUs on 14% (3 of 21) and 21% (6 of 28), respectively[907].

Effect of Cleaning on Sterilization Efficacy

The effect of salt and serum on the efficacy of low-temperature sterilization technologies has raised concern regarding the margin of safety of these technologies. Experiments have shown that salts have the greatest impact on protecting microorganisms from killing[426, 469]. However, other studies have suggested that these concerns may not be clinically relevant. One study evaluated the relative rate of removal of inorganic salts, organic soil, and microorganisms from medical devices to better understand the dynamics of the cleaning process[426]. These tests were conducted by inoculating Alfa soil (tissue-culture media and 10% fetal bovine serum) [469] containing 10^6 *G. stearothermophilus* spores onto the surface of a stainless-steel scalpel blade. After drying for 30 minutes at 35°C followed by 30 minutes at room temperature, the samples were placed in water at room temperature. The blades were removed at specified times, and the concentration of total protein and chloride ion was measured. The results showed that soaking in deionized water for 60 seconds resulted in a >95% release rate of chloride ion from NaCl solution in 20 seconds, Alfa soil in 30 seconds, and fetal bovine serum in 120 seconds. Thus, contact with water for short periods, even in the presence of protein, rapidly leads to dissolution of salt crystals and complete inactivation of spores by a low-temperature sterilization process (Table 10). Based on these experimental data, cleaning procedures would eliminate the detrimental effect of high salt content on a low-temperature sterilization process.

These articles [426, 469, 721] assessing low-temperature sterilization technology reinforce the importance of meticulous cleaning before sterilization. These data support the critical need for healthcare facilities to develop rigid protocols for cleaning contaminated objects before sterilization[472]. Sterilization of instruments and medical devices is compromised if the process is not preceded by meticulous cleaning.

The cleaning of any narrow-lumen medical device used in patient care presents a major challenge to reprocessing areas. While attention has been focused on flexible endoscopes, cleaning issues related to other narrow-lumen medical devices such as sphinctertomes have been investigated[913]. This study compared manual cleaning with that of automated cleaning with a narrow-lumen cleaner and found that only retro-flushing with the narrow lumen cleaner provided adequate cleaning of the three channels. If reprocessing was delayed for more than 24 hours, retro-flush cleaning was no longer effective and ETO sterilization failure was detected when devices were held for 7 days [913]. In another study involving simulated-use cleaning of laparoscopic devices, Alfa found that minimally the use of retro-flushing should be used during cleaning of non-ported laparoscopic devices[914].

Other Sterilization Methods

Ionizing Radiation. Sterilization by ionizing radiation, primarily by cobalt 60 gamma rays or electron accelerators, is a low-temperature sterilization method that has been used for a number of medical products (e.g., tissue for transplantation, pharmaceuticals, medical devices). There are no FDA-cleared ionizing radiation sterilization processes for use in healthcare facilities. Because of high sterilization costs, this method is an unfavorable alternative to ETO and plasma sterilization in healthcare facilities but is suitable for large-scale sterilization. Some deleterious effects on patient-care equipment associated with gamma radiation include induced oxidation in polyethylene [915] and delamination and cracking in polyethylene knee bearings[916]. Several reviews [917, 918] dealing with the sources, effects, and application of ionizing radiation may be referred to for more detail.

Dry-Heat Sterilizers. This method should be used only for materials that might be damaged by moist heat or that are impenetrable to moist heat (e.g., powders, petroleum products, sharp instruments). The advantages for dry heat include the following: it is nontoxic and does not harm the environment; a dry heat cabinet is easy to install and has relatively low operating costs; it penetrates materials; and it is noncorrosive for metal and sharp instruments. The disadvantages for dry heat are the slow rate of heat penetration and microbial killing makes this a time-consuming method. In addition, the high temperatures

are not suitable for most materials[919]. The most common time-temperature relationships for sterilization with hot air sterilizers are 170°C (340°F) for 60 minutes, 160°C (320°F) for 120 minutes, and 150°C (300°F) for 150 minutes. *B. atrophaeus* spores should be used to monitor the sterilization process for dry heat because they are more resistant to dry heat than are *G. stearothermophilus* spores. The primary lethal process is considered to be oxidation of cell constituents.

There are two types of dry-heat sterilizers: the static-air type and the forced-air type. The static-air type is referred to as the oven-type sterilizer as heating coils in the bottom of the unit cause the hot air to rise inside the chamber via gravity convection. This type of dry-heat sterilizer is much slower in heating, requires longer time to reach sterilizing temperature, and is less uniform in temperature control throughout the chamber than is the forced-air type. The forced-air or mechanical convection sterilizer is equipped with a motor-driven blower that circulates heated air throughout the chamber at a high velocity, permitting a more rapid transfer of energy from the air to the instruments[920].

Liquid Chemicals. Several FDA-cleared liquid chemical sterilants include indications for sterilization of medical devices (Tables 4 and 5)[69]. The indicated contact times range from 3 hours to 12 hours. However, except for a few of the products, the contact time is based only on the conditions to pass the AOAC Sporicidal Test as a sterilant and not on simulated use testing with devices. These solutions are commonly used as high-level disinfectants when a shorter processing time is required. Generally, chemical liquid sterilants cannot be monitored using a biological indicator to verify sterility[899, 900].

The survival kinetics for thermal sterilization methods, such as steam and dry heat, have been studied and characterized extensively, whereas the kinetics for sterilization with liquid sterilants are less well understood[921]. The information that is available in the literature suggests that sterilization processes based on liquid chemical sterilants, in general, may not convey the same sterility assurance level as sterilization achieved using thermal or physical methods[823]. The data indicate that the survival curves for liquid chemical sterilants may not exhibit log-linear kinetics and the shape of the survivor curve may vary depending of the formulation, chemical nature and stability of the liquid chemical sterilant. In addition, the design of the AOAC Sporicidal Test does not provide quantification of the microbial challenge. Therefore, sterilization with a liquid chemical sterilant may not convey the same sterility assurance as other sterilization methods.

One of the differences between thermal and liquid chemical processes for sterilization of devices is the accessibility of microorganisms to the sterilant. Heat can penetrate barriers, such as biofilm, tissue, and blood, to attain organism kill, whereas liquids cannot adequately penetrate these barriers. In addition, the viscosity of some liquid chemical sterilants impedes their access to organisms in the narrow lumens and mated surfaces of devices[922]. Another limitation to sterilization of devices with liquid chemical germicides is the post-processing environment of the device. Devices cannot be wrapped or adequately contained during processing in a liquid chemical sterilant to maintain sterility following processing and during storage. Furthermore, devices may require rinsing following exposure to the liquid chemical sterilant with water that typically is not sterile. Therefore, due to the inherent limitations of using liquid chemical sterilants, their use should be restricted to reprocessing critical devices that are heat-sensitive and incompatible with other sterilization methods.

Several published studies compare the sporicidal effect of liquid chemical germicides against spores of *Bacillus* and *Clostridium*[78, 659, 660, 715].

Performic Acid. Performic acid is a fast-acting sporicide that was incorporated into an automated endoscope reprocessing system[400]. Systems using performic acid are not currently FDA cleared.

Filtration. Although filtration is not a lethality-based process and is not an FDA-cleared sterilization method, this technology is used to remove bacteria from thermolabile pharmaceutical fluids

that cannot be purified by any other means. In order to remove bacteria, the membrane pore size (e.g., 0.22 μm) must be smaller than the bacteria and uniform throughout[923]. Some investigators have appropriately questioned whether the removal of microorganisms by filtration really is a sterilization method because of slight bacterial passage through filters, viral passage through filters, and transference of the sterile filtrate into the final container under aseptic conditions entail a risk of contamination[924].

Microwave. Microwaves are used in medicine for disinfection of soft contact lenses, dental instruments, dentures, milk, and urinary catheters for intermittent self-catheterization[925-931]. However, microwaves must only be used with products that are compatible (e.g., do not melt) [931]. Microwaves are radio-frequency waves, which are usually used at a frequency of 2450 MHz. The microwaves produce friction of water molecules in an alternating electrical field. The intermolecular friction derived from the vibrations generates heat and some authors believe that the effect of microwaves depends on the heat produced while others postulate a nonthermal lethal effect[932-934]. The initial reports showed microwaves to be an effective microbicide. The microwaves produced by a "home-type" microwave oven (2.45 GHz) completely inactivate bacterial cultures, mycobacteria, viruses, and *G. stearothermophilus* spores within 60 seconds to 5 minutes depending on the challenge organism[933, 935-937]. Another study confirmed these results but also found that higher power microwaves in the presence of water may be needed for sterilization[932]. Complete destruction of *Mycobacterium bovis* was obtained with 4 minutes of microwave exposure (600W, 2450 MHz)[937]. The effectiveness of microwave ovens for different sterilization and disinfection purposes should be tested and demonstrated as test conditions affect the results (e.g., presence of water, microwave power). Sterilization of metal instruments can be accomplished but requires certain precautions.[926]. Of concern is that home-type microwave ovens may not have even distribution of microwave energy over the entire dry device (there may be hot and cold spots on solid medical devices); hence there may be areas that are not sterilized or disinfected. The use of microwave ovens to disinfect intermittent-use catheters also has been suggested. Researchers found that test bacteria (e.g., *E. coli*, *Klebsiella pneumoniae*, *Candida albicans*) were eliminated from red rubber catheters within 5 minutes [931]. Microwaves used for sterilization of medical devices have not been FDA cleared.

Glass Bead "Sterilizer". Glass bead "sterilization" uses small glass beads (1.2-1.5 mm diameter) and high temperature (217 °C -232°C) for brief exposure times (e.g., 45 seconds) to inactivate microorganisms. These devices have been used for several years in the dental profession[938-940]. FDA believes there is a risk of infection with this device because of potential failure to sterilize dental instruments and their use should be discontinued until the device has received FDA clearance.

***Vaporized Hydrogen Peroxide* (VHP®).** Hydrogen peroxide solutions have been used as chemical sterilants for many years. However, the VHP® was not developed for the sterilization of medical equipment until the mid-1980s. One method for delivering VHP to the reaction site uses a deep vacuum to pull liquid hydrogen peroxide (30-35% concentration) from a disposable cartridge through a heated vaporizer and then, following vaporization, into the sterilization chamber. A second approach to VHP delivery is the flow-through approach in which the VHP is carried into the sterilization chamber by a carrier gas such as air using either a slight negative pressure (vacuum) or slight positive pressure. Applications of this technology include vacuum systems for industrial sterilization of medical devices and atmospheric systems for decontaminating for large and small areas[853]. VHP offers several appealing features that include rapid cycle time (e.g., 30-45 minutes); low temperature; environmentally safe by-products (H_2O, oxygen [O_2]); good material compatibility; and ease of operation, installation and monitoring. VHP has limitations including that cellulose cannot be processed; nylon becomes brittle; and VHP penetration capabilities are less than those of ETO. VHP has not been cleared by FDA for sterilization of medical devices in healthcare facilities.

The feasibility of utilizing vapor-phase hydrogen peroxide as a surface decontaminant and sterilizer was evaluated in a centrifuge decontamination application. In this study, vapor-phase hydrogen peroxide was shown to possess significant sporicidal activity [941]. In preliminary studies, hydrogen

peroxide vapor decontamination has been found to be a highly effective method of eradicating MRSA, *Serratia marcescens, Clostridium botulinum spores* and *Clostridium difficile* from rooms, furniture, surfaces and/or equipment; however, further investigation of this method to demonstrate both safety and effectiveness in reducing infection rates are required[942-945].

Ozone. Ozone has been used for years as a drinking water disinfectant. Ozone is produced when O_2 is energized and split into two monatomic (O_1) molecules. The monatomic oxygen molecules then collide with O_2 molecules to form ozone, which is O_3. Thus, ozone consists of O_2 with a loosely bonded third oxygen atom that is readily available to attach to, and oxidize, other molecules. This additional oxygen atom makes ozone a powerful oxidant that destroys microorganisms but is highly unstable (i.e., half-life of 22 minutes at room temperature).

A new sterilization process, which uses ozone as the sterilant, was cleared by FDA in August 2003 for processing reusable medical devices. The sterilizer creates its own sterilant internally from USP grade oxygen, steam-quality water and electricity; the sterilant is converted back to oxygen and water vapor at the end of the cycle by a passing through a catalyst before being exhausted into the room. The duration of the sterilization cycle is about 4 h and 15 m, and it occurs at 30-35°C. Microbial efficacy has been demonstrated by achieving a SAL of 10^{-6} with a variety of microorganisms to include the most resistant microorganism, *Geobacillus stearothermophilus*.

The ozone process is compatible with a wide range of commonly used materials including stainless steel, titanium, anodized aluminum, ceramic, glass, silica, PVC, Teflon, silicone, polypropylene, polyethylene and acrylic. In addition, rigid lumen devices of the following diameter and length can be processed: internal diameter (ID): > 2 mm, length ≤ 25 cm; ID > 3 mm, length ≤ 47 cm; and ID > 4 mm, length ≤ 60 cm.

The process should be safe for use by the operator because there is no handling of the sterilant, no toxic emissions, no residue to aerate, and low operating temperature means there is no danger of an accidental burn. The cycle is monitored using a self-contained biological indicator and a chemical indicator. The sterilization chamber is small, about 4 ft^3 (Written communication, S Dufresne, July 2004).

A gaseous ozone generator was investigated for decontamination of rooms used to house patients colonized with MRSA. The results demonstrated that the device tested would be inadequate for the decontamination of a hospital room[946].

Formaldehyde Steam. Low-temperature steam with formaldehyde is used as a low-temperature sterilization method in many countries, particularly in Scandinavia, Germany, and the United Kingdom. The process involves the use of formalin, which is vaporized into a formaldehyde gas that is admitted into the sterilization chamber. A formaldehyde concentration of 8-16 mg/l is generated at an operating temperature of 70-75°C. The sterilization cycle consists of a series of stages that include an initial vacuum to remove air from the chamber and load, followed by steam admission to the chamber with the vacuum pump running to purge the chamber of air and to heat the load, followed by a series of pulses of formaldehyde gas, followed by steam. Formaldehyde is removed from the sterilizer and load by repeated alternate evacuations and flushing with steam and air. This system has some advantages, e.g., the cycle time for formaldehyde gas is faster than that for ETO and the cost per cycle is relatively low. However, ETO is more penetrating and operates at lower temperatures than do steam/formaldehyde sterilizers. Low-temperature steam formaldehyde sterilization has been found effective against vegetative bacteria, mycobacteria, *B. atrophaeus* and *G. stearothermophilus* spores and *Candida albicans*[947-949].

Formaldehyde vapor cabinets also may be used in healthcare facilities to sterilize heat-sensitive medical equipment[950]. Commonly, there is no circulation of formaldehyde and no temperature and humidity controls. The release of gas from paraformaldehyde tablets (placed on the lower tray) is slow and produces a low partial pressure of gas. The microbicidal quality of this procedure is unknown[951].

Reliable sterilization using formaldehyde is achieved when performed with a high concentration of gas, at a temperature between 60° and 80°C and with a relative humidity of 75 to 100%.

Studies indicate that formaldehyde is a mutagen and a potential human carcinogen, and OSHA regulates formaldehyde. The permissible exposure limit for formaldehyde in work areas is 0.75 ppm measured as a 8-hour TWA. The OSHA standard includes a 2 ppm STEL (i.e., maximum exposure allowed during a 15-minute period). As with the ETO standard, the formaldehyde standard requires that the employer conduct initial monitoring to identify employees who are exposed to formaldehyde at or above the action level or STEL. If this exposure level is maintained, employers may discontinue exposure monitoring until there is a change that could affect exposure levels or an employee reports formaldehyde-related signs and symptoms[269, 578]. The formaldehyde steam sterilization system has not been FDA cleared for use in healthcare facilities.

Gaseous chlorine dioxide. A gaseous chlorine dioxide system for sterilization of healthcare products was developed in the late 1980s[853, 952, 953]. Chlorine dioxide is not mutagenic or carcinogenic in humans. As the chlorine dioxide concentration increases, the time required to achieve sterilization becomes progressively shorter. For example, only 30 minutes were required at 40 mg/l to sterilize the 10^6 *B. atrophaeus* spores at 30° to 32°C[954]. Currently, no gaseous chlorine dioxide system is FDA cleared.

Vaporized Peracetic Acid. The sporicidal activity of peracetic acid vapor at 20, 40, 60, and 80% relative humidity and 25°C was determined on *Bacillus atrophaeus* spores on paper and glass surfaces. Appreciable activity occurred within 10 minutes of exposure to 1 mg of peracetic acid per liter at 40% or higher relative humidity[955]. No vaporized peracetic acid system is FDA cleared.

Infrared radiation. An infrared radiation prototype sterilizer was investigated and found to destroy *B. atrophaeus* spores. Some of the possible advantages of infrared technology include short cycle time, low energy consumption, no cycle residuals, and no toxicologic or environmental effects. This may provide an alternative technology for sterilization of selected heat-resistant instruments but there are no FDA-cleared systems for use in healthcare facilities [956].

The other sterilization technologies mentioned above may be used for sterilization of critical medical items if cleared by the FDA and ideally, the microbicidal effectiveness of the technology has been published in the scientific literature. The selection and use of disinfectants, chemical sterilants and sterilization processes in the healthcare field is dynamic, and products may become available that are not in existence when this guideline was written. As newer disinfectants and sterilization processes become available, persons or committees responsible for selecting disinfectants and sterilization processes should be guided by products cleared by FDA and EPA as well as information in the scientific literature.

Sterilizing Practices

Overview. The delivery of sterile products for use in patient care depends not only on the effectiveness of the sterilization process but also on the unit design, decontamination, disassembling and packaging of the device, loading the sterilizer, monitoring, sterilant quality and quantity, and the appropriateness of the cycle for the load contents, and other aspects of device reprocessing. Healthcare personnel should perform most cleaning, disinfecting, and sterilizing of patient-care supplies in a central processing department in order to more easily control quality. The aim of central processing is the orderly processing of medical and surgical instruments to protect patients from infections while minimizing risks to staff and preserving the value of the items being reprocessed[957]. Healthcare facilities should promote the same level of efficiency and safety in the preparation of supplies in other areas (e.g., operating room, respiratory therapy) as is practiced in central processing.

Ensuring consistency of sterilization practices requires a comprehensive program that ensures operator competence and proper methods of cleaning and wrapping instruments, loading the sterilizer,

operating the sterilizer, and monitoring of the entire process. Furthermore, care must be consistent from an infection prevention standpoint in all patient-care settings, such as hospital and outpatient facilities.

Sterilization Cycle Verification. A sterilization process should be verified before it is put into use in healthcare settings. All steam, ETO, and other low-temperature sterilizers are tested with biological and chemical indicators upon installation, when the sterilizer is relocated, redesigned, after major repair and after a sterilization failure has occurred to ensure they are functioning prior to placing them into routine use. Three consecutive empty steam cycles are run with a biological and chemical indicator in an appropriate test package or tray. Each type of steam cycle used for sterilization (e.g., vacuum-assisted, gravity) is tested separately. In a prevacuum steam sterilizer three consecutive empty cycles are also run with a Bowie-Dick test. The sterilizer is not put back into use until all biological indicators are negative and chemical indicators show a correct end-point response[811-814, 819, 958].

Biological and chemical indicator testing is also done for ongoing quality assurance testing of representative samples of actual products being sterilized and product testing when major changes are made in packaging, wraps, or load configuration. Biological and chemical indicators are placed in products, which are processed in a full load. When three consecutive cycles show negative biological indicators and chemical indicators with a correct end point response, you can put the change made into routine use[811-814, 958]. Items processed during the three evaluation cycles should be quarantined until the test results are negative.

Physical Facilities. The central processing area(s) ideally should be divided into at least three areas: decontamination, packaging, and sterilization and storage. Physical barriers should separate the decontamination area from the other sections to contain contamination on used items. In the decontamination area reusable contaminated supplies (and possibly disposable items that are reused) are received, sorted, and decontaminated. The recommended airflow pattern should contain contaminates within the decontamination area and minimize the flow of contaminates to the clean areas. The American Institute of Architects [959] recommends negative pressure and no fewer than six air exchanges per hour in the decontamination area (AAMI recommends 10 air changes per hour) and 10 air changes per hour with positive pressure in the sterilizer equipment room. The packaging area is for inspecting, assembling, and packaging clean, but not sterile, material. The sterile storage area should be a limited access area with a controlled temperature (may be as high as 75°F) and relative humidity (30-60% in all works areas except sterile storage, where the relative humidity should not exceed 70%)[819]. The floors and walls should be constructed of materials capable of withstanding chemical agents used for cleaning or disinfecting. Ceilings and wall surfaces should be constructed of non-shedding materials. Physical arrangements of processing areas are presented schematically in four references[811, 819, 920, 957].

Cleaning. As repeatedly mentioned, items must be cleaned using water with detergents or enzymatic cleaners [465, 466, 468] before processing. Cleaning reduces the bioburden and removes foreign material (i.e., organic residue and inorganic salts) that interferes with the sterilization process by acting as a barrier to the sterilization agent[179, 426, 457, 911, 912]. Surgical instruments are generally presoaked or prerinsed to prevent drying of blood and tissue. Precleaning in patient-care areas may be needed on items that are heavily soiled with feces, sputum, blood, or other material. Items sent to central processing without removing gross soil may be difficult to clean because of dried secretions and excretions. Cleaning and decontamination should be done as soon as possible after items have been used.

Several types of mechanical cleaning machines (e.g., utensil washer-sanitizer, ultrasonic cleaner, washer-sterilizer, dishwasher, washer-disinfector) may facilitate cleaning and decontamination of most items. This equipment often is automated and may increase productivity, improve cleaning effectiveness, and decrease worker exposure to blood and body fluids. Delicate and intricate objects and heat- or moisture-sensitive articles may require careful cleaning by hand. All used items sent to the central processing area should be considered contaminated (unless decontaminated in the area of origin), handled with gloves (forceps or tongs are sometimes needed to avoid exposure to sharps), and decontaminated by one of the aforementioned methods to render them safer to handle. Items composed

of more than one removable part should be disassembled. Care should be taken to ensure that all parts are kept together, so that reassembly can be accomplished efficiently[811].

Investigators have described the degree of cleanliness by visual and microscopic examination. One study found 91% of the instruments to be clean visually but, when examined microscopically, 84% of the instruments had residual debris. Sites that contained residual debris included junctions between insulating sheaths and activating mechanisms of laparoscopic instruments and articulations and grooves of forceps. More research is needed to understand the clinical significance of these findings [960] and how to ensure proper cleaning.

Personnel working in the decontamination area should wear household-cleaning-type rubber or plastic gloves when handling or cleaning contaminated instruments and devices. Face masks, eye protection such as goggles or full-length faceshields, and appropriate gowns should be worn when exposure to blood and contaminated fluids may occur (e.g., when manually cleaning contaminated devices)[961]. Contaminated instruments are a source of microorganisms that could inoculate personnel through nonintact skin on the hands or through contact with the mucous membranes of eyes, nose, or mouth[214, 811, 813]. Reusable sharps that have been in contact with blood present a special hazard. Employees must not reach with their gloved hands into trays or containers that hold these sharps to retrieve them[214]. Rather, employees should use engineering controls (e.g., forceps) to retrieve these devices.

Packaging. Once items are cleaned, dried, and inspected, those requiring sterilization must be wrapped or placed in rigid containers and should be arranged in instrument trays/baskets according to the guidelines provided by the AAMI and other professional organizations[454, 811-814, 819, 836, 962]. These guidelines state that hinged instruments should be opened; items with removable parts should be disassembled unless the device manufacturer or researchers provide specific instructions or test data to the contrary[181]; complex instruments should be prepared and sterilized according to device manufacturer's instructions and test data; devices with concave surfaces should be positioned to facilitate drainage of water; heavy items should be positioned not to damage delicate items; and the weight of the instrument set should be based on the design and density of the instruments and the distribution of metal mass[811, 962]. While there is no longer a specified sterilization weight limit for surgical sets, heavy metal mass is a cause of wet packs (i.e., moisture inside the case and tray after completion of the sterilization cycle)[963]. Other parameters that may influence drying are the density of the wraps and the design of the set[964].

There are several choices in methods to maintain sterility of surgical instruments, including rigid containers, peel-open pouches (e.g., self-sealed or heat-sealed plastic and paper pouches), roll stock or reels (i.e., paper-plastic combinations of tubing designed to allow the user to cut and seal the ends to form a pouch) [454] and sterilization wraps (woven and nonwoven). Healthcare facilities may use all of these packaging options. The packaging material must allow penetration of the sterilant, provide protection against contact contamination during handling, provide an effective barrier to microbial penetration, and maintain the sterility of the processed item after sterilization [965]. An ideal sterilization wrap would successfully address barrier effectiveness, penetrability (i.e., allows sterilant to penetrate), aeration (e.g., allows ETO to dissipate), ease of use, drapeability, flexibility, puncture resistance, tear strength, toxicity, odor, waste disposal, linting, cost, and transparency[966]. Unacceptable packaging for use with ETO (e.g., foil, polyvinylchloride, and polyvinylidene chlorine [kitchen-type transparent wrap]) [814] or hydrogen peroxide gas plasma (e.g., linens and paper) should not be used to wrap medical items.

In central processing, double wrapping can be done sequentially or nonsequentially (i.e., simultaneous wrapping). Wrapping should be done in such a manner to avoid tenting and gapping. The sequential wrap uses two sheets of the standard sterilization wrap, one wrapped after the other. This procedure creates a package within a package. The nonsequential process uses two sheets wrapped at the same time so that the wrapping needs to be performed only once. This latter method provides

multiple layers of protection of surgical instruments from contamination and saves time since wrapping is done only once. Multiple layers are still common practice due to the rigors of handling within the facility even though the barrier efficacy of a single sheet of wrap has improved over the years[966]. Written and illustrated procedures for preparation of items to be packaged should be readily available and used by personnel when packaging procedures are performed[454].

Loading. All items to be sterilized should be arranged so all surfaces will be directly exposed to the sterilizing agent. Thus, loading procedures must allow for free circulation of steam (or another sterilant) around each item. Historically, it was recommended that muslin fabric packs should not exceed the maximal dimensions, weight, and density of 12 inches wide x 12 inches high x 20 inches long, 12 lbs, and 7.2 lbs per cubic foot, respectively. Due to the variety of textiles and metal/plastic containers on the market, the textile and metal/plastic container manufacturer and the sterilizer manufacturers should be consulted for instructions on pack preparation and density parameters[819].

There are several important basic principles for loading a sterilizer: allow for proper sterilant circulation; perforated trays should be placed so the tray is parallel to the shelf; nonperforated containers should be placed on their edge (e.g., basins); small items should be loosely placed in wire baskets; and peel packs should be placed on edge in perforated or mesh bottom racks or baskets[454, 811, 836].

Storage. Studies in the early 1970s suggested that wrapped surgical trays remained sterile for varying periods depending on the type of material used to wrap the trays. Safe storage times for sterile packs vary with the porosity of the wrapper and storage conditions (e.g., open versus closed cabinets). Heat-sealed, plastic peel-down pouches and wrapped packs sealed in 3-mil (3/1000 inch) polyethylene overwrap have been reported to be sterile for as long as 9 months after sterilization. The 3-mil polyethylene is applied after sterilization to extend the shelf life for infrequently used items[967]. Supplies wrapped in double-thickness muslin comprising four layers, or equivalent, remain sterile for at least 30 days. Any item that has been sterilized should not be used after the expiration date has been exceeded or if the sterilized package is wet, torn, or punctured.

Although some hospitals continue to date every sterilized product and use the time-related shelf-life practice, many hospitals have switched to an event-related shelf-life practice. This latter practice recognizes that the product should remain sterile until some event causes the item to become contaminated (e.g., tear in packaging, packaging becomes wet, seal is broken)[968]. Event-related factors that contribute to the contamination of a product include bioburden (i.e., the amount of contamination in the environment), air movement, traffic, location, humidity, insects, vermin, flooding, storage area space, open/closed shelving, temperature, and the properties of the wrap material[966, 969]. There are data that support the event-related shelf-life practice[970-972]. One study examined the effect of time on the sterile integrity of paper envelopes, peel pouches, and nylon sleeves. The most important finding was the absence of a trend toward an increased rate of contamination over time for any pack when placed in covered storage[971]. Another evaluated the effectiveness of event-related outdating by microbiologically testing sterilized items. During the 2-year study period, all of the items tested were sterile[972]. Thus, contamination of a sterile item is event-related and the probability of contamination increases with increased handling[973].

Following the sterilization process, medical and surgical devices must be handled using aseptic technique in order to prevent contamination. Sterile supplies should be stored far enough from the floor (8 to 10 inches), the ceiling (5 inches unless near a sprinkler head [18 inches from sprinkler head]), and the outside walls (2 inches) to allow for adequate air circulation, ease of cleaning, and compliance with local fire codes (e.g., supplies must be at least 18 inches from sprinkler heads). Medical and surgical supplies should not be stored under sinks or in other locations where they can become wet. Sterile items that become wet are considered contaminated because moisture brings with it microorganisms from the air and surfaces. Closed or covered cabinets are ideal but open shelving may be used for storage. Any package that has fallen or been dropped on the floor must be inspected for damage to the packaging and

contents (if the items are breakable). If the package is heat-sealed in impervious plastic and the seal is still intact, the package should be considered not contaminated. If undamaged, items packaged in plastic need not be reprocessed.

Monitoring. The sterilization procedure should be monitored routinely by using a combination of mechanical, chemical, and biological indicators to evaluate the sterilizing conditions and indirectly the microbiologic status of the processed items. The mechanical monitors for steam sterilization include the daily assessment of cycle time and temperature by examining the temperature record chart (or computer printout) and an assessment of pressure via the pressure gauge. The mechanical monitors for ETO include time, temperature, and pressure recorders that provide data via computer printouts, gauges, and/or displays[814]. Generally, two essential elements for ETO sterilization (i.e., the gas concentration and humidity) cannot be monitored in healthcare ETO sterilizers.

Chemical indicators are convenient, are inexpensive, and indicate that the item has been exposed to the sterilization process. In one study, chemical indicators were more likely than biological indicators to inaccurately indicate sterilization at marginal sterilization times (e.g., 2 minutes)[847]. Chemical indicators should be used in conjunction with biological indicators, but based on current studies should not replace them because they indicate sterilization at marginal sterilization time and because only a biological indicator consisting of resistant spores can measure the microbial killing power of the sterilization process.[847, 974]. Chemical indicators are affixed on the outside of each pack to show that the package has been processed through a sterilization cycle, but these indicators do not prove sterilization has been achieved. Preferably, a chemical indicator also should be placed on the inside of each pack to verify sterilant penetration. Chemical indicators usually are either heat-or chemical-sensitive inks that change color when one or more sterilization parameters (e.g., steam-time, temperature, and/or saturated steam; ETO-time, temperature, relative humidity and/or ETO concentration) are present. Chemical indicators have been grouped into five classes based on their ability to monitor one or multiple sterilization parameters[813, 819]. If the internal and/or external indicator suggests inadequate processing, the item should not be used[815]. An air-removal test (Bowie-Dick Test) must be performed daily in an empty dynamic-air-removal sterilizer (e.g., prevacuum steam sterilizer) to ensure air removal.

Biological indicators are recognized by most authorities as being closest to the ideal monitors of the sterilization process [974, 975] because they measure the sterilization process directly by using the most resistant microorganisms (i.e., *Bacillus* spores), and not by merely testing the physical and chemical conditions necessary for sterilization. Since the *Bacillus* spores used in biological indicators are more resistant and present in greater numbers than are the common microbial contaminants found on patient-care equipment, the demonstration that the biological indicator has been inactivated strongly implies that other potential pathogens in the load have been killed[844].

An ideal biological monitor of the sterilization process should be easy to use, be inexpensive, not be subject to exogenous contamination, provide positive results as soon as possible after the cycle so that corrective action may be accomplished, and provide positive results only when the sterilization parameters (e.g., steam-time, temperature, and/or saturated steam; ETO-time, temperature, relative humidity and/or ETO concentration) are inadequate to kill microbial contaminates[847].

Biological indicators are the only process indicators that directly monitor the lethality of a given sterilization process. Spores used to monitor a sterilization process have demonstrated resistance to the sterilizing agent and are more resistant than the bioburden found on medical devices[179, 911, 912]. *B. atrophaeus* spores (10^6) are used to monitor ETO and dry heat, and *G. stearothermophilus* spores (10^5) are used to monitor steam sterilization, hydrogen peroxide gas plasma, and liquid peracetic acid sterilizers. *G. stearothermophilus* is incubated at 55-60°C, and *B. atrophaeus* is incubated at 35-37°C. Steam and low temperature sterilizers (e.g., hydrogen peroxide gas plasma, peracetic acid) should be monitored at least weekly with the appropriate commercial preparation of spores. If a sterilizer is used frequently (e.g., several loads per day), daily use of biological indicators allows earlier discovery of

equipment malfunctions or procedural errors and thus minimizes the extent of patient surveillance and product recall needed in the event of a positive biological indicator[811]. Each load should be monitored if it contains implantable objects. If feasible, implantable items should not be used until the results of spore tests are known to be negative.

Originally, spore-strip biological indicators required up to 7 days of incubation to detect viable spores from marginal cycles (i.e., when few spores remained viable). The next generation of biological indicator was self-contained in plastic vials containing a spore-coated paper strip and a growth media in a crushable glass ampoule. This indicator had a maximum incubation of 48 hours but significant failures could be detected in ≤24 hours. A rapid-readout biological indicator that detects the presence of enzymes of *G. stearothermophilus* by reading a fluorescent product produced by the enzymatic breakdown of a nonfluorescent substrate has been marketed for the more than 10 years. Studies demonstrate that the sensitivity of rapid-readout tests for steam sterilization (1 hour for 132°C gravity sterilizers, 3 hrs for 121°C gravity and 132°C vacuum sterilizers) parallels that of the conventional sterilization-specific biological indicators [846, 847, 976, 977] and the fluorescent rapid readout results reliably predict 24- and 48-hour and 7-day growth[978]. The rapid-readout biological indicator is a dual indicator system as it also detects acid metabolites produced during growth of the *G. stearothermophilus* spores. This system is different from the indicator system consisting of an enzyme system of bacterial origin without spores. Independent comparative data using suboptimal sterilization cycles (e.g., reduced time or temperature) with the enzyme-based indicator system have not been published[979].

A new rapid-readout ETO biological indicator has been designed for rapid and reliable monitoring of ETO sterilization processes. The indicator has been cleared by the FDA for use in the United States[400]. The rapid-readout ETO biological indicator detects the presence of *B. atrophaeus* by detecting a fluorescent signal indicating the activity of an enzyme present within the *B. atrophaeus* organism, beta-glucosidase. The fluorescence indicates the presence of an active spore-associated enzyme and a sterilization process failure. This indicator also detects acid metabolites produced during growth of the *B. atrophaeus* spore. Per manufacturer's data, the enzyme always was detected whenever viable spores were present. This was expected because the enzyme is relatively ETO resistant and is inactivated at a slightly longer exposure time than the spore. The rapid-readout ETO biological indicator can be used to monitor 100% ETO, and ETO-HCFC mixture sterilization cycles. It has not been tested in ETO-CO_2 mixture sterilization cycles.

The standard biological indicator used for monitoring full-cycle steam sterilizers does not provide reliable monitoring flash sterilizers[980]. Biological indicators specifically designed for monitoring flash sterilization are now available, and studies comparing them have been published[846, 847, 981].

Since sterilization failure can occur (about 1% for steam)[982], a procedure to follow in the event of positive spore tests with steam sterilization has been provided by CDC and the Association of periOperative Registered Nurses (AORN). The 1981 CDC recommendation is that "objects, other than implantable objects, do not need to be recalled because of a single positive spore test unless the steam sterilizer or the sterilization procedure is defective." The rationale for this recommendation is that single positive spore tests in sterilizers occur sporadically. They may occur for reasons such as slight variation in the resistance of the spores[983], improper use of the sterilizer, and laboratory contamination during culture (uncommon with self-contained spore tests). If the mechanical (e.g., time, temperature, pressure in the steam sterilizer) and chemical (internal and/or external) indicators suggest that the sterilizer was functioning properly, a single positive spore test probably does not indicate sterilizer malfunction but the spore test should be repeated immediately [983]. If the spore tests remain positive, use of the sterilizer should be discontinued until it is serviced[1]. Similarly, AORN states that a single positive spore test does not necessarily indicate a sterilizer failure. If the test is positive, the sterilizer should immediately be rechallenged for proper use and function. Items, other than implantable ones, do not necessarily need to be recalled unless a sterilizer malfunction is found. If a sterilizer malfunction is discovered, the items must be considered nonsterile, and the items from the suspect load(s) should be recalled, insofar as

possible, and reprocessed [984]. A suggested protocol for management of positive biological indicators is shown in Table 12[839]. A more conservative approach also has been recommended [813] in which any positive spore test is assumed to represent sterilizer malfunction and requires that all materials processed in that sterilizer, dating from the sterilization cycle having the last negative biologic indicator to the next cycle showing satisfactory biologic indicator challenge results, must be considered nonsterile and retrieved, if possible, and reprocessed. This more conservative approach should be used for sterilization methods other than steam (e.g., ETO, hydrogen peroxide gas plasma). However, no action is necessary if there is strong evidence for the biological indicator being defective [983] or the growth medium contained a *Bacillus* contaminant[985].

If patient-care items were used before retrieval, the infection control professional should assess the risk of infection in collaboration with central processing, surgical services, and risk management staff. The factors that should be considered include the chemical indicator result (e.g., nonreactive chemical indicator may indicate temperature not achieved); the results of other biological indicators that followed the positive biological indicator (e.g., positive on Tuesday, negative on Wednesday); the parameters of the sterilizer associated with the positive biological indicator (e.g., reduced time at correct temperature); the time-temperature chart (or printout); and the microbial load associated with decontaminated surgical instruments (e.g., 85% of decontaminated surgical instruments have less than 100 CFU). The margin of safety in steam sterilization is sufficiently large that there is minimal infection risk associated with items in a load that show spore growth, especially if the item was properly cleaned and the temperature was achieved (e.g., as shown by acceptable chemical indicator or temperature chart). There are no published studies that document disease transmission via a nonretrieved surgical instrument following a sterilization cycle with a positive biological indicator.

False-positive biological indicators may occur from improper testing or faulty indicators. The latter may occur from improper storage, processing, product contamination, material failure, or variation in resistance of spores. Gram stain and subculture of a positive biological indicator may determine if a contaminant has created a false-positive result[839, 986]. However, in one incident, the broth used as growth medium contained a contaminant, *B. coagulans*, which resulted in broth turbidity at 55°C[985]. Testing of paired biological indicators from different manufacturers can assist in assessing a product defect[839]. False-positive biological indicators due to extrinsic contamination when using self-contained biological indicators should be uncommon. A biological indicator should not be considered a false-positive indicator until a thorough analysis of the entire sterilization process shows this to be likely.

The size and composition of the biological indicator test pack should be standardized to create a significant challenge to air removal and sterilant penetration and to obtain interpretable results. There is a standard 16-towel pack recommended by AAMI for steam sterilization [813, 819, 987] consisting of 16 clean, preconditioned, reusable huck or absorbent surgical towels each of which is approximately 16 inches by 26 inches. Each towel is folded lengthwise into thirds and then folded widthwise in the middle. One or more biological indicators are placed between the eight and ninth towels in the approximate geometric center of the pack. When the towels are folded and placed one on top of another, to form a stack (approximately 6 inch height) it should weigh approximately 3 pounds and should have a density of approximately 11.3 pounds per cubic foot[813]. This test pack has not gained universal use as a standard pack that simulates the actual in-use conditions of steam sterilizers. Commercially available disposable test packs that have been shown to be equivalent to the AAMI 16 towel test pack also may be used. The test pack should be placed flat in an otherwise fully loaded sterilizer chamber, in the area least favorable to sterilization (i.e., the area representing the greatest challenge to the biological indicator). This area is normally in the front, bottom section of the sterilizer, near the drain[811, 813]. A control biological indicator from the lot used for testing should be left unexposed to the sterilant, and then incubated to verify the presterilization viability of the test spores and proper incubation. The most conservative approach would be to use a control for each run; however, less frequent use may be adequate (e.g., weekly). There also is a routine test pack for ETO where a biological indicator is placed in a plastic syringe with plunger, then placed in the folds of a clean surgical towel, and wrapped. Alternatively, commercially available disposal

test packs that have been shown to be equivalent to the AAMI test pack may be used. The test pack is placed in the center of the sterilizer load[814]. Sterilization records (mechanical, chemical, and biological) should be retained for a time period in compliance with standards (e.g., Joint Commission for the Accreditation of Healthcare Facilities requests 3 years) and state and federal regulations.

In Europe, biological monitors are not used routinely to monitor the sterilization process. Instead, release of sterilizer items is based on monitoring the physical conditions of the sterilization process that is termed "parametric release." Parametric release requires that there is a defined quality system in place at the facility performing the sterilization and that the sterilization process be validated for the items being sterilized. At present in Europe, parametric release is accepted for steam, dry heat, and ionizing radiation processes, as the physical conditions are understood and can be monitored directly[988]. For example, with steam sterilizers the load could be monitored with probes that would yield data on temperature, time, and humidity at representative locations in the chamber and compared to the specifications developed during the validation process.

Periodic infection control rounds to areas using sterilizers to standardize the sterilizer's use may identify correctable variances in operator competence; documentation of sterilization records, including chemical and biological indicator test results; sterilizer maintenance and wrapping; and load numbering of packs. These rounds also may identify improvement activities to ensure that operators are adhering to established standards[989].

REUSE OF SINGLE-USE MEDICAL DEVICES

The reuse of single-use medical devices began in the late 1970s. Before this time most devices were considered reusable. Reuse of single-use devices increased as a cost-saving measure. Approximately 20 to 30% of U.S. hospitals reported that they reuse at least one type of single-use device. Reuse of single-use devices involves regulatory, ethical, medical, legal and economic issues and has been extremely controversial for more than two decades[990]. The U.S. public has expressed increasing concern regarding the risk of infection and injury when reusing medical devices intended and labeled for single use. Although some investigators have demonstrated it is safe to reuse disposable medical devices such as cardiac electrode catheters, [991-993] additional studies are needed to define the risks [994] and document the benefits. In August 2000, FDA released a guidance document on single-use devices reprocessed by third parties or hospitals[995]. In this guidance document, FDA states that hospitals or third-party reprocessors will be considered "manufacturers" and regulated in the same manner. A reused single-use device will have to comply with the same regulatory requirements of the device when it was originally manufactured. This document presents FDA's intent to enforce premarket submission requirements within 6 months (February 2001) for class III devices (e.g., cardiovascular intra-aortic balloon pump, transluminal coronary angioplasty catheter); 12 months (August 2001) for class II devices (e.g., blood pressure cuff, bronchoscope biopsy forceps); and 18 months (February 2002) for class I devices (e.g., disposable medical scissors, ophthalmic knife). FDA uses two types of premarket requirements for nonexempt class I and II devices, a 510(k) submission that may have to show that the device is as safe and effective as the same device when new, and a premarket approval application. The 510(k) submission must provide scientific evidence that the device is safe and effective for its intended use. FDA allowed hospitals a year to comply with the nonpremarket requirements (registration and listing, reporting adverse events associated with medical devices, quality system regulations, and proper labeling). The options for hospitals are to stop reprocessing single-use devices, comply with the rule, or outsource to a third-party reprocessor. FDA guidance document does not apply to permanently implantable pacemakers, hemodialyzers, opened but unused single-use devices, or healthcare settings other than acute-care hospitals. The reuse of single use medical devices continues to be an evolving area of regulations. For this reason, healthcare workers should refer to FDA for the latest guidance (www.fda.gov)[996].

CONCLUSION

When properly used, disinfection and sterilization can ensure the safe use of invasive and non-invasive medical devices. However, current disinfection and sterilization guidelines must be strictly followed.

WED-BASED DISINFECTION AND STERILIZATION RESOURCES

Additional information about disinfection and sterilization is available at the following dedicated websites:

Food and Drug Administration, Rockville, Maryland
http://www.fda.gov/dcrh/ode/germlab.html

Environmental Protection Agency, Washington, D.C.
http://www.epa.gov/oppad001/chemregindex.htm

Centers for Disease Control and Prevention, Atlanta, Georgia
http://www.cdc.gov/ncidod/dhqp/sterile.html

University of North Carolina, Chapel Hill, North Carolina
http://www.disinfectionandsterilization.org

RECOMMENDATIONS FOR DISINFECTION AND STERILIZATION IN HEALTHCARE FACILITIES

A. Rationale

The ultimate goal of the Recommendations for Disinfection and Sterilization in Health-Care Facilities, 2008, is to reduce rates of health-care–associated infections through appropriate use of both disinfection and sterilization. Each recommendation is categorized according to scientific evidence, theoretical rationale, applicability, and federal regulations. Examples are included in some recommendations to aid the reader; however, these examples are not intended to define the only method of implementing the recommendation. The CDC system for categorizing recommendations is defined in the following (Rankings) section.

B. Rankings

Category IA. Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.

Category IB. Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies, and by a strong theoretical rationale.

Category IC. Required by state or federal regulations. Because of state differences, readers should not assume that the absence of an *IC* recommendation implies the absence of state regulations.

Category II. Suggested for implementation and supported by suggestive clinical or epidemiologic studies or by a theoretical rationale.

No recommendation. Unresolved issue. These include practices for which insufficient evidence or no consensus exists regarding efficacy.

C. Recommendations

1. *Occupational Health and Exposure*

a. Inform each worker of the possible health effects of his or her exposure to infectious agents (e.g., hepatitis B virus [HBV], hepatitis C virus, human immunodeficiency virus [HIV]), and/or chemicals (e.g., EtO, formaldehyde). The information should be consistent with Occupational Safety and Health Administration (OSHA) requirements and identify the areas and tasks in which potential exists for exposure. *Category II, IC*[214, 320, 959, 997, 998]

b. Educate health-care workers in the selection and proper use of personal protective equipment (PPE). *Category II, IC*

c. Ensure that workers wear appropriate PPE to preclude exposure to infectious agents or chemicals through the respiratory system, skin, or mucous membranes of the eyes, nose, or mouth. PPE can include gloves, gowns, masks, and eye protection. The exact type of PPE depends on the infectious or chemical agent and the anticipated duration of exposure. The employer is responsible for making such equipment and training available. *Category II, IC*. [214, 997-999]

d. Establish a program for monitoring occupational exposure to regulated chemicals (e.g., formaldehyde, EtO) that adheres to state and federal regulations. *Category II, IC*. [997, 1000, 1001]

e. Exclude healthcare workers with weeping dermatitis of hands from direct contact with patient-care equipment. *Category IB*. [1002, 1003]

2. *Cleaning of Patient-Care Devices*

a. In hospitals, perform most cleaning, disinfection, and sterilization of patient-care devices in a central processing department in order to more easily control quality. *Category II*. [454, 836, 959]

b. Meticulously clean patient-care items with water and detergent, or with water and enzymatic cleaners before high-level disinfection or sterilization procedures. *Category IB*. [6, 83, 101, 104-106, 124, 179, 424-426, 436, 465, 471, 911-913, 1004]

i. Remove visible organic residue (e.g., residue of blood and tissue) and inorganic salts with cleaning. Use cleaning agents that are capable of removing visible organic and inorganic residues. *Category IB*. [424-426, 466, 468, 469, 471, 908, 910]

ii. Clean medical devices as soon as practical after use (e.g., at the point of use) because soiled materials become dried onto the instruments. Dried or baked materials on the instrument make the removal process more difficult and the disinfection or sterilization process less effective or ineffective. *Category IB.* [55, 56, 59, 291, 465, 1005, 1006]

c. Perform either manual cleaning (i.e., using friction) or mechanical cleaning (e.g., with ultrasonic cleaners, washer-disinfector, washer-sterilizers). *Category IB.* [426, 456, 471, 999]

d. If using an automatic washer/disinfector, ensure that the unit is used in accordance with the manufacturer's recommendations. *Category IB.* [7, 133, 155, 725]

e. Ensure that the detergents or enzymatic cleaners selected are compatible with the metals and other materials used in medical instruments. Ensure that the rinse step is adequate for removing cleaning residues to levels that will not interfere with subsequent disinfection/sterilization processes. *Category II.* [836, 1004]

f. Inspect equipment surfaces for breaks in integrity that would impair either cleaning or disinfection/sterilization. Discard or repair equipment that no longer functions as intended or cannot be properly cleaned, and disinfected or sterilized. *Category II.* [888]

g.

3. ***Indications for Sterilization, High-Level Disinfection, and Low-Level Disinfection***

a. Before use on each patient, sterilize critical medical and surgical devices and instruments that enter normally sterile tissue or the vascular system or through which a sterile body fluid flows (e.g., blood). See recommendation 7g for exceptions. *Category IA.* [179, 497, 821, 822, 907, 911, 912]

b. Provide, at a minimum, high-level disinfection for semicritical patient-care equipment (e.g., gastrointestinal endoscopes, endotracheal tubes, anesthesia breathing circuits, and respiratory therapy equipment) that touches either mucous membranes or nonintact skin. *Category IA.* [6-8, 17, 20, 99, 101, 108, 113-115, 129, 138, 139, 147, 152-154, 471, 1007]

c. Perform low-level disinfection for noncritical patient-care surfaces (e.g., bedrails, over-the-bed table) and equipment (e.g., blood pressure cuff) that touch intact skin (see Recommendation 5g). *Category II.* [17, 46-48, 50-52, 67, 68, 372, 373, 378, 382, 401]

4. ***Selection and Use of Low-Level Disinfectants for Noncritical Patient-Care Devices***

a. Process noncritical patient-care devices using a disinfectant and the concentration of germicide listed in Table 1. *Category IB.* [17, 46-48, 50-52, 67, 68, 378, 382, 401]

b. Disinfect noncritical medical devices (e.g., blood pressure cuff) with an EPA-registered hospital disinfectant using the label's safety precautions and use directions. Most EPA-registered hospital disinfectants have a label contact time of 10 minutes. However, multiple scientific studies have demonstrated the efficacy of hospital disinfectants against pathogens with a contact time of at least 1 minute. By law, all applicable label instructions on EPA-registered products must be followed. If the user selects exposure conditions that differ from those on the EPA-registered product label, the user assumes liability from any injuries resulting from off-label use and is potentially subject to enforcement action under FIFRA. *Category IB.* [17, 47, 48, 50, 51, 53-57, 59, 60, 62-64, 355, 378, 382]

c. Ensure that, at a minimum, noncritical patient-care devices are disinfected when visibly soiled and on a regular basis (such as after use on each patient or once daily or once weekly). *Category II.* [378, 380, 1008]

d. If dedicated, disposable devices are not available, disinfect noncritical patient-care equipment after using it on a patient who is on contact precautions before using this equipment on another patient. *Category IB.* [47, 67, 391, 1009]

5. ***Cleaning and Disinfecting Environmental Surfaces in Healthcare Facilities***

a. Clean housekeeping surfaces (e.g., floors, tabletops) on a regular basis, when spills occur, and when these surfaces are visibly soiled. *Category II.* [23, 378, 380, 382, 1008, 1010]

b. Disinfect (or clean) environmental surfaces on a regular basis (e.g., daily, three times per week) and when surfaces are visibly soiled. *Category II.* [378, 380, 402, 1008]

c. Follow manufacturers' instructions for proper use of disinfecting (or detergent) products — such as recommended use-dilution, material compatibility, storage, shelf-life, and safe use and

disposal. *Category II.* [327, 365, 404]

d. Clean walls, blinds, and window curtains in patient-care areas when these surfaces are visibly contaminated or soiled. *Category II.* [1011]

e. Prepare disinfecting (or detergent) solutions as needed and replace these with fresh solution frequently (e.g., replace floor mopping solution every three patient rooms, change no less often than at 60-minute intervals), according to the facility's policy. *Category IB.* [68, 379]

f. Decontaminate mop heads and cleaning cloths regularly to prevent contamination (e.g., launder and dry at least daily). *Category II.* [68, 402, 403]

g. Use a one-step process and an EPA-registered hospital disinfectant designed for housekeeping purposes in patient care areas where 1) uncertainty exists about the nature of the soil on the surfaces (e.g., blood or body fluid contamination versus routine dust or dirt); or 2) uncertainty exists about the presence of multidrug resistant organisms on such surfaces. See 5n for recommendations requiring cleaning and disinfecting blood-contaminated surfaces. *Category II.* [23, 47, 48, 51, 214, 378, 379, 382, 416, 1012]

h. Detergent and water are adequate for cleaning surfaces in nonpatient-care areas (e.g., administrative offices). *Category II.* [23]

i. Do not use high-level disinfectants/liquid chemical sterilants for disinfection of non-critical surfaces. *Category IB.* [23, 69, 318]

j. Wet-dust horizontal surfaces regularly (e.g., daily, three times per week) using clean cloths moistened with an EPA-registered hospital disinfectant (or detergent). Prepare the disinfectant (or detergent) as recommended by the manufacturer. *Category II.* [68, 378, 380, 402, 403, 1008]

k. Disinfect noncritical surfaces with an EPA-registered hospital disinfectant according to the label's safety precautions and use directions. Most EPA-registered hospital disinfectants have a label contact time of 10 minutes. However, many scientific studies have demonstrated the efficacy of hospital disinfectants against pathogens with a contact time of at least 1 minute. By law, the user must follow all applicable label instructions on EPA-registered products. If the user selects exposure conditions that differ from those on the EPA-registered product label, the user assumes liability for any injuries resulting from off-label use and is potentially subject to enforcement action under FIFRA. *Category II, IC.* [17, 47, 48, 50, 51, 53-57, 59, 60, 62-64, 355, 378, 382]

l. Do not use disinfectants to clean infant bassinets and incubators while these items are occupied. If disinfectants (e.g., phenolics) are used for the terminal cleaning of infant bassinets and incubators, thoroughly rinse the surfaces of these items with water and dry them before these items are reused. *Category IB.* [17, 739, 740]

m. Promptly clean and decontaminate spills of blood and other potentially infectious materials. Discard blood-contaminated items in compliance with federal regulations. *Category IB, IC.* [214]

n. For site decontamination of spills of blood or other potentially infectious materials (OPIM), implement the following procedures. Use protective gloves and other PPE (e.g., when sharps are involved use forceps to pick up sharps, and discard these items in a puncture-resistant container) appropriate for this task. Disinfect areas contaminated with blood spills using an EPA-registered tuberculocidal agent, a registered germicide on the EPA Lists D and E (i.e., products with specific label claims for HIV or HBV or freshly diluted hypochlorite solution. *Category II, IC.* [214, 215, 557, 1013] If sodium hypochlorite solutions are selected use a 1:100 dilution (e.g., 1:100 dilution of a 5.25-6.15% sodium hypochlorite provides 525-615 ppm available chlorine) to decontaminate nonporous surfaces after a small spill (e.g., <10 mL) of either blood or OPIM. If a spill involves large amounts (e.g., >10 mL) of blood or OPIM, or involves a culture spill in the laboratory, use a 1:10 dilution for the first application of hypochlorite solution before cleaning in order to reduce the risk of infection during the cleaning process in the event of a sharp injury. Follow this decontamination process with a terminal disinfection, using a 1:100 dilution of sodium hypochlorite. *Category IB, IC.* [63, 215, 557]

o. If the spill contains large amounts of blood or body fluids, clean the visible matter with disposable absorbent material, and discard the contaminated materials in appropriate, labeled containment. *Category II, IC.* [44, 214]

p. Use protective gloves and other PPE appropriate for this task. *Category II, IC.* [44, 214]

q. In units with high rates of endemic *Clostridium difficile* infection or in an outbreak setting, use dilute solutions of 5.25%–6.15% sodium hypochlorite (e.g., 1:10 dilution of household bleach) for routine environmental disinfection. Currently, no products are EPA-registered specifically for inactivating *C. difficile* spores. *Category II.* [257-259]

r. If chlorine solution is not prepared fresh daily, it can be stored at room temperature for up to 30 days in a capped, opaque plastic bottle with a 50% reduction in chlorine concentration after 30 days of storage (e.g., 1000 ppm chlorine [approximately a 1:50 dilution] at day 0 decreases to 500 ppm chlorine by day 30). *Category IB.* [327, 1014]

s. An EPA-registered sodium hypochlorite product is preferred, but if such products are not available, generic versions of sodium hypochlorite solutions (e.g., household chlorine bleach) can be used. *Category II.* [44]

6. ***Disinfectant Fogging***

a. Do not perform disinfectant fogging for routine purposes in patient-care areas. *Category II.* [23, 228]

7. ***High-Level Disinfection of Endoscopes***

a. To detect damaged endoscopes, test each flexible endoscope for leaks as part of each reprocessing cycle. Remove from clinical use any instrument that fails the leak test, and repair this instrument. *Category II.* [113, 115, 116]

b. Immediately after use, meticulously clean the endoscope with an enzymatic cleaner that is compatible with the endoscope. Cleaning is necessary before both automated and manual disinfection. *Category IA.* [83, 101, 104-106, 113, 115, 116, 124, 126, 456, 465, 466, 471, 1015]

c. Disconnect and disassemble endoscopic components (e.g., suction valves) as completely as possible and completely immerse all components in the enzymatic cleaner. Steam sterilize these components if they are heat stable. *Category IB.* [115, 116, 139, 465, 466]

d. Flush and brush all accessible channels to remove all organic (e.g., blood, tissue) and other residue. Clean the external surfaces and accessories of the devices by using a soft cloth or sponge or brushes. Continue brushing until no debris appears on the brush. *Category IA* [6, 17, 108, 113, 115, 116, 137, 145, 147, 725, 856, 903]

e. Use cleaning brushes appropriate for the size of the endoscope channel or port (e.g., bristles should contact surfaces). Cleaning items (e.g., brushes, cloth) should be disposable or, if they are not disposable, they should be thoroughly cleaned and either high-level disinfected or sterilized after each use. *Category II.* [113, 115, 116, 1016]

f. Discard enzymatic cleaners (or detergents) after each use because they are not microbicidal and, therefore, will not retard microbial growth. *Category IB.* [38, 113, 115, 116, 466]

g. Process endoscopes (e.g., arthroscopes, cystoscope, laparoscopes) that pass through normally sterile tissues using a sterilization procedure before each use; if this is not feasible, provide at least high-level disinfection. High-level disinfection of arthroscopes, laparoscopes, and cytoscopes should be followed by a sterile water rinse. *Category IB.* [1, 17, 31, 32, 35, 89, 90, 113, 554]

h. Phase out endoscopes that are critical items (e.g., arthroscopes, laparoscopes) but cannot be steam sterilized. Replace these endoscopes with steam sterilizable instruments when feasible. *Category II.*

i. Mechanically clean reusable accessories inserted into endoscopes (e.g., biopsy forceps or other cutting instruments) that break the mucosal barrier (e.g., ultrasonically clean biopsy forceps) and then sterilize these items between each patient. *Category IA.* [1, 6, 8, 17, 108, 113, 115, 116, 138, 145, 147, 153, 278]

j. Use ultrasonic cleaning of reusable endoscopic accessories to remove soil and organic material from hard-to-clean areas. *Category II.* [116, 145, 148]

k. Process endoscopes and accessories that contact mucous membranes as semicritical items, and use at least high-level disinfection after use on each patient. *Category IA.* [1, 6, 8, 17, 108, 113, 115, 116, 129, 138, 145-148, 152-154, 278]

l. Use an FDA-cleared sterilant or high-level disinfectant for sterilization or high-level disinfection (Table 1). *Category IA.* [1, 6-8, 17, 85, 108, 113, 115, 116, 147]

m. After cleaning, use formulations containing glutaraldehyde, glutaraldehyde with phenol/phenate,

ortho-phthalaldehyde, hydrogen peroxide, and both hydrogen peroxide and peracetic acid to achieve high-level disinfection followed by rinsing and drying (see Table 1 for recommended concentrations). *Category IB.* [1, 6-8, 17, 38, 85, 108, 113, 145-148]

n. Extend exposure times beyond the minimum effective time for disinfecting semicritical patient-care equipment cautiously and conservatively because extended exposure to a high-level disinfectant is more likely to damage delicate and intricate instruments such as flexible endoscopes. The exposure times vary among the Food and Drug Administration (FDA)-cleared high-level disinfectants (Table 2). *Category IB.* [17, 69, 73, 76, 78, 83]

o. Federal regulations are to follow the FDA-cleared label claim for high-level disinfectants. The FDA-cleared labels for high-level disinfection with >2% glutaraldehyde at 25°C range from 20-90 minutes, depending upon the product based on three tier testing which includes AOAC sporicidal tests, simulated use testing with mycobacterial and in-use testing. *Category IC.*

p. Several scientific studies and professional organizations support the efficacy of >2% glutaraldehyde for 20 minutes at 20°C; that efficacy assumes adequate cleaning prior to disinfection, whereas the FDA-cleared label claim incorporates an added margin of safety to accommodate possible lapses in cleaning practices. Facilities that have chosen to apply the 20 minute duration at 20°C have done so based on the IA recommendation in the July 2003 SHEA position paper, "Multi-society Guideline for Reprocessing Flexible Gastrointestinal Endoscopes [12, 17, 19, 26, 27, 49, 55, 57, 58, 60, 73, 76, 79-81, 83-85, 93, 94, 104-106, 110, 111, 115-121, 124, 125, 233, 235, 236, 243, 265, 266, 609]

q. When using FDA-cleared high-level disinfectants, use manufacturers' recommended exposure conditions. Certain products may require a shorter exposure time (e.g., 0.55% ortho-phthalaldehyde for 12 minutes at 20°C, 7.35% hydrogen peroxide plus 0.23% peracetic acid for 15 minutes at 20°C) than glutaraldehyde at room temperature because of their rapid inactivation of mycobacteria or reduced exposure time because of increased mycobactericidal activity at elevated temperature (e.g., 2.5% glutaraldehyde at 5 minutes at 35°C). *Category IB.* [83, 100, 689, 693, 694, 700]

r. Select a disinfectant or chemical sterilant that is compatible with the device that is being reprocessed. Avoid using reprocessing chemicals on an endoscope if the endoscope manufacturer warns against using these chemicals because of functional damage (with or without cosmetic damage). *Category IB.* [69, 113, 116]

s. Completely immerse the endoscope in the high-level disinfectant, and ensure all channels are perfused. As soon as is feasible, phase out nonimmersible endoscopes. *Category IB.* [108, 113-116, 137, 725, 856, 882]

t. After high-level disinfection, rinse endoscopes and flush channels with sterile water, filtered water, or tapwater to prevent adverse effects on patients associated with disinfectant retained in the endoscope (e.g., disinfectant induced colitis). Follow this water rinse with a rinse with 70% - 90% ethyl or isopropyl alcohol. *Category IB.* [17, 31-35, 38, 39, 108, 113, 115, 116, 134, 145-148, 620-622, 624-630, 1017]

u. After flushing all channels with alcohol, purge the channels using forced air to reduce the likelihood of contamination of the endoscope by waterborne pathogens and to facilitate drying. *Category IB.* [39, 113, 115, 116, 145, 147]

v. Hang endoscopes in a vertical position to facilitate drying. *Category II.* [17, 108, 113, 115, 116, 145, 815]

w. Store endoscopes in a manner that will protect them from damage or contamination. *Category II.* [17, 108, 113, 115, 116, 145]

x. Sterilize or high-level disinfect both the water bottle used to provide intraprocedural flush solution and its connecting tube at least once daily. After sterilizing or high-level disinfecting the water bottle, fill it with sterile water. *Category IB.* [10, 31-35, 113, 116, 1017]

y. Maintain a log for each procedure and record the following: patient's name and medical record number (if available), procedure, date, endoscopist, system used to reprocess the endoscope (if more than one system could be used in the reprocessing area), and serial number or other identifier of the endoscope used. *Category II.* [108, 113, 115, 116]

z. Design facilities where endoscopes are used and disinfected to provide a safe environment for healthcare workers and patients. Use air-exchange equipment (e.g., the ventilation system, out-exhaust ducts) to minimize exposure of all persons to potentially toxic vapors (e.g.,

glutaraldehyde vapor). Do not exceed the allowable limits of the vapor concentration of the chemical sterilant or high-level disinfectant (e.g., those of ACGIH and OSHA). *Category IB, IC.* [116, 145, 318, 322, 577, 652]

aa. Routinely test the liquid sterilant/high-level disinfectant to ensure minimal effective concentration of the active ingredient. Check the solution each day of use (or more frequently) using the appropriate chemical indicator (e.g., glutaraldehyde chemical indicator to test minimal effective concentration of glutaraldehyde) and document the results of this testing. Discard the solution if the chemical indicator shows the concentration is less than the minimum effective concentration. Do not use the liquid sterilant/high-level disinfectant beyond the reuse-life recommended by the manufacturer (e.g., 14 days for *ortho*-phthalaldehyde). *Category IA.* [76, 108, 113, 115, 116, 608, 609]

bb. Provide personnel assigned to reprocess endoscopes with device-specific reprocessing instructions to ensure proper cleaning and high-level disinfection or sterilization. Require competency testing on a regular basis (e.g., beginning of employment, annually) of all personnel who reprocess endoscopes. *Category IA.* [6-8, 108, 113, 115, 116, 145, 148, 155]

cc. Educate all personnel who use chemicals about the possible biologic, chemical, and environmental hazards of performing procedures that require disinfectants. *Category IB, IC.* [116, 997, 998, 1018, 1019]

dd. Make PPE(e.g., gloves, gowns, eyewear, face mask or shields, respiratory protection devices) available and use these items appropriately to protect workers from exposure to both chemicals and microorganisms (e.g., HBV). *Category IB, IC.* [115, 116, 214, 961, 997, 998, 1020, 1021]

ee. If using an automated endoscope reprocessor (AER), place the endoscope in the reprocessor and attach all channel connectors according to the AER manufacturer's instructions to ensure exposure of all internal surfaces to the high-level disinfectant/chemical sterilant. *Category IB.* [7, 8, 115, 116, 155, 725, 903]

ff. If using an AER, ensure the endoscope can be effectively reprocessed in the AER. Also, ensure any required manual cleaning/disinfecting steps are performed (e.g., elevator wire channel of duodenoscopes might not be effectively disinfected by most AERs). *Category IB.* [7, 8, 115, 116, 155, 725]

gg. Review the FDA advisories and the scientific literature for reports of deficiencies that can lead to infection because design flaws and improper operation and practices have compromised the effectiveness of AERs. *Category II.* [7, 98, 133, 134, 155, 725]

hh. Develop protocols to ensure that users can readily identify an endoscope that has been properly processed and is ready for patient use. *Category II.*

ii. Do not use the carrying case designed to transport clean and reprocessed endoscopes outside of the healthcare environment to store an endoscope or to transport the instrument within the healthcare environment. *Category II.*

jj. No recommendation is made about routinely performing microbiologic testing of either endoscopes or rinse water for quality assurance purposes. *Unresolved Issue.* [116, 164]

kk. If environmental microbiologic testing is conducted, use standard microbiologic techniques. *Category II.* [23, 116, 157, 161, 167]

ll. If a cluster of endoscopy-related infections occurs, investigate potential routes of transmission (e.g., person-to-person, common source) and reservoirs. *Category IA.* [8, 1022]

mm. Report outbreaks of endoscope-related infections to persons responsible for institutional infection control and risk management and to FDA. *Category IB.* [6, 7, 113, 116, 1023] Notify the local and the state health departments, CDC, and the manufacturer(s). *Category II.*

nn. No recommendation is made regarding the reprocessing of an endoscope again immediately before use if that endoscope has been processed after use according to the recommendations in this guideline. *Unresolved issue.* [157]

oo. Compare the reprocessing instructions provided by both the endoscope's and the AER's manufacturer's instructions and resolve any conflicting recommendations. *Category IB.* [116, 155]

8. ***Management of Equipment and Surfaces in Dentistry***

a. Dental instruments that penetrate soft tissue or bone (e.g., extraction forceps, scalpel blades, bone chisels, periodontal scalers, and surgical burs) are classified as critical and should be

sterilized after each use or discarded. In addition, after each use, sterilize dental instruments that are not intended to penetrate oral soft tissue or bone (e.g., amalgam condensers, air-water syringes) but that might contact oral tissues and are heat-tolerant, although classified as semicritical. Clean and, at a minimum, high-level disinfect heat-sensitive semicritical items. *Category IA.* [43, 209-211]

b. Noncritical clinical contact surfaces, such as uncovered operatory surfaces (e.g., countertops, switches, light handles), should be barrier-protected or disinfected between patients with an intermediate-disinfectant (i.e., EPA-registered hospital disinfectant with a tuberculocidal claim) or low-level disinfectant (i.e., EPA-registered hospital disinfectant with HIV and HBV claim). *Category IB.* [43, 209-211]

c. Barrier protective coverings can be used for noncritical clinical contact surfaces that are touched frequently with gloved hands during the delivery of patient care, that are likely to become contaminated with blood or body substances, or that are difficult to clean. Change these coverings when they are visibly soiled, when they become damaged, and on a routine basis (e.g., between patients). Disinfect protected surfaces at the end of the day or if visibly soiled. *Category II.* [43, 210]

9. Processing Patient-Care Equipment Contaminated with Bloodborne Pathogens (HBV, Hepatitis C Virus, HIV), Antibiotic-Resistant Bacteria (e.g., Vancomycin-Resistant Enterococci, Methicillin-Resistant Staphylococcus aureus, Multidrug Resistant Tuberculosis), or Emerging Pathogens (e.g., Cryptosporidium, Helicobacter pylori, Escherichia coli O157:H7, Clostridium difficile, Mycobacterium tuberculosis, Severe Acute Respiratory Syndrome Coronavirus), or Bioterrorist Agents

a. Use standard sterilization and disinfection procedures for patient-care equipment (as recommended in this guideline), because these procedures are adequate to sterilize or disinfect instruments or devices contaminated with blood or other body fluids from persons infected with bloodborne pathogens or emerging pathogens, with the exception of prions. No changes in these procedures for cleaning, disinfecting, or sterilizing are necessary for removing bloodborne and emerging pathogens other than prions. *Category IA.* [22, 53, 60-62, 73, 79-81, 105, 118-121, 125, 126, 221, 224-234, 236, 244, 265, 266, 271-273, 279, 282, 283, 354-357, 666]

10. Disinfection Strategies for Other Semicritical Devices

a. Even if probe covers have been used, clean and high-level disinfect other semicritical devices such as rectal probes, vaginal probes, and cryosurgical probes with a product that is not toxic to staff, patients, probes, and retrieved germ cells (if applicable). Use a high-level disinfectant at the FDA-cleared exposure time. (See Recommendations 7o and 11e for exceptions.) *Category IB.* [6-8, 17, 69]

b. When probe covers are available, use a probe cover or condom to reduce the level of microbial contamination. *Category II.* [197-201] Do not use a lower category of disinfection or cease to follow the appropriate disinfectant recommendations when using probe covers because these sheaths and condoms can fail. *Category IB* [197-201]

c. After high-level disinfection, rinse all items. Use sterile water, filtered water or tapwater followed by an alcohol rinse for semicritical equipment that will have contact with mucous membranes of the upper respiratory tract (e.g., nose, pharynx, esophagus). *Category II.* [10, 31-35, 1017]

d. There is no recommendation to use sterile or filtered water rather than tapwater for rinsing semicritical equipment that contact the mucous membranes of the rectum (e.g., rectal probes, anoscope) or vagina (e.g., vaginal probes). *Unresolved issue.* [11]

e. Wipe clean tonometer tips and then disinfect them by immersing for 5-10 minutes in either 5000 ppm chlorine or 70% ethyl alcohol. None of these listed disinfectant products are FDA-cleared high-level disinfectants. *Category II.* [49, 95, 185, 188, 293]

11. Disinfection by Healthcare Personnel in Ambulatory Care and Home Care

a. Follow the same classification scheme described above (i.e., that critical devices require sterilization, semicritical devices require high-level disinfection, and noncritical equipment

requires low-level disinfection) in the ambulatory-care (outpatient medical/surgical facilities) setting because risk for infection in this setting is similar to that in the hospital setting (see Table 1). *Category IB.* [6-8, 17, 330]

b. When performing care in the home, clean and disinfect reusable objects that touch mucous membranes (e.g., tracheostomy tubes) by immersing these objects in a 1:50 dilution of 5.25%-6.15% sodium hypochlorite (household bleach) (3 minutes), 70% isopropyl alcohol (5 minutes), or 3% hydrogen peroxide (30 minutes) because the home environment is, in most instances, safer than either hospital or ambulatory care settings because person-to-person transmission is less likely. *Category II.* [327, 328, 330, 331]

c. Clean noncritical items that would not be shared between patients (e.g., crutches, blood pressure cuffs) in the home setting with a detergent or commercial household disinfectant. *Category II.* [53, 330]

12. *Microbial Contamination of Disinfectants*

a. Institute the following control measures to reduce the occurrence of contaminated disinfectants: 1) prepare the disinfectant correctly to achieve the manufacturer's recommended use-dilution; and 2) prevent common sources of extrinsic contamination of germicides (e.g., container contamination or surface contamination of the healthcare environment where the germicide are prepared and/or used). *Category IB.* [404, 406, 1024]

13. *Flash Sterilization*

a. Do not flash sterilize implanted surgical devices unless doing so is unavoidable. *Category IB.* [849, 850]

b. Do not use flash sterilization for convenience, as an alternative to purchasing additional instrument sets, or to save time. Category II. [817, 962]

c. When using flash sterilization, make sure the following parameters are met: 1) clean the item before placing it in the sterilizing container (that are FDA cleared for use with flash sterilization) or tray; 2) prevent exogenous contamination of the item during transport from the sterilizer to the patient; and 3) monitor sterilizer function with mechanical, chemical, and biologic monitors. *Category IB.* [812, 819, 846, 847, 962]

d. Do not use packaging materials and containers in flash sterilization cycles unless the sterilizer and the packaging material/container are designed for this use. *Category IB.* [812, 819, 1025]

e. When necessary, use flash sterilization for patient-care items that will be used immediately (e.g., to reprocess an inadvertently dropped instrument). *Category IB.* [812, 817, 819, 845]

f. When necessary, use flash sterilization for processing patient-care items that cannot be packaged, sterilized, and stored before use. *Category IB.* [812, 819]

14. *Methods of Sterilization*

a. Steam is the preferred method for sterilizing critical medical and surgical instruments that are not damaged by heat, steam, pressure, or moisture. *Category IA.* [181, 271, 425, 426, 827, 841, 1026, 1027]

b. Cool steam- or heat-sterilized items before they are handled or used in the operative setting. *Category IB.* [850]

c. Follow the sterilization times, temperatures, and other operating parameters (e.g., gas concentration, humidity) recommended by the manufacturers of the instruments, the sterilizer, and the container or wrap used, and that are consistent with guidelines published by government agencies and professional organizations. *Category IB.* [811-814, 819, 825, 827, 841, 1026-1028]

d. Use low-temperature sterilization technologies (e.g., EtO, hydrogen peroxide gas plasma) for reprocessing critical patient-care equipment that is heat or moisture sensitive. *Category IA* [469, 721, 825, 856, 858, 878, 879, 881, 882, 890, 891, 1027]

e. Completely aerate surgical and medical items that have been sterilized in the EtO sterilizer (e.g., polyvinylchloride tubing requires 12 hours at 50°C, 8 hours at 60°C) before using these items in patient care. *Category IB.* [814]

f. Sterilization using the peracetic acid immersion system can be used to sterilize heat-sensitive

immersible medical and surgical items. *Category IB.* [90, 717-719, 721-724]

g. Critical items that have been sterilized by the peracetic acid immersion process must be used immediately (i.e., items are not completely protected from contamination, making long-term storage unacceptable). *Category II.* [817, 825]

h. Dry-heat sterilization (e.g., 340°F for 60 minutes) can be used to sterilize items (e.g., powders, oils) that can sustain high temperatures. *Category IB.* [815, 827]

i. Comply with the sterilizer manufacturer's instructions regarding the sterilizer cycle parameters (e.g., time, temperature, concentration). *Category IB.* [155, 725, 811-814, 819]

j. Because narrow-lumen devices provide a challenge to all low-temperature sterilization technologies and direct contact is necessary for the sterilant to be effective, ensure that the sterilant has direct contact with contaminated surfaces (e.g., scopes processed in peracetic acid must be connected to channel irrigators). *Category IB.* [137, 725, 825, 856, 890, 891, 1029]

15. *Packaging*

a. Ensure that packaging materials are compatible with the sterilization process and have received FDA 510[k] clearance. *Category IB.* [811-814, 819, 966]

b. Ensure that packaging is sufficiently strong to resist punctures and tears to provide a barrier to microorganisms and moisture. *Category IB.* [454, 811-814, 819, 966]

16. *Monitoring of Sterilizers*

a. Use mechanical, chemical, and biologic monitors to ensure the effectiveness of the sterilization process. *Category IB.* [811-815, 819, 846, 847, 975-977]

b. Monitor each load with mechanical (e.g., time, temperature, pressure) and chemical (internal and external) indicators. If the internal chemical indicator is visible, an external indicator is not needed. *Category II.* [811-815, 819, 846, 847, 975-977, 980]

c. Do not use processed items if the mechanical (e.g., time, temperature, pressure) or chemical (internal and/or external) indicators suggest inadequate processing. *Category IB* [811-814, 819].

d. Use biologic indicators to monitor the effectiveness of sterilizers at least weekly with an FDA-cleared commercial preparation of spores (e.g., *Geobacillus stearothermophilus* for steam) intended specifically for the type and cycle parameters of the sterilizer. *Category IB.* [1, 811, 813-815, 819, 846, 847, 976, 977]

e. After a single positive biologic indicator used with a method other than steam sterilization, treat as nonsterile all items that have been processed in that sterilizer, dating from the sterilization cycle having the last negative biologic indicator to the next cycle showing satisfactory biologic indicator results. These nonsterile items should be retrieved if possible and reprocessed. *Category II.* [1]

f. After a positive biologic indicator with steam sterilization, objects other than implantable objects do not need to be recalled because of a single positive spore test unless the sterilizer or the sterilization procedure is defective as determined by maintenance personnel or inappropriate cycle settings. If additional spore tests remain positive, consider the items nonsterile and recall and reprocess the items from the implicated load(s). *Category II.* [1]

g. Use biologic indicators for every load containing implantable items and quarantine items, whenever possible, until the biologic indicator is negative. *Category IB.* [811-814, 819]

17. *Load Configuration.*

a. Place items correctly and loosely into the basket, shelf, or cart of the sterilizer so as not to impede the penetration of the sterilant. *Category IB.* [445, 454, 811, 813, 819, 836]

18. *Storage of Sterile Items*

a. Ensure the sterile storage area is a well-ventilated area that provides protection against dust, moisture, insects, and temperature and humidity extremes. *Category II.* [454, 819, 836, 969]

b. Store sterile items so the packaging is not compromised (e.g., punctured, bent). *Category II.* [454, 816, 819, 968, 969, 1030]

c. Label sterilized items with a load number that indicates the sterilizer used, the cycle or load number, the date of sterilization, and, if applicable, the expiration date. *Category IB.* [811, 812, 814, 816, 819]

d. The shelf life of a packaged sterile item depends on the quality of the wrapper, the storage conditions, the conditions during transport, the amount of handling, and other events (moisture) that compromise the integrity of the package. If event-related storage of sterile items is used, then packaged sterile items can be used indefinitely unless the packaging is compromised (see f and g below). *Category IB.* [816, 819, 836, 968, 973, 1030, 1031]

e. Evaluate packages before use for loss of integrity (e.g., torn, wet, punctured). The pack can be used unless the integrity of the packaging is compromised. *Category II.* [819, 968]

f. If the integrity of the packaging is compromised (e.g., torn, wet, or punctured), repack and reprocess the pack before use. *Category II.* [819, 1032]

g. If time-related storage of sterile items is used, label the pack at the time of sterilization with an expiration date. Once this date expires, reprocess the pack. *Category II.* [819, 968]

19. ***Quality Control***

a. Provide comprehensive and intensive training for all staff assigned to reprocess semicritical and critical medical/surgical instruments to ensure they understand the importance of reprocessing these instruments. To achieve and maintain competency, train each member of the staff that reprocesses semicritical and/or critical instruments as follows: 1) provide hands-on training according to the institutional policy for reprocessing critical and semicritical devices; 2) supervise all work until competency is documented for each reprocessing task; 3) conduct competency testing at beginning of employment and regularly thereafter (e.g., annually); and 4) review the written reprocessing instructions regularly to ensure they comply with the scientific literature and the manufacturers' instructions. *Category IB.* [6-8, 108, 114, 129, 155, 725, 813, 819]

b. Compare the reprocessing instructions (e.g., for the appropriate use of endoscope connectors, the capping/noncapping of specific lumens) provided by the instrument manufacturer and the sterilizer manufacturer and resolve any conflicting recommendations by communicating with both manufacturers. *Category IB.* [155, 725]

c. Conduct infection control rounds periodically (e.g., annually) in high-risk reprocessing areas (e.g., the Gastroenterology Clinic, Central Processing); ensure reprocessing instructions are current and accurate and are correctly implemented. Document all deviations from policy. All stakeholders should identify what corrective actions will be implemented. *Category IB.* [6-8, 129]

d. Include the following in a quality control program for sterilized items: a sterilizer maintenance contract with records of service; a system of process monitoring; air-removal testing for prevacuum steam sterilizers; visual inspection of packaging materials; and traceability of load contents. *Category II* [811-814, 819].

e. For each sterilization cycle, record the type of sterilizer and cycle used; the load identification number; the load contents; the exposure parameters (e.g., time and temperature); the operator's name or initials; and the results of mechanical, chemical, and biological monitoring. *Category II* [811-814, 819].

f. Retain sterilization records (mechanical, chemical, and biological) for a time period that complies with standards (e.g., 3 years), statutes of limitations, and state and federal regulations. *Category II, IC.* [1033]

g. Prepare and package items to be sterilized so that sterility can be achieved and maintained to the point of use. Consult the Association for the Advancement of Medical Instrumentation or the manufacturers of surgical instruments, sterilizers, and container systems for guidelines for the density of wrapped packages. *Category II.* [811-814, 819]

h. Periodically review policies and procedures for sterilization. *Category II.* [1033]

i. Perform preventive maintenance on sterilizers by qualified personnel who are guided by the manufacturer's instruction. *Category II.* [811-814, 819]

20. Reuse of Single-Use Medical Devices

a. Adhere to the FDA enforcement document for single-use devices reprocessed by hospitals. FDA considers the hospital that reprocesses a single-use device as the manufacturer of the device and regulates the hospital using the same standards by which it regulates the original equipment manufacturer. *Category II, IC.* [995]

PERFORMANCE INDICATORS

1. Monitor adherence to high-level disinfection and/or sterilization guidelines for endoscopes on a regular basis. This monitoring should include ensuring the proper training of persons performing reprocessing and their adherence to all endoscope reprocessing steps, as demonstrated by competency testing at commencement of employment and annually.
2. Develop a mechanism for the occupational health service to report all adverse health events potentially resulting from exposure to disinfectants and sterilants; review such exposures; and implement engineering, work practice, and PPE to prevent future exposures.
3. Monitor possible sterilization failures that resulted in instrument recall. Assess whether additional training of personnel or equipment maintenance is required.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge Eva P. Clontz, M.S., for her assistance in referencing this guideline. The Healthcare Infection Control Practices Advisory Committee thanks the following experts for reviewing a draft of this guideline: Martin S. Favero, Ph.D., Syed A. Sattar, Ph.D., A. Denver Russell, D.Sc., and Martin Exner, M.D. The opinions of the reviewers might not be reflected in all the recommendations contained in this document.

GLOSSARY

Action level: concentration of a regulated substance (e.g., ethylene oxide, formaldehyde) within the employee breathing zone, above which OSHA requirements apply.

Activation of a sterilant: process of mixing the contents of a chemical sterilant that come in two containers (small vial with the activator solution; container of the chemical) Keeping the two chemicals separate until use extends the shelf life of the chemicals.

Aeration: method by which ethylene oxide (EtO) is removed from EtO-sterilized items by warm air circulation in an enclosed cabinet specifically designed for this purpose.

Antimicrobial agent: any agent that kills or suppresses the growth of microorganisms.

Antiseptic: substance that prevents or arrests the growth or action of microorganisms by inhibiting their activity or by destroying them. The term is used especially for preparations applied topically to living tissue.

Asepsis: prevention of contact with microorganisms.

Autoclave: device that sterilizes instruments or other objects using steam under pressure. The length of time required for sterilization depends on temperature, vacuum, and pressure.

Bacterial count: method of estimating the number of bacteria per unit sample. The term also refers to the estimated number of bacteria per unit sample, usually expressed as number of colony-forming units.

Bactericide: agent that kills bacteria.

Bioburden: number and types of viable microorganisms with which an item is contaminated; also called *bioload* or *microbial load*.

Biofilm: accumulated mass of bacteria and extracellular material that is tightly adhered to a surface and cannot be easily removed.

Biologic indicator: device for monitoring the sterilization process. The device consists of a standardized, viable population of microorganisms (usually bacterial spores) known to be resistant to the sterilization process being monitored. Biologic indicators are intended to demonstrate whether conditions were adequate to achieve sterilization. A negative biologic indicator does not prove that all items in the load are sterile or that they were all exposed to adequate sterilization conditions.

Bleach: Household bleach (5.25% or 6.00%–6.15% sodium hypochlorite depending on manufacturer) usually diluted in water at 1:10 or 1:100. Approximate dilutions are 1.5 cups of bleach in a gallon of water for a 1:10 dilution (~6,000 ppm) and 0.25 cup of bleach in a gallon of water for a 1:100 dilution (~600 ppm). Sodium hypochlorite products that make pesticidal claims, such as sanitization or disinfection, must be registered by EPA and be labeled with an EPA Registration Number.

Bleach Solution	Dilution	Chlorine (ppm)
5.25-6.15%	None	52,500-61,500
	1:10	5,250-6,150
	1:100	525-615
	1:1000	53-62

Bowie-Dick test: diagnostic test of a sterilizer's ability to remove air from the chamber of a prevacuum steam sterilizer. The air-removal or Bowie-Dick test is not a test for sterilization.

Ceiling limit: concentration of an airborne chemical contaminant that should not be exceeded during any part of the workday. If instantaneous monitoring is not feasible, the ceiling must be assessed as a 15-minute time-weighted average exposure.

Centigrade or **Celsius**: a temperature scale (0°C = freezing point of water; 100°C = boiling point of water at sea level). Equivalents mentioned in the guideline are as follows: 20°C = 68°F; 25°C = 77°F; 121°C = 250°F; 132°C = 270°F; 134°C = 273°F. For other temperatures the formula is: $F° = (C° \times 9/5) + 32$ *or* $C° = (F° - 32) \times 5/9$.

Central processing or **Central service department**: the department within a health-care facility that processes, issues, and controls professional supplies and equipment, both sterile and nonsterile, for some or all patient-care areas of the facility.

Challenge test pack: pack used in installation, qualification, and ongoing quality assurance testing of health-care facility sterilizers.

Chemical indicator: device for monitoring a sterilization process. The device is designed to respond with a characteristic chemical or physical change to one or more of the physical conditions within the sterilizing chamber. Chemical indicators are intended to detect potential sterilization failures that could result from incorrect packaging, incorrect loading of the sterilizer, or malfunctions of the sterilizer. The "pass" response of a chemical indicator does not prove the item accompanied by the indicator is necessarily sterile. The Association for the Advancement of Medical Instrumentation has defined five classes of chemical indicators: Class 1 (process indicator); Class 2 (Bowie-Dick test indicator); Class 3 (single-parameter indicator); Class 4 (multi-parameter indicator); and Class 5 (integrating indicator).

Contact time: time a disinfectant is in direct contact with the surface or item to be disinfected For surface disinfection, this period is framed by the application to the surface until complete drying has occurred.

Container system, rigid container: sterilization containment device designed to hold medical devices for sterilization, storage, transportation, and aseptic presentation of contents.

Contaminated: state of having actual or potential contact with microorganisms. As used in health care, the term generally refers to the presence of microorganisms that could produce disease or infection.

Control, positive: biologic indicator, from the same lot as a test biologic indicator, that is left unexposed to the sterilization cycle and then incubated to verify the viability of the test biologic indicator.

Cleaning: removal, usually with detergent and water or enzyme cleaner and water, of adherent visible soil, blood, protein substances, microorganisms and other debris from the surfaces, crevices, serrations, joints, and lumens of instruments, devices, and equipment by a manual or mechanical process that prepares the items for safe handling and/or further decontamination.

Culture: growth of microorganisms in or on a nutrient medium; to grow microorganisms in or on such a medium.

Culture medium: substance or preparation used to grow and cultivate microorganisms.

Cup: 8 fluid ounces.

Decontamination: according to OSHA, "the use of physical or chemical means to remove, inactivate, or destroy bloodborne pathogens on a surface or item to the point where they are no longer capable of transmitting infectious particles and the surface or item is rendered safe for handling, use, or disposal" [29 CFR 1910.1030]. In health-care facilities, the term generally refers to all pathogenic organisms.

Decontamination area: area of a health-care facility designated for collection, retention, and cleaning of soiled and/or contaminated items.

Detergent: cleaning agent that makes no antimicrobial claims on the label. They comprise a hydrophilic component and a lipohilic component and can be divided into four types: anionic, cationic, amphoteric, and non-ionic detergents.

Disinfectant: usually a chemical agent (but sometimes a physical agent) that destroys disease-causing pathogens or other harmful microorganisms but might not kill bacterial spores. It refers to substances applied to inanimate objects. EPA groups disinfectants by product label claims of "limited," "general," or "hospital" disinfection.

Disinfection: thermal or chemical destruction of pathogenic and other types of microorganisms. Disinfection is less lethal than sterilization because it destroys most recognized pathogenic microorganisms but not necessarily all microbial forms (e.g., bacterial spores).

D value: time or radiation dose required to inactivate 90% of a population of the test microorganism under stated exposure conditions.

Endoscope: an instrument that allows examination and treatment of the interior of the body canals and hollow organs.

Enzyme cleaner: a solution used before disinfecting instruments to improve removal of organic material (e.g., proteases to assist in removing protein).

EPA Registration Number or **EPA Reg. No.**: a hyphenated, two- or three-part number assigned by EPA to identify each germicidal product registered within the United States. The first number is the company identification number, the second is the specific product number, and the third (when present) is the company identification number for a supplemental registrant.

Exposure time: period in a sterilization process during which items are exposed to the sterilant at the specified sterilization parameters. For example, in a steam sterilization process, exposure time is the period during which items are exposed to saturated steam at the specified temperature.

Flash sterilization: process designed for the steam sterilization of unwrapped patient-care items for immediate use (or placed in a specially designed, covered, rigid container to allow for rapid penetration of steam).

Fungicide: agent that destroys fungi (including yeasts) and/or fungal spores pathogenic to humans or other animals in the inanimate environment.

General disinfectant: EPA-registered disinfectant labeled for use against both gram-negative and gram-positive bacteria. Efficacy is demonstrated against both *Salmonella choleraesuis* and *Staphylococcus aureus*. Also called *broad-spectrum disinfectant*.

Germicide: agent that destroys microorganisms, especially pathogenic organisms.

Germicidal detergent: detergent that also is EPA-registered as a disinfectant.

High-level disinfectant: agent capable of killing bacterial spores when used in sufficient concentration under suitable conditions. It therefore is expected to kill all other microorganisms.

Hospital disinfectant: disinfectant registered for use in hospitals, clinics, dental offices, and any other medical-related facility. Efficacy is demonstrated against *Salmonella choleraesuis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. EPA has registered approximately 1,200 hospital disinfectants.

Huck towel: all-cotton surgical towel with a honey-comb weave; both warp and fill yarns are tightly twisted. Huck towels can be used to prepare biologic indicator challenge test packs.

Implantable device: according to FDA, "device that is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more" [21 CFR 812.3(d)].

Inanimate surface: nonliving surface (e.g., floors, walls, furniture).

Incubator: apparatus for maintaining a constant and suitable temperature for the growth and cultivation of microorganisms.

Infectious microorganisms: microorganisms capable of producing disease in appropriate hosts.

Inorganic and organic load: naturally occurring or artificially placed inorganic (e.g., metal salts) or organic (e.g., proteins) contaminants on a medical device before exposure to a microbicidal process.

Intermediate-level disinfectant: agent that destroys all vegetative bacteria, including tubercle bacilli, lipid and some nonlipid viruses, and fungi, but not bacterial spores.

Limited disinfectant: disinfectant registered for use against a specific major group of organisms (gram-negative or gram-positive bacteria). Efficacy has been demonstrated in laboratory tests against either *Salmonella choleraesuis* or *Staphylococcus aureus* bacteria.

Lipid virus: virus surrounded by an envelope of lipoprotein in addition to the usual core of nucleic acid surrounded by a coat of protein. This type of virus (e.g., HIV) is generally easily inactivated by many types of disinfectants. Also called *enveloped* or *lipophilic virus*.

Low-level disinfectant: agent that destroys all vegetative bacteria (except tubercle bacilli), lipid viruses, some nonlipid viruses, and some fungi, but not bacterial spores.

Mechanical indicator: devices that monitor the sterilization process (e.g., graphs, gauges, printouts).

Medical device: instrument, apparatus, material, or other article, whether used alone or in combination, including software necessary for its application, intended by the manufacturer to be used for human beings for

- diagnosis, prevention, monitoring treatment, or alleviation of disease;
- diagnosis, monitoring, treatment, or alleviation of or compensation for an injury or handicap;
- investigation, replacement, or modification of the anatomy or of a physiologic process; or
- control of conception

and that does not achieve its primary intended action in or on the human body by pharmacologic, immunologic, or metabolic means but might be assisted in its function by such means.

Microbicide: any substance or mixture of substances that effectively kills microorganisms.

Microorganisms: animals or plants of microscopic size. As used in health care, generally refers to bacteria, fungi, viruses, and bacterial spores.

Minimum effective concentration (MEC): the minimum concentration of a liquid chemical germicide needed to achieve the claimed microbicidal activity as determined by dose-response testing. Sometimes used interchangeably with *minimum recommended concentration*.

Muslin: loosely woven (by convention, 140 threads per square inch), 100% cotton cloth. Formerly used as a wrap for sterile packs or a surgical drape. Fabric wraps used currently consist of a cotton-polyester blend.

Mycobacteria: bacteria with a thick, waxy coat that makes them more resistant to chemical germicides than other types of vegetative bacteria.

Nonlipid viruses: generally considered more resistant to inactivation than lipid viruses. Also called nonenveloped or hydrophilic viruses.

One-step disinfection process: simultaneous cleaning and disinfection of a noncritical surface or item.

Pasteurization: process developed by Louis Pasteur of heating milk, wine, or other liquids to 65–77°C (or the equivalent) for approximately 30 minutes to kill or markedly reduce the number of pathogenic and spoilage organisms other than bacterial spores.

Parametric release: declaration that a product is sterile on the basis of physical and/or chemical process data rather than on sample testing or biologic indicator results.

Penicylinder: carriers inoculated with the test bacteria for in vitro tests of germicides. Can be constructed of stainless steel, porcelain, glass, or other materials and are approximately 8 x 10 mm in diameter.

Permissible exposure limit (PEL): time-weighted average maximum concentration of an air contaminant to which a worker can be exposed, according to OSHA standards. Usually calculated over 8 hours, with exposure considered over a 40-hour work week.

Personal protective equipment (PPE): specialized clothing or equipment worn by an employee for protection against a hazard. General work clothes (e.g., uniforms, pants, shirts) not intended to function as protection against a hazard are not considered to be PPE.

Parts per million (ppm): common measurement for concentrations by volume of trace contaminant gases in the air (or chemicals in a liquid); 1 volume of contaminated gas per 1 million volumes of contaminated air or 1¢ in $10,000 both equal 1 ppm. Parts per million = µg/mL or mg/L.

Prions: transmissible pathogenic agents that cause a variety of neurodegenerative diseases of humans and animals, including sheep and goats, bovine spongiform encephalopathy in cattle, and Creutzfeldt-Jakob disease in humans. They are unlike any other infectious pathogens because they are composed of an abnormal conformational isoform of a normal cellular protein, the prion protein (PrP). Prions are extremely resistant to inactivation by sterilization processes and disinfecting agents.

Process challenge device (PCD): item designed to simulate product to be sterilized and to constitute a defined challenge to the sterilization process and used to assess the effective performance of the process. A PCD is a challenge test pack or test tray that contains a biologic indicator, a Class 5 integrating indicator, or an enzyme-only indicator.

QUAT: abbreviation for *quaternary ammonium compound*, a surface-active, water-soluble disinfecting

substance that has four carbon atoms linked to a nitrogen atom through covalent bonds.

Recommended exposure limit (REL): occupational exposure limit recommended by NIOSH as being protective of worker health and safety over a working lifetime. Frequently expressed as a 40-hour time-weighted-average exposure for up to 10 hours per day during a 40-work week.

Reprocess: method to ensure proper disinfection or sterilization; can include: cleaning, inspection, wrapping, sterilizing, and storing.

Sanitizer: agent that reduces the number of bacterial contaminants to safe levels as judged by public health requirements. Commonly used with substances applied to inanimate objects. According to the protocol for the official sanitizer test, a sanitizer is a chemical that kills 99.999% of the specific test bacteria in 30 seconds under the conditions of the test.

Shelf life: length of time an undiluted or use dilution of a product can remain active and effective. Also refers to the length of time a sterilized product (e.g., sterile instrument set) is expected to remain sterile.

Spaulding classification: strategy for reprocessing contaminated medical devices. The system classifies a medical device as critical, semicritical, or noncritical on the basis of risk to patient safety from contamination on a device. The system also established three levels of germicidal activity (sterilization, high-level disinfection, and low-level disinfection) for strategies with the three classes of medical devices (critical, semicritical, and noncritical).

Spore: relatively water-poor round or elliptical resting cell consisting of condensed cytoplasm and nucleus surrounded by an impervious cell wall or coat. Spores are relatively resistant to disinfectant and sterilant activity and drying conditions (specifically in the genera *Bacillus* and *Clostridium*).

Spore strip: paper strip impregnated with a known population of spores that meets the definition of biological indicators.

Steam quality: steam characteristic reflecting the dryness fraction (weight of dry steam in a mixture of dry saturated steam and entrained water) and the level of noncondensable gas (air or other gas that will not condense under the conditions of temperature and pressure used during the sterilization process). The dryness fraction (i.e., the proportion of completely dry steam in the steam being considered) should not fall below 97%.

Steam sterilization: sterilization process that uses saturated steam under pressure for a specified exposure time and at a specified temperature, as the sterilizing agent.

Steam sterilization, dynamic air removal type: one of two types of sterilization cycles in which air is removed from the chamber and the load by a series of pressure and vacuum excursions (prevacuum cycle) or by a series of steam flushes and pressure pulses above atmospheric pressure (steam-flush-pressure-pulse cycle).

Sterile or **Sterility**: state of being free from all living microorganisms. In practice, usually described as a probability function, e.g., as the probability of a microorganism surviving sterilization being one in one million.

Sterility assurance level (SAL): probability of a viable microorganism being present on a product unit after sterilization. Usually expressed as 10^{-6}; a SAL of 10^{-6} means $\leq$1/1 million chance that a single viable microorganism is present on a sterilized item. A SAL of 10^{-6} generally is accepted as appropriate for items intended to contact compromised tissue (i.e., tissue that has lost the integrity of the natural body barriers). The sterilizer manufacturer is responsible for ensuring the sterilizer can achieve the desired SAL. The

user is responsible for monitoring the performance of the sterilizer to ensure it is operating in conformance to the manufacturer's recommendations.

Sterilization: validated process used to render a product free of all forms of viable microorganisms. In a sterilization process, the presence of microorganisms on any individual item can be expressed in terms of probability. Although this probability can be reduced to a very low number, it can never be reduced to zero.

Sterilization area: area of a health-care facility designed to house sterilization equipment, such as steam ethylene oxide, hydrogen peroxide gas plasma, or ozone sterilizers.

Sterilizer: apparatus used to sterilize medical devices, equipment, or supplies by direct exposure to the sterilizing agent.

Sterilizer, gravity-displacement type: type of steam sterilizer in which incoming steam displaces residual air through a port or drain in or near the bottom (usually) of the sterilizer chamber. Typical operating temperatures are 121–123°C (250–254°F) and 132–135°C (270–275°F).

Sterilizer, prevacuum type: type of steam sterilizer that depends on one or more pressure and vacuum excursions at the beginning of the cycle to remove air. This method of operation results in shorter cycle times for wrapped items because of the rapid removal of air from the chamber and the load by the vacuum system and because of the usually higher operating temperature (132–135°C [270–275°F]; 141–144°C [285–291°F]). This type of sterilizer generally provides for shorter exposure time and accelerated drying of fabric loads by pulling a further vacuum at the end of the sterilizing cycle.

Sterilizer, steam-flush pressure-pulse type: type of sterilizer in which a repeated sequence consisting of a steam flush and a pressure pulse removes air from the sterilizing chamber and processed materials using steam at above atmospheric pressure (no vacuum is required). Like a prevacuum sterilizer, a steam-flush pressure-pulse sterilizer rapidly removes air from the sterilizing chamber and wrapped items; however, the system is not susceptible to air leaks because air is removed with the sterilizing chamber pressure at above atmospheric pressure. Typical operating temperatures are 121–123°C (250–254°F), 132–135°C (270–275°F), and 141–144°C (285–291°F).

Surfactant: agent that reduces the surface tension of water or the tension at the interface between water and another liquid; a wetting agent found in many sterilants and disinfectants.

Tabletop steam sterilizer: a compact gravity-displacement steam sterilizer that has a chamber volume of not more than 2 cubic feet and that generates its own steam when distilled or deionized water is added.

Time-weighted average (TWA): an average of all the concentrations of a chemical to which a worker has been exposed during a specific sampling time, reported as an average over the sampling time. For example, the permissible exposure limit for ethylene oxide is 1 ppm as an 8-hour TWA. Exposures above the ppm limit are permitted if they are compensated for by equal or longer exposures below the limit during the 8-hour workday as long as they do not exceed the ceiling limit; short-term exposure limit; or, in the case of ethylene oxide, excursion limit of 5 ppm averaged over a 15-minute sampling period.

Tuberculocide: an EPA-classified hospital disinfectant that also kills *Mycobacterium tuberculosis* (tubercle bacilli). EPA has registered approximately 200 tuberculocides. Such agents also are called *mycobactericides*.

Use-life: the length of time a diluted product can remain active and effective. The stability of the chemical and the storage conditions (e.g., temperature and presence of air, light, organic matter, or metals)

determine the use-life of antimicrobial products.

Vegetative bacteria: bacteria that are devoid of spores and usually can be readily inactivated by many types of germicides.

Virucide: an agent that kills viruses to make them noninfective.

Adapted from Association for the Advancement of Medical Instrumentation; [811-814, 819] Association of periOperating Registered Nurses (AORN), [815] American Hospital Association, [319] and Block. [16, 1034]

Table 1. Methods of sterilization and disinfection.

	Sterilization		Disinfection		
	Critical items (will enter tissue or vascular system or blood will flow through them)		High-level (semicritical items; [except dental] will come in contact with mucous membrane or nonintact skin)	Intermediate-level (some semicritical items[1] and noncritical items)	Low-level (noncritical items; will come in contact with intact skin)
Object	**Procedure**	**Exposure time**	**Procedure (exposure time 12-30 min at ≥20°C)[2,3]**	**Procedure (exposure time ≥ 1 m)[9]**	**Procedure (exposure time ≥ 1 m)[9]**
Smooth, hard Surface[1,4]	A	MR	D	K	K
	B	MR	E	L[5]	L
	C	MR	F	M	M
	D	10 h at 20-25°C	H	N	N
	F	6 h	I[6]		O
	G	12 m at 50-56°C	J		
	H	3-8 h			
Rubber tubing and catheters[3,4]	A	MR	D		
	B	MR	E		
	C	MR	F		
	D	10 h at 20-25°C	H		
	F	6 h	I[6]		
	G	12 m at 50-56°C	J		
	H	3-8 h			
Polyethylene tubing and catheters[3,4,7]	A	MR	D		
	B	MR	E		
	C	MR	F		
	D	10 h at 20-25°C	H		
	F	6 h	I[6]		
	G	12 m at 50-56°C	J		
	H	3-8 h			
Lensed instruments[4]	A	MR	D		
	B	MR	E		
	C	MR	F		
	D	10 h at 20-25°C	H		
	F	6 h	J		
	G	12 m at 50-56°C			
	H	3-8 h			
Thermometers (oral and rectal)[8]					K[8]
Hinged instruments[4]	A	MR	D		
	B	MR	E		
	C	MR	F		
	D	10 h at 20-25°C	H		
	F	6 h	I[6]		
	G	12 m at 50-56°C	J		
	H	3-8 h			

Modified from Rutala and Simmons.[15,17,18,421] The selection and use of disinfectants in the healthcare field is dynamic, and products may become available that are not in existence when this guideline was written. As newer disinfectants become available, persons or committees responsible for selecting disinfectants and sterilization processes should be guided by products cleared by the FDA and the EPA as well as information in the scientific literature.

A. Heat sterilization, including steam or hot air (see manufacturer's recommendations, steam sterilization processing time from 3-30 minutes)
B. Ethylene oxide gas (see manufacturer's recommendations, generally 1-6 hours processing time plus aeration time of 8-12 hours at 50-60°C)
C. Hydrogen peroxide gas plasma (see manufacturer's recommendations for internal diameter and length restrictions, processing time between 45-72 minutes).
D. Glutaraldehyde-based formulations (≥2% glutaraldehyde, caution should be exercised with all glutaraldehyde formulations when further in-use dilution is anticipated); glutaraldehyde (1.12%) and 1.93% phenol/phenate. One glutaraldehyde-based product has a high-level disinfection claim of 5 minutes at 35°C.
E. Ortho-phthalaldehyde (OPA) 0.55%
F. Hydrogen peroxide 7.5% (will corrode copper, zinc, and brass)
G. Peracetic acid, concentration variable but 0.2% or greater is sporicidal. Peracetic acid immersion system operates at 50-56°C.
H. Hydrogen peroxide (7.35%) and 0.23% peracetic acid; hydrogen peroxide 1% and peracetic acid 0.08% (will corrode metal instruments)
I. Wet pasteurization at 70°C for 30 minutes with detergent cleaning
J. Hypochlorite, single use chlorine generated on-site by electrolyzing saline containing >650-675 active free chlorine; (will corrode metal instruments)
K. Ethyl or isopropyl alcohol (70-90%)
L. Sodium hypochlorite (5.25-6.15% household bleach diluted 1:500 provides >100 ppm available chlorine)
M. Phenolic germicidal detergent solution (follow product label for use-dilution)
N. Iodophor germicidal detergent solution (follow product label for use-dilution)
O. Quaternary ammonium germicidal detergent solution (follow product label for use-dilution)
MR. Manufacturer's recommendations
NA. Not applicable

[1] See text for discussion of hydrotherapy.
[2] The longer the exposure to a disinfectant, the more likely it is that all microorganisms will be eliminated. Follow the FDA-cleared high-level disinfection claim. Ten-minute exposure is not adequate to disinfect many objects, especially those that are difficult to clean because they have narrow channels or other areas that can harbor organic material and bacteria. Twenty-minute exposure at 20°C is the minimum time needed to reliably kill *M. tuberculosis* and nontuberculous mycobacteria with a 2% glutaraldehyde. Some high-level disinfectants have a reduced exposure time (e.g., ortho-phthalaldehyde at 12 minutes at 20°C) because of their rapid activity against mycobacteria or reduced exposure time due to increased mycobactericidal activity at elevated temperature (e.g., 2.5% glutaraldehyde at 5 minutes at 35°C, 0.55% OPA at 5 min at 25°C in automated endoscope reprocessor).
[3] Tubing must be completely filled for high-level disinfection and liquid chemical sterilization; care must be taken to avoid entrapment of air bubbles during immersion.
[4] Material compatibility should be investigated when appropriate.
[5] A concentration of 1000 ppm available chlorine should be considered where cultures or concentrated preparations of microorganisms have spilled (5.25% to 6.15% household bleach diluted 1:50 provides > 1000 ppm available chlorine). This solution may corrode some surfaces.
[6] Pasteurization (washer-disinfector) of respiratory therapy or anesthesia equipment is a recognized alternative to high-level disinfection. Some data challenge the efficacy of some pasteurization units.
[7] Thermostability should be investigated when appropriate.
[8] Do not mix rectal and oral thermometers at any stage of handling or processing.
[9] By law, all applicable label instructions on EPA-registered products must be followed. If the user selects exposure conditions that differ from those on the EPA-registered products label, the user assumes liability from any injuries resulting from off-label use and is potentially subject to enforcement action under FIFRA.

Table 2. Properties of an ideal disinfectant.

Broad spectrum: should have a wide antimicrobial spectrum
Fast acting: should produce a rapid kill
Not affected by environmental factors: should be active in the presence of organic matter (e.g., blood, sputum, feces) and compatible with soaps, detergents, and other chemicals encountered in use
Nontoxic: should not be harmful to the user or patient
Surface compatibility: should not corrode instruments and metallic surfaces and should not cause the deterioration of cloth, rubber, plastics, and other materials
Residual effect on treated surfaces: should leave an antimicrobial film on the treated surface
Easy to use with clear label directions
Odorless: should have a pleasant odor or no odor to facilitate its routine use
Economical: should not be prohibitively high in cost
Solubility: should be soluble in water
Stability: should be stable in concentrate and use-dilution
Cleaner: should have good cleaning properties
Environmentally friendly: should not damage the environment on disposal

Modified from Molinari[1035].

Table 3. Epidemiologic evidence associated with the use of surface disinfectants or detergents on noncritical environmental surfaces.

Justification for Use of Disinfectants for Noncritical Environmental Surfaces

Surfaces may contribute to transmission of epidemiologically important microbes (e.g., vancomycin-resistant Enterococci, methicillin-resistant *S. aureus*, viruses)

Disinfectants are needed for surfaces contaminated by blood and other potentially infective material

Disinfectants are more effective than detergents in reducing microbial load on floors

Detergents become contaminated and result in seeding the patient's environment with bacteria

Disinfection of noncritical equipment and surfaces is recommended for patients on isolation precautions by the Centers for Disease Control and Prevention.

Advantage of using a single product for decontamination of noncritical surfaces, both floors and equipment

Some newer disinfectants have persistent antimicrobial activity

Justification for Using a Detergent on Noncritical Environmental Surfaces

Noncritical surfaces contribute minimally to endemic healthcare-associated infections

No difference in healthcare-associated infection rates when floors are cleaned with detergent versus disinfectant

No environmental impact (aquatic or terrestrial) issues with disposal

No occupational health exposure issues

Lower costs

Use of antiseptics/disinfectants selects for antibiotic-resistant bacteria (?)

More aesthetically pleasing floor

Modified from Rutala[378].

Figure 1. Decreasing order of resistance of microorganisms to disinfection and sterilization and the level of disinfection or sterilization.

Resistant	Level
Prions (Creutzfeldt-Jakob Disease)	Prion reprocessing
Bacterial spores (*Bacillus atrophaeus*)	Sterilization
Coccidia (*Cryptosporidium*)	
Mycobacteria (*M. tuberculosis, M. terrae*)	High
Nonlipid or small viruses (polio, coxsackie)	Intermediate
Fungi (*Aspergillus, Candida*)	
Vegetative bacteria (*S. aureus, P. aeruginosa*)	Low
Lipid or medium-sized viruses (HIV, herpes, hepatitis B)	
Susceptible	

Modified from Russell and Favero [13, 344].

Table 4. Comparison of the characteristics of selected chemicals used as high-level disinfectants or chemical sterilants.

	HP (7.5%)	PA (0.2%)	Glut (≥2.0%)	OPA (0.55%)	HP/PA (7.35%/0.23%)
HLD Claim	30 m @ 20°C	NA	20-90 m @ 20°-25°C	12 m @ 20°C, 5 m @ 25°C in AER	15m @ 20°C
Sterilization Claim	6 h @ 20°	12m @ 50-56°C	10 h @ 20°-25°C	None	3 h @ 20°C
Activation	No	No	Yes (alkaline glut)	No	No
Reuse Life[1]	21d	Single use	14-30 d	14d	14d
Shelf Life Stability[2]	2 y	6 mo	2 y	2 y	2 y
Disposal Restrictions	None	None	Local[3]	Local[3]	None
Materials Compatibility	Good	Good	Excellent	Excellent	No data
Monitor MEC[4]	Yes (6%)	No	Yes (1.5% or higher)	Yes (0.3% OPA)	No
Safety	Serious eye damage (safety glasses)	Serious eye and skin damage (conc soln)[5]	Respiratory	Eye irritant, stains skin	Eye damage
Processing	Manual or automated	Automated	Manual or automated	Manual or automated	Manual
Organic material resistance	Yes	Yes	Yes	Yes	Yes
OSHA exposure limit	1 ppm TWA	None	None[6]	None	HP-1 ppm TWA
Cost profile (per cycle)[7]	+ (manual), ++ (automated)	+++++ (automated)	+ (manual), ++ (automated)	++ (manual)	++ (manual)

Modified from Rutala [69].

Abbreviations: HLD=high-level disinfectant; HP=hydrogen peroxide; PA=peracetic acid; glut=glutaraldehyde; PA/HP=peracetic acid and hydrogen peroxide; OPA =ortho-phthalaldehyde (FDA cleared as a high-level disinfectant, included for comparison to other chemical agents used for high-level disinfection); m=minutes; h=hours; NA=not applicable; TWA=time-weighted average for a conventional 8-hour workday.

[1]number of days a product can be reused as determined by re-use protocol

[2]time a product can remain in storage (unused)

[3]no U.S. EPA regulations but some states and local authorities have additional restrictions

[4]MEC=minimum effective concentration is the lowest concentration of active ingredients at which the product is still effective

[5]Conc soln=concentrated solution

[6]The ceiling limit recommended by the American Conference of Governmental Industrial Hygienists is 0.05 ppm.

[7]per cycle cost profile considers cost of the processing solution (suggested list price to healthcare facilities in August 2001) and assumes maximum use life (e.g., 21 days for hydrogen peroxide, 14 days for glutaraldehyde), 5 reprocessing cycles per day, 1-gallon basin for manual processing, and 4-gallon tank for automated processing. + = least expensive; +++++ = most expensive

Table 5. Summary of advantages and disadvantages of chemical agents used as chemical sterilants[1] or as high-level disinfectants.

Sterilization Method	Advantages	Disadvantages
Peracetic Acid/Hydrogen Peroxide	• No activation required • Odor or irritation not significant	• Materials compatibility concerns (lead, brass, copper, zinc) both cosmetic and functional • Limited clinical experience • Potential for eye and skin damage
Glutaraldehyde	• Numerous use studies published • Relatively inexpensive • Excellent materials compatibility	• Respiratory irritation from glutaraldehyde vapor • Pungent and irritating odor • Relatively slow mycobactericidal activity • Coagulates blood and fixes tissue to surfaces • Allergic contact dermatitis • Glutaraldehyde vapor monitoring recommended
Hydrogen Peroxide	• No activation required • May enhance removal of organic matter and organisms • No disposal issues • No odor or irritation issues • Does not coagulate blood or fix tissues to surfaces • Inactivates *Cryptosporidium* • Use studies published	• Material compatibility concerns (brass, zinc, copper, and nickel/silver plating) both cosmetic and functional • Serious eye damage with contact
Ortho-phthalaldehyde	• Fast acting high-level disinfectant • No activation required • Odor not significant • Excellent materials compatibility claimed • Does not coagulate blood or fix tissues to surfaces claimed	• Stains skin, mucous membranes, clothing, and environmental surfaces • Repeated exposure may result in hypersensitivity in some patients with bladder cancer • More expensive than glutaraldehyde • Eye irritation with contact • Slow sporicidal activity
Peracetic Acid	• Rapid sterilization cycle time (30-45 minutes) • Low temperature (50-55°C) liquid immersion sterilization • Environmental friendly by-products (acetic acid, O_2, H_2O) • Fully automated • Single-use system eliminates need for concentration testing • Standardized cycle • May enhance removal of organic material and endotoxin • No adverse health effects to operators under normal operating conditions • Compatible with many materials and instruments • Does not coagulate blood or fix tissues to surfaces • Sterilant flows through scope facilitating salt, protein, and microbe removal • Rapidly sporicidal • Provides procedure standardization (constant dilution, perfusion of channel, temperatures, exposure)	• Potential material incompatibility (e.g., aluminum anodized coating becomes dull) • Used for immersible instruments only • Biological indicator may not be suitable for routine monitoring • One scope or a small number of instruments can be processed in a cycle • More expensive (endoscope repairs, operating costs, purchase costs) than high-level disinfection • Serious eye and skin damage (concentrated solution) with contact • Point-of-use system, no sterile storage

Modified from Rutala[69].

[1]All products effective in presence of organic soil, relatively easy to use, and have a broad spectrum of antimicrobial activity (bacteria, fungi, viruses, bacterial spores, and mycobacteria). The above characteristics are documented in the literature; contact the manufacturer of the instrument and sterilant for additional information. All products listed above are FDA-cleared as chemical sterilants except OPA, which is an FDA-cleared high-level disinfectant.

Table 6. Summary of advantages and disadvantages of commonly used sterilization technologies.

Sterilization Method	Advantages	Disadvantages
Steam	• Nontoxic to patient, staff, environment • Cycle easy to control and monitor • Rapidly microbicidal • Least affected by organic/inorganic soils among sterilization processes listed • Rapid cycle time • Penetrates medical packing, device lumens	• Deleterious for heat-sensitive instruments • Microsurgical instruments damaged by repeated exposure • May leave instruments wet, causing them to rust • Potential for burns
Hydrogen Peroxide Gas Plasma	• Safe for the environment • Leaves no toxic residuals • Cycle time is 28-75 minutes (varies with model type) and no aeration necessary • Used for heat- and moisture-sensitive items since process temperature <50°C • Simple to operate, install (208 V outlet), and monitor • Compatible with most medical devices • Only requires electrical outlet	• Cellulose (paper), linens and liquids cannot be processed • Sterilization chamber size from 1.8-9.4 ft^3 total volume (varies with model type) • Some endoscopes or medical devices with long or narrow lumens cannot be processed at this time in the United States (see manufacturer's recommendations for internal diameter and length restrictions) • Requires synthetic packaging (polypropylene wraps, polyolefin pouches) and special container tray • Hydrogen peroxide may be toxic at levels greater than 1 ppmTWA
100% Ethylene Oxide (ETO)	• Penetrates packaging materials, device lumens • Single-dose cartridge and negative- pressure chamber minimizes the potential for gas leak and ETO exposure • Simple to operate and monitor • Compatible with most medical materials	• Requires aeration time to remove ETO residue • Sterilization chamber size from 4.0-7.9 ft^3 total volume (varies with model type) • ETO is toxic, a carcinogen, and flammable • ETO emission regulated by states but catalytic cell removes 99.9% of ETO and converts it to CO_2 and H_2O • ETO cartridges should be stored in flammable liquid storage cabinet • Lengthy cycle/aeration time
ETO Mixtures 8.6% ETO/91.4% HCFC 10% ETO/90% HCFC 8.5% ETO/91.5% CO_2	• Penetrates medical packaging and many plastics • Compatible with most medical materials • Cycle easy to control and monitor	• Some states (e.g., CA, NY, MI) require ETO emission reduction of 90-99.9% • CFC (inert gas that eliminates explosion hazard) banned in 1995 • Potential hazards to staff and patients • Lengthy cycle/aeration time • ETO is toxic, a carcinogen, and flammable
Peracetic Acid	• Rapid cycle time (30-45 minutes) • Low temperature (50-55°C liquid immersion sterilization • Environmental friendly by-products • Sterilant flows through endoscope which facilitates salt, protein and microbe removal	• Point-of-use system, no sterile storage • Biological indicator may not be suitable for routine monitoring • Used for immersible instruments only • Some material incompatibility (e.g., aluminum anodized coating becomes dull) • One scope or a small number of instruments processed in a cycle • Potential for serious eye and skin damage (concentrated solution) with contact

Modified from Rutala.[625]

Abbreviations: CFC=chlorofluorocarbon, HCFC=hydrochlorofluorocarbon.

Table 7. Minimum cycle times for steam sterilization cycles

Type of sterilizer	Item	Exposure time at 250°F (121°C)	Exposure time at 270°F (132°C)	Drying time
Gravity displacement	Wrapped instruments	30 min	15 min	**15-30** min
	Textile packs	30 min	25 min	**15** min
	Wrapped utensils	30 min	15 min	**15-30** min
Dynamic-air-removal (e.g., prevacuum)	Wrapped instruments		4 min	**20-30** min
	Textile packs		4 min	**5-20** min
	Wrapped utensils		4 min	20 min

Modified from Association for the Advancement of Medical Instrumentation. [813, 819]

Table 8. Examples of flash steam sterilization parameters.

Type of sterilizer	Load configuration	Temperature	Time
Gravity displacement	Nonporous items only (i.e., routine metal instruments, no lumens)	132°C (270°F)	3 minutes
	Nonporous and porous items (e.g., rubber or plastic items, items with lumens) sterilized together	132°C (270°F)	10 minutes
Prevacuum	Nonporous items only (i.e., routine metal instruments, no lumens)	132°C (270°F)	3 minutes
	Nonporous and porous items (e.g., rubber or plastic items, items with lumens) sterilized together	132°C (270°F)	4 minutes
Steam-flush pressure-pulse	Nonporous or mixed nonporous/porous items	132° (270°F) Manufacturers' instruction	4 minutes

Modified from Association for the Advancement of Medical Instrumentation. [812, 819]

Table 9. Characteristics of an ideal low-temperature sterilization process.

High efficacy: the agent should be virucidal, bactericidal, tuberculocidal, fungicidal and sporicidal
Rapid activity: ability to quickly achieve sterilization
Strong penetrability: ability to penetrate common medical-device packaging materials and penetrate into the interior of device lumens
Material compatibility: produces only negligible changes in the appearance or the function of processed items and packaging materials even after repeated cycling
Nontoxic: presents no toxic health risk to the operator or the patient and poses no hazard to the environment
Organic material resistance: withstands reasonable organic material challenge without loss of efficacy
Adaptability: suitable for large or small (point of use) installations
Monitoring capability: monitored easily and accurately with physical, chemical, and biological process monitors
Cost effectiveness: reasonable cost for installation and for routine operation

Modified from Schneider.[851]

Table 10. Factors affecting the efficacy of sterilization.

Factors	Effect
Cleaning[1]	Failure to adequately clean instrument results in higher bioburden, protein load, and salt concentration. These will decrease sterilization efficacy.
Bioburden[1]	The natural bioburden of used surgical devices is 10^0 to 10^3 organisms (primarily vegetative bacteria), which is substantially below the 10^5-10^6 spores used with biological indicators.
Pathogen type	Spore-forming organisms are most resistant to sterilization and are the test organisms required for FDA clearance. However, the contaminating microflora on used surgical instruments consists mainly of vegetative bacteria.
Protein[1]	Residual protein decreases efficacy of sterilization. However, cleaning appears to rapidly remove protein load.
Salt[1]	Residual salt decreases efficacy of sterilization more than does protein load. However, cleaning appears to rapidly remove salt load.
Biofilm accumulation[1]	Biofilm accumulation reduces efficacy of sterilization by impairing exposure of the sterilant to the microbial cell.
Lumen length	Increasing lumen length impairs sterilant penetration. May require forced flow through lumen to achieve sterilization.
Lumen diameter	Decreasing lumen diameter impairs sterilant penetration. May require forced flow through lumen to achieve sterilization.
Restricted flow	Sterilant must come into contact with microorganisms. Device designs that prevent or inhibit this contact (e.g., sharp bends, blind lumens) will decrease sterilization efficacy.
Device design and construction	Materials used in construction may affect compatibility with different sterilization processes and affect sterilization efficacy. Design issues (e.g., screws, hinges) will also affect sterilization efficacy.

Modified from Alfa and Rutala.[470, 825]

[1] Factor only relevant for reused surgical/medical devices

Table 11. Comparative evaluation of the microbicidal activity of low-temperature sterilization technology.

	Carriers Sterilized by Various Low-Temperature Sterilization Technologies						
Challenge	**ETO 12/88**	**100% ETO**	**HCFC-ETO**	**HPGP 100**	**HPGP 100S**	**PA**	**Reference**
No salt or serum[1]	100%	100%	96%	100%	ND	ND	Alfa [721]
10% serum and 0.65% salt[2]	97%	60%	95%	37%	ND	ND	Alfa [721]
Lumen (125 cm long x 3 mm wide) without serum or salt[1]	ND	96%	96%	ND	ND	ND	Alfa [721]
Lumen (125 cm long x 3 mm wide) with 10% serum and 0.65% salt[2]	44%	40%	49%	35%	ND	100%[1]	Alfa [721]
Lumen (40 cm long x 3 mm wide)[3]	ND	ND	100%	95%	100%	8%	Rutala [856]
Lumen (40 cm long x 2 mm wide)[3]	ND	ND	100%	93%	100%	ND	Rutala [856]
Lumen (40 cm long x 1 mm wide)[3]	ND	ND	100%	26%	100%	ND	Rutala [856]
Lumen (40 cm long x 3 mm wide)[4]	ND	ND	100%	100%	100%	ND	Rutala [856]

Modified from Rutala. [825]
Abbreviations: ETO=ethylene oxide; HCFC=hydrochlorofluorocarbon; ND=no data; HPGP=hydrogen peroxide gas plasma; PA=peracetic acid.

[1]Test organisms included *Enterococcus faecalis*, *Mycobacterium chelonae*, and *Bacillus atrophaeus* spores.
[2]Test organisms included *E. faecalis*, *P. aeruginosa*, *E. coli*, *M. chelonae*, *B. atrophaeus* spores, *G. stearothermophilus* spores, and *B. circulans* spores.
[3]Test organism was *G. stearothermophilus* spores . The lumen test units had a removable 5 cm center piece (1.2 cm diameter) of stainless steel sealed to the narrower steel tubing by hard rubber septums.
[4]Test organism was *G. stearothermophilus* spores. The lumen test unit was a straight stainless steel tube.

Table 12. Suggested protocol for management of positive biological indicator in a steam sterilizer.

1. Take the sterilizer out of service. Notify area supervisor and infection control department.
2. Objects, other than implantable objects, do not need to be recalled because of a single positive spore test unless the sterilizer or the sterilization procedure is defective. As soon as possible, repeat biological indicator test in three consecutive sterilizer cycles. If additional spore tests remain positive, the items should be considered nonsterile, and supplies processed since the last acceptable (negative) biological indicator should be recalled. The items from the suspect load(s) should be recalled and reprocessed.
3. Check to ensure the sterilizer was used correctly (e.g., verify correct time and temperature setting). If not, repeat using appropriate settings and recall and reprocess all inadequately processed items.
4. Check with hospital maintenance for irregularities (e.g., electrical) or changes in the hospital steam supply (i.e., from standard ≥97% steam, <3% moisture). Any abnormalities should be reported to the person who performs sterilizer maintenance (e.g., medical engineering, sterilizer manufacturer).
5. Check to ensure the correct biological indicator was used and appropriately interpreted. If not, repeat using appropriate settings.

If steps 1 through 5 resolve the problem

6. If all three repeat biological indicators from three consecutive sterilizer cycles (step 2 above) are negative, put the sterilizer back in service.

If one or both biological indicators are positive, do one or more of the following until problem is resolved.

7. A. Request an inspection of the equipment by sterilizer maintenance personnel.
   B. Have hospital maintenance inspect the steam supply lines.
   C. Discuss the abnormalities with the sterilizer manufacturer.
   D. Repeat the biological indicator using a different manufacturer's indicator.

If step 7 does not resolve the problem

Close sterilizer down until the manufacturer can assure that it is operating properly. Retest at that time with biological indicators in three consecutive sterilizer cycles.

Modified from Bryce.[839]

Disclosure of Financial Interests and Relationships (2000- July 2004)

William A. Rutala: Honoraria from Advanced Sterilization Products, Kimberly-Clark; consultation with Advanced Sterilization Products, Aesculap, Clorox, 3M, SC Johnson, Intelligent Biocides, Metrex; and an educational grant from Consumer Specialty Products Association, Kimberly-Clark.

David J. Weber: Honoraria from Consumer Specialty Products Association; consultation with Clorox; and educational grant from Consumer Specialty Products Association.

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