

MEDICAL DEVICE & DIAGNOSTIC INDUSTRY

VALIDATING REUSABLE MEDICAL DEVICES: AN OVERVIEW

Susanne Anderson, Ed Arscott, John Broad, and Dave Parente

REUSABLE DEVICES

Validating Reusable Medical Devices: An Overview

Susanne Anderson, Ed Arscott, John Broad, and Dave Parente

Reusable medical devices have been used in health-care facilities since the turn of the century. Over the years, advances in diagnostic and therapeutic medicine have led to increasingly sophisticated device designs. As the designs have become more complex, the process of cleaning, disinfecting, and sterilizing reusable devices has become more complex as well.

Manufacturers of reusable medical devices are responsible for supporting their claims for product reuse. Typically, meeting this responsibility involves developing instructions for preparing the device for reuse, and then conducting tests that validate those instructions. Although important, proving sterilization or disinfection efficacy is not the only consideration; other issues related to device function, physical integrity, and biocompatibility must also be addressed.

During the past few years, scientific guidelines have been developed to assist device manufacturers in designing, testing, and labeling devices intended for reuse in health-care facilities. These guidelines are discussed in *Designing, Testing, and Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: A Guide for Device Manufacturers*, a technical information report published by the Association for the Advancement of Medical Instrumentation (AAMI) in 1994.¹ The report, known as AAMI TIR12, covers the following general topics:

- Design considerations (physical, material, total system, and user design).
- Decontamination (cleaning agents, water-quality supplies, equipment, and methods used in health-care facilities and cleaning validation programs).
- Disinfection with liquid chemicals (classification of medical devices, based on degree of risk—low, intermediate, and high level—disinfectant selection, toxicity, and material compatibility).
- Sterilization (available processes, design considerations, efficacy testing methods, sterilant residue, and documentation requirements for hospitals).
- Compatibility of the device, sterilant, and equipment.
- Regulatory considerations (FDA regula-

tory classification and requirements).

The new guidelines raise a number of device design, testing, and labeling issues that are of concern to manufacturers considering test programs for new devices, or supporting

Device manufacturers are responsible for supporting their claims for product reuse.

changes in product design or disinfection and sterilization processing instructions.

DESIGN CONSIDERATIONS

Reusable devices must be designed to function safely and effectively following sterilization in a health-care setting. By definition, they must be designed to withstand multiple exposures to sterilants or disinfec-

tants. The number of exposures to which the device can be subjected without losing the ability to function effectively will help determine its useful life.

Most devices composed of sterilant-tolerant materials can withstand more than 100 use cycles. Testing should not be limited to the efficacy of the sterilization cycle; biocompatibility and functional performance of the device should be considered as well. This can be accomplished by exposing a product to multiple cycles equivalent to the projected maximum useful life of the device, including any cleaning steps performed between cycles. Following these exposures, functionality, physical integrity, and biocompatibility should be demonstrated through adequate testing.

When devices are produced for a single use only and the end-user must sterilize them, the manufacturer should provide the user with sterilization instructions. To provide these instructions, the manufacturer must have validation data to support the sterilization process.

A manufacturer should conduct studies along the lines of those recommended in AAMI TIR 12, under sterilization efficacy testing, to provide data to demonstrate that the recommended instructions provide the product with an equivalent sterility assurance level of 10⁻⁶.

Type of Cycle	Type of Load	Temperature	Cycle Time
Gravity displacement	Wrapped metal surgical instruments and heat-stable devices	270°–275°F (132°–135°C)	10–25 min
	Wrapped metal surgical instruments and heat-stable devices	250°F (121°C)	15–30 min
Prevacuum	Wrapped metal surgical instruments and heat-stable devices	270°–275°F (132°–135°C)	3–4 min
Gravity displacement	Unwrapped (flash) metal; nonporous items, without lumens	270°F (132°C)	3 min
	Unwrapped (flash) metal with lumens; porous items (e.g., rubber, plastic items)	270°F (132°C)	10 min
Prevacuum	Unwrapped (flash) metal; nonporous items, without lumens	270°F (132°C)	3 min
	Unwrapped (flash) metal with lumens; porous items	270°F (132°C)	4 min

Table I. Commonly used steam sterilization cycles.

<i>Type of Cycle</i>	<i>Cycle Parameters</i>	
100% EtO	Concentration EtO	883 mg/L
	Temperature	131°F (55°C) or 99°F (37°C)
	Exposure time	60–250 min (depending on temperature)
	Relative humidity	70% RH minimum
	Concentration EtO	725 mg/L
	Temperature	131°F (55°C) or 99°F (37°C)
	Exposure time	60–180 min (depending on temperature)
	Relative humidity	70% RH minimum
12/88 EtO/CFC-12	Because of concerns regarding harmful effects of CFCs on the ozone layer, alternative gas mixtures are under development. Note: 12/88 EtO/CFC-12 will no longer be manufactured as of January 1996. The remaining limited inventory will be sold on a first-come, first-served basis.	
EtO/carbon dioxide	Concentration EtO	Approximately 450 mg/L
	Temperature	130°F (55°C) or 100°F (38°C)
	Exposure time	3 hr or 7.5 hr (depending on temperature)
	Relative humidity	30 to 80% RH
EtO/HCFC	Concentration EtO	Approximately 600 mg/L
	Temperature	130°F (55°C) or 100°F (38°C)
	Exposure time	2 hr or 5 hr (depending on temperature)
	Relative humidity	30 to 80% RH

Table II. Commonly used EtO sterilization cycles.

DECONTAMINATION

A reusable device must be cleaned thoroughly even when disinfectants or sterilants are used. The cleaning process may remove blood, protein, and other potential contaminants from the surfaces, crevices, joints, and lumens of a device. It may also reduce the number of particles, microorganisms, and pyrogens present. If organic material is not removed, it may neutralize the effects of liquid chemical disinfectants and sterilants, such as ethylene oxide (EtO), and protect microorganisms from destruction. Such material can also alter the device surface.

The references in AAMI TIR 12 list several common cleaning and decontamination agents used in hospitals. Furthermore, the TIR provides test procedures that should be conducted to provide test data verifying that the manufacturer's recommended cleaning pro-

cedure, including the use of a specific cleaning agent, is effective for a particular device.

The cleaning procedure should be developed according to the type of contamination expected for the device, the design features, and the potential for patient exposure to pathogens. Verification is usually performed in a laboratory, using a mixture of artificial soil that closely simulates the type of contamination expected in clinical use. Simulated blood or body fluids, for example, may be formulated with a combination of calf serum, dry-milk powder, and a 1:1 mixture of rabbit blood and saline.²

A method proposed by AAMI for evaluating the effectiveness of the cleaning process is to add to the soil *Bacillus stearothermophilus* spores at approximately 10⁴ organisms per device (used as a tag).¹ After the soiled device has been cleaned according to the manufacturer's instructions, the remaining spores are recovered and counted.

The recovery technique must be validated before determining the efficacy of cleaning, which can then be determined by subtracting the number of spores recovered from the device after cleaning from the number recovered from a control sample; that is, one soiled and not cleaned. The testing should be sufficient to ensure that the procedure can be duplicated in health-care facilities.

DISINFECTION

Disinfection is defined as "the destruction of pathogenic microbes by thermal or chemical processes." As defined in AAMI TIR 12, this process is less lethal than sterilization, because disinfection can destroy most pathogens but not bacterial spores. Moreover, disinfection does not guarantee the sterility assurance level normally associated with sterilization cycles.

The disinfection process is divided into three levels of effectiveness: low, which is effective against vegetative microbes, but not tubercle bacilli, spores, or nonlipid viruses; intermediate, which is effective against tubercle bacilli and most viruses; and high, which is effective against most microbes, including bacterial spores. The level of disinfection or sterilization required for a particular device depends on its intended use.

The Centers for Disease Control and Prevention recommend disinfection or sterilization based on three end-use categories.³ The first is *critical items*: devices that come in direct contact with blood or areas of the body not typically in contact with contaminants. Sterilization is required for such devices, which include surgical instruments, endocavity probes, implants, biopsy forceps and scissors, and ophthalmic irrigation devices. *Semicritical items* are noninvasive devices that do not normally come into contact with intact mucous membranes. High-level disinfection is a minimum process requirement for products in this category, which include devices such as flexible endoscopes, endotracheal tubes, and breathing circuits. The only patient contact that *noncritical items* have is with intact skin. These devices, which rarely transmit disease, require low levels of disinfection; products can be cleaned with a simple detergent. Examples include cuffs for measuring blood pressure, beds, and crutches.

STERILIZATION

Device manufacturers use a wide variety of sterilization methods. Three important methods are exposure of the device to steam,

EtO, and chemical agents, respectively. Steam and EtO sterilization, the most common methods (see Tables I and II), can be controlled and monitored by physical means, microbiological means, or both. They can be used on packaged as well as unpackaged products. Liquid chemicals (e.g., glutaraldehyde and peracetic acid), however, require direct contact with the product, which therefore cannot be contained in a package (see Table III). Products sterilized using liquid chemicals are typically used immediately after sterilization.

Other sterilants include chemical gases, such as hydrogen peroxide plasma, peracetic acid, and vapor-phase hydrogen peroxide (see Table IV). These sterilants can be used on packaged products, and allow for low-temperature processing while minimizing product degradation, toxic residues, and processing times. Supporting test data must be provided for each set of sterilization instructions stated in product literature, however.

A manufacturer normally should perform full sterilization efficacy studies for each set of sterilization parameters chosen for each device. These biological studies are intended to demonstrate that the sterilization instructions provided to the end-user will produce a sterile product. Each end-user must also take steps to ensure that the process is validated and capable of delivering the designated cycle parameters.

Under exceptional circumstances, full efficacy studies on each device are not necessary. For example, if it can be shown that a new device poses no greater challenge to the sterilization process than a previously qualified device does, then the manufacturer can adopt the data gathered for that device. In addition, similar products can be grouped into families, and a worst-case representative chosen for testing to qualify the entire product family. A report should be written to justify the adoption of the new device.

NATURAL BIOBURDEN

The number and types of organisms that constitute the natural bioburden in reprocessing environments vary from site to site, and through time at a single site. Natural bioburden therefore cannot be used as a benchmark value for sterilization efficacy. AAMI TIR 12 recommends an overkill method, which uses a microbial load representing a worst-case challenge to the reusable device. This method is based on the principle that the sterilization process inactivates a resistant microbial spore chal-

<i>Type of Sterilant</i>	<i>Cycle Parameters</i>	
Glutaraldehyde	Concentration	2–3.5%
	Temperature	77°F (25°C)
	Exposure time	10 hr
	Note: Qualifying a liquid chemical sterilizing process for devices with lumens may require extended exposure times. Automated systems have been developed primarily for flexible endoscopes and hemodialyzers.	
Peroxyacetic acid	Concentration	0.2%
	Temperature	122°–132°F (50°–55.5°C)
	Exposure	12 min

Table III. Commonly used liquid chemical sterilants.

lenge. In addition, a safety factor can be used to demonstrate an equivalent sterility assurance level.

Validating the sterilization of a device should focus on the area of the device that is most difficult to sterilize. Dead-air spaces, mated surfaces (for example, scissor blades), threaded-screw areas, regions of greatest mass, and surface crevices all pose potential barriers to effective sterilization, and thus are usually appropriate sites on which to place a spore strip or spore inoculum. Direct spore inoculation should be performed with caution because clumping or inadequate drying of the inoculum could result in unreliable data. In cases where drying is particularly challenging, spores can be suspended in ethanol rather than water to accelerate the drying process.

STERILANT RESIDUES

Residues from sterilization and disinfection processes using steam and hydrogen peroxide are composed of nontoxic chemicals, such as water and oxygen, and therefore do not present problems. Other processes, however, such as those using EtO and glutaraldehyde, can leave toxic residues.

In addition, reusable medical devices are sometimes made of polymeric or elastomeric materials, which can react with chemical sterilants to form residues. EtO and its by-products can be determined using the same procedures recommended for single-use devices. For those processes producing residuals that have not yet been characterized as toxic or nontoxic, validation studies should include testing to determine whether toxic residues are present. If they are, the sterilization and disinfection instructions

must include the means to remove the residue (e.g., aeration or rinsing)—or to reduce it to nontoxic levels—before patient use.

The methods outlined in AAMI ST29 recommend practices for determining residual EtO in medical devices.⁴ The International Organization for Standardization (ISO) is in the process of developing standards for EtO residuals, and FDA's revised guidelines in this area are expected to be published shortly.⁵ The ISO requirements will differ from the current FDA and AAMI standards: whereas the latter measure actual EtO concentration values taken at particular points after a product has been sterilized, ISO will focus on EtO limits based on the expected potential for patient exposure. ISO also will not require analysis of ethylene glycol (EG) residues, only those of ethylene chlorohydrin (ECH).

Because a reusable device will be exposed to sterilants multiple times, EtO or its by-products, ECH and EG, may build up on the device. Increasing the aeration time can reduce residuals to low levels; alternatively, cleaning procedures used between cycles can help remove residuals. The analysis of residuals should be conducted on devices that have experienced the full range of reprocessing procedures expected to occur during their useful lives.

CYCLE REQUALIFICATION

Once a validation is completed, cycle requalification is required if a design modification, a material modification, or both might affect the ability to clean, sterilize, or aerate the device, or if a packaging change might affect the permeation and aeration of the sterilizing agent.

<i>Type of Sterilant</i>	<i>Cycle Parameters</i>	
Low-temperature hydrogen peroxide plasma	Concentration	6 mg/L
	Temperature	76°–122°F (24°–50°C)
	Exposure time	65 min
Low-temperature peroxyacetic acid/plasma	Concentration	2 mg/L (initial vapor phase)
	Temperature	≤113°F (45°C)
	Exposure time	3 hr
Vapor-phase hydrogen peroxide	Concentration	35% (initial)
	Temperature	100°–102°F (38°–39°C)
	Exposure time	30–55 min

Table IV. Commonly used chemical sterilant gases.

Upon qualification of a sterilization method for a device, the manufacturer should provide instructions for a minimum of one type of sterilization process. Typically, however, more than one process is qualified, which gives health-care workers the flexibility to choose an appropriate cycle that not only will be effective, but that they can control. The packaging used in the efficacy study should be adequately described, and instructions for disassembly and reassembly as used in the efficacy study should be included, because some device parts may be effectively sterilized in their disassembled, but not assembled, configuration. Cleaning instructions should be properly stated, because inadequate cleaning can lead to a buildup of contaminants, which can compromise sterilization. For products processed in chemicals that can impart a residue, a description of the removal process is appropriate. EtO processing instructions, for example, should include the time and temperature of aeration required to achieve safe levels.

To make a device easy to use by health-care professionals, a manufacturer should validate its products using standard hospital sterilization cycles. This can present problems for particular devices or sterilants. A manufacturer, for example, may have trouble qualifying the sterility of a product at standard hospital autoclave parameters. When attempting to resolve this dilemma, the manufacturer should begin by asking the following questions:

- Were thermocouples used to monitor conditions during the study? Is it possible that the area in which the product or biological

challenge was located did not reach processing temperature?

- What load configuration was used during processing? Can it be altered in order to facilitate sterilization?
- What was the D-value of the biological indicator used? Was it within the specification indicated by AAMI TIR 12?
- How long were the devices processed after inoculation? Long delays between inoculation and sterilization could adversely affect the resistance of the inoculum.

REGULATORY CONSIDERATIONS

The instruction manual for a reusable device must address several FDA recommendations concerning labeling. In March 1995, FDA's Office of Device Evaluation issued a draft guideline titled "Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: FDA Reviewer Guidance."⁶ This document was intended to provide a checklist for evaluating a reusable device's labeling content for conformance with all applicable requirements. The goal was to ensure that a device would be adequately prepared for repeated, multi-patient use.

The responsibility for labeling rests with both the manufacturer and the user of the device. The manufacturer is responsible for supporting the claim for reuse, and for providing procedures that can be reasonably executed by the user. The user of the device (i.e., the health-care site) is responsible for having the facilities and equipment necessary to follow and execute the instructions.

The labeling practice instructing users to "follow routine hospital reprocessing procedures for this device" is not considered acceptable, because for many devices such procedures do not exist. The FDA guidance document identifies seven criteria for reprocessing that must be addressed in the instructions:

1. "The instructions must include initial processing (nonsterile, single use device) or reprocessing (reusable device) instructions."
2. A statement is required indicating that the device "must be thoroughly cleaned before reuse." (The cleaning process for the device is critical for ensuring success in the microbicidal processes.)
3. "The instructions must indicate the appropriate microbicidal process for the device." This relates to the sterilization or level of disinfection appropriate for the device based on its patient-contact category.
4. "The processes must be feasible considering the intended location of reprocessing." The processes and instructions must adequately reflect the equipment and knowledge needed to carry out the reprocessing steps.
5. "The instructions must be understandable."
6. "The instructions must be comprehensive." This is the section of the labeling that needs to describe specifically the procedures necessary "to execute the processing regimen safely and effectively." This section comprises many components; the intent is to be as comprehensive as possible regarding special tools, accessories, maintenance procedures, cleaning agents, and methods for disinfection or sterilization, based on experimental data. Without these instructions, the label may be declared deficient and returned to the manufacturer for further clarification.
7. "The instructions must include only devices and accessories that are legally marketed." Items such as sterilizers used in health-care facilities and liquid chemical disinfectants and sterilants are subject to separate FDA clearance and approval.

These seven criteria combine to form a user-friendly, validated, and informative instruction packet intended to deliver a safe, anti-infective reusable device.

REFERENCES

1. *Designing, Testing, and Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: A Guide for Device Manufacturers*, AAMI TIR 12, Arlington, VA, Associ-

- ation for the Advancement of Medical Instrumentation (AAMI), 1994.
2. Miles RS, "What Standards Should We Use for the Disinfection of Large Equipment?" *J Hospital Infection*, 18:264-272, 1991.
 3. *Centers for Disease Control Guidelines for Handwashing and Hospital Environmental Control, Section 2: Cleaning, Disinfecting, and Sterilizing Patient Care Equipment*, Atlanta, Centers for Disease Control, 1985.
 4. *Recommended Practice for Determining Residual Ethylene Oxide in Medical Devices*, ANSI/AAMI ST29-1988, Arlington, VA, Association for the Advancement of Medical Instrumentation, 1994.
 5. "Biological Evaluation of Medical Devices—Part 7: Ethylene Oxide Sterilization Residual: Draft International Standard ISO/DIS 10993-7," Geneva, Switzerland, International Organization for Standardization, 1995.
 6. "Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: FDA Reviewer Guidance," Rockville, MD, FDA, Center for Devices and Radiological Health,

Office of Device Evaluation, 1995.

Susanne Anderson is the manager of Technical Sales and Services for NAMSA (Irvine, CA). John Broad, NRM, serves as a NAMSA senior scientist, also at the Irvine, CA facility. Dave Parente is a senior scientist and national accounts manager at NAMSA's Kennesaw, GA laboratory. Ed Arscott previously served as microbiology manager at NAMSA (Northwood, OH). ■