Reusable Device Validations

PBL
Pacific BioLabs

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Health care technicians clean reusable medical devices according to the manufacturer's Instructions For Use (IFU).

PART I: INTRODUCTION TO DEVICE REPROCESSING

Reusable medical devices are devices intended for repeated use either on the same or different patients and require appropriate reprocessing between uses. Examples include surgical forceps, stethoscopes, endoscopes and catheters.

Reprocessing is a multistep process which results in the decontamination of the reusable medical device. Reprocessing is divided into two components, the cleaning procedure and the microbicidal procedure.

Cleaning is a crucial component of device reprocessing. During patient use, reusable devices can become soiled with biological material (such as blood) and contaminated with microorganisms. Soil left on a reusable device could prevent the microbicidal action of sterilization and disinfection. The microbicidal process consists of a disinfection step or a sterilization step which will reduce the microbial load to safe levels.

Reprocessing devices safely, effectively and efficiently is more important than ever in today's healthcare ecosystem. Advancements in technology, medicine and diagnostics have allowed manufacturers and medical device engineers to develop increasingly sophisticated device designs. The increased complexity of device designs has made reprocessing of medical devices more challenging. These designs may include electronics requiring alternative sterilization methods and special care when cleaning.

To ensure the reprocessing instructions provided to health care providers are sufficient to clean and decontaminate the device, the FDA requires that reusable device manufacturers validate their reprocessing methods. These reprocessing instructions are collated into the device's Instructions for Use (IFU) which is included in the device's final labeling. Reprocessing validations are usually done at a later stage of the developmental cycle, but manufacturers should design devices with reprocessing in mind to avoid time consuming and complicated reprocessing procedures.

SPAULDING CATEGORIES

Medical devices can be grouped into one of three categories, called Spaulding categories, based on the degree of risk associated with the type of device. The microbicidal reprocessing procedure for a device largely depends on the assigned Spaulding category.

- **Non-Critical:** Medical devices that only contact intact skin. Non-Critical devices also include devices that do not directly contact the patient but may become contaminated with microorganisms and organic soil during patient care. FDA recommends thorough cleaning followed by intermediate or low level disinfection for these devices. Examples include bedpans and blood pressure cuffs.
- **Semi-Critical:** Medical devices that contact intact mucous membrane or non-intact skin but do not ordinarily penetrate the blood barrier or sterile areas of the body. These devices should be sterilized but if that is not feasible, it must be subjected to high-level disinfection. Examples include gastrointestinal endoscopes and respiratory therapy equipment.
- **Critical:** Medical devices which come in contact with the blood stream or sterile areas of the body are required to be sterile. Examples include implants and surgical instruments.

INDUSTRY AND REGULATORY REQUIREMENTS

In March, 2015 the FDA published a guidance, Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling aimed at helping device manufacturers develop safer reusable devices by providing more clarity about testing and labelling requirements. Other common standards include:

1. **AAMI TIR12** - Designing, testing and labeling reusable medical devices for reprocessing in health care settings: A guide for medical device manufacturers
2. **AAMI TIR30** - A compendium of processes, materials, test methods, and acceptance criteria for cleaning reusable medical devices
3. **AAMI ST58** – Chemical sterilization and high-level disinfection in health care facilities
4. **AAMI/ANSI ST81** – Sterilization of medical devices – Information to be provided by the manufacturer for the processing of resterilizable medical devices
5. **AAMI TIR34** - Water for the reprocessing of medical devices
6. **AAMI ST77** – Containment devices for reusable medical device sterilization
7. **AAMI ST41** – Ethylene Oxide Sterilization in Health Care Facilities: Safety and Effectiveness
8. **ANSI/AAMI/ISO 10993-7** – Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals
9. **ANSI/AAMI ST79** – Comprehensive guide to steam sterilization and sterility assurance in health care facilities

Inappropriate reprocessing of endoscopes has led to patient deaths.

Dried organic soil can be difficult to clean. Point-of-use processing helps to remove the soil and the soil that remains on the device will stay moist making the cleaning process more effective.

DEVICE REPROCESSING WORKFLOW

Reprocessing of reusable devices begin at the point-of-use and typically involves the following steps:

USE

POINT OF USE PROCESSING
Prompt initial treatment to remove soil and prevent drying of soil and contaminants.

THOROUGH CLEANING
The device should be thoroughly cleaned following the IFU from the manufacturer. The cleaning process should remove organic soils to make disinfection or sterilization more effective.

DISINFECTION
The device should be disinfected using high, intermediate or low level disinfection. The level of disinfection is determined by the Spaulding category of the device.

STERILIZATION
For critical medical devices a Sterility Assurance Level (SAL) of 10^{-6} is required which means that out of a million sterilized devices one device will contain one microorganism.

Cleaning a reusable medical device is a crucial step in device reprocessing.

PART II: CLEANING VALIDATIONS

Cleaning is the removal of organic material (e.g. patient blood), inorganic material (e.g. salts), and microbial contamination (acquired from the medical procedure or during handling) to ensure that adequate disinfection/sterilization can be achieved, thereby making the device safe for subsequent patient use.

Cleaning is one of the first and the most essential step in determining the device reprocessing workflow. It involves the physical removal of soil and contaminants from the reusable medical device.

Effective cleaning should:

- Minimize the soil transfer from one patient to another or between uses in a single patient.
- Prevent accumulation of residual soil throughout the product's use life.
- Allow for successful, subsequent disinfection/sterilization steps.

COMPONENTS OF A CLEANING VALIDATION:

Many factors need to be considered when developing the cleaning validation protocol therefore cleaning validation studies typically require significant communication between the sponsor and PBL. The information below should help potential sponsors with the decisions that would need to be made regarding their cleaning validation study.

Test Soil –

The test soil should reflect what the device is expected to be contaminated with after it has been used. A test soil that is used for a surgical instrument may not be appropriate for a device that comes in contact with a mucosal membrane such as a dental device. Intravascular devices will be exposed to a lot more blood than a device that comes in contact with the intact surface of the mouth. Drills designed specifically for bones will be contaminated with bone debris. The table below describes some common types of test soil and devices they can be used for. For more information, refer to AAMI TIR30.

Table 1. Commonly used cleaning validation test soils, composition and suitable devices.

NAME OF SOIL	CONSTITUENTS OF SOIL	DEVICE
ATS – Artificial Test Soil	Protein, hemoglobin, carbohydrates, inorganic salt, mucin and endotoxin	Flexible endoscopes and accessories, surgical instruments, bedpans, dental devices and blood contacting devices.
ATS-Bone	Protein, hemoglobin, carbohydrates, inorganic salt, mucin, endotoxin and bone	Drills used to cut into bone during surgery.
Miles Test Soil	Fetal calf serum, dry milk powder, rabbit blood, saline	Not Specified

Soiling Method –

The soiling method will often depend on how the device will be used. If the health care provider is expected to have blood on their gloves while operating the device, it may be prudent to apply soil onto gloves and then operate the device using soiled gloves. If the device is expected to be covered in soil, immersion in the test soil could be an option. For some rotating devices, like a drill, operating the rotating portion of the device in test soil would be an appropriate soiling method. In some cases, if the manufacturer believes that contamination will be isolated to a specific part of the device, the soiling method could be defined as applying a certain amount of soil directly to that portion of the device.

The common ways to contaminate the device are:

1. Pipette the test soil directly onto the device.
2. Handle the device with soiled gloves.
3. Immerse into the test soil.

When exposed to the test soil, moving parts should be actuated to simulate clinical use. The devices are then removed from the soil and allowed to sit for an appropriate time to simulate the wait time between use and reprocessing.

The possibility of the end user contaminating their gloves should be a factor when performing a cleaning validation.

Soil Extraction – Method Suitability

To perform the cleaning validation, PBL technicians will need to be able to extract residual soil from the device in order to determine how much test soil is left on the device after cleaning. Some materials and device designs are easier to extract soil off of than others and to compensate for that PBL performs a suitability study which allows us to determine a soil recovery correction factor. There are two different extraction methods used when determining this correction factor.

Exhaustive Extraction –

Exhaustive extraction is used when an undefined amount of soil has been added to the device. This is the case when the device is submerged into test soil or when soil is added to the device by handling the device with soiled gloves. For exhaustive extraction the analyst will perform an extraction procedure and measure the amount of the soil markers (usually protein and hemoglobin) present in the extraction fluid. The analyst will then repeat the extraction and measuring procedure until the soil marker measurements are below the limit of quantitation. Typically four extraction procedures are performed consecutively. Once the total amount of marker is known, the recovery percentage is calculated. The first extraction must be able to recover at least 70% of the total soil marker amount for the method to be valid.

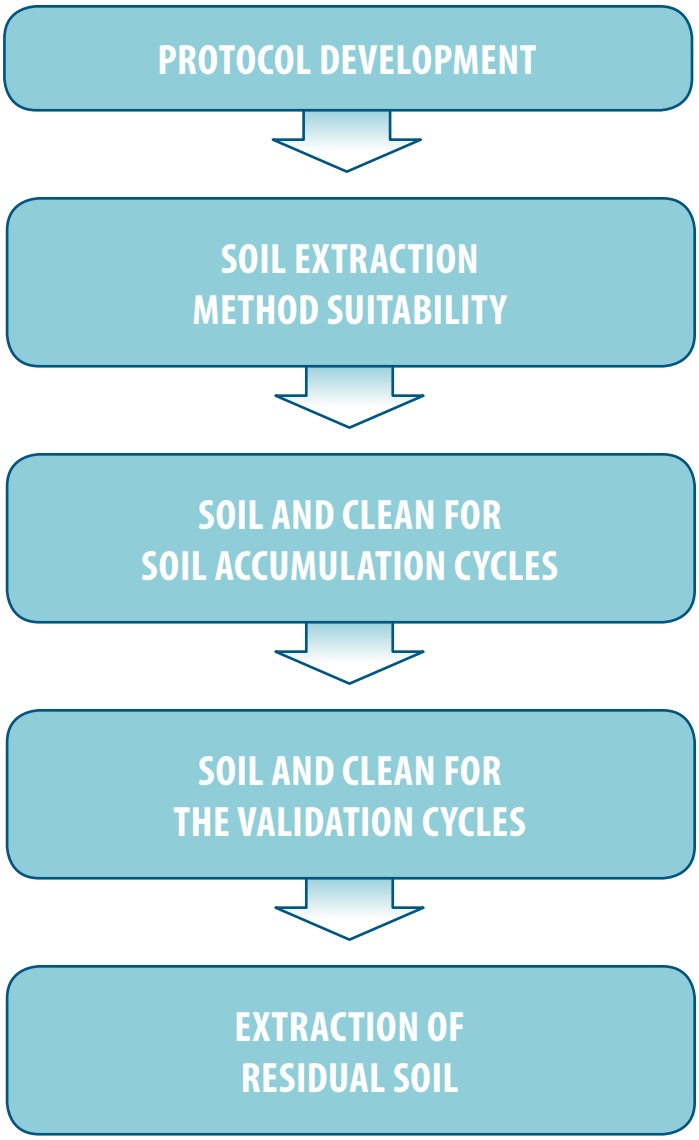
Simulated Extraction –

Simulated extraction is used when a defined amount of soil has been added to the device. For example, 100 µL of test soil may be added to the device. The soil is then extracted from the device and then amount of soil in the extract is compared to the same amount of soil (100 µL in this case) added to the extraction fluid to determine extraction efficiency. The soil markers from each group are measured and compared. The extraction procedure must be able to recover at least 70% of each biomarker.

In both the exhaustive extraction and simulated extraction, the extraction process is done in triplicate and must recover at least 70% of the total soil marker applied to the device. Based on the percentage of soil marker extracted, a recovery factor is determined which will account for the amount of soil that was not able to be extracted from the device.

Soil Accumulation–

Once the extraction method has been shown to be appropriate, the cleaning validation continues by performing soil accumulation cycles. The FDA has found that organic soil builds up over time and the inclusion of soil accumulation cycles in the validation is designed to replicate this phenomenon. The number of soil accumulation cycles will depend on the manufacturer and the life span of the device but PBL recommends performing at least six simulated use cycles. Each cycle will consist of contaminating the device with the test soil and then cleaning the device according to the manufacturer's IFU. The purpose of the soil accumulation cycles is to show that after a specified number of cycles, the device can still be cleaned effectively and build-up is not occurring.



Typical workflow of cleaning validation studies.

Cleaning Cycles –

After the appropriate number of soil accumulation cycles have been completed, the device will be contaminated with test soil again and the cleaning validation cycles begin. At PBL we recommend three validation cycles of three devices each giving a total of nine test data points. The test devices will be cleaned using the cleaning procedure specified in the study protocol. If cost is an issue, PBL could perform one cycle on three devices giving a total of three data points.

The cleaning procedure specified in the protocol will be based on the IFU of the device. The manufacturer will need to have a clear understanding of how they would like the device to be cleaned before starting the validation.

The following will need to be considered before deciding upon a cleaning method:

- Type of detergent
- Need for ultrasonic cleaning
- Brush diameter to clean the lumens of the device
- Duration of cleaning (for example, how long should the technician brush the outside of the device?)
- Conditions (for example, if device has to be immersed in water, how long should it be immersed for and at what temperature?)

The validation procedure should simulate the worst case scenario which means that PBL will use the least amount of time and the coldest temperatures specified in the IFU in order to determine if the worse case procedure can effectively clean the device.

Ultra-sonic cleaners are commonly used to help remove debris from the reusable medical device.

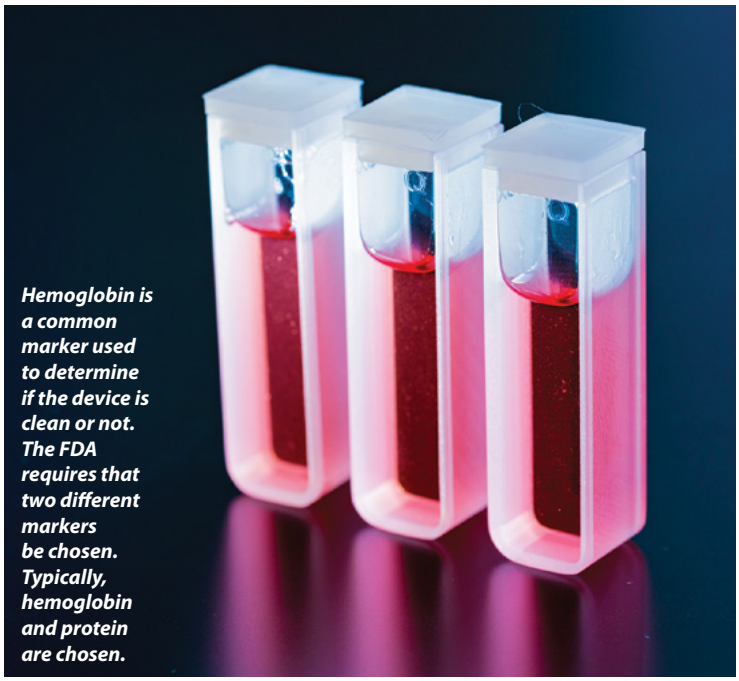
Markers –

After the devices are cleaned, they are inspected visually to ensure that no organic soil is visible on the device. The devices are then extracted using the validated extraction method to remove residual soil that may be present on the device after cleaning. The extraction fluid is then tested to evaluate the amount of test soil remaining on the device.

The FDA requires that two cleaning markers be tested. Protein and hemoglobin are the most commonly tested markers used in a reusable device cleaning validation. Protein is easily quantitated using various methods. Because it is a significant constituent of cell and viral structures it is a good choice as a marker. The amount of protein remaining on the device after cleaning should be less than 6.4 µg/cm^2.

Red blood cells contain hemoglobin and because residual blood is a concern, testing for the presence of hemoglobin after cleaning is an obvious choice. After cleaning the device, the amount of hemoglobin remaining on the device should be less than 2.2 µg/cm^2.

Carbohydrates can be measured as well, as they are also a component of both eukaryotic and prokaryotic cells. Other markers include, total organic carbon, endotoxin, lipids and ATP.



Hemoglobin is a common marker used to determine if the device is clean or not. The FDA requires that two different markers be chosen. Typically, hemoglobin and protein are chosen.

PART III: DISINFECTION AND STERILIZATION VALIDATIONS

The microbicidal step takes place after the cleaning process. Sterilization or disinfection should be a component in the IFU for reusable medical devices and the process must be validated by the manufacturer. The validation process differs depending on the type of sterilization or the level of disinfection. The Spaulding category of the device defines which microbicidal process is required.

- **Critical Devices:** Users should be instructed to disassemble (if applicable), thoroughly clean, and sterilize after each use.
- **Semi-Critical Devices:** Users should be instructed to thoroughly clean these devices and then reprocess them by sterilization. If the device design does not permit sterilization (e.g., device materials cannot withstand sterilization), then high level disinfection should be used.
- **Non-Critical Devices:** FDA recommends thorough cleaning, then intermediate or low level disinfection depending on the nature and extent of contamination.

Sterilization –

Reusable devices must be designed to function safely and effectively following sterilization in a healthcare setting. By definition, they must be designed to withstand multiple exposures to sterilants or disinfectants. The number of exposures to which the device can be subjected to without losing the ability to function effectively will help determine its useful life.

Sterile medical devices should achieve a sterility assurance level (SAL) of at least 10^{-6} which means that one in a million devices will be contaminated with a single organism. All sterilization validation methods use a million bacterial spores and worst-case organisms to prove that a SAL of 10^{-6} is actually achieved.

A wide variety of sterilization methods are available to sterilize reusable devices. Four important common sterilization methods are:

1. Steam sterilization
2. Ethylene Oxide (ETO) sterilization
3. Hydrogen peroxide (such as Sterrad or V-Pro)
4. Liquid Chemical Sterilization

Hospital staff loading reusable devices into an autoclave for sterilization.

Steam Sterilization using an autoclave is the preferred method of sterilization and is the FDA recommended method if the device can withstand high temperatures and exposure to steam.

Steam Sterilization –

Steam sterilization is the most frequently used sterilization method in a health care system and should be considered the microbicidal method of choice if the reusable medical device is able to withstand elevated pressure, high temperatures and exposure to moisture.

Tables 2 and 3 below describes the steam sterilization cycles used in health care facilities. Two different types of sterilization cycles are ran in hospital autoclaves, gravity displacement cycles and pre-vacuum cycles. Gravity displacement cycles force dry air out of the drain at the bottom of the autoclave by injecting steam through the top of the autoclave chamber. Pre-vacuum cycles actively evacuate dry air out of the chamber using a vacuum. Pre-vacuum cycles are more effective at removing the dry air, which makes pre-vacuum cycles more efficient at sterilizing. Because pre-vacuum cycles are more efficient, shorter sterilization cycles can be used to achieve the required sterility assurance level.

Table 2. Gravity displacement steam sterilization cycles.

ITEM	EXPOSURE TIME AT 121°C	EXPOSURE TIME AT 132°C	EXPOSURE TIME AT 135°C	MINIMUM DRYING TIME
Wrapped Instruments	30 min	15 min		15-30 min
			10 min	30 min
Textile Packs	30 min	25 Min		15 min
			10 min	30 min
Wrapped Utensils	30 min	15 min		15-30 min
			10 min	30 min
Nonporous items (e.g., instruments)		3 min	3 min	0-1 min
Unwrapped nonporous and porous items in mixed load		10 min	10 min	0-1 min

Table 3. Pre-vacuum steam sterilization cycles.

ITEM	EXPOSURE TIME AT 132°C	EXPOSURE TIME AT 135°C	MINIMUM DRYING TIME
Wrapped Instruments	4 min		20-30 min
		3 min	16 min
Textile Packs	4 Min		5-20 min
		3 min	3 min
Wrapped Utensils	4 min		20 min
		3 min	16 min
Nonporous items (e.g., instruments)	3 min	3 min	N/A
Unwrapped nonporous and porous items in mixed load	4 min	3 min	N/A

Steam sterilization validations are conducted by inoculating the reusable medical device with at least a million spores of *Geobacillus stearothermophilus* and then exposing the device to a half cycle. For example, if the device manufacturer specifies in their IFU that the sterilization cycle is a pre-vacuum cycle at 135°C for three minutes, the half cycle will be 1.5 minutes.

The organisms inoculated with the device during a sterilization cycle are commonly referred to as biological indicators or BIs for short. *Geobacillus stearothermophilus* is a heat resistant organism and is therefore considered to be worst case over typical bacteria organisms that contaminate medical devices. The spores can either be inoculated directly onto the device using a liquid suspension or the spores can be added onto a paper strip, metal wire or a thread and then the spore carrier can be placed on the device.

The most challenging locations on the device must be inoculated with the biological indictor. In regards to steam sterilization, the challenging areas are areas in which the steam will have the most difficulty in gaining access to. Some challenging areas include long narrow lumens, junctions between parts and partially enclosed areas with limited space for air to flow in and out. Fully enclosed areas will not be able to be sterilized by steam because the steam would not be able to reach the enclosed space.

After the half cycle has been completed the device is immediately removed and taken into a laminar flow hood so that the biological indicators can be removed without contaminating them. The biological indicators are placed into media and then placed in an incubator for seven days. If growth is observed, the sterilization cycle was not sufficient. If growth was not observed after seven days, the half cycle was sufficient to kill a million organisms and therefore the full cycle would be validated.

The steam sterilization dry time would also need to be validated. After the steam exposure the packages are wet and must be dried. Wet devices can introduce microorganisms into the package of the device through wicking. After steam exposure, moisture must be removed from devices. To validate the dry time, the medical device is exposed to the full sterilization cycle temperature and time as well as the full dry time. The cycle is repeated three times and if no moisture is observed on the devices or the packaging immediately after the steam sterilization concludes, the dry time is considered valid.

After steam sterilization, devices should not only be sterile, but also dry.

Ethylene Oxide Sterilization (ETO) –
Ethylene oxide sterilization is often used in health care settings for devices that cannot be steam sterilized. The critical parameters for ETO sterilization are the ethylene oxide concentration, exposure time, relative humidity, temperature and aeration time. ETO concentrations between 450 to 1200 mg/L, temperatures between 37°C to 63°C, exposure times from 60 to 360 minutes and humidity from 40% to 80% are typical. ETO residuals can be toxic and the manufacturer will be expected to show that the amount of ETO residuals after the recommended cycle are below harmful levels.

An ETO validation will rely on biological indicators to show that the sterilization process provides an adequate sterility assurance level (SAL). The BI used for ETO validations is *Bacillus atrophaeus* and the validation will consist of fractional cycles, half cycles and full ETO cycles.

Hydrogen Peroxide Sterilization –
Hydrogen peroxide is commonly used in hospitals to sterilize temperature sensitive medical devices. The most commonly used hydrogen peroxide systems in health care facilities are the Sterrad and V-Pro systems. In both systems, a half cycle can be used to validate a full sterilization cycle. The biological indicator used for hydrogen peroxide validations is *Geobacillus stearothermophilus* and if a million organisms placed at the challenging locations are shown to be killed in the half cycle, the full cycle is considered valid.

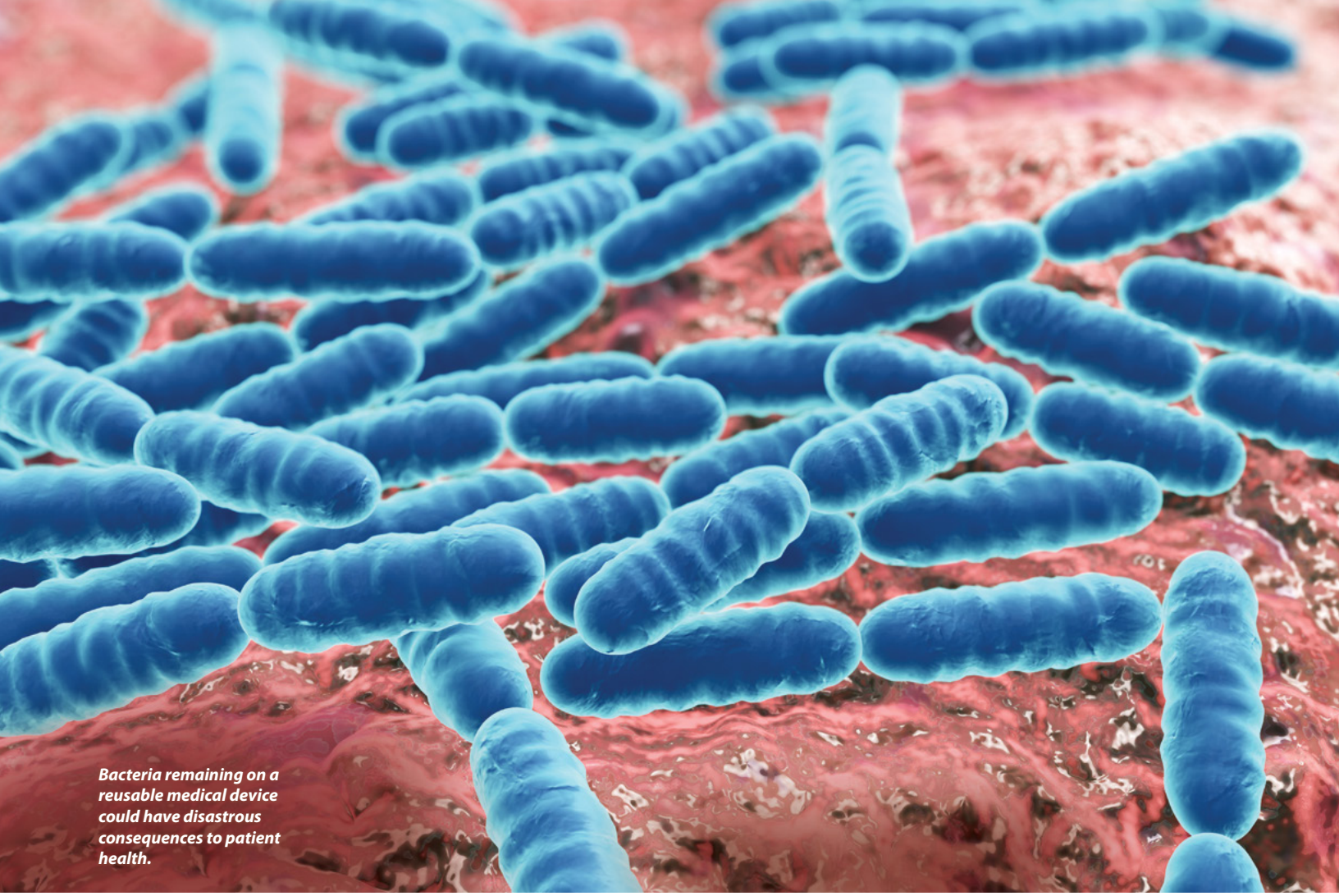
Liquid Chemical Sterilization –
FDA cleared liquid chemical sterilants such as glutaraldehyde and peracetic acid can also be used to sterilize reusable devices. Devices sterilized using liquid chemicals are typically used immediately after sterilization because it is difficult to package the devices after sterilization without exposing the device to air.

The validation of liquid chemical sterilization requires a spore suspension placed at the most challenging locations on the device and then exposing the device to a half cycle. If a liquid chemical sterilization validation is performed, the manufacturer must also show that the chemical residuals are below harmful levels.

Table 4: Commonly used liquid chemical sterilants.

TYPE OF STERILANT	CYCLE PARAMETERS	
Glutaraldehyde	Concentration	2–3.5%
	Temperature	77°F (25°C)
	Exposure time	10 hr
Peracetic acid	Concentration	0.2%
	Temperature	115 - 131°F (46 – 55°C)
	Exposure	6 min

Once the devices are removed from the liquid chemical sterilant, they are exposed to air and are no longer sterile.



Bacteria remaining on a reusable medical device could have disastrous consequences to patient health.

Disinfection –
Disinfection is defined as the destruction of microbes by thermal or chemical processes. This process is less lethal than sterilization, because disinfection can destroy most microorganisms but may not be able to destroy bacterial spores.

The disinfection of medical devices are categorized into high level disinfection, intermediate level disinfection and low level disinfection. High level disinfection may be used on semi-critical devices that cannot be sterilized. High level disinfection can kill most microbes except spores. Intermediate and low level disinfection can be used on non-critical devices. Intermediate level disinfection can kill viruses, mycobacteria, fungi, and vegetative bacteria. Low level disinfection can kill vegetative bacteria, some fungi and lipid viruses.

The different levels of disinfection require different validation testing procedures with different testing end points and test organisms. For high level disinfection, the device is inoculated with over one million Mycobacteria organisms and the high level disinfection validation passes only if a six log reduction achieved. Intermediate level disinfection requires only a three log reduction in Mycobacteria but also six log reduction in four different vegetative organisms. Low level disinfection only requires a six log reduction of four different vegetative microbes.

Table 5. Comparison of the three levels of disinfection.

DISINFECTION TYPE	TYPE OF DEVICE	MICROBES TARGETED	END POINT
High Level	Semi-Critical	Most Microbes, Except Spores	Six Log Reduction of Mycobacteria
Intermediate Level	Non-Critical	Viruses, Mycobacteria, Fungi and Vegetative Bacteria	Three Log Reduction of Mycobacteria and Six Log Reduction of Four Different Vegetative Organisms
Low Level	Non-Critical	Vegetative Bacteria, Some Fungi and Lipid Viruses	Six Log Reduction of Four Different Vegetative Organisms

Thermal vs. Chemical Disinfection –
Devices can be disinfected by thermal means (heat) or by chemical means. Thermal disinfection involves submerging a device into hot water for a set period of time. The temperature of the water determines the amount of exposure time. The higher the water temperature, the shorter the exposure time.

Chemical disinfection uses microbicidal chemicals to kill microorganisms. A variety of different chemical disinfectants are available. Common high level chemical disinfectants are Ortho-phthalaldehyde and Gluteraldehyde.

Automated Units –
Cleaning and disinfection in health care facilities can be conducted manually or by using automated methods. Automated cleaning and disinfection units minimize personnel exposure to harmful organisms, improve cleaning effectiveness, increase productivity, and can be more easily monitored for quality performance.

Automated washer disinfectors clean medical devices as well as disinfect the device. Some automated washer disinfectors perform thermal disinfection while others perform chemical disinfection. Automated washer disinfectors are very common in large heath care facilities such as hospitals. According to AAMI TIR 12, medical devices manufacturers should validate the cleaning and disinfection of their device in at least one type of automated washer disinfector.

Automated Endoscope Reprocessors (AERs) are commonly used to reprocess endoscopes in health care settings. Typically AERs chemically disinfect endoscopes, however some AERs may have cleaning cycles. The chemical disinfectant is exposed to the outside surface of the endoscope as well as through its long interior channels.

Initiate a Reusable Device Validation at PBL
Reusable device validations are a critical factor in getting your device to market. It is important to limit risk as much as possible and by choosing PBL you can be assured that Pacific BioLabs will perform your reusable device validations following rigorous regulatory compliance and scientific integrity. Pacific BioLabs has the experience and expertise needed for your validations and you can trust us to do it right the first time, on time. Call us at 510-964-9000 or email us at Info@PacificBioLabs.com to discuss your reusable device validations.

AAMI TIR 12 recommends that manufacturers validate at least one type of automated washer disinfector.

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