LEARNING OBJECTIVES

1. Describe the validation process performed by medical device manufacturers
2. Discuss the importance of medical device compatibility testing
3. Introduce product families, master products and their role in the validation process
4. Describe how verification testing is performed in healthcare facilities

THE TERMS “VALIDATION” AND “VERIFICATION” ARE FREQUENTLY used when processing medical devices; however, these terms are often used inappropriately and Central Service/Sterile Processing (CS/SP) technicians must understand they are not interchangeable. The purpose of this lesson is to clarify both terms, describe what each term entails and explain how the two activities impact a CS/SP department.

OBJECTIVE 1: DESCRIBE THE VALIDATION PROCESS PERFORMED BY MEDICAL DEVICE MANUFACTURERS

Validation is a documented procedure performed by the device manufacturer; it uses scientifically valid methods to obtain, record and interpret the results required to ensure a process will consistently yield a medical device that complies with predetermined specifications. Before a reusable medical device is introduced to the medical community, its manufacturer must obtain clearance from the US Food and Drug Administration (FDA). To do so, the manufacturer must demonstrate that the medical device can be safely and effectively reprocessed between patient uses.

Two types of risks are associated with the reuse of a medical device:
1. The risk of disease transmission from one patient to another or from environmental sources to a patient; and
2. The risk of inadequate or unacceptable device performance following reprocessing.

Manufacturers of reusable medical devices must provide users with instructions for use (IFU) for reusable
medical devices. The IFU must completely and comprehensively explain how to handle, clean, disinfect, test, package, sterilize and, if applicable, aerate their products. Manufacturers also have the responsibility of conducting and documenting any testing necessary to validate the suitability of these instructions.

Manufacturers bear these obligations under FDA labeling regulations (21 CFR 801). Detailed FDA recommendations are provided in the FDA guidance document, Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling Guidance for Industry and Food and Drug Administration Staff (issued March 17, 2015; Appendix E updated June 9, 2017). This FDA guidance provides recommendations to medical device manufacturers for the formulation and scientific validation of reprocessing instructions for reusable medical devices. The guidance document also provides recommendations for the content and review of premarket notification submissions [510(k)] and premarket approval (PMA) applications concerning labeling instructions for reprocessing reusable medical devices.

Manufacturers of reusable medical devices are responsible for providing labeling that contains adequate IFU, including how to prepare a device for use. While the FDA recognizes the critical role and responsibility of the device manufacturer, it is the responsibility of healthcare facilities to follow the validated reprocessing instructions. The focus of the FDA document is to provide guidance to medical device manufacturers in the complex activities involved in crafting and validating reprocessing instructions to ensure the device can be used safely and for its intended purpose.

The FDA defines reprocessing as validated processes used to render a used or contaminated medical device fit for the next use. The processes must be designed to remove soil and contaminants by cleaning and to inactivate microorganisms by disinfection or sterilization. Reprocessing of reusable devices involves the appropriate steps that begin at the point of use, followed by thorough cleaning and, finally, disinfection or sterilization.

1. **Point-of-Use Processing:** Reprocessing begins with processing at the point of use to aid in the later cleaning steps. Point-of-use processing is the prompt, initial cleaning steps and/or measures to prevent drying of soil and contaminants in and on the device.

2. **Thorough Cleaning:** The device should be thoroughly cleaned after point-of-use processing occurs. Generally, thorough cleaning is done in a dedicated cleaning area. Cleaning is the physical removal of soil and contaminants; the methods and agents used for cleaning should be designed to effectively remove soil and contamination. 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; and
   - Allow for successful, disinfection/sterilization steps.

3. **Disinfection or Sterilization:** Depending on the intended use of the device, the device should be disinfected or sterilized. These processes are intended to kill microorganisms; the methods and agents used for disinfection and sterilization should be designed to achieve appropriate microbicidal efficacy.

Validation studies are performed in accordance with AAMI TIR12, Designing, testing, and labeling reusable medical devices for reprocessing in health care facilities: A guide for medical device manufacturers, and AAMI TIR30, A compendium of processes, materials, test methods, and acceptance criteria for cleaning reusable medical devices. These documents describe design considerations that medical device manufacturers should consider to help ensure their products can be safely and effectively reprocessed; a summary of test methods available is also included. The documents also contain information about decontamination, cleaning, disinfection and sterilization processes commonly used in healthcare facilities. This information helps manufacturers develop and validate reprocessing procedures that can be used by and will be recommended to healthcare facilities for reprocessing in their facilities. It is from this testing that manufacturers can develop reprocessing IFU and demonstrate that the device can be thoroughly cleaned, without being damaged or left with remaining residues.

Reusable medical devices used in today’s healthcare facilities range from a simple non-hinged stainless-steel instrument to a robotic instrument manufactured with varying materials and containing lumens and working mechanisms encompassed in a complex design that is difficult and time consuming to clean. Medical devices between these extremes differ in size, complexity, fragility, immersibility, sensitivity to cleaning agents and water temperatures, and other properties. Validation testing is performed because of these critical variables to ensure devices can be effectively reprocessed in a healthcare setting.

Per the FDA validation methods and labeling document, cleaning validation
activities are based on all-inclusive validation protocols that use soils relevant to how the device is used. These include the worst-case (least rigorous) implementation of the cleaning process, medical devices that represent the worst case (most challenging to reprocess and most contaminated), and at least two quantitative test methods that are as close as possible to the soil in actual use. The cleaning process validation protocols specify predetermined cleaning test endpoints. These protocols are designed to establish that the most inaccessible locations on devices can be adequately cleaned during routine processing. These cleaning methods must be able to be consistently reproduced in a healthcare facility.

Soil inoculation represents worst-case use conditions. Artificial soil is used to inoculate (inject into) the device in all locations likely to contact patient materials, including all locations that are difficult to clean (See Figure 1). If a device has features that can accumulate soil with repeated use, the validation studies will use devices that have undergone some simulated use. They should incorporate multiple full-use cycles and be designed to clean the accumulation of soil over time.

All operative techniques in which the device is expected to be used (e.g., repeated articulations, flexures and/or manipulations to represent worst-case conditions) will be inoculated and tested. If the device is likely to be repeatedly subjected to “pushing” soil into a hard-to-reach area during use, then validation soiling should include repeated soiling to adequately reproduce such a worst-case use situation. If, after clinical use of the device, drying of soil might occur and cleaning might not be performed immediately after use, the validation methods will allow soil to dry for a length of time that simulates the worst-case or longest duration of time. The control devices are prepared and processed in the same manner as the test devices; positive control devices are soiled, and negative control devices are not soiled. The cleaning validation protocols should use the shortest times, lowest temperatures, weakest dilutions, etc., for each step of the cleaning instructions (See Figure 2).

Devices are then subjected to a validated method of extraction for recovery of residual soil.

The extraction method removes the testing soil that was placed on all surfaces. Some device designs include more complex internal structures (e.g., lumens, internal moving parts) that may become soiled during use but are difficult to access during cleaning and extraction. Hence, cleaning methods, including disassembly, should be designed to access these surfaces for cleaning and sterilization. For validation studies, additional disassembly processes may be required to adequately extract residual soil from these difficult-to-access areas. For devices with internal compartments that are not intended to come in contact with clinical soil and fluids, it must be demonstrated that cleaning solutions, rinse water and/or patient materials will not penetrate the internal components of the devices. A description of the validation protocols (to identify and account for all worst-case processing conditions for cleaning) are kept for the FDA submission.

Note: Medical device manufacturers do not validate cleaning solutions. It is
the responsibility of cleaning solution manufacturers to provide information about the water quality, cleaning agent concentration, exposure time and other parameters necessary for effective use of their products.

STERILIZATION
The medical device manufacturer conducts its validation testing in a type of sterilizer that is available to healthcare facilities [e.g., steam, ethylene oxide (EtO), hydrogen peroxide, dry heat, or ozone]. When validating these sterilization methods, the manufacturer packages its devices in an available FDA-cleared packaging system to provide a microbial barrier for sterility maintenance until use.

To qualify sterilization cycle parameters, the device manufacturer must show that the cycle imparts sufficient lethality to produce the desired sterility assurance level (SAL) for the device (typically 10^6). An overkill approach to demonstrating cycle lethality is used when qualifying sterilization processes for reusable devices because the bioburden of reusable devices prior to sterilization processed in healthcare facilities is not known. This approach is based on the concept that the sterilization process will be able to inactivate a resistant microbiological challenge and provide an additional safety factor. An example of cycle overkill is a 6-log reduction in one-half of the cycle exposure time of a microbiological challenge. A full cycle would produce sufficient lethality to effect at least a 12-log reduction.

Steam sterilization is the most widely-used sterilant in healthcare facilities. To validate a medical device for steam sterilization, an overkill method is used. The test uses preparations of Geobacillus stearothermophilus as the biological challenge containing a population of 10^6 spores because they are the most resistant to steam sterilization process.

For devices undergoing ethylene oxide (EtO) sterilization and other low-temperature sterilization, testing is performed to assure the medical device can be sterilized. Additional testing is performed to determine if there are any chemical residuals or byproducts. The aeration phase may have an effect on the device, as might the cleaning process, because washing might help remove small amounts of residuals between sterilization processes.

HIGH-LEVEL DISINFECTION
High-level disinfection (HLD) is the minimum treatment recommended by the Centers for Disease Control and Prevention (CDC) for semi-critical items. The FDA regulates high-level disinfectants and sterilants and these products go through a validation process that is beyond the scope of this lesson; however, the validation process used must confirm that high-level disinfectants show a logarithmic reduction of microorganisms that is time-related. In the case of one specific agent, for example, soaking a device for 20 minutes results in HLD, while extending the time to approximately 10 hours results in sterilization. The process can be performed manually (usually by soaking an item in a basin of solution) or in mechanical equipment such as an automatic endoscope reprocessor (AER). The effectiveness of the process depends
on the chemical agent itself and on the quality control measures established for the procedure, which includes water quality.

The validation process involves the interaction of the disinfecting agent with the materials used in device construction, and the disinfectant’s ability to contact all device surfaces that will become contaminated during normal use. Manufacturers of reusable medical devices intended for HLD must ensure their device can achieve HLD with FDA-cleared disinfection equipment and high-level disinfectants; these methods are specified in their written instructions.

**OBJECTIVE 2: DISCUSS THE IMPORTANCE OF MEDICAL DEVICE COMPATIBILITY TESTING**

After the sterilization process is completed, the manufacturer demonstrates the physical and functional compatibility of the devices with the sterilization process being qualified. The evaluation considers a device’s intended use and the effects of repeated sterilization on the device. Material properties such as physical strength and dimensions, resilience, and permeability (for gas sterilization) are evaluated after multiple sterilization cycles. The device is checked for material effects such as crazing (spiderweb-like cracking of plastics under chemical stress), cracking, embrittlement and phase separation – all of which have potential degradation effects on polymeric materials. Discoloration, staining and other negative aesthetic effects are also determined. During device inspection, all moveable or hinged parts are opened and closed to check for visible soil and ease of movement.

Powered instrumentation is turned on and off to verify that power is supplied when needed.

Device accessories are attached and detached to ensure they fit properly. Any locking mechanisms, clamps and cutting tools are actuated to ensure proper alignment and ease of use.

A sterilization residue check is also performed. Residues are often difficult to see, so the test is performed by a residue reagent test and/or tactile feedback that can reveal sticky or oily surfaces and stiff hinges. Devices with markings, such as the depth or size, are checked to ensure that the markings can be easily seen and are not dull or rubbed off.

The manufacturer also determines if processing in accordance with the provided instructions will harm the device and, therefore, limit its useful life. If degradation is determined, the manufacturer will provide an indication of when the medical device will no longer be able to safely fulfill its intended use.

**OBJECTIVE 3: INTRODUCE PRODUCT FAMILIES AND MASTER PRODUCTS AND THEIR ROLE IN THE VALIDATION PROCESS**

Not every medical device requires validation testing. Testing may not be required if the medical device manufacturer can demonstrate that the device is similar to one that has already been validated. To qualify for this exemption, an equivalency evaluation is performed to demonstrate that the device’s materials and design are the same or present less of a challenge.

There are two other types of exceptions: product family and master products. In these cases, not all medical devices are tested; only representations of them are tested. The devices or instrument sets are broken into product families.

Master products demonstrate the worst-case features or attributes as shown through the testing and assessment process within the products in the family. Manufacturers can select a “master product” that constitutes a worst-case challenge, and it can be used to represent the product family. Product-related variables that potentially affect the cleanability and sterilizability of the products should be considered. Factors in the selection of master products include the following:

- Design configuration;
- Number of components;
- Construction materials;
- Size and density;
- Surface area and porosity;
- Need for disassembly;
- Surface finish or texture;
- Presence of cannulations or lumens;
- Presence of mated surfaces;
- Ability to sterilize in a routine cycle;
- Presence of validated reprocessing instructions; and
- Suitability of test soil.

Not every medical device requires validation testing. Testing may not be required if the medical device manufacturer can demonstrate that the device is similar to one that has already been validated. To qualify for this exemption, an equivalency evaluation is performed to demonstrate that the device’s materials and design are the same or present less of a challenge.
OBJECTIVE 4: DESCRIBE HOW VERIFICATION TESTING IS PERFORMED IN HEALTHCARE FACILITIES

After the manufacturer has performed an in-depth validation testing on its device, Central Service/Sterile Processing (CS/SP) personnel must ensure that the cleaning and sterilization methods recommended by the manufacturer can be duplicated in their environment and that the manufacturer’s instructions can be followed correctly in their facility. This is known as the verification process, and it involves documented procedures performed in a healthcare facility to obtain, record and interpret the results required to establish that pre-determined specifications have been met.

CS/SP professionals must remember that if a device is not clean, it cannot be sterile. Cleaning is the most important part of the sterilization process and it is the first step in reprocessing. When a medical device is introduced into a healthcare facility, cleaning verification can be performed to ensure the facility can disinfect or sterilize the medical device. The development of a cleaning verification involves establishing, clarifying and documenting a standard cleaning process based on published and validated recommended practices or guidelines and the IFU.

The cleaning verification process involves showing that all critical cleaning steps are being properly and consistently followed, and this is done through comprehensive training and observation. All visible organic soil and contamination must be removed and CS/SP technicians must demonstrate the correct cleaning process, without variation. Process controls must be in place to ensure complete and consistent cleaning.

The healthcare facility must have policies and procedures in place that are consistent with standards and recommended practices. The cleaning protocol must be based on the recommendations of the device and detergent manufacturers and, if used, the manufacturer of the automatic processing equipment.

To confirm the device cleaning process was effective, an inspection is performed after cleaning. This process can be performed by visual inspection with the use of a lighted magnifying glass, borescope or camera (See Figure 3). Cleaning inspection processes have evolved to be more precise, so the efficacy of the cleaning process can be quantified. Commercial test kits are available to provide quantitative methods of measuring organic residues such as adenosine triphosphate (ATP) protein and hemoglobin, which are not detectable using visual inspection (See Figure 4).

Commercial test kits are also available to check lumens and other non-accessible surfaces. Cleaning verification tests differ and should be used according to their IFU.

A functionality check should be performed to ensure the device operates as it was intended. This may be defined by the device manufacturer and is a part of the basic inspection, preparation and packaging procedures used. The device manufacturer may provide tests to check for debris and residue in areas that cannot be visually inspected.

Product testing is performed to
verify that the device or devices can be sterilized in a healthcare facility; it is not a substitute for the more extensive validation. Healthcare facilities do not have the scientific equipment or expertise to perform validation testing. For example, unlike the one-half sterilization cycle used by manufacturers for validation, only a full sterilization cycle can be used in a healthcare facility. The sterilization cycle is set by the sterilizer manufacturer. Other than extending time, many of the cycle parameters can only be changed by the sterilizer manufacturer, and the sterilization cycle is dictated by the device manufacturer’s IFU.

To perform product testing in healthcare sterilizers, chemical indicators (CIs) and biological indicators (BIs) validated for that method of sterilization are used to verify the sterility provided the required lethality to yield a sterile product. These indicators are placed strategically throughout the test pack, in areas that pose the greatest sterilization challenge (those areas most resistant to sterilant penetration).

Not all medical devices are tested; only representations of them are. The device or instrument sets are broken out into product families: a concept similar to that used by manufacturers. Product families enable the healthcare facility to ensure a high level of sterility assurance without testing all products being sterilized. This type of testing is performed for new devices, periodically for routine devices, and when major changes are made in packaging, wraps or load configuration (e.g., dimensional changes, weight changes or changes in the type or material of packaging or wrapper). If a change is made in a product family’s composition, designated master product or written sterilization instructions, product testing should be performed.

Instruments and loaned sets are items that are most often tested; however, because of the sizable number of these sets, product families are used. To determine a product family, CS/SP professionals should check for similarities in design configuration; number of components; construction materials; size and/or surface area; need for disassembly; surface finish or texture; the presence of cannulations, lumens or mated surfaces; and the written reprocessing instructions provided by the manufacturer.

When conducting verification testing, each test pack undergoing testing should have BIs and CIs placed in the most difficult area to sterilize (the location should be documented on the indicators). The number of the indicators used will be based on the size and configuration of the test pack. Upon completion of the sterilization cycle, the locations should be recorded, along with the test results. The use of a digital camera provides additional documentation. What follows are examples of BI and CI placement:

- For single layer instrument sets – BIs and CIs are placed together at the end of the tray and among the instruments placed on stringers.
- For sterilization containers – Typically, the most difficult area to sterilize is underneath the lid and away from the filters, such as the upper and lower corners.
- For containment devices (loaned trays) - BIs and CIs are placed together in each corner, center and any other area recommended by the manufacturer of the containment device.
- For multi-layered instrument sets – BIs and CIs are placed together in areas determined by the manufacturer to create the greatest sterilization challenge.
- For miscellaneous items – BIs and CIs for items such as reusable syringe sets and bulk packages of sponges or dressings are placed in the area of the pack least accessible to sterilant penetration.

Product test samples are packaged as normal, labeled “Test Pack” and processed in a routine load with other items. Test packs are placed throughout the sterilizer load in the areas that are most difficult to sterilize or in locations that would be most resistant to steam sterilization, such as over the drain.

Before and during product testing, all sterilizer quality monitors should be checked. Sterilization process monitoring devices include physical monitors, CIs and BIs; each of these devices plays a distinct and specific role in sterilization process monitoring, and each must be checked to verify that the parameters of the sterilization cycle have been met. As with all sterilization loads, the physical parameters should be reviewed to ensure the correct cycle was selected and that the parameters were met.

As soon as the sterilization process is completed, the test pack should be opened, the contents should be checked for moisture, CIs should be reviewed to meet their endpoint, and the BIs should be incubated. The test packs should then be inspected for moisture, and the contents of the test sample should be either reprocessed or discarded.

Unacceptable test results (e.g., positive BIs, CIs that have not reached their endpoint, and/or evidence of moisture) must be investigated. Corrective actions such as load modification, set reconfiguration or sterilizer service are required. Documentation is also important for product testing; this can include the test protocol, placement of BIs and CIs (a digital photograph is especially effective), test results and any corrective actions that were taken.

**RIGID CONTAINER VERIFICATION**

Rigid container verification verifies that the rigid sterilization container system will perform as intended by the manufacturer. Outcomes of testing are
dependent upon multiple variables unique to the healthcare facility, including the load composition, sterilizer and steam supply. Verification testing of sterilization containers is performed to ensure that the necessary conditions for sterilization can be achieved and that the specific configuration of the container contents is acceptable for the sterilization process and for the requirements at the point of use.

Verification of sterilization containers is performed similarly to instrument sets. Before conducting a verification study, the container manufacturer’s IFU must be reviewed for device compatibility and restrictions. Examples include lumen size or textile restrictions. The test for rigid sterilization container system should contain instruments and if the system requires filters, the filters must be in place.

Sterilization containers differ from flat-wrapped instrument sets because of how steam evacuates from the container (through either a filter opening or valve); this may result in a need to extend the dry time. Other factors that can influence the dry time are the design and composition of the container system and the type, number and configuration of instruments.

Each rigid sterilization container system should be tested using BIs and CIs validated for the cycle being used. The rigid sterilization container system manufacturer should be consulted regarding the test procedures, as they may provide specific locations for BI and CI testing locations.

After the sterilization cycle is completed, the user should:

- Retrieve CIs to ensure they met their endpoint;
- Incubate BIs according to the BI manufacturer’s written IFU; and
- Evaluate the container and load for retained moisture.

*Note: The test container and instruments should be reprocessed before use in patient care. Positive BIs can indicate a sterilization process failure and should be investigated.*

It is important to check for moisture at the end of verification testing to ensure the containers are dry. Rigid sterilization container systems occasionally require extend drying times (typically used for wrapped items). Retained moisture can damage instrumentation if contact with moisture is prolonged and wet packs are contaminated. Other factors affect the dry times of the sterilizer, such as the distance from the steam source, effectiveness of moisture removal from the incoming steam and potential differences between sterilizers being used.

**CONCLUSION**

This lesson has explained the differences between validation performed by manufacturers using scientific measurable analysis and verification performed in healthcare facilities using the quality monitors available to healthcare facilities. Healthcare facilities verify that the medical devices validated by manufacturers can be sterilized in their facility.

All manufacturers’ IFU must be carefully followed by healthcare facilities. Any significant changes in the process may require verification testing.

**RESOURCES**

- AAMI TIR12:2010 *Designing, testing, and labeling reusable medical devices for reprocessing in health care facilities.*

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