Sterilization Modality Selection: Role of Sterility Assurance Subject Matter Expert

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Abstract

Selection of a sterilization modality for a medical device is a critical decision that requires sterility assurance subject matter experts (SME)s to work collaboratively with various company functions. The sterility assurance SME is responsible and accountable for the sterilization modality decision for a product. The modality selection process starts with the sterility assurance SME partnering with research and development to ensure that the sterilization modality allows the device to deliver its intended function in patient care. After the sterilization modality is selected, the sterility assurance SME needs to work with other partners, including quality, supply chain/logistics, operations, and regulatory, to ensure that the selected sterilization modality is appropriately integrated into the end-to-end process. Collaborative partnerships between sterility assurance experts and key partners regarding sterilization modality selection reduce the potential for negative impacts within the end-to-end sterility assurance process, including impacts on product functionality, increased regulatory approval timelines, and inefficiencies and risks throughout the supply chain. This article describes aspects of a comprehensive approach to sterilization modality selection, including critical information necessary to address each of the key considerations.

Selection of a sterilization modality for a medical device is a critical decision that affects the entire manufacturing supply chain. Manufacturing firms with traditional supply chains may exhibit individual organizational silos that often result in emphasis on only one aspect of the supply chain, potentially resulting in suboptimal selection of the sterilization modality. During the previous decade, many manufacturing firms have changed from traditional supply chains to take into account the entire end-to-end view of the supply chain. This end-to-end view matches well with the thought process needed when selecting the sterilization modality. An end-to-end view of the complete supply chain, for example, begins with the product design to meet customer needs, supplier selection and management, then scheduling, production, distribution and after-sale customer service. The sterility assurance program supports all steps in the end-to-end supply chain.

The execution and delivery of the sterilization process is only one portion of the sterility assurance program. For medical devices, the delivery of the sterilization process typically occurs during the production step, with sterilization occurring in either the final finished package stage or during final assembly. The delivery of the sterilization process in the manufacturing step is either conducted within the manufacturing firm or through the use of a contract sterilization firm. When using a contract sterilization firm, the delivery of the sterilization process typically occurs after final finished packaging. In this case, the finished product is shipped from the production location to the contractor for sterilization and, following sterilization, shipped to the distribution center.

The sterilization modality selection typically is made during the product design and development stages to ensure that the product can be designed and manufactured to meet the "sterile" label claims. The sterility assurance subject matter expert (SME) is responsible for the sterilization modality selection and sterilization process definition (i.e., detailed specification for the sterilization process).

With traditional supply chains, the modality selection may have been made because companies were only familiar with a single modality, such as the use of an available

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internal sterilization process. During the 1990s, the use of contract sterilization firms increased to augment or replace the use of internal sterilization. Most traditional sterilization processes such as moist and dry heat sterilization processes continue to be predominantly performed internally, and radiation (gamma, electron beam, and X-ray) and ethylene oxide (EO) are, depending on the volume of product, performed either internally or by an external contractor.

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In this transition from internal to external sterilization, increasing emphasis has been placed on ensuring that the roles and responsibilities of the manufacturer and contractor are clearly defined. In the transition from the use of internal sterilization to contract sterilization, some traditional supply chain manufacturers have handed off decisions on sterilization modality selection to external suppliers (e.g., sterilization providers, labs, component/device suppliers, consultants). Unless these external suppliers are involved in the entire sterility assurance program, making appropriate decisions on modality selection is not possible. Therefore, sterility assurance SMEs involved with the entire program need to guide the strategy and selection of sterilization modality and process definition. This decision should not be left in the hands of an external supplier that is not involved with the entire manufacturing process.

Sterility assurance SMEs are proficient in delivering the required sterility assurance level (SAL) and/or microbial control to the product as required; they are expertly familiar with all potential sterilization modalities, impacts to product functionality, and sterilization process definition and validation. These individuals should not be confused with individuals responsible for sterilization operations who are responsible for delivering the validated sterilization process to the product. This division of responsibility exists whether the sterility assurance SME is an internal employee or external consultant to the device manufacturer.

Product Considerations

In a previous publication,[1] a high-level process for selecting a sterilization modality was presented. The first step in this process is to determine whether a device, based on its intended use and mode of patient contact, requires sterilization or if microbial control alone is sufficient. The ability of the product to deliver its intended care to the patient is the primary basis for all decisions regarding sterilization modality selection. Research and development (R&D) is responsible for the detailed aspects/specifications that enable a device to deliver its intended care, and the sterility assurance SME must work with R&D to select a sterilization modality that delivers a sterile, safe product that meets all functional specifications required to deliver the intended care to the patient.

The selection of a sterilization modality should be considered in the design of the product. The sterility assurance SME(s) should actively engage within the design input phase to ensure that R&D teams understand the product functionality impact of the sterilization modalities. Partnering with R&D to understand functional requirements is necessary in the selection of compatible materials that are critical to device quality. If the sterilization modality has been finalized prior to understanding its impact on device functionality, redesigning the product or selecting a different sterilization modality to enable compatibility can be very costly.

Assessing compatibility with sterilization does not have to be complicated; a simple decision tree can enable selection of a relatively simple sterilization modality, such as moist or dry heat.[1] Moist or dry heat processes can be completed at the manufacturing facility with minimal facilities footprint and minimal environmental health and safety concerns with personnel exposure to sterilant residuals. Product design teams may overlook these high-heat modalities because low-temperature sterilization modalities commonly are understood as more advantageous for materials. Moist or dry heat sterilization are great options for

product materials that are both moisture and heat tolerant. Not having to manage the additional element of a chemical sterilant that may interact with materials is another benefit. Chemical sterilants increase the possibility of an adverse biological response, thereby adding potential risk to the device's biocompatibility. With novel modalities, more research is required, as published information is limited and manufacturers have minimal information to leverage from predicate devices. The sterility assurance SME should work with R&D to ensure a thorough understanding of potential sterilization modalities, including high-temperature and novel modalities.

Many classes of polymers used for medical device components have been well characterized for sterilization modalities such as radiation, EO, moist heat, dry heat, hydrogen peroxide, nitrogen dioxide, and peracetic acid (liquid and vapor). A sterility assurance SME can provide the R&D team with the known parameters for a given modality and their potential effects on materials. For example, the SME can use the technical information report AAMI TIR17:2017[2] to identify a material for a component. The selection of polytetrafluoroethylene (PTFE) for this component potentially would be limiting because of the well-known damaging effects of radiation. This does not necessarily mean radiation cannot be selected, particularly if the component's mechanical needs do not feed into the functional requirements of the device. The use of PTFE coating may be used for lubricity. In this case, degradation from radiation could lead to higher particulates, which may or may not be a concern depending on whether the device is blood contacting. If particulates are a concern, a low maximum acceptable dose may be qualified. This lower maximum dose may require a lower minimum sterilization dose, optimization of the packaging configuration to improve dose uniformity, or the exploration of more robust radiation-resistant polymers such as perchlorotrifluoroethylene or polyvinyl fluoride.

Product functionality often is a focus when considering the impact of sterilization modalities, but packaging functionality also must be considered. One of the top reasons for sterilization-related product recalls is nonintact packaging. For gas sterilization modalities, rates of pressure change can stress packaging seals and cause pouches to burst if the permeability of the packaging is not sufficient to allow for pressure equilibration between the inside and outside of the packaging. Sterilization modality selection particularly is important when considering packaging for products that require strict storage conditions to deliver their intended care. A gas or moist heat sterilization process for such products may require complex secondary packaging process. A combination product with a drug that is sensitive to oxidation or temperature might be sterilized with EO in a gas-permeable high-density polyethylene package. The combination product then would need to undergo an additional step of poststerile packaging inside a nonpermeable foil pouch prior to distribution to reduce poststerilization oxidation. Alternatively, a terminal radiation sterilization process might be feasible with the combination product inside the final packaging, which can reduce the time between manufacturing and delivery to the customer. The sterility assurance SME should work with R&D to ensure that the packaging is designed for the appropriate sterilization modality.

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Considerations of product functionality following sterilization often are focused on the potential negative aspects. However, situations exist where the sterilization process can improve aspects of product functionality, such as reducing residual manufacturing solvents, curing of hydrophilic coatings and/or adhesives, and relaxing tensile forces present in delicate metal components. In these cases, changes to sterilization process parameters (e.g., decreasing temperature or time) may affect product functionality negatively. Interaction between all elements of the sterilization process and all aspects of the product that

affect its functional specifications, whether these interactions harm or benefit the product, must be understood in order to avoid unintended negative impacts to functionality. The sterility assurance SME should be familiar with detailed elements of both the sterilization modality process parameters and product functionality in order to guide product and package design and validation of its functionality after exposure to the selected sterilization modality and process definition.

Process Selection/Logistics

After a sterilization modality is selected, the definition of an appropriate supply chain process is a critical aspect of enabling a sterile product to deliver its intended function in patient care. In this context, "supply chain process" encompasses raw materials, component manufacturing, assembly, packaging, transportation, sterilization, and distribution. Key logistical considerations are affected by decisions around sterilization modality selection. These considerations include where the sterilization process is delivered (e.g., in-house, outsourced), whether the sterilization equipment can process devices of a certain size or configuration, whether there is sufficient availability of equipment and sterilant, and whether major safety issues exist with the selected sterilization modality. This section presents important examples on how the sterility assurance SME needs to partner with various functions to ensure critical information is understood and used to ensure that the process(es) used to deliver the selected sterilization modality is effectively incorporated into the end-to-end supply chain.

Volume/Capacity

Physical product volume (i.e., physical dimensions of packaged product to be sterilized), as well as manufacturing volume (i.e., amount of product requiring sterilization per unit time), are key considerations for the selected sterilization modality. The frequency and volume of manufactured product, whether pallets or individual boxes are produced regularly, have implications for the selected sterilization modality and location. The sterility assurance SME should partner with R&D and packaging to ensure an understanding of physical volume constraints of the sterilization equipment, as well as with operations to ensure that the facility sterilizing the product can accommodate the device packaging.

The ability to accommodate production volume as volume increases from development, to clinical use, and to full commercial scale is another logistical consideration related to sterilization modality and location selection. If manufacturing volumes are initially small but will scale up quickly, the throughput of the sterilization modality and location should be able to scale up to meet increasing demand. Some sterilization modalities may efficiently process a wide range of batch sizes, whereas others are more suited and efficient with multiple pallet-size batches. Certain modalities may only process small volumes and may be unable to scale up capacity to meet demands of production ramp-up. The sterility assurance SME should work with logistics and operations to ensure that the available capacity is sufficient to sterilize product volumes associated with each phase of production ramp-up.

Some sterilization equipment cannot accommodate large packaging. The sterilization equipment (i.e., conveyer, chamber) must be able to fit the device packaging such that the required sterilization is delivered. Some devices may need to be packaged in a particular configuration to meet their functional specifications. For example, a long imaging catheter that is required to maintain shape, and would be compromised by curving or coiling, is required to be packaged in a long configuration (e.g., >80 in). This size package presents problems for many sterilization modalities and sterilization equipment. In this situation, the selected sterilization modality may be available but with fewer sterilization location/equipment options for processing compared with other devices with smaller packaging configuration. The sterility assurance SME should work with R&D to understand the requirements for the product and packaging configuration and identify sterilization locations and/or equipment that can accommodate the packaged device, as well as with logistics to

Sterility assurance subject matter experts play a vital role in ensuring that a selected sterilization modality and validation approach is appropriately integrated into the end-to-end process.

secure available sterilization capacity that can accommodate the packaged device.

Medical devices may have varying needs as production volume ramps up from feasibility to full commercialization. Certain products may go from sending very few items at a time to sending many pallets of product at a time, while others may experience periodic or seasonal variations in needed sterilization capacity. Some small-volume products may need several weeks to produce enough quantity (e.g., multiple pallets) to fill large sterilization equipment, which might result in delays in patient care. The sterility assurance SME should work with logistics/supply chain to ensure that all intricacies of needed sterilization capacity are fully understood and that available capacity meets demand from initial product development to full commercialization.

Sterilization Processing Time

Sterilization modality affects the overall processing time for a product as the product transits through the manufacturing process. The proximity of the manufacturing site(s), sterilization location, and distribution location affect total manufacturing time, which might be shortened if sterilization processing occurs at the manufacturing location. Product transit time from beginning of sterilization processing to receipt at distribution varies depending on sterilization modality. For example, EO sterilization processing times typically are five to 10 days, while radiation sterilization processing times are typically one to four days from the time the product is delivered to the sterilization equipment location. The sterility assurance SME should partner with manufacturing and logistics to ensure that times associated with the selected sterilization modality are understood.

Availability of Equipment and Sterilant

Supply chain planning for sterilized product should consider the effect of limits or delays in available sterilization capacity on sterile product availability. The availability of the selected sterilization modality is an important consideration for supply chain and business continuity. The medical device

industry is expected to grow approximately 4% to 5.4% per year,[3–5] creating a need for expansion of global sterilization capacity to meet this growing demand. The sterility assurance SME should partner with logistics and supply chain to ensure that the selected modality has sufficient availability for both primary and back-up sterilization processing capacity and ensure understanding future sterilization processing capacity needs. Validating back-up sterilization processing capacity is important for maintaining business continuity, as it can mitigate potential delays and provide an insurance policy in the event that availability of a sterilization process decreases (e.g., sterilization processing capacity at vendor no longer available). Lack of sterilization availability for both primary and back-up capacity for current and future production capacity results in potential delay in release of sterile product and increased risk of supply chain interruption. Failure to understand the balance between needed and available capacity results in disrupted business continuity and, ultimately, delays in patient care.

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In addition, availability of some sterilization modalities is affected by single-source sterilant suppliers, namely EO, gamma, and certain novel modalities. Sterility assurance SMEs should work with internal logistics and external sterilization providers to optimize sterilant use and ensure a consistent supply of available sterilant.

Location

The relative location of the device manufacturing site, sterilization equipment location, distribution center, and site of use should be considered when implementing the selected sterilization modality. If a product needs to be manufactured, sterilized, and distributed to the patient in a relatively short time, the proximity of the manufacturer, sterilization equipment location, distribution center, and patient must be considered. Examples of where this is a concern include products that support microbial growth, products with a relatively short shelf-life, products requiring secondary packaging after sterilization and before distribution, and custom-made products for which manufacturing, including the sterilization process, must be completed quickly in order to deliver customized patient care. For products with these types of requirements, a sterilization process performed by a contract manufacturer far away from the rest of the production chain can add substantial delays to delivering the product to the patient. The sterility assurance SME should work with R&D to understand all device requirements affected by sterilization and partner with logistics to select a modality that meets these requirements. These types of requirements may lead to a decision to bring sterilization to the manufacturing location to minimize time to product release. Understanding the relationship among the product requirements, sterilization equipment location, applicable poststerilization manufacturing locations, and patient location is critical to delivering the intended care of a product.

Safety

The safety of the selected modality also is a key consideration. The occupational safety of the individuals executing the sterilization process, as well as safety of the patient, must be considered for the selected sterilization modality. Given the required degree of microbial inactivation, all sterilants used for the treatment of medical devices, whether used in traditional or novel sterilization modalities, present potential hazards. The sterility assurance SME should work with the appropriate environmental health professionals to ensure that appropriate safety measures are in place. Regarding patient safety, the sterility assurance SME must work closely with R&D during the selection of product materials, as sterilization processes can interact with materials by leaving sterilant residuals or drawing leachable substances out of materials. The sterility assurance SME should guide in the selection of materials and/or appropriate processing conditions so that the safety of the process is balanced with the safety of the product.

The sterilization process must be safe to operate in order to deliver sterile product in a timely fashion. If a gaseous sterilant modality is used, the sterility assurance SME should work with R&D and packaging to create product load configurations that will retain minimal amounts of sterilant after processing. When sterilization takes place at the manufacturing facility, the sterility assurance SME should also work with environmental health and safety to ensure that sterilization facilities protect workers against unintentional exposure to the sterilant. For gaseous sterilization processes, appropriate gas sensors must be used to ensure that sterilant gas does not escape the vacuum chambers or is emitted from sterilized product in transit or storage. For radiation sterilization processes, appropriate sensors to ensure radiation is at safe levels around the irradiator must be used. Failure to consider sterilant emissions can result in environmental alarms in sterilization processing facilities, which can interrupt and delay timely completion of sterilization processing, thereby delaying release of sterile product.

For gaseous sterilization modalities, residual sterilant and sterilant by-products must be reduced on sterilized devices such that they do not cause harm to patients. The sterility assurance SME should work with R&D to understand whether product and/or packaging materials are susceptible to sterilant residual retention. If materials are susceptible to residual retention, the sterility assurance SME should adapt the sterilization processing parameters to efficiently remove sterilant residuals from the device. If, for example, gaseous sterilization processing parameters are designed to minimize exposure to the sterilant, the amount of postprocessing aeration required to remove sterilant residuals may be reduced by several hours. If processing parameters are not designed to minimize exposure to the sterilant, the amount of postprocessing aeration could be substantial (i.e., days to weeks). This situation leads to delays in product release and ultimately delays patient care.

Some device materials may release harmful leachable substances after exposure to heat and humidity conditions associated with sterilization. Constituents (e.g., plasticizers, fillers, additives, antioxidants) often are added to polymer components to reach a required durometer, achieve stability to ultraviolet light, or gain other desired characteristics. These materials can be bound or encapsulated within a material and could be bioavailable in toxic amounts during clinical use if conditions during sterilization release these agents. The sterility assurance SME should have knowledge of which materials may be particularly susceptible to leaching harmful substances, work with R&D to understand if these materials are critical to delivering the device's intended function in patient care, and use this information to select a sterilization modality and process definition that minimizes the risk of creating nonbiocompatible substances.

Speed to Market

Sterilization modality selection affects the speed at which a device comes to market. Whereas the previous section discussed impacts of sterilization modality on manufacturing time, this section focuses on the time associated with activities involved in development and regulatory approval prior to product distribution. Timely validation of product functionality requires detailed understanding of elements that a product experiences as a result of sterilization processing. Also, regulatory agency familiarity with the sterilization modality can have a considerable impact on approval timelines. Traditional sterilization modalities with a long history of validation and use may result in faster regulatory approvals compared with nontraditional[6] sterilization modalities, for which the manufacturer may need to provide new precedent for validation. The sterility assurance SME must partner with R&D, quality, and regulatory to ensure timely approval.

Understanding the impact of sterilization processing parameters on product and/or packaging functionality is critical in avoiding failures during design validation. If a novel sterilization modality is selected, the conditions experienced by the product during the most challenging sterilization conditions may not be as well understood by R&D compared with a sterilization modality with

a longer history of use. The sterility assurance SME should work closely with R&D so that impacts to device functionality after exposure to sterilization conditions, including temperature, humidity, pressure changes, and chemical interactions, are well understood. Pursuing product functionality testing in the event that sterilization processing parameters are not well understood can result in failures of functionality validation testing, which result in time-consuming and costly redesign and ultimately approval delays. Detailed knowledge of sterilization processing parameters also is valuable when moving product from one sterilization process definition to another (e.g., moving radiation dose limits of 25–40 kGy to limits of 15–50 kGy) or from one modality to another (e.g., EO to moist/dry heat, gamma to electron beam or X-ray), as these data may be leveraged in place of repeating product functionality testing, potentially saving several months of development time.

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The sterility assurance SME may be able to assist in reducing the amount of work required by understanding how new products fit into established product families (i.e., devices with similar materials, density, packaging, or difficulty of sterilization determined to be equivalent for evaluation and processing purposes[7]) or processing categories (i.e., collection of products or product families that can be processed together[7]) for various sterilization modalities. Product families and processing categories allow for substantially reduced amounts of testing when qualifying a new product into an existing sterilization modality using established processing parameters. Lack of established product families could lead to the need to perform costly and time-consuming validation testing, which ultimately will delay a device from reaching market. Validation without an established product family and/or processing category may take roughly six to 18 months, whereas validation time with an established product family/processing category may only take several weeks to several months (e.g., one to three months).

The sterility assurance SME also should respond appropriately to pressure when faced with aggressive project timelines involving the iterative product development process for the purpose of bringing product to market more quickly. Consider the explosion of the Space Shuttle Challenger in 1986: Many are aware of the determined root cause of this accident being failure of seals in the solid rocket boosters in cold weather. It may not be as well known that this failure was a result of extreme pressure to meet aggressive timelines in the Space Shuttle program. If the engineers had delayed launch and spent additional time on correcting known issues with the booster seals, this tragic disaster could have been avoided. The appropriate SMEs must ensure that all aspects of product functionality are thoroughly assessed, even if this may extend the project time, in order to avoid failures.

Examples of these situations involving sterility assurance include assessment of design changes made after sterilization processing parameter qualifications are completed or only validating functionality after one-time exposure to sterilization processing parameters compared with validating multiple processes or maximum exposure. The sterility assurance SME should work with R&D to ensure an understanding of the risks of only performing the minimum required assessments during the development process. However, if shortening the lead time to get products to market, further assessments should be followed with additional testing to provide sustainable sterilization processing capability. Although spending a few weeks to conduct additional testing may increase the timeline of bringing a product to market, this decision may impede long-term capability if multiple process parameter exposures or maximum conditions are not validated.

If a novel sterilization modality is required for the device to deliver its intended care, the regulatory timeline may be longer than if a traditional sterilization modality is selected. The sterility assurance SME should work with regulatory and R&D to develop a

workable validation strategy for the selected modality, taking into account all applicable requirements and standards. Issues that may arise with a novel sterilization modality include lack of established modality-specific standards for validation and/or lack of established biological or chemical indicator. If a novel sterilization modality is selected, speed to market will be improved if the sterility assurance SME promotes active education, collaboration, and research/evaluation among both internal and external (e.g., regulatory agencies) functions regarding validation of a novel sterilization modality. Speed to market with a novel sterilization modality may be shorter if the microbial inactivation rates can be established as similar to traditional modalities (see AAMI/ISO 14937:2009/(R)2013[8]). If these inactivation rates are different, regulatory approval time may be considerably longer (e.g., years). Failure to work with the sterility assurance SME to gain this critical understanding can result in longer approval times, which ultimately will delay product availability for patient care.

Economic Impact/ Environmental Sustainability

Environmental sustainability is a primary initiative across companies in many industries around the world. To improve overall environmental sustainability, companies are taking key actions, such as maximizing energy efficiency, innovating in manufacturing and engineering, and opting for greener alternatives with packaging and materials. Environmental sustainability in sterilization is not a novel concept, and it involves far more than the reduction of the amount of sterilant used in sterilization processing. Pursuing environmentally sustainable sterilization processes improves sustainability across the entire sterilization supply chain. Environmental sustainability of sterilization processes may involve changes to sterilization process parameters and product and/or packaging materials.

Companies that sterilize with EO are working to optimize cycles to reduce the amount of EO used. Sterility assurance SMEs can help design processing parameters that are not only compatible with the product but also promote validation approaches that correlate with the microbiological quality of the product. When validated using overkill methods, sterilization processes often provide a greater SAL than required, with no additional benefit to the patient from this additional degree of lethality. The sterility assurance SME should partner with the sterilization processing function to provide EO cycles that have optimized gas concentrations and exposure times, which may be accomplished through validation methods closely linked to the bioburden of the product (e.g., bioburden or biological indicator/bioburden based[9]). Typically, a switch to a validation method other than overkill requires more testing up front (time and expense); however, the long-term benefits for the shorter/lower sterilization processes include a short time frame for return on investment when comparing the overall benefits with the product and process (cost of sterilization and reduction in residues).

When validated using overkill methods, sterilization processes often provide a greater SAL than required, with no additional benefit to the patient from this additional degree of lethality.

Radiation sterilization also may be optimized by validating a sterilization dose that correlates closely to the microbiological quality of the product. Many radiation-sterilized products are validated with a traditionally used minimum sterilization dose (e.g., 25 kGy) that is not directly linked to the level and type of natural product bioburden. The use of product families may increase the minimum sterilization dose if the included products have a wide range of microbiological quality.

Lowering sterilization doses can lead to increased throughput by maximizing isotope utilization for gamma radiation and less energy consumption for electron beam and X-ray irradiators. In addition to the increase in throughput, a lower sterilization dose can open a window of opportunity for resterilization capability. A product may not be qualified for two-times sterilization in radiation if its validated dose range is too narrow. Sterilizing in a loading configuration that enables a

narrower dose distribution ratio may allow the option of resterilization. In addition, testing product and package functionality to failure, rather than just to anticipated maximum doses, may open the ability to sterilize two times or with other sterilization modalities. The sterility assurance SME should partner with supply chain and R&D/packaging to define and balance this need.

Packaging design and materials also can be optimized to aid sustainability efforts. Fewer packaging materials combined with use of materials that do not retain sterilant residuals can lead to improved sterilant penetration to achieve lethality and reduce sterilization and postprocessing time. Loading configurations for radiation sterilization processes can be optimized by adjusting treatment parameters to be more efficient. All of these changes can lead to shorter cycle times and increased throughput, which contributes to improved energy efficiency.

The sterility assurance SME has the in-depth knowledge required to guide various functions through each related decision process so that the associated required testing is well thought out and understood.

Environmental sustainability also may be improved by sterilization processing at the manufacturing site. On-site sterilization (e.g., in-house) has the advantage of reducing shipment costs and decreasing carbon emissions in cases where sterilization processing takes place far from the manufacturing site and distribution center. In the interest of improving sustainability, novel (e.g., nitrogen dioxide, vaporized peracetic acid, hydrogen peroxide) or traditional (e.g., moist or dry heat) sterilization modalities may be viable alternatives for some products, as these modalities are more readily brought in-house than other larger-scale traditional sterilization modalities (e.g., radiation or EO). These alternative modalities do not have some of the safety concerns of flammability or the requirement of a larger facility footprint required for EO or gamma sterilization. In addition, because of the composition of the sterilant, these modalities do not require extensive equipment to abate exhausted sterilant. These alternative modalities can support improved environmental sustainability, as they are incompatible with cellulosic materials and thus require products to be sterilized in their primary packaging pouches or trays. With this situation, sterilant use is reduced as less sterilant is absorbed by packaging and other paper materials.

Conclusion

Several functions of the end-to-end supply chain process are affected by the sterilization modality selected for a product, including R&D, quality, regulatory, logistics/supply chain, and operations. In this article, the criticality of the sterility assurance SME was described.

Sterility assurance SMEs must partner with R&D during the initial stages of product development to select a sterilization modality based on the requirements of product functionality and to ensure that the product's intended SAL is achieved. This article reviewed examples of how this interaction is effective, the type of critical information required by the sterility assurance SME in guiding this decision, and how the sterility assurance SME partners with other functions to ensure successful assessment, planning, and implementation of the selected sterilization modality. All of these aspects ultimately are geared toward the delivery of safe and effective patient care.

Selection of an appropriate sterilization modality is a critical decision that has implications throughout the entire end-to-end supply chain and ultimately to delivering safe and effective patient care. The sterility assurance SME has detailed knowledge of these implications and therefore should be involved with the modality selection and throughout the entire process. Each decision around sterilization modality selection has requirements and a timeline for completion. The sterility assurance SME has the in-depth knowledge required to guide various functions through each related decision process so that the associated required testing is well thought out and understood.

The sterility assurance SME should be considered responsible and accountable for sterilization modality selection, and he/she

should collaborate with other functions involved in the end-to-end process. The SME serves as a connection among the various functions involved, ensuring that all implications of a sterilization modality are considered. This partnership promotes solid decision making around sterilization modality selection and helps to avoid costly and time-consuming delays and repetition of testing. If companies have not promoted these relationships, now is the time to put this structure into practice, as this positioning of the sterility assurance SME ultimately is a critical enabler of timely and effective patient care.

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