Corporate Sterilization Programs: 
Facing Change in the Worldwide Market

Navigating thru the upcoming Regulatory Changes impacting EO Sterilization

During the past ten years manufacturers have continued to employ three standard sterilization processes for the majority of medical device processing worldwide: Gamma & Electron Beam Radiation and Ethylene Oxide (EO) Gas Diffusion sterilization. Within this group Gamma and Ethylene Oxide together account in some estimates for as much as 90% to 97% of all medical devices sterilized by industrial scale manufacturers worldwide. Specifically, ethylene oxide continues to flourish as a robust and flexible method for the industrial sterilization of medical devices into the 21st century.

EO is considered the oldest of the three major technologies used for industrial sterilization. Once thought of as an anachronism, this sterilization method has shown to be highly useful when dealing with innovative developments in medical devices. The growth of new precise medical products designed for maximum patient benefit requires a sterilization modality that will not diminish the product’s potency and effectiveness. The role of industrial EO sterilization includes providing an industrial level process that meets the need for rapid medical device development required today to meet critical patient needs. Ethylene Oxide provides, as a reliable method for the growing sterilization needs in many places of the world where sensitive, single use devices cannot be reprocessed without loss of functionality resulting in reduced patient benefit. Finally EO meets the needs when combinations of medical devices, materials and packaging are placed into a single complex kit. These kits require a method suitable for all materials while maintaining stringent sterility assurance levels.

The highly reactive nature of the ethylene oxide molecule (epoxy ring molecule) presents an excellent method of sterilization but also present a significant number of regulatory challenges. For the use of EO for medical device sterilization is a highly regulated process requiring adherence to a number of local, state, national and international regulatory bodies in the areas of patient health, environmental safety, worker safety and construction requirements. These regulatory requirements and the increasing challenges presented highlight the need for continual innovation and insightful process development, upgrading of equipment and the need for reliable sterilization services on a worldwide scale. Such as:
Alternative mixtures of 100% EO gas, steam and inert gases patterned for maximum lethality and product safety;

Introduction of humidified gases concentrated to aid in EO penetration and removal;

While maintaining lethality requirements based on the ISO 11135 guidelines, significantly reduce EO gas concentrations and dwell time through experimental studies and validations using fractional negative approaches, combination of Biological Indicator and Bioburden approach or Bioburden Approach to sterilization development. All leading to a reduction of residual and residual by-products.

Methods to reduce loss of product heat (and accordingly, energy in the load) to prevent slowing of EO residuals from product.

From a regulatory aspect there are currently two key ISO documents that are in the process of making several changes that will impact the sterilization of medical devices with ethylene oxide gas:

a) ISO 10993-07: Addresses and regulates the level of EO residue (and EO by-product) levels on medical devices in contact with patients. This standard document includes a restructuring of requirements for short term exposure that will necessitate strategic focus by each medical device manufacture to assure compliance, and,

b) ISO 11135-1: This standard, which addresses Ethylene Oxide sterilization, has been updated and includes a revision to the qualification requirements of Medical Device manufacturers for utilizing parametric release. These changes will require Medical Device manufacturers to review their supply chain timeframes in order to discern what if any potential advantages will aid their speed to market needs.

Perhaps the question that needs to be asked by each manufacturer of sterile medical devices is ‘how are we prepared to address these changes/challenges?’

Though these changes have been under discussion for several years, these separate documents and committees also appear to directly impact the manufacturer, albeit unfortunately, perhaps at cross-purposes relative to product and patient supply needs. The changes to the ISO 11135 requirements will most likely allow for more medical device manufacturers to access the provisions under the parametric release criteria resulting in improved product to the hospital and clinician. Parametric release allows for the acceptance of validated processes based on conformance to parameters and eliminates the requirement for post process incubation of biological indicators for conformation. There are a number of revisions under consideration within the ISO 10993-07 document, such that a review by an appropriate
Sterilization professional (i.e. Chemist, Sterilization Engineer, Consultant, or Microbiologist, etc) is needed to ascertain the total impact on a medical device manufacturer’s process release. Medical devices used for short-term duration (24 hours) will need to conform to significantly reduce residual criteria prior to release for patient use. Without significant changes to the sterilization process or ventilation of the packaging the medical device manufacturer may expect an extension to product quarantine time pending necessary EO residual levels being met.

Table A shows the quarantine release period necessary for two medical products based on residual release criteria. Product B meets the current requirements and is releasable after approximately 72 hours of quarantine aeration time. Product A, though close requires additional testing to confirm the time in which the residual levels meet the release criteria. However, neither product is remotely close to the new levels under consideration currently. Table B shows the same data however with the additional data achieved through the use of an all in one process utilizing some of the techniques identified above in this article. Though more work must be performed by this client in order to meet the new requirements the level of EO residuals have been significantly removed as measured immediately from the chamber (Time: 0 hours).
Regulatory Changes Necessitate Focused Response by Manufacturers:

Options available to Medical Device Manufacturers & Sterilizers include:

2. Perform a ‘GAP’ analysis immediately:
   a. Move now to perform scientific evaluations to determine the gap between the current product status and the upcoming requirements
   b. Calculate EO residue reduction (and reduction rate over time) based on empirical data performed utilizing additional time in quarantine.
   c. Perform appropriate studies with reduced EO gas exposure and new de-gassing techniques to evaluate lethality and residues.
3. Calculate the potential impact on costs and loss of inventory velocity versus the reliability of EO sterilization as an accepted method of terminal sterilization.
4. Consider Package Redevelopment and Revalidation to aid in the increase ventilation and vapor barrier out gassing of the package. Move to evaluate:
   a. Increased product venting for improved gas and vapor transmission;
   b. Reduction in sterilization load density; and
   c. Alternatives to improve breathable surfaces involving kit over-wraps;
5. Redevelopment of the EO Process methodology to include all in one technologies available to lower EO concentrations and EO gas dwells which result in a reduction of residual levels;
6. Utilize new EO direct measurement technologies to evaluate EO out-gassing levels in entire loads post processing.
7. Once the product residues are considered and the quarantine time is minimized then Product Release Methodologies (i.e. parametric release, Reduced incubation Time Studies, Rapid Incubation Biologic products, new testing methods for rapid detection of biological indicator growth, etc) can insure the minimization of release time.

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All In One Sterilization: 3 step process performed in chamber: Conditioning, Delivery of Lethality and Removal of EO residue.

The Product leaves the chamber ready for immediate shipment
ALL in One Parametric Process.
Total Process and Inventory Hold Time *Reduced from: 250 hours to 15 hours*