Methods to Reduce Sterilization Process Time

Changes in ethylene oxide sterilization are providing manufacturers with improved speed to market. This report examines several developments that are influencing processing times.

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EtO sterilization is continuing its progression toward a ‘technology-neutral’ solution.Peter Strain is the vice president of technology at Sterigenics EMEAA in the UK, and Bill Young is the vice president of EtO technology at Sterigenics U.S.A., 2015 Spring Rd., Ste. 650, Oak Brook, IL 60523. Strain has more than 20 years of experience in the field of sterilization in the medical device industry and represents the UK as a delegate on ISO/TC 198 Working Group 1 EtO Sterilization. Bill Young, who has been working on a patent-pending one-day-one-chamber EtO process, is a member of the Association for the Advancement of Medical Instrumentation and has served on several key AAMI committees. More information on EtO sterilization is available by contacting Young at 800-928-1700 or byoung@sterigenics.com.

By Peter Strain and Bill Young
Over the past 8 to 10 years, the growth of single-use medical devices has been followed by the increased use of traditional terminal sterilization methods such as ethylene oxide (EtO), electron beam, and gamma irradiation. Within this market, there has been a movement toward the presentation of medical devices in customized procedure packs for use in specific medical and surgical procedures. This change has created a number of sterilization challenges because of the diversity of product designs, material types, and packaging applications. The relative suitability of EtO with a broad range of materials, coupled with the flexibility of sterilization process variables, has meant that EtO has often emerged as the sterilization method of choice.
The effort to reduce overall sterilization process time has provided a strongincentive to develop and optimize large-scale EtO sterilization technology whilealso continuing to deliver the required product sterility assurance levels. Historically,60 to 80 percent of the EtO sterilization process time is taken up with twoactivities. One is the post-processing quarantine period when products are heldpending the completion of a microbiological test. The other is the validatedaeration time to ensure that process residual levels in devices are compliantwith the requirements of ISO 10993, Biological Evaluation of Medical Device,Part 7: Ethylene Oxide Sterilization Residuals. The most recent revised ISO 10993-7draft indicates that the acceptable residual levels will be reduced in the future,thus requiring even longer aeration times or the intention on the part of themanufacturer to address the issue through re-examination of the sterilizationprocess.

Validation Optimization

Contract sterilizers have responded to the demand for improved processing time in a number of ways. Originally, it was common to focus on the microbiological test period for optimization, particularly for products that required less than two or three days of aeration. Approaches used to achieve this included the two described below.

1. Validation of a reduced incubation period for biological indicators used for monitoring the process delivered a reduction typically from seven days to between two and five days.
2. Implementation of parametric release (i.e., product is sterile) is based on adherence to validated physical process parameters rather than microbiological tests. Speed to market for the product is then dependent on aeration time and conditions that are validated to ensure compliance with ISO 10993, Part 7.

Benefits for manufacturers arising from these initiatives include a faster response to market and a reduction in work-in-progress materials.

It has been the validation and implementation of parametric release with the attendant increase in the understanding of the “kinetics of inactivation” in the sterilization chamber that has allowed further significant developments. Validation of parametric release in compliance with ISO 11135, Medical Devices, Routine Control, and Validation of Ethylene Oxide Sterilization, (EN 550) requires monitoring the parameters of load temperature, relative humidity in the chamber, and EtO concentration by direct measurement. Much has been learned about product distribution within the chamber and the temperature of the sterilization load, relative humidity in the chamber, and EtO, which has translated into further improvements for all phases of the process.

Preconditioning Phase Eliminated

The use of dynamic conditioning&#151the application of pulsed steam in combination with nitrogen in the sterilization chamber&#151has expedited the rate of heat-up of products to attain the required sterilization temperature and achieved optimal relative humidity levels throughout the load. As a result, the preconditioning phase has been significantly reduced or eliminated.

Optimized Microbial Inactivation

Proprietary studies using a design of experiments (DOE) method with standardized process challenge devices (microbiological and residual), in addition to unique combinations of nitrogen, steam, and EtO, have been tailored for specific product families to produce optimal conditions for microbial inactivation. This provides two benefits: reduced dwell times and a reduction in EtO concentration used in the gas dwell phase. Both of these are primary drivers for EtO residuals in product. These improvements have brought the additional benefit that residue levels in product are minimized as it transfers into the aeration phase.

Aeration Time Eliminated

Additionally, combinations of gases, pressure setpoints, vacuum rates, and gas-

injection rates have been reviewed for specific product families, which have allowed enhanced outgassing of EtO from materials. Calculated design of this outgassing phase in the chamber has resulted in major reductions or the elimination of the need for subsequent aeration of products. Indeed, product is compliant with the requirements of ISO 10993, Part 7, directly from the sterilization chamber, and extremely low levels (less than 5 ppm) of “environmental EtO” have been observed, which has provided additional environmental, health, and safety benefits.

Technology Time Savers

By combining these approaches, recent case studies have shown that substantialimprovements have been achieved for various product families.
The flexibility of EtO sterilization as a traditional gas-diffusion process has been greatly enhanced by overall improvements afforded by microprocessing capabilities and more than five years of direct measurement of key process variables as well as improvements in the design of the chamber to maximize effective gas distribution and better process design achieved through scientific modeling and experimental evidence.
The culmination of these factors has permitted significant development of each process phase. In addition, it has resulted in an overall reduction in sterilization process time and the ability to deliver a sterile and safe product to market. In terms of speed to market, EtO sterilization is continuing its progression toward a “technology-neutral” solution compared with other sterilization methods.

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For additional information on the technologies discussed in this article, see *Medical Design Technology* online at www.mdtmag.com or Sterigenics at www.sterigenics.com.