December 6, 2019

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re:  Docket No. FDA-2019-N-3793 General Hospital and Personal Use Devices
Panel of the Medical Devices Advisory Committee; Notice of Meeting;
Establishment of a Public Docket; Request for Comments

Dear Sir/Madam:

The Advanced Medical Technology Association (AdvaMed) provides these comments in response to a request regarding the Food and Drug Administration (FDA or “Agency”) Center for Devices and Radiological Health Federal Register notice “General Hospital and Personal Use Panel of the Medical Devices Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments”; Federal Register Volume 84, Number 171 (Wednesday, September 4, 2019).

AdvaMed is the world’s largest trade association representing medical device and diagnostics manufacturers. AdvaMed member companies produce the innovations that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. AdvaMed has more than 400 member companies, ranging from the largest to the smallest medical technology innovators and manufacturers. AdvaMed advocates for a legal, regulatory and economic environment that advances global health care by assuring worldwide patient access to the benefits of medical technology. The Association promotes policies that foster the highest ethical standards, efficient product approvals, appropriate reimbursement, and access to international markets.

Ethylene oxide (EtO) gas is the most common way to sterilize medical devices, a process that is critical for preventing infections and ensuring patients have safe surgeries and medical treatments. Since its discovery as an effective sterilant in 1938, EtO has played a critical role in the sterilization of medical devices. Decades later, EtO is now used to sterilize more than 20 billion health care products each year in the U.S. alone. This represents more than 50 percent of all medical devices sterilized annually in the U.S.

For many medical devices, due to their material composition, size, shape or complexity, EtO is the only effective method for sterilization. EtO provides the ongoing capacity and scale to process the billions of medical devices required by today’s modern health care...
systems in delivering care to patients. Heart valves, pacemakers, implantable cardioverter/defibrillators, drug-eluting stents, feeding tubes and breathing tubes, surgical drapes and kits, and syringes are just a few of the many products critical to modern patient care that can only be sterilized using EtO. Ethylene oxide’s compatibility and effectiveness with the plastics and polymers commonly used in medical products allows for the sterilization of many medical devices that would otherwise be rendered ineffective or unsafe if sterilized by radiation, moist heat, dry heat, or other alternative methods.

FDA and other global regulators play an important role in assuring that manufacturers’ sterilization methods are properly validated to ensure their safety and effectiveness. FDA regulations, guidance and harmonized international standards have provisions that address the use of EtO and other sterilants for medical devices. Medical device manufacturers have invested in microbiologists, sterility assurance experts, process safety and environmental engineers, and industrial hygienists who have worked for decades to ensure that they have standards and controls in place to responsibly manage the use of EtO. Manufacturers must conduct extensive studies to demonstrate that the required sterility assurance levels are achieved and maintained by their equipment and processes, and to confirm that exposure to the sterilization process does not adversely affect the device’s performance, safety or effectiveness over the shelf life of the device.

AdvaMed appreciates the value of convening the advisory panel meeting and providing the opportunity for open and constructive discussions on the topic of industrial ethylene oxide (EtO) sterilization of medical devices and its role in maintaining public health. AdvaMed commends FDA for their efforts to monitor device shortages, create the FDA Innovation Challenges and continue to engage with other federal agencies and stakeholders.

AdvaMed has reviewed the panel recommendations as recorded in the FDA 24-hour summary of the advisory panel meeting and provides the following comments:

“The panel discussed how FDA can help mitigate device shortages due to reduced device sterilization capabilities. The panel’s consensus reemphasized the need for stakeholder communication and collaboration to help manage shortages, including working collaboratively with other government entities, on the federal and state level.”

- AdvaMed supports the need for timely communication and collaboration among all stakeholders. AdvaMed government affairs staff are actively working with state and federal legislators to inform them of the impact of sterilization facility closures on medical device availability, the challenges of finding alternatives to EtO and other issues.

“The panel also recommended that it may be appropriate to enhance FDA’s ability to respond to device shortages by incorporating processes currently used with drug shortages that would necessitate additional authorities for FDA.”
• AdvaMed will continue to work with FDA, as appropriate, to respond to any potential device shortages. When considering methods used for drug shortages, it must be determined if those methods are suitable for medical devices.

“The panel deliberated on the possibility of changing EtO sterilization cycles or sterilization loads to reduce EtO use while maintaining effective sterilization. The panel’s consensus was that there were potential methods that appeared viable, but no single method would address all issues and that manufacturers and contract sterilizers should pursue all applicable methods for reducing EtO use.”

• AdvaMed agrees that modifications to sterilization cycles or loads could potentially reduce the amount of EtO used. AdvaMed members will continue to explore various sterilization process changes that would reduce amounts of EtO used.

“The panel considered various methods to validate EtO sterilization cycles in hopes of reducing EtO-use while still maintaining an effective sterilization process. The panel recommended that FDA encourage the use of alternatives to the overkill validation method which are included in the consensus standards for EtO sterilization processes.”

• AdvaMed supports the consideration of the use of alternatives to the overkill method of cycle validation. The current AAMI standard for EtO sterilization cycle validation allows for other methods and therefore companies can maintain compliance with the international standard.

“The panel discussed the sterilization of some medical devices to a less rigorous sterility assurance level (SAL) (e.g. 10^-5, 10^-4, etc. instead of 10^-6) be considered as part of the approach to reduce sterilant use. The panel’s consensus was that consistent with current standards, FDA should consider moving to a risk-based assessment of the SAL for some sterilized medical devices.”

• AdvaMed supports the consideration of a risk-based assessment of SAL. The recent recognition by FDA of the ISO/TS “Guidance on aspects of a risk-based approach to assuring sterility of terminally sterilized, single-use health care product that is unable to withstand processing to achieve maximally a sterility assurance level of 10^-6” provides a risk-based approach to less rigorous SAL and should assist FDA and industry in this consideration.

“The panel discussed existing large-scale industrial sterilization modalities as a possibility that can take over a portion of the EtO sterilization. The panel deliberations identified that none of the currently available large-scale industrial modalities have the capacity or material compatibility necessary to take over a significant fraction of the medical devices currently sterilized via EtO. At the same time, the panel saw merit in actively pursuing exploration of the alternative modalities that could potentially provide some relief to the ecosystem, recognizing that the capacity for EtO sterilization is
significantly constrained at present. The panel recommended that manufacturers review which sterilization modalities may be compatible with their devices and where possible validate alternate methods. The panel also recommended that FDA continue to collaborate with industrial stakeholders to facilitate industrial efforts to develop alternatives to EtO sterilization as well as utilization of optimized EtO processes that use less EtO and emit less EtO into the environment in the near term.”

- AdvaMed agrees that there are currently no suitable alternative sterilization modalities for certain medical devices. Developers of alternate methods who presented information on their sterilization modalities at the panel meeting concurred that no one method is a suitable replacement for EtO, and it is unlikely that a replacement will be available for at least 10 years. However, AdvaMed continues to support the ongoing efforts to develop alternatives to EtO.

AdvaMed member companies are committed to further reducing the amount of EtO used for effective sterilization processes by actively exploring methods and processes that reduce the amount of EtO used for a sterilization cycle. The industry is committed to investigating alternate sterilization methods that provide appropriate sterility levels and maintain device performance. Until there is a safe and effective replacement for EtO, we will continue to pursue our goal to reduce the amount of EtO used. Optimizing the EtO process itself, the medical device packaging and the approach to validation are examples of possible ways to minimize the amount of EtO sterilant necessary to sterilize devices.

However, none of these potential solutions can be achieved quickly or easily. Any change to minimize EtO use, if even feasible, may require extensive product and/or process modifications; validation and verification testing; and required notifications, clearances and approvals from FDA.

In summary, AdvaMed member companies are committed to the safe and effective use of EtO for the sterilization of certain medical devices for which there is currently no acceptable alternate method. We are also committed to reducing the amount of EtO needed for an effective sterilization cycle, thereby reducing the amount of EtO that must be abated. We will continue to research alternative sterilization methods and implement them once they are proven to be safe, effective and feasible. We look forward to working with FDA and other stakeholders on this important public health issue.

Sincerely,

/s/

Ruey C. Dempsey
Vice President
Technology & Regulatory Affairs