April 26, 2019

U.S. Environmental Protection Agency
EPA Docket Center
Mail Code 28221T
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460


Dear Sir/Madam:

The Advanced Medical Technology Association (AdvaMed) is the world’s largest trade association representing medical device and diagnostics manufacturers. AdvaMed 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 members, 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, rapid product approvals, appropriate reimbursement, and access to international markets. Many AdvaMed members provide sterile devices that depend on the use of ethylene oxide (EO) as a sterilant.

AdvaMed supports efforts to ensure the safety of people who may be exposed to ethylene oxide. The mission of any medical device company is to protect and improve the health of the patients we serve. This interest naturally carries over to our concern for our employees and the general public. Medical device companies implement industrial hygiene programs to monitor potential workplace exposures to EO including, individual and industrial environment work area EO exposure monitoring systems, employee training programs, emergency management systems, and risk management practices that typically exceed federal requirements for employee and public safety. We underscore the high regard our industry places on human health and safety – including that of our own employees and the communities in which we operate.

Our members are committed to ensuring employee safety and reducing the environmental impact of EO. Because EO is critical to the safe sterilization of numerous medical devices, over the past decade, our members have invested hundreds of millions of dollars
to improve workplace safety and environmental health, and to monitor potential exposure to EO. Through implementation of new technology our members have continued to reduce employee exposures and emissions in accordance with current federal regulations.

AdvaMed members have significant concerns regarding the U.S. Environmental Protection Agency’s (EPA) cancer risk estimates for EO and the agency’s Integrated Risk Information System (IRIS) assessment. We fully support the issues raised by the American Chemistry Council’s (ACC) EO Panel and the Ethylene Oxide Sterilization Association, Inc. (EOSA). We are deeply concerned about the reliability and accuracy of the IRIS assessment and the potential negative impact the assessment could have on the healthcare industry and, most importantly, patient health and safety.

Many medical devices, including those used for infusion therapy and administration of medications; implantable devices such as pacemakers; and devices used in surgical settings must be sterilized before use. In order to ensure patient safety, the Food and Drug Administration (FDA) has established requirements for the assurance of sterility for medical devices. The mode of sterilization must be validated to ensure its safety and effectiveness as well as its impact on device performance. The mode of sterilization must be shown to be compatible with the product as well as its packaging and ensure sterility of the device over the transportation supply chain.

Although medical device sterilization accounts for less than 1% of the overall EO usage in the U.S., our members currently sterilize hundreds of millions of medical devices each year in the U.S. with EO. Many of these devices cannot be sterilized in any other way because of the sensitive nature of the device materials, the components, or the complexity of design. The majority of these devices are not resistant to damage caused by moist heat, radiation, and other modes of sterilization. Examples of devices that can only be sterilized using EO include implantable devices containing electronic components and batteries, anesthesia products, combination products (devices that contain drugs), MRI conditional/safe devices and IV devices. For a number of other types of products, our members utilize other modes of sterilization, such as gamma irradiation and electron beam sterilization when possible, but for many devices there is currently no viable alternative technology to EO.

The direct impact of any elimination or severe restriction on the use of EO as a sterilant would compromise the U.S. healthcare system. At best, inventory shortages would likely result, and at worst, many life-sustaining medical devices such as pacemakers and implantable cardioverter/defibrillators would no longer be available to patients. It should also be noted that changes in sterilization processes and methods would require clearance or approval by the FDA prior to implementation. Supporting evidence would have to be provided by the manufacturer demonstrating that the new sterilization process does not adversely affect the device and that the same level of sterility is achieved.
While we agree that the National Institute for Occupational Safety and Health (NIOSH) study contains data collected from the community, AdvaMed agrees with the concerns expressed by ACC and EOSA and thereby disagrees with the broad categorization of such data and in the gross estimation of exposure to EO prior to 1978. Because the information is used in a model, the inputs to the model are critical to the use of the model for establishing guidance to the regulatory community. Categorical exposure estimates from the NIOSH study are subject to a number of potential errors which could include random errors in estimating historical exposures, errors and misclassification in establishing category boundaries, and manipulation of category boundaries. Upon review of this data, it is unclear why some data from the NIOSH cohort were discarded, when in fact this data appeared relevant to the evaluation and statistically important. In addition, we believe that the application of a single, long lag is more suitable for this cohort than the single 15-year lag used in the evaluation.

We disagree with the use of categorical data in linear regression modeling to determine low-exposure risk. We also disagree with the use of a two-piece linear spline to estimate cancer potency as this incorrectly overestimates the carcinogenicity of EO and has not been used to estimate potency of other carcinogens.

Furthermore, we contend that the evaluation failed to consider several studies deemed relevant by the Science Advisory Board (SAB). This includes, but is not limited to, studies by Teta (Teta et al, 1993, 1999) and Greenberg (Greenberg et al, 1990). Failure to include relevant data may further bias the results of the evaluation. The failure to evaluate these relevant studies as part of the modeling exercise skews the model to an unsupportable conclusion.

Thank you for the opportunity to provide comments. AdvaMed members are committed to ensuring the availability of safe and effective medical devices and diagnostics to patients and healthcare professionals in the United States and around the world. We are also committed to doing so in an environmentally responsible manner. The availability of ethylene oxide as a sterilant for certain medical devices is an essential requirement for their safety and effectiveness.

Respectfully Submitted,

/s/

Ruey C. Dempsey
Vice President
Technology & Regulatory Affairs