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November 10, 2014

Mr. Aaron Yeow
Designated Federal Officer (DFO)
Science Advisory Board Staff Office
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460-4164

Re: Comments to the Chemical Assessment Advisory Committee for the Integrated Risk Information System Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide (Revised External Review Draft - August 2014)

Dear Mr. Yeow:

The Advanced Medical Technology Association (AdvaMed) welcomes the opportunity to provide comments to the Chemical Assessment Advisory Committee for the Integrated Risk Information System Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide (revised external draft-August 2014).

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

AdvaMed supports the committee's efforts to ensure the safety of people exposed to ethylene oxide (EO). 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. Medical device companies implement 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 safety. We underscore the high regard our industry places on human health and safety – including that of our own employees.



Our members are committed to ensuring employee safety and reducing environmental impact. Over the past decade, our members have invested hundreds of millions of dollars to improve workplace safety and environmental health. Through implementation of new technology our members have continued to reduce employee exposures and emissions in accordance with current OSHA and NESHAP regulations.

AdvaMed members have significant concerns regarding the U.S. Environmental Protection Agency's (EPA) cancer risk estimates for ethylene oxide and the revised draft IRIS assessment. We fully support the comments submitted 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 terminally 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 packaging, and ensure sterility of the device.

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) 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 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 NIOSH study contains relevant data, AdvaMed disagrees with the broad categorization of such data and in the gross estimation of exposure to EO prior to 1978. 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 was 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 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.

We respectfully request that the SAB-Chemical Assessments Advisory Committee (CAAC) carefully consider not only the inaccuracy and bias of the IRIS assessment, but the impact on the proposed risk estimate on the ability to supply sterile medical products to patients, clinicians, and the general public.

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. The availability of ethylene oxide as a sterilant for these devices is an essential requirement for the safety and effectiveness of sterile devices.

Sincerely,

/s/

Ruey C. Dempsey RAC
Associate Vice President
Technology and Regulatory Affairs