Sterigenics®

November 12, 2014

Via E-Mail (Yeow.Aaron@epa.gov)

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: Sterigenics 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:

Sterigenics U.S., LLC ("Sterigenics") appreciates the opportunity to submit these comments to the Science Advisory Board (SAB) Chemical Assessment Advisory Committee (CAAC) for consideration in responding to the draft charge questions for the revised draft Integrated Risk Information System (IRIS) assessment for ethylene oxide (EO).

Sterigenics is the global market leader in contract sterilization services. We have 39 global contract sterilization facilities and utilize four different types of sterilization technologies to treat medical and food products. These technologies include ethylene oxide processing, cobalt gamma radiation, electron-beam radiation, and x-ray radiation. With our EO processing technology, we sterilize medical device and pharmaceutical products as well as reduce the bioburden on some spice products. Some of the medical device and pharmaceutical products that we treat with EO can only be sterilized with EO processing. EO sterilization plays a critical role in protecting public health and reducing the risk of infection with the safe and efficient delivery of sterile medical devices and pharmaceutical products to the medical community.

As users of EO, the accuracy and completeness of the scientific basis for the draft IRIS assessment is extremely important to Sterigenics and our EO sterilization customers. Sterigenics has significant concerns regarding the U.S. Environmental Protection Agency's (EPA) cancer risk estimates for EO and the revised draft IRIS assessment as a whole. In addition to our specific comments, we fully support all comments submitted by the American Chemistry Council's (ACC) EO Panel and the Ethylene Oxide Sterilization Association (EOSA). Sterigenics believes the current assessment results in the risk of EO being inappropriately magnified. The EO levels that are deemed to be "safe" in this risk assessment are significantly lower than natural background levels of EO in the atmosphere and endogenous EO levels in humans. If this assessment is finalized, EO would also be identified as one of the most potent chemicals within

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the IRIS database. This exaggerated risk will not only severely and adversely impact the EO sterilization industry, but it will significantly disrupt an established sterilization method for medical devices essential to the general public. The CAAC must consider the benefits of EO sterilization as they review the draft IRIS risk assessment that we believe is not accurate regarding the EO risk estimates.

EO Sterilization Worker Exposure Levels

One of the main concerns raise by the IRIS risk assessment is in regard to Worker Exposure levels. We agree that this is an important focus and one that the EO sterilization industry has paid particular attention to as well. In recent decades, improvements to the EO sterilization equipment and processes have continuously been evolving to greatly reduce potential employee exposures. Ambient air monitoring and sterilization processes are designed to minimize potential exposure of workers. In addition, the industry has utilized emission controls to significantly reduce environmental EO emissions during the past several years.

The draft IRIS assessment evaluates occupational exposure EO risk estimates in Section 4.7. In Table 1-1, Summary of major findings, they report the extra risk estimates for occupational exposure scenarios to be a range of 0.047 to 0.14 per $\mu g/m^3$ for the maximum likelihood estimates of the extra risk of lymphoid cancer and breast cancer combined for the range of occupational exposure scenarios considered. From these risk estimates, industry could estimate EPA acceptable worker exposure levels to be at or less than 0.001 ppm or 1 ppb. Current worker exposure levels in the sterilization industry range from 0.1 to 1.0 ppm. It would be impossible to accurately and reliably measure or achieve worker exposure levels at the 1 ppb exposure limit.

Benefits and Use of EO Sterilization

As mentioned previously, EO plays a critical role in antimicrobial sterilization to protect public health. It is used to sterilize more than 20 billion medical devices each year in the U.S. alone. This represents more than 50 percent of all medical devices that are sterilized. In fact, some medical products and surgical kits can only be sterilized with EO because of the various complexities and components within these products. The use of EO sterilization provides unparalleled benefits to society by its use throughout the medical community. Numerous medical, hospital, and laboratory processes rely on EO to sterilize devices and equipment to protect millions of patients from the real risks of infectious diseases from bacteria, viruses, and fungi. EO sterilization is critical in the delivery of sterile devices and safe medical care.

The nature of EO sterilization and its low temperatures at which the process occurs gives great flexibility and utility regarding the devices and products that it can sterilize. Many critical healthcare products are highly sensitive and sophisticated pieces of equipment. For the majority of these healthcare products, EO sterilization is not just the most effective and efficient sterilization technology; it is the only acceptable method. EO sterilization allows for

the sterilization of healthcare products and devices that would otherwise be destroyed and rendered inoperable by the high heat, harsh chemicals, and/or other properties of alternative sterilization methods.

Adverse Impacts on Public Health

Sterigenics believes the current draft IRIS assessment will have significant adverse impacts on those who use EO to sterilize healthcare products, and the medical community at large. By inappropriately magnifying the risk associated with the use of EO, users could be forced to switch to less effective, impractical alternatives with significant adverse public health consequences. A change in sterilization technology could introduce significant risks involving medical device integrity and biocompatibility issues. Also changing to a different technology requires considerable time and effort in conducting validation studies for demonstrating acceptable sterilization of medical devices and other products. For some medical devices and pharmaceutical products, proper sterility assurance levels might not be achieved with a change in sterilization technology.

Medical devices and healthcare products are frequently designed for a specific sterilization method. Any change to the sterilization technology would often require such medical products to be redesigned completely. In fact, some complex products may not be able to be redesigned to be effectively sterilized without EO sterilization. The costs and timing associated with such medical product redesigns and validations are significant. In the United States, alternative sterilization methods may require submissions of new 510(k)s, premarket approvals (PMAs), or PMA supplements to the Food and Drug Administration (FDA), depending on the regulatory classification of the product. Such product changes with new FDA submissions could require significant costs in the multi-million dollar range and several years before the changes are proven and accepted. The significant costs and timing delays could also impact any further advances in the healthcare community.

In its current form, the revised draft IRIS assessment would result in more than 50 percent of all medical devices and over 90% of pre-sterilized surgical kits becoming unavailable. These kits include devices such as syringes, endotracheal tubes, catheters, vascular stents, and many other components required for surgeries. These single-use medical products are critical items in hospitals, doctor's offices, and clinics across the U.S. In addition, many reusable devices are currently only qualified for EO sterilization. A reduction in the EO exposure limits as proposed would result in these products no longer being able to be sterilized adequately and would have significant impacts on public health. The inability to sterilize these products and equipment with EO would significantly increase the risk of infection and impact public health. Such risks are far greater than those suggested by the draft IRIS assessment.

Comments on Specific Charge Questions

Sterigenics agrees with and supports comments made by the American Chemistry Council's (ACC) EO Panel and the Ethylene Oxide Sterilization Association (EOSA).

In addition, Sterigenics would like to address one specific Charge Question:

Charge Question #4 -- Uncertainty in the cancer risk estimates. *Please comment on whether the qualitative discussions of uncertainty (Sections 4.1.4, 4.5, and 4.7 and Chapter 1) are clear, objective and scientifically appropriate.*

EPA has dismissed the Union Carbide Corporation (UCC) exposure assessment study for dose-response assessment due to certain uncertainties and therefore relies solely on the NIOSH exposure assessment. We recommend that EPA includes the data from the UCC study so that increase the power and breadth of the dose-response assessment. The NIOSH study included workers who began working in the EO industry as early as 1943. In fact, Sterigenics had employees included in the NIOSH studies and are familiar with the workplace controls during this time frame. During this time, the workplace exposure limit for EO was as high as 100 parts per million (ppm) until 1957 when the American Conference of Governmental Industrial Hygienists (ACGIH) set the Threshold Limit Value (TLV) Time-Weighted Average (TWA) to 50 ppm. This level was reduced to 10 ppm in 1981 and then reduced further to 1 ppm in 1984. The U.S. Occupational Safety and Health Administration (OSHA) followed a similar pattern reducing the workplace exposure limit from 50 ppm in 1971 to 1 ppm in 1984. The sterilization equipment, workplace controls and EO measurement devices do not represent what is place in the industry today. The workplace exposures during previous periods of much higher EO TLV and TWA limits are orders or magnitude higher than what is in place today. Using this data alone does not seem representative of the risks today.

Therefore, the limitations contained within the NIOSH study largely invalidate the decision to solely rely on it and EPA has failed to justify the exclusion of the UCC study. As the IRIS assessment can lead to the further regulation of EO exposure, the CAAC should recommend that, at a minimum, the results from both the UCC and NIOSH studies should be presented and considered to improve the credibility of the assessment.

Sterigenics appreciates the opportunity to submit these comments on the draft IRIS assessment for EO. We urge the CAAC to review this information, and the comments submitted by the ACC EO Panel and EOSA as it develops draft responses to the charge questions. If you have any questions, or would like to request additional information, please do not hesitate to contact me at 630.928.1758 of khoffman@sterigenics.com.

Sincerely,

Kathleen Hoffman
Senior Vice President of Global Environmental, Health & Safety