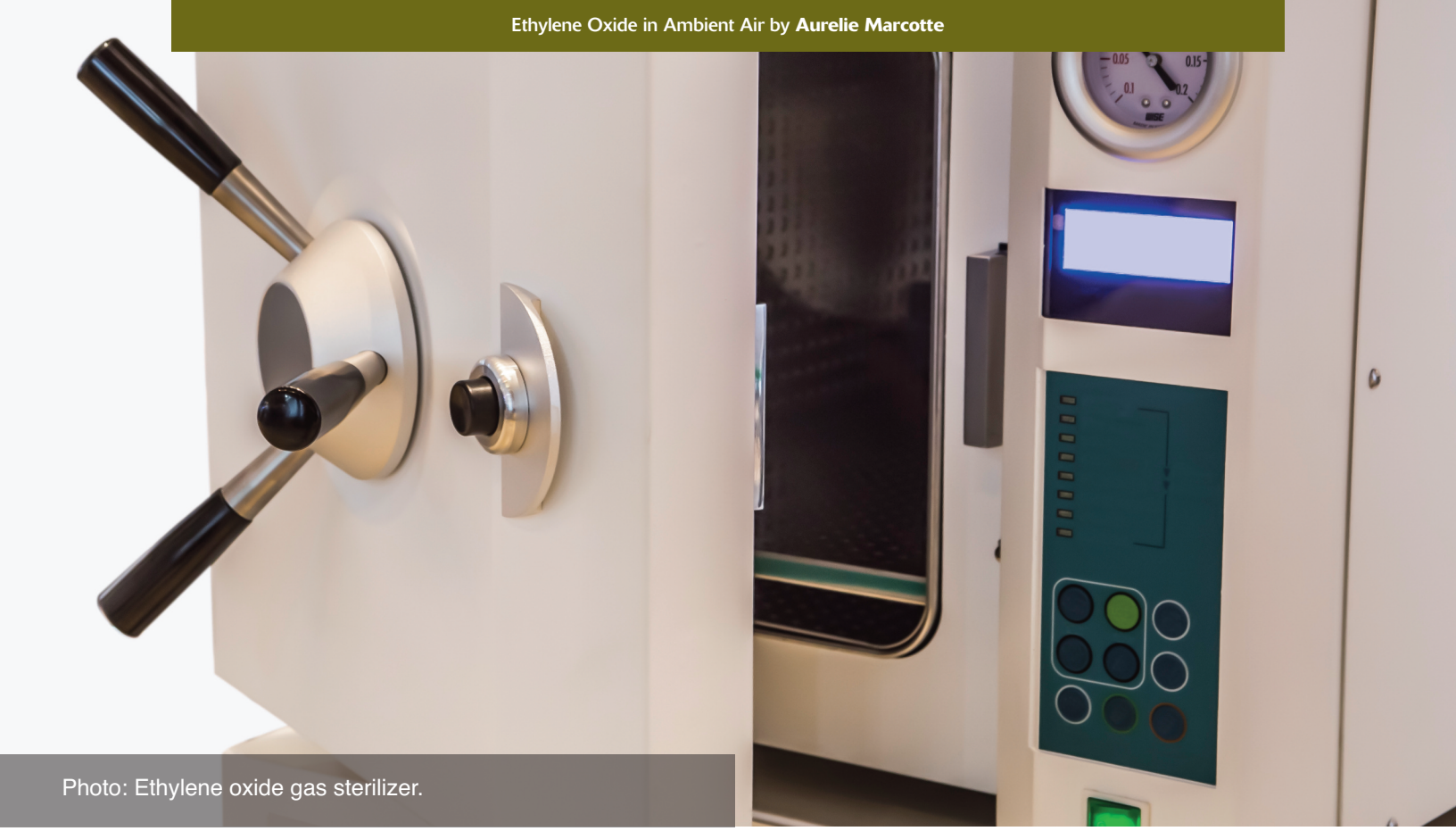


Photo: Ethylene oxide gas sterilizer.

The Current State of Ethylene Oxide in Ambient Air

by Aurelie Marcotte

Ethylene oxide (abbreviated as EO or EtO) is an important industrial precursor, critical element in the medical device supply chain, and also a known carcinogen, even at low concentrations. A particularly challenging compound to analyze, measurement technologies are only now catching up to the sensitivity and accuracy required to understand the sources and impacts of this contaminant of emerging concern. For the first time, new technologies are making it possible to measure ethylene oxide in ambient air to part-per-trillion concentrations.

Ethylene oxide is a gaseous compound at room temperature that is a valuable tool by itself and a key component in a variety of manufacturing processes. Ethylene oxide is a widespread chemical precursor often used in the manufacturing of chemicals that produce consumer household products and is an essential building block for synthetic fibers, plastics, PVC pipes, and cosmetics. Most notably, ethylene oxide is a sterilizing agent for a wide variety of medical and dental equipment due to its ability to penetrate various materials and safely sterilize the equipment without causing damage to sensitive components. At present, nearly 50% of all medical devices are sterilized with ethylene oxide.[1]

A Brief History of EO

The use of ethylene oxide for sterilization dates to the 1940s, when it was used to sterilize food during World War II. In the 1950s, ethylene oxide became widely used to sterilize medical instruments.[2] While the use of ethylene oxide grew quickly, understanding of exposure risks grew more slowly, the first study to be published about the exposure risks was in 1948 by Rapoport,[3] which found ethylene oxide to be mutagenic and potentially cancerous.

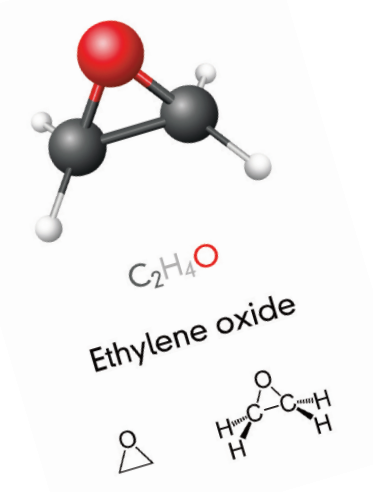
In 1984, the U.S. Occupational Health and Safety Administration (OSHA) set the permissible exposure limit to 1 part-per-million (ppm) ethylene oxide, measured as an 8-hr time-weighted average, based on animal and human data showing that exposure to ethylene oxide is a potential carcinogenic, mutagenic, genotoxic, reproductive, neurologic, and sensitization hazard to exposed workers.[4] An extensive 2004 study by the National Institute for Occupational Safety and Health (NIOSH) reported that workers at sterilization facilities with very high ethylene oxide exposures had an elevated risk for blood cancers among men and breast cancers among women.[5,6]

Under the 1990 U.S. Clean Air Act Amendments, the U.S. Environmental Protection Agency (EPA) designated 187 pollutants as hazardous (called hazardous air pollutants or HAPs), including ethylene oxide. Specific national emission standards for ethylene oxide from commercial sterilization and fumigation operations were proposed under the Clean Air Act in 1994, requiring these operations to report their emissions to the Toxic Release Inventory.[7] The current emission standards are under review by EPA and a proposed rule is expected to be issued in 2022. Despite the health risks related to acute and chronic exposure, ethylene oxide sterilization is a critical part of the medical supply chain and helps to prevent countless infections each year.

Recent Risk Assessments for Ambient EO

In the 2016 Integrated Risk Information System (IRIS) report on the "Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide," EPA updated its risk assessment showing that the long-term exposure risk of ethylene oxide is greater than previously thought. It was calculated that the concentration of ethylene oxide associated with a 100-in-a-million cancer risk, for a lifetime of continuous exposure, is 0.02 µg/m^3 (approximately 11 parts per trillion by volume, or pptv).[8] EPA uses the National Air Toxics Assessment (NATA), and more recently, the Air Toxics Screening Assessment (AirToxScreen, a screening tool to evaluate the human-health risks posed by HAPs released in March 2022),[9] to provide estimates of cancer risk and other health effects from inhaling air toxics. In 2018, EPA published a NATA report indicating that more areas of the country showed elevated risks caused by emissions from ethylene oxide based on the latest risk assessment.[10]

Not all stakeholders agree with EPA's current risk assessment for ethylene oxide. In 2020, the Texas Commission on Environmental Quality published their assessment of the carcinogenic dose–response of ethylene oxide, which showed that ethylene oxide was far less hazardous than stated in the 2018 EPA report.[11] In addition to differing calculations of the long-term exposure risk levels of ethylene oxide, there are



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also uncertainties and limitations with current measurement techniques to monitor ethylene oxide in ambient air. Until recently, there were no readily deployable methods that were capable of measuring ppt concentrations of ethylene oxide in ambient air to reach the 100-in-a-million excess cancer risk level reported by EPA. Without accurate and sensitive measurement technologies, there is limited information about the concentrations of ethylene oxide in the ambient environment making it challenging for air agencies and communities to understand their long-term exposure risk of ethylene oxide.

Current Measurement Techniques for EO in Air

Ethylene oxide in ambient air is typically measured by EPA Method TO-15/TO-15A, which is a canister-based sampling method with Gas Chromatography-Mass Spectrometry (GC/MS) analysis. The main challenge with this method is that typical detection limits are around 18–25 pptv ethylene oxide, which is not below regulatory risk assessment.[12,13] Alternative methodologies include Proton-Transfer Reaction Mass Spectrometry (PTR-MS), Cavity Ring-Down Spectroscopy (CRDS), and Fourier Transform Infrared Spectroscopy (FTIR). Though, many of these techniques also come with associated challenges, including ease of use, instrument detection limits, accuracy, and cost.

In 2021, Entanglement Technologies (San Bruno, CA) released their AROMA-ETO analyzer capable of measuring ethylene oxide in ambient air below 10 pptv.[14,15] In recent years companies, including Entanglement Technologies, Aerodyne Research (Billerica, MA), and Nikira Labs (Mountain View, CA), have been funded by EPA Small Business Innovation Research Awards to develop instrumentation capable of measuring ethylene oxide below the cancer risk assessment levels. EPA's Office of Research and Development is currently evaluating the best measurement practices for monitoring ethylene oxide in ambient air.[15]

EO Measurements in Ambient Air

The fate, transport, and persistence of ethylene oxide in the ambient environment is not well-understood. EPA estimates that the half-life of ethylene oxide in the atmosphere ranges from 69–149 days in the summer and winter months, respectively.[16] At ambient air concentrations that have been monitored or modeled near emission sources, ethylene oxide cannot be smelled (the odor threshold for ethylene oxide is 470 ppm) or seen. Since the release of the 2014 air toxics data,[10] many state air monitoring agencies have been working to better understand ambient air concentrations downwind of industrial sources, as well as background concentrations, using the best available tools. In one example, the Michigan Department of Environment, Great Lakes, and Energy (EGLE) conducted an air quality modeling study and EPA Method TO-15 analysis of ethylene oxide in ambient air around the largest medical sterilization facility in Michigan. Their findings estimated peak 24-hr exposure to ethylene oxide caused by the sterilization facility in nearby neighborhoods was

1.83 µg/m^3 above the background level.[17] Georgia, Utah, and West Virginia are among some of the other states that have conducted ethylene oxide monitoring. Ethylene oxide, along with the other air toxics, is also measured at National Air Toxics Trends Stations (NATTS) across the country.

In recent years, EPA has funded several projects to study air toxics in communities. In 2020, US$5 million was awarded to 11 state and local agencies to support monitoring in communities and provide important information on air toxics; approximately half of these agencies highlighted ethylene oxide as a contaminant of concern.[18] In 2021, EPA announced US$2.4 million available to develop and evaluate measurement methods for air toxics and contaminants of emerging concern in the atmosphere.[19] Most recently, as part of US$50 million allotted for environmental justice initiatives under the American Rescue Plan, EPA announced in December 2021 a US$20 million funding opportunity for enhancing air quality monitoring in communities, including monitoring for air toxics such as ethylene oxide.[20]

Conclusion

In preparing for enforcement of new regulations regarding emissions, and to ensure that communities are safe, robust measurement capabilities for atmospherically relevant concentrations of ethylene oxide are required. Since the release of the 2014 NATA report in 2018, several industries utilizing ethylene oxide have worked to reduce their emissions.[21] It is more important than ever to make accurate and sensitive ethylene oxide measurements to fully understand ambient background levels and to verify the performance of existing and upgraded ethylene oxide control devices. **em**

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