UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: March 27, 2023

SUBJECT: **Ethylene Oxide (EtO).** Addendum to "Draft Human Health and Ecological Risk Assessment in Support of Registration Review" - Inhalation Exposure Risk Assessment in Support of Registration Review.

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Executive Summary

In November 2020, the Office of Pesticide Programs (OPP) issued a draft human health and ecological risk assessment (2020 DRA) for the currently registered conventional and antimicrobial pesticidal uses of ethylene oxide (EtO) in support of Registration Review (US EPA, 2020). This memorandum updates and revises the aspects of the 2020 DRA that relate to human health inhalation cancer risk. In the 2020 DRA, OPP conducted a quantitative dietary risk assessment for exposures from EtO use to sterilize spices and determined there were no dietary risks of concern for either EtO or the metabolites ethylene glycol (EG) or ethylene chlorohydrin (ECH). This addendum does not present any revisions to the human health dietary risk assessment nor does it update the ecological risk assessment. With regard to effects to listed species, the Agency was not able to make a 'no effect' determination in the 2020 DRA due to potential exposure to terrestrial species.

The 2020 DRA presented multiple perspectives on cancer evaluations for EtO but did not choose a single value for risk extrapolation. Inhalation exposures to EtO were qualitatively assessed based on the variety of cancer dose response evaluations for inhalation exposure, and risks of concern were expected for the inhalation route based on the qualitative assessment. Since the publication of the DRA, and in contexts[1] other than the registration review of EtO, EPA has continued to consider the best approach for characterizing the cancer risk associated with inhalation exposure to EtO. While there are some uncertainties associated with all of the approaches to characterizing the cancer risk (as discussed in the 2020 DRA), the EPA has determined that the Integrated Risk Information System (IRIS) assessment of EtO (US EPA, 2016) should be used to characterize the cancer risk associated with inhalation exposure to EtO.

The IRIS assessment (US EPA, 2016) went through "unusually extensive processes for the consideration of public comment and external peer review," and is considered by EPA's Office of Research and Development (ORD) to be the "best available scientific information regarding cancer risks from EtO[2]." Further, since the publication of the DRA, the EPA has repeatedly expressed favorable views of the IRIS assessment, including in comparison to the other EtO cancer inhalation risk characterization approaches cited in the 2020 DRA[3,4].

Therefore, the EtO 2020 DRA is being revised here for the human health inhalation risk assessment using the IRIS Assessment (US EPA, 2016) to characterize the cancer risk from inhalation exposure.

Registered Uses of EtO

The registered antimicrobial uses of EtO include medical or laboratory equipment, pharmaceuticals, and aseptic packaging; and artifacts, archival material, library objects, and musical instruments. EtO is also registered for use on whole and ground spices or other

[1] US EPA, 2022. Reconsideration of the 2020 National Emission Standards for Hazardous Air Pollutants: Miscellaneous Organic Chemical Manufacturing Residual Risk and Technology Review – Final Action. FR Doc. 2022-27522 Filed 12-20-2022

[2] US EPA, 2021. Memo from W. Cascio (ORD) to J. Goffman (OAR), ORD Review of Comments on the IRIS Ethylene Oxide Assessment Contained in the ACC Request for Correction Submitted Regarding EPA's National Air Toxics Assessment, Aug. 25, 2021, Page 1.

[3] US EPA, 2022.

[4] US EPA, 2021a. EPA Should Conduct New Residual Risk and Technology Reviews for Chloroprene- and Ethylene Oxide-Emitting Source Categories to Protect Human Health, Report No. 21-P-0129, US EPA Office of Inspector General, May 6, 2021

seasoning materials. Additionally, a special local need (SLN) registration (North Carolina) is currently in place for the treatment of beekeeping equipment.

Hazard Assessment

The 2020 DRA (US EPA, 2020) includes a complete toxicological profile of EtO that addresses non-cancer effects such as neurotoxicity and effects from all exposure routes including oral, inhalation and dermal. In this document, only the cancer risks from inhalation exposure are being evaluated. Regulating on the risks from cancer effects is protective of non-cancer effects such as neurotoxicity because the non-cancer effects occur at much higher exposures in comparison to cancer effects. The effects from inhalation exposure are also protective of the other exposure routes.

Because the weight of evidence supports a mutagenic mode of action for EtO carcinogenicity, and as there are no chemical-specific data from which to assess early-life susceptibility, increased early-life susceptibility was assumed and age dependent adjustment factors (ADAFs) were incorporated to calculate lifetime risks, in accordance with the EPA's Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens (US EPA, 2005). The total cancer inhalation unit risk estimate for lifetime exposures is 5.0×10^{-3} per $\mu g/m^3$ (9.15×10^{-3} per ppb). This unit risk already accounts for application of the ADAFs for early life exposures and, therefore, can be used with exposures that have not been adjusted for ADAFs to estimate inhalation cancer risk. The total cancer inhalation unit risk estimate for adult exposure is 3.0×10^{-3} per ug/m^3 (5.5×10^{-3} per ppb). This unit risk does not include the ADAF adjustments. If exposures have already been adjusted using ADAFs for early life exposures, then this unit risk can also be used with these exposures to estimate the cancer risk.

For occupational exposures, a maximum likelihood estimate (MLE) and an upper-bound estimate are provided. An upper bound estimate is considered a "higher" value that is still considered reasonable with regard to its probability of occurring (e.g., a 95th percentile value); whereas a MLE is the most probable overall, but not the most probable "high" value like the upper bound estimate.

Under the Federal Insecticide Fungicide and Rodenticide Act, OPP applies a "no unreasonable risk" standard for both dietary and non-dietary exposures in making a risk management decisions. To help initially identify chemicals which may pose such unreasonable risks, OPP considers whether the risks from a chemical exceed a specified level of concern. If a given risk exceeds this level, OPP decides what further action, if any, is needed. OPP generally seeks to reduce the risk to 1×10^{-6} (1 in a million) for both occupational and residential exposures. In some cases, when it is not possible to mitigate to this level of risk and benefits are high, a risk target of up to 1×10^{-4} (100 in a million) may be used for occupational exposures.

Occupational Safety and Health Administration (OSHA) Exposure Limits

The permissible exposure limits (PELs) for EtO are 1.0 ppm as an eight hour time weighted average (TWA) and 5.0 ppm as a 15 minute short term excursion limit (STEL) and are enforceable under 29 CFR 1910.1047. These limits were established in the 1980s and have not

been updated. They are noted as being outdated and inadequate for ensuring protection of worker health on the OSHA website at https://www.osha.gov/annotated-pels.

Residential Handler and Post Application Exposure

There are no uses of EtO resulting in direct residential applications; therefore, residential handler and post-application exposures from residential uses are not expected (see non-occupational "bystander" exposures).

Aggregate Risk Assessment

An aggregate assessment for EtO was not conducted since there are no food or drinking water exposures to EtO. For the metabolites of EtO (ECH and EG), there are no water or non-dietary residential exposures; the only exposure route is through food. Thus, an aggregate assessment was not conducted for ECH or EG (US EPA, 2020).

Non-Occupational Bystander Exposure (Residential and Non-Residential)

There is the potential for non-occupational bystander exposure for people who live near sterilization facilities (residential non-occupational bystanders) or who spend significant time in the area for non-work related activities (e.g., school, daycare, shopping, etc.) near sites where sterilization or fumigation occurs (non-residential non-occupational bystanders). The exposure can occur from EtO emissions from commercial sterilizers, hospitals/health care facilities and beekeeping equipment fumigation chambers.

The Office of Air and Radiation (OAR) is proposing to address non-occupational residential bystander exposures from commercial sterilization facilities through proposed amendments to the National Emission Standards for Hazardous Air Pollutants (NESHAP) for the Commercial Sterilization Facilities source category. Exposures to non-occupational non-residential bystanders are not addressed by the proposed OAR rulemaking and are included below. These exposures are represented by children attending day care centers and schools because these exposures occur more frequently and with a longer duration than other non-work related activities.

Commercial Sterilization Facilities
The EtO average daily air concentration which corresponds to a cancer risk target of 1×10^{-6} (i.e., one in one million[5]) was back calculated using the unit risk estimates from the IRIS Assessment (US EPA, 2016). These air concentrations are as follows:

- Residential Non-Occupational Bystanders Living Near Sterilization Facilities - A lifetime average daily EtO air concentration of 0.00011 parts per billion (ppb) or 0.11 parts per trillion (ppt) has a cancer risk of 1×10^{-6} assuming continuous exposure (i.e., 24 hours a day for seven days a week) for a 70 year lifetime starting at birth. The cancer risk will be greater than 1×10^{-6} if the lifetime average daily concentration is greater than 0.11 ppt.

[5] The cancer risk target of 1×10^{-6} (i.e. one in a million) is normally used by OPP as a risk management goal for non-occupational exposures.

- Non-Residential Non-Occupational Bystanders (Daycare Centers and Schools) - An average daily concentration of 0.0012 ppb (1.2 ppt) has a cancer risk of 1 x 10^{-6} assuming children attend daycare 8 hours per day for 240 days per year for 6 years and school for 6 hours a day for 180 days per year for 12 years near a sterilization facility. The cancer risk will be greater than 1 x 10^{-6} if the average daily concentration is greater than 1.2 ppt.

Beekeeping Equipment Fumigations

For the beekeeping equipment fumigation use in North Carolina, there is the potential for both residential and non-residential non-occupational bystander exposure. A quantitative residential non-occupational bystander assessment, assuming someone lives near a fumigation chamber for a full lifetime (70 years), was conducted using the Probabilistic Exposure and Risk Model for Fumigants (PERFUM) (US EPA, 2019). This assessment would be protective of any non-residential exposures which would have a shorter exposure duration (e.g., 35 working years vs 70 lifetime years). Two application rates were modeled as provided on the product label: 28.3 lb ai/1,000 ft^3 and 46.5 lb ai/1,000 ft^3. The concentration distribution output from PERFUM for various percentiles (50^{th}, 75^{th}, 80^{th}, 85^{th}, and 90^{th}) was used to calculate cancer risk estimates assuming four or eight exposure days (24 hrs/day) per year based on specific use information for the beekeeping use and 70 years of exposure per lifetime. The IRIS inhalation unit risk for environmental exposures for a full lifetime [5.0 x 10^{-3} per $\mu g/m^3$ (9.15 x 10^{-3} per ppb)] was used to estimate cancer risks.

The distances from the fumigation chamber at which the cancer risk estimates are less than 1 x 10^{-6} increase from lower to higher percentiles. For example, at the lower percentiles (e.g., 75^{th} and 80^{th}), the distance from the fumigation chamber at which the cancer risk is less than 1 x 10^{-6} is only 10 meters, while at the higher percentiles (e.g., 90^{th}), distances of 300 meters or more are necessary to reach cancer risk estimates less than 1 x 10^{-6}. Because the model only provides results at specific distances from the fumigation chamber (e.g., 1, 5, 10, 15 meters, etc) and not at continuous distances, the distances at which risks are greater than 1 x 10^{-6} do not change based on the model results whether assuming four or eight exposure days per year. It is likely that the exact distances change, but per the model results which are only reported at specific distances, the distance at which the cancer risk estimate is not of concern does not change between four and eight exposure days.

Hospitals/Healthcare Facilities

Since 2010, health care sterilization facilities have been required to operate on an all-in-one basis in accordance with the EtO Reregistration Eligibility Decision (US EPA, 2008). These facilities sterilize material in oven-sized chambers using 4.5 to 170 grams of EtO per load. The exhaust from the chambers is typically routed to an air pollution control device and the room air is typically ventilated though an exhaust stack (ANSI/AAMI, 2018). Given this information, exposures to non-occupational bystanders are expected to be minimal, but the exact air concentrations are not known and therefore the risks are not quantitatively assessed in this DRA. It is known, however, that the exposures that would result in a cancer risk of 1 in a million are the same as those calculated for contract sterilization facilities (i.e., 0.11 ppt for residential areas and 1.2 ppt for children in schools/daycares. These potential exposures around health care sterilization facilities can be addressed in the Preliminary Interim Decision (PID) by requiring control measures that are recommended in ANSI/AAMI (2018).

Occupational Handler Exposure

There is potential for occupational handler inhalation exposure from the registered uses of EtO. OPP has obtained personal breathing zone (PBZ) air monitoring data from registrant-submitted studies for commercial sterilization plants, health care facilities and spice treatment facilities (MRIDs 50231101, 50231102 and 47338301). These PBZ air monitoring data represent observational monitoring during routine workdays and are expressed as 8-hour TWAs when compared to the OSHA PEL-TWA of 1.0 ppm or as 15-minute TWAs when compared to the OSHA PEL-STEL of 5 ppm. It should be noted that workers involved in all various activities were monitored. Some of these activities did not require the use of a respirator, such as working with untreated product in receiving areas or in the warehouse.

Antimicrobial Uses: Exposure data for commercial sterilization plant workers were included in a registrant submission of 1,273 results from 25 facilities (MRID 50231101). The EtO air concentrations were measured[6] in the PBZ outside the respirator and ranged from non-detect to 35 ppm with a mean of 1.3 ppm. The measured air concentrations along with the time that a respirator was worn were used to calculate 8-hour TWA exposures to EtO. These 8-hour TWAs of EtO range from 0.002 to 4.6 ppm with an arithmetic mean of 0.23 ppm. The 8-hour TWAs for workers who wore respirators were calculated by assuming that they wore full face supplied air respirators. These respirators have an assigned protection factor of 1,000 (OSHA, 2009), which means that the respirators reduce exposures by a factor 1,000x when workers were wearing the respirators. The 8-hour TWAs for workers involved in activities that did not require a respirator were not adjusted for use of a respirator.

Air concentration data for EtO in health care facilities were included in a registrant submission of 647 sample results that were collected in health care facilities in 2012 (MRID 50231102). The results ranged from 0.0007 ppm (the limit of detection) to 10.1 ppm with an arithmetic mean of 0.12 ppm and a 90^{th} percentile value of 0.16 ppm. These air concentration data represent actual exposures and have not been modified to account for respiratory protection because the use of respirators was not documented in the submission. It is likely that respirators were not used in most cases because the 90^{th} percentile exposures were less than the PEL.

Based on the exposure data that were provided for the commercial sterilization plant workers and health care facilities and the IRIS MLE and upper bound unit risks, the cancer risks range from 6×10^{-2} (1 in 17) to 1×10^{-1} (1 in 10) for sterilization facilities and 4×10^{-2} (1 in 25) to 8×10^{-2} (1 in 12) for health care facilities. These risks are greater than the maximum risk target of 1×10^{-4} that OPP normally uses for managing occupational cancer risk.

Conventional Uses: In support of the use of EtO for the sterilization of spices, the American Spice Trade Association (ASTA) submitted exposure monitoring of two workers at each of two facilities[7]. Each worker was monitored for 10 days and indicated what tasks they were doing throughout the day and whether they were wearing respirators for those tasks. While the study

[6] This study is not subject to the requirements of EPA's Rule for the Protection of Human Subjects of Research (40 CFR part 26) as discussed in US EPA 2022a.

[7] This study was reviewed by OPP's Human Research Ethics Reviewer, who found no barrier in law or regulation to reliance on this study in EPA actions taken under FIFRA or Section 408 of FFDCA (Arling, M., 2022, "Ethics Review of Ethylene Oxide Worker Exposure Study"). The study does not involve intentional exposure of human subjects, therefore, the requirement to consult the Human Studies Review Board does not apply.

reported that a PF50 respirator was worn, these respirators are no longer available for EtO[8]; therefore, when adjusting for the use of respirators, it was assumed that workers would be wearing self-contained breathing apparatus (SCBA) which are more protective than PF50 respirators. EtO 8-hour time-weighted averages (TWAs) for all activities, including those where respirators were not worn and those where respirators were worn, ranged from 0.01 to 0.841 ppm, with an overall average of 0.075 ppm. The 8-hr TWAs for only those activities where respirators were not worn was 0.092 ppm and the 8-hr TWAs for only those activities where SCBA was worn was 0.00002 ppm, highlighting the fact that exposures while conducting activities where a respirator was not required were driving overall exposure. The cancer risk estimate for workers conducting all activities monitored ranged from a maximum likelihood estimate (MLE) of 3×10^{-2} (1 in 36) to an upper bound of 6×10^{-2} (1 in 16). If the SCBA was worn for all tasks, the 8-hour TWA of 0.092 ppm for the non-respirator tasks would be reduced by 10,000; however, it is not likely feasible for workers to wear SCBAs for entire workdays.

For the beekeeping equipment fumigation use, there are no monitoring data specific to this use; therefore, the spice facility air concentration data were used as a surrogate. In order to account for the differences in potential exposure between workers in an indoor spice facility and workers fumigating beekeeping equipment in an outdoor chamber, the activities reported were limited to include only those that would likely occur during outdoor beekeeping equipment fumigation. A lifetime average concentration (LAC) was calculated assuming either four or eight exposure days per year, and then the cancer risks were calculated using the LAC and the adult specific inhalation unit risk of 5.5×10^{-3} per ppb. Cancer risks range from 2×10^{-4} (1 in 5,000) when assuming 4 exposure days per year to 4×10^{-4} (1 in 2,500) when assuming 8 exposure days per year.

OSHA Exposure Data

To provide context for the occupational handler exposures assessed using submitted data, EtO chemical exposure health data (i.e., PBZ air samples) that were collected during OSHA inspections were downloaded from the OSHA website[9] for the years 2008 through 2020. Combined TWAs were calculated for each facility rather than for each worker because the identity of the worker associated with each sample is not included in the chemical exposure health data. The combined TWAs range from 0.0013 ppm to 1.5 ppm for the medical equipment production and sterilization facilities, with two facilities above the OSHA PEL of 1 ppm. The combined TWAs for the health and veterinary care facilities ranged from 0.0061 to 0.022 ppm and were all below the OSHA PEL. The combined TWA of 0.082 ppm for the spice and extract manufacturing facility is also below the OSHA PEL. The OSHA data represent exposures that occur in the breathing zone and do not account for the use of respiratory protection.

Occupational Bystander Exposure

OPP considers the potential for exposure to occupational bystanders who work in non-processing areas of treatment facilities or who work near sterilization facilities. Occupational bystanders are estimated to have a cancer risk of 1×10^{-6} if their average daily concentration is 0.002 ppb. This

[8] The NIOSH approval for the PF-50 respirators (i.e., gas masks) that were previously used for EtO has been cancelled. There are no air purifying respirators approved for EtO. Only air supplying respirators can be used.
[9] https://www.osha.gov/opengov/health-samples

is based on the assumptions that these workers do not wear respirators and are exposed 8 hours per day for 240 days per year for 35 years out of a 70-year lifetime. Using the same assumptions, a cancer risk of 1×10^{-4} corresponds to an average daily concentration of 0.2 ppb.

1.0 Introduction

This memorandum revises and updates the aspects of the 2020 DRA (US EPA, 2020) that relate to human health inhalation cancer risk using the inhalation unit risk estimates from the Integrated Risk Information System (IRIS) Assessment of EtO (US EPA, 2016). This addendum does not revise the human health dietary risk assessment nor does it update the ecological risk assessment.

1.1 Review of the 2020 DRA

The 2020 Draft Risk Assessment (DRA) for ethylene oxide (EtO) included both antimicrobial and conventional uses (US EPA, 2020). The antimicrobial uses assessed include sterilization of medical supplies and equipment in commercial sterilization facilities and health care facilities and the sterilization of artifacts, archival material, library objects, cosmetics and musical instruments in commercial sterilization facilities. The conventional uses assessed include fumigation/sterilization of spices or other seasoning materials and a special local need (SLN) registration (North Carolina) for the treatment of beekeeping equipment. The 2020 DRA primarily focused on EtO (for the inhalation route) and the EtO reaction product ethylene chlorohydrin (ECH) for the dietary route – from the spice sterilization use. A quantitative dietary assessment was conducted for exposures from the spice sterilization use. Inhalation exposures to EtO were qualitatively assessed based on a variety of cancer dose response evaluations for inhalation exposure. There were no dietary risks of concern; however, risks of concern were expected for the inhalation route based on the qualitative assessment. With regard to effects to listed species, the Agency was not able to make a 'no effect' determination in the 2020 DRA due to potential exposure to terrestrial species.

1.2 Office of Air Rulemaking of EtO Emissions from Commercial Sterilization Facilities

EtO is a listed hazardous air pollutant (HAP) under Clean Air Act (CAA) section 112(b). Within EPA, the responsibility for developing the CAA emission standards and other requirements applicable to the commercial sterilizer and fumigation operations source category rests with the Office of Air and Radiation's (OAR) Office of Air Quality Planning and Standards (OAQPS). The OAR is proposing amendments to the National Emission Standards for Hazardous Air Pollutants (NESHAP) for the Commercial Sterilization Facilities source category. OAR is proposing decisions concerning the risk and technology review (RTR), including proposing amendments pursuant to the technology review for certain point source emissions and proposing amendments pursuant to the risk review to specifically address ethylene oxide (EtO) emissions from point source and room air emissions from certain groups of facilities. OPP is collaborating with OAR in these efforts.

1.3 Rationale for Use of the IRIS Assessment for Risk Assessment

In the 2020 DRA, OPP presented multiple perspectives on cancer evaluations for EtO, including the IRIS assessment (US EPA, 2016), but did not choose a single value for risk assessment. Since the publication of the 2020 DRA, and in contexts[10] other than the registration

[10]US EPA, 2022 Reconsideration of the 2020 National Emission Standards for Hazardous Air Pollutants: Miscellaneous Organic Chemical Manufacturing Residual Risk and Technology Review – Final Action. FR Doc. 2022-27522 Filed 12-20-2022.

review of EtO, EPA has continued to consider the best approach for characterizing the cancer risk associated with inhalation exposure to EtO. While there are some uncertainties associated with all of the approaches in characterizing the cancer risk (as discussed in the 2020 DRA), the EPA has determined that the IRIS assessment should be used to characterize the cancer risk associated with inhalation exposure to EtO. Therefore, OPP is using the same inhalation unit risk estimates from the IRIS assessment that are being used by OAR in their rulemaking of EtO emissions from commercial sterilization facilities.

The IRIS assessment went through "unusually extensive processes for the consideration of public comment and external peer review," and is considered by EPA's Office of Research and Development (ORD) to be the "best available scientific information regarding cancer risks from EtO[11]." In developing the IRIS assessment, ORD "utilized extensive advice" from the Science Advisory Board (SAB) and incorporated recommendations from the SAB into the IRIS assessment to address uncertainties identified by the SAB[12]. Further, since the publication of the DRA, EPA has repeatedly expressed favorable views of the IRIS assessment, including in relation to the other EtO cancer inhalation risk characterization approaches cited in the 2020 DRA[13,14].

1.4 Ethylene Oxide Formulations and Use Patterns

As of November 29, 2022, there were fifteen Section 3 end use product registrations and one Section 24(c) Special Local Need registration for EtO as an active ingredient (a.i.). EtO is formulated as a pressurized gas. The end-use products are all gas mixtures of EtO and other gases (e.g., carbon dioxide) in varying concentrations that are formulated from EPA Reg No. 36736-8, which is a manufacturing use product. Table 1 presents a summary of the registered antimicrobial and conventional end use products and uses of EtO.

Antimicrobial Uses: The registered antimicrobial uses of EtO include the fumigation/ sterilization of medical or laboratory equipment, pharmaceuticals, and aseptic packaging (21 CFR §201.1(d)(5)); and to sterilize artifacts, cosmetics, archival material, library objects, and musical instruments. The antimicrobial products are packaged in returnable bulk cylinders for use in tractor trailer sized chambers in commercial sterilization facilities or as single use cartridges or ampules for use in oven-sized chambers in health care facilities.

The application rates are not generally listed on the labels of EtO products registered for antimicrobial uses. There are two voluntary consensus standards (ANSI AAMI ISO 11135:2014 and ANSI AAMI ISO 10993-7:2008) that describe how to develop, validate, and control EtO sterilization processes for medical devices and the acceptable levels of residual EtO and ECH left on a device after it has undergone EtO sterilization. These standards help ensure levels of EtO on medical devices are within safe limits since long-term and occupational exposure to EtO has been linked to cancer. These standards are included in the FDA database of recognized consensus standards.

[11]US EPA, 2021. Memo from W. Cascio (ORD) to J. Goffman (OAR), page 1.
[12]US EPA, 2021. Memo from W. Cascio (ORD) to J. Goffman (OAR), page 4.
[13]US EPA, 2022.
[14]US EPA, 2021a. EPA Should Conduct New Residual Risk and Technology Reviews for Chloroprene- and Ethylene Oxide-Emitting Source Categories to Protect Human Health, Report No. 21-P-0129, US EPA Office of Inspector General, May 6, 2021.

Conventional Uses: EtO is a commodity fumigant/sterilant registered for use to reduce microbials on whole and ground spices or other seasoning materials (40 CFR §180.151). Additionally, a special local need registration (North Carolina) is currently in place for the treatment of beekeeping equipment. The use of EtO for the treatment of spices currently represents less than 10 percent of the total EtO pesticide use. The American Spice Trade Association (ASTA) estimates that less than 50% of spices in the U.S. are treated with EtO each year[15]. There are eight products currently registered for treatment of spices. These are all formulated as pressurized gas contained in cylinders. Sterilization/fumigation with EtO must be performed only in vacuum or gas tight chambers designed for use with EtO. The maximum application rate is 500 mg/L (or 31.22 lb a.i./1,000 ft^3) in a sealed chamber.

Table 1. Summary of EtO Registered End Use Products and Use Sites

EPA Reg. No.	% a.i.	Packaging (ETO Content)	Use Site
36736-2	100	Bulk Cylinder	Medical or laboratory items, pharmaceuticals, and aseptic packaging, (21 CFR 201.1(d)(5)), whole and ground spices or other seasoning materials (40 CFR 180.151) artifacts, archival material, library objects, cosmetics and musical instruments.
36736-3	80	Bulk Cylinder	
36736-4	10	Bulk Cylinder	
36736-5	20	Bulk Cylinder	
36736-6	12	Bulk Cylinder	
36736-7	8.5	Bulk Cylinder	
69340-2	97	Ampule (18.15 g)	Surgical instruments; hospital instruments; hospital critical equipment; heat labile materials; oral and inhalation equipment; diagnostic instruments/equipment; hospital critical rubber/plastic items; hospital materials; first aid equipment; veterinary hospital instruments; veterinary hospital critical equipment; human face gear; contact lens.
69340-4	96	Cartridge (5 to 14 g)	
69340-5	90	Cartridge (4.5 g)	
69340-6	96	Cartridge (10.5 g)	
69340-7	97	Ampule (17.6 g)	
69340-9	97	Cartridge (17.6 g)	
7182-1	100	Cartridge (100 to 170 g)	Medical equipment and supplies, musical instruments, library/museum artifacts, and cosmetics.
73711-5	100	Ampule (100 to 170 g)	Medical or laboratory items, pharmaceuticals, and aseptic packaging, cosmetics, and artifacts, archival material or library objects.
89514-1	100	Bulk Cylinder	Medical or laboratory items, pharmaceuticals, and aseptic packaging, cosmetics, spices or other seasoning materials, artifacts, archival material or library objects, musical instruments.
NC140003	8.5	Bulk Cylinder (parent label)	Special Local Need for beekeeping equipment in North Carolina. The parent label is 36736-7.

1.5 Anticipated Exposures

As stated previously, the purpose of this document is to quantitatively assess the cancer risks from inhalation exposures to EtO. In commercial sterilization facilities, where there are separate treatment chambers and aeration rooms, occupational inhalation exposures primarily occur when moving treated materials, such as medical equipment, from the treatment chambers to the aeration rooms and when moving the aerated material out of the aeration rooms to the warehouse for shipping. These transfers are typically done using forklifts. In some commercial sterilization facilities, such as those for spices, treatment and aeration is done in the same chamber (all-in-one treatment) which eliminates the exposure that is associated with moving materials prior to

[15]ASTA, 2017. Clean, Safe Spices: Guidance from the American Spice Trade Association. 2017 Update. https://www.astaspice.org/food-safety/clean-safe-spices-guidance-document/.

aeration. Exposures also occur in commercial sterilization facilities when changing cylinders and when repairing leaks.

The all-in-one treatment method is also used on a much smaller scale in health care and veterinary facilities where the treatment and aeration occur in the same oven-sized chamber using cartridges and ampules that contain 4.5 to 170 grams of EtO. For the beekeeping use, the treatment is done in a 126 ft^3 chamber that is located at an off-campus research facility of a state university.

In addition to the occupational exposures that occur within the processing areas of a treatment facility, health care facility, or beekeeping equipment treatment area, occupational bystander exposures may occur in non-processing areas of a treatment facility, health care facility, or beekeeping equipment treatment area, in "downstream" facilities where the treated product is shipped and stored, or in other businesses or workplaces that are near the treatment facility, health care facility or beekeeping equipment treatment area.

There are no EtO products that can be purchased by consumers, therefore, there is no potential for residential handler applications; however, there is the potential for non-occupational/ residential bystander exposures to persons living near commercial sterilization facilities. OAR is proposing to address residential bystander exposures through amendments to the NESHAP for the Commercial Sterilization Facilities source category. EtO emissions from hospitals where EtO is used are addressed in a different NESHAP that OAR promulgated in 2006—the NESHAP for Hospital Ethylene Oxide Sterilizers— and OAR plans to evaluate the risks from hospital sterilizers in an upcoming regulatory review. In addition, there is the potential for non-occupational/non-residential exposure for people who spend significant time for non-work related activities (e.g., school, daycare, shopping, etc.) in the areas that are between the fence line of a commercial sterilization facility and the nearest residence. OPP's assessment of risks from non-occupational/residential bystander and non-occupational/non-residential bystander exposures are included in this addendum.

1.6 Label Requirements

Currently, all labels indicate the Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) is an 8-hr time weighted average (TWA) of 1 ppm[16] and the short term excursion limit (STEL) for 15 minutes is 5 ppm. All labels require personal protective equipment (PPE) consisting of a long-sleeved shirt, long pants, shoes plus socks, chemical-resistant gloves and a respirator. If the worker could have eye or skin contact with EtO or EtO solutions, they must wear chemical-resistant attire (e.g., apron or footwear) and face-sealing goggles, a full-face shield, or a full-face respirator. There are no EtO solutions registered, only gas, and therefore, language relating to EtO solutions is not necessary. Labels for the spice uses also include language that requires all applications to be made using an EtO sterilization method that uses a single sterilization chamber to precondition and aerate (i.e., an all-in-one system).

[16]Per the Ethylene Oxide Standard 29 CFR 1910.1047.

2.0 Toxicological Effects and Endpoints for Human Health Risk Assessment

The agency's published 2020 DRA includes a complete toxicological profile of EtO that characterizes non-cancer effects from all exposure routes including oral, inhalation and dermal. In this current 2023 DRA addendum, only cancer risks from inhalation exposures to EtO are being evaluated. Carcinogenic effects of EtO are observed at lower exposures (i.e., ppb and below) compared to non-carcinogenic effects; thus, any mitigation for carcinogenic effects is also protective of non-carcinogenic effects, including neurotoxicity, because the non-cancer effects occur at much higher exposures (i.e., ppm levels). The effects from inhalation exposure are also protective of the other exposure routes, because EtO is a gas at room temperature, and inhalation exposure is the predominant route of exposure to gases. In addition, the pulmonary region of the respiratory tract (i.e. the lungs) for the average adult has a surface area of 54 m^2 (US EPA, 1994) which is 27 times greater than the surface area of the skin which is 2.2 m^2 for the average adult (US EPA, 2011).

2.1 Inhalation Unit Risk Estimates for Carcinogenicity

In the 2020 DRA, the Agency cited several data sources that characterized the carcinogenicity of EtO. The Agency presented multiple perspectives on the carcinogenicity of EtO and summarized the risks from these perspectives. A single perspective was not chosen at that time.

As discussed in Section 1.0, the Agency has now determined in this 2023 DRA addendum that the inhalation unit risk estimates published in the IRIS assessment (US EPA, 2016), which was one of the risk estimates discussed in the 2020 DRA, should be used to characterize the cancer inhalation risk from EtO for the purpose of this Registration Review.

2.1.1 Inhalation Unit Risk Estimates for Continuous Environmental Exposures

The inhalation unit risk estimates for environmental exposure are listed in Table 2. These unit risks are the preferred estimates highlighted in bold in Table 1.1 of the IRIS assessment (US EPA, 2016). These unit risks were developed for use with continuous environmental exposure (i.e., 24 hours a day for seven days a week for a 70 year lifetime) to EtO where maximum modeled levels are on the order of 1−2 µg/m^3 (0.5 to 1.0 ppb) as discussed on page 99 of section 4 of the IRIS assessment. These unit risks are not applicable to higher level exposures, such as those that may occur occupationally, which appear to have a different exposure-response relationship.

Because the weight of evidence supports a mutagenic mode of action for EtO carcinogenicity, and as there are no chemical-specific data from which to assess early-life susceptibility, increased early-life susceptibility was assumed, in accordance with the EPA's Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens (US EPA, 2005). To calculate lifetime risks, the risk associated with each of the three relevant time periods is calculated using age dependent adjustment factors (ADAFs). The ADAF is 10 for the first 2 years of life, 3 for ages 2 through <16, and 1 for ages 16 and above.

The inhalation unit risk estimate for full lifetime exposures is **5.0 x 10^{-3} per µg/m^3 (9.15 x 10^{-3} per ppb)** as listed in Table 2. The unit risk accounts for the application of ADAF adjustments for

the exposures that occur in the first 16 years of life and, therefore, can be used with exposures that have not been adjusted for ADAFs to estimate inhalation cancer risk. The inhalation unit risk estimate for adult-based exposures is **3.0 x 10^{-3} per ug/m^3 (5.5 x 10^{-3} per ppb**). This unit risk does not include the ADAF adjustments because it is intended for use to evaluate exposures that occur from age 17 to age 70.[17] If exposures are available that have already been adjusted using ADAFs for early life exposures, then this unit risk can also be used for lifetime exposures.

Table 2. IRIS Inhalation Unit Risks for Environmental Exposures to EtO

Basis	Exposure Duration	Inhalation Unit Risk Estimate		Comment
		$(\mu g/m^3)^{-1}$	$(ppb)^{-1}$	
Total cancers based on human data – lymphoid cancers incidence and breast cancer incidence in females	Full Lifetime	5.0 x10^{-3}	9.15 x10^{-3}	Includes ADAF adjustments for lifetime exposures. Can be used with exposures that do not account for the ADAF adjustments.
	Adult - Based	3.0 x10^{-3}	5.5 x10^{-3}	Requires that ADAF adjustments be applied to the estimated exposure at each lifestage up to 16 years if used for lifetime exposures.
Note. The unit risks are listed as $(\mu g/m^3)^{-1}$ in Table 1.1 of the IRIS assessment (US EPA, 2016). They were converted to ppb by multiplying by 1.83 $\mu g/m^3$ per ppb. [*i.e.* $(\mu g/m^3)^{-1}$ * 1.83 $\mu g/m^3$ per ppb = $(ppb)^{-1}$]				

Source: Table 1-1 of the IRIS Assessment (US EPA, 2016).

2.1.2 Inhalation Unit Risk Estimates for Occupational Exposures

In the IRIS assessment (US EPA, 2016), cancer risk estimates are provided for occupational exposures. These exposures are assumed to occur for eight hours a day, 240 days per year for 35 years at a certain concentration. Cancer risk estimates are provided for exposures in the range of 0.1 to 1.0 ppm and for exposures that are less than 0.1 ppm.

Continuous Occupational Exposures from 0.1 ppm to 1.0 ppm

According to IRIS assessment (US EPA, 2016, Section 4, page 99), "*The unit risk estimates derived in the preceding sections were developed for environmental exposure levels, where maximum modeled levels are on the order of 1−2 μg/m^3 … i.e., roughly 0.5−1 ppb, and are not applicable to higher exposures, including some occupational exposure levels…The occupational exposure scenarios of interest to the EPA include …exposure levels in the nonlinear range of some of the models (i.e., above the maximum exposure level at which the low-dose-linear unit risk estimates apply). Therefore, extra risk estimates were calculated for a number of occupational exposure scenarios of possible concern. Extra risk estimates are estimates of the extra cancer risk above background and are the same type of estimate that one gets from multiplying a unit risk estimate by an exposure level*."

The extra cancer risk estimates presented in the IRIS assessment (US EPA, 2016) for total cancers (lymphoid and breast cancers) are shown in Table 3. The EtO air concentrations used to illustrate the cancer risks range from 0.1 ppm to a maximum of 1.0 ppm, which is the Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL). For occupational exposures, a maximum likelihood estimate (MLE) and an upper-bound estimate are provided. An upper bound estimate is considered a "higher" value that is still considered

[17]In page 4-25 of the IRIS assessment (US EPA, 2016), the EPA default average lifespan is listed as 70 years. This value is also listed in the EPA's Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens (US EPA, 2005).

reasonable with regard to its probability of occurring (e.g., a 95th percentile value); whereas a MLE is the most probable overall, but not the most probable "high" value like the upper bound estimate.

Table 3. IRIS Extra Risk Est. for Total Cancer Incidence for Occupational Exposure Levels

8-hour TWA (ppm EtO)	Maximum likelihood [risk] estimate[a,b]	Upper-bound [risk] estimate[a,b]
0.1	0.037	0.081
0.2	0.058	0.13
0.3	0.072	0.15
0.4	0.085	0.18
0.5	0.094	0.19
0.6	0.10	0.20
0.7	0.10	0.21
0.8	0.11	0.21
0.9	0.11	0.21
1.0	0.11	0.22

[a]Assuming a 35-yr exposure between ages 20 and 55 years.
[b]From combining results for lymphoid cancer incidence in both sexes and breast cancer incidence in females.
*Source: Table 4-30 of EPA/635/R-16/350Fa, December 2016 (US EPA 2016).

Continuous Occupational Exposures from less than 0.1 ppm to 0.001 ppm

The cancer risks for occupational exposures that are less than 0.1 ppm can be calculated using the formulas listed in Section 4, page 111 of the IRIS assessment (US EPA, 2016). There are formulas for the 95% upper confidence limit (UCL)[18] and MLE of extra risk for total cancer incidence. According to the IRIS assessment: *"For total cancer risk, low-exposure linear extrapolation from the total cancer extra risk estimates for the 0.1 ppm 8-hour TWA exposure level presented in Table 4-30 of the assessment is recommended. Both of the underlying models are linear in the low-exposure range (e.g., at the 0.1 ppm TWA and below); thus, their sum is also linear. For 35-year exposures, the following formulae would apply:"*

95% UCL on extra risk for total cancer incidence ≈ (8-h TWA occ exp [in ppm]) × (0.081/0.1 ppm)
= (8-h TWA occ exp [in ppm]) × (0.81/ppm)

MLE of extra risk for total cancer incidence = (8-h TWA occ exp [in ppm]) × (0.037/0.1ppm)
= (8-h TWA occ exp [in ppm]) × (0.37/ppm)

For the purposes of this assessment, the above formulas have been simplified as follows:

- 95% UCL, Total Cancer Incidence = 8-hour TWA (ppm) x (0.81/ppm)
- MLE, Total Cancer Incidence = 8-hour TWA (ppm) x (0.37/ppm)

[18] The sum of the 95% UCLs for the two cancer types is the upper bound shown in Table 4-30 (US EPA, 2016, section 4, page 109).

Continuous Occupational Exposures less than 0.001 ppm

The cancer risks for occupational exposures that are less than 0.001 ppm (i.e. 1 ppb) are calculated using the adult specific inhalation unit risk of $5.5x10^{-3}$ per ppb from Table 2. This is because the inhalation unit risks in Table 2 were developed for environmental exposure levels, where maximum modeled levels are on the order of roughly 0.5−1 ppb (US EPA, 2016).

Intermittent Occupational Exposures

The beekeeping equipment use, where applications are made on an "as needed" basis instead of on a daily basis, results in intermittent occupational exposures. The IRIS assessment does not provide specific cancer risk estimates for these exposures. Normally, these exposures are assessed by calculating a lifetime average concentration (LAC) and multiplying the LAC by the continuous exposure unit risk. In the case of EtO, this approach is only valid if the LAC is less than 0.001 ppm (1 ppb). If the LAC is greater than 1 ppb, then the section 4 formulas should be used with adjustments made to account for the days of exposure per working year.

As noted in the 2020 DRA (US EPA, 2020), in 2008, information specific to the beekeeping equipment use was received from North Carolina indicating that use is approximately 40 times per year (electronic mail correspondence from Dan Hopkins, NC Dept. of Agriculture to Susan Bartow, EPA/OPP/SRRD; 2/7/2008), as opposed to a potential year-round operation like the spice treatment facilities. In 2020, updated information was received that there had been eight treatments for beekeeping equipment between January 2019 and October 2020 (call held with NCDA-CS on 10/20/20). Therefore, a range of exposure days per year was assumed (four or eight exposure days) for the cancer assessment for the beekeeping equipment fumigation use. Worker monitoring data specific to the beekeeping use are not available and it has been assumed that estimated exposures for the spice industry would be protective of the treatment of beekeeping equipment with EtO. Therefore, the exposure data for the spice use has been adjusted for the difference in exposure days per year (i.e., 4 or 8 days/240 days).

2.2 Levels of Concern for Cancer Risks

Levels of concern for cancer risks are typically determined during risk mitigation (rather than risk assessment), when benefits of the use and feasibility of reducing exposures are also considered. Under the Federal Insecticide Fungicide and Rodenticide Act, OPP applies a "no unreasonable risk" standard for both dietary and non-dietary exposures in making a risk management decisions. To help initially identify chemicals which may pose such unreasonable risks, OPP considers whether the risks from a chemical exceed a specified level of concern. If a given risk exceeds this level, OPP decides what further action, if any, is needed. OPP generally seeks to reduce the risk to 1×10^{-6} (1 in a million) for both occupational and residential exposures. In some cases, a risk target of up to 1×10^{-4} (100 in a million) may be used for occupational exposures in consideration of benefits and feasibility of mitigation measures.

In the OAR assessment of EtO risk from commercial sterilizers, community cancer risks that are greater than 100 in a million are considered to be elevated[19]. OAR is proposing to require emissions controls to reduce the risk to less than 100 in a million.

2.3 Occupational Exposure Limits for Ethylene Oxide (EtO)

Occupational exposure limits have been established for EtO by the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH) and the California Division of Occupational Safety and Health (Cal/OSHA). These limits are summarized in Table 4. The limits are expressed as 8-hour time weighted averages (TWAs), which represent the average exposure during an 8-hour workday, or as short-term exposure limits (STELs), which represents the exposure of a 10- or 15-minute period within the workday. The purpose of these limits is to reduce cancer risks for workers exposed to EtO. In 1984, OSHA established a permissible exposure limit (PEL) of 1 ppm as an 8-hour TWA and in 1988, OSHA added a short term excursion limit of 5 ppm as a 15-minute TWA. These values are enforceable by OSHA under 29 CFR 1910.1047. These values were also adopted by Cal/OSHA in 1985 and are enforceable under section 5220 of Title 8 of the California Code of Regulations. NIOSH established the recommended exposure limit (REL) of <0.1 ppm as an 8-hour TWA in 1981 and added the REL-STEL of 5 ppm as a 10 minute TWA in 1983. ACGIH established a threshold limit value (TLV) of 1.0 ppm as an 8-hour TWA in 1984. Both the NIOSH RELs and the ACGIH TLV are recommended values that are not enforceable.

In 2019, the ACGIH adopted the biological exposure indexes (BEIs) for EtO that were proposed in 2018 (ACGIH, 2018). These include a BEI of 5,000 pmol HEV/g globin for N-(2-hydro-xyethy) valine (HEV) hemoglobin adducts in blood and a BEI of 5 ug HEMA/g creatinine for S-(2-hydroxyethyl)mercapturic acid (HEMA) in urine. The BEI for HEV is set at a level that is associated with airborne equivalent to the TLV of 1 ppm integrated over the past 120 days. The BEI for HEMA is based on the upper 95th percentile reported in the 2014 correction of the 2011/2012 National Human and Nutrition Examination study (CDC, 2014 as cited in ACGIH, 2018).

With the exception of the new BEIs adopted by the ACGIH, the above exposure limits have not been updated since they were established in the 1980s. In a regulatory review of the OSHA EtO Standard (OSHA, 2005), it was concluded that the EtO Standard should be continued without change and does not need to be revised or rescinded to minimize economic impacts on small entities. The OSHA website at https://www.osha.gov/annotated-pels currently indicates that "OSHA recognizes that many of its permissible exposure limits (PELs) are outdated and inadequate for ensuring protection of worker health".

[19] https://www.epa.gov/hazardous-air-pollutants-ethylene-oxide/forms/ethylene-oxide-risk-commercial-sterilizers

Table 4. Ethylene Oxide Occupational Exposure Limits

Organization and Year Established	Exposure Limit Type	8-hour TWA	10- or 15-Minute STEL	Action Level[a]
OSHA (1984)	Permissible Exposure Limit (PEL)	1 ppm[b]	5 ppm[c]	0.5 ppm
NIOSH (1981)	Recommended Exposure Limit (REL)	< 0.1 ppm[d]	5 ppm[e]	Not Applicable
ACGIH (1984)	Threshold Limit Value (TLV)	1 ppm	Not Applicable	Not Applicable
Cal OSHA (1985)	Permissible Exposure Limit (PEL)	1 ppm	5 ppm	0.5 ppm

[a] Action Level: Concentration as an 8-hour TWA, above which the employer must initiate certain compliance activities such as periodic employee exposure monitoring and medical surveillance.
[b] The employer shall ensure that no employee is exposed to EtO in excess of the PEL as an 8-hour TWA.
[c] The employer shall ensure that no employee is exposed to EtO in excess of the STEL as averaged over a period of 15 minutes.
[d] The REL of <0.1 ppm is based on the limit of detection.
[e] The NIOSH REL-STEL is based on a sampling period of 10 minutes.

3.0 Occupational Exposure and Risk Assessment

There is potential for occupational handler inhalation exposure from the registered uses of EtO. Occupational dermal exposures are not expected given the high vapor pressure of EtO and based on the delivery systems used (which include pressurized cylinders).

In the 2020 DRA (US EPA, 2020), OPP summarized personal breathing zone (PBZ) air monitoring data from registrant-submitted studies for sterilization plant workers, health care facilities and workers involved in the treatment of spices. These PBZ air monitoring data represent observational monitoring during routine workdays and are expressed as 8-hour TWA air concentrations when compared to the OSHA PEL of 1.0 ppm or as 15-minute TWAs when compared to the OSHA EL of 5 ppm. No new occupational exposure data have been submitted since the 2020 DRA.

3.1 Occupational Handler Exposures and Cancer Risks

3.1.1 Occupational Exposure Data Submitted to EPA

A summary of available exposure data included in the 2020 DRA is presented in Table 5.

Antimicrobial Uses - Sterilization Plants: Air concentration data from a sterilization plant worker study (MRID 50231101) were submitted. The study contains 1,273 PBZ air samples that were collected using 3M passive sampling badges. These badges are typically fastened to the workers' lapel and they represent the exposure that occurs outside the respirator.

Only data with a reporting time of 210 minutes or more were used. The study report indicates that this was done because OSHA defines full-shift sampling "…as a minimum of the total time of the work shift less one hour (e.g., seven hours of an 8-hour work shift or nine hours of a ten-hour work shift)…" and samples from periods of at least half a day (i.e., 420 / 2) were considered to reflect TWA exposures. The sample times ranged from 210 to 420 minutes for four samples, 420 to 480 minutes for 1,121 samples and 480 to 772 minutes for 148 samples.

The reported EtO air concentrations for all 1,273 samples ranged from 0.002 ppm to 35 ppm[20]. Of the 1,273 samples, 80 samples (6.3%) were reported as less than the level of detection (LOD). The reported LOD for a 480-minute sample was 0.026 ppm and one half the LOD (i.e., 0.013 ppm) was used for calculating exposures. This LOD is comparable to the reporting limit of 0.01 ppm[21] for an 8-hour sample using a 3M badge that has a sampling rate of 12 ml minute (3M, 2021).

The study report indicates the current industry standard is to use supplied air respiratory protection with a protection factor of 1,000 or a pressure-demand self-contained breathing apparatus (SCBA) with a protection factor of 10,000. The protection factor of 1,000 for airline respirators operated in pressure demand mode (OSHA, 2009) was used to estimate exposure for the workers that wore respirators. Of the 1,273 samples, respirators were worn at all times for 6 samples and respirators were worn part of the time for 605 samples. For these 611 samples, the use of respirators was accounted for by dividing the sample result for exposure period when the respirator was worn by the protection factor of 1,000. Respirators were not worn at any time during monitoring for 662 samples; therefore, the respirator exposure adjustments were not made for these samples. As shown in Table 7, the calculated exposures for all 1,273 samples ranges from 0.002 to 4.6 ppm with an arithmetic mean of 0.23 ppm. The calculated exposures for the 611 samples when workers wore a respirator at any time during sampling ranges from 0.013 to 2.2 ppm with an arithmetic mean of 0.18 ppm. 22.5 percent of these calculated exposures are below the LOD and are reported as one half the LOD. If the actual calculated exposures are reported rather than half the LOD, the calculated exposures range from 0.00011 to 2.2 ppm with an arithmetic mean of 0.18 ppm (US EPA, 2023). The exposures for the 662 workers who did not wear a respirator at any time during sampling ranges from 0.002 to 4.6 ppm with an arithmetic mean of 0.27 ppm.

The estimates for the 605 samples when workers wore respirators part of the time is based on 6 different calculation methods that attempted to quantify the EtO air concentrations during the times respirators were and were not worn during the period that the air samples were collected. This was done because only one 8 hour air sample is typically collected per worker per day in accordance with the OSHA standard and because respirators are only required in certain areas during certain tasks (i.e., moving a load from the treatment cylinder to the aeration cylinder). These tasks are done at intermittent times and are mixed in with other tasks (such as monitoring the process in the control room or working in the warehouse) that do not require respiratory protection. Ideally, a separate air sample would have been taken for each interval when a worker was in a certain area doing a certain task. The results of these samples in combination with information on when respirators were worn would allow for a more accurate estimation of the worker exposure that occurs underneath the respirator.

In addition, when accounting for the use of respirators, only those exposure estimates reflecting respirator use were adjusted for the protection factors. Exposure estimates not reflective of the use of a respirator were not adjusted. Because of this, the exposure estimates are driven by exposures that occur when respirators are not worn and are not significantly different when the

[20]In the DRA (US EPA 2020), it is stated that "the reported TWA EtO concentrations for all 1,273 workers ranged from 0.002 ppm to 4.6 ppm". These values are actually the calculated TWAs that included the use of respirators. The reported air concentrations are the values that were measured and they ranged from 0.002 to 35 ppm.

[21]In the DRA (US EPA 2020), the LOD was reported to be 0.7 ppb (0.0007 ppm) for an 8 hour sample based on OSHA Method 49 for EtO. This was based on the 3M badge airflow rate of 49.3 mL/minute and the detection limit of 0.03 ug/sample.

protection factors are increased from PF-1,000 to PF-10,000 (US EPA, 2023). The arithmetic mean exposure is 0.22 ppm when the PF is 10,000 which is only slightly less than the arithmetic mean exposure of 0.23 ppm when the PF is 1,000.

Antimicrobial Uses - Health Care Facilities: The 3M Health Care Facility data from 2012 (MRID 50231102) were presented at a May 15, 2015, meeting at the U.S. Food and Drug Administration (FDA). The exposures range from 0.026 ppm to 10.2 ppm with an average of 0.12 ppm and a 90th percentile value of 0.16 ppm. The lowest value was not reported in the submission and is estimated to be 0.026 ppm, which is the LOD for an 8-hour badge sample that was reported for sterilization worker study. Since the data were provided only as summary as included in the presentation to show how exposures have decreased since the implementation of the OSHA – PEL in hospitals, it is not known exactly how many health care facilities were included or what tasks were associated with the measured exposures. These data are the actual exposures and have not been modified to account for respiratory protection because respirator use information was not included in the submission. It is likely that respirators were not used in most cases because the 90th percentile value of 0.16 ppm is below the OSHA PEL of 1.0 ppm.

Conventional Uses -Spice Sterilization Facilities: In support of the use of EtO for the sterilization of spices, the ASTA submitted exposure monitoring of two workers at each of two facilities (MRID 47338301; D347717). Each worker was monitored for 10 days at facilities that ASTA claims treat the majority of spices in the United States. Activities monitored included unloading/loading chambers, cleaning chambers, charging the chamber with EtO, receiving untreated product, shipping treated product, sampling EtO treated product, etc. (see Appendix A for a full list of activities). For some of these activities, workers wore a respirator (per the label requirements); however, for some activities workers did not wear a respirator and would not be required to per the product label. The Agency believes the data – representing a total of 40 EtO exposure-days – are a reasonable representation of EtO exposure throughout the spice industry.

Air concentrations were collected utilizing a continuous monitoring instrument (BW Technologies, Inc. GasAlert Extreme) set to record EtO exposure throughout the day with a LOD of 0.1 ppm. Results submitted to the Agency included the following:

- 5-minute instantaneous readings (e.g., 0.2 ppm at 7:05 AM, 0.1 ppm at 7:10 AM, etc.);
- 15-minute rolling averages;
- 8-hour rolling averages;
- Activity specific information corresponding to each 5-minute reading;
- "Yes/No" indication for respiratory protection (a PF50 MSA Ethylene Oxide Gas Mask – NIOSH Certification TC 14G-0202) worn during time of reading; and,
- 8-hour TWA results from a ChemChip™ Ethylene Oxide Personal Monitor by Assay Technologies, Inc.

While the study reported that a PF50 respirator was worn, these respirators are no longer available for EtO[22]; therefore, it was assumed that workers would be wearing self-contained breathing apparatus (SCBA) which are more protective than PF50 respirators. A protection factor of 10,000 was then applied to those 5-minute averages where a respirator was worn, and daily averages were calculated. For results showing no exposure (i.e., non-detects), half the

[22] The NIOSH approval for the PF-50 respirators (i.e., gas masks) that were previously used for EtO has been cancelled. There are no air purifying respirators approved for EtO. Only air supplying respirators can be used.

LOD (0.1 ppm) was used as is standard Agency practice; unless EtO was detected, breaks and lunch were not included. Of note, many of the samples for the workers were less than the LOD and therefore, many values were included in the calculations as ½ LOD or 0.05 ppm, which impacted the overall arithmetic mean calculated.

Also of note, MRID 50231101 (mentioned above under the antimicrobial uses) indicates on page 6, *"whereas most of the data were obtained from facilities that sterilized medical equipment, badge data were obtained from two facilities which treat spices exclusively and from at least one other facility which treated both medical equipment and spices on days when badge monitoring was conducted."* Therefore, some of the data from this study would also be representative of spice facility fumigations as well.

Conventional Uses - Beekeeping Equipment:

Based on information provided at the time of the EtO RED (US EPA 2008), the beekeeping equipment use of EtO is limited to a state-managed facility in North Carolina. The North Carolina Department of Agriculture and Consumer Affairs (NCDA&CS) uses 2 vacuum tight chambers designed for use with EtO. Both chambers are located outdoors. Monitoring data specific to the beekeeping equipment fumigation use are not available; however, based on the label directions and requirements for the SLN beekeeping equipment use (related to EPA Reg. # 36736-7), it is anticipated that the ASTA monitoring data for the spice facilities would be protective of the beekeeping use and was used as a surrogate. While the exact tasks and environment (indoor spice facility versus outdoor beekeeping equipment fumigation chamber) may not be the same between the two uses, the data provide an estimate of potential exposure. In order to better represent the potential exposures from fumigating beekeeping equipment, the activities reported were limited to those that would likely occur during outdoor beekeeping equipment fumigation (see Appendix A).

Previously, information submitted to the Agency for EtO sterilization of beekeeping equipment in North Carolina indicated that use is approximately 40 times per year (electronic mail correspondence from Dan Hopkins, NC Dept. of Agriculture to Susan Bartow, EPA/OPP/SRRD; 2/7/2008), as opposed to a potential year round operation like the spice treatment facilities. However, this number has reportedly decreased even more in recent years; information provided in 2020 from North Carolina indicated that only eight treatments had been conducted between January 2019 and October 2020 (i.e., about 4 per year). In order to account for any potential variation in number of treatments, both four and eight treatments per year were assumed for the beekeeping equipment fumigation use.

Table 5. EtO Occupational Air Concentration and Exposure Data Submitted to EPA

Data Source	Number of Facilities Monitored	Number of Air Samples Collected	EtO Exposures (ppm)	
			Range	Arithmetic Mean
Sterilization & Spice Plant Worker Exposure Study (MRID 50231101)[a]	25	1,273	0.002 to 4.6	0.23
3M Health Care Facility Data (MRID 50231102)[b]	More than 34	647	0.026 to 10.1	0.12
ASTA Worker Exposure Study (MRID 47338301; D347717)[c]	2 (2 workers at each facility)	40	0.01 – 0.841	0.075

[a] MRID 50231101. Ethylene Oxide Exposures for Ethylene Oxide Sterilization Plant Workers, Acta Group, 3/31/2017. The EtO exposures reflect the use of PF 1,000 respiratory protection when it was worn for specific tasks.
[b] MRID 50231102. Supplemental Information on State Controls Affecting Ethylene Oxide Emissions, Targeted Monitoring Data near Operating Chambers, and Monitoring Data from Health Care Facilities. Acta Group, 3/31/2017. Includes data from passive EtO monitors in health care facilities across 33 states and Puerto Rico in 2012. The EtO exposures are the actual measured air concentrations and do not reflect the use of respiratory protection.
[c] MRID 47338301. Render, C. 2008. Ethylene Oxide Worker Exposure Study. Sponsored by the American Spice Trade Association (ASTA). The EtO exposures reflect the use of SCBA respiratory protection for only certain activities when it was indicated that respirators were worn.

3.1.2 Occupational Cancer Risks for Handlers Using EtO

Antimicrobial Uses – The cancer risks for the antimicrobial uses were calculated using the arithmetic mean of the submitted exposure data for commercial sterilizer and health care facilities. Since these facilities operate on a continuous basis, the submitted exposure data were assumed to represent a 35-year occupational exposure between ages 20 and 55 years. The cancer risks for the exposure were, therefore, estimated using the table "Extra Risk Est. for Total Cancer Incidence for Occupational Exposure Levels" which is included as Table 3 in this document and Table 4-30 of the IRIS assessment (US EPA, 2016). The MLE and upper bound cancer risk estimates are included in Table 6 and range from 4×10^{-2} (1 in 25) to 1×10^{-1} (1 in 10), depending upon which facility type and cancer risk estimate is considered. The upper bound cancer risks are approximately twice the MLE cancer risks.

Table 6. Occupational Handler Cancer Risks for the Antimicrobial Uses

Data Source	Arithmetic Mean 8-hr TWA (ppm)	Cancer Risks[c]	
		MLE	Upper Bound
Sterilization Plant Worker Exposure Study (MRID 50231101)	0.23[a]	6×10^{-2} (1 in 17)	1×10^{-1} (1 in 10)
3M Health Care Facility Data (MRID 50231102)	0.12[b]	4×10^{-2} (1 in 25)	8×10^{-2} (1 in 12)

[a] Air samples were adjusted to account for the use of PF-1,000 Supplied Air Respirators if the worker wore a respirator during the sampling period. This adjustment was made for 611 of the 1273 samples.
[b] Air samples were not adjusted to account for respirators since it is not known if respirators were worn.
[c] Risks are for total cancers and are taken from IRIS Table 4-30. Risks are rounded to one significant figure.

Conventional Uses – Spice Facilities: The cancer risks for the conventional spice uses were calculated using the arithmetic mean of the submitted exposure data for the spice facilities. Since these facilities operate on a continuous basis, the submitted exposure data were assumed to represent a 35-year occupational exposure between ages 20 and 55 years. Since the exposure is less than 0.1 ppm, however, the cancer risks for the exposure could not be estimated using Table 4-30 of the IRIS assessment (US EPA, 2016) and instead MLE and Upper Bound cancer risks were calculated using the formulae listed on page 4-111 of the IRIS assessment (as described in Section 2.1.2 above, for *Continuous Occupational Exposures from less than 0.1 ppm to 0.001 ppm*).

As noted above, some of the workers did not wear respirators during the time that they were monitored when they were doing activities for which a respirator was not required. Therefore, when calculating exposures, respiratory protection factors were only applied to concentrations measured during activities when a respirator was worn. Concentrations measured during activities when no respirator was worn (and is not required to be worn according to the product labels) were not adjusted for any respiratory protection factors. A summary of the cancer risks is

presented in Table 7. Cancer risks range from 3 x 10^{-2} (1 in 36) for the MLE to 6 x 10^{-2} (1 in 16) for the upper bound.

Table 7. Occupational Handler Cancer Risks for the Conventional Spice Uses

Data Source	Arithmetic Mean 8-hr TWA (ppm)	Cancer Risks[a]	
		MLE	Upper Bound
ASTA Worker Exposure Study (MRID 47338301; D347717)	0.075	3 x 10^{-2} (1 in 36)	6 x 10^{-2} (1 in 16)

[a] MLE of extra risk for total cancer incidence = (8-h TWA [ppm]) × (0.37/ppm). Upper Bound (95% UCL) on extra risk for total cancer incidence = (8-h TWA [ppm]) × (0.81/ppm).

Special Local Need –Beekeeping Equipment Fumigations: As noted above, the cancer risks for the beekeeping equipment use were calculated using the arithmetic mean of the submitted exposure data for the spice facilities. In order to account for the differences in potential exposure between workers in an indoor spice facility and workers fumigating beekeeping equipment in an outdoor chamber, the activities reported were limited to those that would likely occur during outdoor beekeeping equipment fumigation (see Appendix A). Since the beekeeping fumigation exposures are considered "intermittent occupational exposures", as noted above in Section 2.1.2, a lifetime average concentration (LAC) was calculated, assuming either four or eight exposure days per year, and then the cancer risks were calculated using the LAC and the adult specific inhalation unit risk of 5.5 x 10^{-3} per ppb.

A summary of the cancer risks is presented in Table 8. Cancer risks range from 2 x 10^{-4} (1 in 5,000) when assuming four exposure days per year to 4 x 10^{-4} (1 in 2,500) when assuming eight exposure days per year.

Table 8. Occupational Handler Cancer Risks for the Beekeeping Use

Data Source	Arithmetic Mean[a] 8-hr TWA (ppm)	Assumed Exposure Days Per Year for Beekeeping Use	Lifetime Average Concentration[b] (LAC) (ppm)	Cancer Risks[c]
ASTA Worker Exposure Study (MRID 47338301; D347717)	Subset of spice fumigation activities reported			
	0.02	4 days	3.7 x 10^{-5}	2 x 10^{-4} (1 in 5,000)
		8 days	7.3 x 10^{-5}	4 x 10^{-4} (1 in 2,500)

[a] Spice facility air sample data subset to account for tasks most likely to occur with an outdoor fumigation chamber (see Appendix A). For some of these activities, workers wore a respirator, and an adjustment was made to account for use of SCBA for those activities. For activities where a respirator was not reported to be worn, no adjustment was made.
[b] LAC = 8-hr TWA Arithmetic Mean (ppm) * (8 hour/24 hour) * [(4 or 8 exposure days) / 365 days] * (35 years / 70 years)
[c] Cancer Risk = LAC (ppm) * 1,000 ppb per ppm * Inhalation Unit Risk (5.5 x 10^{-3} per ppb).

3.1.3 Comparison to Occupational Exposure Data Available from OSHA

To provide context for the occupational exposures assessed above, EtO chemical exposure health data (i.e., air samples) that were collected during OSHA inspections are included in Table 9 below. These data were downloaded as Chemical Exposure Health Data from the OSHA website at https://www.osha.gov/opengov/healthsamples.html. Data for the years 2008 through

2020[23] were downloaded and screened to eliminate area samples, bulk samples and blank values leaving only personal breathing zone samples. Data were also deleted for industries, such as chemical manufacturing, that are not relevant for FIFRA registered uses. The remaining data are summarized in Table 9 below. Numerical results were calculated for the samples reported as, non-detect (ND) by dividing the reliable quantitation limit (RQL) of 0.032 µg/sample for the method used (OSHA, 2014) by the sample air volume. Given that the OSHA PEL is 1 ppm for the 8-hour TWA and 5 ppm for the 15-minute short term excursion limit (STEL), the data for EtO include both samples of up to 480 minutes that were collected for comparison to the PEL and samples of less than 30 minutes for comparison to the STEL.

The combined sample TWA values reported in Table 9 for each facility inspection are the time weighted averages (TWAs) for all the samples collected during that inspection. These TWAs were calculated for each facility rather than for each worker because the identity of the worker associated with each sample is not included in the chemical exposure health data. Combined sample durations that are greater than 480 minutes indicate that more than one worker was sampled during the inspection. For example, the combined sample duration of 3,150 minutes for the 21 samples collected during Inspection #315303131 suggests that at least seven workers were sampled. It also is likely that multiple samples were collected on each worker sampled at a particular facility because the PEL of EtO is expressed both as an 8-hour TWA and as a 15-minute EL. For some of the inspections listed in Table 9, the upper end of the range of results includes samples that were collected to evaluate the EL. This is particularly true for Inspection #1192822 which includes a result of 19.5 ppm. This result of 19.5 ppm and the next highest result of 4.4 ppm were from 19-minute samples that were taken to evaluate the EL of 5 ppm. The remaining results are from samples of approximately 240 minutes in duration that were collected to evaluate the PEL of 1 ppm. The combined TWAs range from 0.0013 ppm to 1.5 ppm for the medical equipment production and sterilization facilities, with two facilities above the PEL of 1 ppm. The combined TWAs for the health and veterinary care facilities ranged from 0.0061 to 0.022 ppm and were all below the PEL. The combined TWA of 0.082 ppm for the spice and extract manufacturing facility is also below the PEL. The OSHA data represent exposures that occur in the breathing zone and do not account for the use of respiratory protection; therefore, they were not used to calculate cancer risks.

Table 9. OSHA EtO Data for EPA Registered Uses (2008 through 2020)

OSHA Inspection Number	Year	Industry	Number of Samples	Range of Results[a] (ppm EtO)	Combined Sample Duration[b] (Minutes)	Combined Sample TWA[c] (ppm EtO)
Medical Equipment Production and Sterilization Facilities						
315303131 1192822	2011 2017	Medical Equipment Wholesale	21 15	0.05 to 0.74 **0.05** to 19.5	3150 2903	0.22 1.5
1169775	2016	Scientific and Technical Consulting[d]	8	**0.0008 to 0.03**	2074	0.0013
317586501	2014	Surgical Equipment and Supplies Manufacturing	11	**0.0015** to 0.60	1065	0.23

[23] The data for 2008 through 2019 were included in the 2020 DRA. The data for 2020 became available in 2021. There are no data for 2021.

OSHA Inspection Number	Year	Industry	Number of Samples	Range of Results[a] (ppm EtO)	Combined Sample Duration[b] (Minutes)	Combined Sample TWA[c] (ppm EtO)
314845975	2011	Surgical and Medical Equipment Manufacturing	4	**0.005** to 0.18	350	0.11
810881	2013		6	**0.005** to 0.85	603	0.43
1013403	2015		6	**0.02** to 2.4	906	1.4
1400790	2019		13	**0.001** to 0.23	2280	0.15
1428553	2020		16	**0.0008** to 0.23	2578	0.063[e]
Health and Veterinary Care Facilities						
312835390	2009	Health Care Facilities	4	**0.003 to 0.02**	217	0.0061
310770896	2009		4	**0.0008** to 0.89[f]	460	0.031
315129924	2011		3	**0.005 to 0.03**	99	0.010
1147145	2016		5	**0.001 to 0.03**	445	0.0040
312226533	2008		6	**0.009 to 0.02**	150	0.013
1007452	2015	Veterinary Care Facilities	2	**0.02, 0.02**	30	0.024
1276007	2017		2	**0.006, 0.002**	75	0.0095
Non-Medical Facilities						
1241931	2017	Spice and Extract Manufacturing	5	**0.002** to 0.16[g]	472	0.083

[a] Results in bold font are based on the air sample volume and the reliable quantitation limit of 0.032 ug/sample.
[b] The combined sample duration is the duration of all of the samples taken during the inspection.
[c] The combined TWA is the TWA of all of the samples taken during the inspection.
[d] This facility does sterilization protocol development and testing.
[e] For this inspection it was possible to identify the employees by field number. Five employees were sampled for 458 to 480 minutes each. The average 8 hour TWA is 0.058 ppm for these five employees. An additional employee was sampled for 229 minutes. The combined sample TWA of 0.063 ppm includes all six employees.
[f] Only one sample was above the RQL. This sample was collected for 15 minutes.
[g] The highest result of 0.16 ppm is from a 240 minute sample.

3.2 Occupational Bystander Exposures and Cancer Risks

Occupational bystander exposures may occur in non-processing areas of a treatment facility, health care facility, or beekeeping equipment treatment area; in downstream facilities where the treated product is shipped and stored; or in other workplaces that are near the treatment facilities, health care facilities, or beekeeping equipment treatment areas. To aide in mitigation planning for these types of exposures where respiratory protection is not used, the EtO concentration at which the cancer risk equals a certain target level (1×10^{-4} or 1×10^{-6}) was back calculated from the inhalation unit risk for adults as shown in Table 9. This calculation indicates that if the EtO exposure in these areas does not exceed 0.19 parts per billion (ppb) as an 8-hour TWA, the cancer risk will not exceed 1×10^{-4} (100 in 1 million). If the EtO exposure does not exceed 0.0019 ppb, the cancer risk will not exceed 1×10^{-6} (1 in 1 million). This calculation is relevant to both the antimicrobial and conventional uses of EtO.

Table 10. Occupational Bystander Exposure Associated with Cancer Risk Targets

Cancer Risk Target	8-hr TWA (ppb)	Hours Per Day	Days Per Year	Years Per Lifetime	LAC[a,b] (ppb)	Inhalation Unit Risk[c]	Cancer Risk[d]
1×10^{-4}	0.19	8	240	35	0.021	5.5×10^{-3} per ppb	1×10^{-4}
1×10^{-6}	0.0019				0.00021		1×10^{-6}

[a] LAC = Lifetime Average Concentration
[b] LAC = 8-hr TWA (ppb) * (8 hours exposure per day/24 hours) * (240 days exposure per year/365 days) * (35 years/70 years)

[c] Adult Inhalation Unit Risk from Table 2.
[d] Cancer Risk = LAC (ppb) * Inhalation Unit Risk (per ppb)

4.0 Non-Occupational Bystander Exposure and Risk Assessment

4.1 Commercial Sterilization Facilities (Antimicrobial and Conventional Uses)

Non-occupational bystander exposures around commercial sterilization facilities are considered either "residential" exposure occurring where people live (i.e., their homes) or "non-residential" meaning exposures occurring at places other than homes where people may spend a significant amount of time (i.e., daycare centers, schools).

4.1.1 Commercial Sterilization Facility Emissions

In proposing amendments to the NESHAP for the Commercial Sterilization Facilities source category, OAR is assessing and proposing to regulate only residential exposure (i.e., exposure where people live). Exposures to workers and non-residential bystanders are not addressed in this proposed rulemaking.

4.1.2 Residential Bystander Exposures and Risks

There is the potential for EtO exposure to children and adults who live near sterilization facilities. These exposures are also being addressed by the proposed OAR rulemaking (US EPA, 2022). The EtO average daily concentration at which the cancer risk is 1×10^{-6} was back calculated from the inhalation unit risk for lifetime exposure as shown in Table 11. This calculation indicates that if the average daily concentration in these areas does not exceed 0.00011 ppb (0.11 ppt), the cancer risk will not exceed 1×10^{-6} (1 in 1 million). As discussed in Section 5.0 below, this is below the LOD of 20 to 90 ppt for EtO in ambient air.

Table 11. Residential Bystander Exposures Associated with a Cancer Risk of 1×10^{-6}

ETO Average Daily Concentration (ADC)	ETO Lifetime Average Concentration[a] (LAC)	Inhalation Unit Risk[b]	Cancer Risk[c]	Cancer Risk[d]
0.00011 ppb (0.11 ppt)	0.00011 ppb	9.15×10^{-3} per ppb	1×10^{-6}	1 in 1 million

[a] LAC = ADC * (24 hour / 24 hours) * (365 days / 365 days) * (70 years / 70 years)
[b] Full Lifetime Inhalation Unit Risk Estimate from Table 2.
[c] Cancer Risk (unitless) = LAC (ppb) * Inhalation Unit Risk (9.15×10^{-3} per ppb for lifetime exposures)
[d] Cancer Risk (in a million) = Cancer Risk (unitless) x 1,000,000

4.1.3 Non-Residential Bystander Exposures and Risks (Daycare Centers and Schools)

Non-residential bystander exposures can occur at a variety of facilities such as retail establishments, restaurants, gyms, swimming pools, music studios, movie theatres, etc., that are between the fence line of a sterilization facility and the nearest residence. These exposures are best represented by children attending day care centers and schools because they occur more frequently and with a longer daily duration and because EtO is a mutagen that requires the use of ADAFs to assess childhood exposures. The EtO concentration at which the cancer risk equals 1×10^{-6} was back calculated from the inhalation unit risk as shown in Table 12. These calculations indicate that the cancer risk is 1×10^{-6} (1 in 1 million) for children who attend

daycare and school where the average daily EtO concentration is 0.0012 ppb (1.2 ppt). As discussed in Section 5.0 below, this is below the LOD of 20 to 90 ppt for EtO in ambient air.

Table 12. Daycare and School Bystander Exposures Associated with a Cancer Risk of 1 x 10^{-6}

ETO ADC[a]	Age	Hours Per Day	Days Per Year	Years Per Lifetime	LAC[b,c] (ppb)	ADAF[d]	Inhalation Unit Risk[e]	Cancer Risk[f]
0.0012 ppb (1.2 ppt)	0 to 2	8	240	2	7.5×10^{-6}	10	5.5×10^{-3} per ppb	4.1×10^{-7}
	3 to 6	8	240	4	1.5×10^{-5}	3		2.5×10^{-7}
	7 to 16	6	180	10	2.1×10^{-5}	3		3.5×10^{-7}
	17 to 18	6	180	2	4.2×10^{-6}	1		2.3×10^{-8}
	0 to 18	N/A	N/A	18	N/A	N/A		1×10^{-6}

[a] ADC = Average Daily Concentration (24 hours)
[b] LAC = Lifetime Average Concentration
[c] LAC = ADC (ppb) * (hours per day/24 hours) * (days per year/365 days) * (years per lifetime/70 years)
[d] ADAF = Age Dependent Adjustment Factor
[e] Adult for Use with ADAFs Inhalation Unit Risk Estimate from Table 3.
[f] Cancer Risk = LAC (ppb) * ADAF * Inhalation Unit Risk (per ppb)

4.2 Health Care Facility Residential and Non-Residential Bystander Exposures

Since 2010, health care sterilization facilities have been required to operate on an all-in-one basis in accordance with the EtO Reregistration Eligibility Decision (US EPA, 2008). These facilities sterilize material in oven-sized chambers using 4.5 to 170 grams of EtO per load. The exhaust from the chambers is typically routed to an air pollution control device and the room air is typically ventilated though an exhaust stack to minimize exposures as recommended in the American National Standard Institute/Association for the Advancement of Medical Instrumentation (ANSI/AAMI) standard ST41 (ANSI/AAMI, 2018). Given this information, exposures to non-occupational bystanders are expected to be minimal, but the exact air concentrations are not known and, therefore, the risks are not quantitatively assessed in this DRA. It is known, however, that the exposures that would result in a cancer risk of 1 in a million are the same as those calculated for contract sterilization facilities (i.e., 0.11 ppt for residential areas and 1.2 ppt for children in schools/daycares). The potential exposures around health care sterilization facilities can be addressed in the Preliminary Interim Decision (PID) by requiring control measures that are recommended in ANSI/AAMI (2018). In addition, the NESHAP for Hospital Ethylene Oxide Sterilizers addresses EtO emissions from hospitals where EtO is used, and OAR plans to evaluate the risks from hospital sterilizers in an upcoming regulatory review of this NESHAP.

4.3 Beekeeping Equipment Fumigations (Special Local Need)

For the beekeeping equipment use in North Carolina, a quantitative residential bystander assessment was conducted using the Probabilistic Exposure and Risk Model for Fumigants (PERFUM). This approach was taken since the use is limited to one area and information was available on the fumigation chambers and process to allow for the exposure to be modeled. Details on the PERFUM inputs and a table of the outputs at various percentiles is provided in Appendix B. A summary of the inputs and outputs is provided below.

EPA reached out to the North Carolina Department of Agriculture and Consumer Affairs (NCDA&CS) to obtain information about the chamber set up and operations for the beekeeping

equipment fumigations. Based on the information provided, the approach taken was to model the beekeeping equipment use as an area source in PERFUM, with passive aeration from the source, and assuming the mass of EtO in the chamber all comes out during the first hour (first flushing out of the chamber after fumigation). NCDA&CS indicated that the chamber is flushed 3 times after fumigation and given the size of the chamber (126 ft^3), this process would not be expected to take longer than an hour, and by releasing all the mass in one hour, a conservative air concentration would be modeled. NCDA&CS also provided information on the chamber and aeration set up, and based on this information, EPA assumed the source to be a circular area, with a radius of 15 cm (0.15 m). The emission rate was entered for hour 1 (assumed to be noon based on the information from NCDA&CS which stated that the treatments start midday and run until the following midday) and then zero emissions assumed for the rest of the day. The meteorological data for Raleigh, North Carolina was used as this would be the closest to the actual location of the fumigation.

Two application rates were modeled as provided on the product label: 450 mg/L (28.3 lb ai/1,000 ft^3) and 740 mg/L (46.5 lb ai/1,000 ft^3). Information provided by North Carolina indicated the chamber size to be 126 ft^3 (3.57 m^3). The mass of EtO released and the corresponding emission rate modeled were the following:

- For the 28.3 lb ai/1,000 ft^3 rate:
  - Mass of EtO released: 3.6 lb (1,617,409,181 µg or 1,617 grams)
  - Emission rate: 6,370,963 µg/(m^2-s)
- For the 46.5 lb ai/1,000 ft^3 rate:
  - Mass of EtO released: 5.9 lb (2,657,600,376 µg or 2,657 grams)
  - Emission rate: 10,468,269 µg/(m^2-s)

The PERFUM output provides distributions of modeled air concentrations at various distances from the chamber. These air concentrations are then used to estimate inhalation cancer risk assuming four or eight exposure days per year and 70 years of exposure per lifetime. The IRIS inhalation unit risk for environmental exposures for a full lifetime [5.0×10^{-3} per µg/m^3 (9.15×10^{-3} per ppb) from Table 2] was used to estimate cancer risks. For the purposes of this assessment, a summary of the cancer risk estimates for the 50th, 75th, 80th, 85th, and 90th percentiles assuming 4 and 8 days (24 hrs/day) per year, based on specific use information for the beekeeping use, are provided below in Table 12 from 10 to 300 meters from the chamber. While the cancer risks are twice as high when assuming 8 days per year, the distances at which risks are greater than 1×10^{-6} (1E-06) do not change. It is likely that the exact distance at which the cancer risks change from "of concern" to "not of concern" are different when assuming 4 versus 8 exposure days; however, the model results are only reported at specific distances (e.g., 1, 5, 10, 15 meters, etc) and not at continuous distances from the fumigation chamber. Therefore, the distance, as reported by the model, at which the cancer risk estimate is not of concern does not change between four and eight exposure days.

The distances from the fumigation chamber at which the cancer risk estimates are less than 1×10^{-6} increase from lower to higher percentiles. For example, at the lower percentiles (e.g., 75th and 80th), the distance from the fumigation chamber at which the cancer risk is less than 1×10^{-6} is only 10 meters, while at the higher percentiles (e.g., 90th) distances of 300 meters or more are necessary to reach cancer risk estimates less than 1×10^{-6}. Cancer risk estimates are less than

1 x 10^{-6} at all percentiles for both application rates when the distance is equal to or greater than 300 meters.

Table 13. Cancer Risks at Buffer Distances from the Beekeeping Fumigation Chambers

Application Rate (lb a.i./1000 ft^3)	Modeled Air Concentration Distribution Percentile	Cancer Risk at Buffer Distances				
		10 meters	50 meters	100 meters	200 meters	300 meters
4 Exposure Days Per Year						
46.5	50	6E-41	5E-41	2E-41	3E-41	3E-41
	75	3E-16	1E-12	2E-15	3E-18	2E-21
	80	**2E-06**	7E-09	4E-11	6E-14	9E-15
	85	**3E-04**	**3E-06**	1E-07	2E-09	3E-10
	90	**5E-03**	**4E-04**	**4E-05**	**3E-06**	4E-07
28.3	50	6E-41	3E-41	2E-41	5E-41	2E-41
	75	2E-16	7E-13	9E-16	2E-18	1E-20
	80	1E-06	4E-09	3E-11	4E-14	5E-15
	85	**2E-04**	**2E-06**	8E-08	1E-09	2E-10
	90	**3E-03**	**2E-04**	**3E-05**	**2E-06**	3E-07
8 Exposure Days Per Year						
46.5	50	1E-40	1E-40	4E-41	5E-41	6E-41
	75	5E-16	2E-12	3E-15	5E-18	4E-21
	80	**4E-06**	1E-08	9E-11	1E-13	2E-14
	85	**7E-04**	**6E-06**	3E-07	3E-09	6E-10
	90	**1E-02**	**7E-04**	**9E-05**	**6E-06**	9E-07
28.3	50	1E-40	6E-41	5E-41	1E-40	4E-41
	75	3E-16	1E-12	2E-15	3E-18	3E-20
	80	**3E-06**	9E-09	5E-11	8E-14	1E-14
	85	**4E-04**	**4E-06**	2E-07	2E-09	4E-10
	90	**6E-03**	**4E-04**	**5E-05**	**4E-06**	5E-07

Bolded values are greater than 1x10^{-6} (1E-06)

5.0 Ambient Air Monitoring Data and Analytical Uncertainties

Ambient air data are normally used to provide context for the exposures and risks that are being assessed. In the case of EtO; however, there are risks of concern for levels that are below the levels of detection for the methods that are used to measure EtO in ambient air. To achieve a residential population cancer risk that is less than 1 x 10^{-6}, for example, the lifetime average EtO concentration would need to be less than 0.11 ppt. As discussed below, this level is less than the detection limit of 20 to 90 ppt and this detection limit can only be achieved under optimum conditions.

EtO has been measured in the outdoor air in areas away from specific sources of EtO. Monitoring data are available in EPA's Air Quality System (AQS), which houses outdoor air quality data collected by EPA, state, local, and tribal air pollution control agencies across the country (see https://www.epa.gov/aqs).

For most of the sites included in the AQS, the EtO air concentrations were measured as 24-hour air samples using 6 liter evacuated stainless steel canisters. The air collected in the canisters was then analyzed using gas chromatography and mass spectrometry. When the method was initially developed, it had a detection limit of 0.25 ppb using EPA's traditional approach of seven

replicate analyses of a low-level standard and 0.20 ppb using a novel probabilistic approach (Eklund et al., 2004). Since that time, the method has been incorporated into EPA Method TO-15, which has recently been updated to EPA Method TO-15A (US EPA, 2019a). The method now has an analytical method detection limit (MDL) of approximately 0.020 to 0.09 ppb (20 to 90 ppt). The overall method MDL will be higher than the analytical MDL ranges noted above when sampling media and sampling handling are taken into consideration (US EPA, 2021b).

The interior surfaces of the stainless-steel air sampling canisters are typically electropolished or coated with a silicon-ceramic film (US EPA, 2019a). There are concerns that if electropolished canisters are used, the EtO concentration in the canister will increase after sample collection due to interaction with canister wall surfaces (i.e., the canister wall effect). In a preliminary study conducted by ORD (Gitipour, 2022), initial one-week results showed EtO concentrations in the samples stored in the silicon ceramic-lined canisters were below the method detection limit (MDL) for all samples, whereas EtO was measured at detectable concentrations in all of the samples stored in electropolished canisters. After the 4 - 5 week holding period, the background EtO concentrations observed in the silicon-ceramic canisters were below the MDL for the majority of the samples. However, the EtO concentrations in the electropolished canisters had increased over the 4 - 5 week hold time by a factor of 7 to 10 times from the initial one-week values. These concentrations were substantially higher than typical ambient EtO concentrations. The type of canister that was used is not listed in the AQS dataset.

In addition to the effects of the canister lining, there are concerns regarding the cleaning and preparation of the canisters for air sampling. If cleaning is not done thoroughly, even silicon-ceramic lined canisters can yield results that are biased due to contamination and wall effects. Due to the uncertainties associated with the currently available ambient air sampling results, many of the results reported in the AQS are biased high and do not reflect actual ambient EtO air concentrations. In addition, the working limits of detection achieved by the commercial laboratories that analyze ambient air samples are typically greater than the MDL of 20 to 90 ppt. For these reasons, it cannot be concluded that measured ambient air concentrations of EtO are less than the level (0.11 ppt) which corresponds to a cancer risk of 1×10^{-6}. ORD is actively working in this area to improve sampling methods for ambient levels of EtO[24].

6.0 Comparison of Bystander Exposures and Risks to OAR Model Results

To get a better understanding of how the back-calculated concentrations that exceed risks of concern for non-residential bystanders (e.g., children who attend school) and occupational bystanders (adults who work near sterilization facilities) relate to concentrations around facilities, the air concentrations developed by the Office of Air and Radiation (OAR) in their recent proposed rulemaking were considered[25]. Air concentrations for polar receptor rings around each sterilizing facility were modeled and annual average air concentrations were derived by OAR. The model results indicate that there is a potential for EtO concentrations to exceed the level of 1.2 ppt that corresponds to a cancer risk of 1×10^{-6} for children in schools/daycares that are in non-residential areas near sterilization facilities. The model results also indicate that EtO concentrations in the non-residential areas modeled by OAR could exceed the level of 0.0019

[24] See https://www.epa.gov/hazardous-air-pollutants-ethylene-oxide/epas-work-understand-background-levels-ethylene-oxide

[25] See OAR's residual risk assessment for the commercial sterilization facilities source category document in support of the 2022 Risk and Technology Review Proposed Rule. This document is currently an internal draft and will be posted to Regulations.Gov for Docket Number: EPA-HQ-OAR-2019-0178 when it is finalized.

ppb (1.9 ppt) that corresponds to cancer risk of 1 x 10^{-6} for adults who work near facilities modeled by OAR.

7.0 Risk Summary and Characterization

The inhalation cancer risks are likely of concern for all of the scenarios considered in this 2023 DRA addendum. These risks are driven by the high inhalation unit risk estimates which suggest that EtO is a potent carcinogen. Based on these unit risks, the EtO exposures that are associated with the risk targets that OPP normally uses for cancer risks (i.e., 1 x 10^{-4} for occupational exposure and 1 x10^{-6} for non-occupational exposure) are so low that they cannot be measured using existing air monitoring technologies and analytical methods. For example, to achieve the risk target of 1 x 10^{-6} for continuous residential exposures, the EtO air concentration must not exceed 0.11 parts per trillion (ppt). This level is over one hundred times less than the analytical MDL of 20 to 90 ppt for the 24-hour canister method that is used for ambient air sampling. For worker exposures, to achieve the target risk level of 1 x 10^{-4}, the average EtO air concentration should not exceed 0.2 ppb. This level is 5,000 times less than the OSHA PEL of 1.0 ppm. The level of 0.2 ppb is also 100 times lower than the LOD of 0.026 ppm (26 ppb) for the passive badge method that is most commonly used by employers to measure EtO and 7.5 times less than the reliable quantification limit of 1.5 ppb for the sampling tube and pump method (OSHA, 2014) that OSHA inspectors use to measure EtO.

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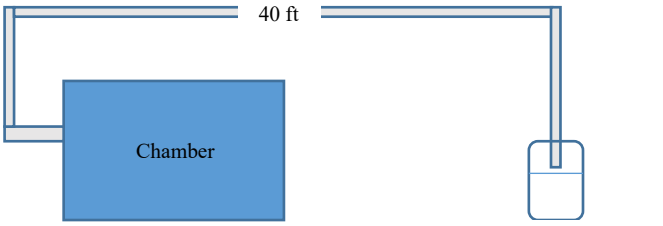
Appendix A. Reported Work Activities in Spice Facilities (from MRID 47338301) and the Work Activity Subset Assumed for Beekeeping Equipment Fumigations

Worker Activities Listed in ASTA Study Protocol	Worker Activities Listed in ASTA Study Submission	Respirator Worn?	Included in Spice Facility Occupational Handler Exposure Assessment	Included in Beekeeping Equipment Occupational Handler Exposure Assessment	Reason for including/not including for Beekeeping Equipment Fumigation
Forklift Checklist	Forklift Checklist	N	X		Beekeeping equipment fumigation chamber not inside
Working Control (Computer) Room	Computer room	N	X		Beekeeping equipment fumigation chamber not inside – would not be in same facility/space as office
Shipping Treated Product	Shipping	N	X		Beekeeping equipment fumigation chamber not inside – would not be in same facility/space as shipping area
Present in another building	Office for tickets, Office, Warehouse	N	X		Beekeeping equipment fumigation chamber not inside – would not be in same facility/space as office
Paperwork	Chamber Sheet, Paperwork	N	X		Beekeeping equipment fumigation chamber not inside – would not be in same facility/space as office
Empty Trash	Empty Trash, Cleaning	N	X		Beekeeping equipment fumigation chamber not inside – would not be in same facility/space as office
not listed	Sampling	N	X		Assumed to be sampling of untreated product; specific to spices
not listed	Control H2O chamber	N	X		Assumed specific to indoor spice facility
Receiving Untreated Product	Ticket/Tag/Labels on Product, Untreated Product, Restack/working with spices, Pull untreated product for chamber, Receiving, Moving Product	N	X		Activities assumed to occur inside spice treatment facility; not applicable to beekeeping equipment fumigation

Worker Activities Listed in ASTA Study Protocol	Worker Activities Listed in ASTA Study Submission	Respirator Worn?	Included in Spice Facility Occupational Handler Exposure Assessment	Included in Beekeeping Equipment Occupational Handler Exposure Assessment	Reason for including/not including for Beekeeping Equipment Fumigation
Clean mask	Clean mask, Clean respirator, Clean SCUBA	N	X	X	Assumed to occur regardless of product being treated
not listed	Receipt of EtO Gas	N	X	X	
Vacuum down EtO cylinders for shipment	Vacuum	N	X	X	
not listed	Start, Start up Chamber, Heat Chamber, Heat Product	N	X	X	
Unloading Chamber	Open Chamber, Unload Chamber	Y	X	X	
Loading Chamber	Load Chamber	Y	X	X	
Charging Chamber with EtO	Chamber “X”, Gassing Chamber “X”	Y	X	X	
Cleaning (sweeping) chamber	Clean chamber room, Sweep Chamber	Y	X	X	
Sampling EtO Treated Product	Work with Treated Product, Sampling	Y	X	X	
Draining empty gas cylinder	Drain cylinder	Y	X	X	
not listed	New EtO Cylinder	Y	X	X	
not listed	Remove EtO Cylinder	Y	X	X	
not listed	Caps in EtO Cylinders	Y	X	X	

Appendix B. Details on the PERFUM modeling for the Bystander Assessment for the Beekeeping Equipment Fumigation Use

The Special Local Need beekeeping equipment fumigation use is not a typical fumigation/warehouse type use as these chambers are smaller and the aeration configuration is somewhat unique. According to information provided by North Carolina, the chamber is vented through a pipe into a bucket located approximately 40 feet from the chamber. The set up was described as something akin to this:



The approach taken to model bystander exposure was to assume an area source, with the bucket as the "source," with passive aeration from the source, and assuming the mass of EtO in the chamber all comes out during the first hour (first flushing out of the chamber after fumigation). The area source was modeled as a circular area source, with a radius of 15 cm (0.15 m). The emission rate was entered for hour 1 (assumed to be noon) and then zero emissions assumed for the rest of the day. The meteorological data for Raleigh, North Carolina was used as this would be the closest to the actual location of the fumigation.

App rates: two app rates

- 28.3 lb ai/1,000 ft^3 (treatment time = 16 hours)
- 46.5 lb ai/1,000 ft^3 (treatment time = 8 hours)

Chamber size: 126 ft^3 (3.57 m^3)

The emission rate has been calculated based on the bucket being the source as follows:

Radius = 0.15 m
Area = πr^2 = 0.0705 m^2
Mass of EtO released:

(1) for 28.3 lb ai/1,000 ft^3 rate =

$$28.3\ \frac{lb\ ai}{1{,}000\ ft3} \times 453.59\ \frac{g}{lb} \times 35.315\ \frac{ft^3}{m^3} = 453.32\ \frac{g}{m^3} \times 3.57\ m^3 \times 1{,}000{,}000\ \frac{ug}{g} = 1{,}617{,}409{,}181\ ug$$

(2) for 46.5 lb ai/1,000 ft^3 rate =

$$46.5\ \frac{lb\ ai}{1{,}000\ ft^3} \times 453.59\ \frac{g}{lb} \times 35.315\ \frac{ft^3}{m^3} = 744.86\ \frac{g}{m^3} \times 3.57\ m^3 \times 1{,}000{,}000\ \frac{ug}{g} = 2{,}657{,}600{,}376\ ug$$

- Emission rates:

  (1) for 28.3 lb ai/1,000 ft^3 rate =

$$1{,}617{,}409{,}181\ ug\ \div 0.0705\ m^2\ \div 3600\ seconds = \mathbf{6{,}370{,}963}\ \frac{\boldsymbol{ug}}{\boldsymbol{m^2 - s}}$$

  (2) for 46.5 lb ai/1,000 ft^3 rate =

$$2{,}657{,}600{,}376\ ug\ \div 0.0705\ m^2\ \div 3600\ seconds = \mathbf{10{,}468{,}269}\ \frac{\boldsymbol{ug}}{\boldsymbol{m^2 - s}}$$

Table B1. Cancer Risks at Modeled Buffer Distances from the Beekeeping Fumigation Chambers at a rate of 28.3 lb ai/1000 ft^3 and an Assumption of 4 Exposure Days per Year

Percentile	Statistic	Distance (meters)									
		1	5	10	15	25	50	100	150	200	300
50	Concentration (ug/m^3)	3.40E-37	5.10E-37	1.10E-36	5.30E-37	8.20E-37	5.80E-37	4.30E-37	3.80E-37	1.00E-36	4.10E-37
	Lifetime Average Concentration (LAC) (ug/m^3)	3.7E-39	5.6E-39	1.2E-38	5.8E-39	9.0E-39	6.4E-39	4.7E-39	4.2E-39	1.1E-38	4.5E-39
	Cancer risk	2E-41	3E-41	6E-41	3E-41	4E-41	3E-41	2E-41	2E-41	5E-41	2E-41
75	Concentration (ug/m^3)	9.60E-21	5.50E-09	3.00E-12	1.90E-13	1.30E-12	1.20E-08	1.70E-11	2.00E-13	3.00E-14	2.30E-16
	LAC (ug/m^3)	1.1E-22	6.0E-11	3.3E-14	2.1E-15	1.4E-14	1.3E-10	1.9E-13	2.2E-15	3.3E-16	2.5E-18
	Cancer risk	5E-25	3E-13	2E-16	1E-17	7E-17	7E-13	9E-16	1E-17	2E-18	1E-20
80	Concentration (ug/m^3)	2.90E-17	1.80E-03	2.30E-02	1.50E-03	1.70E-04	8.00E-05	4.90E-07	1.80E-08	7.20E-10	1.00E-10
	LAC (ug/m^3)	3.2E-19	2.0E-05	2.5E-04	1.6E-05	1.9E-06	8.8E-07	5.4E-09	2.0E-10	7.9E-12	1.1E-12
	Cancer risk	2E-21	1E-07	1E-06	8E-08	9E-09	4E-09	3E-11	1E-12	4E-14	5E-15
85	Concentration (ug/m^3)	1.10E-13	3.10E-01	3.80E+00	2.90E+00	7.60E-01	3.40E-02	1.50E-03	6.90E-05	1.80E-05	3.50E-06
	LAC (ug/m^3)	1.2E-15	3.4E-03	4.2E-02	3.2E-02	8.3E-03	3.7E-04	1.6E-05	7.6E-07	2.0E-07	3.8E-08
	Cancer risk	6E-18	**2E-05**	**2E-04**	**2E-04**	**4E-05**	**2E-06**	8E-08	4E-09	1E-09	2E-10
90	Concentration (ug/m^3)	7.10E-11	8.60E+00	5.90E+01	5.00E+01	2.20E+01	4.10E+00	4.80E-01	1.10E-01	3.20E-02	4.80E-03
	LAC (ug/m^3)	7.8E-13	9.4E-02	6.5E-01	5.5E-01	2.4E-01	4.5E-02	5.3E-03	1.2E-03	3.5E-04	5.3E-05
	Cancer risk	4E-15	**5E-04**	**3E-03**	**3E-03**	**1E-03**	**2E-04**	**3E-05**	**6E-06**	**2E-06**	3E-07

Bolded values are greater than 1x10^{-6}

Table B2. Cancer Risks at Modeled Buffer Distances from the Beekeeping Fumigation Chambers at a rate of 46.5 lb ai/1000 ft^3 and an Assumption of 4 Exposure Days per Year

Percentile	Statistic	Distance (meters)									
		1	5	10	15	25	50	100	150	200	300
50	Concentration (ug/m^3)	3.40E-37	1.00E-36	1.10E-36	9.30E-37	4.60E-37	9.20E-37	3.70E-37	4.50E-37	5.00E-37	5.80E-37
	LAC (ug/m^3)	3.7E-39	1.1E-38	1.2E-38	1.0E-38	5.0E-39	1.0E-38	4.1E-39	4.9E-39	5.5E-39	6.4E-39
	Cancer risk	2E-41	5E-41	6E-41	5E-41	3E-41	5E-41	2E-41	2E-41	3E-41	3E-41
75	Concentration (ug/m^3)	1.60E-20	9.30E-09	4.70E-12	3.20E-13	2.20E-12	1.90E-08	2.80E-11	3.50E-13	4.60E-14	3.40E-17
	LAC (ug/m^3)	1.8E-22	1.0E-10	5.2E-14	3.5E-15	2.4E-14	2.1E-10	3.1E-13	3.8E-15	5.0E-16	3.7E-19
	Cancer risk	9E-25	5E-13	3E-16	2E-17	1E-16	1E-12	2E-15	2E-17	3E-18	2E-21
80	Concentration (ug/m^3)	4.70E-17	2.90E-03	3.70E-02	2.60E-03	2.80E-04	1.30E-04	8.00E-07	3.00E-08	1.10E-09	1.70E-10
	LAC (ug/m^3)	5.2E-19	3.2E-05	4.1E-04	2.8E-05	3.1E-06	1.4E-06	8.8E-09	3.3E-10	1.2E-11	1.9E-12
	Cancer risk	3E-21	2E-07	**2E-06**	1E-07	2E-08	7E-09	4E-11	2E-12	6E-14	9E-15
85	Concentration (ug/m^3)	1.80E-13	5.00E-01	6.30E+00	4.70E+00	1.20E+00	5.60E-02	2.50E-03	1.10E-04	3.00E-05	5.80E-06
	LAC (ug/m^3)	2.0E-15	5.5E-03	6.9E-02	5.2E-02	1.3E-02	6.1E-04	2.7E-05	1.2E-06	3.3E-07	6.4E-08
	Cancer risk	1E-17	**3E-05**	**3E-04**	**3E-04**	**7E-05**	**3E-06**	1E-07	6E-09	2E-09	3E-10
90	Concentration (ug/m^3)	1.20E-10	1.40E+01	9.70E+01	8.20E+01	3.60E+01	6.80E+00	8.00E-01	1.90E-01	5.20E-02	8.00E-03
	LAC (ug/m^3)	1.3E-12	1.5E-01	1.1E+00	9.0E-01	3.9E-01	7.5E-02	8.8E-03	2.1E-03	5.7E-04	8.8E-05
	Cancer risk	7E-15	**8E-04**	**5E-03**	**4E-03**	**2E-03**	**4E-04**	**4E-05**	**1E-05**	**3E-06**	4E-07

Bolded values are greater than the cancer target risk of 1x10^{-6}

Table B3. Cancer Risk at Modeled Buffer Distances from the Beekeeping Fumigation Chambers at a rate of 28.3 lb ai/1000 ft^3 and an assumption of 8 Exposure Days per Year.

Percentile	Statistic	Distance (meters)									
		1	5	10	15	25	50	100	150	200	300
50	Concentration (ug/m^3)	3.40E-37	5.10E-37	1.10E-36	5.30E-37	8.20E-37	5.80E-37	4.30E-37	3.80E-37	1.00E-36	4.10E-37
	LAC (ug/m^3)	7.5E-39	1.1E-38	2.4E-38	1.2E-38	1.8E-38	1.3E-38	9.4E-39	8.3E-39	2.2E-38	9.0E-39
	Cancer risk	4E-41	6E-41	1E-40	6E-41	9E-41	6E-41	5E-41	4E-41	1E-40	4E-41
75	Concentration (ug/m^3)	9.60E-21	5.50E-09	3.00E-12	1.90E-13	1.30E-12	1.20E-08	1.70E-11	2.00E-13	3.00E-14	2.30E-16
	LAC (ug/m^3)	2.1E-22	1.2E-10	6.6E-14	4.2E-15	2.8E-14	2.6E-10	3.7E-13	4.4E-15	6.6E-16	5.0E-18
	Cancer risk	1E-24	6E-13	3E-16	2E-17	1E-16	1E-12	2E-15	2E-17	3E-18	3E-20
80	Concentration (ug/m^3)	2.90E-17	1.80E-03	2.30E-02	1.50E-03	1.70E-04	8.00E-05	4.90E-07	1.80E-08	7.20E-10	1.00E-10
	LAC (ug/m^3)	6.4E-19	3.9E-05	5.0E-04	3.3E-05	3.7E-06	1.8E-06	1.1E-08	3.9E-10	1.6E-11	2.2E-12
	Cancer risk	3E-21	2E-07	**3E-06**	2E-07	2E-08	9E-09	5E-11	2E-12	8E-14	1E-14
85	Concentration (ug/m^3)	1.10E-13	3.10E-01	3.80E+00	2.90E+00	7.60E-01	3.40E-02	1.50E-03	6.90E-05	1.80E-05	3.50E-06
	LAC (ug/m^3)	2.4E-15	6.8E-03	8.3E-02	6.4E-02	1.7E-02	7.5E-04	3.3E-05	1.5E-06	3.9E-07	7.7E-08
	Cancer risk	1E-17	**3E-05**	**4E-04**	**3E-04**	**8E-05**	**4E-06**	2E-07	8E-09	2E-09	4E-10
90	Concentration (ug/m^3)	7.10E-11	8.60E+00	5.90E+01	5.00E+01	2.20E+01	4.10E+00	4.80E-01	1.10E-01	3.20E-02	4.80E-03
	LAC (ug/m^3)	1.6E-12	1.9E-01	1.3E+00	1.1E+00	4.8E-01	9.0E-02	1.1E-02	2.4E-03	7.0E-04	1.1E-04
	Cancer risk	8E-15	**9E-04**	**6E-03**	**5E-03**	**2E-03**	**4E-04**	**5E-05**	**1E-05**	**4E-06**	5E-07

Bolded values are greater than 1x10^{-6}

Table B4. Cancer Risk at Modeled Buffer Distances from the Beekeeping Fumigation Chambers at a rate of 46.5 lb ai/1000 ft^3 and an assumption of 8 Exposure Days per Year.

Percentile	Statistic	Distance (meters)									
		1	5	10	15	25	50	100	150	200	300
50	Concentration (ug/m^3)	3.40E-37	1.00E-36	1.10E-36	9.30E-37	4.60E-37	9.20E-37	3.70E-37	4.50E-37	5.00E-37	5.80E-37
	LAC (ug/m^3)	7.5E-39	2.2E-38	2.4E-38	2.0E-38	1.0E-38	2.0E-38	8.1E-39	9.9E-39	1.1E-38	1.3E-38
	Cancer risk	4E-41	1E-40	1E-40	1E-40	5E-41	1E-40	4E-41	5E-41	5E-41	6E-41
75	Concentration (ug/m^3)	1.60E-20	9.30E-09	4.70E-12	3.20E-13	2.20E-12	1.90E-08	2.80E-11	3.50E-13	4.60E-14	3.40E-17
	LAC (ug/m^3)	3.5E-22	2.0E-10	1.0E-13	7.0E-15	4.8E-14	4.2E-10	6.1E-13	7.7E-15	1.0E-15	7.5E-19
	Cancer risk	2E-24	1E-12	5E-16	4E-17	2E-16	2E-12	3E-15	4E-17	5E-18	4E-21
80	Concentration (ug/m^3)	4.70E-17	2.90E-03	3.70E-02	2.60E-03	2.80E-04	1.30E-04	8.00E-07	3.00E-08	1.10E-09	1.70E-10
	LAC (ug/m^3)	1.0E-18	6.4E-05	8.1E-04	5.7E-05	6.1E-06	2.8E-06	1.8E-08	6.6E-10	2.4E-11	3.7E-12
	Cancer risk	5E-21	3E-07	**4E-06**	3E-07	3E-08	1E-08	9E-11	3E-12	1E-13	2E-14
85	Concentration (ug/m^3)	1.80E-13	5.00E-01	6.30E+00	4.70E+00	1.20E+00	5.60E-02	2.50E-03	1.10E-04	3.00E-05	5.80E-06
	LAC (ug/m^3)	3.9E-15	1.1E-02	1.4E-01	1.0E-01	2.6E-02	1.2E-03	5.5E-05	2.4E-06	6.6E-07	1.3E-07
	Cancer risk	2E-17	**5E-05**	**7E-04**	**5E-04**	**1E-04**	**6E-06**	3E-07	1E-08	3E-09	6E-10
90	Concentration (ug/m^3)	1.20E-10	1.40E+01	9.70E+01	8.20E+01	3.60E+01	6.80E+00	8.00E-01	1.90E-01	5.20E-02	8.00E-03
	LAC (ug/m^3)	2.6E-12	3.1E-01	2.1E+00	1.8E+00	7.9E-01	1.5E-01	1.8E-02	4.2E-03	1.1E-03	1.8E-04
	Cancer risk	1E-14	**2E-03**	**1E-02**	**9E-03**	**4E-03**	**7E-04**	**9E-05**	**2E-05**	**6E-06**	9E-07

Bolded values are greater than 1x10^{-6}