OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
WASHINGTON, D.C. 20460

Ethylene Oxide

Interim Registration Review Decision
Case Number 2275

January 2025

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Definition of Terms

AAMI - Association for the Advancement of Medical Instrumentation
Action Level – As defined in OSHA 29 C.F.R. § 1910.1047, the action level is a concentration of airborne EtO of 0.5 ppm calculated as an 8-hour time-weighted average. Exceedances of the OSHA Action Level would result in the following: personal air monitoring, information and training programs, medical surveillance programs, and warning labels.
ANSI - American National Standard Institute
ATSDR – Agency for Toxic Substances and Disease Registry
CDC – Centers for Disease Control and Prevention
DCI – Data Call-In
DRA – Draft Risk Assessment
EBH - Ethylene bromohydrin
ECH - Ethylene chlorohydrin
EDSP – Endocrine Disruptor Screening Program
EG - Ethylene glycol
EPA – Environmental Protection Agency
ESA – Endangered Species Act
EtO – Ethylene Oxide
FDA – Food and Drug Administration
FDA CDRH – Food and Drug Administration, Center for Devices and Radiological Health
FDA CFSAN – Food and Drug Administration, Center for Food Safety and Applied Nutrition
FDA-HFP – Food and Drug Administration, Human Foods Program (Formerly CFSAN)
FIFRA – Federal Insecticide, Fungicide, and Rodenticide Act
FWP – Final Work Plan
ID – Interim Decision
NESHAP – National Emission Standards for Hazardous Air Pollutants
NIOSH – National Institute for Occupational Safety and Health
OAR – Office of Air and Radiation
OPP – Office of Pesticide Programs
OSHA – Occupational Safety and Health Administration
PBZ – Personal breathing zone
PEL - As defined in OSHA 29 C.F.R. § 1910.1047, the PEL or Permissible Exposure Limit, is the worker exposure limit based on an 8-hour time weighted average (TWA) set at 1 part per million (ppm). Exceedances of the OSHA PEL would result in the following: written compliance program, regulated areas, and respirator use.
PID – Proposed Interim Decision
PWP – Preliminary Work Plan
STEL - As defined in OSHA 29 C.F.R. § 1910.1047, the STEL or Short-Term Exposure Limit, is the worker exposure limit based on a 15-minute time weighted average (TWA) set at 5 parts per million (ppm). OSHA also refers to this value as the Excursion Limit. Exceedances of the OSHA STEL would result in the following: personal air monitoring, information and training programs, warning labels, written compliance program, and regulated areas.
TWA – Time-weighted average

Table of Contents

I. INTRODUCTION

Executive Summary

Ethylene Oxide (EtO) is a flammable, colorless gas that is primarily used to make other chemicals that are used in making a range of products, including antifreeze, textiles, plastics, detergents, and adhesives. This Interim Decision (ID), in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) focuses on the pesticidal uses of EtO. Other activities involving EtO, including manufacturing, may be regulated under other statutes and/or by other agencies.

As a pesticide, EtO is primarily used as a sterilant for medical devices and equipment, and it is highly valuable because it is a penetrative gas that has a high throughput capacity, is effective at a wide range of temperatures, and is compatible with a broad range of materials. EtO is used on approximately 50% of all sterilized medical devices, annually, including an estimated 95% of all surgical kits. Despite the availability of alternative sterilization methods, such as gamma irradiation, X-ray sterilization, electron beam sterilization, and steam, EPA understands the limitations of alternative sterilization methods for use with medical devices due to their lack of compatibility with materials and/or packaging; and also due to their lack of scalability or

capacity, application method, and/or lack of standardized validation measures for sterility assurance or efficacy data.[1] For these reasons, it is difficult to replace EtO without changing other inherent parts of the supply chain, which would result in a loss of efficiency within a system that is already at capacity. The identification of alternatives is being developed on a product-by-product basis, and as such the capacity for alternatives is not sufficient to begin replacing EtO at scale. The absence of EtO for use on medical devices and equipment would cause widespread disruption to the availability of sterile medical devices including feeding tubes used in neonatal intensive care units, drug-eluting cardiac stents, catheters, shunts, and other implantable devices. Sterile medical equipment is necessary to prevent the transmission of infectious pathogens to patients/users, especially with devices and instruments that are used in normally sterile body tissue or within the vascular system. In the U.S., EtO is also used during the processing and reconditioning of food commodities (e.g., dried herbs and spices) to reduce foodborne pathogens of concern such as *Salmonella* and *Escherichia coli*.

EtO is a known carcinogen. The registered pesticidal uses of EtO pose inhalation risks to workers inside commercial sterilization facilities and healthcare facilities across the country, and to those treating beekeeping equipment with EtO (a use that only occurs in North Carolina). EtO also has the potential to pose inhalation risks to people who live in communities near facilities where EtO is used. Therefore, EPA has identified mitigation to reduce inhalation risk concerns, including the termination of certain uses, a reduced concentration rate for medical device sterilization, more protective occupational exposure limits, respiratory protection for workers engaged in high exposure tasks, respiratory protection for other workers based on the more protective occupational exposure limits, monitoring, training, and recordkeeping, as well as venting to reduce exposure to workers and bystanders inside of healthcare facilities and abatement devices to reduce exposure to surrounding communities nearby healthcare facilities. Furthermore, EPA has identified a need to obtain worker exposure data for commercial sterilizers and warehouses in order to understand the impacts of complying with EPA's requirements under the Clean Air Act (CAA) and implementing the mitigation measures in this Interim Registration Review Decision under FIFRA, and to better understand how to further reduce worker exposure. Once these data become available, the Agency may promptly reevaluate this Interim Decision.

On April 5, 2024, EPA's Office of Air and Radiation (OAR) published their Rulemaking for EtO commercial sterilizers, *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review*.[2] OAR revised the NESHAP for commercial sterilization facilities by both amending existing standards and establishing additional standards in order to reduce EtO emissions and associated exposure to EtO of residential communities.

[1] See Section III.C. and *Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation* in this docket.

[2] EPA-HQ-OAR-2019-0178-1482 at www.regulations.gov.

This document is the Environmental Protection Agency's (EPA or the Agency) Interim Registration Review Decision (ID) for ethylene oxide, henceforth referred to as EtO (PC Code 042301, case 2275). In a final registration review decision under FIFRA, the Agency determines whether a pesticide continues to meet FIFRA's registration standard.[3] Where appropriate, the Agency may issue an Interim Registration Review Decision before completing a registration review.[4] Among other things, the ID may determine that new risk mitigation measures are necessary, lay out interim risk mitigation measures, identify data or information required to complete the review, and include schedules for submitting the required data, conducting the new risk assessment and completing the registration review.[5] For more information on EtO, see EPA's public docket for this chemical's registration review case (EPA-HQ-OPP-2013-0244) at www.regulations.gov.

FIFRA[6] mandates the continuous review of existing pesticides. All pesticides distributed or sold in the United States must be registered by EPA based on scientific data showing that they will not cause unreasonable adverse effects to human health or to the environment when used as directed on product labeling. In 2006, the Agency began implementing the registration review program. EPA generally reviews each registered pesticide every 15 years. Through the registration review program, the Agency intends to verify that all registered pesticides continue to meet the registration standard as the ability to assess and reduce risk evolves and as policies and practices change. By periodically re-evaluating pesticides as science, public policy, and pesticide-use practices change, the Agency ensures that the public can continue to use products in the marketplace that do not present unreasonable adverse effects. For more information on the registration review program, see http://www.epa.gov/pesticide-reevaluation.

EtO was first registered as a pesticide in the U.S. in 1966. Because it was registered before 1984, it was subject to reregistration, and a Reregistration Eligibility Decision was completed by EPA in 2008.[7] There is currently one supplier of EtO for sterilization in the U.S., ARC Specialty Products of Balchem Corporation.

In addition to the registration review of EtO as a pesticide under FIFRA, the Agency also conducts a periodic review of air emission standards for air pollutants, including EtO, through the National Emission Standards for Hazardous Air Pollutants (NESHAP) under the Clean Air Act. On April 5, 2024, EPA's Office of Air and Radiation (OAR) published their Rulemaking for EtO commercial sterilizers, *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology*

[3] Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) § 3(g), 7 U.S.C. § 136a(g); 40 C.F.R. § 155.57.
[4] 40 C.F.R. §§ 155.56, 155.58.
[5] 40 C.F.R. § 155.56.
[6] As amended by the Food Quality Protection Act (FQPA) of 1996, Pub. L. No. 104-170, 110 Stat. 1489 and by the Consolidated Appropriations Act, 2023, Pub L. No. 117-328, § 711, 136 Stat. 4459 (2022).
[7] https://www.epa.gov/pesticide-reevaluation/reregistration-and-other-review-programs-predating-pesticide-registration.

Review.[8] The mitigations set forth in each Agency action are complementary in that they are intended to reduce public health risks from EtO exposure. The OAR rulemaking focuses on reducing EtO emissions released outside the commercial sterilization facilities for residential bystanders. EPA's Office of Pesticide Programs' (OPP's) mitigation measures for commercial sterilizers and other facilities that use EtO will also reduce EtO exposure to people outside the facilities, including residential and non-residential bystanders (i.e., those who go to work or school near facilities), as well as reduce exposures to workers exposed to EtO inside the facilities. OPP's mitigation applies to all use of EtO in commercial sterilization facilities in the U.S. OPP has also identified mitigation measures for the use of EtO in healthcare facilities and all niche uses of EtO (i.e., beekeeping equipment; museum, library, and archival materials, cosmetics; and musical instruments). Conversely, OAR's mitigation is focused only on the commercial sterilizers source category.

The Agency is issuing an ID for EtO so that it can move forward with aspects of the registration review and identify necessary risk mitigation measures (see Appendices A and B). EPA has not yet fully evaluated EtO's effects on federally threatened and endangered (listed) species or designated critical habitats. However, consistent with its obligations under the Endangered Species Act (ESA),[9] EPA expects to complete effects determinations and any necessary consultation with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service (the Services) before completing the EtO registration review and issuing a final registration review decision. For more information on EPA's ESA obligations during registration review, see Appendix C.

EPA continues to work with the Services to improve the consultation process for pesticides in registration review. In April 2022, EPA released its ESA Workplan, which outlines strategies and actions for the Agency to meet its ESA obligations for FIFRA actions.[10] Consistent with the ESA Workplan, EPA is focused on steps it will take during registration review to reduce exposure for listed species as it moves toward fulfilling its ESA obligations and making final registration review decisions. In November 2022, EPA released its first ESA Workplan Update.[11] As part of this update, EPA announced that, going forward, EPA may include a variety of FIFRA Interim Ecological Mitigation (IEM) measures in its registration review decisions that seek to reduce exposures for nontarget organisms based on its FIFRA ecological risk assessment(s). EPA expects that this mitigation may also reduce pesticide exposures for listed species.

As part of this ID, EPA has considered a variety of risk mitigation measures based on the risks and benefits of EtO, including measures that may mitigate ecological risks, while EPA works

[8] EPA-HQ-OAR-2019-0178-1482 at www.regulations.gov.
[9] Endangered Species Act (ESA) § 7, 16 U.S.C. § 1536.
[10] Balancing Wildlife Protections and Responsible Pesticide Use (Apr. 2022), https://www.epa.gov/system/files/documents/2022-04/balancing-wildlife-protection-and-responsible-pesticide-use_final.pdf.
[11] ESA Workplan Update: Nontarget Species Mitigation for Registration Review and Other FIFRA Actions (Nov. 2022), https://www.epa.gov/system/files/documents/2022-11/esa-workplan-update.pdf.

toward a final registration review decision. While these mitigation measures do not fully satisfy EPA's ESA obligations, EPA has determined that early mitigation may shorten the consultation process and improve protections for listed species from currently registered pesticide products. EPA also has determined that risk mitigation measures that the Agency has identified for EtO in this ID (Section V) satisfy EPA's obligations under Section 711 of the Consolidated Appropriations Act, PL-117-328 (Dec. 29, 2022). Among other things, Section 711 requires EPA to "include, where applicable, measures to reduce the effect of the applicable pesticide on" listed species and designated critical habitats in any ID noticed in the Federal Register between December 29, 2022, and October 1, 2026 for which EPA has not "made effects determinations or completed any necessary consultation under [ESA Section 7(a)(2)]."

The identified mitigation is expected to reduce the extent of environmental exposure and may reduce risk to listed species whose range or designated critical habitat co-occur with the use of EtO (Section V.A.). Exposure to wildlife from the use of EtO will be reduced through OPP's mitigation to reduce EtO usage through the cancellation of minor uses of EtO, phased cancellation of the use of EtO on certain food commodities, and the reduced concentration rate of EtO for medical device sterilization for new cycles. Additionally, environmental exposure will be further reduced through the current emissions controls required under OAR's NESHAP, which have been further strengthened by the publication of the *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review* on April 5, 2024.[12]

In this ID, the Agency is not making any human health or environmental safety findings associated with the Endocrine Disruptor Screening Program (EDSP) screening of EtO. The Agency will make an EDSP determination before issuing a final registration review decision for EtO. For more information, see Appendices C and D.

This document is organized into six sections:

- *Introduction* (summarizing the registration review milestones and responding to public comments);
- *Use and Usage* (discussing how and where EtO is used);
- *Scientific Assessments* (summarizing EPA's risk and benefits assessments, updating or revising previous risk assessments, and discussing risk characterization);
- *Interagency Considerations* (discussing EPA's coordination with OSHA and FDA on mitigation of EtO exposures);
- *Interim Registration Review Decision* (presenting EPA's interim decision on mitigation measures to address risks of concern identified at this point in the registration review process); and
- *Next Steps and Timeline* (discussing how and when EPA intends to complete registration review).

[12] EPA-HQ-OAR-2019-0178-1482 at www.regulations.gov.

A. Summary of EtO Registration Review Timeline

On September 25, 2013, the Agency formally initiated registration review for EtO with the opening of the registration review docket for the case.[13] The following summary highlights the docket opening and other significant milestones that have occurred thus far during the registration review of EtO:

- September 2013 – EPA posted the EtO *Preliminary Work Plan* (PWP) (September 25, 2013) to the public docket for a 60-day public comment period. Along with the PWP, the following documents were also posted in the ethylene oxide registration review docket (EPA-HQ-OPP-2013-0244):
    - *Ethylene Oxide (ETO): Review of Human Incidents* (May 8, 2013)
    - *BEAD Chemical Profile for Registration Review: Ethylene Oxide (ETO) (042301) (September 25, 2013)*

- April 2014 – EPA posted the EtO *Final Work Plan* (FWP) (April 4, 2014) to the public docket. The Agency received 12 comments on the PWP. Public comments on the PWP did not change the schedule, risk assessment needs, or anticipated data requirements in the FWP. In the FWP, EPA corrected the anticipated Registration Review schedule and noted that no additional data were needed outside of what was required in the PWP. After the PWP public comment period closed, the Agency received additional information from the Ethylene Oxide Sterilization Association, Inc. that was considered in the risk assessment phase of registration review. This additional information can be found in docket EPA-HQ-OPP-2013-0244 at www.regulations.gov.

- October 2014 – EPA issued a generic data call-in (GDCI) for EtO to obtain data needed to conduct the registration review risk assessments (GDCI-042301-1428). The registrants satisfied all required data except the non-guideline study Monitoring Data on Fumigated Commodities (required for the spice use only). The registrants submitted a waiver request for this study (MRID 50384901) on September 8, 2017. However, this waiver request was denied on July 17, 2018, due to a lack of information related to potential exposures within the various channels of trade after fumigation, dissipation of EtO beyond the facility, and the analytical method used to measure air concentrations.[14] The Agency has been coordinating with the Ethylene Oxide Task Force (EOTF) to fulfill this data requirement and is awaiting a protocol submission by EOTF. Accordingly, all data requirements have not been satisfied. For more information, see Sections III.A. and III.B.

- November 2020 – EPA posted the *Ethylene Oxide (EtO) Draft Human Health and Ecological Risk Assessment in Support of Registration Review* (2020 DRA) for a 60-day

[13] 40 C.F.R. § 155.50.
[14] Ethylene Oxide (EtO): Response to registrant's inhalation exposure monitoring requirements waiver request. Decision Number 533138. June 21, 2018.

public comment period. The Agency received 15 comments from 10 commenters. After the DRA public comment period closed, the Agency received additional submissions from the Ethylene Oxide Task Force and the American Chemistry Council. The Agency determined that the submissions included information that had already been considered during development of the DRA. All comments can be found in the docket for the EtO case. The Agency summarized and responded to these comments in the Proposed Interim Decision (PID). The comments did not change the risk assessments or registration review timeline for EtO.

- March 2023 – The Agency completed the Proposed Interim Decision (PID) for EtO. The PID was posted to the docket for a 75-day public comment period. Along with the PID, the following documents were also posted to the EtO docket.

    - Response to Public Comments for the Ethylene Oxide (EtO) Draft Risk Assessment (DRA). March 27, 2023.
    - 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. March 27, 2023.
    - Review of MRID 50231101. Ethylene Oxide Exposures for Ethylene Oxide Sterilization Plant Workers Submitted in Response to the Registration Review GDCI for EtO. March 23, 2023.
    - Food and Drug Administration Center for Devices and Radiological Health (FDA-CDRH) Medical Device Benefits Statement. March 15, 2023.
    - Ethylene Oxide (EtO) Spice Sterilizing Facilities. Center for Food Safety and Applied Nutrition (CFSAN), Food and Drug Administration (FDA) responses to questions from Office of Pesticide Programs (OPP), Environmental Protection Agency (EPA). December 20, 2022.
    - Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation. December 1, 2022.
    - Ethylene Oxide (EtO): Response to registrant's ambient air monitoring requirements waiver request. October 12, 2022.
    - Letter from Dr. Girvin Liggans, Acting Deputy Director for Plant Derived Foods, Office of Food Safety, Center for Food Safety and Applied Nutrition, Food and Drug Administration to Edward Messina, Director, Office of Pesticide Programs, Environmental Protection Agency. August 18, 2022.
    - Email Response to FDA and EPA Questions. Shannen Kelly, American Spice Trade Association (ASTA) to Aparna Tatavarthy, Office of Food Safety, Center for Food Safety and Applied Nutrition, Food and Drug Administration. August 12, 2022.
    - Ethylene Oxide (EtO): Summary of Hazard and Science Policy Council (HASPOC) Meeting on June 9th, 2022: Recommendations on the Need for a Special Acute Inhalation Toxicity Study. June 14, 2022.
    - Overview of Application Methods and Factors, Use, Usage, and Benefits of Commodity and Structural Fumigants: Phosphine [(066500) including Aluminum

Phosphide (066501) and Magnesium Phosphide (066504)], Propylene Oxide (042501), Sulfur Dioxide (077601), Sodium Metabisulfite (111409), Sulfuryl Fluoride, (078003), Ethylene Oxide (042301), and Methyl Bromide (053201). October 5, 2020.

- Letter from Laura Shumow, Executive Director, American Spice Trade Association (ASTA) to Susan Bartow, Pesticide Re-evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. June 25, 2020.
- Ethylene Oxide (ETO): Response to registrant's inhalation exposure monitoring requirements waiver request. June 21, 2018.
- Ethylene Oxide (ETO): Review of MRID 50231103 "Supplemental Information on Ethylene Oxide Industry Usage and Product Use Information." July 19, 2018.
- Ethylene Oxide: Revised Response to Data Waiver Requests Submitted by the Ethylene Oxide Task Force. March 9, 2018. Ethylene Chlorohydrin: Summary of Hazard and Science Policy Council (HASPOC) Meeting of January 21, 2016. Recommendations on the Requirement for a Chronic/Cancer Study. June 16, 2016.
- Ethylene Oxide: Response to Data Waiver Requests Submitted by the Ethylene Oxide Task Force. January 21, 2016.
- Ethylene Oxide/Ethylene Chlorohydrin: Summary of Hazard and Science Policy Council (HASPOC) Meeting of April 11, 2013. Recommendations on the need for multiple toxicology studies. May 14, 2013.

- January 2025 – The Agency completes the Interim Decision (ID) for EtO. The ID is posted to the docket. Along with the ID, the following documents were also posted to the EtO docket.

  - Response to Public Comments on the Ethylene Oxide (EtO) Draft Risk Assessment (DRA) Addendum.
  - Comment submitted by Thermo Fisher Scientific (posted December 8, 2023).
  - Ethylene Oxide – AdvaMed Response to FIFRA Proposed Interim Decision – May 17, 2024.
  - Ethylene Oxide – EOTF and EOSA Proposal for the Interim Decision – June 26, 2024.
  - EOTF Proposal for EtO Short Term Exposure Limit - July 2024.
  - Ethylene Oxide (EtO) Response to Registrant's Ecological Data Requirements Waiver Request. October 9, 2018.
  - EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders AdvaMed September 2023 - May 2024.
  - EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders American Federation of Labor and Congress of Industrial Organizations (AFL-CIO) May - June 2024.
  - EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Agri Neo July 17, 2023.

- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen September - December 2023.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders American Spice Trade Association (ASTA) November 2020 - September 2024.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders American Veterinary Medical Association (AVMA) December 7, 2023.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Balchem February - June 2024.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Becton Dickinson (BD) June 3, 2024.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Earthjustice et. al. June 12, 2023.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Ethylene Oxide Task Force (EOTF) and Ethylene Oxide Sterilization Association (EOSA) September 2023 - June 2024.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders European Union November 29, 2023.
- EPA Office of Pesticide Programs (OPP) Meetings Regarding Ethylene Oxide (EtO) Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) July 2023 - August 2024.
- EPA Office of Pesticide Programs (OPP) Meetings Regarding Ethylene Oxide (EtO) Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition (CFSAN) July 2022 - August 2024.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Kreyenbourg August 2, 2023.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders McCormick & Company, Incorporated November 2023 - May 2024.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Midwest Sterilization Corporation (MSC) September – October 2023.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders North Carolina Department of Agriculture & Consumer Services (NCDA&CS) October 2020 - November 2022.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders National Institute for Occupational Safety and Health (NIOSH) September 12, 2023.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Occupational Safety and Health Administration (OSHA) January – August 2024.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Picarro September 18, 2023.

- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Steris April 23, 2024.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Thermo Fisher August 16, 2023.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders U.S. Department of Agriculture (USDA) Office of Pest Management Policy (OPMP) December 2022 – September 2024.
- U.S. EPA, 2024. *Ethylene Oxide (EtO)/Ethylene Chlorohydrin (ECH). Chronic Dietary (Food Only) Exposure and Risk Assessment for Registration Review*. William H. Donovan. September 24, 2024.
- American Spice Trade Association (ASTA) Responses to EPA Questions on EtO Concentrations and Food Safety for Spices from Meeting on December 1, 2023.
- ASTA Responses to EPA Questions on Reconditioning and Proposed Phase-Out. June 28, 2024.
- Letter from Brian Hammons, President, Hammons Products Company to Jessica Bailey, Antimicrobials Division, Office of Pesticide Programs, Environmental Protection Agency. August 21, 2023.
- Email from Paul Bailey, Director, Plant Industries, Missouri Department of Agriculture to Wilfredo Rosado-Chaparro, Branch Supervisor, Environmental Protection Agency Region 7. December 2, 2024.
- American Black Walnut Marketing Board. Undated. *Black Walnuts A Nutritional Powerhouse from America's Forests*.
- EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Missouri Department of Agriculture (MDA) September 13, 2024.
- Email from Laura Shumow, Executive Director, ASTA, to Susan Bartow, Pesticide Re-Evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. November 26, 2024.
- Email from Food and Drug Administration (FDA) Human Foods Program (HFP), to Susan Bartow, Pesticide Re-Evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. December 2, 2024.

B. EtO Special Review

As discussed above, through the registration review of EtO, EPA will determine whether EtO continues to meet the standard for registration under FIFRA – i.e., does not cause unreasonable adverse effects to human health and the environment. Based on this determination, the Agency also intends to initiate termination of its Special Review of EtO. The Special Review process predates, and is distinct from, the registration review and reregistration processes. EPA may initiate the Special Review process if EPA determines that the use of a pesticide may pose significant risks. EtO entered EPA's Special Review process in 1978 based on concern for potential developmental toxicity, mutagenicity, and neurotoxic effects in workers who are exposed to EtO. A Position Document 1 (PD1) was published in the Federal Register on January

27, 1978, to announce the initiation of the Special Review.[15] In the early 1980s, the carcinogenicity of EtO became of concern and was included for consideration in the Special Review.

To terminate the Special Review of a chemical substance, EPA must publish first a Notice of Preliminary Determination, followed by a Notice of Final Determination, addressing the Agency's determination of whether the use of a pesticide causes unreasonable adverse effects to human health or the environment. On October 29, 2008, the Agency announced in the Federal Register the availability of Position Document 2/3 (PD 2/3). PD 2/3 presented the Agency's preliminary determination to terminate the Special Review of EtO after publication of the Reregistration Eligibility Decision (RED).[16] The Agency has not published a final determination terminating the Special Review of EtO, and since publication of the preliminary determination has received additional data about EtO which EPA has incorporated into the human health assessment for the registration review of EtO.

However, because through registration review EPA will be making a determination as to whether the use of EtO causes unreasonable adverse effects to human health or the environment – the same purpose for which Special Review is undertaken - EPA intends to initiate termination of the Special Review of EtO pursuant to the Agency's Special Review regulations based on the outcome of registration review. Following the publication of a final registration review decision, EPA will publish the Notice of Preliminary Determination, then publish the Notice of Final Determination after the public comment period on the Notice of Preliminary Determination. EPA will continue to review the registration of EtO as part of the ongoing registration review process.

C. Summary of Public Comments on the Proposed Interim Decision (PID)

During the 75-day public-comment period for the EtO PID (April 13, 2023 to June 27, 2023), the Agency received over 30,000 public comments, the majority of which were mass mailers. Comments were submitted by representatives from government, non-profit groups, private citizens, hospitals, bioscience industry, physicians' organizations, medical device distributors, medical device manufacturers, states, small businesses, and commercial sterilization facilities. The Agency has summarized and responded to all substantive comments and comments of a broader regulatory nature in Appendix E. The Agency thanks all commenters for participating and has considered all comments in developing this ID.

II. USE AND USAGE

[15] 43 Fed. Reg. 3,801.
[16] 73 Fed. Reg. 64,318.

EtO was first registered as a pesticide in the U.S. in 1966. Because it was registered before 1984, it was subject to reregistration, and a Reregistration Eligibility Decision (RED) was completed by EPA in 2008. There is currently one source of EtO for sterilization in the U.S.—ARC Specialty Products of Balchem Corporation.

There are 14 registered FIFRA Section 3 products containing EtO as an active ingredient (a.i.), and one FIFRA section 24(c) registration for the use of EtO in beekeeping in North Carolina. On October 16, 2024, EPA published the Federal Register Notice (FRN) *Pesticide Registration Maintenance Fee: Product Cancellation Order for Certain Pesticide Registrations*, which included Andersen EtO products EPA Reg. No. 69340-5 Eogas AN1005 and EPA Reg. No. 69340-9 AN7514.[17] EtO is formulated and marketed as a pressurized gas. The end-use formulations are all gas mixtures of EtO and other gases (e.g., carbon dioxide) in varying concentrations. Table 1 below presents a summary of the registered antimicrobial and conventional uses of EtO.

Table 1. Summary of EtO Registered Uses

EPA Reg. No.	% a.i.	Packaging (EtO Content)	Use Site
36736-2	100	Bulk Cylinder	Medical or laboratory items, pharmaceuticals, and aseptic packaging, (21 C.F.R. 201.1(d)(5)), whole and ground spices or other seasoning materials (40 C.F.R. 180.151), artifacts, archival material, library objects, cosmetics, and musical instruments.
36736-3	80	Bulk Cylinder	Medical or laboratory items, pharmaceuticals, and aseptic packaging, (21 C.F.R. 201.1(d)(5)), whole and ground spices or other seasoning materials (40 C.F.R. 180.151), artifacts, archival material, library objects, cosmetics, and musical instruments.
36736-4	10	Bulk Cylinder	Medical or laboratory items, pharmaceuticals, and aseptic packaging, (21 C.F.R. 201.1(d)(5)), whole and ground spices or other seasoning materials (40 C.F.R. 180.151), artifacts, archival material, library objects, cosmetics, and musical instruments.
36736-5	20	Bulk Cylinder	Medical or laboratory items, pharmaceuticals, and aseptic packaging, (21 C.F.R. 201.1(d)(5)), whole and ground spices or other seasoning materials (40 C.F.R. 180.151), artifacts, archival material, library objects, cosmetics, and musical instruments.
36736-6	12	Bulk Cylinder	Medical or laboratory items, pharmaceuticals, and aseptic packaging, (21 C.F.R. 201.1(d)(5)), whole and ground spices or other seasoning materials (40 C.F.R. 180.151), artifacts, archival material, library objects, cosmetics, and musical instruments.
36736-7	8.5[18]	Bulk Cylinder	Medical or laboratory items, pharmaceuticals, and aseptic packaging, (21 C.F.R. 201.1(d)(5)), whole and ground spices or other seasoning materials (40 C.F.R. 180.151), artifacts, archival material, library objects, cosmetics, and musical instruments.

[17] https://www.federalregister.gov/documents/2024/10/16/2024-23381/pesticide-registration-maintenance-fee-product-cancellation-order-for-certain-pesticide.

[18] A company in Missouri commented on the PID that they use this formulation to treat black walnuts.

Table 1. Summary of EtO Registered Uses

EPA Reg. No.	% a.i.	Packaging (EtO Content)	Use Site
36736-8	100	Bulk cylinder / Manufacturing use product[19]	Medical/lab items; pharmaceuticals; packaging; spices; seasonings; artifacts, archival material, library objects
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)	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.
69340-6	96	Cartridge (10.5 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.
69340-7	97	Ampule (17.6 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.
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.

EtO is registered for the sterilization of medical devices and equipment (including veterinary equipment), laboratory items, pharmaceuticals, and aseptic packaging. EtO is registered to reduce the microbial load on certain food commodities (e.g., whole and ground spices or other seasoning materials (see 40 C.F.R. 180.151)), archival and museum materials, musical instruments, and cosmetics. Additionally, EtO is registered for use under a special local needs registration in North Carolina for use on beekeeping equipment contaminated with American

[19] A manufacturing use product is a registered pesticide product that is used to formulate other pesticide products.

foulbrood (AFB) or other pests. A company commented on the PID that they also use EtO to treat black walnuts in a commercial sterilization facility in Missouri.[20] For more information on black walnuts see Section V.A. (*Label Consistency and Clarification* subsection).

EPA's Office of Air and Radiation's Office of Air Quality Planning and Standards (OAR OAQPS) estimates that the overall EtO usage as a pesticide (sterilant) in the U.S. is 14 million pounds annually.[21] As a pesticide, the majority of EtO usage in the U.S. is for sterilization of medical equipment. Usage of EtO for dried herb and spice fumigation is the second most common use pattern and represents approximately 5 - 6% of the total EtO used within the U.S. The American Spice Trade Association (ASTA) reports that the spice industry uses approximately 800,000 pounds of EtO on an annual basis in the U.S.[22] For beekeeping equipment, the use of EtO is limited via a FIFRA section 24(c) registration to one facility in North Carolina, and the amount of EtO used pursuant to this registration is likely to be low. The Agency expects the total EtO usage for other registered use sites—musical instruments, cosmetics, museum, library, and archival materials—to be very low or zero. There are 93 commercial sterilization facilities using EtO in the U.S. (along with 11 research and development facilities); six of the facilities treat only food commodities, four facilities treat both medical devices and food commodities, and the remaining 83 facilities treat only medical devices and pharmaceutical products. EtO also is used to treat medical equipment in healthcare facilities such as hospitals, veterinarian offices, and dental offices; the amount of EtO used in healthcare facilities is a much lower as compared to the commercial sterilization use.

Antimicrobial Uses: EtO is generally used as a sterilant for single use, and reusable medical devices and equipment (see, e.g., 21 C.F.R. § 880.6100, 880.6860). EtO is used to sterilize approximately 50% of all sterilized medical devices, annually, including an estimated 95% of all

[20] Letter from Brian Hammons, President, Hammons Products Company to Jessica Bailey, Antimicrobials Division, Office of Pesticide Programs, Environmental Protection Agency. August 21, 2023.
[21] Usage information was collected for the year for which the most recent information was available at each facility, ranging from 2005 to 2019, and was compiled from a number of sources including Clean Air Act Section 114 Information Collection Request for Chemical Manufacturers, EPA, state, or local government inspection reports, company reports, and facility usage logs.
[22] American Spice Trade Association (ASTA). 2020. ASTA's reply to EPA questions regarding ethylene oxide use on spices. Email from Laura Shumow, Executive Directors, ASTA to Susan Bartow, Pesticide Re-Evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. June 25, 2020.

surgical kits[23, 24, 25, 26]. The other registered antimicrobial uses of EtO include the fumigation/sterilization of artifacts, archival material, library objects, cosmetics, and musical instruments. The antimicrobial products are packaged as bulk cylinders for use in tractor trailer-sized chambers in commercial sterilization facilities or as cartridges for use in oven-sized chambers in healthcare facilities.

The application rates are not generally listed on the labels. The FDA website indicates that two voluntary consensus standards (ANSI AAMI ISO 11135:2014 and ANSI AAMI ISO 10993-7:2008(R)2012) describe how to develop, validate, and control EtO sterilization processes for medical devices and the acceptable levels of residual EtO and ethylene chlorohydrin (an EtO reaction product) left on a device after it has undergone EtO sterilization.[27] These standards help ensure levels of EtO on medical devices are within safe limits for patient use. These standards also ensure devices meet sterility assurance levels.[28]

Conventional Uses: EtO is a commodity fumigant/sterilant registered for use to reduce pathogen load (such as *Salmonella* and *Escherichia coli*) on dried herbs and spices, processed vegetables that have been dried or dehydrated, and/or other seasoning materials. A company in Missouri commented on the PID that they also use EtO to treat black walnuts. This document uses the term 'food uses' and 'food commodities' to designate these various uses. ASTA estimates that approximately 40% of dried spices in the U.S. are treated with EtO each year.[29] There are eight products currently registered for treatment of food commodities. One of these products is also used to treat black walnuts. All of these products are formulated as pressurized gas contained in cylinders.

[23] Gamma Industry Processing Alliance (GIPA). 2017. A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products. Found at http://gipalliance.net/wp-content/uploads/2013/01/GIPA-WP-GIPA-iia-Sterilization-Modalities-FINAL-Version-2017-October-308772.pdf. Accessed August 2021.

[24] Federal Advisory Committee Act (FACA). 2019. General Hospital and Personal Use Devices Panel of the Medical Devices Advisory Committee Meeting Announcement, FDA Executive Summary - EtO. https://www.fda.gov/advisory-committees/advisory-committee-calendar/november-6-7-2019-general-hospital-and-personal-use-devices-panel-medical-devices-advisory-committee#event-materials. Accessed August 2021.

[25] Ethylene Oxide Task Force (EOTF). 2020. Ethylene Oxide Benefits Statement submitted by B&C Consortia Management, L.L.C. on behalf of the EOTF. EOTF email to EPA regarding benefits of ethylene oxide for medical devices. Email sent from Lisa Campbell, Partner, Bergeson & Campbell PC to Jessica Bailey, Antimicrobial Division, Office of Pesticide Programs, Environmental Protection Agency. May 6, 2020.

[26] B&C Consortia Management, LLC. 2014. Registration Review of Ethylene Oxide Stakeholder Meeting presentation. Docket ID: EPA-HQ-OPP-2013-0244-0018. https://www.regulations.gov/document/EPA-HQ-OPP-2013-0244-0018. Accessed July 2022.

[27] Ethylene chlorohydrin is a reaction product of EtO. See ANSI AAMI ISO 10993-7:2008(R)2012.

[28] For additional information on sterilization for medical devices, please see: https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/ethylene-oxide-sterilization-medical-devices.

[29] American Spice Trade Association (ASTA). 2020. ASTA's reply to EPA questions regarding ethylene oxide use on spices. Email from Laura Shumow, Executive Director, ASTA, to Susan Bartow, Pesticide Re-Evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. June 25, 2020.

Sterilization/fumigation with EtO must be performed only in vacuum or gas tight chambers designed for use with EtO. The EtO sterilization method must use a single chamber to pre-condition and aerate. The maximum application rate for treatment of food commodities is 500 mg/L (or 31.22 lb a.i./1,000 ft^3) in a sealed chamber.

III. SCIENTIFIC ASSESSMENTS

A. Human Health Risks

The Agency has summarized the human health sections of the 2020 DRA and 2023 DRA Addendum below. The Agency used the most current science policies and risk assessment methodologies to prepare the risk assessment and addendum in support of the registration review of EtO. For additional details on the 2020 DRA and 2023 DRA Addendum, see *Ethylene Oxide (EtO) Draft Human Health and Ecological Risk Assessment in Support of Registration Review* and *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* in EPA's public docket (EPA-HQ-OPP-2013-0244).

Definition of terms

For purposes of the registration review of EtO, EPA is using the following definitions for describing the different groups of individuals exposed to EtO:

- *Occupational handler*: A person who is directly involved in EtO sterilization, in commercial sterilization facilities, healthcare facilities or beekeeping operations. This worker, for example, would be loading or unloading sterilization or aeration chambers/areas.

- *Occupational bystander*: A person who, by nature of their employment, could be exposed to EtO. This includes workers within a facility or area where EtO is used, but who do not directly handle EtO (for example, workers in control rooms or storage warehouses). This also includes persons employed at other workplaces nearby facilities or areas where EtO is used, who would spend a significant amount of time at that location (e.g., 8 hours per day, 5 days per week). A worker who is employed nearby a facility in another workplace may also be referred to as a "non-residential bystander" (see below).

- *Non-residential bystander*: A person who may be exposed to EtO who does not live near a facility or area where EtO is used, but who may otherwise spend a significant amount of time near the facility. For example, children in schools or daycares who typically spend several hours per day and five days per week in that location, or persons employed at other workplaces, nearby facilities or areas where EtO is used, who would

spend a significant amount of time at that location (e.g., 8 hours per day, 5 days per week).

- *Residential bystander*: A person who may be exposed to EtO who lives nearby a facility or area where EtO is used.

Risk Summary and Characterization

Under FIFRA, OPP applies a "no unreasonable adverse effects" standard, considering both dietary and non-dietary exposures, in making risk management decisions. To help initially identify chemicals which may pose such unreasonable adverse effects, 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. With respect to cancer risks, OPP generally seeks to reduce the risk to less than 1×10^{-6} (1 in 1 million) for both occupational and residential exposures. At that level, OPP generally considers risks to be negligible and would not pursue additional risk mitigation measures. In some cases, when it is not possible to mitigate to this level of risk and the benefits of the pesticide are high, a risk target of up to 1×10^{-4} (100 in 1 million) may be used for occupational exposures. Please see Appendix F for more details on the risk decision frameworks in both EPA's Office of Pesticide Programs (OPP) and EPA's Office of Air and Radiation (OAR). [30]

As explained in the following sections, 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 (IUR) for adults. Given the high benefits of EtO, OPP examined risks from occupational exposures in the range of 1×10^{-4} (100 in 1 million) to determine whether benefits of use outweigh the risks and whether mitigation is appropriate to reduce those risks. For EtO, risks exceed 100 in 1 million; however, the pesticidal uses of EtO also provide significant benefits, as described in Section III.C. For occupational bystanders employed in commercial sterilization facilities, healthcare facilities, and beekeeping equipment treatment areas, EPA is establishing a risk threshold of 100 in 1 million. For non-residential bystanders who are employed nearby EtO treatment facilities, EPA is establishing a risk threshold of 1 in 1 million. Calculations in all scenarios indicate EtO concentrations would have to be extremely low in order to meet either risk threshold. As explained in the following sections, this calculation indicates that if the EtO exposure for workers in contract sterilization facilities in these areas does not exceed 0.19 ppb

[30] EPA's Office of Air and Radiation (OAR) "considers all health information, including risk estimation uncertainty, and includes a presumptive limit on maximum individual lifetime [cancer] risk (MIR) 1 of approximately 1 in 10 thousand." (54 FR 38045, September 14, 1989). If risks are unacceptable, the EPA must determine the emissions standards necessary to reduce risk to an acceptable level without considering costs. EPA considers whether the emissions standards provide an ample margin of safety to protect public health ''in consideration of all health information, including the number of persons at risk levels higher than approximately 1 in 1 million, as well as other relevant factors, including costs and economic impacts, technological feasibility, and other factors relevant to each particular decision." After conducting the ample margin of safety analysis, OAR considers whether a more stringent standard is necessary to prevent, taking into consideration costs, energy, safety, and other relevant factors, an adverse environmental effect.

as an 8-hour time-weighted average (TWA), the cancer risk will not exceed 1 x 10^{-4} (100 in 1 million). If the EtO exposure for workers employed in nearby workplaces (i.e., not the commercial sterilization facility) does not exceed 0.0019 ppb, the cancer risk will not exceed 1 x 10^{-6} (1 in 1 million). This calculation of 0.0019 ppb is relevant to both the antimicrobial and conventional uses of EtO.

EtO is a colorless, highly reactive gas. The primary route of exposure is by inhalation. Once absorbed, EtO is distributed throughout the body and metabolized to ethylene glycol and to glutathione conjugates. EtO is an electrophilic agent and alkylates (introduces an alkyl radical to) nucleophilic groups in macromolecules such as hemoglobin and deoxyribonucleic acid (DNA). EtO is genotoxic in almost all available studies, and the weight of evidence supports a mutagenic mode of action for carcinogenicity of EtO. For workers employed in EtO-manufacturing facilities and in sterilizing facilities, there is evidence of an increased association with cancer of the lymphohematopoietic system and of breast cancer mortality in females. EPA's 2016 Integrated Risk Information System (IRIS) cancer assessment of EtO characterized EtO as "carcinogenic to humans" by the inhalation route of exposure and established a cancer unit risk estimate that represents both cancer types combined.[31] The 2023 DRA Addendum includes a quantitative risk assessment based on the 2016 EPA Integrated Risk Information System (IRIS) cancer assessment.

Neurotoxicity is also observed in repeat dose toxicity studies with EtO in experimental animals and from exposure in humans. Peripheral neuropathy, impaired hand-eye coordination and memory loss have been reported in workers exposed to EtO for longer periods.

OPP collaborated with the Office of Research and Development (ORD) and Office of Air and Radiation (OAR) during their assessment process of EtO to further inform the cancer evaluation characterization and ongoing work to characterize and mitigate exposures in the sterilizer industry. Additionally, as part of the pesticide registration review process, OPP routinely meets with stakeholders, including the EtO industry, and federal agencies such as the Occupational Safety and Health Administration (OSHA) and the Food and Drug Administration (FDA). See Section IV.

In the 2020 *Ethylene Oxide Draft Risk Assessment,* OPP presented multiple perspectives on cancer evaluations for EtO but did not choose a single value for risk extrapolation, nor did OPP provide a critical review of the available approaches. Based on the range of cancer inhalation unit risks (IUR) provided in the qualitative assessment, OPP believed that additional mitigation of EtO exposure would be necessary to address cancer risk from inhalation exposure to EtO.

[31] U.S. EPA. Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide (CASRN 75–21– 8) In Support of Summary Information on the Integrated Risk Information System (IRIS). December 2016. EPA/635/R–16/350Fa. Available at: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/1025tr.pdf.
See Docket ID No. EPA–HQ–OAR–2018–0746 at www.regulations.gov.

In the 2023 DRA Addendum, OPP updated a portion of the EtO risk characterization by providing a quantitative risk assessment that used the inhalation unit risk (IUR) value from the 2016 EPA IRIS cancer assessment to assess inhalation cancer risk to workers and bystanders. The 2016 IRIS assessment went through "unusually extensive processes for the consideration of public comment and external peer review," and is considered by EPA to be the "best available scientific information regarding cancer risks from EtO." Further, since the publication of the 2020 DRA, EPA has repeatedly reviewed and responded to comments on the EtO IRIS assessment and its use in risk assessments in support of Agency actions. [32, 33, 34] The EPA has confirmed its use of the IRIS IUR for EtO in its risk assessments and its rejection of the use of alternative IURs for EtO.[35] Therefore, the 2023 DRA Addendum updates the EtO 2020 DRA for the human health inhalation risk assessment using the IUR values from the IRIS Assessment to characterize the cancer risk from inhalation exposure.[36] However, for reasons described in this document, the mitigation measures found to be necessary are not intended to establish a level of exposure to EtO that is without risk for all risk assessment scenarios, but rather to substantially reduce exposure based on technological feasibility. Please see Section V.A. for a full description of mitigation measures.

For the conventional food commodity fumigation use of EtO, the assessment included EtO and its reaction products ethylene bromohydrin (EBH), ethylene chlorohydrin (ECH), and ethylene

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[32] U.S. EPA. 2022. Reconsideration of the 2020 National Emission Standards for Hazardous Air Pollutants: Miscellaneous Organic Chemical Manufacturing Residual Risk and Technology Review. (87 FR 77985; December 21, 2022). Docket ID No. EPA-HQ-OAR-2018-0746. Available at: https://www.regulations.gov/search?documentTypes=Rule&filter=EPA-HQ-OAR-2018-0746.
U.S. EPA. 2022. Summary of Public Comments and Responses for the Reconsideration of the 2020 National Emission Standards for Hazardous Air Pollutants: Miscellaneous Organic Chemical Manufacturing Residual Risk and Technology Review. December 2022. Docket ID No. EPA-HQ-OAR-2018-0746-0327. Available at: https://www.regulations.gov/search?filter=EPA-HQ-OAR-2018-0746-0327.

[33] U.S. EPA. 2024. National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review. (89 FR 24090; April 5, 2024). Docket ID No. EPA-HQ-OAR-2019-0178-1482. Available at: https://www.regulations.gov/search?filter=EPA-HQ-OAR-2019-0178-1482. U.S. EPA. 2024. Summary of Public Comments and Responses for Risk and Technology Review for Ethylene Oxide Commercial Sterilization Facilities. Docket ID No. EPA-HQ-OAR-2019-0178-1595. Available at www.regulations.gov in the document EPA-HQ-OAR-2019-0178-1595 (See Chapter 5: IRIS EtO Assessment).

[34] U.S. EPA. 2024. New Source Performance Standards for the Synthetic Organic Chemical Manufacturing Industry and National Emission Standards for Hazardous Air Pollutants for the Synthetic Organic Chemical Manufacturing Industry and Group I & II Polymers and Resins Industry. (89 FR 42932; May 16, 2024). Docket ID No. EPA-HQ-OAR-2022-0730. Available at: https://www.regulations.gov/search?filter=EPA-HQ-OAR-2022-0730.
U.S. EPA. 2024. Summary of Public Comments and Responses for New Source Performance Standards for the Synthetic Organic Chemical Manufacturing Industry and National Emission Standards for Hazardous Air Pollutants for the Synthetic Organic Chemical Manufacturing Industry and Group I & II Polymers and Resins Industry. Docket ID No. EPA-HQ-OAR-2022-0730-2764. Available at: https://www.regulations.gov/search?filter=EPA-HQ-OAR-2022-0730-2764.

[35] U.S. EPA. 2022. Reconsideration of the 2020 National Emission Standards for Hazardous Air Pollutants: Miscellaneous Organic Chemical Manufacturing Residual Risk and Technology Review. (87 FR 77985; December 21, 2022). Docket ID No. EPA-HQ-OAR-2018-0746. Available at: https://www.regulations.gov/search?documentTypes=Rule&filter=EPA-HQ-OAR-2018-0746.

[36] 87 Fed. Reg. 77, 985 (Dec. 21, 2022).

glycol (EG). Formation of EBH and ECH results from fumigation of foods with EtO due to interaction with natural bromides and chlorides present in the food. Formation of EG results from high sterilization concentrations of EtO, where EtO reacts with moisture to form EG. The 2020 DRA primarily focused on EtO (for the inhalation route) and ECH (for the dietary route) since (1) residue level comparisons from sterilization studies and toxicity comparisons from literature reports indicate that dietary assessments of ECH are protective for residues of EG, (2) residue levels of EBH are insignificant compared to the residue levels of ECH, and thus it is sufficient to regulate only residues of ECH for dietary exposure, and (3) measurements of EtO from a spice sterilization study indicate that it dissipates rapidly after sterilization and is unlikely to be found in spices available for consumption. In the 2020 DRA and 2023 DRA Addendum, EPA concluded that dietary risks from exposures to EtO and its reaction products in food and drinking water are not of concern.

In September 2024, the Agency updated the dietary assessment using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID) Version 4.02 and incorporating information submitted during the PID public comment period and additional outreach to stakeholders.[37] The 2024 assessment is titled *Ethylene Oxide (EtO)/Ethylene Chlorohydrin (ECH). Chronic Dietary (Food Only) Exposure and Risk Assessment for Registration Review*. This updated assessment also concludes that dietary risks from exposures to EtO and its reaction products in food and drinking water are not of concern.

Dietary (Food + Water) Risks

EPA did not identify any dietary risks of concern for EtO or ECH. A quantitative dietary assessment was not conducted for EtO since sterilization studies[38] show that EtO residues disappear rapidly after sterilization and are unlikely to be found in treated commodities available for consumption. EtO residues are expected to be present on commodities immediately after the fumigation process (e.g., 24 hours) and may be present as the commodity enters the channels of trade; therefore, a tolerance for EtO is needed and was established with 2005 residue data for the single chamber fumigation process required on product labels. However, the EtO residues are expected to completely dissipate by the time the commodity is available for consumption (e.g., two months)[39, 40] and thus a quantitative dietary assessment for EtO was not conducted. Because exposures to residues of EtO in food and drinking water are expected to be minimal to none, no dietary risks are expected.

[37] U.S. EPA, 2024. *Ethylene Oxide (EtO)/Ethylene Chlorohydrin (ECH). Chronic Dietary (Food Only) Exposure and Risk Assessment for Registration Review*. William H. Donovan. September 24, 2024.
[38] MRID 46625301. Magnitude of the Residue of Ethylene Oxide and Ethylene Chlorohydrin in/on Spices. Wright, M. (2005). Study sponsored by American Spice Trade Association. 829 p.
[39] MRID 46625301. Magnitude of the Residue of Ethylene Oxide and Ethylene Chlorohydrin in/on Spices. Wright, M. (2005). Study sponsored by American Spice Trade Association. 829 p.
[40] Memorandum. *Ethylene Oxide. Case 2275. Results of Trade Practices Survey on Spices & Anticipated Residues for Dietary Exposure Assessment*. Leung Cheng, Health Effects Division. March 26, 1997.

ECH is a reaction product formed during the EtO fumigation. ECH residues are present on commodities immediately after the fumigation process and when the commodities are available for consumption. Therefore, both tolerances and a dietary assessment are needed for ECH. The updated 2024 food-only chronic dietary risk assessment was conducted for ECH using the Dietary Exposure Evaluation Model - Food Consumption Intake Database (DEEM-FCID, ver.4.02) which incorporates food consumption data from the United States Department of Agriculture (USDA) National Health and Nutrition Examination Survey, What We Eat in America (NHANES/WWEIA; 2005-2010).

The updated assessment also incorporated information that the Agency received from the American Spice Trade Association (ASTA) in the public comments on the 2023 PID and in follow up communications. In the PID comments, ASTA indicated that EtO remains critical for the safety of various dried vegetable commodities including onion, garlic, turmeric, ginger, pepper (*Capsicum* spp.), and galangal (*Alpinia officinarum* Hance).[41] ASTA also noted that dried vegetables including pumpkin flakes, dehydrated diced tomatoes, and dried bell peppers are critical for the spice and seasoning industries and are often handled within the same facilities as other spices and herbs.

More recently, ASTA informed the Agency that the following additional dried vegetable commodities may be treated with EtO as components of seasoning blends: asparagus, artichoke, green bean, green bell pepper, red bell pepper, broccoli, cabbage, carrot, celery stalk, corn, kelp, leek, mushroom, tomato, pumpkin flakes, and meleguenta (also known as Grains of paradise).[42] Accordingly, the dietary assessment was updated to reflect the new information from ASTA to ensure that the current use of EtO on dried vegetables in the spice and seasoning industries does not result in dietary risks of concern.

EPA did not conduct a quantitative acute dietary risk assessment as toxicological effects attributable to a single dose were not present (i.e., no acute endpoint identified). In addition, a separate cancer dietary risk assessment was not conducted because the chronic assessment adequately accounts for all chronic toxicity, including potential carcinogenicity. The conservative chronic dietary risk assessment assumed 100% of registered food commodities were treated with EtO post-harvest, and that the ECH residues on such crops reflected tolerance-level residues.[43] All processing factors were set to 1 since drying procedures are performed prior to sterilization. No residues were included in the dietary exposure assessment for drinking water, as uses of EtO for indoor food and nonfood uses will result in negligible exposures from drinking water because EtO is a volatile gas and its use in sterilization chambers is unlikely to result in EtO residues in groundwater or surface water.

Moreover, residential exposures to ECH are not expected because ECH is a reaction product that forms on the surface of the treated commodity during EtO fumigation. ECH is not volatile

[41] EPA-HQ-OPP-2013-0244-0130 at www.regulations.gov.
[42] EPA-HQ-OPP-2013-0244-0433 at www.regulations.gov.
[43] 40 C.F.R. §180.151.

and will remain on the commodity; therefore, the only relevant exposure pathway is through dietary sources. The resulting chronic exposure estimates do not exceed the Agency's level of concern (LOC; 100% of the chronic population adjusted dose (cPAD)); children 3-5 years old were the most highly exposed population subgroup at 15% the cPAD, while that for the U.S. population was 6.2% cPAD. The 2024 updated dietary assessment did not change OPP's conclusions about dietary risks.

Commercial Sterilization Facilities: Residential Bystander Exposures and Risks

There is the potential for EtO exposure to children and adults who live near sterilization facilities. These exposures were also addressed by the OAR rulemaking.[44] The EtO average daily concentration at which the cancer risk is 1 x 10^{-6}, and therefore not considered by OPP to be of concern for non-occupational exposures, was back calculated from the IUR for lifetime exposure. This is assuming continuous exposure (i.e., 24 hours a day for seven days a week) for a 70-year lifetime starting at birth, which likely represents a conservative exposure scenario. The IUR already accounts for application of the age dependent adjustment factors (ADAFs) for early life exposures and, therefore, can be used with exposures that have not been adjusted for ADAFs to estimate inhalation cancer risk. 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 x 10^{-6} (1 in 1 million). This concentration is below the limit of detection (LOD) of 20-90 ppt for EtO in ambient air.

Commercial Sterilization Facilities: Non-Residential Bystander Exposures and Risks (Daycare Centers and Schools)

Non-residential bystander exposures can occur at a variety of facilities such as daycare centers, schools, 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. Exposures to children attending daycare centers and schools are protective of other non-residential bystander exposures because they occur more frequently and with a longer daily duration. In addition, EtO is a mutagen that requires the use of age dependent adjustment factors (ADAFs) to assess childhood exposures. The EtO concentration at which the cancer risk equals 1 x 10^{-6} was back calculated from the unadjusted IRIS IUR using child/lifestage-specific ADAFs, and 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. These calculations indicate that the cancer risk is 1 x 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). This concentration is below the LOD of 20-90 ppt for EtO in ambient air.

[44] U.S. EPA, 2022. Reconsideration of the 2020 National Emission Standards for Hazardous Air Pollutants: Miscellaneous Organic Chemical Manufacturing Residual Risk and Technology Review. FR Doc. 2022-01923, Filed: 02/03/2022. See OAR's residual risk assessment for the commercial sterilization facilities source category document in support of the 2024 Risk and Technology Review Required Rule located at www.regulations.gov in docket EPA-HQ-OAR-2019-0178-1576.

To get a better understanding of how the back-calculated concentrations that exceed risks of concern for residential and non-residential bystanders (e.g., children who attend school) relate to concentrations around facilities, the air concentrations developed by the Office of Air and Radiation (OAR) in their recent rulemaking were considered.[45] Air concentrations were modeled around each sterilization facility 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 x 10^{-6} for children in schools/daycare centers that are in non-residential areas near sterilization facilities, which means that they also exceed the level of 0.11 ppt that corresponds to a cancer risk of 1 x 10^{-6} for children and adults who live near sterilization facilities.

Health Care Facilities: Residential and Non-Residential Bystander Exposures

Since 2010, healthcare sterilization facilities have been required to utilize all-in-one sterilizers (i.e., materials are treated and aerated in the same chamber to reduce worker exposure) in accordance with the EtO RED.[46] These facilities sterilize material in oven-sized chambers using 4.5 to 170 grams of EtO per load (in comparison, EtO usage is much smaller in healthcare facilities compared to commercial sterilization facilities, where fumigation takes place in tractor trailer sized chambers). 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.[47] Given this information, exposures to residential and non-residential bystanders near health care facilities are expected to be minimal, but the exact concentrations are not known and therefore the risks were not quantitatively assessed in the 2020 DRA or 2023 DRA Addendum. It is known, however, that the exposures that would result in a cancer risk of 1 in 1 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 and daycares). EPA OPP does not have monitoring data from health care facilities to confirm potential exposure concentrations to bystanders. EPA OAR regulates hospital sterilizers using EtO as a separate source category under 40 C.F.R. part 63 subpart WWWWW National Emission Standards for Hospital Ethylene Oxide Sterilizers. The hospital sterilizers NESHAP applies to hospitals that provide medical care and treatment for patients on an inpatient basis under supervision of licensed physicians and under nursing care offered 24 hours per day. The hospital sterilizers rule is currently undergoing review in OAR and is outside the scope of OAR's recent rulemaking effort, which focused on conducting a NESHAP review for the commercial sterilizer facilities source category under 40 C.F.R part 63 subpart O.

[45] See OAR's residual risk assessment for the commercial sterilization facilities source category document in support of the 2024 Risk and Technology Review Required Rule located at www.regulations.gov in docket EPA-HQ-OAR-2019-0178-1576.
[46] Reregistration Eligibility Decision for Ethylene Oxide. March 31, 2008.
[47] ANSI/AAMI, 2018. American National Standard: Ethylene Oxide Sterilization in Health Care Facilities: Safety and Effectiveness. ANSI/AAMI ST41:2008/(R)2018. American National Standards Institute/Association for the Advancement of Medical Instrumentation (ANSI/AAMI). 2018.

Beekeeping Equipment Fumigations in North Carolina: Residential and Non-Residential Bystander Exposures and Risks

For the FIFRA section 24(c) 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 (24 hours/day for four or eight exposure days per year for 70 years of exposure per lifetime), was conducted using the Probabilistic Exposure and Risk Model for Fumigants (PERFUM)[48]. 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 and 70 years of exposure per lifetime. The IRIS inhalation unit risk for environmental exposures for a full lifetime [5.0×10^{-3} per $\mu g/m^3$ (9.15×10^{-3} per ppb)] was used to estimate cancer risks.

The distances from the fumigation chamber at which the cancer risk estimates are less than 1×10^{-6} increase from lower to higher percentiles. For example, at the 75^{th} and 80^{th} percentiles, the distance from the fumigation chamber at which the cancer risk is less than 1×10^{-6} is only 10 meters, while at the 90^{th} percentiles, distances of 300 meters or more are necessary to reach cancer risk estimates less than 1×10^{-6}. A specific percentile has not been selected for regulation (and correspondingly a buffer distance from the fumigation chamber has not been established) since the Agency has determined that it is necessary to terminate the use of EtO on beekeeping equipment in North Carolina (see Section V.A for details).

Occupational Bystander and Occupational Post Application Risk

OPP considers the potential for exposure to occupational bystanders who work in non-processing areas of treatment facilities, healthcare facilities, or beekeeping equipment treatment areas; in downstream facilities such as warehouses where the treated product is shipped and stored; or in other workplaces that are near the treatment facilities, healthcare facilities, or beekeeping equipment treatment areas.

To get a better understanding of how the back calculated EtO concentrations that exceed risks of concern for occupational bystanders (adults who work near sterilization facilities) relate to concentrations around facilities, the air concentrations modeled by the Office of Air and

[48] PERFUM is a model that adapts EPA air dispersion algorithms to develop probabilistic estimates of acute exposures to bystanders following fumigant applications. See U.S. EPA, 2019. User's Guide for the Probabilistic Exposure and Risk model for Fumigants PERFUM Version 3.0. Prepared by Exponent, 1800 Diagonal Road, Suite 500 Alexandria, VA 22314. Sponsored by U.S. EPA, OPP, Health Effects Division (HED). October 28, 2019.

Radiation (OAR) in their recent rulemaking were considered.[49] Air concentrations were modeled around each sterilizing facility 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 0.0019 ppb (1.9 ppt) that corresponds to cancer risk of 1×10^{-6} for adults who work near facilities modeled by OAR. The IRIS inhalation unit risk for adult-based less-than-lifetime exposure scenarios [3×10^{-3} per $\mu g/m^3$ (5.5×10^{-3} per ppb)] was used to estimate cancer risks.

Aggregate Risks

In an aggregate assessment conducted to support the safety of EtO tolerances, EPA considers the combined pesticide exposures and risks from three major sources: food, drinking water, and residential / non-occupational exposures. In the context of discussing the FFDCA aggregate assessment, EPA is using the term "residential" to reflect the FFDCA requirement to consider non-occupational sources of exposure to the pesticide chemical residue. The Agency sums the exposures from these sources and compares the aggregate exposure to quantitative estimates of hazard. EPA considers the route, duration, and potential for co-occurrence of exposure when assessing aggregate risks.

EtO

EPA did not conduct a quantitative aggregate assessment for EtO, although it has determined that exposures to EtO will not result in aggregate risks of concern for purposes of supporting the EtO tolerances. EPA has concluded that dietary risks from exposures to EtO in food and drinking water are not of concern. This conclusion is based on residue data showing that there is no expectation of residues of EtO on food when consumed. Although residue data show that there are residues on food treated with EtO following fumigation, for 24 hours, the available data indicates that most spices are not available for purchase until at least 2 months after treatment, at which time, extrapolated residues indicate no residues of EtO on food.[50, 51] Moreover, EPA does not expect any residues in drinking water, because EtO is a volatile gas and its use in sterilization chambers is unlikely to result in EtO residues in groundwater or surface water.

Under EPA's General Principles for Performing Aggregate Exposure and Risk Assessments, EPA considers many factors in determining whether to aggregate exposures. For example, EPA's guidance says that exposure scenarios should not be combined when there are different

[49] See OAR's residual risk assessment for the commercial sterilization facilities source category document in support of the 2024 Risk and Technology Review Required Rule located at www.regulations.gov in docket EPA-HQ-OAR-2019-0178-1576.
[50] MRID 46625301. Magnitude of the Residue of Ethylene Oxide and Ethylene Chlorohydrin in/on Spices. Wright, M. (2005). Study sponsored by American Spice Trade Association. 829 p.
[51] Memorandum. *Ethylene Oxide. Case 2275. Results of Trade Practices Survey on Spices & Anticipated Residues for Dietary Exposure Assessment*. Leung Cheng, Health Effects Division. March 26, 1997.

toxicological effects via different routes of exposure. Moreover, EPA may consider the temporal nature of exposure to residues and the likelihood of co-occurrence of those exposures.

Although there may be some residues of EtO in or on food soon after treatment, EPA does not expect consumption of those spices while parent EtO residues persist. At the time of consumption of treated food commodities, there will be no residues of parent EtO in or on food.[52, 53] At that time, there is no co-occurrence of residues in or on food with any potential residential exposures; therefore, there cannot be an additive effect. The FFDCA requires aggregation to ensure that residues in or on food are safe; if people are not being exposed to residues in or on their food, then there is no risk from exposures on food with which to aggregate risks from other exposures.

Based on the lack of dietary risk and the nonadditive nature of any negligible residues on food with residential exposures, EPA concludes that the aggregate risk from exposure to EtO consists only of exposures to residues on food, of which there are none at the time of consumption. Therefore, aggregate risk does not exceed the Agency's level of concern.

EtO Reaction Products

For the reaction products of EtO (ECH and EG), there are no drinking water or non-dietary residential exposures; the only exposure route is through food. Thus, the aggregate risk from exposure to ECH is equal to the risk from dietary exposure alone; a separate aggregate assessment was not conducted for ECH or EG. Since dietary exposure alone does not exceed EPA's risks of concern, aggregate exposure does not exceed the Agency's level of concern.

Cumulative Risks

EPA has not made a common-mechanism-of-toxicity finding for EtO and any other substance. EtO does not appear to produce a toxic metabolite produced by other substances. Therefore, EPA has premised this ID and the underlying risk assessments on the belief that EtO does not have a common mechanism of toxicity with other substances.

Occupational Handler Risks

Antimicrobial Uses in Commercial Sterilization Facilities (Occupational Handler). The cancer risks for the antimicrobial uses were calculated using the arithmetic mean of the submitted exposure data for commercial sterilizer and healthcare 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 (8 hours per day, 40 hours per week). The

[52] MRID 46625301. Magnitude of the Residue of Ethylene Oxide and Ethylene Chlorohydrin in/on Spices. Wright, M. (2005). Study sponsored by American Spice Trade Association. 829 p.
[53] Memorandum. *Ethylene Oxide. Case 2275. Results of Trade Practices Survey on Spices & Anticipated Residues for Dietary Exposure Assessment*. Leung Cheng, Health Effects Division. March 26, 1997.

cancer risks for the exposure were, therefore, estimated using the table in the 2016 IRIS assessment titled "Extra Risk Est. for Total Cancer Incidence for Occupational Exposure Levels" found in the IRIS cancer assessment (and referenced in table 9 of the 2020 DRA). The Maximum Likelihood [Risk] Estimate (MLE) and upper-bound cancer risk estimates range from 4×10^{-2} (1 in 25) to 1×10^{-1} (1 in 10), depending upon which facility type and cancer risk estimate are considered. The upper-bound cancer risks are approximately twice the MLE cancer risks. For commercial sterilization facilities, the MLE cancer risk is 1 in 17 and the upper bound cancer risk is 1 in 10. EPA expects the mitigation in Section V.A. to reduce exposures from commercial sterilization facilities.

Conventional Uses in Commercial Sterilization Facilities (Occupational Handler). The cancer risks for the use of EtO on food commodities (i.e., conventional uses) in commercial sterilization facilities were calculated using the arithmetic mean of the submitted exposure data for the commercial 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, the cancer risks were calculated using the formulas listed in Section 4, page 111 of the IRIS assessment.[54]

Submitted exposure data from commercial sterilization facilities indicate that 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. Cancer risks range from 3×10^{-2} (1 in 36) for the MLE to 6×10^{-2} (1 in 16) for the upper bound.

Beekeeping Equipment Use in North Carolina (Occupational Handler). Monitoring data specific to the beekeeping equipment fumigation use are not available; however, based on the label directions and requirements for the Special Local Need (SLN) beekeeping equipment use (related to EPA Reg. # 36736-7), it is anticipated that the ASTA monitoring data for the commercial spice sterilization facilities would be protective of the beekeeping use and was used as a surrogate. Cancer risks for the beekeeping equipment use were calculated using the arithmetic mean of the submitted exposure data for the commercial spice sterilization facilities. To account for the differences in potential exposure between workers in an indoor commercial spice sterilization 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 in the 2023 DRA Addendum for details). Since the beekeeping fumigation exposures are considered "intermittent occupational

[54] U.S. EPA, 2016. Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide, (CASRN 75-21-8), In Support of Summary Information on the Integrated Risk Information System (IRIS). EPA/635/R-16/350Fa. NCEA, ORD, U.S. EPA, Washington, DC. December 2016.

exposures," 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 IUR of 5.5 x 10^{-3} ppb. 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. These risk estimates, which also assume that self-contained breathing apparatus (SCBA) PPE is in use, exceed the Agency target of 1 x 10^{-4} for occupational risks.

Antimicrobial Uses in Healthcare Facilities (Occupational Handler). In healthcare facilities, the MLE cancer risk is 1 in 25 and the upper bound cancer risk is 1 in 12. 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[16]. 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). EPA expects the mitigation in Section V.A. to reduce exposures from healthcare sterilization facilities.

Human Incidents and Epidemiology

EPA reviewed EtO incidents reported to the Incident Data System (IDS). As of EPA's latest search on November 18, 2024, the IDS showed nine medium- to high-severity incidents from March 1, 2008 to December 1, 2022. Six of these incidents were in an international setting using a U.S. EPA-registered product in Barbados, Sri Lanka, Korea (two), Taiwan, and Thailand. Two incidents, which occurred in the U.S., involved a spill and a misuse of the product, which were associated with acute symptoms such as headache, light-headedness, and racing heart. The remaining incident in the U.S. described a hospital worker who was diagnosed with leukemia after six years of employment. Although EtO is a known carcinogen, it is not possible to determine if the cancer in this incident was caused by EtO exposure and/or some other factor(s) based on the available information. The Agency intends to monitor human incidents for EtO and will conduct additional analyses if necessary.[55]

Tolerances

EtO is registered for uses that result in residues in or on food. Generally, a tolerance or tolerance exemption must cover the residues, or the affected food is considered adulterated.[56] EPA has established most of the necessary tolerances for residues resulting from EtO's legal use.

The Agency has established tolerances for EtO and the EtO reaction product, ethylene chlorohydrin (ECH), under 40 C.F.R. § 180.151. However, during the risk assessment process, EPA determined that revisions to the tolerances and tolerance expressions are necessary. EtO

[55] OSHA additionally has publicly available information on EtO incidents and enforcement, which can be accessed at https://www.osha.gov/data.
[56] 21 U.S.C. §§ 342, 346(a).

and ECH tolerances need to be revised for several commodities to reflect updated commodity definitions. The 2020 DRA notes that the tolerance expressions for EtO and ECH need to be updated per current practice concerning tolerance expressions. Tolerance changes will be required through a separate rulemaking process.

In the 2020 DRA, the Agency determined that the EtO tolerance for walnuts needs to be revised to reflect the lower residues resulting from the required single chamber process. The 2020 DRA also states an ECH tolerance for walnuts needs to be established based on the documented level of quantification (LOQ). In the PID, the Agency noted that it was not aware of EtO use on walnuts and proposed revoking the walnut tolerance. The Agency received a public comment that a facility in Missouri is using EtO to sterilize black walnuts.[57] The Missouri Department of Agriculture also provided information about the importance of EtO use on black walnuts and the importance of black walnuts as a commodity to the state.[58, 59 ,60]

No tolerance changes are anticipated for international harmonization. Codex has not set Maximum Residue Limits (MRLs) for EtO or ECH. Canada has not set MRLs for walnut for EtO or ECH. Canada has set MRLs for herbs and spices (and sesame seed) for both EtO and ECH. As these levels match the U.S. tolerances, there are no international harmonization issues at this time. For more information on tolerances, see Section V.C, below.

Human Health Data Needs

The human health database for EtO is not considered complete. Although not all human health data requirements have been completely met, EPA has determined that available data were sufficient to conduct the 2020 HHRA, the 2023 DRA Addendum, and the 2024 updated dietary assessment and are sufficient to support this ID. Based on the occupational risk estimates for EtO, EPA believes that further mitigation of EtO exposure is required. The Agency intends to continue working with the registrants to satisfy the data requirements under the existing DCI notice (GDCI-042301-1428).

One data requirement is still outstanding and will be used to inform future risk assessments. The following study is outstanding for the EtO GDCI-042301-1428:

- Non-Guideline Study Monitoring Data on Fumigated Commodities (food use)

[57] Letter from Brian Hammons, President, Hammons Products Company to Jessica Bailey, Antimicrobials Division, Office of Pesticide Programs, Environmental Protection Agency. August 21, 2023.
[58] Email from Paul Bailey, Director, Plant Industries, Missouri Department of Agriculture to Wilfredo Rosado-Chaparro, Branch Supervisor, Environmental Protection Agency Region 7. December 2, 2024.
[59] American Black Walnut Marketing Board. Undated. *Black Walnuts A Nutritional Powerhouse from America's Forests*.
[60] EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Missouri Department of Agriculture (MDA) September 13, 2024.

This study is required to evaluate emission rates for EtO from treated commodities/materials and the potential for occupational exposure due to those emissions in the channels of trade after fumigation activities are complete. The registrants submitted a waiver request for this study (MRID 50384901) on September 8, 2017. However, this waiver request was denied on July 17, 2018, due to a lack of information related to potential exposures within the various channels of trade after fumigation, dissipation of EtO beyond the facility, and the analytical method used to measure air concentrations.[61]

Additionally, in order to quantify worker exposure in commercial sterilizers and warehouses, EPA will issue a DCI for OSCPP GLN 875.1400 Inhalation Exposure Indoor to understand the impacts of complying with EPA's recently amended Clean Air Act (CAA) NESHAP for EtO commercial sterilizers and implementing mitigation measures identified in this ID issued under FIFRA, and to better understand how to further lower the occupational exposure limit discussed in Section V.A. of this ID. EPA will require a protocol before monitoring for the study begins. Based on previously submitted worker exposure data that lacked specificity and detail, EPA will require time-weighted average personal breathing zone (PBZ) monitoring of the handlers specifically involved in activities related to the sterilization/fumigation (e.g., loading and unloading chambers, routine maintenance, product transfer, etc), documentation of the activities each worker performed while monitored, and whether they were wearing a respirator (and what type of respirator). For non-handlers in the facility (e.g., office workers, warehouse workers), EPA also intends to require PBZ monitoring data to monitor their exposures. Data would also have to include whether or not the facility has complied with the NESHAP requirements.

In order to verify the occupational exposure limits identified in this ID (0.5 ppm, 0.25 ppm, 0.1 ppm) are attainable, EPA will gather annual worker exposure data through a DCI and assess those data.[62] Specifically, EPA has determined it is necessary for EtO registrants to collect worker monitoring data from their customers on an annual basis.[63] Further, EtO registrants may not continue to sell EtO products to customers who do not provide worker monitoring data. See Appendix G for the updated terms and conditions of registration for EtO products. EPA can change the implementation timing and target occupational exposure limit concentration, if necessary, as demonstrated by data, prior to the 10-year deadline for the final implementation tier of the worker exposure limit of 0.1 ppm. In order to make this determination, EPA will reevaluate the occupational exposure limit and any other needed mitigations, based on data, within 8 years. See Section V.A. for details on the lowered worker exposure limit for EtO.

[61] Ethylene Oxide (EtO): Response to registrant's inhalation exposure monitoring requirements waiver request. Decision Number 533138. June 21, 2018.
[62] See "Ethylene Oxide – EOTF and EOSA Proposal for the Interim Decision – June 26, 2024" in the EtO public docket at www.regulations.gov under document ID EPA-HQ-OPP-2013-0244-0406.
[63] A "registrant" is defined as a person who has registered any pesticide [with EPA] pursuant to [FIFRA]. 7 U.S.C. § 136(y).

Additionally, EPA will issue a DCI requiring a special study for monitoring data on fumigated commodities for medical devices to better understand post-application exposure to EtO in warehouses. Through these data, EPA is seeking information on the exposure scenario from emissions from treated medical device commodities and materials and the potential for post-application occupational exposure due to those emissions in the channels of trade after sterilization activities are complete. The environments in which worker activities are monitored would also be evaluated, which may include monitoring off-gassing properties of fumigated commodities over time. Data are required for occupational sites, such as warehouses, if the human activity data indicate that workers are likely to have post-application exposures while participating in typical activities. EPA will require a protocol before monitoring for the study begins.

EPA has authority to require the registrants of EtO products to obtain or develop data necessary for EPA to evaluate EtO exposures in warehouses that store products fumigated with EtO if the data are necessary for EPA to maintain the registration of EtO (i.e., necessary for the Agency to determine that the use of EtO will not cause unreasonable adverse effects), even if the activities at the warehouses are not subject to direct regulation under FIFRA. EPA data requirement regulations specifically envision the Agency requiring submission of data relating to post-application exposures.[64] Because EPA has identified significant risks from EtO exposures, and the potential for exposure to nearby communities and workers in warehouses where commodities fumigated with EtO are stored, the call-in of post-application exposure data is necessary.[65] Specifically for warehouses that are not co-located with sterilization facilities, there is a need for additional data because data from warehouses co-located with sterilization facilities may be skewed by emissions from the sterilization facilities themselves. The Agency has previously required registrants of propylene oxide (PPO) to submit data allowing EPA to assess post-application exposure to fumigated commodities.[66] EPA has also considered data on post-application exposures during the registration review of the wood preservatives.[67]

In the PID, EPA proposed to issue a DCI for data on commercially available technologies that can monitor below 10 ppb in real time, while also documenting other instruments that can quantify levels around 0.19 ppb, which is the Agency's concentration of concern for worker exposure. However, EPA is no longer requiring these data at this time because the Agency acquired

[64] See 40 C.F.R. § 158.2270(d), (e) ("Data are required for occupational and residential uses if the human activity data indicate the potential for post-application dermal and/or inhalation exposures while participating in typical activities and no acceptable modeling options are available."); *see also* 40 C.F.R. § 158.75 (providing that EPA may impose additional data requirements if necessary for EPA to evaluate the potential of a pesticide product to cause unreasonable adverse effects on the environment).
[65] The data call-in will address worker exposure; however, these data could potentially also be used to help inform worst case exposure to bystanders in nearby communities where EtO sterilized products are stored.
[66] See Propylene Oxide (PPO) Interim Registration Review Decision Case Number 2560 at www.regulations.gov document ID EPA-HQ-OPP-2013-0156-0052.
[67] See Creosote Draft Risk Assessment (DRA) discussing post-application exposure to users installing treated wood (page 28) at www.regulations.gov document ID EPA-HQ-OPP-2014-0823-0014.

sufficient information through the public comment period on available monitoring technologies. For more information on public comments on available monitoring technologies and EPA's responses, please see Appendix E.

Once these data become available, the Agency may promptly reevaluate this Interim Decision.

B. Ecological Risks

The Agency assessed ecological risks in the 2020 DRA, which are summarized below. EPA did not reassess ecological risks as part of the 2023 DRA Addendum, which focused on human health risks. The Agency used the most current science policies and risk assessment methodologies to prepare a risk assessment in support of the registration review of EtO.[68] For additional details on the 2020 DRA, see *Ethylene Oxide (EtO) Draft Human Health and Ecological Risk Assessment in Support of Registration Review* in EPA's public docket (EPA-HQ-OPP-2013-0244).

EPA has not yet fully evaluated EtO's effects on federally threatened and endangered (listed) species or designated critical habitats. However, consistent with its obligations under the Endangered Species Act (ESA),[69] EPA expects to complete effects determinations and any necessary consultation with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service (the Services) before completing the EtO registration review and issuing a final registration review decision. For more information on EPA's ESA obligations during registration review, see Appendix C.

EPA continues to work with the Services to improve the consultation process for pesticides in registration review. In April 2022, EPA released its ESA Workplan, which outlines strategies and actions for the Agency to meet its ESA obligations for FIFRA actions.[70] Consistent with the ESA Workplan, EPA is focused on steps it will take during registration review to reduce exposure for listed species as it moves toward fulfilling its ESA obligations and making final registration review decisions. In November 2022, EPA released its first ESA Workplan Update.[71] As part of this update, EPA announced that, going forward, EPA may include a variety of FIFRA Interim Ecological Mitigation (IEM) measures in its registration review decisions that seek to reduce

[68] The 2020 Eco DRA only addresses potential risks to species not listed under the Endangered Species Act. EPA is working with its federal partners and other stakeholders to implement a Revised Method (EPA-HQ-OPP-2019-0185-0054) for assessing potential risk to listed species and their designated critical habitats. The Agency expects to complete EtO's listed-species assessment and any necessary consultation before completing the EtO registration review and issuing a final registration review decision. For more details, see Appendix C.
[69] Endangered Species Act (ESA) § 7, 16 U.S.C. § 1536.
[70] Balancing Wildlife Protections and Responsible Pesticide Use (Apr. 2022), https://www.epa.gov/system/files/documents/2022-04/balancing-wildlife-protection-and-responsible-pesticide-use_final.pdf.
[71] ESA Workplan Update: Nontarget Species Mitigation for Registration Review and Other FIFRA Actions (Nov. 2022), https://www.epa.gov/system/files/documents/2022-11/esa-workplan-update.pdf.

exposures for nontarget organisms based on its FIFRA ecological risk assessment(s). EPA expects that this mitigation may also reduce pesticide exposures for listed species.

As part of this ID, EPA has considered a variety of risk mitigation measures based on the risks and benefits of EtO, including measures that may mitigate ecological risks, while EPA works toward a final registration review decision. While these mitigation measures do not satisfy EPA's ESA obligations, EPA has determined that early mitigation may shorten the consultation process and improve protections for listed species from currently registered pesticide products. EPA also has determined that the risk mitigation measures that the Agency has identified for EtO in this ID (Section V) satisfy EPA's obligations under Section 711 of the Consolidated Appropriations Act, PL-117-328 (Dec. 29, 2022). Among other things, Section 711 requires EPA to "include, where applicable, measures to reduce the effect of the applicable pesticide on" listed species and designated critical habitats in any ID noticed in the Federal Register between December 29, 2022, and October 1, 2026, for which EPA has not "made effects determinations or completed any necessary consultation under [ESA Section 7(a)(2)]."

The mitigation identified in this ID is expected to reduce the extent of environmental exposure and may reduce effects to listed species whose range or critical habitat co-occur with the use of EtO (Section V.A.). Exposure to wildlife from the use of EtO will be reduced through OPP's mitigation measures to reduce EtO usage through the cancellation of minor uses of EtO, phased cancellation of the use of EtO on certain food commodities, and the reduced concentration rate of EtO for medical device sterilization for new cycles. Additionally, environmental exposure will be further reduced through the current emissions controls from OAR's NESHAP, which have been further strengthened as of the publication of the *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review* on April 5, 2024.[72]

Potential risks for non-listed species only are described below.

Risk Summary and Characterization

The Agency assessed ecological risks in the 2020 DRA, which are summarized below. EPA did not reassess ecological risks as part of the 2023 DRA Addendum. In the document *Ethylene Oxide (EtO) Response to Registrant's Ecological Data Requirements Waiver Request* dated October 9, 2018, EPA stated, "The Agency is waiving the vegetative vigor (850.4150), honeybee acute vapor exposure (SS-1233), and avian acute inhalation toxicity (SS-1252) data requirements in GDCI-042301-1428, but some (or all of these) data requirements may be required in the future." During development of this ID, the Agency has determined that there are remaining uncertainties, such as the ecological exposure from small facilities, which include healthcare facilities, which could be addressed with data. Therefore, EPA will include the

[72] EPA-HQ-OAR-2019-0178-1482 at www.regulations.gov.

aforementioned ecological data requirements in a future DCI, as well as include others, as policies and practices change.

Under ambient environmental conditions, EtO released to air is expected to result in potential inhalation exposure of terrestrial wildlife. The ecotoxicity data available for EtO is limited, however EtO is expected to be toxic to terrestrial animals via the inhalation route of exposure. Since uses of EtO are not expected to have a significant component that is available for runoff or leaching, aquatic exposures are not expected. Therefore, for aquatic organisms, risks are not expected due to limited exposure potential. This means that, for both the food commodity and medical equipment commercial sterilization uses, due to the toxicity of EtO to non-target organisms and the potential for exposure, only terrestrial animals in the vicinity or downwind of a treatment vent may be at risk. For aquatic organisms, risks are not expected due to limited exposure potential.[73]

EtO sterilization is performed indoors in vacuum or gas tight chambers. Sterilization in commercial sterilization facilities must follow National Emissions Standards for Hazardous Air Pollutants (NESHAP) requirements for emissions control. At the time of the 2018 data waiver, approximately 1% of the EtO used for sterilization was used in medium-sized facilities and approximately 0.1% of the EtO used for sterilization was used in small-sized facilities, and the remainder was used in large-sized facilities.[74] Exposures to EtO from large- and medium-sized facilities had controls achieving greater than or equal to 99% reduction in emissions at the time of the 2018 waiver, consistent with the applicable NESHAP requirements for emissions control at that time. OPP determined in the 2018 waiver response that these exposures are not of concern, and notes that these exposures have further been lessened as part of the 2024 NESHAP.[75, 76] With approximately 99% of sterilization occurring in large- and medium-sized facilities with emissions controls achieving greater than or equal to 99% emissions reductions at the time of the 2018 waiver, any exposure to wildlife from the use of EtO would likely be limited. There was a possible exception of the aforementioned low percentage of small-sized facilities that were not subject to emissions controls by the former NESHAP requirements at the time of the 2018 waiver and may not have achieved 99% emissions reductions. The 2018 waiver response stated that for both the food uses and medical uses in small-sized commercial sterilization facilities, terrestrial organisms in the vicinity or downwind of a treatment vent may be at risk from EtO vapor exposure due to the fugitive emissions. OPP notes that on April 5, 2024, EPA's Office of Air and Radiation (OAR) published their Rulemaking for EtO commercial sterilizers, *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide*

[73] See *Ethylene Oxide (EtO) Draft Human Health and Ecological Risk Assessment in Support of Registration Review* and *Ethylene Oxide (EtO)* in docket EPA-HQ-OPP-2013-0244 at www.regulations.gov.
[74] The size of the facility is determined by the amount of EtO emitted in accordance with section 112 of the Clean Air Act. See https://www.epa.gov/stationary-sources-air-pollution/ethylene-oxide-emissions-standards-sterilization-facilities.
[75] Ethylene Oxide: Revised Response to Data Waiver Requests Submitted by the Ethylene Oxide Task Force. March 9, 2018.
[76] Ethylene Oxide (EtO). Draft Human Health and Ecological Risk Assessment in Support of Registration Review. November 3, 2020.

Emissions Standards for Sterilization Facilities Residual Risk and Technology Review.[77] OAR revised the NESHAP for commercial sterilization facilities by both amending existing standards and establishing additional standards, which included small facilities that use less than 1 ton of EtO per year. The information contained in the 2018 waiver was based on the former, less stringent OAR NESHAP that was current at the time. However, it is also worth noting that the 2024 NESHAP only includes commercial sterilization facilities as part of that source category, and not healthcare facilities, and therefore there is still uncertainty for ecological exposure for the latter facilities.[78]

The Agency could not discount potential risks to terrestrial organisms. For aquatic organisms, risks are not expected due to limited exposure potential since uses of EtO are not expected to create a significant pathway for deposition, runoff, or leaching into water bodies. At the time of the 2018 waiver, EPA determined that (due to lack of NESHAP regulations at the time) emissions of EtO from uses in small-sized facilities may have presented risks of concern to birds, mammals, honey bees, or plants when considering currently available data; however, emissions of EtO uses from large- and medium-sized facilities (after controls achieving ≥ 99% reduction in emissions at the time of the 2018 waiver) did not present risks of concern to non-target organisms.[79, 80] In the absence of toxicity studies, there is greater uncertainty regarding risk near EtO commercial sterilization facilities that either have no or limited (< 99% reduction) emission controls. In those cases, especially for those facilities without emission controls, risk could not be precluded for terrestrial organisms in adjacent areas around EtO treatment facilities. It is also worth noting that the 2024 NESHAP only included commercial sterilization facilities as part of that source category, and not healthcare facilities, and therefore there is still uncertainty for ecological exposure for the latter facilities.

OPP expects that the more stringent emissions controls for commercial sterilization facilities required under the NESHAP, and the rate reductions, phase out of the use of EtO on certain food commodities, and cancellation of minor uses of EtO, as outlined in this ID, will further reduce exposure to nontarget species.

Ecological Incidents

EPA reviewed EtO incidents reported to the Incident Data System (IDS). As of EPA's latest search on November 18, 2024, IDS showed zero incidents reported from March 1, 2008 to January 18, 2023. The Agency intends to monitor ecological incidents for EtO and will conduct additional analyses if necessary.

[77] EPA-HQ-OAR-2019-0178-1482 at www.regulations.gov.
[78] Ethylene Oxide: Revised Response to Data Waiver Requests Submitted by the Ethylene Oxide Task Force. March 9, 2018.
[79] Ethylene Oxide: Revised Response to Data Waiver Requests Submitted by the Ethylene Oxide Task Force. March 9, 2018.
[80] Ethylene Oxide (EtO). Draft Human Health and Ecological Risk Assessment in Support of Registration Review. November 3, 2020.

Ecological and Environmental Fate Data Needs

EPA did not identify a risk concern for acute exposure of adult honeybees to EtO. However, chronic risks to adult honeybees and acute risks to larval honeybees have not been evaluated at this time because of the lack of data. Additional data may be necessary to fully evaluate risks to non-target terrestrial invertebrates, especially pollinators, based on the *Guidance for Assessing Pesticide Risks to Bees* (June 2014).[81]

The ecological and environmental fate data requirements in GDCI-042301-1428 included GLN 850.4150 Vegetative Vigor, Non-guideline study Honeybee Acute Vapor Exposure, and Non-guideline study Avian Acute Inhalation Toxicity. On June 10, 2015, EPA received waiver requests for all three data requirements from the Ethylene Oxide Task Force (EOTF) (MRIDs 49648401, 49648402, and 49688601). In May 2017, EOTF submitted information to fulfill the Product Use Information data requirement (GLN 875.1700) which was also considered when evaluating the ecological data requests. EtO sterilization is performed indoors in vacuum or gas tight chambers. In the document *Ethylene Oxide (EtO) Response to Registrant's Ecological Data Requirements Waiver Request* dated October 9, 2018, EPA waived these data requirements, but stated that "some (or all of these) data requirements may be required in the future." During development of this ID, the Agency has determined that there are remaining uncertainties, such as the ecological exposure from small facilities, which include healthcare facilities, which could be addressed with data. Therefore, EPA will include the aforementioned ecological data requirements in a future DCI, as well as others as policies and practices change.

C. Benefits Assessment

Sterilization of Medical Devices

EtO is primarily used as a sterilant for single use, and reusable medical devices and equipment. EtO is highly valuable in the industrial sterilization setting – or any setting that has the objective of destroying or inactivating all microorganisms to meet defined sterility assurance levels (SALs) – because it is a penetrative gas that has a high throughput capacity, is effective at a wide range of temperatures, and is compatible with a broad range of materials. EtO is used on approximately 50% of all sterilized medical devices, annually, including an estimated 95% of all surgical kits.[82] A key benefit of EtO is its ability to sterilize medical devices in their final packaging as it is able to penetrate palletized materials, cardboard, and other cellulosic packaging material. The ability to sterilize devices in their final packaging is advantageous, as it allows for the devices to remain sterile without additional handling while also meeting medical

[81] https://www.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf.

[82] B&C Consortia Management, LLC. 2014. Registration Review of Ethylene Oxide Stakeholder Meeting presentation. Docket ID: EPA-HQ-OPP-2013-0244-0018. https://www.regulations.gov/document/EPA-HQ-OPP-2013-0244-0018. Accessed July 2022.

device supply demands for prepackaged materials. Presently, there are no viable alternatives to EtO for the sterilization of certain medical devices and equipment because gamma irradiation and e-beam irradiation, the next most commonly employed methods for medical device sterilization, cannot be used on certain materials. Other technologies (e.g., nitrogen dioxide, hydrogen peroxide, chlorine dioxide, vaporized peracetic acid) are currently limited due to issues with material compatibility, scalability, and/or because they lack standardized validation measures for sterility assurance. Sterile medical equipment is necessary to prevent the transmission of infectious pathogens to patients/users, especially with devices and instruments that are used in normally sterile body tissue or within the vascular system. The absence of EtO for use on medical devices and equipment would cause widespread disruption to the availability of sterile medical devices including feeding tubes used in neonatal intensive care units, drug-eluting cardiac stents, catheters, shunts, and other implantable devices.

During the PID public comment period, EPA received several comments regarding the benefits of EtO for both medical device sterilization and food commodity fumigation. In their public comment, Becton Dickinson (BD) stated that approximately 50% of BD products currently can only be sterilized with EtO, including intravenous (IV) catheters, peripherally inserted central (PIC) catheters, surgical prep devices, surgical kits, Foley urinary catheter trays, glass syringes, chemotherapy ports, among many others.[83] The Medical Device Manufacturers Association (MDMA) stated that common medical devices that are EtO-reliant include but are not limited to the following: heart valves; intravenous (IV) sets; catheters; sutures; gowns and drapes; fiberoptic endoscopes; surgical kits; pacemakers; respirators; tubing sets; plastic tubing; inhalation therapy supplies; surgical telescopes; anesthesia masks and circuits; renal peritoneal dialysis sets; renal hemodialysis sets; surgical drills; uterine monitors; surgical staplers; and, diagnostic electrode catheters.[84] Biocom California stated that for products that can be sterilized using other methods, if companies shift away from EtO and begin sterilizing more products using gamma radiation, there could be a strain on gamma resources, which are used for oncology radiotherapy to kill cancer cells, and could in turn delay life-saving oncology treatments.[85] AdvaMed asserted that surgical kits singularly depend upon EtO – 95% of all surgical kits are sterilized using EtO, and about 40 to 50 million surgeries are performed each year in the U.S. (e.g., more than 100,000 surgeries a day).[86] The Ethylene Oxide Task Force (EOTF) and the Ethylene Oxide Sterilization Association (EOSA) stated that a lack of EtO-sterilized medical supplies to operating rooms would result in delayed or even canceled procedures, which would pose grave risk to those in urgent medical need.[87] Terumo Blood and Cell Technologies (BCT) stated that approximately 80% of Terumo BCT products (and 95% of the Terumo BCT products manufactured in the U.S.) currently can only be sterilized with EtO,

[83] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.
[84] EPA-HQ-OPP-2013-0244-0092 at www.regulations.gov.
[85] EPA-HQ-OPP-2013-0244-0103 at www.regulations.gov.
[86] EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.
[87] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.

including the Rika Plasma Donation System, among many others.[88] See Appendix E for detailed information on the comments and EPA's response.

Sterilization of Food Commodities

In the U.S., EtO is used during the processing and reconditioning of dried herbs and spices to reduce food safety pathogens of concern such as *Salmonella* and *Escherichia coli*. The presence of moisture alone may be sufficient for the development of pathogens such as *Salmonella* and keeping moisture out of dried herbs and spices can be challenging during processing, handling, shipping, and storage activities.[89] Additionally, most spices are imported from overseas, which creates more opportunity for pathogens to be introduced due to differing sanitation and food handling practices and regulations. EtO is advantageous for processing and reconditioning dried herbs and spices as it has minimal impact on the desirable characteristics of an herb or spice including its aromatics, color, flavor, or texture. There are a few alternatives to EtO for the sanitization of dried herbs and spices from pathogens, including propylene oxide (PPO), steam, heat, and irradiation. Currently, the alternatives may not be viable for every situation, pathogen, or consumer market. These alternative sterilization methods have limitations including changes to the color, flavor, or texture of herbs and spices that may limit consumer acceptance of herbs and spices treated with these alternative methods, scalability, incompatibility with packaging, and lack of standardized validation methods. PPO is the most likely alternative sterilization method for most herbs and spices where EtO is used, but it is not currently registered for use on all herbs and spices on the current EtO label.

The United States Department of Agriculture (USDA) stated that spices are integral to the U.S. food industry. EtO is one of the primary methods used to sterilize spices prior to their incorporation into other food products, such as commercially prepared foods in the U.S. USDA stated, "Once spices have been dried, bacteria are less likely to multiply due to lower moisture content (making dried spices relatively shelf stable), but when they are added to a food product with higher water content, microbes can quickly multiply to levels that may be dangerous to consumers and/or can lead to food loss when they cause spoilage of a packaged product." Without proper sterilization, there is the potential for increased foodborne pathogens that can cause foodborne illness and other microorganisms that can cause spoilage of products that contain spices and ultimately lead to food loss. The impacts to this market could have significant economic consequences.[90] The American Spice Trade Association (ASTA) noted that raw unprocessed spices commonly harbor large numbers of bacteria and fungi, including organisms that cause spoilage and food borne pathogens such as *Salmonella*, *E. coli*, *Clostridium perfringens*, and *Bacillus cereus*. ASTA provided information for more than 60 food commodities for which EtO treatment is critical for food safety.[91] See Appendix E for detailed information on the comments and EPA's response.

[88] EPA-HQ-OPP-2013-0244-0146 at www.regulations.gov.
[89] EPA-HQ-OPP-2013-0244-0051 at www.regulations.gov.
[90] EPA-HQ-OPP-2013-0244-0128 at www.regulations.gov.
[91] EPA-HQ-OPP-2013-0244-0130 at www.regulations.gov.

Sterilization of Other Items

EtO is also registered for niche uses in beekeeping to manage American foulbrood on equipment (in North Carolina only); the preservation of library, museum, and archival materials against bacteria, fungi, and insects; on musical instruments to prevent the transmission of human diseases, and for the sterilization of cosmetics. For the beekeeping equipment, the use of EtO is limited via a FIFRA section 24(c) registration to one facility in North Carolina. There are alternative chemical, cultural, and mechanical controls available to manage American foulbrood disease on beekeeping equipment. EtO is no longer used for treatment of museum, library, or archival materials due to concerns over human health risks associated with off-gassing from treated materials. Alternatives for the museum, library, and archival materials include freezing, anoxia (oxygen deprivation), and irradiation. For the musical instrument uses, other disinfectant products are available for use that are more practical, low cost, and easily accessible. EPA could not find confirmation that EtO is still used in the cosmetics industry. Gamma irradiation is a viable alternative for cosmetics. Therefore, in these use sites, EtO provides minimal benefits based on the availability of alternatives and/or limited to no current EtO usage. The absence of EtO for use on these use sites is unlikely to impact these industries. For more information on the benefits of EtO, see *Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation*[92] and the letter from Dr. Girvin Liggans to Edward Messina (dated August 18, 2022).[93]

D. Alternatives for Medical Device Sterilization and Food Commodity Fumigation

As described above, the Agency estimates that EtO use results in cancer risks of concern to occupational handlers as well as risks to occupational and non-occupational bystanders. However, EPA recognizes that EtO products are registered for uses which are extremely beneficial and have no currently registered alternatives that can completely replace EtO. Under its Reduced Risk Policy, OPP encourages the submission of applications for pesticides which offer a reduced risk alternative and will give priority consideration to the review of such applications. The registration of such a reduced risk alternative pesticide would allow OPP to achieve greater risk reduction.[94] Even though there is only one registered alternative active ingredient for spice fumigations (propylene oxide) and there are only two registered alternative pesticide active ingredients for medical device sterilization (nitrogen dioxide and chlorine dioxide), there are a variety of alternative sterilization methods described below. However, the current field of alternatives are insufficient to completely replace EtO for reasons described below.

Medical Devices

[92] EPA-HQ-OPP-2013-0244-0051 at www.regulations.gov.
[93] EPA-HQ-OPP-2013-0244-0053 at www.regulations.gov.
[94] https://www.epa.gov/pesticide-registration/conventional-reduced-risk-pesticide-program.

Some medical devices can only be sterilized with EtO. However, there are several alternative methods used to sterilize certain medical devices: gamma irradiation, X-ray sterilization, electron beam sterilization, and steam; as well as alternative sterilization methods in development including vaporized hydrogen peroxide, nitrogen dioxide, chlorine dioxide, and vaporized peracetic acid.

Despite the availability of alternative sterilization methods, EPA understands the limitations of alternative sterilization methods for use with medical devices due to their lack of compatibility with materials and/or packaging; and also due to their lack of scalability or capacity, application method, and/or lack of standardized validation measures for sterility assurance or efficacy data.[95] For these reasons, it is difficult to replace EtO without changing other inherent parts of the supply chain, which would result in a loss of efficiency within a system that is already at capacity. Identifying alternatives may be a decades-long path, and it is difficult to quantify a timeline since the innovations for alternatives are in the early stages. The identification of alternatives is being developed on a product-by-product basis, and as such the capacity for alternatives is not sufficient to begin replacing EtO at scale. Despite these limitations, EPA is seeking to pursue identifying alternatives to EtO sterilization as a long-term risk reduction strategy.

FDA's Center for Devices and Radiological Health (CDRH) assures that patients and providers have timely and continued access to safe, effective, and high-quality medical devices. Before most sterile medical devices are on the market, FDA reviews premarket submissions such as premarket approval applications (PMAs) and premarket notifications (referred to as 510(k)s) to determine if the sterility validation is consistent with the sterility assurance under which the device is labeled and intended for use (e.g., in accordance with internationally agreed upon voluntary consensus standards that FDA recognizes). See Section IV.B. for more information on FDA's jurisdiction over recognizing sterilization modalities and verifying sterility assurance for medical devices.

As part of interagency collaboration, EPA-OPP and FDA-CDRH have held discussions on alternatives to EtO sterilization and have identified regulatory and logistical limitations in prescribing what sterilization modality must be used on specific medical devices. These regulatory and logistical limitations, and additional background regarding FDA's regulatory oversight over medical devices, are described below:

- Given that medical device material makeup varies from manufacturer to manufacturer (even for the same device type), it is not possible to prescribe which types of medical devices must use which sterilization modality, due to material compatibility issues. For example, catheters from different manufacturers could be made from different materials, some of which may or may not be compatible with alternative sterilization modalities.

[95] See Section III.C. and *Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation* in this docket.

- The Federal Food, Drug, and Cosmetic Act (FD&C Act) authorizes FDA to exercise regulatory oversight over medical devices, including through its implementing regulations.[96] In the context of devices labeled as sterile, under the FD&C Act, the information provided to FDA as support for a device sterilization claim must show that the selected sterilization method for a subject device conforms to the labeling and intended use of the device, which may include any applicable FDA-recognized consensus standards or an equivalent sterilization method. A more detailed description of FDA's regulatory oversight in this space is provided below.

    - With respect to devices that are intended to be sterilized using EtO, sponsors may choose to reference certain FDA-recognized standards that include EtO residual information based on the applicable standards and their allowable limits for residual EtO.[97] Accordingly, information related to the residual EtO exposure potential of a subject device, both during the manufacturing and sterilization process and at the time the device is used by an end user (such as a healthcare professional or patient), is generally reviewed and compared to any applicable International Standards defining allowable limits of EtO residuals and exposures.

    - As part of FDA's regulatory oversight, FDA is also required to evaluate whether a subject device, prior to its introduction in the market, offers a reasonable assurance of safety and effectiveness upon the imposition of certain regulatory controls.[98] Fundamental to this evaluation is, among other things, the weighing of any probable benefits to health from the use of a device against any probable risks of injury or illness from such use (i.e., analyzing clinical risks and clinical benefits for a given device).[99] For example, if EtO as a device sterilizing agent poses a cancer exposure risk to an end user or to manufacturing or sterilization staff, FDA is obligated to review that information, together with other probable risks as well as risk mitigations, against the probable benefits offered by the finished sterile device.

[96] FD&C Act Section 501 *et seq*.; 21 C.F.R. Part 800 *et seq*.
[97] ANSI AAMI ST41:2008/(R)(2018); ISO 10993-7, 2nd Ed. 2008-10-15. Additionally, depending on the premarket submission pathway, there may be other applicable regulations that further contextualize how sponsors should submit sterilization data.
[98] See FFDCA Section 513(a)(1).
[99] The safety and effectiveness of a device is determined, among other things, by "weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from such use" FFCDA Section 513(a)(2)(C)). To aid this process, sponsors submit valid scientific evidence, which FDA reviews to determine whether "the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device" FFCDA Section 513(a)(3)(A).

  - Separately, since the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Public Law 105-115),[100] Congress has directed FDA to take a least burdensome approach to medical device premarket evaluation in a manner that eliminates unnecessary burdens that may delay the marketing of beneficial new products, while maintaining the statutory requirements for clearance and approval. In practice, FDA defines least burdensome to refer to the minimum amount of information necessary to address regulatory questions in line with the statutory and regulatory requirements applicable to a subject device, and encourages industry to refer to least burdensome principles in compiling information for premarket review by the FDA.[101] Consequently, if certain information was not provided in a premarket submission, but that information is not needed to support a determination that the device meets the applicable statutory and regulatory standards for marketing authorization, FDA does not request such information.

- EPA's authority under FIFRA does not allow for OPP to prescribe on pesticide product labels FDA's process for validation assessments of sterilization modalities for medical devices. As noted above, FDA's role in this regard under the FD&C Act and its implementing regulations is to evaluate whether the sterilization data (irrespective of method) submitted for premarket review is adequate to support a claim that a subject device is sterile as part of the overall premarket review carried out on FDA-regulated devices.

Despite these limitations, EPA still seeks to pursue identifying alternatives to EtO sterilization as a long-term risk reduction strategy and will continue to communicate with FDA, such as on their work through the *Innovation Challenge: Identify New Sterilization Methods and Technologies*. See Section IV.B for more information on the steps FDA is taking to identify alternatives to EtO sterilization.

During the PID public comment period, EPA received three comments from two submitters regarding alternatives to EtO for medical device sterilization: Noxilizer and ClorDiSys. Noxilizer

[100] Congress enacted additional least burdensome provisions to the FFCDA through the FDA Safety and Innovation Act (Public Law 112-144) and the 21st Century Cures Act (Public Law 114-255).

[101] See, e.g., FFCDA Section 513(i)(1)(D)(i) ("Whenever the Secretary requests information to demonstrate that devices with differing technological characteristics are substantially equivalent, the Secretary shall only request information that is necessary to making substantial equivalence determinations. In making such request, the Secretary shall consider the least burdensome means of demonstrating substantial equivalence and request information accordingly."); FFCDA Section 513(a)(3)(D)(ii) ("Any clinical data, including one or more well-controlled investigations, specified in writing by the Secretary for demonstrating a reasonable assurance of device effectiveness shall be specified as a result of a determination by the Secretary that such data are necessary to establish device effectiveness. The Secretary shall consider, in consultation with the applicant, the least burdensome appropriate means of evaluating device effectiveness that would have a reasonable likelihood of resulting in approval."); see also FDA Guidance entitled "The Least Burdensome Provisions: Concept and Principles," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles.

provided information on nitrogen dioxide and its advantages as well as limitations for material compatibility. ClorDiSys provided information on chlorine dioxide and its advantages and applicability as a growing sterilization modality.[102] See Appendix E for detailed information on the comments and EPA's response.

Neither nitrogen dioxide nor chlorine dioxide can presently fully replace the medical device sterilization uses of EtO due to material compatibility, scalability, and capacity limitations; however, EPA encourages the increased use of alternatives to EtO when possible, to reduce EtO exposures to workers and communities. EPA suggests companies reach out directly to FDA regarding medical device sterilization for their modalities, by email at dice@fda.hhs.gov. Direct phone contacts can also be found at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance.

Food Uses

Spices or herbs discussed in this document refer only to the dried forms, not fresh forms, of herbs and/or spices. Limiting the use of EtO to specific food commodities where its use is deemed critical for food safety and where alternative treatment methods are not available also would result in fewer EtO applications overall, and thus less exposure to workers (including handlers and occupational bystanders), residential bystanders, and non-residential bystanders. There are several alternatives used to treat food commodities: irradiation, heat, steam, and propylene oxide. However, currently these alternatives may not be viable for every food commodity, spice form (e.g., dried leafy-type, ground/powdered), spice blend, or target pathogen[103]. Despite these limitations, EPA still seeks to encourage use of alternatives to EtO sterilization as a long-term risk reduction strategy. See Section III.C. and *Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation* in this docket.

Pesticides can be used to treat food commodities in the U.S. if the commodity is listed on the product label (i.e., the pesticide is registered for use on the commodity). Any food treated with a pesticide may be distributed in interstate commerce only if there is an established tolerance or tolerance exemption for the pesticide residue in or on the commodity. As stated on the EtO product labels, EtO is currently registered to reduce the microbial load on various whole and ground spices (except basil), dried vegetables, and seasonings. Tolerances are established for EtO and ECH residues in or on various dried herbs and spices and dried vegetables (see Table 2 for all commodities with established EtO and ECH tolerances). There is also a tolerance for residues of EtO in or on walnuts. Seasonings are blends of dried herbs and spices. If a seasoning/spice blend is treated with EtO, it can only include commodities identified in Table 2.

[102] EPA-HQ-OPP-2013-0244-0091, EPA-HQ-OPP-2013-0244-0084, EPA-HQ-OPP-2013-0244-0086 at www.regulations.gov.

[103] American Spice Trade Association (ASTA). 2020. ASTA reply to EPA questions regarding ethylene oxide use on spices. Email from Laura Shumow, Executive Directors, ASTA, to Susan Bartow, Pesticide Re-Evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. June 25, 2020.

Table 2. Current Commodities with Tolerances for EtO and ECH in the U.S.[104]

Herbs (crop subgroup 19A)	Spices (crop subgroup 19B)	Other food commodities in 40 C.F.R. § 180.151
Angelica (*Angelica archangelica*)	Allspice (*Pimenta dioica*)	Licorice, roots
Balm (lemon balm) (*Melissa officinalis*)	Anise (anise seed) (*Pimpinella anisum*)	Peppermint, tops, dried
Borage (*Borago officinalis*)	Anise, star (*Illicium verum*)	Sesame seed
Burnet (*Sanguisorba minor*)	Annatto (seed)	Spearmint, tops, dried
Chamomile (Anthemis nobilis)[A]	Caper buds (*Capparis spinosa*)	Vegetable, dried[D]
Catnip (*Nepeta cataria*)	Caraway (*Carum carvi*)	Walnut[E]
Chervil (dried) (*Anthriscus cerefolium*)	Caraway, black (*Nigella sativa*)	
Chive (*Allium schoenoprasum*)	Cardamom (*Elettaria cardamomum*)	
Chive, Chinese (*Allium tuberosum*)	Cassia (bark) (*Cinnamomum aromaticum*)	
Clary (*Salvia sclarea*)	Cassia buds (*Cinnamomum aromaticum*)	
Coriander (cilantro or Chinese parsley) (leaf) (*Coriandrum sativum*)	Celery seed (*Apicum graveolens*)	
Costmary (*Chrysanthemum balsamita*)	Cinnamon (*Cinnamomum verum*)	
Culantro (leaf) (*Eryngium foetidum*)	Clove buds (*Eugenia caryophyllata*)	
Curry (leaf) (*Murraya koenigii*)	Coriander (cilantro) (seed) (*Coriandrum sativum*)	
Dill (dillweed) (*Anethum graveolens*)	Culantro (seed) (*Eryngium foetidum*)	
Horehound (*Marrubium vulgare*)	Cumin (*Cuminum cyminum*)	
Hyssop (*Hyssopus officinalis*)	Dill (seed) (*Anethum graveolens*)	
Lavender (*Lavandula officinalis*)	Fennel (common) (*Foeniculum vulgare*)	
Lemongrass (*Cymbopogon citratus*)	Fennel, Florence (seed) (*Foeniculum vulgare* Azoricum Group)	
Lovage (leaf) (*Levisticum officinale*)	Fenugreek (*Trigonella foenumgraecum*)	
Marigold (*Calendula officinalis*)	Grains of paradise (*Aframomum melegueta*)	
Marjoram (*Origanum spp.*) (includes sweet or annual marjoram, wild marjoram or oregano, and pot marjoram)[B]	Juniper berry (*Juniperus communis*)	
Nasturtium (*Tropaeolum majus*)	Lovage (seed) (*Levisticum officinale*)	
Parsley (dried) (*Petroselinum crispum*)	Mace (*Myristica fragrans*)	
Pennyroyal (*Mentha pulegium*)	Mustard (seed) (*Brassica* juncea, *B.* hirta, *B.* nigra)	
Rosemary (*Rosemarinus officinalis*)	Nutmeg (*Myristica fragrans*)	
Rue (*Ruta graveolens*)	Pepper, black (*Piper nigrum*)[C]	
Sage (*Salvia officinalis*)	Pepper, white	

[104] Basil (*Ocimum basilicum*) is included in crop group 19. However, it is excluded from Table 2 because there are no EtO tolerances established for residues of EtO or ECH in or on basil commodities.

Savory, summer and winter (*Satureja spp.*)	Poppy (seed) (*Papaver somniferum*)	
Sweet bay (bay leaf) (*Laurus nobilis*)	Saffron (*Crocus sativus*)	
Tansy (*Tanacetum vulgare*)	Vanilla (*Vanilla planifolia*)	
Tarragon (*Artemisia dracunculus*)		
Thyme (*Thymus spp.*)		
Wintergreen (*Gaultheria procumbens*)		
Woodruff (*Galium odorata*)		
Wormwood (*Artemisia absinthium*)		
A – Chamomile includes both German and Hungarian (46694 Federal Register / Vol. 74, No. 175 / Friday, September 11, 2009). B – Oregano is covered by the preferred term marjoram (46694 Federal Register / Vol. 74, No. 175 / Friday, September 11, 2009). C – Also includes pink peppercorns (46694 Federal Register / Vol. 74, No. 175 / Friday, September 11, 2009). D – Dried vegetables include capsicums, ginger, horseradish, paprika, garlic, onion, turmeric, and arrowroot (46694 Federal Register / Vol. 74, No. 175 / Friday, September 11, 2009). E – An EtO tolerance for walnut is established in 40 C.F.R. § 180.151, but an ECH tolerance is not.		

Based on discussions with industry, USDA-OPMP, and FDA-CFSAN,[105] EPA understands the limitations of the alternative treatment methods due to lack of compatibility with certain food commodities and/or their packaging, lack of scalability of some of the alternatives to an industrial scale, and lack of standardized validation measures or efficacy data. Despite these limitations, due to the inhalation risk estimates associated with the use of EtO, EPA still seeks to shift the use of EtO to identified alternatives for treating food commodities wherever possible.

In the PID, the Agency solicited comments on the specific commodities in Table 2 for which there is a critical need for the use of EtO and for which there are no viable alternatives to EtO (e.g., steam, irradiation, or propylene oxide cannot be used for pathogen control on a particular spice, spice form, or spice blend). The Agency noted that any commodities without documented support for continued treatment with EtO would be considered for a phased cancellation to reduce exposure to workers (including handlers and occupational bystanders), residential bystanders, and non-residential bystanders. The Agency further noted its intention to include language in the ID stating that registrants should submit requests to voluntarily terminate uses on these commodities (see Section V.A.).

Based on information submitted to the Agency during the development of the PID, EPA understood that the following spices often have high pathogen loads—black pepper, paprika,

[105] On October 1, 2024, FDA's CFSAN was combined into FDA's Human Foods Programs (HFP). See https://www.fda.gov/about-fda/fda-organization/fda-modernization-efforts-establishing-unified-human-foods-program-new-model-field-operations-and.

celery seed, coriander, turmeric, and thyme[106, 107]. The Agency sought public comment on alternative treatment options for those spices and target pathogens (e.g., *Salmonella*, *E. coli*.). In addition, the Agency requested information regarding any other commodities that typically have high pathogen loads for which there are not efficacious treatment options besides EtO. Finally, the Agency requested information about the importance of EtO to spice blends (e.g., seasonings) and the specific spices in the blends for which EtO fumigation is critical.

During the public comment period, the Agency received public comments providing information about specific food commodities for which commenters identified EtO treatment as critical to ensure food safety.[108] Most of the commodities identified are listed in Table 2 above. However, several specific commodities mentioned in the public comments are not listed in the table. These are cassia bark (*Cinnamomum burmannii*), galangal (*Alpinia officinarum* Hance), Mediterranean oregano (*Origanum vulgare*), Mexican oregano (*Lippia graveolens*), green pepper (*Piper nigrum*), sassafras, turmeric, pumpkin flakes, dehydrated diced tomatoes, dried bell peppers, and pink peppercorns. The Agency determined that galangal,[109] turmeric,[110] pumpkin flakes,[111] dehydrated diced tomatoes,[112] and dried bell peppers[113] are considered *dried vegetables*. Similarly, the Agency determined that cassia bark (*Cinnamomum burmannii*),[114] Mediterranean oregano (*Origanum vulgare*),[115] green pepper (*Piper nigrum*),[116]

[106] EOTF email to EPA regarding benefits of ethylene oxide for medical devices. Email sent from Lisa Campbell, Partner, Bergeson & Campbell PC to Jessica Bailey, Antimicrobial Division, Office of Pesticide Programs, Environmental Protection Agency. May 6, 2020.
[107] American Spice Trade Association (ASTA). 2017. Clean, Safe Spices, Guidance from the American Spice Trade Association, 2017 Update. https://www.astaspice.org/food-safety-technical-guidance/best-practices-and-guidance/clean-safe-spices-guidance-document/. Accessed September 2020.
[108] EPA-HQ-OPP-2013-0244-0130, EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[109] The Agency considers galangal (*Alpinia officinarum* Hance) to be similar to ginger since it is in the Zingiberaceae (ginger) family, and therefore, considers it to be included in the *Dried Vegetables* tolerance similar to ginger.
[110] 46694 Federal Register / Vol. 74, No. 175 / Friday, September 11, 2009 states, "… (Capsicums, ginger, horseradish, paprika, garlic, onion, turmeric, and arrowroot) are covered by the proposed tolerances on ''vegetable, dried.''"
[111] Since pumpkins are cucurbit vegetables (as identified in Cucurbit Vegetable crop subgroup 9B), the Agency considers dried pumpkin flakes to be dried vegetables and covered by the *Dried Vegetables* tolerance.
[112] Since tomatoes are fruiting vegetables (as identified in Fruiting Vegetable crop group 8-10), the Agency considers dehydrated diced tomatoes to be dried vegetables and covered by the *Dried Vegetables* tolerance.
[113] 46694 Federal Register / Vol. 74, No. 175 / Friday, September 11, 2009, states, "… (Capsicums, ginger, horseradish, paprika, garlic, onion, turmeric, and arrowroot) are covered by the proposed tolerances on ''vegetable, dried.''" Bell peppers are the fruit of plants in the species *Capsicum* and thereby covered by the *Dried Vegetables* tolerance.
[114] Crop group 19B lists "Cassia bark (*Cinnamomum aromaticum*)". The Agency considers cassia bark (*Cinnamomum burmannii*) similar to Cassia bark (*Cinnamomum aromaticum*) because they are both in the *Cinnamomum* genus.
[115] Crop group 19A lists "Marjoram (*Origanum spp*.) (includes sweet or annual marjoram, wild marjoram or oregano, and pot marjoram)". The Agency considers Mediterranean oregano (*Origanum vulgare*) to be included under Marjoram (*Origanum spp*.) because they are both in the *Origanum* genus.
[116] Crop group 19B lists "Pepper, black (*Piper nigrum*)". The Agency considers green pepper (*Piper nigrum*) to be the same plant as black pepper; the green pepper is the unripe fruit.

and pink peppercorns[117] are included in the existing tolerances for crop group 19. However, Mexican oregano (*Lippia graveolens*) and sassafras are not included in crop group 19, and there are no EtO or ECH tolerances for those commodities. Therefore, EtO is not currently allowed for treatment of those commodities.

Dried vegetables is identified as a commodity with a tolerance in 40 C.F.R. § 180.151. EtO is the only active ingredient with a *dried vegetables* tolerance. EPA's tolerance regulation does not define the exact list of dried vegetables that are included in the *dried vegetables* tolerance, and public comments on the PID suggest that this list has evolved over time. Comments submitted by ASTA identify certain dried vegetables for which EtO treatment is critical for food safety. The dried vegetables identified in their comments include additional dried vegetables not previously identified by EPA as included in the tolerance for *dried vegetables* (46694 Federal Register / Vol. 74, No. 175 / Friday, September 11, 2009).

After receiving public comment on the PID, the Agency reached out to ASTA to obtain a list of all dried vegetables currently treated with EtO to help clarify this use pattern. ASTA provided information that the following dried vegetables may be treated with EtO as part of seasoning blends, "asparagus, artichoke, green bean, green bell pepper, red bell pepper, broccoli, cabbage, carrot, celery stalk, corn, kelp, leek, mushroom, tomato, and meleguenta."[118, 119] EPA has not confirmed whether EtO is in fact being used to treat these dried vegetables. However, the dietary assessment was updated to reflect the new information from ASTA to ensure that the current use of EtO on dried vegetables in the spice and seasoning industries does not result in dietary risks of concern. The assessment confirmed that no dietary risks are anticipated from the use of EtO to treat the identified dried vegetables. To eliminate any further confusion of the dried vegetables that can be treated with EtO under the *dried vegetables* tolerance, the Agency has determined the need to define the commodities included within the *dried vegetables* tolerance and list the dried vegetables on the product labels.

IV. INTERAGENCY CONSIDERATIONS

The federal government has taken an all-agency approach to addressing concerns about the use of EtO since the establishment of the Ethylene Oxide Interagency Task Force in February 2020. Members of the Task Force include EPA Office of Pesticide Programs (EPA-OPP), EPA Office of Air and Radiation (EPA-OAR), EPA Office of Research and Development (EPA-ORD), the Centers for Disease Control and Prevention and Agency for Toxic Substances and Disease Registry (CDC-ATSDR), the Occupational Safety and Health Administration (OSHA), the Food and Drug Administration Center for Food Safety and Applied Nutrition (FDA-CFSAN), and the Food and Drug Administration Center for Devices and Radiological Health (FDA-CDRH). Members meet

[117] 46694 Federal Register / Vol. 74, No. 175 / Friday, September 11, 2009 states, "…pink peppercorns is covered by black pepper within the proposed tolerance on ''herb and spice, group 19, dried, except basil.''".
[118] EPA-HQ-OPP-2013-0244-0433 at www.regulations.gov.
[119] Meleguenta is also known as Grains of paradise and is included as a spice in crop subgroup 19B.

monthly to discuss the on-going regulatory concerns for EtO. In particular, for the regulation of the pesticidal registrations of EtO, OPP worked closely with OSHA and FDA on the registration review mitigation to address exposures to workers and nearby communities, as discussed below. EPA thanks all federal partners for their collaboration.

A. Occupational Safety and Health Administration (OSHA)

OSHA standards are issued pursuant to the OSH Act and are found in title 29 of the Code of Federal Regulations (C.F.R.). There are separate standards for general industry, construction, maritime and agriculture activities, as well as general standards applicable to a number of sectors (e.g., OSHA's Respiratory Protection standard). OSHA has a standard on ethylene oxide at 29 C.F.R. § 1910.1047.[120]

OSHA sets legally enforceable limits on the concentrations of hazardous chemicals in the air in a workplace, referred to as permissible exposure limits (PELs), to protect workers against the health effects of exposure to such chemicals (29 C.F.R. 1910 Subpart Z, 1915 Subpart Z, 1926 Subparts D and Z). Under section 6(a) of the OSH Act, OSHA was permitted an initial two-year window after the passage of the Act to adopt "any national consensus standard and any established Federal standard." 29 U.S.C. 655(a). OSHA used this authority in 1971 to establish PELs that were adopted from federal health standards originally set by the Department of Labor through the Walsh-Healy Act, pursuant to which approximately 400 occupational exposure limits were selected based on the American Conference of Governmental Industrial Hygienists (ACGIH) 1968 list of Threshold Limit Values (TLVs). In addition, about 25 exposure limits recommended by the American Standards Association (now called the American National Standards Institute (ANSI)) were adopted as PELs.

Following the two-year window provided under section 6(a) of the OSH Act for adoption of national consensus and existing Federal standards, OSHA has issued health standards following the requirements in section 6(b) of the Act. OSHA has established approximately 30 PELs under section 6(b)(5) as part of comprehensive substance-specific standards that include additional requirements for protective measures such as establishment of regulated areas, exposure assessment, medical surveillance, and training.

With few exceptions, OSHA's PELs have not been updated since they were first established starting in 1971. At this time, the EtO PEL was established at 50 ppm, based on the 1968 ACGIH TLV. The PEL for EtO has not been revised since 1984, when it was set at 1 ppm. Yet, in many instances, scientific evidence has accumulated suggesting that the current limits are not sufficiently protective. As stated on OSHA's annotated PELs webpage, OSHA has recognized that "many of its PELs are outdated and inadequate for ensuring protection of worker health."[121] In addition, health standards issued under section 6(b)(5) of the OSH Act must reduce significant risk only to the extent that it is technologically and economically feasible. OSHA's legal

[120] https://www.osha.gov/laws-regs/regulations/standardnumber/1910/1910.1047.
[121] https://www.osha.gov/annotated-pels.

requirement to demonstrate that its 6(b)(5) standards are technologically and economically feasible often precludes OSHA from imposing exposure control requirements sufficient to ensure that a chemical no longer presents a significant risk to workers. In sum, there is concern that OSHA's chemical standards are outdated or do not eliminate significant risk as defined by the Supreme Court's interpretation of the OSH Act.[122] These standards may not address unreasonable adverse effects to workers within the meaning of FIFRA, which allows EPA to consider more sensitive endpoints and working populations than OSHA's risk evaluations typically contemplate.

OSHA, under limited circumstances, has cited the General Duty Clause for worker exposure to hazardous chemicals that are not sufficiently addressed under 29 C.F.R. 1910 Subpart Z, 1915 Subpart Z, 1926 Subparts D and Z. To prove a violation of the General Duty Clause, OSHA must prove employer or industry recognition of the hazard, that the hazard was causing or likely to cause death or serious physical harm, and a feasible method was available to eliminate or materially reduce the hazard. In rare situations, OSHA has cited employers for violation of the General Duty Clause where exposures were below a chemical-specific OSHA PEL. In such situations, OSHA must demonstrate that the employer had actual knowledge that the PEL was inadequate to protect its employees from death or serious physical harm. Because of the heavy evidentiary burden on OSHA to establish violations of the General Duty Clause, it is not frequently used to cite employers for employee exposure to chemical hazards.

Thus, it is appropriate that EPA conduct risk assessments and, where it finds risks of concern to workers, develop risk mitigation measures to address risks from the pesticidal uses of chemicals that OSHA also regulates, and it is expected that EPA's findings and mitigation measures may sometimes diverge from OSHA's. However, it is also appropriate that EPA consider the chemical standards that OSHA has already developed, so as to limit the compliance burden to employers, where alignment will ensure that the use of a pesticide will not cause unreasonable adverse effects on the environment, including to workers.

When developing mitigation measures to address risks of concern to workers for this ID, EPA has: 1) striven for consistency with OSHA requirements and industry best practices, including appropriate application of the hierarchy of controls (e.g., elimination, substitution, engineering controls, administrative controls, PPE), to address risks of concern to workers; 2) ensured the EPA mitigation measures apply to all workers potentially exposed to risks from pesticidal uses of EtO; and 3) developed occupational risk mitigation measures to address any risks of concern identified by EPA.

EPA's risk assessment on EtO has found risks of concern to workers associated with the registered uses of EtO, even when the applicable OSHA requirements are being met. Therefore, to ensure that the use of EtO does not cause unreasonable adverse effects to workers, as

[122] Am. Petroleum Inst., 448 U.S. at 655.

required under FIFRA, EPA has developed risk mitigation measures that go beyond those included in OSHA's standard for EtO.

In the *Reregistration Eligibility Decision for Ethylene Oxide* (2008), OPP required registrants to implement label amendments for respirator requirements and air monitoring requirements based on the OSHA PEL of 1 ppm. Since 2008, there have been considerable updates to the scientific database on EtO exposure and risk, including the 2016 IRIS assessment on EtO, OPP's 2020 EtO DRA, and OPP's 2023 EtO DRA Addendum. EPA thus considers the OSHA PEL of 1 ppm to no longer ensure that the use of EtO will not cause unreasonable adverse effects, including effects to workers, as required under FIFRA. Therefore, EPA has determined that it is necessary for registrants to amend their EtO label to revise language regarding the OSHA PEL and to include lowered occupational exposure limits necessary to address unreasonable adverse effects to workers from the pesticidal use of EtO. See Section V.A. for details on worker mitigation and Appendix B for EtO product label changes.

EPA notes that since the publication of the PID and DRA, OSHA has updated its Safety and Health Topics Webpage for Ethylene Oxide to acknowledge EPA's publications.[123]

Training Requirements

Commercial Sterilization Facilities for Medical Devices and Food Commodities

OSHA Standard 29 C.F.R. § 1910.1047(j)(3)(iii) *Information and Training* states that employee training shall include at least:

- Methods and observations that may be used to detect the presence or release of EtO in the work area (such as monitoring conducted by the employer, continuous monitoring devices, etc.);
- The physical and health hazards of EtO,[124] which must include at a minimum cancer; reproductive effects; mutagenicity; central nervous system; skin sensitization; skin, eye, and respiratory tract irritation; acute toxicity effects; and flammability per 1910.1047(j)(1)(ii);
- The measures employees can take to protect themselves from hazards associated with EtO exposure, including specific procedures the employer has implemented to protect employees from exposure to EtO, such as work practices, emergency procedures, and personal protective equipment to be used; and
- The details of the hazard communication program developed by the employer, including an explanation of the labeling system and how employees can obtain and use the appropriate hazard information.

[123] https://www.osha.gov/ethylene-oxide.

[124] This includes all classified hazards as per 1910.1200, and at a minimum include at a minimum Cancer; reproductive effects; mutagenicity; central nervous system; skin sensitization; skin, eye and respiratory tract irritation; acute toxicity effects; and flammability as per 29 C.F.R. § 1910.1047(j)(1)(ii).

For information on training identified as necessary by EPA, see Section V.A.

Engagement with OSHA Following the Publication of the PID

Following the publication of the PID, EPA met with OSHA to discuss the mitigation to reduce worker exposure to EtO. In these meetings, the agencies discussed OSHA's existing requirements applicable to EtO use, as well as mitigation included in this ID.[125]

B. Food and Drug Administration (FDA)

Medical Devices

FDA's Center for Devices and Radiological Health (CDRH) assures that patients and providers have timely and continued access to safe, effective, and high-quality medical devices.[126] Before most sterile medical devices are on the market, FDA reviews submissions to determine if the sterility information is consistent with the sterility assurance under which the device is labeled and intended for use (e.g., in accordance with internationally agreed upon voluntary consensus standards that FDA recognizes).

For EtO sterilization, two voluntary consensus standards (ANSI AAMI ISO 11135:2014 and ANSI AAMI ISO 10993-7:2008(R)2012) describe how to develop, validate, and control EtO sterilization processes for medical devices and the acceptable levels of residual EtO and ethylene chlorohydrin (ECH) left on a device after it has undergone EtO sterilization. FDA also inspects industrial facilities that sterilize medical devices and medical device manufacturing facilities to make sure that they have validated sterilization processes that meet FDA-recognized standards. State health departments inspect healthcare facilities that use EtO to sterilize medical devices.

FDA actively works with sterilization experts, medical device manufacturers, and other government agencies to advance innovative ways to sterilize medical devices with lower levels of EtO and employ new agents or alternatives, while maintaining device safety and effectiveness and helping to prevent potential medical device shortages.[127] In May and November 2019, FDA engaged the infection control community at the Healthcare Infection Control Practices Advisory Committee (HICPAC) and General Hospital and Personal Use Panel of the Medical Devices Advisory Committee meetings, respectively, to update the public on FDA's work and engagement with industry on sterilization modalities with devices that are normally sterilized using EtO.[128]

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[125] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide Stakeholders Occupational Safety and Health Administration (OSHA) January – August 2024* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0426.

[126] https://www.fda.gov/about-fda/fda-organization/center-devices-and-radiological-health.

[127] https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-steps-agency-taking-prevent-potential-medical-device.

[128] https://www.fda.gov/advisory-committees/advisory-committee-calendar/november-6-7-2019-general-hospital-and-personal-use-devices-panel-medical-devices-advisory-committee.

On July 15, 2019, FDA announced two public innovation challenges to encourage development of new approaches to medical device sterilization, which could include identifying alternatives to EtO sterilization methods or strategies to reduce EtO emissions:

- Challenge 1: Identify New Sterilization Methods and Technologies.
- Challenge 2: Reduce Ethylene Oxide Emissions.

On November 25, 2019, FDA announced that 46 applications were received, and 12 participants were selected for the challenges. For details regarding Innovation Challenges 1 and 2, please visit the respective FDA websites.[129, 130]

Approvals/Clearances for Changes to Sterilization Processes

Typically, for premarket application (PMA) approved devices, if a medical device manufacturer changes the method, process, or the facility identified in its original PMA submission for sterilizing its devices, the manufacturer needs to submit a PMA supplement so that FDA can review these changes and determine if the sterility information remains consistent with the sterility assurance under which the device is labeled and approved for use (e.g., in accordance with internationally agreed-upon voluntary standards that FDA recognizes). For manufacturers that are 510(k) holders, sterilization method, process or site modifications can be assessed as recommended in the FDA guidance document: "Deciding When to Submit a 510(k) for a Change to an Existing Device" for determination on whether the sterilization modifications would trigger the need for a new submission.[131]

Master File Program

FDA announced a series of master file pilot programs to include the Ethylene Oxide Sterilization Master File Pilot Program for sterilization facilities and PMA holders and 510(k) Sterility Change Master File Pilot Program. For more details on these pilots, please visit the respective FDA website and Federal Register postings.[132, 133, 134]

[129] https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-1-identify-new-sterilization-methods-and-technologies.
[130] https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-2-reduce-ethylene-oxide-emissions.
[131] https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/ethylene-oxide-sterilization-medical-devices.
[132] https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/ethylene-oxide-sterilization-medical-devices.
[133] https://www.federalregister.gov/documents/2019/11/26/2019-25631/center-for-devices-and-radiological-health-ethylene-oxide-sterilization-master-file-pilot-program.
[134] https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/ethylene-oxide-sterilization-medical-devices#MasterFile.

Technical Information Reports (TIR) and Sterilization Standards

In July 2023, the FDA announced complete recognition of a sterilization standard and two Technical Information Reports (TIRs) to help advance innovation in medical device sterilization processes. The FDA's recent recognitions further support supply chain resiliency. For details on these recognitions, please visit the FDA website.[135]

Recognition of Vaporized Hydrogen Peroxide (vH2O2) as an Established Method

In January 2024, the FDA revised the final guidance, *Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile*, to list vH2O2 as an example of an Established Category A method of sterilization. VH2O2 is a type of sterilization method that FDA has seen in a variety of sterile products, and it is generally viewed as an established Category A method if sterilization, per FDA guidance. For more information on this guidance, please visit the FDA docket FDA-2008-D-0611 at www.regulations.gov.

Food Commodities

FDA also is an important federal partner with respect to EtO fumigation of spices. FDA's Human Food Program's vision is "to ensure that food is a source of wellness for all U.S. consumers, and our day-to-day activities are focused at protecting and promoting the health and wellness of all people through science-based approaches to prevent foodborne illness, reduce diet related chronic disease, and ensure chemicals in food are safe."[136] Passage of the Food Safety Modernization Act (FSMA) in 2011 expanded FDA's authority under the Federal Food, Drug, and Cosmetic Act to ensure the food supply in the United States is safe. FDA's authority covers domestically grown and produced food as well as food and ingredients imported from abroad, except for meat; poultry; Siluriformes fish, including catfish; and certain egg products for which the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture (USDA) is responsible. FDA is responsible for ensuring that food, including spices, is not adulterated, or misbranded. Foods, including spices, can be adulterated for reasons such as they contain pathogens or pesticide residues such as EtO or ECH at unsafe levels, or because they are produced under unsanitary conditions and may contain filth (e.g., mold, sticks, insect fragments, hair).

Many herbs and spices are imported into the U.S.[137, 138] FDA inspects foreign facilities that import food into the U.S. and inspects shipments at the port of entry. FSMA also established

[135] CDRH Announces New Standards Recognition to Support Innovation in Medical Device Sterilization | FDA.
[136] https://www.fda.gov/about-fda/fda-organization/human-foods-program.
[137] FDA Center for Food Safety and Applied Nutrition (FDA CFSAN). 2017. Draft Risk Profile: Pathogens and Filth in Spices. Center for Food Safety and Applied Nutrition, Food and Drug Administration. U.S. Department of Health and Human Services. https://www.fda.gov/media/108126/download. Accessed August 2021.
[138] American Spice Trade Association (ASTA). 2020. ASTA reply to EPA questions regarding ethylene oxide use on spices. Email from Laura Shumow, Executive Directors, ASTA, to Susan Bartow, Pesticide Re-Evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. June 25, 2020.

prevention-based programs to ensure the safety of imported foods before they reach the U.S.[139] These include the Foreign Supplier Verification Program and the Voluntary Qualified Importer Program, as well as accrediting third-party certification bodies to conduct food safety audits of foreign food entities. The Foreign Supplier Verification Program requires importers to verify the safety of the food they import, and FDA inspects importers to make sure they are doing so. The Voluntary Qualified Importer Program involves expedited review of food from eligible importers that meet rigorous standards.

Treatment (including reconditioning) of food commodities for pathogen control

Herbs and spices can contain pathogens of public health significance. Spices may be treated for pathogen reduction as a preventive measure to control pathogens, due to the confirmed presence of a pathogen, such as *Salmonella*, or due to the appearance of adulteration. The primary treatment options for pathogen reduction on dried herbs and spices are EtO, steam, and irradiation; propylene oxide (PPO) also is used occasionally. If a contaminated shipment is identified during FDA's screening of imported commodities at the U.S. border, the importer can either return, destroy, or recondition the shipment. When reconditioning is selected, the firm submits a reconditioning proposal to FDA with intent to bring the product into compliance.[140] The reconditioning proposal must identify the required treatment option and treatment location. If the reconditioning proposal is accepted by FDA, the shipment is then sent to the facility for treatment. After the treatment process, the manufacturer or importer of the lot will generally provide testing results of the treated lot for FDA review to verify that the treatment was effective, and the product is safe.[141] FDA will then release the shipment into U.S. commerce. FDA may also place specific importers or commodities from certain countries on automatic detention (i.e., import alert, detention without physical examination (DWPE)) based on historical contamination incidents. In this situation, reconditioning of the shipment may be required regardless of whether there is confirmed presence of human pathogens.

Reconditioning occurs in less than one percent of the dried herb and spice shipments to the U.S.[142, 143] From 2018-2023, the majority of shipments detained for reconditioning were because of microbial contamination (i.e., *Salmonella*). Of the reconditioning proposals submitted to FDA for those imported herbs and spices detained for microbial contamination, roughly half of the reconditioning proposals were for EtO treatment. The other half proposed alternative treatment methods (e.g., irradiation, steam, propylene oxide). Some examples of spices that were submitted for reconditioning by EtO treatment were thyme, black pepper, and

[139] https://www.fda.gov/food/cfsan-risk-safety-assessments/questions-answers-improving-safety-spices.
[140] https://www.fda.gov/industry/fda-import-process/reconditioning-imported-fda-regulated-products.
[141] *Ethylene Oxide (EtO) Spice Sterilizing Facilities*. Center for Food Safety and Applied Nutrition (CFSAN), Food and Drug Administration (FDA) responses to questions from Office of Pesticide Programs (OPP), Environmental Protection Agency (EPA). December 20, 2022.
[142] EPA-HQ-OPP-2013-0244-0420 at www.regulations.gov.
[143] EPA-HQ-OPP-2013-0244-0433 at www.regulations.gov.

sesame seeds. Reconditioning proposals are generally for whole spices or single spice powders.[144, 145]

FDA also may inspect commercial sterilization facilities. Regardless of the facility location and type, FDA's review of reconditioning proposals ensures that each treatment process for microbial reduction is effective. In addition, when a manufacturing/processing facility is subject to the requirements for hazard analysis and preventive controls in the Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food (PCHF) regulation in 21 C.F.R. part 117 and is using a certain process for pathogen reduction as a preventive control, it must validate the process to ensure it is adequate for controlling the identified hazards (21 C.F.R. 117.160(a)).[146]

According to ASTA,[147] many spice companies conduct internal analyses for *Salmonella* to verify their food safety plans as well as to ensure product safety and regulatory compliance. If *Salmonella* is detected, companies will re-treat the product before it leaves the facility. The frequency of retreatment of spices by spice companies varies by the spice type and by the initial treatment method. ASTA provided information indicating that approximately 1% of spice products are retreated internally, with potentially as much as 12-15% of spice commodities being retreated. ASTA noted that the variation in treatment occurrence can be a result of different factors such as some spices are more resistant to treatment due to their form, starting microbial load, or inherent chemical properties. The effectiveness of the initial treatment method is another factor in determining if retreatment is necessary.

ASTA developed documents to assist sterilization facilities in developing validations for fumigations of herbs and spices entitled, *General Protocol for the Validation of Microbiocidal Processes on Pathogen Contaminated Spices and Culinary Herbs (2001) and Validation of Microbial Reduction Processes for Spices (2013).* These documents may assist commercial sterilization facilities with complying with portions of the PCHF regulation as mandated by FSMA. FDA is also developing a multichapter, *Draft Guidance for Industry: Hazard Analysis and Risk-Based Preventive Controls for Human Food*, and has released most of the chapters to the public, outlining FDA's current thinking on how to comply with the PCHF regulation.[148] As new technologies become available for spice microbial remediation, these methods will require

[144] *Ethylene Oxide (EtO) Spice Sterilizing Facilities*. Center for Food Safety and Applied Nutrition (CFSAN), Food and Drug Administration (FDA) responses to questions from Office of Pesticide Programs (OPP), Environmental Protection Agency (EPA). December 20, 2022.
[145] EPA-HQ-OPP-2013-0244-0420 at www.regulations.gov.
[146] *Ethylene Oxide (EtO) Spice Sterilizing Facilities*. Center for Food Safety and Applied Nutrition (CFSAN), Food and Drug Administration (FDA) responses to questions from Office of Pesticide Programs (OPP), Environmental Protection Agency (EPA). December 20, 2022.
[147] EPA-HQ-OPP-2013-0244-0433 at www.regulations.gov.
[148] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/draft-guidance-industry-hazard-analysis-and-risk-based-preventive-controls-human-food.

validations. New technologies can take up to ten years to be implemented because research and validation are required.[149, 150, 151]

Engagement with FDA Following the Publication of the PID

EPA met with FDA-CDRH 16 times since the publication of the PID to discuss mitigation measures to be included in the ID, in order to keep FDA informed of any EPA mitigation measures that may have an impact on the supply chain of medical devices.[152]

Since the publication of the PID in April 2023, EPA OPP received several public comments that raised concerns about the availability of sterilized medical devices if EPA's mitigation was adopted as proposed (see Appendix E). EPA has taken steps to more fully understand potential impacts to the medical device supply chain, including consulting FDA-CDRH. EPA shares the concerns for a stable supply chain of medical devices and uninterrupted access to patient care. For these reasons, EPA has amended several aspects of the PID to refine the Agency's mitigation strategy to allow facilities the flexibility to meet the demand for sterilized medical devices while also reducing worker exposure. It is worth noting that there are several proposed mitigation measures from the PID that remain part of this Interim Decision based on the reductions in worker exposure provided by these measures and the impacts of these measures on the availability of sterile medical devices, which EPA expects to be low. See Section V.A. for a detailed explanation of all mitigation measures.

EPA also met with FDA-CFSAN (now FDA-HFP) four times since the publication of the PID to discuss public comments received on the PID and revised mitigation measures under consideration that are specific to the food use of EtO.[153] EPA has consulted FDA-CFSAN to understand the current importation of dried herbs and spices and the use of EtO for reconditioning contaminated shipments.

[149] *Ethylene Oxide (EtO) Spice Sterilizing Facilities*. Center for Food Safety and Applied Nutrition (CFSAN), Food and Drug Administration (FDA) responses to questions from Office of Pesticide Programs (OPP), Environmental Protection Agency (EPA). December 20, 2022.
[150] EPA-HQ-OPP-2013-0244-0432 at www.regulations.gov.
[151] EPA-HQ-OPP-2013-0244-0420 and EPA-HQ-OPP-2013-0422 at www.regulations.gov.
[152] See *EPA Office of Pesticide Programs (OPP) Meetings Regarding Ethylene Oxide (EtO) Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) July 2023 – August 2024* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0419.
[153] See *EPA Office of Pesticide Programs (OPP) Meetings Regarding Ethylene Oxide (EtO) Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition (CFSAN) July 2022 – August 2024* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0420.

V. INTERIM REGISTRATION REVIEW DECISION

A. Risk Mitigation and Rationale

EtO is a known carcinogen. EtO is also a critical tool for the medical sterilization market and is beneficial when used on food commodities (e.g., dried herbs and spices) to control microbes which may cause food-borne illnesses, but has low benefits in other registered use sites, including beekeeping equipment, due to the availability of viable alternatives. The registered uses of EtO pose inhalation risks to workers inside commercial sterilization facilities, healthcare facilities, and to those treating beekeeping equipment in North Carolina. EtO also has the potential to pose inhalation risks to communities near facilities where EtO is used. See Section III.A.-B. above. Therefore, EPA has identified mitigation necessary at this time to address these inhalation risk concerns, including the termination of certain minor uses, the phase-out of certain food commodity uses, a phased-in reduced concentration rate for new medical device sterilization cycles, respiratory protection for workers involved in high exposure tasks, lowered occupational exposure limits and associated respiratory protection, monitoring, training, and recordkeeping, as well as venting and abatement devices for healthcare facilities. Furthermore, EPA will be issuing a DCI to require submission of worker exposure data for commercial sterilizers and warehouses in order to understand the worker exposure impacts of complying with EPA's CAA EtO commercial sterilization NESHAP and implementing the mitigation measures identified in this ID, issued under FIFRA, and to better understand how to further lower the occupational exposure limit. In order to make this determination, EPA will reevaluate the occupational exposure limit and any other needed mitigations, based on data, within 8 years.

During the 75-day public-comment period for the EtO PID (April 13, 2023 to June 27, 2023), the Agency received over 30,000 public comments, many of which were mass mailers. Comments were submitted by representatives from government, non-profit groups, private citizens, hospitals, bioscience industry, physicians' organizations, medical device distributors, medical device manufacturers, states, small businesses, and commercial sterilization facilities. The Agency has summarized and responded to all substantive comments and comments of a broader regulatory nature in Appendix E. The Agency thanks all commenters for participating and has considered all comments in developing this ID.

Many of the changes made to the PID for this ID are in response to concerns about impacts to the medical device supply chain that could have resulted from the unintended consequences of the proposed mitigation. During the public comment period, EPA received 36 public comments expressing concerns about the effects of the proposed mitigation on the medical device supply chain. Commenters represented stakeholders from hospitals, the bioscience industry, physicians' organizations, medical device distributors, medical device manufacturers, states, small businesses, and commercial sterilization facilities. Of note, commenters stated that if the mitigation measures were to be adopted as proposed in the PID, this would cause widespread and catastrophic disruption to the medical device supply chain in the U.S. and subsequent

limited patient access to medical care since the U.S. medical device supply chain is already at capacity. Commenters requested the maximum amount of implementation time for mitigation. Finally, commenters reiterated that EtO is the only suitable sterilization method for a variety of medical devices, and no available alternatives could replace EtO. EPA shares the concerns of the submitters for a stable supply chain of medical devices and uninterrupted access to patient care. For these reasons, EPA has amended several aspects of the PID to refine the Agency's mitigation strategy to allow facilities the flexibility to meet the demand for sterilized medical devices while also reducing worker exposure. It is worth noting that there are several proposed mitigation measures from the PID that remain part of this ID based on the reductions in worker exposure provided by these measures and the impacts of these measures on the availability of sterile medical devices, which are expected to be low.

Following review of the public comments, the Agency met with representatives from non-profit organizations, industry, and other federal agencies to better understand the content of the public comments and refine the risk mitigation strategy.[154]

In Table 3 below, EPA has summarized the changes from the proposed mitigation in the PID to the mitigation measures identified in this ID for the continued use of EtO.

Table 3. Summary of Changes to Mitigation Proposed in PID

Mitigation Measure	Proposed Mitigation in PID	Mitigation in ID
Use Termination	Terminate uses for: museum, library, archival materials; cosmetics; musical instruments; and beekeeping equipment. 60-day implementation timeframe.	**No change.** Remove from product registrations and labels the uses for: museum, library, archival materials; cosmetics; musical instruments; and beekeeping equipment. Immediate upon approved label.[155, 156]
	Requested public comment on specific spices/commodities for which use of EtO is critical for food	**Revised.** Cancellation of specific food commodities for which EtO use is not considered critical for food safety, and phased cancellation for

[154] EPA-HQ-OPP-2013-0244-0408, EPA-HQ-OPP-2013-0244-0409, EPA-HQ-OPP-2013-0244-0410, EPA-HQ-OPP-2013-0244-0411, EPA-HQ-OPP-2013-0244-0412, EPA-HQ-OPP-2013-0244-0413, EPA-HQ-OPP-2013-0244-0414, EPA-HQ-OPP-2013-0244-0415, EPA-HQ-OPP-2013-0244-0416, EPA-HQ-OPP-2013-0244-0417, EPA-HQ-OPP-2013-0244-0418, EPA-HQ-OPP-2013-0244-0419, EPA-HQ-OPP-2013-0244-0420, EPA-HQ-OPP-2013-0244-0421, EPA-HQ-OPP-2013-0244-0422, EPA-HQ-OPP-2013-0244-0423, EPA-HQ-OPP-2013-0244-0424, EPA-HQ-OPP-2013-0244-0425, EPA-HQ-OPP-2013-0244-0426, EPA-HQ-OPP-2013-0244-0427, EPA-HQ-OPP-2013-0244-0428, EPA-HQ-OPP-2013-0244-0429, EPA-HQ-OPP-2013-0244-0430 at www.regulations.gov.

[155] EPA expects that registrants will submit label amendments within 60 days after the decision. The Agency would review such label amendments as expeditiously as feasible.

[156] Following the removal of the uses from the EtO product labels, registrants would follow the use termination process according to the FIFRA 6(f) procedure. See https://www.epa.gov/pesticide-registration/voluntary-cancellation-pesticide-product-or-use.

Mitigation Measure	Proposed Mitigation in PID	Mitigation in ID
	safety and there are no viable alternatives.	specific food commodities for which EtO use is considered critical for food safety but have potential alternatives to EtO.
	Revoke tolerances for any spices/commodities that might be proposed for cancellation.	**Revised.** Retain tolerances for any cancelled food uses. There are no anticipated dietary risks.
Concentration Rate Limits	Concentration limit at 500 mg/L for medical devices. 2-year implementation timeframe for new cycles and 5-year implementation timeframe for existing cycles.	**Revised.** Concentration limit at 600 mg/L for medical devices for new cycles only. 10-year implementation timeframe.
	Requested public comment on examples of efficacious EtO treatments for pathogen control on spices at rates lower than the maximum label rate and expressed an interest in establishing an alternative method for the product labels that uses a lower rate of EtO.	**Revised.** Not pursuing a lower rate on food commodities at this time given the phased cancellation and need to establish alternative methods for treatment. This potential mitigation will be revisited at the next round of registration review or sooner for any spices/commodities that retain EtO use.
Engineering Controls	Air pressure gradient, ventilation of storage areas, covered conveyors, all-in-one sterilization systems, and separated HVAC systems in commercial sterilization facilities. 3-year implementation timeframe.	**Revised.** ID does not identify specific engineering controls for commercial sterilization facilities (except for separated HVAC systems). Facilities may choose which engineering and process controls to use in order to meet lowered occupational exposure limits, as described below.
	Separation of HVAC systems for processing and non-processing areas. 2-year implementation timeframe.	**Revised implementation timeframe.** Separation of HVAC systems for processing and non-processing areas. 3-year implementation timeframe.
Personal Protective Equipment (PPE)	Respirators for indoor levels exceeding 10 ppb (based on stationary continuous monitoring) in commercial sterilization facilities. 2-year implementation timeframe.	**Revised.** Respirators for exceedances of occupational exposure limit of 1 ppm (1,000 ppb) (8-hour time weighted average) and short-term exposure limit (STEL) of 5 ppm (5,000 ppb) (15-minute time

Mitigation Measure	Proposed Mitigation in PID	Mitigation in ID
		weighted average) in commercial sterilization facilities and healthcare facilities. The occupational exposure limit to be lowered to 0.5 ppm (500 ppb) (3-year implementation timeframe), 0.25 ppm (250 ppb) (5-year implementation timeframe), and 0.1 ppm (100 ppb) (10-year implementation timeframe). Short-Term Exposure Limit (STEL) of 5 ppm (5,000 ppb) duration to be lowered to 10-minute time weighted average from the current 15-minute duration (10-year implementation timeframe).
	Respirators for connecting and disconnecting EtO containers from sterilization process equipment; unloading processed products from the sterilization chamber; loading and unloading product from the aeration area; removing validation test materials from processed product at any time prior to the completion of aeration; opening process lines or equipment that may contain EtO (e.g., for repairs or routine maintenance tasks). 60-day implementation timeframe.	**Revised implementation timeframe.** Respirators for connecting and disconnecting EtO containers from sterilization process equipment; unloading processed products from the sterilization chamber; loading and unloading product from the aeration area; removing validation test materials from processed product at any time prior to the completion of aeration; opening process lines or equipment that may contain EtO (e.g., for repairs or routine maintenance tasks). 12-month implementation timeframe.
Stationary Indoor Air Monitoring	Continuous stationary indoor monitoring at 10 ppb. Respirators for exceedances of 10 ppb. 2-year implementation timeframe.	**Revised.** Continuous stationary indoor air monitoring at 0.1 ppm (100 ppb) with monitoring results that are to be made visible to workers. 1-year implementation timeframe.
Training	Training to state risks at 1 in 17 for MLE and 1 in 10 for upper bound for EtO handlers (medical devices) and 1 in 36 for MLE and 1 in 16 for upper bound for EtO handlers	**Revised.** Training on the potential health effects from EtO exposure for workers in commercial sterilization facilities and healthcare facilities, including information on

Mitigation Measure	Proposed Mitigation in PID	Mitigation in ID
	(spices) in commercial sterilization facilities. 60-day implementation timeframe.	acute risks and chronic cancer risks. Immediate upon approved label.[157]
Recordkeeping	Recordkeeping for sterilization concentration rates on medical devices, indoor EtO concentrations and corresponding worker protection measures, and worker training. Implementation timeframe based on associated mitigation.	**Revised.** Recordkeeping that demonstrates adherence to the TWA occupational exposure limit and short-term exposure limit; readings from stationary continuous monitoring of room air; documents the method of initial treatment for food commodities as well as the need for reconditioning/retreatment with EtO; worker training; and adherence to the 600 mg/L limit on new sterilization cycles. Implementation timeframe based on associated mitigation.
Data Requirements	Worker exposure data for commercial sterilizers and warehouses (OSCPP GLN 875.1400 Inhalation Exposure Indoor) to quantify the effect of mitigation on worker exposure in commercial sterilization facilities and warehouses, using OSHA Method 1010 as the monitoring method. The PID stated EPA would collect data upon publication of the ID, and again after mitigation is put in place.	**Revised.** Worker exposure data for commercial sterilizers and warehouses (OSCPP GLN 875.1400 Inhalation Exposure Indoor) in order to understand the impacts of complying with EPA's CAA requirements and implementing FIFRA ID mitigation, and to better understand how the occupational exposure limit may be further lowered. Additionally, EPA is requiring a special study on fumigated commodities for medical devices to better understand exposure to EtO in warehouses.
	Data call-in to collect data on commercially available technologies that can monitor	**Revised.** Not included in ID. EPA acquired sufficient information through the public comment period

[157] EPA expects that registrants will submit label amendments within 60 days after the decision. The Agency would review such label amendments as expeditiously as feasible.

Mitigation Measure	Proposed Mitigation in PID	Mitigation in ID
	below 10 ppb in real time. 2-year compliance timeframe.	on available monitoring technologies.
Healthcare Facilities Engineering Controls	Physical separation of EtO sterilization spaces. 2-year implementation timeframe.	**Revised.** Not included in ID. Sterilization devices available for purchase by healthcare facilities include air pumps that maintain a negative pressure gradient, which prevents EtO from flowing from the device to the surrounding spaces.
	Negative air pressure. 2-year implementation timeframe.	**Revised.** Not included in ID. Sterilization devices available for purchase by healthcare facilities include air pumps that maintain a negative pressure gradient, which prevents EtO from flowing from the device to the surrounding spaces.
	Ventilation of EtO through exterior ventilation exhaust, located at least 7.6 meters (25 feet) away from the building air intake source and must be engineered according to existing codes. 2-year implementation timeframe.	**No change.** Ventilation of EtO through exterior ventilation exhaust, located at least 7.6 meters (25 feet) away from the building air intake source and must be engineered according to existing codes. 2-year implementation timeframe.
	EtO single chamber sterilization/aeration devices must utilize an abatement device in order to reduce EtO emissions. 2-year implementation timeframe.	**Revised.** EtO single chamber sterilization/aeration devices must utilize an abatement device in order to reduce EtO emissions. 2-year implementation timeframe. Healthcare facilities using a total of less than 10 lbs of EtO within the same building per year are exempted from the use of abatement devices. Recordkeeping is needed to demonstrate less than 10 lbs of EtO is used per year if the facility seeks an exemption.
Healthcare Facilities Training	Training to state risks at 1 in 25 for MLE and 1 in 12 for upper bound for EtO handlers. 60-day implementation timeframe.	**Revised.** Training on the potential health effects from the levels of EtO in the facility, including information on acute risks and chronic cancer

Mitigation Measure	Proposed Mitigation in PID	Mitigation in ID
		risks. 60-day implementation timeframe.

In order to reduce EtO exposure, EPA is implementing the hierarchy of controls, in the following order: elimination, substitution, engineering controls, administrative controls, and lastly personal protective equipment (PPE). Firstly, EPA is eliminating uses for which there are limited benefits. Secondly, EPA is driving industry to look for alternatives to EtO for food commodity fumigation by providing deadlines for the termination of its use where alternatives are possible. Next, EPA has identified necessary label changes to require facilities to reach an occupational exposure limit lower than the current OSHA PEL. This may be accomplished through elimination or substitution, or to the extent feasible engineering controls and/or administrative controls. Finally, where it is not feasible to meet the exposure limits through elimination, substitution, engineering or administrative controls, the use of PPE would be required in situations where the lowered occupational exposure limits are exceeded. EPA has also identified necessary label changes requiring the use of PPE for certain high exposure tasks.

Termination of Uses

EPA has identified as necessary the termination of the following EtO uses:

- Museum materials
- Library materials
- Archival materials
- Cosmetics
- Musical instruments
- Beekeeping equipment

<u>Use of EtO by Commercial Sterilization Facilities for Museum, Library, and Archival Materials, Cosmetics, and Musical Instruments</u>

EtO is registered for use to treat museum, library, and archival materials, as well as cosmetics and musical instruments, in commercial sterilization facilities. For occupational handlers at commercial sterilization facilities, cancer risk estimates are estimated from 4×10^{-2} (1 in 25 workers) to 1×10^{-1} (1 in 10 workers). Cancer risks of concern are also anticipated for occupational and non-residential and residential bystanders. Because there are viable EtO alternatives available for these uses, continued registration of EtO provides minimal benefits. Alternatives for the museum, library, and archival materials include freezing, anoxia (oxygen deprivation), and irradiation. EtO is no longer used for treatment of museum, library, or archival materials due to concerns over human health risks associated with off-gassing from treated

materials.[158] Gamma irradiation is a viable alternative for cosmetics and EtO is likely no longer used in the cosmetics industry. For the musical instrument uses, other disinfectant products are available for use that are more practical. These products are low cost and easily accessible as compared to EtO sterilization in commercial sterilization facilities. Therefore, EPA has identified that it is necessary for these uses to be terminated.

There is low to no impact expected as a result of the termination of these uses because viable alternative sterilization methods are available and already in use. For more information on the alternatives to EtO and impacts of termination of these uses, see *Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation* in this docket. EPA did not receive any requests that these uses be retained during the PID public comment period.

Beekeeping Equipment (in NC only)

EtO is approved for the treatment of beekeeping equipment in North Carolina under FIFRA section 24(c) SLN registration NC140003. EtO is used for the sterilization of beekeeping equipment to control American foulbrood (AFB) disease in the state. The North Carolina Department of Agriculture and Consumer Services (NCDACS) currently operates one treatment chamber in the Raleigh, NC area for this purpose. There is the potential for non-occupational bystander exposure for people who live near the treatment chamber (residential non-occupational bystanders) or who spend significant time in the area for non-work-related activities (e.g., school, daycare, shopping) (non-residential non-occupational bystanders).

The distances from the fumigation chamber at which the cancer risk estimates are less than 1 x 10^{-6} increase from 10 meters to 300 meters or more depending on the percentile considered (e.g., 75th and 90th respectively). A specific percentile has not been selected (and correspondingly a buffer distance from the fumigation chamber has not been established) since the Agency has identified that it is necessary for the use of EtO on beekeeping equipment in North Carolina to be terminated.

There also is the potential for occupational exposure for people who operate the treatment chamber in NC. Cancer risks range from 2 x 10^{-4} (1 in 5,000) when assuming 4 exposure days per year to 4 x 10^{-4} (1 in 2,500) when assuming 8 exposure days per year. These risk estimates also assume that self-contained breathing apparatus (SCBA) PPE is in use. These cancer risk estimates exceed the Agency target of 1 x 10^{-4} for occupational risks. For more information, see section III. A above and *Ethylene Oxide (EtO). Addendum to "Draft Human Health and Ecological*

[158] Email communication between Jessica Johnson, Head of Conservation, Museum Conservation Institute, Smithsonian Institution and Jessica Bailey, Antimicrobial Division, Office of Pesticide Program, Environmental Protection Agency. March 18, 2021.; Email communication between Lindsey Oakley, Director of Heritage Science Research and Testing, U.S. National Archives and Records Administration and Jessica Bailey, Antimicrobial Division, Office of Pesticide Program, Environmental Protection Agency. March 30, 2021.; Email communication between Hayes Robinson III, Associate Director, Environmental Management Division, Office of Safety, Health and Environmental Management at the Smithsonian Institution and Jessica Bailey, Antimicrobial Division, Office of Pesticide Program, Environmental Protection Agency. March 18, 2021.

Risk Assessment in Support of Registration Review" - Inhalation Exposure Risk Assessment in Support of Registration Review in this docket.

Beekeepers have several chemical and non-chemical alternatives to EtO for preventing and disinfecting beekeeping equipment of AFB. Chemical control alternatives include antibiotics such as terramycin, tylan (tylosin), or lincomix soluble powder. Non-chemical control tactics include cultural and mechanical/physical controls. Examples of cultural controls include practices such as purchasing several new frames for hives each year, sanitizing hands with alcohol-based hand sanitizer and wearing non-leather gloves when working with a hive, sanitizing equipment/tools with isopropyl alcohol, irradiation, or autoclave prior to working with a hive and/or between seasons, and hive placement. Examples of mechanical controls include fire scorching small equipment with a blowtorch followed by a bleach spray, or the burning or destruction of infected colonies and equipment. Beekeepers can also sanitize infected equipment including frames by boiling infected materials in sodium hydroxide (lye), although this may involve culling the hive if the equipment is in use.

Given that the risk estimates for this use assume the use of the highest level of respiratory protection (SCBA) and, nonetheless, exceed the Agency target of 1×10^{-4} for occupational risks, and that there are alternative control methods for AFB in place in the other states that are feasible in North Carolina, the Agency stated in the PID that the benefits of the use do not outweigh the risk. Therefore, the Agency determined that it is necessary for this use to be terminated.

There is low to no impact expected from the termination of the use to sterilize beekeeping equipment in North Carolina (the only state with this registered use). There are alternative chemical, cultural, and mechanical controls available to manage AFB, a contagious disease that affects honey bees. For more information on the impacts of the cancellation of this use, see *Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation* in this docket.

In the PID public comment period, EPA received three comments on the proposed cancellation of the use of EtO on beekeeping equipment in North Carolina which are discussed in further detail in Appendix E. The 11 Attorneys General and the Environmental Protection Network (EPN) concurred with terminating the use of EtO on beekeeping equipment.[159] USDA commented that even though alternatives to EtO are promoted in North Carolina, cases of AFB still exist. USDA also commented that other states' management of AFB without EtO does not mean that EtO does not provide benefits in North Carolina. USDA further commented that there is the potential that the occupational exposure is overestimated in the Agency's risk assessment and asked if EPA would be willing to assess the occupational and bystander risks using additional monitoring data or if EPA would be willing to allow beekeeping equipment to be a labeled use on current products if risks can be mitigated. The Agency maintains that there are chemical, cultural, and mechanical controls available to manage AFB and does not believe

[159] EPA-HQ-OPP-2013-0244-0106, EPA-HQ-OPP-2013-0244-0142 at www.regulations.gov.

that the benefits of this use outweigh the estimated risks. Therefore, the Agency has not changed its decision regarding the cancellation.

Voluntary Use Cancellations

EPA has determined it is necessary for the registrants to submit requests to voluntarily terminate the uses of EtO for museum materials, library materials, archival materials, cosmetics, musical instruments, and beekeeping equipment (in accordance with FIFRA section 6(f)) and to submit amended labels to remove these uses, as soon as practicable but no later than 60 days from the publication of the ID.

Regarding the process outlined in FIFRA section 6(f), the registrant would submit a letter to EPA requesting voluntary cancellation of the product use(s). After receipt of the letter, EPA will publish a notice in the Federal Register with a comment period of at least 30 days. At the conclusion of the comment period, unless there are substantive comments or the registrant rescinds the cancellation request, EPA publishes the final cancellation order and, for products with retained uses, approves the revised label. If the Agency has received substantive comments, EPA may modify or reconsider the cancellation as appropriate.

Food Commodities

In the PID, the Agency requested public comment on specific commodities for which use of EtO is critical for food safety and there are no viable alternatives. The Agency also indicated that any commodities without documented support for continued treatment with EtO will be considered for a phased-out cancellation to reduce exposure to workers and bystanders.

Public comments were received on the PID that requested the Agency prohibit the use of EtO on spices similar to the European Union (EU). To inform the EtO ID, the Agency discussed the control of pathogens on dried herbs and spices in the European Union with the European Commission Directorate-General for Health & Food Safety[160] and also contacted the European Spice Association (ESA). EPA confirmed that EtO is not used in the EU and learned about the alternative treatment methods in place there. Spices imported into the EU cannot have a level of EtO that exceeds the EU maximum residue level (MRL).[161] The Agency also learned about differences between the EU and the U.S. with respect to assessing the risk of EtO and regulations affecting the use of EtO. U.S. companies must comply with FDA's Food Safety Modernization Act (FSMA) and the regulations supporting FSMA. This includes the requirements for hazard analysis and preventive controls in the Current Good Manufacturing

[160] EPA-HQ-OPP-2013-0244-0418 at www.regulations.gov.

[161] "Ethylene oxide may not be used for sterilising purposes in food additives. No residue above 0,1 mg/kg, irrespective of its origin, of ethylene oxide (sum of ethylene oxide and 2-chloro-ethanol expressed as ethylene oxide (ethylene oxide + 0,55* 2-chloroethanol) shall be present in food additives listed in Annexes II and III to Regulation (EC) No 1333/2008, including mixtures of food additives." at https://eur-lex.europa.eu/eli/reg/2022/1396. Accessed December 5, 2024.

Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food (PCHF) regulation in 21 C.F.R. part 117 which requires companies that use a certain process for pathogen reduction as a preventive control to validate the process to ensure it is adequate for controlling the identified hazards (21 C.F.R. 117.160(a)).[162] Transitioning to EtO alternatives will require the development of validations for the alternatives to comply with FSMA.[163] This transition often takes seven to ten years.[164, 165] See Appendix E for detailed information on the comments and EPA's response.

Public comments did not identify several commodities for which EtO treatment is currently allowed (see Table 2) as commodities for which EtO use is considered to be critical for food safety. EPA has determined it is necessary for these uses to be cancelled and for the registrants to submit requests to voluntarily cancel the use of EtO on those commodities as soon as practicable, but no later than 60 days from the publication of the ID. The commodities are angelica, borage, burnet, catnip, costmary, culantro leaf, culantro seed, curry leaf, licorice roots, lovage leaf, lovage seed, marigold, nasturtium, pennyroyal, rue, tansy, wintergreen, woodruff and wormwood.

Public comments were submitted for other commodities indicating that EtO use remains critical for food safety and that currently no viable alternatives exist.[166] Comments provide details on various alternatives to EtO and the constraints of each for these specific commodities. The Agency has considered the comments submitted and determined a phased cancellation is appropriate for many of the specific commodities identified as needing EtO treatment for food safety but that may have potential alternative treatments. EPA acknowledges that industry will need time to select an alternative treatment method, develop validations to comply with FSMA, and scale the method for industrial use. In light of the steps that facilities must take before transitioning to an alternative treatment method, the Agency has determined at this time that it is appropriate to retain the use of EtO for the following commodities for seven years (until January 1, 2032): allspice, anise seed, anise star, annatto seed, balm, chamomile (German and

[162] *Ethylene Oxide (EtO) Spice Sterilizing Facilities*. Center for Food Safety and Applied Nutrition (CFSAN), Food and Drug Administration (FDA) responses to questions from Office of Pesticide Programs (OPP), Environmental Protection Agency (EPA). December 20, 2022.

[163] If the parameters for which a food commodity/product was validated are the same, then one facility could potentially treat another facility's food commodity/product; however, if the parameters are not the same, a new validation would be required. (ASTA. 2024. Email from Laura Shumow, Executive Director, ASTA, to Susan Bartow, Pesticide Re-Evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. November 26, 2024. and FDA-HFP. 2024. Email from FDA-HFP to Susan Bartow, Pesticide Re-Evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. December 2, 2024). Further, industry has indicated that currently there is not enough capacity for companies using alternative (non-EtO) treatment methods to treat all of the product currently being treated with EtO (ASTA. 2024. Email from Laura Shumow, Executive Director, ASTA, to Susan Bartow, Pesticide Re-Evaluation Division, Office of Pesticide Programs, Environmental Protection Agency. November 26, 2024).

[164] EPA-HQ-OPP-2013-0244-0412, EPA-HQ-OPP-2013-0244-0420, EPA-HQ-OPP-2013-0244-0422 at www.regulations.gov.

[165] EPA-HQ-OPP-2013-0244-0432 at www.regulations.gov.

[166] EPA-HQ-OPP-2013-0244-0130, EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.

Hungarian), caper buds, caraway, black caraway, cardamom, cassia bark and buds, celery seed, dried chervil, Chinese chive, chive, cinnamon, clary, clove buds, coriander leaf, coriander seed, cumin, dill seed, dillweed, common fennel, Florence fennel seed, fenugreek, grains of paradise, horehound, hyssop, juniper berry, lavender, lemongrass, mace, marjoram (*Origanum* spp.), mustard seed, nutmeg, dried parsley, black pepper (and pink peppercorns), white pepper, poppy seed, rosemary, saffron, sage, savory (summer and winter), sweet bay, tarragon, thyme, vanilla, and black walnuts.

EtO is an important option for the reconditioning of dried herbs, dried spices, and dried vegetables that have been detained for the presence of human pathogens at the borders of the U.S. EtO is also the primary tool for retreatment of dried herbs, dried spices, and dried vegetables contaminated during processing. Alternatives to EtO are generally either incompatible with packaging materials (e.g., PPO, steam), cannot be used if the commodities are in the ground form (e.g., steam), and/or can result in dried herbs, dried spices, and dried vegetables that are unmarketable to the public (e.g., irradiation, steam). Firms are required to comply with the adulteration provisions of the FD&C Act and applicable FSMA rules including the Current Good Manufacturing Practice, Hazard Analysis and Risk-Based Preventive Controls for Human Food rule (21 C.F.R. part 117, CGMP & PC rule), which requires certain domestic and foreign facilities to establish and implement hazard analysis and risk-based preventive controls for human food. As a result, if herbs/spices are contaminated and cannot be retreated, the batch will likely be destroyed. Given the importance of EtO for reconditioning and retreatment and the limited amount of reconditioning and retreatment that occurs, the Agency has determined that it is necessary to restrict EtO to use as a treatment method for FDA-approved reconditioning proposals and retreatment for human pathogens when a primary EtO-alternative treatment fails for the following commodities after January 1, 2032: allspice, anise seed, anise star, annatto seed, balm, chamomile (German and Hungarian), caper buds, caraway, black caraway, cardamom, cassia bark and buds, celery seed, dried chervil, Chinese chive, chive, cinnamon, clary, clove buds, coriander leaf, coriander seed, cumin, dill seed, dillweed, common fennel, Florence fennel seed, fenugreek, grains of paradise, horehound, hyssop, juniper berry, lavender, lemongrass, mace, marjoram (*Origanum* spp.), mustard seed, nutmeg, dried parsley, black pepper (and pink peppercorns), white pepper, poppy seed, rosemary, saffron, sage, savory (summer and winter), sweet bay, tarragon, thyme, vanilla, and black walnuts. New recordkeeping measures will apply to the reconditioning/retreatment use; to comply with the EtO label, the facility will need documentation (e.g., correspondence documenting FDA-approval of reconditioning) that indicates the method of initial treatment for the food commodities as well as the need for reconditioning/retreatment with EtO.

Public comments were submitted for certain dried herbs, dried spices, and dried vegetables that indicate the potential alternatives are extremely limited at this time.[167, 168] These commodities are dried peppermint tops, sesame seed, dried spearmint tops and dried

[167] PPO tolerances do not exist for these commodities. Establishing tolerances and adding new uses to PPO product registrations will take time to complete in addition to the time necessary to develop validations.
[168] EPA-HQ-OPP-2013-0244-0128 and EPA-HQ-OPP-2013-0244-0130 at www.regulations.gov.

vegetables. For those commodities, the Agency has determined that a phased cancellation is not practicable at this time. EPA will re-evaluate the continued need for EtO treatment on these commodities in the next round of registration review or sooner.

In the PID, the Agency indicated that tolerances for those dried herbs and spices for which uses are cancelled would be proposed to be revoked in a separate process. Based on the public comments received explaining the need to retain the tolerances for global trade,[169, 170] EPA is no longer planning to proceed with revoking the tolerances for any food commodities at this time. See Appendix E for detailed information on the comments and EPA's response.

EtO Use Rate Reduction

Medical Devices

An EtO sterilization cycle is defined as "treatment in a sealed chamber, which includes air removal, conditioning (if used), injection of ethylene oxide, inert gas (if used), exposure to ethylene oxide, removal of ethylene oxide and flushing (if used), and air/inert gas admission." (See: International Standard ISO 11135. Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation, and routing control of a sterilization process for medical devices. 2014). A sterilization calculation includes validated parameters such as pressure, concentration, temperature, humidity, and exposure time. Assessment of a company's cycle validation data by FDA includes specifications for products, load configuration, packaging, and sterility assurance level.

Based on discussions with industry, it is EPA's understanding that many sterilization facilities sterilize medical devices using much higher concentrations of EtO than what may be required for achieving the target sterility assurance level – specifically, the Agency has been informed that double the necessary concentration is used on some devices. Furthermore, it is the Agency's understanding, through discussions with industry, that the current EtO concentration may be as high as 700 mg/L for medical device sterilization. The increased application rate is related to the way in which facilities sterilize large quantities of mixed devices in order to meet demand, as the devices in these mixed loads will have varying EtO exposure requirements. For example, if a few devices in a large mixed load require 700 mg/L, then all of the devices will be sterilized at that rate, even those that may need less EtO to ensure sterility. Surgical kits are an example, which are pre-packaged in order to be quickly sent to operating rooms and contain a variety of devices which may require differing levels of EtO for sterilization. Batching devices in mixed loads also helps to reduce the total number of EtO cycles run, potentially reducing overall EtO usage. If a lower EtO concentration were used, an increased frequency of running

[169] EPA-HQ-OPP-2013-0244-0128, EPA-HQ-OPP-2013-0244-0130, EPA-HQ-OPP-2013-0244-0133, EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[170] Letter from Brian Hammons, President, Hammons Products Company to Jessica Bailey, Antimicrobials Division, Office of Pesticide Programs, Environmental Protection Agency. August 21, 2023.

EtO cycles may be needed to meet device demand and could result in the need for additional chambers, staff, and possibly more EtO being used overall.

In the PID, EPA sought public comment on the feasibility of a EtO concentration limit of 500 mg/L, with a 5-year implementation timeframe for existing cycles and a 2-year implementation timeframe for new cycles. EPA also sought public comment on alternative EtO concentration limits. For existing cycles in particular, commenters stated that given the thousands of cycles that currently are in place, it would take decades for validation and FDA review. Commenters further stated that any requirement to create a new validation for existing cycles would result in adverse impacts on the medical device supply chain and access to patient care. During the PID public comment period, EPA was informed that the proposed 500 mg/L concentration limit may not achieve appropriate assurance of sterility for many devices, but that a limit of 600 mg/L would be obtainable for a greater number of products. EPA was further informed that 10 years would be needed to make these changes for new cycles because designing a cycle can take up to 18 months, validation can take six months, submission to and approval by FDA can take two years, and approvals by regulatory bodies in other countries where the product will be sold can take up to five years.[171] For details on these comments and the Agency's response, please see Appendix E. Taking into account public comments received from the medical device sterilization industry, and subsequent engagement with FDA, EPA is not adopting the PID's proposal to limit EtO concentrations to 500 mg/L for new and existing cycles, or the proposed timelines of 2 years for new cycles and 5 years for existing cycles.

Thus, rather than the proposed 500 mg/L concentration limit for new cycles within two years, EPA has instead identified a 600 mg/L concentration limit for new cycles only, with a 10-year implementation timeframe. A new cycle is defined as a newly validated cycle specification that is not in use by any device regulated by the FDA as of January 1, 2035. Existing cycles that have previous FDA approval above 600 mg/L concentration and are in use before January 1, 2035, will continue to be permitted. The concentration rate limit is applicable to all settings where EtO is applied for medical device sterilization, including commercial sterilization facilities and healthcare facilities.

Food Commodities

ISO standard 11135 described above does not apply to food commodity treatments and there are no other ISO standards in place for treatments of food commodities as there are for sterilization of medical devices. The treatment process for food commodities is currently specified on the FIFRA product labels as follows:

> "This product may not be used on or in any form of basil.

[171] EPA-HQ-OPP-2013-0244-0141, EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.

> After August 1, 2008, this product may only be applied to or on spices, dried vegetables or seasonings utilizing an EtO sterilization method that uses a single sterilization chamber to precondition and aerate with an alternating vacuum and aeration purging procedure. If you wish to employ an alternative method to that described below, you must contact the Environmental Protection Agency Office of Pesticide Programs for instruction on how to receive authorization.
>
> Place spices in the treatment chamber. Assure that the mixture of ethylene oxide and air is compatible with the chamber design, then, introduce into the chamber a concentration of Ethylene Oxide not to exceed 500 mg/L, with a dwell time not to exceed 6 hours. Then evacuate the gas from the chamber using a sequence of not less than 21 steam washes (injections and evacuations) between 1.5 PSIA (27" Hg) and 5.0 PSIA (20" Hg) while maintaining a minimum chamber temperature of 115°F."

In the PID, the Agency discussed an interest in establishing an alternative method for EtO fumigations at a lower rate than 500 mg/L that is effective for pathogen control and continues to meet the dietary safety standards. ASTA provided comments indicating that it is possible and efficacious to treat spices at levels lower than the 500 mg/L limit currently permitted. However, they noted that many companies have validated their current treatment operations at 500 mg/L and a reduction in the concentration limit of EtO would require new validations to be established for the lower rate.[172] The Environmental Protection Network also commented on establishing a lower rate and recommended that the Agency propose a two-year timeframe for establishing a new maximum application rate.

Taking into account the comments received and the phased cancellation outlined in this ID that will require new validations to be established for the alternative treatment methods, EPA is not pursuing a lower EtO rate at this time. The Agency is prioritizing the shift to alternatives and the establishment of validations for those methods over developing validations for EtO at lower application rates. Establishing a lower rate will be revisited at the next round of registration review or sooner for any spices/commodities with continued EtO use.

Mitigation for Residential Bystander Risk

Bystander exposures around commercial sterilization facilities are considered "residential" if the exposures occur where people live (i.e., their homes).

In addition to the registration review of EtO as a pesticide under FIFRA, the Agency also conducts a periodic review of air emission standards for air pollutants, including EtO, through the National Emission Standards for Hazardous Air Pollutants (NESHAP) under the Clean Air Act (CAA). On April 5, 2024, EPA's Office of Air and Radiation (OAR) published their final rule for EtO commercial sterilizers, *National Emission Standards for Hazardous Air Pollutants (NESHAP):*

[172] EPA-HQ-OPP-2013-0244-0130 and EPA-HQ-OPP-2013-0244-0432 at www.regulations.gov.

Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review.[173] OAR revised the NESHAP for commercial sterilization facilities by both amending existing standards and establishing additional standards for this source category, exercising authority under multiple provisions of section 112 of the Clean Air Act (CAA). In the risk assessment for this rulemaking, OAR relied upon the cancer risk value from the EPA's 2016 EtO IRIS assessment, which indicated that EtO is a far more potent carcinogen than EPA had understood at the time of the previous risk and technology review for this source category. There are 93 commercial sterilization facilities in this source category, many of which are located near residences, schools, and other public facilities. Many of these facilities are also located in communities with environmental justice concerns. OAR had determined that without the mitigation measures included in the final NESHAP, approximately 23 of these facilities pose elevated lifetime cancer risks to the surrounding communities, some of which are exceptionally high.

Through the final NESHAP rule, OAR is requiring mitigation to reduce EtO emissions from commercial sterilizers to residential populations.[174, 175] Specifically, OAR is requiring that emission sources in existing and new facilities reduce emissions by a certain percentage depending on the emission source and EtO usage per year.[176, 177]

While the OAR and OPP proposals are based on different statutory authorities and mandates, they complement each other in their shared objective of reducing exposure to EtO. At this time, OPP has not identified mitigation measures additional to OAR's required mitigation to address residential bystander risks from inhalation exposure to EtO because emissions reductions are expected to result from action required to be taken by OAR under the authority of the Clean Air Act. The emissions limits required by OAR will significantly reduce residential and non-residential bystander exposure without causing adverse impacts to the U.S. supply of sterilized medical devices needed for a variety of medical procedures. The phased cancellation of food commodities outlined in this ID will reduce residential bystander risk as well.

Implementation of mitigation measures associated with both Agency actions, including this OPP ID and the OAR rulemaking, will impose costs on commercial sterilization facilities. While the mitigation measures set forth in each Agency action may be complementary in that they both reduce public health risks from EtO exposure, the costs to commercial sterilization facilities to

[173] EPA-HQ-OAR-2019-0178-1482 at www.regulations.gov.
[174] The Rulemaking from OAR is based on risk to residential areas only. OPP's analysis and mitigation includes residential, non-residential, and worker exposure.
[175] At the time of OAR's assessment on commercial sterilizers, 23 out of 85 facilities were identified that exceeded a 100 in 1 million risk threshold. See Appendix F.
[176] Emission sources in sterilization facilities include: sterilization chamber vents, aeration room vents, chamber exhaust vents, Group 1 room air emissions (emissions from indoor EtO storage, EtO dispensing, vacuum pump operations, and pre-aeration handling of sterilized material), and Group 2 room air emissions (emissions from post-aeration handling of sterilized material).
[177] Note that existing Group 2 room air emissions for facilities using less than 4 tons per year are only required to implement a management practice to reduce emissions.

implement both Agency actions are additive in some respects. The *Regulatory Impact Analysis for the Required National Emission Standards for Hazardous Air Pollutants: Ethylene Oxide Commercial Sterilization and Fumigation Operations* provides estimates of the cost to industry to comply with the required OAR rule.[178] In the OPP analysis titled *Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation*, the Agency concluded that EtO remains critical for certain uses based on the assessment of impacts if EPA were to cancel uses of EtO. As it is not obligated, OPP did not conduct a quantitative cost analysis for the mitigation measures included in this ID but qualitatively considered how various measures could impede the use of EtO and the impacts on industry.[179] During the PID public comment period, EPA received two public comments with cost information for the proposed mitigation in the PID from the Medical Device Manufacturers Association (MDMA) and AdvaMed, both of whom represent industry.[180] For details on these comments and the Agency's response, please see Appendix E.

Mitigation for Non-Residential Bystander Risk

Bystander exposures around commercial sterilization facilities are considered "non-residential" if the exposures occur at locations other than homes where people may spend a significant amount of time (i.e., daycare centers, schools).

Emissions controls required by OAR to address risks from residential exposure to EtO will also reduce exposure to non-residential bystanders. See *Mitigation for Residential Bystander Risk* above. In addition, the phased cancellation of food commodities outlined in this ID will reduce non-residential bystander risk.

Mitigation for Occupational Risk

Engineering Controls for Commercial Sterilization Facilities

According to OSHA's hazard prevention principles, the first and best strategy is to control the hazard at its source. Engineering controls do this, unlike other controls that generally focus on

[178] EPA-HQ-OAR-2019-0178-1557 at www.regulations.gov.

[179] There is no statutory requirement to quantify costs of mitigation measures under FIFRA's risk-benefit standard. See 40 C.F.R. § 155.40(a); 7 U.S.C. § 136a(c)(5); see also 7 U.S.C. §§ 136(bb), which define "unreasonable adverse effects on the environment" as encompassing both "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide" (FIFRA's risk-benefit standard), and "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the [FFDCA safety standard]". While FIFRA requires EPA to evaluate the economic, social, and environmental costs and benefits of the use of any pesticide," the statute provides discretion to figure out how to describe, evaluate, and weigh those factors. Consistent with other EPA and federal government guidance, OPP does not view this evaluation of risks and benefits as requiring a quantitative comparison. EPA guidance advises that "if important costs or benefits categories cannot be expressed quantitatively, they should be discussed qualitatively."

[180] EPA-HQ-OPP-2013-0244-0097, EPA-HQ-OPP-2013-0244-0092 at www.regulations.gov.

reducing exposures to the worker exposed to the hazard, such as the use of PPE. Under these principles, the work environment, and the job itself should be designed to eliminate hazards or reduce exposure to hazards.[181] The National Institute for Occupational Safety and Health (NIOSH) states that well-designed engineering controls can be highly effective in protecting workers.

Separation of HVAC Systems

To reduce exposure to EtO at commercial sterilization facilities, EPA has identified as necessary label changes requiring the separation of office and sterilization area heating, ventilation, and air conditioning (HVAC) systems. Specifically, EtO processing areas must have separate HVAC systems from non-processing areas, such as office space and control rooms. Based on comments received during the public comment period about delays in the delivery of needed equipment and materials and regular shortages of trained personnel to install equipment, this measure must be in place 3 years from the publication date of the ID, which is a 1-year extension from the proposed 2 years in the PID.[182] For details on these comments and the Agency's response, please see Appendix E.

Other Engineering Controls

Taking into account public comments received from the medical device sterilization industry and the spice industry, and subsequent engagement with FDA (see *Interagency Considerations* section), EPA is not adopting the PID's proposal for air pressure gradients, ventilation of storage areas, covered conveyors, and all-in-one sterilization systems for medical device sterilization in commercial sterilization facilities.

In the PID, EPA requested public comment on the costs and feasibility of the proposed engineering controls, including public comments on the impact of these engineering controls on the medical device supply chain, as well as public comment on the availability of other methods and controls to reduce worker exposure to EtO. Commenters on the PID asserted that if the engineering controls were to be adopted as proposed in the PID, this would cause a severe disruption to the medical device supply chain and impair the healthcare system as a whole. Commenters stated that almost all the proposed measures were too costly, not logistically feasible, and not able to be implemented within the proposed implementation timeframes. Of note, commenters stated that some of the proposed engineering controls would require a new validation and subsequent FDA review, which would not be feasible given the need to conduct research and perform the validations. For details on these comments and the Agency's response, please see Appendix E. EPA confirmed with FDA that certain proposed engineering

[181]https://www.osha.gov/sites/default/files/Hierarchy_of_Controls_02.01.23_form_508_2.pdf
[182] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.

and process controls would require new validations and subsequent FDA review, which may lead to impacts on the medical device supply chain.[183]

Based on the public comments received about the significant costs and infeasibility of the engineering control measures identified in the PID, and the impact of such measures on the medical device supply chain, EPA has decided to not include specific engineering controls in commercial sterilization facilities, except for the separation of HVAC systems, in this ID. Rather, facilities may choose which engineering and process controls to use in order to meet lowered occupational exposure limits as described below. This approach will allow facilities the flexibility to meet the demand for sterilized medical devices while reducing worker exposure.

In order to reach the lowered occupational exposure limits, there are a series of engineering and process controls available, including those proposed in the PID: concentration rate reduction for sterilizing medical devices, covered conveyor systems, and all-in-one processing systems. Additionally, industry has asserted there are other methods available to reduce worker exposure such as ensuring the highest level of negative pressure in the facility is either in the sterilization chamber or aeration space, automated (i.e., driverless) fork lifts, reducing the amount of EtO remaining in the chamber post-sterilization, improved back vents, chamber door cracking procedures, exhaust fans, changes to pallet packaging (i.e., avoid solid plastic wrap when possible), and faster transfer times of sterilized products.[184] Commercial sterilization facilities may implement any variety of these, or other, engineering and process controls in order to meet the lowered occupational exposure limits.

Lowered Occupational Exposure Limit for Commercial Sterilization Facilities

OSHA Permissible Exposure Limit (PEL)

As noted in Section IV.A., EtO product labels currently cite the OSHA PEL of 1 ppm 8-hour time-weighted average (TWA) exposure to trigger the requirement that workers wear a respirator. EPA understands that OSHA's EtO PEL has not been updated since it was established in 1984. Health standards issued under section 6(b)(5) of the OSH Act must reduce significant risk only to the extent that it is technologically and economically feasible, which may preclude OSHA from imposing exposure control requirements sufficient to ensure that a chemical no longer presents a significant risk to workers.[185]

Furthermore, since the publication of the RED in 2008, there have been considerable updates to the scientific database on EtO exposure and risk, including the 2016 IRIS assessment on EtO,

[183] See *EPA Office of Pesticide Programs (OPP) Meetings Regarding Ethylene Oxide (EtO) Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) July 2023 – August 2024* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0419.
[184] EPA-HQ-OPP-2013-0244-0408, EPA-HQ-OPP-2013-0244-0417, EPA-HQ-OPP-2013-0244-0423, EPA-HQ-OPP-2013-0244-0428 at www.regulations.gov.
[185] https://www.federalregister.gov/citation/49-FR-25734.

OPP's 2020 EtO Draft Risk Assessment (DRA), and 2023 EtO DRA Addendum. Therefore, EPA has concluded that the OSHA PEL of 1 ppm is no longer sufficiently protective and, consistent with FIFRA's mandate to ensure that the use of EtO will not cause unreasonable adverse effects, including effects to workers, EPA has determined it is necessary for registrants amend to their EtO label language regarding the OSHA PEL. Please see Appendix B for label language changes for the occupational exposure limits.

EtO PID's Proposed 10 ppb Limit

In the PID, EPA requested public comment on the feasibility of continuous, real-time monitoring to a 10-ppb level inside of commercial sterilization facilities and the impacts of such monitoring on the operations of commercial sterilization facilities. During the PID public comment period, EPA received considerable input that opposed the PID's proposed occupational exposure limit of 10 ppb. Commenters asserted that the limit should be an 8-hour time weighted average measured near the worker's breathing zone, not based on an instantaneous reading of room air emissions as proposed, citing that time weighted averages are the typical method for measuring worker exposure over the course of a workday. EOTF and EOSA stated that a time-weighted average value would allow for variations in concentration accounting for the working eight-hour average and is appropriate for chronic risks.[186] AdvaMed stated that location and temporal differences in concentrations require monitoring within the worker's breathing zone, as reflected by OSHA's regulations for exposure monitoring.[187] Commenters also provided alternative occupational exposure limits. For details on these comments and the Agency's response, please see Appendix E.

Supporting Evidence for 0.1 ppm Limit

EPA has several lines of evidence supporting that a 0.1 ppm occupational exposure limit is advisable and achievable under certain conditions. In the U.S., there is a recommended exposure limit (REL) from the National Institute for Occupational Safety & Health (NIOSH) set at 0.1 ppm.[188, 189] In Germany, 0.1 ppm is the workplace exposure concentration corresponding to the required preliminary acceptable cancer risk.[190, 191, 192] In order to inform the EtO ID, EPA

[186] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[187] EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.
[188] https://www.cdc.gov/niosh/npg/npgd0275.html.
[189] https://www.cdc.gov/niosh/npg/pgintrod.html.
[190] The MAK Collection for Occupational Health and Safety 2019, Vol 4, No 3. A. Hartwig, MAK Commission, DOI: 10.1002/3527600418.mb7521d0067.
[191] In Germany, 1 ppm is the workplace exposure concentration corresponding to the required tolerable cancer risk, while 0.1 ppm is the workplace exposure concentration corresponding to the required preliminary acceptable cancer risk. The German Committee on Hazardous Substances (Ausschuss für Gefahrstoffe, or AGS) sets risk-based limits for carcinogens based on social policy wherein there are "acceptable" and "tolerable" risks. For occupational lifetime cancer risks, acceptable risk in Germany is 4 in 100,000, which may be exceeded if specific measures are complied with; and tolerable risk is 4 in 1,000, which may not be exceeded.
[192] Occupational Limit Values (Arbeitsplatzgrenzwerte – AGW). https://ilv.ifa.dguv.de/limitvalues/27861

corresponded with the German Committee on Hazardous Substances on their worker exposure policies. Representatives confirmed that, in Germany, if worker monitoring shows that the 0.1 ppm acceptable concentration is exceeded, it is necessary to reduce the exposure, firstly by substitution, if technically feasible, secondly by state-of-the art technical measures (*i.e.*, engineering controls), thirdly by organizational measures (*i.e.*, administrative controls), and fourthly by providing personal protective equipment (similar to the concept of hierarchy of controls).[193] EPA notes that there may be differences in German workplace exposure scenarios compared to workplace exposure scenarios in the U.S.

In the PID, EPA noted that OSHA's EtO PEL has not been updated since it was established in 1984, and that the Agency does not consider the current OSHA PEL to be protective of workers. EPA therefore sought public comment on lower exposure limits that have been voluntarily implemented by commercial sterilization facilities to address worker exposure. During the public comment period, EPA received public comments on this topic, discussed in further detail in Appendix E. Additionally, after the closing of the EtO PID public comment period, EPA received a proposal to include lower occupational exposure limits on EtO labels from industry representatives from the Advanced Medical Technology Association (AdvaMed) on May 17, 2024. The proposal was published in the EtO public docket on May 29, 2024. In their proposal, AdvaMed supported the use of the 0.1 ppm NIOSH REL, and stated that using a phased approach, industry could reach a 0.1 ppm 8-hour time-weighted average occupational exposure limit within 10 years. AdvaMed cited some uncertainties regarding measurement capabilities and available technologies and stated that they are not aware of any AdvaMed member companies who are currently able to implement a 0.1 ppm occupational exposure limit at this time. However, AdvaMed stated their commitment to achieving the goal of reduced worker exposure and collaborating with EPA on this effort.[194, 195]

EPA Occupational Exposure Limit

A 0.1 ppm occupational exposure limit is supported by NIOSH, German occupational standards, and AdvaMed, an U.S. association which represents a large number of EtO sterilizers. Because of the risks identified to occupational handlers and bystanders from exposure to EtO in commercial sterilization facilities, EPA asserts that an occupational exposure limit of 0.1 ppm is necessary to address unreasonable adverse effects and has determined that it is achievable over time.

[193] Email correspondences between U.S. EPA Chemical Review Manager Jessica Bailey and Dr. Thomas A.J. Kuhlbusch, Section Head of the Hazardous Substances, Chemical Safety at the German Federal Institute of Occupational Safety and Health. January 30, 2024 – March 20, 2024.
[194] AdvaMed proposal can be found in the EtO public docket on www.regulations.gov under document ID EPA-HQ-OPP-2013-0244-0405.
[195] EPA received an alternative proposal from the industry groups Ethylene Oxide Sterilization Association (EOSA) and Ethylene Oxide Task Force (EOTF). However, the Agency decided the proposal from AdvaMed is more protective and achievable over time. See "Ethylene Oxide – EOTF and EOSA Proposal for the Interim Decision – June 26, 2024" in the EtO public docket at www.regulations.gov under document ID EPA-HQ-OPP-2013-0244-0406.

To reduce worker exposure, EPA has identified necessary label changes establishing lowered occupational exposure limits of 0.5 ppm (3-year implementation timeframe), 0.25 ppm (5-year implementation timeframe), and 0.1 ppm (10-year implementation timeframe) based on an 8-hour time weighted average. EtO labels will require that respirators must be worn by workers if these occupational exposure limits are exceeded. Additionally, EPA has determined it is necessary for EtO labels to include language requiring facilities to monitor exposures and follow all accompanying requirements outlined in OSHA Standard 29 C.F.R. § 1910.1047, which include a written compliance program and established regulated areas.[196]

At this time, EPA believes that these lowered occupational exposure limits can be achieved while minimizing disruptions to the medical device supply chain and to the availability of sterile medical devices needed for a wide range of medical treatments and procedures. This understanding is based on comments received from industry stakeholders.[197] However, in order to verify the occupational exposure limits in this ID are attainable, EPA will gather and assess annual worker exposure data.[198] EPA can change the implementation timing and target occupational exposure limit concentrations, if necessary, as demonstrated by data, prior to the 10 year deadline for the final implementation tier of the 0.1 ppm exposure limit. In order to make this determination, EPA will reevaluate the occupational exposure limit and any other needed mitigations, based on data, within 8 years. EtO product registrants will be subject to additional terms of registration which will require registrants to collect worker monitoring data from their customers (i.e., EtO commercial sterilization facilities) annually. As part of this condition of registration, if a customer does not provide worker monitoring data to the registrant, the registrant may no longer sell their EtO product to that customer. This data will be formally collected by EPA through a data call-in (DCI).

Additionally, EPA has identified necessary label changes to revise the current OSHA 5 ppm Short-Term Exposure Limit (STEL) duration of 15 minutes referenced on EtO labels to a 10-minute duration (10-year implementation timeframe). This short-term duration is supported by the recommendation from NIOSH.[199] Because of the risks identified to occupational handlers

[196] For information on monitoring frequency, see OSHA Technical Manual (OTM) Section II: Chapter 1; Personal Sampling for Air Contaminants and OSHA Field Safety and Health Management System (SHMS) Manual Chapter 27 Exposure Monitoring. For information on calculating the time-weighted average exposure, see OSHA Technical Manual (OTM) Section II: Chapter 1 Personal Sampling for Air Contaminants; 1910 Subpart Z Toxic and Hazardous Substances 1910.1000 Air Contaminants; and 1910 Subpart Z Toxic and Hazardous Substances 1910.1047 App D Sampling and Analytical Methods for Ethylene Oxide (Non-Mandatory).

[197] See, e.g. EPA-HQ-OPP-2013-0244-0405 at www.regulations.gov.; EPA-HQ-OPP-2013-0244-0147 (suggesting that EPA consider "a value of no less than 0.5 ppm eight-hour time weight average (TWA) with compliance required in two to three years or more" and "a value of no less than 0.25 ppm TWA with compliance required in five to ten years or more"); EPA-HQ-OPP-2013-0244-0141 (noting that EPA should "allow industry at least five years" for implementation of an exposure limit of 0.25 ppm and, in the interim, "implement a 0.5 ppm PEL within two to three years").

[198] See "Ethylene Oxide – EOTF and EOSA Proposal for the Interim Decision – June 26, 2024" in the EtO public docket at www.regulations.gov under document ID EPA-HQ-OPP-2013-0244-0406.

[199] See the CDC NIOSH Pocket Guide to Chemical Hazards Ethylene oxide NIOSH REL at https://www.cdc.gov/niosh/npg/npgd0275.html.

and bystanders from exposure to EtO in commercial sterilization facilities, EPA asserts that a short-term exposure limit of 5 ppm at a shortened duration of 10 minutes is necessary to address unreasonable adverse effects and has determined that it is achievable over time.

The Agency encourages use of a badge method using Gas Chromatography with Electron Capture Detector or the OSHA ID 1010 tube method for the collection of occupational exposure data using the time-weighted average in the personal breathing zone.[200, 201]

Per language on EtO labels, facilities will be required to maintain records of EtO worker exposure levels.

Quantified Risk Reduction at 0.1 ppm

Reducing the occupational exposure limit from the current OSHA Standard 29 C.F.R. § 1910.1047 permissible exposure limit (PEL) of 1 ppm to the EPA occupational exposure limit of 0.1 ppm would reduce exposure, as described in this Interim Decision, would reduce exposure by 10-fold. However, EPA notes that risk remains at a 0.1 ppm occupational exposure limit. EPA has nevertheless identified as necessary a 0.1 ppm occupational exposure limit, as this is the lowest level achievable at this time, given the limits to technology and concerns for the medical device supply chain. EPA will reevaluate the occupational exposure limit, based on data, within 8 years.

Lowered Action Level for Commercial Sterilization Facilities

The current OSHA Action Level for EtO is 0.5 ppm, based on an 8-hour time-weighted average.[202] To further inform worker exposure levels, EPA has determined it is necessary for EtO labels to include language establishing a lowered action level of 0.1 ppm based on an 8-hour time weighted average in commercial sterilization facilities, with an implementation timeline of one year. If a worker's exposure may be at or exceed this new action level, increased worker monitoring and medical surveillance, as well as training, are required by language on the EtO labels cross-referencing OSHA Standard 29 C.F.R. § 1910.1047.

Per language on EtO labels cross-referencing OSHA Standard 29 C.F.R. § 1910.1047, facilities will be required to maintain records of EtO monitoring.

[200] For example, 3M Badge Analytical Method: Modified ASTM D5578: Desorption in 90/10 toluene/acetonitrile. Ethylene oxide is adsorbed and converted to 2-Bromoethanol; analysis by Gas Chromatography with Electron Capture Detector (GC/ECD).
[201] For example, OSHA Method 1010 Procedure: Samples are collected by drawing workplace air through sampling tubes containing hydrobromic acid coated carbon beads using personal sampling pumps. Samples are extracted with a mixture of water and a 1:1 (v/v) solution of acetonitrile/toluene. Analysis is performed by gas chromatography using an electron capture detector (GC-ECD).
[202] See 29 C.F.R. § 1910.1047 for details and requirements of the Action Level.

Table 4. Summary of Worker Exposure Limit, Short Term Exposure Limit, and Action Level for EtO Commercial Sterilization Facilities

Description	Current OSHA Standard	New EPA Limit	Timeline
Exposure Limit (8-hr TWA)	1 ppm	0.5 ppm	3 years
		0.25 ppm	5 years
		0.1 ppm	10 years
Short Term Exposure Limit (STEL) 5 ppm	5 ppm (as 15-minute TWA)	5 ppm (as 10-minute TWA)	10 years
Action Level (8-hr TWA)	0.5 ppm	0.1 ppm	1 year

Personal Protective Equipment for Commercial Sterilization Facilities

New Respiratory PPE Mitigation for EtO Handlers: The Agency has identified as necessary the addition of a respirator statement to EtO product labels to mitigate potential inhalation exposure risks to workers involved in the EtO commercial sterilization process. Supplied air/airline (SAR) respirators or self-contained breathing apparatus (SCBA) respirators (full facepiece) are required for workers engaged in the following tasks:

- Connecting and disconnecting EtO containers from sterilization process equipment.
- Unloading processed products from the sterilization chamber, whether at the end of a cycle for an all-in-one process, or, for a conventional process, prior to moving product to the aeration area.
- Loading and unloading product from the aeration area.
- Removing validation test materials from processed product at any time prior to the completion of aeration.
- Opening process lines or equipment that may contain EtO (e.g., for repairs or routine maintenance tasks).

In addition to these task-based respirator requirements, EPA has determined it is necessary for EtO labels to include requirements for SAR or SCBA respirators for exceedances of the lowered occupational exposure limits and short-term exposure limits as explained previously.

Previous requirements to wear PPE on EtO product labels were triggered by the OSHA PEL of 1 ppm, which EPA has now determined is not protective based on the Agency's updated risk

analysis. Thus, EPA has determined that the previous requirements to wear respiratory PPE are not sufficient to ensure that the use of EtO will not cause unreasonable adverse effects to workers. The new respiratory mitigation to wear PPE is anticipated to reduce EtO exposure to workers involved with the EtO sterilization process at points when the potential for exposure is highest. The use of respirators is subject to requirements of OSHA's respiratory protection standard (29 C.F.R. § 1910.134), including the fit testing, training, and medical evaluation requirements.

EPA's 2023 DRA Addendum assumes National Institute for Occupational Safety and Health (NIOSH) protection factors in estimating the inhalation risks and the risk reduction associated with different respirators. If the respirator does not fit properly, EPA's PPE mitigation measures for EtO may not reduce exposure and thus the use of EtO may result in exposure and risks to the pesticide handler and others involved in the sterilization process that may need to wear a respirator.

During the PID public comment period, EPA received several comments regarding the use of respirators, including comments from the American Federation of Labor and Congress of Industrial Organizations (AFL-CIO) and the California Division of Occupational Safety and Health (Cal/OSHA).[203] Commenters stated that overuse of respirators has risks of its own to worker health and safety, including exertion, risks of snags, falls, and reduced visual ability. As stated earlier, EPA considers the implementation of the hierarchy of controls to be the best method for reducing worker exposure for EtO and as such is implementing a strategy, in the following order for elimination, substitution, engineering controls, administrative controls, and lastly personal protective equipment (PPE). Furthermore, EPA does not expect the mitigation measures included in this ID to result in constant respirator use, unlike what may have occurred based on the 10-ppb instantaneous reading occupational exposure limit proposed in the PID. For more details on these comments and the Agency's responses, please see Appendix E.

Requiring a respirator could impose a cost on handlers or employers. Per Agency discussions with industry leaders, use of the SCBA or SAR systems may already be standard industry practice for the performance of several of the tasks for which a SCBA or SAR system is required pursuant to the label language identified as necessary in this ID; therefore, the overall impacts from this requirement are expected to be low. However, use of a SCBA or SAR system may not be part of current practice for some of the tasks at some facilities, meaning that facilities would need to purchase additional SCBA or SAR systems. Prices for an industrial-use SCBA system range from $2,300 to $9,300 depending on the duration of air supply needed (30 or 60 minutes), cylinder pressure, tank material (typically aluminum or carbon fiber), and mask

[203] EPA-HQ-OPP-2013-0244-0114, EPA-HQ-OPP-2013-0244-0138 at www.regulations.gov.

size[204, 205, 206]. In addition to the original SCBA system purchase, replacement air cylinders range in price from $600 to $3,500[207, 208, 209] . Facilities may also opt to purchase on-site tank air cylinder fill stations to refill cylinders on site instead of purchasing additional replacements. Complete SAR systems range from $1,500 to $4,100 depending on hose length, air pump horsepower, and mask size[210, 211, 212]. SCBA or SAR systems can only be used by a single person that has been fit for the system, so these costs are per user. Facilities with multiple users would have to incur these costs for every individual they employ that may require the system. Additional costs may also arise from the maintenance of SCBA or SAR systems and necessary replacement parts. Applicators may also incur additional costs of training and fit testing as required under OSHA's respiratory protection standard. EPA received two public comments during the PID public comment period which contained cost information for the proposed respiratory PPE mitigation measures, from the Medical Device Manufacturers Association (MDMA) and AdvaMed.[213] For more details on these comments and the Agency's responses, please see Appendix E.

Data on Worker Exposure

In order to further quantify worker exposure in commercial sterilizers and warehouses, EPA will issue a data call-in for OSCPP GLN 875.1400 Inhalation Exposure Indoor to understand the impacts of complying with EPA's Clean Air Act (CAA) NESHAP for EtO commercial sterilizers and implementing mitigation measures identified in this ID issued under FIFRA, and to better understand how to further lower the occupational exposure limit. EPA will require a protocol before monitoring for the study begins. Based on previously submitted worker exposure data that lacked specificity and detail, EPA will require that the data include time-weighted average personal breathing zone (PBZ) monitoring of the handlers specifically involved in activities related to the sterilization/fumigation (e.g., loading and unloading chambers, routine

[204] AirGas. 2022. Respiratory Protection, https://www.airgas.com/Safety-Products/Respiratory-Protection/category/177. Accessed December 2022.
[205] Fisher Science. 2022. Atmosphere-Supplying Respirators. https://www.fishersci.com/us/en/browse/90411025/atmosphere-supplying-respirators. Accessed December 2022.
[206] Grainger. 2022. Respiratory Protection. https://www.grainger.com/category/safety/respiratory-protection. Accessed December 2022.
[207] AirGas. 2022. Respiratory Protection, https://www.airgas.com/Safety-Products/Respiratory-Protection/category/177. Accessed December 2022.
[208] Fisher Science. 2022. Atmosphere-Supplying Respirators. https://www.fishersci.com/us/en/browse/90411025/atmosphere-supplying-respirators. Accessed December 2022.
[209] Grainger. 2022. Respiratory Protection. https://www.grainger.com/category/safety/respiratory-protection. Accessed December 2022.
[210] AirGas. 2022. Respiratory Protection, https://www.airgas.com/Safety-Products/Respiratory-Protection/category/177. Accessed December 2022.
[211] Fisher Science. 2022. Atmosphere-Supplying Respirators. https://www.fishersci.com/us/en/browse/90411025/atmosphere-supplying-respirators. Accessed December 2022.
[212] Grainger. 2022. Respiratory Protection. https://www.grainger.com/category/safety/respiratory-protection. Accessed December 2022.
[213] EPA-HQ-OPP-2013-0244-0092, EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.

maintenance, product transfer, etc), documentation of the activities each worker performed while monitored, and whether they were wearing a respirator (and what type of respirator). For non-handlers in the facility (e.g., office workers, warehouse workers), EPA will also require the data include PBZ monitoring data to monitor their exposures. Data must also include whether or not the facility has complied with the NESHAP requirements.

In order to verify the occupational exposure limits in this ID are attainable, EPA will gather and assess annual worker exposure data.[214] Specifically, EPA has determined it is necessary to add a condition of registration that requires EtO registrants to collect worker monitoring data from their customers on an annual basis. Further, EtO registrants may not continue to sell EtO products to customers who do not provide worker monitoring data. EPA will collect this data through a DCI. EPA can change the implementation timing and target occupational exposure limit concentrations, if necessary, as demonstrated by data, prior to the 10-year deadline for the final implementation tier of the exposure limit of 0.1 ppm. In order to make this determination, EPA will reevaluate the occupational exposure limit and any other needed mitigations, based on data, within 8 years.

Additionally, EPA will issue a DCI for a special study for monitoring data on fumigated commodities for medical devices to better understand exposure to EtO in warehouses. Through these data, EPA is seeking information on the exposure scenario from emissions from treated medical device commodities and materials and the potential for occupational exposure due to those emissions in the channels of trade after sterilization activities are complete. The environments in which worker activities are monitored should also be evaluated which may include monitoring off-gassing properties of fumigated commodities over time. Data are required for occupational sites if the human activity data indicate that workers are likely to have post-application exposures while participating in typical activities. EPA will require a protocol before monitoring for the study begins.

Under FIFRA, if EPA determines that "additional data are required to maintain in effect an existing registration of a pesticide," the Agency may notify the pesticide registrants of the need for that data.[215] EPA data requirement regulations specifically envision the Agency requiring submission of data relating to post-application exposures.[216] Because EPA has identified significant hazards from EtO exposures, and the potential for exposure to workers in warehouses where commodities fumigated with EtO are stored, EPA has determined that it is necessary to call-in post-application exposure data. Specifically, for warehouses that are not co-located with sterilization facilities, there is a need for additional data because data from warehouses co-located with sterilization facilities may be skewed by emissions from the sterilization facilities themselves. The Agency has previously required registrants of propylene

[214] See "Ethylene Oxide – EOTF and EOSA Proposal for the Interim Decision – June 26, 2024" in the EtO public docket at www.regulations.gov under document ID EPA-HQ-OPP-2013-0244-0406.
[215] 7 U.S.C. § 136a(c)(2)(B)(i); see also 40 C.F.R. § 155.48 (providing that EPA may issue a data call-in "at any time if the Agency believes that the data are needed to conduct the registration review").
[216] See, e.g., 40 C.F.R. § 158.2270(d), (e).

oxide (PPO) to submit data allowing EPA to assess post-application exposure to fumigated commodities.[217] EPA has also considered data on post-application exposures during the registration review of the wood preservatives.[218]

Once these data become available, the Agency may promptly reevaluate this Interim Decision.

Stationary Continuous Monitoring in Commercial Sterilization Facilities

In the PID, EPA proposed indoor monitoring at 10 ppb and requested public comment on the feasibility of monitoring at this level and the impacts of this proposed monitoring on the operations of commercial sterilization facilities. The Agency received several comments regarding the feasibility of such a requirement. Due to considerations for the medical device supply chain related to costs to facilities, EPA has instead identified as necessary label language requiring continuous stationary indoor air monitoring using systems that can reliably measure to 0.1 ppm or lower. Facilities may choose which type of monitoring system to implement, so long as its measurement capabilities meet the monitoring threshold of 0.1 ppm or lower. For more information on public comments on available monitoring technologies and EPA's responses, please see Appendix E.

EPA has also identified as necessary label language requiring recordkeeping of indoor EtO levels by room/area throughout the facility, as described in the *Record Keeping* section of this ID.

Training in Commercial Sterilization Facilities

In the PID, EPA proposed training for persons who work in commercial sterilization facilities to state risks at 1 in 17 for MLE and 1 in 10 for upper bound for EtO handlers (medical devices) and 1 in 36 for MLE and 1 in 16 for upper bound for EtO handlers (spices) in commercial sterilization facilities. However, EPA asserts in this ID that training that includes information on the acute and chronic health effects from EtO exposure that aligns with information from OSHA is implementable and understandable by workers and would enable continuity with respect to how workers are provided information about risks associated with EtO. OSHA has identified EtO as a carcinogen that may cause leukemia and other cancers as a result of long term (chronic) exposure, and acute exposure (short term) to EtO may cause eye pain, sore throat, difficult breathing, blurred vision, dizziness, nausea, headache, convulsions, blisters, vomiting, coughing, spontaneous abortion, genetic damage, nerve damage, peripheral paralysis, muscle weakness, impaired thinking, and impaired memory.

Labels on EtO products registered by EPA require safety and awareness training for all workers in commercial sterilization facilities, including office staff. Information and training must be

[217] See Propylene Oxide (PPO) Interim Registration Review Decision Case Number 2560 at www.regulations.gov document ID EPA-HQ-OPP-2013-0156-0052.
[218] See Creosote Draft Risk Assessment (DRA) discussing post-application exposure to users installing treated wood (page 28) at www.regulations.gov document ID EPA-HQ-OPP-2014-0823-0014.

provided to all workers in the facility at the time of initial assignment and annually thereafter. The safety training must include, at a minimum, the following information:

- The most recent monitored ambient levels of EtO in the facility.[219]
- The potential health effects from the levels of EtO in the facility. Safety training materials must include the following verbiage: "EtO is a carcinogen that may cause leukemia and other cancers due to chronic exposure. Acute exposure to EtO may cause eye pain, sore throat, difficult breathing, blurred vision, dizziness, nausea, headache, convulsions, blisters, vomiting, coughing, spontaneous abortion, genetic damage, nerve damage, peripheral paralysis, muscle weakness, impaired thinking, and impaired memory."
- The emergency response plan and how to respond in an emergency.
- The availability of the Safety Data Sheet and other materials related to the health hazards of exposure to EtO.

As stated earlier, EtO labels will also require additional training if worker exposure may be at or exceed the Action Level. This requirement for additional training is consistent with OSHA's requirements in 29 C.F.R. § 1910.1047.

Recordkeeping for Commercial Sterilization Facilities

EPA has identified as necessary label language requiring recordkeeping of concentration rates that demonstrates adherence to the 600 mg/L limit on new sterilization cycles, worker personal breathing zone (PBZ) data that demonstrates adherence to the TWA occupational exposure limit and mitigation measures associated with exceedances of the action level, readings from stationary continuous monitoring of room air, and required worker training. EPA has also determined that it is necessary for EtO labels to include language directing facilities to continue recordkeeping practices which are described in the OSHA EtO Standard at 29 C.F.R. § 1910.1047.

Recordkeeping: Concentration Rates

EPA has determined that it is necessary for EtO labels to include language specifying that as of January 1, 2035, the EtO application rate for new cycles must be less than or equal to 600 mg/L unless a higher concentration rate is required to meet FDA sterility requirements. By January 1, 2035, facilities must also maintain records of concentration rates for new cycles per label language. If sterilization of a device requires more than 600 mg/L, due to the device design, facilities must additionally maintain records for a justification for the increased application rate. Records are required to be maintained for two years from the date of sterilization.

[219] The most recent monitored ambient levels would also be available to the workers by stationary continuous monitoring.

Recordkeeping: Worker PBZ Data (Adherence to Occupational Exposure Limit, EPA Short-Term Exposure Limit, and EPA Action Level)

To reduce worker exposure, EPA has determined it is necessary for EtO labels to be revised to include a more stringent occupational exposure limit, short-term exposure limit, and action level. Upon amendment of the EtO labels following the publication of this ID, records of PBZ monitoring data and the exposure results must be maintained to show adherence to the current exposure limit, short-term exposure limit, and mitigation measures associated with exceedances of the action level. Recordkeeping requirements, consistent with the requirements found in OSHA's EtO standard at 29 C.F.R. § 1910.1047(k)(2), remain for the new occupational exposure limit, short-term exposure limit, and action level. Records are required to be maintained according to 29 C.F.R. § 1910.1047(k)(2) from the date of monitoring. A record retention time of 30 years per § 1910.1047(k)(2) is needed because a facility may not conduct 8-hour time-weighted average worker exposure monitoring for extended periods of time absent an event triggering such monitoring, such as changes to the facility, as described in 29 C.F.R. § 1910.1047(d). Because exposure monitoring results dictate whether facilities must take additional steps to reduce worker exposure and what steps they must take—such as providing workers with PPE—it is necessary for facilities to maintain exposure monitoring records supporting the steps they did or did not take for as long as facilities may rely on such records.

Recordkeeping: Readings from Stationary Continuous Monitoring

EPA has identified as necessary label language requiring recordkeeping for readings of continuous stationary indoor air monitoring at 0.1 ppm by January 1, 2026. Records must show indoor EtO levels by room/area throughout the entire facility. Records are required to be maintained for two years from the date of monitoring.

Recordkeeping: Worker Training

EPA has identified as necessary label language requiring commercial sterilization facilities to maintain records on worker training. Specifically, recordkeeping should identify the training materials provided to workers upon assignment and annually thereafter, and the dates individual workers are trained. Records are required to be maintained for two years from the date of training, including if the trainee leaves the place of employment before two years.

Recordkeeping: Documentation of Food Commodity Sterilization

EPA has identified as necessary label language requiring commercial sterilization facilities to maintain records after January 1, 2032, for reconditioning and retreatment when a secondary treatment is necessary for human pathogen control for the following commodities: allspice, anise seed, anise star, annatto seed, balm, chamomile (German and Hungarian), caper buds, caraway, black caraway, cardamom, cassia bark and buds, celery seed, dried chervil, Chinese

chive, chive, cinnamon, clary, clove buds, coriander leaf, coriander seed, cumin, dill seed, dillweed, common fennel, Florence fennel seed, fenugreek, grains of paradise, horehound, hyssop, juniper berry, lavender, lemongrass, mace, marjoram (*Origanum* spp.), mustard seed, nutmeg, dried parsley, black pepper (and pink peppercorns), white pepper, poppy seed, rosemary, saffron, sage, savory (summer and winter), sweet bay, tarragon, thyme, vanilla, and black walnuts. Reconditioning may occur when identified in an FDA-approved reconditioning proposal. Retreatment may occur after an initial treatment with an alternative to EtO. Specifically, records must include the initial treatment method (i.e., EtO alternative treatment) and the necessity for reconditioning or retreatment with EtO. In certain situations, an initial treatment may have been made with EtO (e.g., prior to import into the U.S.), and then the commodity is re-contaminated with human pathogens. Reconditioning may also occur in those situations and records must include the initial treatment method and the necessity for reconditioning with EtO. Records would be required to be maintained for two years from the time of reconditioning or retreatment.

Mitigation for Healthcare Facilities

Healthcare facilities such as hospitals, dental offices and veterinary facilities are expected to use significantly smaller volumes of EtO than commercial sterilization facilities. Exposure scenarios in healthcare facility settings differ significantly from commercial sterilization exposure scenarios because in health care facilities, EtO sterilization is intermittent, and devices are typically used soon after sterilization (i.e., not stored for shipping). As of the 2008 RED, sterilization is required to be performed in all-in-one systems. However, given the low concentration at which EtO may present inhalation cancer risks of concern, at this time EPA believes additional risk mitigation measures are needed.

Healthcare Facilities: Engineering Controls

To reduce exposure to EtO in and around healthcare facilities, EPA has identified label changes requiring implementation of the following engineering controls.

Ventilation of EtO through exterior ventilation exhaust

EPA has identified necessary label changes requiring that all exhaust from all-in-one EtO healthcare facility sterilization devices be directed through exterior ventilation exhaust. This will ensure that there is minimal EtO exposure for workers and bystanders within healthcare facilities. EtO exhaust must be vented to a dedicated exhaust ventilation system composed of local exhaust ducts that serve the sterilizer area only (i.e., the area containing the all-in-one sterilization device, EtO ampules, etc.) and route EtO directly to the outside of the building by maintaining a net suction on all of the exhaust ductwork.[220] The exhaust duct is also required to terminate away from areas where people walk or work, to be located at least 7.6 meters (25

[220] https://www.cdc.gov/niosh/docs/89-115/default.html.

feet) away from the building air intake source, and to be engineered according to existing codes.[221]

Abatement Devices

EPA has determined that label changes are necessary to require that additional abatement devices be used along with all-in-one EtO sterilization devices in healthcare settings as of January 1, 2027. Both all-in-one sterilization device manufacturers offer accessory abatement devices that reduce EtO emissions by more than 99%.[222, 223] By requiring that all EtO sterilization devices are used with dedicated abator systems, EtO levels will be kept to a minimum in their outgoing emissions. Recognizing that risks to bystanders from healthcare facilities were not quantitatively assessed, EPA expects abatement devices to reduce exposures to bystanders as well. Healthcare facilities using less than 10 lbs (4,536g) EtO per year are exempted from the requirement to utilize abatement devices. This exemption was established in coordination with sterilization device manufacturers and represents the approximate amount of EtO used by running a small EtO sterilization device once per weekday for a full year.[224] EPA does not have data on EtO usage at this low level or the associated exposures, and so cannot preclude the possibility of risk; however, in light of this low level of EtO usage and associated exposure and the financial burden of requiring small scale healthcare facilities using this amount of EtO to use abatement devices, the amount of anticipated risk reduction does not justify the burden at this time. Specifically, the financial burden of installing an abatement device may result in forcing small scale healthcare facilities to shut down, which could compromise patient access to care.[225] EtO labels will require recordkeeping to demonstrate less than 10 lbs of EtO is used per year if a facility seeks an exemption. Records must include an identification of the sterilization device, time and date of each cycle and quantity of EtO used per cycle.

[221] ANSI/AAMI ST41:2008/(R)2018 Section 3.9.2.6: Exhaust Ducts (pg. 15).
[222] https://multimedia.3m.com/mws/media/1427940O/3m-steri-vac-sterilizer-gs-series-safety-summary.pdf.
[223] https://www.sterility.com/gas-abatement-equipment-eto-abator-sterility/.
[224] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen Sterilizers September – December 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0411.
[225] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen Sterilizers September – December 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0411 and *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders American Veterinary Medical Association (AVMA) December 7, 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0413.

Healthcare Facilities: Lowered Exposure Limit

Because of the risks identified to occupational handlers and bystanders from exposure to EtO in healthcare facilities, EPA asserts that an occupational exposure limit of 0.1 ppm is necessary to address unreasonable adverse effects and has determined that it is achievable over time. EPA has determined it is necessary for EtO labels to include language establishing lowered occupational exposure limits of 0.5 ppm (3-year implementation timeframe), 0.25 ppm (5-year implementation timeframe), and 0.1 ppm (10-year implementation timeframe) based on an 8-hour time weighted average in healthcare facilities. The Agency believes that most healthcare facilities already achieve exposure limits below 0.1 ppm, so this measure is intended to standardize the limit for enforcement purposes and to harmonize requirements between commercial and healthcare facilities. The Agency is also addressing risks from exposure to EtO in healthcare facilities through PPE and engineering controls as described in the following sections.

EtO labels will include language requiring that respirators must be worn by workers if these occupational exposure limits are exceeded. EPA has also determined that it is necessary for EtO labels to also include language requiring facilities to monitor exposures and follow all accompanying requirements outlined in OSHA Standard 29 C.F.R. § 1910.1047, which include a written compliance program and established regulated areas.[226]

Additionally, EPA has determined it is necessary for EtO labels to include language revising the current 5 ppm Short-Term Exposure Limit (STEL) duration of 15 minutes referenced on EtO labels to a 10-minute duration (10-year implementation timeframe). This short-term duration is supported by the recommendation from the National Institute for Occupational Safety and Health (NIOSH).[227]

The Agency encourages use of a badge method using Gas Chromatography with Electron Capture Detector or the OSHA ID 1010 tube method for the collection of occupational exposure data using the time-weighted average in the personal breathing zone.[228, 229]

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[226] For information on monitoring frequency, see OSHA Technical Manual (OTM) Section II: Chapter 1; Personal Sampling for Air Contaminants and OSHA Field Safety and Health Management System (SHMS) Manual Chapter 27 Exposure Monitoring. For information on calculating the time-weighted average exposure, see OSHA Technical Manual (OTM) Section II: Chapter 1 Personal Sampling for Air Contaminants; 1910 Subpart Z Toxic and Hazardous Substances 1910.1000 Air Contaminants; and 1910 Subpart Z Toxic and Hazardous Substances 1910.1047 App D Sampling and Analytical Methods for Ethylene Oxide (Non-Mandatory).

[227] See the CDC NIOSH Pocket Guide to Chemical Hazards Ethylene oxide NIOSH REL at https://www.cdc.gov/niosh/npg/npgd0275.html.

[228] 3M Badge Analytical Method: Modified ASTM D5578: Desorption in 90/10 toluene/acetonitrile. Ethylene oxide is adsorbed and converted to 2-Bromoethanol; analysis by Gas Chromatography with Electron Capture Detector (GC/ECD).

[229] OSHA Method 1010 Procedure: Samples are collected by drawing workplace air through sampling tubes containing hydrobromic acid coated carbon beads using personal sampling pumps. Samples are extracted with a mixture of water and a 1:1 (v/v) solution of acetonitrile/toluene. Analysis is performed by gas chromatography using an electron capture detector (GC-ECD).

EPA has identified as necessary label language requiring that facilities maintain records of EtO worker exposure levels.

Healthcare Facilities: Lowered Action Level

Similar to commercial sterilization facilities, to further inform worker exposure levels, EPA has determined it is necessary for EtO labels to include language establishing a lowered action level of 0.1 ppm based on an 8-hour time weighted average in healthcare facilities, with an implementation timeline of one year. If a worker's exposure may be at or exceed this new action level, increased worker monitoring and medical surveillance, as well as training, are required by language on the EtO labels cross-referencing OSHA Standard 29 C.F.R. § 1910.1047.

Table 5. Summary of Worker Exposure Limit, Short Term Exposure Limit, and Action Level for Healthcare Facilities

Description	Current OSHA Standard	New EPA Limit	Timeline
Exposure Limit (8-hr TWA)	1 ppm	0.5 ppm	3 years
		0.25 ppm	5 years
		0.1 ppm	10 years
Short Term Exposure Limit (STEL)	5 ppm (as 15-minute TWA)	5 ppm (as 10-minute TWA)	10 years
Action Level (8-hr TWA)	0.5 ppm	0.1 ppm	1 year

Healthcare Facilities: Personal Protective Equipment

EPA has determined it is necessary for EtO labels to include language requiring respirators for workers exposed to EtO at levels in exceedance of the lowered occupational exposure limits and/or short-term exposure limits in healthcare facilities, as explained in the ID section *Healthcare Facilities: Lowered Exposure Limit*.

Following conversations with the manufacturers of EtO sterilization devices used in healthcare facilities, EPA believes that the design of all-in-one EtO sterilization devices used in healthcare settings, in addition to the minimal amount of EtO used in these devices will rarely, if ever, result in exceedances of occupational exposure limits when used as directed. Additionally, it is EPA's understanding that it is already common practice for device manufacturers to

troubleshoot problems that sterilization device operators experience with their devices, so a respirator requirement is not expected to be overly burdensome on end users.[230]

Healthcare Facilities: Training

In the PID, EPA proposed training for persons who work in healthcare facilities to state risks at 1 in 25 for MLE and 1 in 12 for upper bound for EtO handlers in healthcare facilities. However, EPA asserts in this ID that training that includes information on the acute and chronic health effects from EtO exposure that aligns with information from OSHA is implementable and understandable by workers and would enable continuity with respect to how workers are provided information about risks associated with EtO. OSHA has identified EtO as a carcinogen that may cause leukemia and other cancers as a result of long term (chronic) exposure, and acute exposure (short term) to EtO may cause eye pain, sore throat, difficult breathing, blurred vision, dizziness, nausea, headache, convulsions, blisters, vomiting, coughing, spontaneous abortion, genetic damage, nerve damage, peripheral paralysis, muscle weakness, impaired thinking, and impaired memory.

In healthcare facilities, training is currently recommended by the Association for the Advancement of Medical Instrumentation (AAMI) in their EtO Standard (ANSI/AAMI ST41:2008/(R)2018) for personnel who work with EtO sterilization devices. It is common industry practice that healthcare facilities follow the guidelines in the AAMI Standard – Personnel Considerations. Specifically, ANSI/AAMI ST41 states: "Education and training materials and information are available from the sterile processing vendors, associations and journals; in addition, OSHA has education materials available for loan.[231] Personnel may receive in-service training for all new instrumentation, devices and equipment. All orientation, on-the-job and in-service training may be documented."[232]

Similar to the training for workers in commercial sterilization facilities, labels on EtO products registered by EPA for use in healthcare settings will require safety and awareness training for all workers including office staff. Information and training must be provided to all workers in the facility at the time of initial assignment and annually thereafter. The safety training must include, at a minimum, the following information: [233]

- The potential health effects from the levels of EtO in the facility. Safety training materials must include the following verbiage: "EtO is a carcinogen that may cause leukemia and other cancers due to chronic exposure. Acute exposure to EtO may cause eye pain, sore throat, difficult breathing, blurred vision, dizziness, nausea, headache,

[230] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen Sterilizers September – December 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0411.
[231] https://www.osha.gov/etools/hospitals/central-supply/hazardous-chemicals.
[232] ANSI/AAMI ST41:2008/(R)2018. Page 20.
[233] For healthcare facilities, training on the most recent monitored ambient levels of EtO in the facility is not necessary because there is no continuous indoor air monitoring measure for healthcare facilities.

convulsions, blisters, vomiting, coughing, spontaneous abortion, genetic damage, nerve damage, peripheral paralysis, muscle weakness, impaired thinking, and impaired memory."

- The emergency response plan and how to respond in an emergency.
- The availability of the Safety Data Sheet and other materials related to the health hazards of exposure to EtO.

As stated earlier, EtO labels will also require additional training if worker exposure may be at or exceed the Action Level and cross-reference all other training requirements in OSHA Standard 29 C.F.R. § 1910.1047.

For additional details and resources related to training workers, healthcare facility employers may refer to the Association for the Advancement of Medical Instrumentation's (AAMI's) most recent version of the standard *Ethylene Oxide Sterilization in Health Care Facilities: Safety and Effectiveness* and OSHA's *Small Business Guide for Ethylene Oxide*.

EPA expects the registrants to submit label amendments to implement the aforementioned training provisions within 60 days.

Healthcare Facilities: Recordkeeping

EPA has determined it is necessary for EtO labels to include language requiring recordkeeping that demonstrates adherence to the TWA occupational exposure limit, worker training, and records of EtO usage for the purposes of exemption from abatement devices, if applicable. The Agency has also determined it is necessary for EtO labels to include language directing facilities to maintain records pertinent to the Action Level as outlined in OSHA Standard 29 C.F.R. § 1910.1047.

Healthcare Facility Recordkeeping: Worker Personal Breathing Zone Data (Adherence to Occupational Exposure Limit and Mitigation Associated with EPA Action Level Exceedances)

To reduce worker exposure, EPA has determined it is necessary for EtO labels to be revised to include a more stringent occupational exposure limit, short-term exposure limit, and action level. Upon amendment of the EtO labels following the publication of this ID, records of PBZ monitoring data and the exposure results must be maintained to show adherence to the current exposure limit, short-term exposure limit, and mitigation measures associated with exceedances of the action level. Recordkeeping requirements, consistent with the requirements found in OSHA's EtO standard at 29 C.F.R. § 1910.1047(k)(2), remain for the new occupational exposure limit, short-term exposure limit, and action level. Records are required to be maintained according to 29 C.F.R. § 1910.1047(k)(2) from the date of monitoring. A record retention time of 30 years per § 1910.1047(k)(2) is needed because a facility may not conduct worker exposure monitoring for extended periods of time absent an event triggering such monitoring, such as changes to the facility, as described in 29 C.F.R. § 1910.1047(d).

Because exposure monitoring results dictate whether facilities must take additional steps to reduce worker exposure and what steps they must take—such as providing workers with PPE—it is necessary for facilities to maintain exposure monitoring records supporting the steps they did or did not take for as long as facilities may rely on such records.

Healthcare Facility Recordkeeping: Worker Training

EPA has determined it is necessary for EtO labels to include language requiring healthcare facilities maintain records on worker training. Specifically, training materials provided to workers upon assignment and annually thereafter and records of the dates individual workers are trained should be maintained as part of the recordkeeping requirement. Records would be required to be maintained for two years from the date of training, including if the trainee leaves the place of employment before two years.

Healthcare Facility Recordkeeping: Abatement Devices Exemption

EPA has determined it is necessary for EtO labels to include language directing facilities to record the number of cycles run in each sterilization device. As of January 1, 2027, recordkeeping will be required to demonstrate that less than 10 lbs of EtO is used per year if a facility seeks an exemption from the abatement device requirement on the EtO labels. Records must include: 1) Quantity of EtO in the facility's inventory on January 1, 2027; 2) Quantity and proof of purchase for each EtO acquisition made on and following January 1, 2027; and 3) Quantity of EtO used, including an identification of the sterilization device, time and date of each cycle and quantity of EtO used per cycle. Records must be kept for two years from the date they are created.

Label Consistency and Clarification

The Agency has identified several label changes necessary for consistency and clarification as specified in Appendix B.

Black Walnuts

In the PID, EPA expressed its intent to withdraw the EtO tolerance for black walnut, noting that "the Agency is not aware of current EtO use on walnuts and none of the EtO products are currently labeled for use on walnuts." During the development of this ID, EPA learned of an ongoing use of EtO for the fumigation of black walnuts. EPA also learned that there is not currently an available alternative for the fumigation of black walnuts and that, if EtO usage on black walnuts were to be prohibited in the short-term, there would be a significant adverse economic impact not only to the user of EtO but also to communities involved in other steps of the black walnut harvesting, fumigation, and distribution process.

The existence of a tolerance for a pesticide on a specific commodity does not mean that application of the pesticide to that commodity is permissible under FIFRA. Rather, a registered pesticide product may only be applied to commodities listed on the product label; application to other commodities would be considered use of a pesticide in a manner inconsistent with the labeling in violation of FIFRA section 12(a)(2)(G). While there is a tolerance for residues of EtO on walnuts, including black walnuts, no currently registered pesticide product bears specific directions for use of EtO on black walnuts. Rather, registered EtO products permit the application of EtO to "reduce microbial load" on "whole and ground spices or other seasoning materials" and include a cross-reference to the EtO tolerance at 40 C.F.R. § 180.151.

However, EPA has historically acknowledged the use of EtO, despite noting that no registered EtO products bear specific directions for use on black walnuts. For example, during the reregistration of EtO, EPA stated that "[e]thylene oxide is used as a postharvest fumigant on spices and black walnut." Revised Residue Chemistry Chapter for Ethylene Oxide Reregistration Eligibility Decision (RED) Document per Registrant's Error Corrections (July 12, 2005), at 1. EPA also noted that "[s]pecific directions for treatment of spices and black walnut are not listed on any label of the active [EtO] labels," and recommended that "[d]irections for use must be clearly defined on all labels that are allowed for the fumigation of spices and black walnut." Id. at 2, 8. However, no changes were subsequently made to EtO product labels to specifically address use of EtO on black walnuts.

Additionally, black walnuts have been fumigated with EtO for a long time, with the tolerance for EtO residues on black walnut originally being established in 1962. 27 Fed. Reg. 817, 822 (Jan. 27, 1962). At that time, pesticides were generally regulated by USDA, and tolerances were established by FDA. EPA's acknowledgment of this use is similarly long-standing. See, e.g., 43 Fed. Reg. 3,693, 3,803 (Jan. 27, 1978) ("EtO is used primarily for sterilization of medical supplies and equipment (see Appendix A for examples) on which FDA establishes tolerances (53), and as an insecticidal, fungicidal, and bactericidal fumigant on copra, black walnuts, and spices."). Furthermore, EtO labels have not historically listed specific commodities, instead referring generally to spices and seasoning materials with references to the tolerance regulation in effect when the label was approved. See, e.g., OxyFume 12 Label (1973) (referring to 21 C.F.R. 121.1232);[234] OxyFume 12 Label (1983) (referring to 21 C.F.R. 193.200);[235] OxyFume 12 Label (1996) (referring to 40 C.F.R. 180.151 and 40 C.F.R. 185.2850).[236]

Based on the long-standing use of EtO for the fumigation of black walnuts, EPA's acknowledgment of such use, and the historical approach to identifying use sites on EtO pesticide product labels, EPA has determined that registrants of EtO products that currently bear directions for use to "reduce microbial load" on "whole and ground spices or other seasoning materials" and include a cross-reference to the EtO tolerance at 40 C.F.R. § 180.151 may choose to specify black walnut as a use site for EtO. Because the use of EtO on black

[234] https://www3.epa.gov/pesticides/chem_search/ppls/010330-00005-19730815.pdf.
[235] https://www3.epa.gov/pesticides/chem_search/ppls/010330-00005-19830613.pdf.
[236] https://www3.epa.gov/pesticides/chem_search/ppls/067470-00003-19961219.pdf.

walnuts is ongoing, specifying this use on EtO product labels is not expected to increase use of EtO. Additionally, specifying this use on EtO product labels will ensure that the mitigation measures applicable to users of EtO on dried herbs, spices, and vegetables will also apply to users of EtO on black walnuts. EPA also does not currently intend to revoke the tolerance for EtO residues on walnuts. Further, EPA has identified as necessary a January 1, 2032, phase-out deadline for the use of EtO on black walnut. This deadline is based on information that EPA has received from the only known user of EtO on black walnuts provided that there are not currently available alternatives for EtO on black walnut; however, the user is actively exploring alternative fumigation methods.

Following the revision of EtO product labels to remove the reference to the EtO and ECH tolerances at 40 C.F.R. 180.151 as described in Appendix B, only EtO pesticide products that are specifically labeled for use on black walnuts may be applied to this commodity. Allowing registrants to specify black walnuts as a use site on their EtO product labels is consistent with the recommendation from the reregistration of EtO that products include specific directions for use on black walnuts and with revisions to EtO labels described in this ID to identify the specific herbs, spices, and dried vegetables to which EtO may be applied. EPA's approach with respect to the black walnut use of EtO is based on the unique history of this use and label language for EtO pesticide products. Application of a pesticide to a commodity not identified on a pesticide product label is use of the pesticide in a manner inconsistent with its labeling, even if a tolerance exists for that pesticide residue on the commodity.

Other Label Changes

These label changes are also directionally correct with respect to reducing the amount of EtO exposure to workers and to those near commercial sterilization facilities that use EtO.

- Current EtO labels contain general, undefined terms for use on dried herbs and spices and the language used is not consistent within the product labels. Specifically, the *Directions for Use* section of the labels says, "This product may be used only…to reduce microbial load on cosmetics, whole and ground spices or other seasoning materials (see 40 C.F.R. 180.151)..." The same section also states, "After August 1, 2008, this product may only be applied to or on spices, dried vegetables or seasonings…"

  To clarify the acceptable use sites on the product labels, the Agency has determined it is necessary to standardize the label language within each label (and as a result across all the labels) to reflect registered uses. The Agency has determined it is necessary for registrants to amend EtO product labels to specifically identify the dried herbs, dried spices, and dried vegetables on the label for which EtO is registered for use. See Appendix B for the necessary label language.

  In addition, the phrase "other seasoning materials" on the labels is vague and undefined. The Agency has determined it is necessary for registrants to amend their

labels to delete the use of "other seasoning materials" since the Agency understands this term to mean a blend of any of the dried commodities specified in the newly added list of dried herbs, spices, and vegetables on the label.

- Currently, EtO product labels contain references to the OSHA Permissible Exposure Limit (PEL). However, since the establishment of the OSHA limits in 1984, there have been considerable updates to the scientific database on EtO exposure and risk, including the 2016 IRIS assessment on EtO, OPP's 2020 EtO DRA, and OPP's 2023 EtO DRA Addendum. EPA thus considers the OSHA PEL of 1 ppm to no longer ensure that the use of EtO will not cause unreasonable adverse effects, including effects to workers, as required under FIFRA, and has therefore determined it is necessary that registrants amend their EtO label language regarding the OSHA PEL. See Appendix B.

- Current labels do not clearly specify the type of facility in which an EtO product is intended to be used. Since the application rate and method for sterilization in healthcare settings compared to commercial sterilization settings differ greatly (e.g., in small oven sized systems versus large chambers), the Agency has identified as necessary changes to EtO product labels to clarify which products are intended to be used in which settings. EPA has identified as necessary that the following statement be added to EtO product labels intended for use in commercial sterilization facilities: "This product is only approved for use in commercial sterilization facilities. This product is not approved for use in healthcare facilities (hospitals, veterinary facilities, dental offices, etc.)." The Agency also has identified as necessary clarification of which products are intended to be used in healthcare facilities through the addition of the following statement to EtO product labels intended for use in such facilities: "This product is only approved for use in single chamber sterilization/aeration devices in healthcare facilities (e.g., hospitals, veterinary facilities, dental offices, etc.)."

B. Environmental Justice

"Environmental justice" means the just treatment and meaningful involvement of all people, regardless of income, race, color, national origin, Tribal affiliation, or disability, in agency decision-making and other Federal activities that affect human health and the environment.[237] EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. Throughout the registration review process, EPA has sought to include all communities and persons, including minority, low-income, and indigenous populations who may be disproportionately overburdened by the exposure to EtO.

[237] See EO 14096 Sec. 2(b) at https://www.federalregister.gov/documents/2023/04/26/2023-08955/revitalizing-our-nations-commitment-to-environmental-justice-for-all#p-11

The Agency sought information during the public comment period of the PID on any other groups or segments of the population who, as a result of their proximity and exposure to pesticides, unique exposure pathway (e.g., as a result of cultural practices), location relative to physical infrastructure, exposure to multiple stressors and cumulative impacts, lower capacity to participate in decision making, or other factors, may have unusually high exposure to EtO disproportionately affected by the use of EtO as a pesticide. During the PID public comment period, EPA received several comments regarding environmental justice, including those from private citizens, the Environmental Protection Network (EPN), and the Attorneys General of New York, Connecticut, Illinois, Maryland, Massachusetts, Michigan, New Jersey, Oregon, Rhode Island, Vermont, and Wisconsin.[238] For more details on these comments and the Agency's responses, please see Appendix E.

EPA's Office of Air and Radiation (OAR) conducted an in-depth Environmental Justice analysis as part of the *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review*.[239] OAR examined the potential for the 88 facilities that were assessed to pose concerns to environmental justice (EJ) communities both in the baseline and under the control options considered in their proposal. Overall, the results of this proximity demographic analysis indicated that the percent of the population living within 10 km of the 88 facilities that is Hispanic or Latino is substantially higher than the national average, driven largely by the seven facilities in Puerto Rico. The baseline proximity analysis indicated that the proportion of other demographic groups living within 10 km of commercial sterilizers is closer to the national average. The baseline risk-based demographic analysis, which focused on those specific locations that are expected to have higher cancer risks as identified by OAR (defined by OAR for the purpose of this analysis as cancer risks greater than or equal to 1-in-1 million, greater than or equal to 50-in-1 million, and greater than 100-in-1 million), suggested that African Americans were disproportionally represented at the higher risk levels.

The final control requirements under the OAR NESHAP reduce the number of individuals exposed to unacceptable cancer risk (i.e., greater than 100-in-1 million) to zero individuals. Thus, the final requirements reduce risk to acceptable levels for all population groups, including groups with potential EJ concerns. EPA recognizes that a disproportionate share of the individuals that would remain at somewhat elevated risk (albeit at risk levels generally considered acceptable based on the greater than 100-in-1 million threshold) after implementation of the standards are Hispanic or Latino, driven largely by the facilities in Puerto Rico. While absolute risk declines significantly for Hispanic or Latino individuals after implementing the final requirements, the distribution of the remaining risk is more disproportionately concentrated among Hispanic or Latino individuals compared to the baseline.

[238] EPA-HQ-OPP-2013-0244-0106, EPA-HQ-OPP-2013-0244-0142, EPA-HQ-OPP-2013-0244-0260 at www.regulations.gov.
[239] EPA-HQ-OAR-2019-0178-1482 at www.regulations.gov.

OPP has identified risks to workers handling EtO or who may be exposed to EtO within the facilities where it is used. Because people tend to live and work within their community, individuals who would be employed in these facilities could be disproportionally drawn from the Hispanic or Latino communities, as identified by OAR, since many facilities are located in Puerto Rico.

Additionally, according to the 2023 data from the U.S. Bureau of Labor Statistics, people working in warehousing and storage, such as those who would be employed in these facilities, moving materials into and out of chambers for fumigation, could be disproportionally drawn from population groups with potential EJ concerns. The national average of employed persons working in warehousing and storage are about 23% Black or African American and 37% Hispanic or Latino.[240]

EPA anticipates that through the identified mitigation, including the NESHAP emissions controls and workplace protections, substantial benefits in risk reduction and associated health risks in communities with EJ concerns will be achieved.

C. Tolerance Actions

The Agency plans to exercise its FFDCA authority to update the tolerance expressions to appropriately cover the metabolites and degradates of EtO and the EtO reaction product, ethylene chlorohydrin (ECH), and to specify the residues to be measured for each commodity for enforcement purposes. EPA anticipates amending the tolerance expressions to read as follows:

> (a) General.
> (1) Tolerances are established for residues of the fumigant ethylene oxide (EtO),[241] including its metabolites and degradates except ethylene chlorohydrin, in or on the commodities listed in the table to paragraph (a)(1). Compliance with the tolerance levels specified below is to be determined by measuring only EtO in or on the commodity.
>
> (2) Tolerances are established for residues of the EtO reaction product ethylene chlorohydrin, including its metabolites and degradates, in or on the commodities listed in the table to paragraph (a)(2) as a result of applications of EtO to the commodities listed below. Compliance with the tolerance levels specified below is to be determined by measuring only ethylene chlorohydrin (2-chloroethanol), in or on the commodity.

The Agency also plans to exercise its FFDCA authority to modify certain commodity definitions associated with the tolerances for EtO and ECH, as summarized in Table 6, below. The tolerances listed in Table 6 only include those for which changes are recommended.

[240] U.S. Bureau of Labor Statistics. Household Data Annual Averages: Employed persons by detailed industry, sex, race, and Hispanic or Latino ethnicity. 2023. Accessed December 30, 2024.https://www.bls.gov/cps/cpsaat18.htm.
[241] The Agency plans to revise the tolerance expression to be consistent with other fumigants (e.g., PPO).

EtO. EPA intends to revise the commodity definitions for Peppermint, dried leaves; and Spearmint, dried leaves. In addition, EPA intends to revise the commodity definition for Herbs and spices group 19, dried (except basil). These revisions would not change the established tolerance of 7 ppm for each of these commodities, as listed in 40 C.F.R. § 180.151. The changes will be implemented through separate rulemaking. The Agency has also determined that it is necessary for EtO product labels to identify that the vegetables included under *Dried Vegetables* are capsicums, ginger, horseradish, paprika, garlic, onion, turmeric, arrowroot, asparagus, artichoke, green bean, green bell pepper, red bell pepper, broccoli, cabbage, carrot, celery stalk, corn, kelp, leek, mushroom, tomato, galangal, and pumpkin flakes.

ECH. EPA intends to revise the commodity definitions for Peppermint, dried leaves; and Spearmint, dried leaves. In addition, EPA intends to revise the commodity definition for the Herbs and spices group 19, dried (except basil). These revisions would not change the established tolerance of 940 ppm for each of these commodities, as listed in 40 C.F.R. § 180.151. The Agency determined that a tolerance is needed for walnuts and intends to establish a tolerance of 100 ppm. The changes will be implemented through separate rulemaking. The Agency has also determined that it is necessary for EtO product labels to identify that the vegetables included under *Dried Vegetables* are capsicums, ginger, horseradish, paprika, garlic, onion, turmeric, arrowroot, asparagus, artichoke, green bean, green bell pepper, red bell pepper, broccoli, cabbage, carrot, celery stalk, corn, kelp, leek, mushroom, tomato, galangal, and pumpkin flakes.

In the PID, EPA proposed revoking tolerances for specific commodities cancelled during a phased cancellation. The Agency received several comments regarding the importance of retaining the EtO tolerances for global trade even if the commodity is no longer treated with EtO in the U.S. As a result, EPA has instead determined that the tolerances will be retained for such commodities.

Table 6. Summary of Anticipated Tolerance Actions (40 C.F.R. § 180.151)

Commodity	Established Tolerance (ppm)	Anticipated Tolerance (ppm)	Comments
40 C.F.R. § 180.151(a)(1) ethylene oxide			
Herbs and spices group 19, dried, except basil	--	7	Commodity definition revision.
Herb and spice, group 19, dried, except basil	7	remove	
Peppermint, dried leaves	--	7	Commodity definition revision.
Peppermint, tops, dried	7	remove	
Spearmint, dried leaves	--	7	Commodity definition revision.
Spearmint, tops, dried	7	remove	
40 C.F.R. § 180.151(a)(2) ethylene chlorohydrin			
Herbs and spices group 19, dried, except basil	--	940	Commodity definition revision.
Herb and spice, group 19, dried, except basil	940	remove	
Peppermint, dried leaves	--	940	Commodity definition revision.
Peppermint, tops, dried	940	remove	
Spearmint, dried leaves	--	940	Commodity definition revision.
Spearmint, tops, dried	940	remove	
Walnut	--	100	Spice sterilization study level of quantification (LOQ).

D. Interim Registration Review Decision

The Agency is issuing this ID in accordance with 40 C.F.R. §§ 155.56 and 155.58. Based on the Agency's review of EtO at this time in the registration review process, EPA has identified certain changes to the affected registrations and their labeling that will be implemented through label amendments and/or registration changes. EPA has identified the mitigations in Section V and Appendix B as necessary to address specific concerns identified at this point in the ongoing registration review process.

At the end of the registration review process, EPA will determine whether each EtO pesticide registration "continues to satisfy the FIFRA standard for registration."[242] However, this ID is not a decision on whether EtO registrations continue to satisfy the FIFRA standard for registration and implementing the mitigation identified in this ID may not be sufficient for EPA to determine

[242] 40 C.F.R. §§ 155.40(a), 155.57; 7 U.S.C. § 136a(g); *see also* 7 U.S.C. §§ 136a(c)(5) (FIFRA registration standard), 136(bb) (defining "unreasonable adverse effects on the environment" as encompassing both "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide" [FIFRA's risk-benefit standard] and "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the [FFDCA safety standard]"). This document is not a "registration review decision" within the meaning of FIFRA Section 3(g) and 40 C.F.R. § 155.57.

that EtO registrations do so ultimately. EPA may determine that additional mitigations or other measures are necessary in a subsequent interim determination or its final registration review decision. For EtO, EPA has identified in this ID additional information that is needed to complete registration review and will issue a data call-in for that information, as discussed in section V.E. Once the aforementioned data become available, the Agency may promptly reevaluate this Interim Decision.

"Unreasonable adverse effects on the environment" is defined by FIFRA to be "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits." In considering whether mitigation measures are necessary to address risks of concern during the registration review process, EPA's Office of Pesticide Programs conducts a risk-benefit analysis. This analysis involves weighing the benefits (e.g., sterilization of medical devices) of the use of a pesticide against the potential ecological and human health risks. Risk-benefit analysis is conceptually equivalent to more traditional benefit-cost analysis (BCA) conducted elsewhere in the Agency. Risk-benefit analysis and benefit-cost analysis need not exhaustively quantify costs in monetary terms. EPA guidance advises that "benefits and costs that cannot be quantified should be presented qualitatively."[243] The Office of Management and Budget's Circular A-4, which defines good regulatory analysis and standardizes the way benefits and costs of Federal regulatory actions are measured and reported, advises that "if you are not able to quantify the [cost or benefit] effects, you should present any relevant quantitative information along with a description of the unquantified effects."[244] Through implementation of risk-benefit analysis, OPP takes into account the "economic, social, and environmental costs and benefits of the use of any pesticide."

The Agency conducted a DRA in 2020, as well as a detailed Addendum to the DRA in 2023. In these risk assessments, EPA identified inhalation risks for workers and nearby communities from continuing to register EtO. For occupational handlers at commercial sterilization and healthcare facilities, cancer risk estimates are estimated from 4×10^{-2} (1 in 25) to 1×10^{-1} (1 in 10). Cancer risks of concern are also anticipated for occupational, residential, and non-residential bystanders. These risks are not quantified in dollars, but they represent the Agency's assessment of risk from the use of EtO. EPA has identified mitigation necessary at this stage in the registration review process to help address inhalation risk concerns, including the termination of certain uses, a reduced concentration rate for medical device sterilization for new cycles, respiratory protection for workers engaged in high exposure tasks, respiratory protection for lowered occupational exposure limits, monitoring, training, and recordkeeping, as well as venting and abatement devices for healthcare facilities. These mitigation measures are expected to reduce EtO exposure to workers and residential and non-residential bystanders. EPA has information on the marginal risk reduction from the reduced occupational exposure limit; however, at this time, EPA has not conducted a quantitative analysis of the risk

[243] Environmental Protection Agency (EPA). 2010. Guidelines for preparing economic analyses. Accessed online on January 6, 2023, at: https://www.epa.gov/environmental-economics/guidelines-preparing-economic-analyses.
[244] Office of Management and Budget (OMB). 2003. Executive Office of the President, OMB Circular A-4, Regulatory Analysis.

reduction that would result from the collection of all of the mitigation measures in this ID. EPA will be requiring worker exposure data for commercial sterilizers and warehouses in order to understand the impacts of complying with EPA's CAA NESHAP requirements and implementing the mitigation measures identified in this ID issued under FIFRA, and to better understand how to further lower the occupational exposure limit. Once these data become available, the Agency may promptly reevaluate this Interim Decision. Since the risk reduction is not quantitatively assessed, and since the air concentrations need to be very low to meet risk thresholds, the Agency is taking an approach of "as low as reasonably achievable" (ALARA) for EtO use and application. Under FIFRA, cancellation is an option for achieving risk reduction; however, at this stage in the registration review of EtO, EPA has identified mitigation measures consistent with the "ALARA" approach. Such measures would result in a reasonable level of exposure reduction at this stage in the registration review process, considering the benefits of EtO and the current unavailability of alternatives, particularly for medical device sterilization.

EPA expects inhalation cancer risks of concern to remain for workers inside sterilization and healthcare facilities, and residential and non-residential bystanders, even after the implementation of the identified mitigation.[245] 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 and/or quantification for the methods that are used to measure EtO in ambient air. To achieve a residential population cancer risk that is less than 1 in 1 million, for example, the lifetime average EtO concentration would need to be less than 0.11 ppt. This level is less than the detection limit of 20-90 ppt and this detection limit can only be achieved under optimum conditions.[246]

Despite these risks, at this time EtO remains a critical pesticide for certain uses, as it is critical for the sterilization of new and reusable medical devices, instruments, and equipment. Industrial EtO sterilization has a high throughput capacity, broad material compatibility, low cost, and effective bactericidal, sporicidal, and virucidal activity. EtO is used to sterilize approximately 50% of all sterilized medical devices, or 20 billion devices, annually. EPA has investigated alternatives to EtO for sterilizing medical devices, including engaging in discussions with FDA about alternatives to EtO. EPA understands that, while there are alternative sterilization methods for some medical devices, there are currently no available alternatives—pesticidal or non-pesticidal—for some devices due to challenges such as material compatibility, scalability, and capacity. Therefore, if commercial sterilization and healthcare facilities no longer had access to EtO to sterilize medical devices, the result would likely be a disruption to the medical device supply chain, which could in turn result in a nationwide public health crisis.

[245] OPP notes that for residential bystander risk, even though OAR and OPP have different thresholds for when residential cancer risks are considered to be of concern (100 in a million and 1 in a million, respectively), OPP believes that the emissions controls required by OAR would significantly reduce bystander exposure without causing adverse impacts to the U.S. supply of sterilized medical devices needed for a variety of medical procedures.

[246] 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.

There is also a public health benefit from the use of EtO for food commodity fumigation. The threat of food-borne contamination from pathogens such as *Salmonella* and *Escherichia coli*, and the potential for serious illness from exposure to these pathogens, is a concern for the Agency, food manufacturers, and the general public. EtO is used in the U.S. during the processing of food commodities (e.g., herbs and spices) to reduce microbial activity. As with medical devices, EPA has investigated the availability of alternatives to EtO in food use fumigation, including discussing potential alternatives with FDA. EPA understands that while alternatives may be available to treat certain food commodities, EtO currently may be the only viable option for the treatment of certain commodities and their specific forms. See Section III.C.

EPA has determined that there is no human dietary risk from registered uses of EtO that is inconsistent with the FFDCA safety standard. An aggregate assessment for EtO was not conducted since there are no food or drinking water exposures to EtO. For the reaction products 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. For more information, see *Ethylene Oxide (EtO) Draft Human Health and Ecological Risk Assessment in Support of Registration Review* (2020 DRA) and *Ethylene Oxide (EtO)/Ethylene Chlorohydrin (ECH). Chronic Dietary (Food Only) Exposure and Risk Assessment for Registration Review* (dated September 24, 2024) in this docket. EPA concludes that there is a reasonable certainty that no harm will result from dietary exposure to EtO or ECH. Therefore, the EtO and ECH residues are safe. EPA intends to leave the tolerances in place as well as make several non-substantive modifications, as EPA's analysis indicates that such actions would be safe.

EPA has not yet fully evaluated EtO's effects on federally threatened and endangered (listed) species or designated critical habitats. However, consistent with its obligations under the Endangered Species Act (ESA),[247] EPA expects to complete effects determinations and any necessary consultation with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service (the Services) before completing the EtO registration review and issuing a final registration review decision. For more information on EPA's ESA obligations during registration review, see Appendix C.

EPA continues to work with the Services to improve the consultation process for pesticides in registration review. In April 2022, EPA released its ESA Workplan, which outlines strategies and actions for the Agency to meet its ESA obligations for FIFRA actions.[248] Consistent with the ESA Workplan, EPA is focused on steps it will take during registration review to reduce exposure for listed species as it moves toward fulfilling its ESA obligations and making final registration

[247] Endangered Species Act (ESA) § 7, 16 U.S.C. § 1536.
[248] Balancing Wildlife Protections and Responsible Pesticide Use (Apr. 2022), https://www.epa.gov/system/files/documents/2022-04/balancing-wildlife-protection-and-responsible-pesticide-use_final.pdf.

review decisions. In November 2022, EPA released its first ESA Workplan Update.[249] As part of this update, EPA announced that, going forward, EPA may include a variety of FIFRA Interim Ecological Mitigation (IEM) measures in its registration review decisions that seek to reduce exposures for nontarget organisms based on its FIFRA ecological risk assessment(s). EPA expects that this mitigation may also reduce pesticide exposures for listed species.

As part of this ID, EPA has considered a variety of risk mitigation measures based on the risks and benefits of EtO, including mitigation measures that may mitigate ecological risks, while EPA works toward a final registration review decision. While these mitigation measures do not satisfy EPA's ESA obligations, EPA has determined that early mitigation may shorten the consultation process and improve protections for listed species from currently registered pesticide products. EPA also has determined that the risk mitigation measures that the Agency has identified for EtO in this ID (Section V) satisfy EPA's obligations under Section 711 of the Consolidated Appropriations Act, PL-117-328 (Dec. 29, 2022). Among other things, Section 711 requires EPA to "include, where applicable, measures to reduce the effect of the applicable pesticide on" listed species and designated critical habitats in any ID noticed in the Federal Register between December 29, 2022, and October 1, 2026, for which EPA has not "made effects determinations or completed any necessary consultation under [ESA Section 7(a)(2)]."

The identified mitigation is expected to reduce the extent of environmental exposure and may reduce risk to listed species whose range or critical habitat co-occur with the use of EtO (Section V.A.). Exposure to wildlife from the use of EtO will be reduced through OPP's mitigation to reduce EtO usage through the cancellation of minor uses of EtO, phased cancellation of certain food commodities (see Table 7), and the reduced concentration rate of EtO for medical device sterilization for new cycles. Additionally, environmental exposure will be further reduced through the current emissions controls from OAR's NESHAP, which have been further strengthened as of the publication of the *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review* on April 5, 2024.[250]

Table 7. EtO Phased Cancellation Plan for Food Uses

Phased Cancellation Plan	
Commodities	**Mitigation**
Group 1 (26%)[251]	Immediate cancellation: no use allowed afterwards.

[249] ESA Workplan Update: Nontarget Species Mitigation for Registration Review and Other FIFRA Actions (Nov. 2022), https://www.epa.gov/system/files/documents/2022-11/esa-workplan-update.pdf.
[250] EPA-HQ-OAR-2019-0178-1482 at www.regulations.gov.
[251] Angelica, borage, burnet, catnip, costmary, culantro leaf, culantro seed, curry leaf, licorice roots, lovage leaf, lovage seed, marigold, nasturtium, pennyroyal, rue, tansy, wintergreen, woodruff, and wormwood.

Group 2 (68%)[252]	7-year phase out; afterwards, allow use only for reconditioning and retreatment when a secondary treatment is necessary for human pathogen control. Reconditioning with this product may occur when identified in an FDA-approved reconditioning proposal. Retreatment may occur after initial treatment with an alternative to EtO if the initial treatment was ineffective or if the food becomes re-contaminated after the initial treatment.*
Group 3 (6%)[253]	No change in the use of EtO on these commodities.**
* Recordkeeping requirements to begin January 1, 2032. ** Reevaluate need for continued EtO use on these commodities within 8 years.	

In this ID, the Agency is not making any human health or environmental safety findings associated with the Endocrine Disruptor Screening Program (EDSP) screening of EtO. The Agency will make an EDSP determination before issuing a final registration review decision for EtO. For more information, see Appendices C and D.

E. Data Requirements

Outstanding Data from GDCI-042301-1428

The human health database for EtO is not considered complete. The Agency intends to continue working with the registrants to satisfy the data requirements under the existing DCI notice GDCI-042301-1428, which was issued in 2014. One data requirement is still outstanding and will be used to inform future risk assessments: Non-Guideline Study Monitoring Data on Fumigated Commodities (food commodity use).

This study is required to evaluate emission rates for EtO from treated commodities/materials and the potential for occupational exposure due to those emissions in the channels of trade after fumigation activities are complete. The registrants submitted a waiver request for this study (MRID 50384901) on September 8, 2017. However, this waiver request was denied on July 17, 2018, due to a lack of information related to potential exposures within the various channels of trade after fumigation, dissipation of EtO beyond the facility, and the analytical method used to measure air concentrations.[254]

[252] Allspice, anise seed, anise star, annatto seed, balm, chamomile (German and Hungarian), caper buds, caraway, black caraway, cardamom, cassia bark and buds, celery seed, dried chervil, Chinese chive, chive, cinnamon, clary, clove buds, coriander leaf, coriander seed, cumin, dill seed, dillweed, common fennel, Florence fennel seed, fenugreek, grains of paradise, horehound, hyssop, juniper berry, lavender, lemongrass, mace, marjoram (Origanum spp.), mustard seed, nutmeg, dried parsley, black pepper (and pink peppercorns), white pepper, poppy seed, rosemary, saffron, sage, savory (summer and winter), sweet bay, tarragon, thyme, vanilla, and black walnuts.
[253] Dried peppermint tops, sesame seed, dried spearmint tops, and dried vegetables.
[254] Ethylene Oxide (EtO): Response to registrant's inhalation exposure monitoring requirements waiver request. Decision Number 533138. June 21, 2018.

Additional Required Data

In order to quantify worker exposure in commercial sterilizers and warehouses, EPA will issue a data call-in for OSCPP GLN 875.1400 Inhalation Exposure Indoor to understand the impacts of complying with EPA's recently amended Clean Air Act (CAA) NESHAP for EtO commercial sterilizers and implementing mitigation measures identified in this ID issued under FIFRA, and to better understand how to further lower the occupational exposure limit. Based on previously submitted worker exposure data that lacked specificity and detail, EPA is requiring the data include time-weighted average personal breathing zone (PBZ) monitoring of the handlers specifically involved in activities related to the sterilization/fumigation (e.g., loading and unloading chambers, routine maintenance, product transfer, etc.), documentation of the activities each worker performed while monitored, and whether they were wearing a respirator (and what type of respirator). For non-handlers in the facility (e.g., office workers, warehouse workers), EPA also is requiring the data include PBZ monitoring data to monitor their exposures. Data must also include whether or not the facility has complied with the NESHAP requirements.

The Agency encourages use of a badge method using Gas Chromatography with Electron Capture Detector or the OSHA ID 1010 tube method for the collection of occupational exposure data using the time-weighted average in the personal breathing zone.[255, 256]

In order to verify the occupational exposure limits in this ID are attainable, EPA will gather annual worker exposure data and assess those data.[257] Specifically, EPA has determined it is necessary for EtO registrants to collect worker monitoring data from their customers on an annual basis. Further, EtO registrants may not continue to sell EtO products to customers who do not provide worker monitoring data. EPA will collect these data through a DCI. EPA can change the implementation timing and target occupational exposure limit concentration, if necessary, as demonstrated by data, prior to the deadline for the final implementation tier of the exposure limit of 0.1 ppm. In order to make this determination, EPA will reevaluate the occupational exposure limit and any other needed mitigations, based on data, within 8 years.

Additionally, EPA will issue a DCI for a special study for monitoring data on fumigated commodities for medical devices to better understand exposure to EtO in warehouses. Through this data, EPA is seeking information on the exposure scenario from emissions from treated medical device commodities and materials and the potential for occupational exposure due to

[255] 3M Badge Analytical Method: Modified ASTM D5578: Desorption in 90/10 toluene/acetonitrile. Ethylene oxide is adsorbed and converted to 2-Bromoethanol; analysis by Gas Chromatography with Electron Capture Detector (GC/ECD).
[256] OSHA Method 1010 Procedure: Samples are collected by drawing workplace air through sampling tubes containing hydrobromic acid coated carbon beads using personal sampling pumps. Samples are extracted with a mixture of water and a 1:1 (v/v) solution of acetonitrile/toluene. Analysis is performed by gas chromatography using an electron capture detector (GC-ECD).
[257] See "Ethylene Oxide – EOTF and EOSA Proposal for the Interim Decision – June 26, 2024" in the EtO public docket at www.regulations.gov under document ID EPA-HQ-OPP-2013-0244-0406.

those emissions in the channels of trade after sterilization activities are complete. The environments in which worker activities are monitored should also be evaluated which may include monitoring off-gassing properties of fumigated commodities over time. Data are required for occupational sites if the human activity data indicate that workers are likely to have post-application exposures while participating in typical activities. EPA will require a protocol before monitoring for the study begins.

EPA has authority to require the registrants of EtO products to obtain or develop data necessary for EPA to evaluate EtO exposures in warehouses that store products fumigated with EtO if the data are necessary for EPA to maintain the registration of EtO (i.e., necessary for the Agency to determine that the use of EtO will not cause unreasonable adverse effects), even if the activities at the warehouses are not subject to direct regulation under FIFRA. EPA data requirement regulations specifically envision the Agency requiring submission of data relating to post-application exposures.[258] Because EPA has identified significant hazards from EtO exposures, and the potential for exposure to workers in warehouses where commodities fumigated with EtO are stored, the call-in of post-application exposure data is necessary. Specifically for warehouses that are not co-located with sterilization facilities, there is a need for additional data because data from warehouses co-located with sterilization facilities may be skewed by emissions from the sterilization facilities themselves. The Agency has previously required registrants of propylene oxide (PPO) to submit data allowing EPA to assess post-application exposure to fumigated commodities.[259] EPA has also considered data on post-application exposures during the registration review of the wood preservatives.[260]

The ecological and environmental fate data requirements in GDCI-042301-1428 included GLN 850.4150 Vegetative Vigor, Non-guideline study Honeybee Acute Vapor Exposure, and Non-guideline study Avian Acute Inhalation Toxicity. On June 10, 2015, EPA received waiver requests for all three data requirements from the Ethylene Oxide Task Force (EOTF) (MRIDs 49648401, 49648402, and 49688601). In May 2017, EOTF submitted information to fulfill the Product Use Information data requirement (GLN 875.1700) which was also considered when evaluating the ecological data requests. In the document *Ethylene Oxide (EtO) Response to Registrant's Ecological Data Requirements Waiver Request* dated October 9, 2018, EPA waived these data requirements, but additionally stated that "some (or all of these) data requirements may be required in the future." During development of this ID, the Agency has determined that there are remaining uncertainties, such as the ecological exposure from small facilities, which include healthcare facilities, which could be addressed with data. Therefore, EPA will include the

[258] See 40 C.F.R. § 158.2270(d), (e) ("Data are required for occupational and residential uses if the human activity data indicate the potential for post-application dermal and/or inhalation exposures while participating in typical activities and no acceptable modeling options are available.").
[259] See Propylene Oxide (PPO) Interim Registration Review Decision Case Number 2560 at www.regulations.gov document ID EPA-HQ-OPP-2013-0156-0052.
[260] See Creosote Draft Risk Assessment (DRA) discussing post-application exposure to users installing treated wood (page 28) at www.regulations.gov document ID EPA-HQ-OPP-2014-0823-0014.

aforementioned ecological data requirements in a future DCI, as well as include others as policies and practices change.

Once these data become available, the Agency may promptly reevaluate this ID.

Data Proposed in PID But Not Required for the ID

In the PID, EPA proposed to issue a DCI for data on commercially available technologies that can monitor below 10 ppb in real time, while also documenting other instruments that can quantify levels around 0.19 ppb, which is the Agency's concentration of concern for worker exposure. However, EPA is no longer requiring this data at this time because the Agency acquired sufficient information through the public comment period on available monitoring technologies. For more information on public comments on available monitoring technologies and EPA's responses, please see Appendix E.

VI. NEXT STEPS AND TIMELINE

A. Announcement of this Interim Registration Review Decision

A Federal Register Notice will announce the availability of the EtO ID. A final registration review decision for EtO will only be made after EPA completes (1) endangered species effects determinations and any necessary consultation with the Services, and (2) an EDSP determination. At the end of the registration review process, EPA will determine whether each EtO pesticide registration "continues to satisfy the FIFRA standard for registration."[261] However, this ID is not a decision on whether EtO registrations continue to satisfy the FIFRA standard for registration and implementing the mitigation identified in this ID may not be sufficient for EPA to determine that EtO registrations do so ultimately. EPA may determine that additional mitigations or other measures are necessary in a subsequent interim determination or its final registration review decision. For EtO, EPA has identified in this ID additional information that is needed to complete registration review and will issue a data call-in for that information, as discussed in section V.E. The Agency will reevaluate this Interim Decision within 8 years.

B. Implementation of Mitigation Measures

EPA expects that registrants will submit label amendments within 60 days after the announcement of this ID. The Agency would review such label amendments as expeditiously as

[261] 40 C.F.R. §§ 155.40(a), 155.57; 7 U.S.C. § 136a(g); *see also* 7 U.S.C. §§ 136a(c)(5) (FIFRA registration standard), 136(bb) (defining "unreasonable adverse effects on the environment" as encompassing both "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide" [FIFRA's risk-benefit standard] and "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the [FFDCA safety standard]"). This document is not a "registration review decision" within the meaning of FIFRA Section 3(g) and 40 C.F.R. § 155.57.

feasible and expects that products distributed by registrants would bear the revised labeling as described in the mitigation section of this ID after EPA has approved the revised labeling.

The mitigations discussed in this ID are implemented through label amendments and/or registration changes. Registrants: Submit a cover letter, a completed Application for Registration (EPA form 8570-1) and electronic copies of the amended product labels within 60 days after the announcement of this ID in the Federal Register. Submit two copies for each label, a clean copy and an annotated copy with changes. Include the following statement on the Application for Registration (EPA form 8570-1):

> "I certify that this amendment is consistent with the EtO Interim Registration Review Decision and satisfies the requirements of EPA regulations at 40 C.F.R. Section 152.44, and no other changes have been made to the labeling of this product. I understand that it is a violation of 18 U.S.C. Section 1001 to willfully make any false statement to EPA. I further understand that if this amendment is found not to satisfy the requirements of the statute or regulations, this product may be in violation of FIFRA and may be subject to regulatory and/or enforcement action and penalties under FIFRA."

Submit the required documents to EPA's Pesticide Submission Portal (PSP), which can be accessed through EPA's Central Data Exchange (CDX) using the following link: https://cdx.epa.gov/. Once in the CDX system, in the Pesticide Submission Portal home page, under Submissions and Tools, click on "Registration & Exemptions" and then click on "General Registration." DO NOT use the "Reevaluation" links in CDX for Registration Review label amendments.

After all the label amendments and/or registration changes have been submitted, EPA will review them to ensure that they incorporate the necessary mitigation. If they incorporate the necessary changes, EPA intends to approve the requested changes and/or amendments. If the registrant does not submit the label amendments or registration changes, EPA reserves the right to take appropriate action under FIFRA. 40 C.F.R. § 155.58. This ID does not effect a change in the existing registration, and EPA will not involuntarily cancel any registration without following the procedures and substantive requirements of FIFRA section 6 or unless EPA is otherwise compelled to cancel.

Appendix A: Summary of Mitigation for EtO

Registration Review Case #: 2275 PC Code: 042301 Chemical Type: Fumigant Chemical Family: Oxirane Mode of Action: Alkylation						
Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Mitigation	Comment
Occupational handler	Air	Inhalation	Lifetime	Cancer	• Delete uses for which alternatives exist. • Concentration rate limit for new cycles. • Commercial sterilization facilities: Separated HVAC systems for processing and non-processing areas. • Lowered occupational exposure limits. • Commercial sterilization facilities and healthcare facilities: SCBA or supplied air respirators for specific tasks and when EtO concentrations exceed lowered occupational exposure limits.	

					• Healthcare facilities: venting and abatement devices.	
Occupational bystander	Air	Inhalation	Lifetime	Cancer	• Delete uses for which alternatives exist. • Concentration rate limit for new cycles. • Commercial sterilization facilities: Separated HVAC systems for processing and non-processing areas. • Lowered occupational exposure limits. • Commercial sterilization facilities and healthcare facilities: SCBA or supplied air respirators for specific tasks and when EtO concentrations exceed lowered occupational exposure limits. • Healthcare facilities: venting and abatement devices.	
Bystanders (residential and non-residential)	Air	Inhalation	Lifetime	Cancer	• Delete uses for which alternatives exist. • Concentration rate limit for new cycles.	

					• Healthcare facilities: abatement devices. • Commercial sterilization facilities: Emissions reductions as required per OAR's EtO Emissions Standards for Sterilization Facilities.[262]	

[262] EPA-HQ-2019-0178-1482 at www.regulations.gov.

Appendix B: Labeling Changes for EtO Products

Description	Label Language for EtO Products	Placement on Label
Manufacturing Use Products For formulating products for the uses indicated		
Product Formulation	"Formulators using this product are responsible for providing data for the EPA registration of their formulated products."	Directions for Use
Use Deletion	Remove from the label references to the following use sites for which this product can be used for formulation: Museum materials, Library materials, Archival materials, Cosmetics, Musical instruments, Beekeeping equipment.* [* The beekeeping equipment use is on Special Local Needs registration NC140003.]	Directions for Use
Food Use Definition/Identification: Specifying allowable spices and herbs from Crop Group 19, dried vegetables covered by the *Dried Vegetables* tolerance, and black walnut	Deletions are shown with a strikethrough and insertions are shown with an underline. "As A Sterilant and Fumigant Gas This product may be used for formulation into a sterilant/fumigant for the following pesticidal uses only: to sterilize devices (as defined under 21 U.S.C. 321(h)), drugs (as defined under 21 U.S.C. 321(g)(1)), and any associated containers, cartons, inserts, or other packaging of such devices or drugs thereof, or to reduce microbial load on ~~cosmetics, whole and ground spices or other seasoning materials (see 40 C.F.R. 180.151) and artifacts, archival material or library objects~~ the following lists of dried commodities: List 1: Peppermint, tops, dried; Sesame seed; Spearmint, tops, dried; and Vegetable, dried (capsicums, ginger, horseradish, paprika, garlic,	Directions for Use

	onion, turmeric, arrowroot, asparagus, artichoke, green bean, green bell pepper, red bell pepper, broccoli, cabbage, carrot, celery stalk, corn, kelp, leek, mushroom, tomato, galangal, and pumpkin flakes); and List 2: Allspice, Anise (seed); Anise, star; Annatto (seed); Balm, Chamomile (German and Hungarian); Caper (buds); Caraway; Caraway, black; Cardamom; Cassia (bark and buds); Celery (seed); Chervil (dried); Chinese chive; Chive; Cinnamon; Clary; Clove (buds); Coriander (leaf); Coriander (seed); Cumin; Dill (seed); Dillweed; Fennel, common; Fennel, Florence (seed); Fenugreek; Grains of paradise; Horehound; Hyssop; Juniper (berry); Lavender; Lemongrass; Mace; Marjoram (*Origanum* spp.); Mustard (seed); Nutmeg; Parsley (dried); Pepper, black (and pink peppercorns); Pepper, white; Poppy (seed); Rosemary; Saffron; Sage; Savory (summer and winter); Sweet bay; Tarragon; Thyme; Vanilla; and Black Walnut until January 1, 2032. After January 1, 2032, this product may only be used on the commodities in List 2 for reconditioning and retreatment when a secondary treatment is necessary for human pathogen control. Reconditioning with this product may occur when identified in an FDA-approved reconditioning proposal. Retreatment may occur after initial treatment with an alternative to EtO if the initial treatment was ineffective or if the food becomes re-contaminated after the initial treatment. **Reconditioning** is a process by which a food containing unsafe levels of microbial pathogens is subjected to a treatment that reduces the microbial pathogens to an acceptable level. When a food needs reconditioning, a firm submits a reconditioning proposal to FDA to bring the food into compliance. **Retreatment** is the process by which a food is treated for human pathogen control a second time because an initial treatment with an	

	alternative to EtO was ineffective or because the food became re-contaminated after the initial treatment." "This product may only be applied to or on ~~spices, dried vegetables or seasonings~~ the listed commodities utilizing an ETO sterilization method that uses a single sterilization chamber for pre-conditioning, sterilization and aeration …"	
End Use Products for Commercial Sterilization Facilities		
Use Deletion	Remove the following use sites from the label: Museum materials, Library materials, Archival materials, Cosmetics, Musical instruments, and Beekeeping equipment.* [* The beekeeping equipment use is on Special Local Needs registration NC140003.]	Directions for Use
Food Use Definition/Identification: Specifying allowable spices and herbs from Crop Group 19, dried vegetables covered by the *Dried Vegetables* tolerance, and black walnut	Deletions are shown with a strikethrough and insertions are shown with an underline. "As A Sterilant and Fumigant Gas This product may be used only to sterilize devices (as defined under 21 U.S.C. 321(h)), drugs (as defined under 21 U.S.C. 321(g)(1)), and any associated containers, cartons, inserts, or other packaging of such devices or drugs thereof, or to reduce microbial load on ~~cosmetics, whole and ground spices or other seasoning materials (see 40 C.F.R. 180.151) and artifacts, archival material or library objects~~ the following lists of dried commodities: List 1: Peppermint, tops, dried; Sesame seed; Spearmint, tops, dried; and Vegetable, dried (capsicums, ginger, horseradish, paprika, garlic, onion, turmeric, arrowroot, asparagus, artichoke, green bean, green bell pepper, red bell pepper, broccoli, cabbage, carrot, celery stalk,	Directions for Use

	corn, kelp, leek, mushroom, tomato, galangal, and pumpkin flakes); and List 2 Allspice, Anise (seed); Anise, star; Annatto (seed); Balm, Chamomile (German and Hungarian); Caper (buds); Caraway; Caraway, black; Cardamom; Cassia (bark and buds); Celery (seed); Chervil (dried); Chinese chive; Chive; Cinnamon; Clary; Clove (buds); Coriander (leaf); Coriander (seed); Cumin; Dill (seed); Dillweed; Fennel, common; Fennel, Florence (seed); Fenugreek; Grains of paradise; Horehound; Hyssop; Juniper (berry); Lavender; Lemongrass; Mace; Marjoram (*Origanum* spp.); Mustard (seed); Nutmeg; Parsley (dried); Pepper, black (and pink peppercorns); Pepper, white; Poppy (seed); Rosemary; Saffron; Sage; Savory (summer and winter); Sweet bay; Tarragon; Thyme; Vanilla; and Black Walnut until January 1, 2032. After January 1, 2032, this product may only be used on the commodities in List 2 for reconditioning and retreatment when a secondary treatment is necessary for human pathogen control. Reconditioning with this product may occur when identified in an FDA-approved reconditioning proposal. Retreatment may occur after initial treatment with an alternative to EtO if the initial treatment was ineffective or if the food becomes re-contaminated after the initial treatment. **Reconditioning** is a process by which a food containing unsafe levels of microbial pathogens is subjected to a treatment that reduces the microbial pathogens to an acceptable level. When a food needs reconditioning, a firm submits a reconditioning proposal to FDA to bring the food into compliance. **Retreatment** is the process by which a food is treated for human pathogen control a second time because an initial treatment with an alternative to EtO was ineffective or because the food became re-contaminated after the initial treatment.”	

	"This product may only be applied to or on ~~spices, dried vegetables or seasonings~~ the listed commodities utilizing an ETO sterilization method that uses a single sterilization chamber for pre-conditioning, sterilization and aeration …"	
Specification of Use Site for Commercial Sterilization Facilities	"This product is only approved for use in commercial sterilization facilities. This product is not approved for use in healthcare facilities (hospitals, veterinary facilities, dental offices, etc.)."	Directions for Use
Concentration Rate Limit for Medical Device Sterilization	"By January 1, 2035, this product may not be used for medical device sterilization at concentrations greater than 600 mg/L for new cycles unless sterilization of a device requires a concentration of EtO greater than 600 mg/L due to the device design and the facility maintains records to justify the increased application rate. A new cycle is defined as a newly validated cycle specification to be submitted to the FDA that is not in use by any device regulated by FDA as of January 1, 2035. Existing cycles that have previous FDA approval above 600 mg/L concentration and are in use before January 1, 2035, are permitted to continue after January 1, 2035. The sterilization/fumigation cycle parameters are prescribed by the equipment manufacturer. Safety and efficacy validations must be reviewed by FDA and are the responsibility of the user."	Directions for Use
HVAC Systems in Commercial Sterilization Facilities	"By January 1, 2028, this product may not be used in facilities unless non-processing areas, such as office space and control rooms, have separate HVAC systems from EtO processing areas such as sterilization, aeration, and sterilized product storage areas. Each system must have	Directions for Use

	independent intake and exhaust systems that ensure no interaction of air distribution between processing and non-processing areas."	
Removal of references to OSHA 1 ppm Permissible Exposure Limit (PEL), 5 ppm 15-minute Short-Term Exposure Limit (STEL), and 0.5 ppm Action Level	References to OSHA's current 1 ppm PEL, 5 ppm 15-minute STEL, and 0.5 ppm Action Level must be removed from EtO product labels.	Throughout label
EPA Occupational Exposure Limit (8-hour time-weighted average)	"This product may not be used in facilities unless the facility conducts monitoring of worker exposure consistent with 29 C.F.R. § 1910.1047(d) and 1910.1047(l). Determinations of worker exposure shall be made from breathing zone air samples that are representative of the 8-hour time-weighted average of each worker. Facilities must follow the exposure monitoring methods defined in OSHA 29 C.F.R. § 1910.1047(d). Through December 31, 2027, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration greater than an 8-hour time-weighted average occupational exposure limit of 1 ppm. By January 1, 2028, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration greater than an 8-hour time-weighted average occupational exposure limit of 0.5 ppm. By January 1, 2030, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration greater than an 8-hour time-weighted average occupational exposure limit of 0.25 ppm. By January 1, 2035, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration of greater than an 8-hour time-weighted average occupational exposure limit of 0.1 ppm. These occupational exposure limits will apply in lieu of the OSHA PEL of 1 ppm.	Directions for Use

	In meeting these lowered occupational exposure limits, facilities must comply with all requirements outlined in OSHA 29 C.F.R. § 1910.1047 (e)-(i), (j)(1), (j)(2)(i), (j)(3), and (k). For information on monitoring frequency, see OSHA Technical Manual (OTM) Section II: Chapter 1."	
EPA Short-Term Exposure Limit (STEL)	"This product may not be used in facilities unless that facility conducts monitoring of worker exposure consistent with 29 C.F.R. § 1910.1047(d) and 1910.1037(l). Determinations of worker exposure shall be made from breathing zone air samples that are representative of the short-term exposures of each worker. Facilities must follow the exposure monitoring methods defined in OSHA 29 C.F.R. § 1910.1047(d). Through December 31, 2034, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration of greater than a 15-minute time-weighted average short-term exposure limit of 5 ppm. By January 1, 2035, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration of greater than a 10-minute time-weighted average short-term exposure limit of 5 ppm. The EPA STEL will apply in lieu of the OSHA STEL. In meeting with this lowered short-term exposure limit, facilities must comply with all requirements outlined in OSHA 29 C.F.R. § 1910.1047 (e)-(i), (j)(1), (j)(2)(i), (j)(3), and (k)."	Directions for Use
EPA Action Level (8-hour time-weighted average)	"Through December 31, 2025, this product may only be used in facilities that conduct periodic monitoring of worker exposure as outlined in 29 C.F.R. § 1910.1047(d)(3) based on an action level of 0.5 ppm. As of January 1, 2026, this product may only be used in facilities that conduct periodic monitoring of exposure as outlined in 29 C.F.R. §1910.1047(d)(3) based on an action level of 0.1 ppm.	Directions for Use

	In conducting monitoring based on these action levels, facilities must comply with all requirements outlined in 29 C.F.R. § 1910.1047 (e)-(i), (j)(1), (j)(2)(i), (j)(3), and (k)."	
Updated Respirator Language for Commercial Sterilization Facilities	"This product may only be used in facilities in which supplied air/airline (SAR) respirators or self-contained breathing apparatus (SCBA) respirators (full facepiece) are worn by any workers in a commercial sterilization facility engaged in the following tasks, regardless of the EtO concentration inside the facility, by January 1, 2026: • Connecting and disconnecting EtO containers from sterilization process equipment. • Unloading processed products from the sterilization chamber, whether at the end of a cycle for an all-in-one process, or, for a conventional process, preparatory to moving product to the aeration area. • Loading and unloading product from the aeration area. • Removing validation test materials from processed product at any time prior to the completion of aeration. • Opening process lines or equipment that may contain EtO (e.g., for repairs or routine maintenance tasks). Additionally, SAR or SCBA respirators must be worn if the EtO concentration exceeds the EPA occupational exposure limit and/or the short-term exposure limit."	In the Personal Protective Equipment (PPE) section within the Precautionary Statements
Respirator Requirements	**"Respirator Requirements:** See OSHA's Respiratory Protection Standard (29 C.F.R. Part 1910.134) for federal requirements including	In the Personal Protective Equipment

	how to safely fit-test, train, and medically evaluate workers who will be using respirators."	(PPE) within the Precautionary Statements
Stationary Continuous Monitoring Requirement in Commercial Sterilization Facilities	"By January 1, 2026, this product may only be used in commercial sterilization facilities that monitor room air using stationary continuous monitoring devices with detection capabilities at or below 0.1 ppm. Monitoring areas must include all processing (i.e., sterilization, aeration, etc.) and non-processing areas (i.e., office spaces, control rooms, warehouses, etc.). Facilities must follow device manufacturer's instructions for calibration and maintenance of monitoring equipment. Monitoring must be conducted on 2-minute intervals. Data from these monitoring devices must be visible to workers."	Directions for Use
Training Requirements in Commercial Sterilization Facilities	"Information and training must be provided to all workers in the facility at the time of initial assignment to the facility and annually thereafter. The training must be consistent with the training requirements under 29 C.F.R. § 1910.1047 and, to the extent not covered under 29 C.F.R. § 1910.1047, must include the following information: • The most recently monitored levels of EtO in the individual rooms of the facility, using stationary continuous monitoring devices with detection capabilities at or below 0.1 ppm. • The potential health effects from the levels of EtO in the facility. Safety training materials must include the following verbiage: 'EtO is a carcinogen that may cause leukemia and other cancers as a result of long term (chronic) exposure. Acute exposure (short term) to EtO may cause eye pain, sore throat, difficult breathing, blurred vision, dizziness, nausea, headache, convulsions, blisters, vomiting, coughing, spontaneous abortion, genetic damage, nerve damage, peripheral paralysis, muscle weakness, impaired thinking, and impaired memory.'	Directions for Use under the heading "Training Requirements"

	• The emergency response plan and how to respond in an emergency. • The availability of the Safety Data Sheet and other materials related to the health hazards of exposure to EtO."	
Recordkeeping Requirements in Commercial Sterilization Facilities	"This product may not be used in facilities that do not comply with the following recordkeeping requirements. **Recordkeeping Requirements:** Records must be kept in a form suitable and readily available for expeditious review. ***EtO Sterilization Cycle Concentrations*:** By January 1, 2035, facilities must maintain records of the FDA validation for the sterilization of medical devices, which include the EtO concentration rate used to sterilize medical devices. These records must demonstrate adherence to the 600 mg/L concentration rate limit for medical devices for new cycles validated after or not in use before January 1, 2035. If sterilization of a device requires more than 600 mg/L, due to the device design, facilities must additionally maintain records to justify the increased application rate. Records are required to be maintained for two years from the date of sterilization. ***Worker PBZ Monitoring Readings:*** Determinations of worker exposure shall be made from personal breathing zone (PBZ) air samples that are representative of the time-weighted average exposures of each worker. Facilities must follow the exposure monitoring methods as defined in OSHA 29 C.F.R. § 1910.1047 (d). Records of worker PBZ monitoring data and the exposure results must be maintained in facilities to show adherence to the occupational exposure limit and mitigation measures associated with exceedances of the action level. Recordkeeping of worker PBZ monitoring data must be conducted and records maintained consistent with the requirements found in OSHA	Directions for Use under the heading, "Recordkeeping Requirements"

	29 C.F.R. § 1910.1047 (k)(2). Facilities may use improved information technology, including electronic recording, when establishing or maintaining records. ***Indoor EtO Concentrations in Commercial Sterilization Facilities:*** Recordkeeping is required for readings of continuous stationary indoor air monitoring at 0.1 ppm by January 1, 2026. Records must show indoor EtO levels by room/area throughout the entire facility. Facilities must follow device manufacturer's instructions for calibration and maintenance of monitoring equipment and maintain records of equipment calibration. Records are required to be maintained for two years from the date of monitoring. ***Worker Training:*** Facilities must maintain records of training materials that are provided to workers upon assignment and annually thereafter, and records of the dates individual workers are trained. Records are required to be maintained for two years from the date of training, including if the trainee leaves the place of employment before two years. ***Reconditioning/retreatment of dried food commodities:*** After January 1, 2032, facilities must retain records to document an initial treatment, including the method of treatment, and need for reconditioning/retreatment with EtO of Allspice, Anise (seed); Anise, star; Annatto (seed); Balm, Chamomile (German and Hungarian); Caper (buds); Caraway; Caraway, black; Cardamom; Cassia (bark and buds); Celery (seed); Chervil (dried); Chinese chive; Chive; Cinnamon; Clary; Clove (buds); Coriander (leaf); Coriander (seed); Cumin; Dill (seed); Dillweed; Fennel, common; Fennel, Florence (seed); Fenugreek; Grains of paradise; Horehound; Hyssop; Juniper (berry); Lavender; Lemongrass; Mace; Marjoram (*Origanum* spp.); Mustard (seed);	

	Nutmeg; Parsley (dried); Pepper, black (and pink peppercorns); Pepper, white; Poppy (seed); Rosemary; Saffron; Sage; Savory (summer and winter); Sweet bay; Tarragon; Thyme; Vanilla; and Black Walnut. Records are required to be maintained for two years from the date of reconditioning or retreatment."	
End Use Products for Healthcare Facilities		
Specification of Use Site for Healthcare Facility Products	"This product is only approved for use in single chamber sterilization/aeration devices in healthcare facilities (*e.g.*, hospitals, veterinary facilities, dental offices, etc.)."	Directions for Use
Concentration Rate Limit for Medical Device Sterilization	"By January 1, 2035, this product may only be used in facilities that limit the use of EtO for medical device sterilization to concentrations less than or equal to 600 mg/L for new cycles. A new cycle is defined as a newly validated cycle specification to be submitted to the FDA that is not in use by any device regulated by the FDA as of January 1, 2035. If sterilization of a device requires more than 600 mg/L, due to the device design, facilities must maintain records to justify the increased application rate. Existing cycles that have previous FDA approval above 600 mg/L concentration before January 1, 2035, are permitted to continue after January 1, 2035. The sterilization/fumigation cycle parameters are prescribed by the equipment manufacturer. Safety and efficacy validations must be reviewed by FDA and are the responsibility of the user."	Directions for Use
Abatement Devices in Healthcare facilities	"By January 1, 2027, this product may only be used in healthcare facilities (hospitals, veterinary facilities, dental offices, etc.) using EtO single chamber sterilization/aeration devices that utilize emissions-capturing equipment in the form of an abatement device in order to	Directions for Use

	reduce EtO discharge to the environment. Refer to sterilization device manufacturer for information on abatement devices. Healthcare facilities using less than 10 lbs. (4,536g) of EtO per year within the same building are not required to utilize abatement devices. Facilities seeking an exemption from the abatement device requirement must keep the following records: 1) Quantity of EtO in the facility's inventory on January 1, 2027, 2) Quantity and proof of purchase for each EtO acquisition made on and following January 1, 2027, 3) Quantity of EtO used, including an identification of the sterilization device, time and date of each cycle and quantity of EtO used per cycle. Records must be kept for two years from the date they are created."	
Venting of Healthcare Facilities	"By January 1, 2027, this product may only be used in EtO sterilizers in healthcare facilities (hospitals, veterinary facilities, dental offices, etc.) that are vented out of the workplace to the outside atmosphere. A separate exhaust duct to the outside is required. The exhaust duct must terminate away from areas where people walk or work. The duct must be located at least 7.6 meters (25 feet) away from the building air intake source and must be engineered according to existing codes."	Directions for Use
Removal of references to OSHA 1 ppm Permissible Exposure Limit (PEL), 5 ppm 15-minute Short-Term Exposure Limit (STEL), and 0.5 ppm Action Level	References to OSHA's current 1 ppm PEL, 5 ppm 15-minute STEL, and 0.5 ppm Action Level must be removed from EtO product labels.	Throughout label
EPA Occupational Exposure Limit **(8-hour time-weighted average)**	"This product may only be used in facilities that conduct monitoring of worker exposure consistent with 29 C.F.R. § 1910.1047(d) and 1910.1047(l). Determinations of worker exposure shall be made from breathing zone air samples that are representative of the 8-hour time-	Directions for Use

	weighted average of each worker. Facilities must follow the exposure monitoring methods defined in OSHA 29 C.F.R. § 1910.1047 (d). Through December 31, 2027, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration greater than an 8-hour time-weighted average occupational exposure limit of 1 ppm. By January 1, 2028, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration greater than an 8-hour time-weighted average occupational exposure limit of 0.5 ppm. By January 1, 2030, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration greater than an 8-hour time-weighted average occupational exposure limit of 0.25 ppm. By January 1, 2035, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration greater than an 8-hour time-weighted average occupational exposure limit of 0.1 ppm. These occupational exposure limits will apply in lieu of the OSHA PEL of 1 ppm. In meeting these lowered occupational exposure limits, facilities must comply with all requirements outlined in 29 C.F.R. § 1910.1047. For information on monitoring frequency, see OSHA Technical Manual (OTM) Section II: Chapter 1."	
EPA Short-Term Exposure Limit (STEL)	"This product may only be used in facilities that conduct monitoring of worker exposure consistent with 29 C.F.R. § 1910.1047(d) and 1910.1047(l). Determinations of worker exposure shall be made from breathing zone air samples that are representative of the short-term exposure of each worker. Facilities must follow the exposure monitoring methods as defined in OSHA 29 C.F.R. § 1910.1047(d). Through December 31, 2034, facilities are required to ensure that workers are not exposed to EtO at an airborne concentration of greater than a 15-minute time-weighted average short-term exposure limit of 5 ppm. By January 1, 2035, facilities are required to ensure that	Directions for Use

	workers are not exposed to EtO at an airborne concentration of greater than a 10-minute time-weighted average short-term exposure limit of 5 ppm. This EPA STEL will apply in lieu of the OSHA STEL. In meeting this lowered short-term exposure limit, facilities must comply with all requirements outlined in OSHA 29 C.F.R. § 1910.1047."	
EPA Action Level (8-hour time-weighted average)	"Through December 31, 2025, this product may only be used in facilities that conduct periodic monitoring of worker exposure as outlined in 29 C.F.R. § 1910.1047(d)(3) based on an action level of 0.5 ppm. As of January 1, 2026, this product may only be used in facilities that conduct periodic monitoring of exposure as outlined in 29 C.F.R. § 1910.1047(d)(3) based on an action level of 0.1 ppm. In conducting monitoring based on these action levels, facilities must comply with all requirements outlined in 29 C.F.R. § 1910.1047."	Directions for Use
Updated Respirator Language for Healthcare Facilities	"This product may not be used in facilities unless supplied air/airline (SAR) respirators or self-contained breathing apparatus (SCBA) respirators (full facepiece) are worn if the EtO concentration exceeds the occupational exposure limit and/or the short-term exposure limit."	In the Personal Protective Equipment (PPE) within the Precautionary Statements
Respirator Requirements	**"Respirator Requirements:** See OSHA's Respiratory Protection Standard (29 C.F.R. Part 1910.134) for federal requirements including how to safely fit-test, train, and medically examine workers who will be using respirators."	In the Personal Protective Equipment (PPE) within the Precautionary Statements
Training Requirements in Healthcare Facilities	"Information and training must be provided to all workers in the facility at the time of initial assignment and annually thereafter. The training must be consistent with the training requirements under 29 C.F.R. § 1910.1047 and, to the extent not covered under 29 C.F.R. § 1910.1047, must include the following information:	Directions for Use under the heading "Training Requirements"

	• The potential health effects from the levels of EtO in the facility. Safety training materials must include the following verbiage: 'EtO is a carcinogen that may cause leukemia and other cancers due to chronic exposure. Acute exposure to EtO may cause eye pain, sore throat, difficult breathing, blurred vision, dizziness, nausea, headache, convulsions, blisters, vomiting, coughing, spontaneous abortion, genetic damage, nerve damage, peripheral paralysis, muscle weakness, impaired thinking, and impaired memory.' • The emergency response plan and how to respond in an emergency. • The availability of the Safety Data Sheet and other materials related to the health hazards of exposure to EtO. Healthcare facility employers may refer to the Association for the Advancement of Medical Instrumentation's (AAMI's) most recent version of the ANSI/AAMI Standard ST41:2008(R)2018 *Ethylene Oxide Sterilization in Health Care Facilities: Safety and Effectiveness* and OSHA's *Small Business Guide for Ethylene Oxide* for additional details and resources related to training workers."	
Recordkeeping Requirements in Healthcare Facilities	"This product may not be used in facilities that do not comply with the following recordkeeping requirements. **Recordkeeping Requirements:** Records must be kept in a form suitable and readily available for expeditious review. ***EtO Sterilization Cycle Concentrations*:** By January 1, 2035, facilities must maintain records of the FDA validation for the sterilization of medical devices, which include the EtO concentration rate used to sterilize medical devices. These records must demonstrate adherence to the 600 mg/L concentration rate limit for medical devices for new	

	cycles validated after or not in use before January 1, 2035. If sterilization of a device requires more than 600 mg/L, due to the device design, facilities must additionally maintain records to justify the increased application rate. Records are required to be maintained for two years from the date of sterilization. ***Worker PBZ Monitoring Readings:*** Determinations of worker exposure shall be made from personal breathing zone (PBZ) air samples that are representative of the time-weighted average exposures of each worker. Facilities must follow the exposure monitoring methods as defined in 29 C.F.R. § 1910.1047 (d). Records of worker PBZ monitoring data and the exposure results must be maintained in facilities to show adherence to the occupational exposure limit and mitigation measures associated with exceedances of the action level. Recordkeeping of worker PBZ monitoring data must be conducted and records maintained consistent with the requirements found in OSHA 29 C.F.R. § 1910.1047(k)(2). Facilities may use improved information technology, including electronic recording, when establishing or maintaining records. ***Worker Training:*** Facilities must maintain records of training materials that are provided to workers upon assignment and annually thereafter, and records of the dates individual workers are trained. Records are required to be maintained for two years from the date of training, including if the trainee leaves the place of employment before two years. ***Healthcare facilities seeking exemption from abatement device requirement:*** Facilities seeking an exemption from the abatement device requirement must record the number of cycles run in each sterilization device. Recordkeeping is required to demonstrate that	

	less than 10 lbs of EtO is used per year within the same building if a facility seeks an exemption from the abatement requirement. Records must include: 1) Quantity of EtO in the facility's inventory on the January 1, 2027; 2) Quantity and proof of purchase for each EtO acquisition made on and following January 1, 2027; 3) Quantity of EtO used, including an identification of the sterilization device, time and date of each cycle and quantity of EtO used per cycle. Records must be kept for two years from the date they are created."	

Appendix C: Listed-Species Assessment

This Appendix provides general background about the Agency's assessment of the effects of pesticides on listed species and designated critical habitats under the Endangered Species Act (ESA).

Developing Approaches for ESA Assessments and Consultation for FIFRA Actions

In 2015, EPA, along with the Services—the U.S. Fish and Wildlife Service (FWS) and the National Marine Fisheries Service (NMFS)—and the United States Department of Agriculture (USDA) (referred to as "the agencies") released their joint Interim Approaches[263] for assessing the effects of pesticides to listed species. The agencies jointly developed these Interim Approaches in response to the 2013 National Academy of Sciences' recommendations that discussed specific scientific and technical issues related to the development of assessments of pesticides' effects to listed species. Since that time, the agencies have been continuing to work to improve the approaches for assessing effects to listed species. After receiving input from the Services and USDA on required revisions to the interim method and after consideration of public comments received, EPA released an updated *Revised Method for National Level Listed Species Biological Evaluations of Conventional Pesticides* ("Revised Method") in March 2020.[264]

The agencies also continue to work collaboratively through a FIFRA Interagency Working Group (IWG). The IWG was created under the 2018 Farm Bill to recommend improvements to the ESA section 7 consultation process for FIFRA actions and to increase opportunities for stakeholder input. This group is led by EPA and includes representatives from NMFS, FWS, USDA, and the Council on Environmental Quality (CEQ). The IWG outlines its recommendations and progress on implementing those recommendations in reports to Congress.[265]

Consultation on Chemicals in Registration Review

EPA initially conducted biological evaluations (BEs) using the interim method on three pilot chemicals representing the first nationwide pesticide consultations (final pilot BEs for chlorpyrifos, malathion, and diazinon were completed in January 2017). These initial pilot consultations were envisioned as the start of an iterative process. Later that year, NMFS issued a final biological opinion for these three pesticides. In 2019, EPA requested to reinitiate formal consultation with NMFS on malathion, chlorpyrifos and diazinon to consider new information that was not available when NMFS issued its 2017 biological opinion.

[263] https://www.epa.gov/endangered-species/interim-approaches-pesticide-endangered-species-act-assessments-based-nas-report.
[264] https://www.epa.gov/endangered-species/revised-method-national-level-listed-species-biological-evaluations-conventional.
[265] https://www.epa.gov/endangered-species/reports-congress-improving-consultation-process-under-endangered-species-act.

In 2020, EPA released draft BEs for the first two chemicals conducted using the 2020 Revised Method—carbaryl and methomyl. Subsequently, EPA has used the Revised Method to complete final BEs for carbaryl, methomyl, atrazine, simazine, glyphosate, clothianidin, imidacloprid, and thiamethoxam. EPA is currently in consultation with the Services on these active ingredients.

EPA received a final malathion biological opinion from FWS in February 2022 and a final biological opinion from NMFS on malathion, chlorpyrifos and diazinon in June 2022.[266] In August 2023, the Agency implemented the FWS malathion biological opinion by issuing Endangered Species Protection Bulletins[267] and approving malathion label amendments[268] to incorporate measures to protect listed species. In March 2024, EPA implemented the NMFS biological opinion for malathion, chlorpyrifos (for non-food uses), and diazinon.[269] EPA was granted an extension by NMFS to implement the NMFS biological opinion for the food uses of chlorpyrifos by September 2024.

EPA's New Actives Policy and the 2022 Workplan

In January 2022, EPA announced a policy[270] to evaluate potential effects of new conventional pesticide active ingredients to listed species and their designated critical habitat and initiate consultation with the Services, as appropriate, before registering these new pesticides. Before the Agency registers new uses of pesticides for use on pesticide-tolerant crops, EPA will also continue to make effects determinations. If these determinations are "likely to adversely affect," the Agency will not register the use unless it can predict that registering the new use would not have a likelihood of jeopardizing listed species or adversely modifying their designated critical habitats. EPA will also initiate consultation with the Services as appropriate.

In April 2022, EPA released a comprehensive, long-term approach to meeting its ESA obligations, which is outlined in *Balancing Wildlife Protections and Responsible Pesticide Use*.[271] This workplan reflects the Agency's most comprehensive thinking to date on how to create a sustainable ESA-FIFRA program that focuses on meeting EPA's ESA obligations and improving protection for listed species while minimizing regulatory impacts to pesticide users and collaborating with other agencies and stakeholders on implementing the plan.

[266] https://www.epa.gov/endangered-species/biological-opinions-available-public-comment-and-links-final-opinions.
[267] https://www.epa.gov/endangered-species/endangered-species-protection-bulletins.
[268] https://www.regulations.gov/document/EPA-HQ-OPP-2009-0317-0154.
[269] https://www.epa.gov/pesticides/epa-announces-implementation-mitigation-measures-insecticides-chlorpyrifos-diazinon-and#:~:text=For%20chlorpyrifos%2C%20diazinon%2C%20and%20malathion,one%20or%20more%20listed%20species.
[270] https://www.epa.gov/newsreleases/epa-announces-endangered-species-act-protection-policy-new-pesticides.
[271] https://www.epa.gov/endangered-species.

On November 16, 2022, EPA released the *ESA Workplan Update: Nontarget Species Mitigation for Registration Review and Other FIFRA Actions*.[272] As part of this update, EPA announced its plan to consider and include, as appropriate, a menu of FIFRA Interim Ecological Risk Mitigation intended to reduce off-target movement of pesticides through spray drift and runoff in its registration review and other FIFRA actions. These measures are intended to reduce risks to nontarget organisms efficiently and consistently across pesticides with similar levels of risks and benefits. EPA expects that these mitigation measures may also reduce pesticide exposures to listed species.

The *ESA Workplan Update* also discussed additional efforts to expedite and streamline ESA consultation, including the Vulnerable Species Pilot, regional strategies (i.e., a Hawaii strategy), approaches for specific niche pesticide uses (e.g., mosquito adulticide applications), and programmatic approaches to consultation (e.g., the Herbicide Strategy). Recently, EPA has released the following:

- **July 2024:** EPA published the Draft Insecticide Strategy for public comment. The Draft Insecticide Strategy is focused on identifying measures to protect listed species from use of conventional insecticides in agriculture in the lower 48 states.[273]
- **August 2024:** EPA published the Final Herbicide Strategy which is focused on identifying measures to protect listed species from use of conventional herbicides in agriculture in the lower 48 states.[274]
- **September 2024:** EPA announced the Vulnerable Species Action Plan, which provides a framework to adopt early protections to address potential impacts to listed species that EPA identifies as particularly vulnerable to pesticides.[275]

EPA continues to work on these pilot efforts and strategies. Once finalized, EPA expects to implement them through registration review and new active ingredient registration.

[272] https://www.epa.gov/system/files/documents/2022-11/esa-workplan-update.pdf.
[273] https://www.regulations.gov/document/EPA-HQ-OPP-2024-0299-0005.
[274] https://www.regulations.gov/document/EPA-HQ-OPP-2023-0365-1137.
[275] https://www.regulations.gov/document/EPA-HQ-OPP-2023-0327-0208.

Appendix D: Endocrine Disruptor Screening Program

The Federal Food Drug and Cosmetic Act (FFDCA) § 408(p) requires EPA to develop a screening program to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." (21 U.S.C. 346a(p)). In carrying out the Endocrine Disruptor Screening Program (EDSP), FFDCA section 408(p)(3) requires that EPA "provide for the testing of all pesticide chemicals," which includes "any substance that is a pesticide within the meaning of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), including all active and pesticide inert ingredients of such pesticide." (21 U.S.C. 231(q)(1) and 346a(p)(3)). However, FFDCA section 408(p)(4) authorizes EPA to, by order, exempt a substance from the EDSP if the EPA "determines that the substance is anticipated not to produce any effect in humans similar to an effect produced by a naturally occurring estrogen." (21 U.S.C. 346a(p)(4)).

The EDSP initiatives developed by EPA in 1998 includes human and wildlife testing for estrogen, androgen, and thyroid pathway activity and employs a two-tiered approach. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid pathways. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance and establish a dose-response relationship for any adverse estrogen, androgen, or thyroid effect. If EPA finds, based on that data, that the pesticide has an adverse endocrine-related effect on humans, FFDCA § 408(p)(6) also requires EPA, "… as appropriate, [to] take action under such statutory authority as is available to the Administrator … as is necessary to ensure the protection of public health." (21 U.S.C. 346a(p)(6)).[276]

Between October 2009 and February 2010, EPA issued Tier 1 test orders/data call-ins (DCIs) for its first list of chemicals ("List 1 chemicals") for EDSP screening and subsequently required submission of EDSP Tier 1 data for a refined list of these chemicals. EPA received data for 52 List 1 chemicals (50 pesticide active ingredients and 2 inert ingredients). EPA scientists performed weight-of-evidence (WoE) analyses of the submitted EDSP Tier 1 data and other scientifically relevant information (OSRI) for potential interaction with the estrogen, androgen, and/or thyroid signaling pathways for humans and wildlife.[277]

In addition, for FIFRA registration, registration review, and tolerance-related purposes, EPA collects and reviews numerous studies to assess potential adverse outcomes, including potential outcomes to endocrine systems, from exposure to pesticide active ingredients. Although EPA has been collecting and reviewing such data, EPA has not been explicit about how its review of required and submitted data for these purposes also informs EPA's obligations and commitments under FFDCA section 408(p). Consequently, on October 27, 2023, EPA issued a

[276] For additional details of the EDSP, please visit https://www.epa.gov/endocrine-disruption.
[277] Summarized in Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions; EPA-HQ-OPP-2023-0474-0001; https://www.regulations.gov/document/EPA-HQ-OPP-2023-0474-0001.

Federal Register Notice (FRN) providing clarity on the applicability of these data to FFDCA section 408(p) requirements and near-term strategies for EPA to further its compliance with FFDCA section 408(p). This FRN, entitled Endocrine Disruptor Screening Program (EDSP): Near-Term Strategies for Implementation' Notice of Availability and Request for Comment (88 FR 73841) is referred to here as EPA's EDSP Strategies Notice. EPA also published three documents supporting the strategies described in the Notice:

- Use of Existing Mammalian Data to Address Data Needs and Decisions for Endocrine Disruptor Screening Program (EDSP) for Humans under FFDCA Section 408(p);
- List of Conventional Registration Review Chemicals for Which an FFDCA Section 408(p)(6) Determination is Needed; and,
- Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions (referred to here as List 1 Screening Conclusions).

The EDSP Strategies Notice and the support documents are available on www.regulations.gov in docket number EPA-HQ-OPP-2023-0474. As explained in these documents, EPA is prioritizing its screening for potential impacts to the estrogen, androgen, and thyroid systems in humans, focusing first on conventional active ingredients. Although EPA voluntarily expanded the scope of the EDSP to screening for potential impacts to the estrogen, androgen, and thyroid systems in wildlife, EPA announced that it is not addressing this discretionary component of the EDSP at this time, taking into account its current focus on its comprehensive, long-term approach to meeting its Endangered Species Act obligations (See EPA's April 2022 ESA Workplan[278] and November 2022 ESA Workplan Update).[279] However, EPA notes that for 35 of the List 1 chemicals (33 active ingredients and 2 inert ingredients), Tier 1 WoE memoranda[280] indicate that available data were sufficient for FFDCA section 408(p) assessment and review for potential effects to the estrogen, androgen, or thyroid pathways for wildlife. For the remaining 17 List 1 chemicals, Tier 1 WoE memoranda made recommendations for additional testing. EPA expects to further address these issues taking into account additional work being done in concert with researchers within the EPA's Office of Research and Development (ORD).

As discussed in EPA's EDSP Strategies Notice and supporting documents, EPA will be using all available data to determine whether additional data are needed to meet EPA's obligations and discretionary commitments under FFDCA section 408(p). For some conventional pesticide active ingredients, the toxicological databases may already provide sufficient evaluation of the chemical's potential to interact with estrogen, androgen, and/or thyroid pathways and EPA will generally not need to obtain any additional data to reevaluate those pathways, if in registration review, or to provide an initial evaluation for new active ingredient applications. For instance, EPA has endocrine-related data for numerous conventional pesticide active ingredients through

[278] https://www.epa.gov/system/files/documents/2022-04/balancing-wildlife-protection-and-responsible-pesticide-use_final.pdf.
[279] https://www.epa.gov/system/files/documents/2022-11/esa-workplan-update.pdf.
[280] https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and.

either a two-generation reproduction toxicity study performed in accordance with the current guideline (referred to here as the updated two-generation reproduction toxicity study; OCSPP 870.3800 - Reproduction and Fertility Effects) or an extended one-generation reproductive toxicity (EOGRT) study (OECD Test Guideline 443 - Extended One-Generation Reproductive Toxicity Study). In these cases, EPA expects to make FFDCA 408(p)(6) decisions for humans without seeking further estrogen or androgen data. However, as also explained in the EPA's EDSP Strategies Notice, where these data do not exist, EPA will reevaluate the available data for the conventional active ingredient during registration review to determine what additional data, if any, might be needed to confirm EPA's assessment of the potential for impacts to estrogen, androgen, and/or thyroid pathways in humans. For more details on EPA's approach for assessing these endpoints, see EPA's EDSP Strategies Notice and related support documents.

Also described in the EPA's EDSP Strategies Notice is a framework that represents an initial approach by EPA to organize and prioritize the large number of conventional pesticides in registration review. For conventional pesticides with a two-generation reproduction toxicity study performed under a previous guideline (i.e., an updated two-generation reproduction toxicity study or an EOGRT is not available), EPA has used data from the Estrogen Receptor Pathway and/or Androgen Receptor Pathway Models to identify a group of chemicals with the highest priority for potential data collection (described in EPA's EDSP Strategies Notice as Group 1 active ingredients). For these cases, although EPA has not reevaluated the existing endocrine-related data, EPA has sought additional data and information in response to the issuance of EPA's EDSP Strategies Notice to better understand the positive findings in the ToxCast™ data for the Pathway Models and committed to issuing DCIs to require additional EDSP Tier 1 data to confirm the sufficiency of data to support EPA's assessment of potential adverse effects to the estrogen, androgen, and/or thyroid pathways in humans and to inform FFDCA 408(p) data decisions. For the remaining conventional pesticides (described in EPA's EDSP Strategies Notice as Group 2 and 3 conventional active ingredients), EPA committed to reevaluating the available data to determine what additional studies, if any, might be needed to confirm EPA's assessment of the potential for impacts to endocrine pathways in humans.

Although EPA has prioritized conventional active ingredients as presented in EPA's EDSP Strategies Notice, EPA is planning to develop similar strategies for biopesticide and antimicrobial pesticide (i.e., nonconventional) active ingredients and will provide public updates on these strategies, when appropriate. At this time, EPA is making no findings associated with the implementation of EDSP screening of EtO. Such issues will be addressed in future updates by EPA on its strategies for implementing FFDCA section 408(p).

Appendix E: Summary of Public Comments on the Proposed Interim Decision (PID) and Agency Responses

During the 75-day public-comment period for the EtO PID (April 13, 2023 to June 27, 2023), the Agency received over 30,000 public comments, many of which were mass mailers. Comments were submitted by representatives from government, non-profit groups, private citizens, hospitals, bioscience industry, physicians' organizations, medical device distributors, medical device manufacturers, states, small businesses, and commercial sterilization facilities. The Agency has summarized and responded to all substantive comments and comments of a broader regulatory nature below. The Agency thanks all commenters for participating and has considered all comments in developing this ID.

For responses to science-related comments on the *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*, please see the document *Response to Public Comments on the Ethylene Oxide (EtO) Draft Risk Assessment (DRA) Addendum* in docket EPA-HQ-OPP-2013-0244 at www.regulations.gov.

Extension Requests on PID Public Comment Period

Comments Summary:

EPA received 13 requests from 10 commenters to extend the 60-day public comment period on the EtO PID: Medical Alley, Ethylene Oxide Sterilization Association (EOSA), Ethylene Oxide Task Force (EOTF), American Spice Trade Association (ASTA), Illinois Biotechnology Innovation Organization (IBIO), Baxter Healthcare Corporation, Health Industry Distributors Association (HIDA), Sterigenics, Elite Spice, and AdvaMed. The requests spanned from a 30-day extension to a 120-day extension.[281]

EPA Response:

EPA published the EtO PID on April 13, 2023, with an original 60-day public comment period to end on June 12, 2023. EPA granted a 15-day extension, for a total of a 75-day public comment period that ended on June 27, 2023.

[281] EPA-HQ-OPP-2013-0244-0089, EPA-HQ-OPP-2013-0244-0069, EPA-HQ-OPP-2013-0244-0076, EPA-HQ-OPP-2013-0244-0066, EPA-HQ-OPP-2013-0244-0075, EPA-HQ-OPP-2013-0244-0064, EPA-HQ-OPP-2013-0244-0078, EPA-HQ-OPP-2013-0244-0115, EPA-HQ-OPP-2013-0244-0071, EPA-HQ-OPP-2013-0244-0070, EPA-HQ-OPP-2013-0244-0068, EPA-HQ-OPP-2013-0244-0065 at www.regulations.gov.

EPA Use of the IRIS Assessment

Comments Summary:

EPA received two public comments supporting the use of the IRIS assessment as the best available science for the 2023 DRA Addendum. These comments were submitted by the community activist group Stop Sterigenics and the California Division of Occupational Safety and Health (Cal/OSHA).[282]

EPA received ten public comments debating the use of the IRIS assessment for the 2023 DRA Addendum. Most submitters represented industry: Medtronic, the U.S. Chamber of Commerce, American Chemistry Council (ACC), AdvaMed, Sterigenics, Midwest Sterilization Corporation (MSC), Becton Dickinson (BD), and combined comments from CropLife America (CLA) and Responsible Industry for a Sound Environment (RISE), and the Ethylene Oxide Task Force (EOTF) and the Ethylene Oxide Sterilization Association (EOSA). EPA also received a comment from the Texas Commission on Environmental Quality (TCEQ) debating the use of the IRIS assessment.[283] Of these comments, five discussed EPA's use of the Inhalation Unit Risk (IUR) values from the 2016 IRIS Assessment in a manner substantially similar to the comments submitted to the OAR NESHAP proposed rulemaking docket (ACC, AdvaMed, BD, MSC, and EOTF and EOSA), while the remaining four were similar to those submitted to the OAR docket with slight variation (Medtronic, TCEQ, U.S. Chamber of Commerce, and Sterigenics) about the specifics of worker exposure. Of note, regarding worker exposure, TCEQ stated that quantitative comparisons of actual worker risk estimates to EPA's estimated cancer risks demonstrate that EPA over-predicts occupational worker risks.[284] Similarly, regarding worker exposure, Sterigenics stated that the EPA's risk calculations and proposed worker protection measures are contrary to the findings of the NIOSH study upon which they are based.[285] CLA and RISE characterized the 2016 IRIS assessment as flawed science and also discussed concerns with its application in the registration review process and potential resulting risks of supply chains disruptions impacting American agriculture, homes, and businesses.[286]

EPA Response:

The EPA acknowledges the comments from Stop Sterigenics and Cal/OSHA in support of the current IRIS cancer risk value for EtO and agrees that it reflects the latest scientific knowledge and is the result of an extensive review process.

[282] EPA-HQ-OPP-2013-0244-0144, EPA-HQ-OPP-2013-0244-0138 at www.regulations.gov.
[283] EPA-HQ-OPP-2013-0244-0116, EPA-HQ-OPP-2013-0244-0129, EPA-HQ-OPP-2013-0244-0093, EPA-HQ-OPP-2013-0244-0143, EPA-HQ-OPP-2013-0244-0097, EPA-HQ-OPP-2013-0244-0141, EPA-HQ-OPP-2013-0244-0119, EPA-HQ-OPP-2013-0244-0121, EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[284] EPA-HQ-OPP-2013-0244-0129 at www.regulations.gov.
[285] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.
[286] EPA-HQ-OPP-2013-0244-0133 at www.regulations.gov.

In response to the comments from industry and TCEQ which call into question the use of the IRIS assessment, all topics of concern have been summarized and responded to in the OAR document *Summary of Public Comments and Responses for Risk and Technology Review for Ethylene Oxide Commercial Sterilization Facilities* which can be found at www.regulations.gov in the document EPA-HQ-OAR-2019-0178-1595 (See Chapter 5: IRIS EtO Assessment). To the extent relevant, EPA incorporates the responses to these comments into this Appendix E by reference.

Finally, as discussed further in Appendix F, when the use of a pesticide results in non-dietary cancer risks that exceed 1 x 10^{-4}, EPA generally concludes that such use will result in unreasonable adverse effects. However, in cases with extremely high benefits, this conclusion may vary, and EPA seeks to identify measures, which may range from training and PPE to cancellation or suspension of a pesticide, to reduce individual cancer risks to the greatest extent feasible, preferably to 1 x 10^{-6} or less. Sometimes, however, EPA may not be able to identify feasible mitigation measures that would reduce risks below 1 x 10^{-4}, taking into consideration the benefits of the use of the pesticide and the costs associated with mitigation measures that would reduce such risks. In that case, EPA would identify mitigation measures that would reduce cancer risks to the greatest extent feasible.

Notably, commenters do not argue that there are not risks of concern to workers—in fact Sterigenics expressed support for certain of the risk mitigation measures proposed in the PID[287] —but rather raise arguments about the extent of such risks. Here, based on public comments received on the PID and extensive engagement with stakeholders, EPA believes that the mitigation measures included in this ID are necessary to reduce inhalation risks of concern greater than 1 x 10^{-4} to the greatest extent feasible at this time considering the technological feasibility of the mitigation measures and the impacts on the most highly beneficial uses of EtO—the sterilization of medical devices and fumigation of certain food commodities. Finally, EPA does not expect that the mitigation measures included in this ID will reduce risks to workers to below 1 x 10^{-4}. As a result, the concerns raised by commenters about EPA's consideration of the IRIS IUR values in developing risk mitigation measures described in the PID are not relevant to the mitigation measures identified by EPA as necessary in this ID.

Use of Protection Factors for Respirators in Worker Exposure Assessment

Comments Summary:

EPA received a comment from Cal-OSHA regarding the use of respirator protection factors to adjust exposure concentrations in the Sterilization Plants study in the 2023 Draft Risk Assessment Addendum (DRA). Cal-OSHA stated that this reduction could underestimate the risk for workers, especially occupational bystanders not subject to the higher levels of protection called for in the PID. Cal-OSHA further stated that PPE is the hardest control to effectively

[287] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.

implement and has the highest failure rate. Cal-OSHA suggested that using the actual air concentrations in the Sterilization Plants study would provide a more accurate estimate of exposure for workers not directly handling EtO.[288]

EPA Response:

EPA received a similar comment on the 2020 Draft Risk Assessment (DRA) from Earthjustice et. al.[289] The response to this comment was posted in the public docket with the PID.[290] The study report indicates the current industry standard is to use supplied air respiratory protection. Therefore, EPA determined that it was appropriate here to consider respirator use when calculating exposure. As stated in the 2020 DRA RTC, 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.

EPA stated in the 2023 DRA Addendum that 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. As stated in the ID, since the previously submitted data did not provide detailed enough information for EPA to make this more accurate estimation, the Agency will issue a Data Call-In (DCI) for OCSPP GLN 875.1400 Indoor Inhalation and require a protocol before monitoring begins. Based on non-specificity and lack of detail in previously submitted worker exposure data from commercial sterilization facilities treating medical devices, EPA intends to require, through a DCI, air monitoring of the occupational handlers specifically involved in fumigation activities (e.g., loading and unloading chambers, routine maintenance, product transfer), documentation of what activities each worker did while monitored, and whether they were wearing a respirator or not (and what type) for all commercial sterilization facilities. For non-handlers in the facility (e.g., office workers, warehouse workers), EPA also intends to require air monitoring data through a DCI.

[288] EPA-HQ-OPP-2013-0244-0138 at www.regulations.gov.
[289] EPA-HQ-OPP-2013-0244-0038 at www.regulations.gov.
[290] Response to Public Comments for the Ethylene Oxide (EtO) Draft Risk Assessment (DRA). March 27, 2023. EPA-HQ-OPP-2013-0244-0046 at www.regulations.gov.

Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Food Quality Protection Act (FQPA) Requirements

Comments Summary:

EPA received three comments that stated OPP is not meeting their obligations under FIFRA and FQPA. Earthjustice et. al. asserted that EPA's proposed changes to the EtO's registration fall short of FIFRA's mandate to eliminate unreasonable risks, including risks to communities near off-site warehouses where EtO sterilized products are stored and to communities near healthcare facilities where EtO is used—both because EPA has understated the extent of those risks and because it has failed to adequately mitigate the risks it did find. Earthjustice et. al. suggested EPA strengthen its interim registration review decision by prohibiting all unnecessary uses of EtO sterilization and imposing greater protections on any uses that remain. Earthjustice et. al. further asserted that the proposed mitigation in the Sterilizers NESHAP satisfying EPA's obligations under the Clean Air Act is wholly separate from whether the mitigation in the PID satisfies FIFRA's registration standard.[291]

EPA also received a comment from the Attorneys General of New York, Connecticut, Illinois, Maryland, Massachusetts, Michigan, New Jersey, Oregon, Rhode Island, Vermont, and Wisconsin. The Attorneys General stated that EPA failed to quantitatively assess risks to residential bystanders near healthcare facilities. The Attorneys General further stated that EPA's proposed mitigation measures do not reduce risk to acceptable levels.[292]

Conversely, Terumo, who represents industry, stated that the proposed mitigation measures are not supported by the administrative record, and that the explanations for some of the proposed mitigation measures in the PID are incomplete. Terumo did not approve of the use of Data Call Ins ("DCI") to request information from registrants to supplement EPA's analysis, asserting that EPA should not rely on this DCI information without publicly providing it in a supplemental proposal.[293]

EPA Response:

EPA has identified inhalation risks of concern from EtO to workers inside commercial sterilization facilities, healthcare facilities, and to those treating beekeeping equipment in North Carolina. EtO also has the potential to pose inhalation risks of concern to communities near facilities where EtO is used. Therefore, EPA has identified mitigation necessary to mitigate these risks at this point in the ongoing registration review process. However, this ID is not a decision on whether EtO registrations continue to satisfy the FIFRA standard for registration and implementing the mitigation identified in this ID may not be sufficient for EPA to determine that EtO registrations do so ultimately. Based on information received from data call-ins (DCI's)

[291] EPA-HQ-OPP-2013-0244-0140 at www.regulations.gov.
[292] EPA-HQ-OPP-2013-0244-0106 at www.regulations.gov.
[293] EPA-HQ-OPP-2013-0244-0146 at www.regulations.gov.

that the Agency plans to issue to better understand worker exposure in commercial sterilization facilities and warehouses, EPA may determine that additional mitigations or other measures are necessary in a subsequent interim determination or its final registration review decision.

In identifying mitigation measures necessary at this point in the registration review process, EPA has considered the available information about the risks of EtO, the benefits of the use of EtO, and how mitigation measures to address risks would impact the benefits of the use of EtO. While FIFRA requires EPA to evaluate the economic, social, and environmental costs and benefits of the use of any pesticide," the statute provides discretion to determine how to describe, evaluate, and weigh those factors. Consistent with other EPA and federal government guidance, OPP does not view this evaluation of risks and benefits as requiring a quantitative comparison. EPA guidance advises that "if important costs or benefits categories cannot be expressed quantitatively, they should be discussed qualitatively."[294]

When considering risk mitigation measures to address identified risk, EPA considers the impact of imposing each mitigation measure. In short, this involves weighing how much risk reduction may be achieved by a particular mitigation measure against how much impact imposing that mitigation measure will have on the net benefits of using the pesticide. Generally, if a pesticide is determined to provide high benefits, that means that its use is of great importance (e.g., the pesticide is highly effective, and lacks identified alternatives). If identified measures to fully mitigate risk would significantly impact or reduce the benefits estimated from the use of the pesticide (i.e., essentially or actually prohibiting the use of the pesticide), the Agency may consider whether a less stringent mitigation strategy could effectively reduce risks to the point where any remaining risks are outweighed by the high benefits of the pesticide. This strategy is consistent with the FIFRA standard to ensure that risks are not "unreasonable" while "taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."

In identifying mitigation measures necessary to address identified risks of concern at this point in the registration review process, EPA carefully considered the risks and benefits of the use of EtO. While EPA did not quantify certain risks, or the impact that available mitigation measures would have on those risks, EPA considered the risks identified by commenters, consistent with its obligations under FIFRA. For example, with respect to the risks to residential and non-residential bystanders from the use of EtO at healthcare facilities, EPA explained in the PID (page 18) that exposures to these populations are expected to be "minimal" because the amount of EtO used at healthcare facilities is "much smaller" than at commercial sterilization facilities.

[294] Environmental Protection Agency (EPA). 2010. Guidelines for preparing economic analyses, https://www.epa.gov/environmental-economics/guidelines-preparing-economic-analyses; *see also* Office of Management and Budget (OMB). 2003. Executive Office of the President, OMB Circular A-4, Regulatory Analysis. https://www.whitehouse.gov/wp-content/uploads/legacy_drupal_files/omb/circulars/A4/a-4.pdf ("if you are not able to quantify the [cost or benefit] effects, you should present any relevant quantitative information along with a description of the unquantified effects").

Regarding risks from post-sterilization exposures to EtO resulting from the storage of sterilized devices in areas such as warehouses, EPA assessed risk to workers in sterilization facilities based on a summary of worker exposure data that was provided by the registrants. These data were collected on workers in sterilization facilities; however, details on where the workers were working in the facility or what they were doing were not provided. It is likely however, that the data were not collected from off-site warehouses because: (1) registrants may not be aware of off-site warehouses where sterilized product is stored because pesticide products are not used at such warehouses; and (2) employers would not focus exposure monitoring efforts in these areas because they expected the exposures to be low in comparison with the OSHA PEL of 1 ppm. EPA intends to issue a data call in for a special study for monitoring data on fumigated commodities, specifically medical devices, to better understand exposure to workers in warehouses, including off-site warehouses. See Sections V.A. and V.E. for a full explanation of the data requirement.

The Agency concluded that mitigation measures are necessary at this point in the registration review process to help address inhalation risks of concern from the use of EtO and proposed such measures in the PID. These proposed mitigation measures included the termination of certain uses, a concentration rate reduction for all medical device sterilization cycles, real-time monitoring, an indoor concentration limit, engineering controls, and respiratory protection requirements. Based on feedback received during the public comment period, this ID includes a modified set of mitigation measures, including the termination of certain uses, a concentration rate reduction only for new medical device sterilization cycles, an 8-hour time-weighted average occupational exposure limit, recordkeeping, and respiratory protection.

EPA has identified the following exposure scenarios for which potential human health risks from the use of EtO are expected to remain after implementation of the mitigation measures identified in the ID: inhalation risks to workers inside commercial sterilization and healthcare facilities. Regarding residential bystander risk, although EPA OPP and EPA OAR consider different risk thresholds (see Appendix F), OAR included measures to address bystander risk in their recently published *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review*.[295]; at this time, OPP has not identified other mitigation measures necessary to address residential bystander risk. EPA considered whether other mitigation measures, including prohibition of uses, could be implemented at this time that would address remaining occupational risks. However, EPA has not identified additional mitigation measures that could be implemented at this time to help address these risks of concern that would not result in a significant reduction in the benefits provided by the use of EtO (e.g., the availability of sterilized medical devices and access to patient care). As explained in this Appendix, based on feedback from the public comment period, there were several mitigation measures proposed in the PID that are not included as part of the ID, due to their impact on the benefits of the use of EtO,

[295] EPA-HQ-OAR-2019-0178-1482 at www.regulations.gov.

including mandatory engineering controls which would impact the supply chain of sterilized medical devices.

Thus, while EPA expects that human health risks of concern will remain following the implementation of the mitigation measures identified in the EtO ID, EPA has not identified additional mitigation measures that could be implemented at this time without causing significant detrimental effects on the benefits of the use of EtO (and adverse effects on public health that could be caused as a result). For example, based on conversations with medical device sterilization experts, industrial hygienists, and engineers, EPA has identified reductions in the occupational exposure limit that will be implemented as quickly as possible taking into consideration impacts on the sterilized medical device supply chain, resulting in a reduction from the OSHA PEL of 1 ppm which will reduce allowable worker exposure initially in half (0.5 ppm) within three years, four-fold (0.25 ppm) within five years, and ten-fold (0.1 ppm) within 10 years.[296]

With respect to residential bystanders, while FIFRA and the Clean Air Act have different statutory standards, EPA may consider compliance with a NESHAP when identifying whether mitigation measures are necessary to address risks of concern from the use of a pesticide, consistent with the requirement under FIFRA that EPA consider whether the use of a pesticide when used "in accordance with widespread and commonly recognized practice," causes unreasonable adverse effects on the environment.[297] Similarly, while the commenter correctly stated that the referenced ANSI/AAMI standard is not binding, industry standards like this may represent "widespread and commonly recognized practice" and are appropriately considered when identifying necessary mitigation measures.

In response to the comment about the lack of rationale for the proposed mitigation, and the Agency's decision to issue a DCI after the ID, EPA regulations provide that the Agency must publish proposed interim registration review decisions and provide a comment period of at least 60 days on these decisions.[298] EPA must then "consider any comments," and include in an interim decision "an explanation of any changes to the proposed decision and the Agency's response to significant comments."[299] Consistent with these requirements, the EtO PID included a description of the proposed mitigation measures and EPA's basis for those proposed measures. EPA received a significant number of public comments on the PID, has considered those comments, has made changes to the mitigation measures included in the ID, and has explained the basis for those changes. For example, rather than specifying engineering controls as proposed in the PID, this ID includes an 8-hour time-weighted average occupational exposure limit which allows facilities to choose which engineering and process controls to

[296] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders AdvaMed September 2023 – May 2024* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0408.
[297] 7 U.S.C. § 136a(c)(5)(D).
[298] (40 C.F.R. § 155.58(a)). A PID must include, among others, EPA's "proposed risk mitigation measures or other remedies as needed and describe the basis for such proposed requirements." (Id. § 155.58(b)).
[299] (Id. § 155.58(c)).

implement in order to meet this limit, based on the unique designs and layouts of individual facilities. Furthermore, EPA has the ability to issue DCIs during the registration review process, including following the issuance of the ID and could consider data received in response to those DCI's to promptly reevaluate this ID. Consistent with 40 C.F.R. § 155.58, EPA will provide an opportunity for public comment on any future PID for EtO.

In Support of Mitigation and Requests for More Stringency

Comments Summary:

EPA received over 100 individual comments in support of mitigating the risks of EtO to nearby communities and workers. These comments came from private citizens; community activist groups such as Stop Sterigenics; American Federation of Labor and Congress of Industrial Organizations (AFL-CIO); Earthjustice et. al.; Environmental Protection Network (EPN); California Division of Occupational Safety and Health (Cal/OSHA); and Attorneys General of New York, Connecticut, Illinois, Maryland, Massachusetts, Michigan, New Jersey, Oregon, Rhode Island, Vermont, and Wisconsin. Commenters showed support for EPA's proposed mitigation and requested the Agency do more to protect exposed populations, including warehouse workers and communities nearby warehouses, and to terminate all unnecessary uses of EtO.[300]

One private citizen in Fort Myers, Florida requested that EPA ensure the LeeSar American Contract Systems plant, which is located in close proximity to a school, is closed and relocated.[301] The Environmental Protection Network (EPN) suggested that healthcare facility workers be required to wear respirators, specifically those who are loading or unloading sterilization chambers or those who enter spaces where this is being performed.[302] The Attorneys General from the aforementioned states, as well as Earthjustice et. al., asserted that EPA cannot solely rely on the OAR commercial sterilizer proposal and must propose additional mitigation measures to reduce risk to acceptable levels for communities near healthcare facilities and warehouses.[303]

AFL-CIO suggested workers and their collective bargaining representatives have access to information regarding the hazards in their workplace and the measures employers are taking to keep them safe.[304] Earthjustice et. al. suggested EPA improve its outreach to labor organizations, since workers experience the greatest risk and may have valuable input in registration review decisions. Earthjustice et. al. further suggested that workers and their collective bargaining representatives should have records made available to them regarding EtO application rates, indoor EtO levels, and worker training; and the availability of these

[300] EPA-HQ-OPP-2013-0244-0144, EPA-HQ-OPP-2013-0244-0114, EPA-HQ-OPP-2013-0244-0140, EPA-HQ-OPP-2013-0244-0142, EPA-HQ-OPP-2013-0244-0138, EPA-HQ-OPP-2013-0244-0106 at www.regulations.gov.
[301] EPA-HQ-OPP-2013-0244-0151 at www.regulations.gov.
[302] EPA-HQ-OPP-2013-0244-0142 at www.regulations.gov.
[303] EPA-HQ-OPP-2013-0244-0106, EPA-HQ-OPP-2013-0244-0140 at www.regulations.gov.
[304] EPA-HQ-OPP-2013-0244-0114 at www.regulations.gov.

records be added to the information workers are provided during their training and, consistent with 29 C.F.R. § 1910.1020, when requested. Finally, Earthjustice et. al. suggested that EPA review EtO's registration every five years and impose additional mitigation measures as they become available.[305]

USDA commented that it is generally supportive of adding personal protective equipment (PPE) and engineering controls to reduce occupational exposure to EtO. USDA agreed with the Agency's proposal to modify labels to require use of a supplied air respirator (SAR) or SCBA for the activities described in the PID. USDA also agreed with EPA's proposal to issue a data call-in for more detailed air monitoring data. USDA recommended that monitoring data be collected specifically from facilities that have separate HVAC systems for non-processing areas, from facilities that use closed conveyor systems to transport product between fumigation and aeration chambers, and from facilities that use closed conveyor systems to transport product between all-in-one chambers and storage/shipping areas to inform whether these engineering controls are effective. USDA expressed concern that requirements for engineering controls requiring facility upgrades, especially a requirement for covered conveyors, might increase the cost of fumigation without changing the risk profile. However, if monitoring data indicates that the facilities sampled with these controls have lower ambient levels of EtO, they could serve as a useful model or a starting point for a properly designed system in other facilities.[306]

EPA Response:

EPA thanks the commenters for their support to mitigate the risks of EtO use. EPA's responses to comments regarding medical device sterilization alternatives, warehouses, healthcare facilities, the food commodity fumigation use, and specific changes to proposed mitigation measures can be found in dedicated responses in this appendix.

In response to the request to close and relocate specific facilities, the final standards under the OAR NESHAP will reduce risk to acceptable levels (based on a threshold of greater than 100-in-1 million).[307] Additionally, under FIFRA, EPA regulates the sale, distribution, and use of pesticides. EPA may regulate under FIFRA whether and how a facility may use a pesticide but does not regulate the location of the facility.

In response to the request to improve outreach to labor organizations, EPA may consider this during the registration review process. EPA agrees that records could be provided to workers and unions. EtO registrants may add an advisory statement to their labels encouraging users to share information with their workers. However, EPA has determined that the addition of such a

[305] EPA-HQ-OPP-2013-0244-0140 at www.regulations.gov.
[306] EPA-HQ-OPP-2013-0244-0128 at www.regulations.gov.
[307] Regarding residential bystander risk, although EPA OPP and EPA OAR consider different risk thresholds (see Appendix F), OAR included measures to address bystander risk in their recently published *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review*.

statement is not necessary at this time based on the training and recordkeeping requirements on EtO product labels. See Section V.A. for a full description of training and recordkeeping measures. EPA notes that since the publication of the PID, the Agency has met two times with AFL-CIO to discuss worker exposures to EtO and possible mitigation measures.[308]
In response to the request for EPA to review EtO's registration every five years, EPA has the ability to issue DCIs following the issuance of the ID and could consider data received in response to those DCIs to promptly reevaluate this Interim Decision.

Impacts to OPP Proposed Mitigation Measures from the OAR NESHAP Proposed Requirements

Comments Summary:

EOTF and EOSA asserted that the air exchanges per hour in the PID, meant to reduce worker exposure, would be constrained by the proposed mass-based emissions limits in EPA's Office of Air and Radiation's (OAR) EtO Commercial Sterilizers NESHAP. EOTF and EOSA also stated that the number of air exchanges per hour is product-, facility-, and cycle-dependent because the amount of ventilation required depends on a variety of factors (such as the percentage of the space that is occupied by products, the amount of off-gassing that is present, the off-gassing rate, and the temperature of the space). Furthermore, each sterilization facility is unique since variations in room design, air mixing, air flow within the space, and release rate of the contaminant impact the concentration in the space.[309]

BD agreed that negative pressure systems are helpful in capturing and controlling fugitive emissions from processing areas. However, they expressed concerns that the proposed measures under FIFRA may contradict what was proposed in the Office of Air and Radiation's (OAR) EtO Commercial Sterilizers NESHAP, specifically regarding Method 204.[310]

EPA Response:

The comments submitted were based on the OPP and OAR proposals, both of which have been modified as part of each individual final action. OPP is no longer including as a mitigation measure ventilation or negative air pressure systems for commercial sterilization facilities. OAR has also amended their proposal to remove the mass emission rate standards for the final rulemaking. EPA asserts that with these revisions from the proposals, the requirements of the CAA and the mitigation measures identified in this ID issued under FIFRA are feasible. Furthermore, several existing commercial sterilizers have already been complying with EPA Method 204. As finalized, the requirements for permanent total enclosure (PTE) under the OAR

[308] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders American Federation of Labor and Congress of Industrial Organizations (AFL-CIO) May – June 2024* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0409.
[309] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[310] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.

NESHAP do not limit air changes per hour, and therefore the lowered indoor occupational exposure limit under FIFRA are also simultaneously attainable.

In order to verify progress in meeting the occupational exposure limits and associated implementation deadlines in this ID in commercial sterilization facilities in the U.S., which are inherently unique in design and layout, EPA will gather annual worker exposure data and assess those data.[311] Specifically, EPA has determined it is necessary for EtO registrants to collect worker monitoring data from their customers on an annual basis. Further, EtO registrants may not continue to sell EtO products to customers who do not provide worker monitoring data to EPA. EPA will collect these data through a DCI. EPA can change the implementation timing and target occupational exposure limit concentration, if necessary, as demonstrated by data, prior to the deadline for the final implementation tier of the exposure limit of 0.1 ppm. In order to make this determination, EPA will reevaluate the occupational exposure limit and any other needed mitigations, based on data, within 8 years.

Requested Changes to Proposed Mitigation to Reduce Stringency

Comments Summary:

EPA received 14 comments, all from industry, requesting the Agency make changes to the mitigation proposed in the PID to reduce stringency: Becton Dickinson (BD), Midwest Sterilization Corporation (MSC), Medical Device Manufacturers Association (MDMA), EDANSA, Biocom California, Medline, AdvaMed, Terumo, Baxter, Sterigenics, Health Industry Distributors Association (HIDA), Elite Spice, and combined comments from CropLife America (CLA) and Responsible Industry for a Sound Environment (RISE), and the Ethylene Oxide Task Force (EOTF) and the Ethylene Oxide Sterilization Association (EOSA). Commenters asserted that if the mitigation were to be adopted as proposed in the PID, this would cause a severe disruption to the medical device supply chain and impair the healthcare system as a whole. Commenters stated that almost all the proposed measures were too costly, not logistically feasible, and/or not able to be implemented within the proposed timeframes. Of note, commenters pointed out that many of the proposed mitigation measures would require a new validation and subsequent FDA review, which would put a halt to the medical device sterilization industry in order to conduct the research and perform the validations necessary to meet the proposed mitigation. CLA and RISE commented that the proposed engineering controls will jeopardize the supply chain and negatively impact essential products to protect the food supply and public health.[312] Elite Spice commented that the Agency proposed several actions that are either infeasible to implement or would require a complete restructuring of current spice manufacturers' operations and would effectively force the spice industry not to use EtO at the

[311] See "Ethylene Oxide – EOTF and EOSA Proposal for the Interim Decision – June 26 2024" in the EtO public docket at www.regulations.gov under document ID EPA-HQ-OPP-2013-0244-0406.
[312] EPA-HQ-OPP-2013-0244-0133 at www.regulations.gov.

end of the implementation period.[313] Provided below are summaries of the commenters' concerns for individual proposed mitigation measures.[314]

Concentration rate limit of 500 mg/L or less

For existing cycles, commenters stated that given the large number of cycles that currently are in place, which number in the thousands, it could take decades or longer to have the cycles validated anew. [315] Any requirement to create a new validation for existing cycles to meet a cycle concentration limit would have immense adverse impacts on the medical device supply chain and would significantly reduce innovation and new product development.

For new cycles, Sterigenics, EOTF, and EOSA stated that any requirement for new cycles to meet a 600 mg/L maximum concentration, which is above the proposed 500 mg/L rate, would take a minimum of 10 years. Sterigenics asserted that the proposed 500 mg/L concentration limit may not achieve appropriate assurance of sterility for many devices, and that a limit of 600 mg/L would be obtainable for a greater number of products. Sterigenics further stated that 10 years would be needed to make these changes because designing a cycle can take up to 18 months, validation can take six months, submission to and approval by FDA can take two years, and approvals by regulatory bodies in other countries where the product will be sold can take up to five years.[316] AdvaMed suggested a timeframe of five years for new cycles to meet a 500 mg/L limit.[317] BD suggested a timeframe of three years for new cycles to meet a 500 mg/L limit.[318]

Commenters asserted that test cycles have been run where the amount of EtO used was reduced by 50 percent or more but did not result in reduction of fugitive emissions or worker exposure. Additionally, commenters expressed concern that all device types may not be effectively sterilized at levels below 500 mg/L, and this limit may result in devices that cannot be sterilized in accordance with FDA requirements. For example, products that are pressure sensitive are often sterilized using a shallow vacuum cycle, which requires a higher concentration of EtO to assure sterility. Furthermore, commenters asserted that a 500 mg/L

[313] EPA-HQ-OPP-2013-0244-0136 at www.regulations.gov.
[314] EPA-HQ-OPP-2013-0244-0121, EPA-HQ-OPP-2013-0244-0119, EPA-HQ-OPP-2013-0244-0092, EPA-HQ-OPP-2013-0244-0126, EPA-HQ-OPP-2013-0244-0103, EPA-HQ-OPP-2013-0244-0100, EPA-HQ-OPP-2013-0244-0097, EPA-HQ-OPP-2013-0244-0146, EPA-HQ-OPP-2013-0244-0109, EPA-HQ-OPP-2013-0244-0141, EPA-HQ-OPP-2013-0244-0147, EPA-HQ-OPP-2013-0244-0117 at www.regulations.gov.
[315] An EtO sterilization cycle is defined as "treatment in a sealed chamber, which includes air removal, conditioning (if used), injection of ethylene oxide, inert gas (if used), exposure to ethylene oxide, removal of ethylene oxide and flushing (if used), and air/inert gas admission." (See: International Standard ISO 11135. Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation, and routing control of a sterilization process for medical devices. 2014). A sterilization calculation includes validated parameters such as pressure, concentration, temperature, humidity, and exposure time. Assessment of a company's cycle validation data by FDA includes specifications for products, load configuration, packaging, and sterility assurance level.
[316] EPA-HQ-OPP-2013-0244-0141, EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[317] EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.
[318] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.

limit could result in longer processing times and would therefore put a strain on the medical device supply chain, which is already at capacity.

MDMA estimated that the total cost for validating anew all existing cycles is $13 billion. MDMA asserted that when factoring in labor, equipment, administrative costs, testing, packaging redesign, logistics, total costs for a complete sterilization validation are estimated at an average cost of $80,000 per validation cycle. The process to determine which cycle to proceed with for a product can take up to three years, with most reporting a time period of six to 18 months. Of this amount, $10,000 is for lab testing that precedes the sterilization cycle validation.[319] Sterigenics stated that the approximate cost to redesign a single EtO sterilization cycle can range from $100,000 to $1 million.[320]

MSC suggested that instead of having a concentration limit of 500 mg/L during sterilization, facilities could be required to have a post-sterilization in-chamber concentration limit of less than 1 ppm (using Ideal Gas Law calculations) before the chamber door is opened.[321]

BD suggested that instead of a 500 mg/L limit, EPA and FDA should continue to work with sterilizers and incentivize them to take steps to innovate their sterilization cycles and processes to minimize EtO usage. BD noted that they are already committed to this process, participating in both FDA's Innovation Challenge 2 ("Reduce Ethylene Oxide Emissions") and the Ethylene Oxide Sterilization Master File Pilot Program.[322]

All-in-one systems

All commenters stated that all-in-one processing systems for the sterilization of all medical devices are not feasible. Commenters stated that all-in-one processing systems take twice as long to process devices, thus reducing the sterilization capacity by 50%. Commenters also stated that all-in-one processing systems use higher temperatures than traditional sterilization systems and would therefore damage certain devices. Furthermore, from these increased temperatures and other changes to cycle parameters, all devices would require a new validation and subsequent FDA review, which would impact the medical device supply chain and availability of devices. Commenters also stated that implementing all-in-one systems would require complete redesign of existing facilities. In order to meet demand, double the number of chambers would be required, since all-in-one systems have 50% output as compared to traditional systems due to longer processing times.

AdvaMed stated that all-in-one systems would conflict with medical device manufacturer compliance with ISO 10993-7, and only on a limited basis can cycles be validated using the "dissipation curve" within this standard. Furthermore, all-in-one chambers are not compatible

[319] EPA-HQ-OPP-2013-0244-0092 at www.regulations.gov.
[320] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.
[321] EPA-HQ-OPP-2013-0244-0119 at www.regulations.gov.
[322] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.

with pulling product for testing at various stages of the aeration process per the ISO standard.[323]

MSC suggested that instead of requiring all-in-one systems, facilities should design sterilization chamber cycles to reduce EtO levels to a calculated 0 ppm prior to transfer to aeration rooms, which would minimize worker exposure and maximize aeration capabilities.[324]

Ventilation

Commenters asserted that the air exchanges per hour in the PID, meant to reduce worker exposure, would be constrained by the proposed mass-based emissions limits in EPA's Office of Air and Radiation's (OAR) EtO Commercial Sterilizers NESHAP. Commenters also stated that the number of air exchanges per hour is product-, facility-, and cycle-dependent because the amount of ventilation required depends on a variety of factors (such as the percentage of the space that is occupied by products, the amount of off-gassing that is present, the off-gassing rate, and the temperature of the space). Furthermore, each sterilization facility is unique since variations in room design, air mixing, air flow within the space, and release rate of the contaminant impact the concentration in the space.[325]

Packaging Materials

Certain commenters were not in support of requiring specific packaging materials to reduce the amount of EtO absorbed and off gassed from product packaging. BD stated that depending on the product, various methods are employed to protect the product and stabilize the load during shipping, handling, and storage. This includes, but is not limited to stretch wrap, vented wrap, netting and corner boards and straps. Requiring a specific material or configuration may result in product damage, or compromise worker safety if loads become unstable during handling.[326] AdvaMed stated that netting is only appropriate if manufacturers account for pallet load stability, and in some cases, netting cannot meet the required strength to support certain loads of products. Accordingly, netting is not feasible in all circumstances, and a mandate would compromise worker safety because of concerns for pallet load stability. The use of netting may also require cardboard corner boards on pallets, which would increase the likelihood of residuals.[327] EOTF and EOSA stated that depending on the commercial sterilizer, various types of product containment are used, including stretch wrap, vented wrap, netting and corner boards and straps. Furthermore, wrapping and banding are used to stabilize loads during transport, processing, and storage. Requiring one kind of product containment may compromise worker safety if loads become unstable during any point of a cycle.[328]

[323] EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.
[324] EPA-HQ-OPP-2013-0244-0119 at www.regulations.gov.
[325] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[326] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.
[327] EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.
[328] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.

Conversely, MSC asserted that they have seen favorable results with vented plastic wrap and netting alternatives and would support this as a potential means for improving aeration efficiency.[329]

Air pressure gradients

Sterigenics stated that specifically requiring air-pressure gradients, to the exclusion of other possible methods to maintain ventilation and lower concentrations, would not improve worker safety and would only limit flexibility when retrofitting facilities. Sterigenics suggested commercial sterilization facilities be required to achieve exposure reductions to the OSHA Permissible Exposure Limit (PEL) by using engineering controls to ventilate spaces (but without specifically mandated air exchange standards, to allow for flexible approaches to different facility designs) and ensure the highest level of negative pressure in the facility is either the sterilization chamber or aeration space.[330]

BD agreed that negative pressure systems are helpful in capturing and controlling fugitive emissions from processing areas. However, they expressed concerns that the proposed mitigation measures under FIFRA may contradict what was proposed in the Office of Air and Radiation's (OAR) EtO Commercial Sterilizers NESHAP, specifically regarding Method 204.[331]

HVAC systems

Sterigenics stated that commercial sterilization facilities would be able to separate HVAC systems of processing areas from HVAC systems of non-processing areas in three years, which is one year longer than the proposed two-year implementation timeframe. Sterigenics expressed concerns about delays in the delivery of needed equipment and materials and regular shortages of trained personnel to install equipment.[332]

Automation using covered conveyors

All commenters stated that covered conveyor systems are not feasible, since this would require a complete redesign of facilities and force facilities to shut down.

EOTF and EOSA stated that many chamber doors swing open on hinges and do not roll/slide open, preventing connection to a conveyor system, and that facility "blast doors" that are often part of chamber room design, pose similar issues. Existing facilities can have multiple chambers and dozens of entrances to aeration rooms, in many cases on multiple levels, resulting in hundreds of product flow combinations that are only feasible with forklift movements and

[329] EPA-HQ-OPP-2013-0244-0119 at www.regulations.gov.
[330] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.
[331] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.
[332] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.

cannot be done via conveyors. The complex and varied product flow options, crossflow, building codes and reclassification, safety protocol and fire hazard issues, and the required control systems make it impossible to automate these movements with a conveyor system. Chambers that are ASME rated would need to be modified and may not be able to be recertified. Finally, adding conveyors in an existing facility will result in emergency access and egress issues.[333]

MSC stated that even for new contract sterilizer facility designs, such a requirement would significantly reduce a contract sterilizer's ability to effectively process products at current healthcare market demand, since the linear design of a conveyor system would impact aeration flexibility.[334]

MDMA estimated the annualized cost of implementing covered conveyors in all 86 EtO commercial sterilization facilities to be $3.1 million and estimated the total cost per facility to be $380,000, annualized at $37,000.[335]

AdvaMed suggested that instead of implementing covered conveyors, commercial sterilization facilities be required to meet a set exposure level while leaving facilities the flexibility to achieve that limit, through engineering and process controls that are achievable at each specific facility.[336] Similarly, MSC suggested facilities design cycles to reduce EtO levels to a calculated 0 ppm prior to transfer to aeration rooms, instead of universally requiring covered conveyors.[337]

The American Spice Trade Association (ASTA) commented that the Agency's proposed automation requirements, particularly covered conveyors, are unnecessarily burdensome. In addition, ASTA commented that conveyor systems are problematic due to spice pallet configuration. They state that sacks of spices are stacked in blocks. The stacks tend to be loose and have overhangs, resulting in shifting of the sacks on the pallet. ASTA noted that personnel would need to re-enter the enclosed areas frequently to restack the sacks of spices.[338]

Respirators

All commenters opposed the use of respirators at the proposed 10 ppb limit. Commenters stated that overuse of respirators has risks of its own to worker health and safety, including exertion, risks of snags, falls, and reduced visual ability. EPA notes that, as stated in the comments summary section for *Hierarchy of Controls*, the American Federation of Labor and Congress of Industrial Organizations (AFL-CIO) and the California Division of Occupational Safety

[333] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[334] EPA-HQ-OPP-2013-0244-0119 at www.regulations.gov.
[335] EPA-HQ-OPP-2013-0244-0092 at www.regulations.gov.
[336] EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.
[337] EPA-HQ-OPP-2013-0244-0119 at www.regulations.gov.
[338] EPA-HQ-OPP-2013-0244-0130 at www.regulations.gov.

and Health (Cal/OSHA) also raised concerns about the overuse of respirators which would be a result of such a low threshold.[339]

EOTF and EOSA stated that despite the maximum wear time of a SCBA being 45 to 60 minutes, in practice this time can be cut in half dependent on the amount of physical exertion and health of the individual. Furthermore, workers must undergo medical clearance before they are allowed to use a SCBA per OSHA's regulations at 29 C.F.R. § 1910.134(e), and many will not be able to meet the requirements for extended usage.[340] MSC asserted that requirements for worker SCBA use will likely result in fewer workers willing to work in such roles, adversely impacting available human resources and reducing site operating capacity.[341]

Regarding task-based respirator use (regardless of EtO levels), most commenters were supportive of the proposal in the PID. However, BD opposed the task-based respirator mitigation, stating that increased use of respirators in general presents risks and hazards to workers (e.g., exertion, risks of snags, etc.).[342]

Occupational Exposure Limit

All commenters opposed the proposed real-time occupational exposure limit of 10 ppb. Commenters asserted that the limit should be an 8-hour time weighted average measured near the worker's breathing zone, not based on an instantaneous reading of room air emissions as proposed, citing that time weighted averages are the typical method for measuring worker exposure over the course of a workday. EOTF and EOSA stated that a time-weighted average value would allow for variations in concentration accounting for the working eight-hour average and is appropriate for chronic risks.[343] AdvaMed stated that location and temporal differences in concentrations require monitoring within the worker's breathing zone, as reflected by OSHA's regulations for exposure monitoring.[344] Commenters also provided alternative occupational exposure limits, as described below.

MSC asserted that the current OSHA PEL of 1 ppm has been determined by a number of countries (e.g., Australia, Canada, Israel, Japan, Singapore, UK) and the EU to be protective of workers.[345] EOTF and EOSA suggested a value of no less than 0.5 ppm eight-hour time weighted average (TWA) with implementation required in two to three years or more; and/or a value of no less than 0.25 ppm TWA with implementation required in five to ten years or more.[346] Sterigenics suggested a 0.25 ppm limit, which they note would be a 75% reduction from the current OSHA PEL of 1 ppm. Sterigenics further suggested EPA allow the industry at least five

[339] EPA-HQ-OPP-2013-0244-0114, EPA-HQ-OPP-2013-0244-0138 at www.regulations.gov.
[340] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[341] EPA-HQ-OPP-2013-0244-0119 at www.regulations.gov.
[342] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.
[343] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[344] EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.
[345] EPA-HQ-OPP-2013-0244-0119 at www.regulations.gov.
[346] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.

years, but likely 10 years to meet this limit, allotting industry the appropriate time for improvements and measurement methods.[347] Finally, both AdvaMed and BD suggested EPA require the NIOSH Recommended Exposure Limit (REL) of 0.1 ppm.[348] EPA notes that the Agency received additional proposals for a lowered occupational exposure limit from EOTF and EOSA and AdvaMed after the close of the PID public comment period. Those proposals can be found in the EtO public docket at www.regulations.gov under documents EPA-HQ-OPP-2013-0244-0405 and EPA-HQ-OPP-2013-0244-0406.

Monitoring

EOTF and EOSA stated that Fourier transform infrared spectroscopy (FTIR) and Cavity ring-down spectroscopy (CRDS) are the only monitoring systems that can achieve a limit of detection (LOD) of 10 ppb, but both have limitations when doing multi-port area sampling. They also stated that facilities would be required to limit and optimize airflows to comply with the requirement for monitoring down to 10 ppb, which could conflict with the Office of Air and Radiation's (OAR) NESHAP proposed requirements.[349]

BD stated that there are additional sources at commercial facilities that can produce EtO, such as gas-fired boilers, heating equipment, emergency generators, and tractor trailers, which all generate EtO as a byproduct of combustion at levels above 10 ppb. BD suggested that the purpose of indoor air monitoring should be to ensure that air inside the facility remains below the OSHA Short-Term Exposure Limit (STEL) and assist facility operators to control indoor EtO concentrations below the action OSHA Permissible Exposure Limit (PEL). BD further suggested that corrective actions, especially facility evacuations, should not be required in response to single readings above 10 ppb.[350]

Sterigenics estimated that a single FTIR system is likely to cost $400,000 to $500,000, and between eight and ten devices would be needed for each facility, totaling $3.2 to $5 million for an average sterilization facility.[351]

The Health Industry Distributors Association (HIDA) commented that implementing the proposed worker monitoring is technologically challenging, if not impossible, at the Agency's current proposed levels. HIDA also commented that it is unlikely that a worker will want to work a full day wearing self-contained breathing apparatus. HIDA recommended that commercial sterilization facilities continue to operate under established OSHA standards regarding permissible exposure limits for EtO.[352]

[347] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.
[348] EPA-HQ-OPP-2013-0244-0097, EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.
[349] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[350] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.
[351] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.
[352] EPA-HQ-OPP-2013-0244-0117 at www.regulations.gov.

ASTA commented that real time monitoring at 10 ppb is not achievable. ASTA stated that they are not aware of technology that can reliably detect in real time to the 10-ppb limit of quantification. They also expressed concern with establishing an action level at the limit of current technology because there can be issues with reading accuracy and interference.[353]

EPA notes that, as stated in the comment summary section for *Monitoring and Capture Technologies,* Picarro, who provides monitoring technologies below 10 ppb, suggested that EPA consider providing extended implementation windows to facilities or adopting a phased approach to implementing new workplace limitations, since this would allow sterilization facilities the necessary time to thoroughly evaluate, install, and implement associated process control strategies.[354]

Training

Sterigenics, EOTF, and EOSA opposed the proposed use of worker risk estimates based on the IRIS assessment for worker training purposes. EOTF and EOSA asserted that the proposed training language is without basis and misleading[355] Sterigenics stated that workers should be made aware of the risks they face but urged EPA to remove from the proposed training requirements any obligation to present specific likelihoods of harm. Sterigenics stated that EPA's proposed training on the statistical likelihood of cancer as calculated by IRIS is aimed at ensuring "employees are apprised of" alleged hazards, not aimed at preventing unreasonable harm, so it exceeds EPA's authority and steps into the jurisdiction of OSHA. Sterigenics further stated that the cancer risks identified in the proposed training are based on average exposure levels across various facilities at present, but they do not reflect exposures in a particular facility or after any additional mitigation measures are implemented.[356]

MDMA estimated the total one-time costs of training to be $440,000. MDMA expected an increase in worker turnover rates, which would mean recurring costs to train new workers on an annual basis at an estimated annual cost of $46,000.[357]

Recordkeeping

EOSA and EOTF stated in their comment that they did not have an adequate opportunity to provide comment on the proposed recordkeeping measures, many of which are not possible or feasible concerning the significant issues posed by the mitigation measures that would be the subject of the recordkeeping.[358] MDMA stated that there are a range of additional costs associated with reporting and recordkeeping practices recommended by OSHA for workers in

[353] EPA-HQ-OPP-2013-0244-0130 at www.regulations.gov.
[354] EPA-HQ-OPP-2013-0244-0123 at www.regulations.gov.
[355] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[356] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.
[357] EPA-HQ-OPP-2013-0244-0092 at www.regulations.gov.
[358] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.

PPE, including creating written control plans for exposure, respiratory protection, medical surveillance, and medical removal. MDMA estimated the cost of recordkeeping to be $160,000 for a one-time cost, and $630,000 for a recurring annual cost.[359]

Data Requirements

For the proposed Data Call-In (DCI) for OCSPP GLN 875.1400 Inhalation Exposure Indoor, BD recommended Method MOD ASTM D5578, using passive dosimeter badges because it is less obtrusive for the person being monitored, and is more cost effective. BD asserted that the proposed exposure monitoring using Method 1010 requires expertise in industrial hygiene monitoring to ensure sampling is performed as intended; it is cumbersome due to the size of the sampling pump and the routing of the tubing which may become entangled in SAR/SCBA equipment; and it also entails additional costs for equipment purchase, maintenance, and calibration. BD further stated that the proposed requirement is unclear as to whether every worker would be required to be monitored (on every shift) or only representative individuals. BD asserted that documenting every task for every worker for the full work shift would not only be disruptive for the workers, but it also likely would require a large number of additional personnel to directly observe all activities during the monitoring period, and would require weeks (if not months) to complete due to availability of sampling media, sampling pumps, calibration equipment for the pumps, etc.[360] Sterigenics stated that the DCI is problematic because EPA wishes to test worker exposure in commercial sterilization facilities, yet the requirement for such testing is placed on the registrants, not on the commercial sterilization facilities. Sterigenics also stated that it is unclear whether EPA intends to test a single facility or multiple facilities. Sterigenics suggested that EPA should wait until all proposed timelines for mitigation implementation have passed, then issue the DCI, instead of issuing it at present.[361]

For the proposed Data Call-In for a special study for registrants to send information on monitoring technologies, BD stated that improving monitoring technology to detect indoor air concentration levels lower than ambient background levels is unreasonable and unnecessary.[362] Sterigenics asserted that EPA cannot issue the proposed DCI regarding commercially available technologies because such a DCI is outside those permitted by FIFRA for the following reasons: it does not relate to whether EtO causes unreasonable adverse effects; EPA cannot require searches for suppliers; it is research into how EPA could monitor exposure in the future, which is not the type of information contemplated by FIFRA or its implementing regulations; EPA may only require new types of studies if the studies are identified in EPA's regulations; and EPA can only require additional data in order to fully characterize the use and properties of specific pesticide products under review.[363]

[359] EPA-HQ-OPP-2013-0244-0092 at www.regulations.gov.
[360] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.
[361] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.
[362] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.
[363] EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.

EPA Response:

EPA thanks the submitters for their comments. EPA shares the concerns of the submitters for a stable supply chain of medical devices and uninterrupted access to patient care as well as the safety of the food supply chain. Furthermore, the comments that EPA received on the feasibility of certain exposure controls, the times required to implement such controls, and suggestions for alternative exposure controls varied greatly between the commenters. These comments suggest that commercial sterilization facilities may differ greatly in their ability to implement specific engineering controls, and in how their operations would be impacted if implementation of such controls was necessary. For these reasons, EPA has amended several aspects of the PID to refine the Agency's mitigation strategy to allow facilities the flexibility to select exposure controls that allow them to meet the demand for sterilized medical devices and food commodities while reducing worker exposure. It is worth noting that there are several proposed mitigation measures from the PID that are still included as part of this Interim Decision. See Section V.A. for a detailed explanation of all mitigation measures.

In response to the statements from Sterigenics regarding EPA's authority to specify worker training measures and EPA's authority to issue DCIs, please see the responses included in the *Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Food Quality Protection Act (FQPA) Requirements* response to comments section and the *OSHA Authority and EPA Authority under FIFRA* response to comments section.

Medical Device Supply Chain

Comments Summary:

EPA received 36 public comments expressing concerns about the effects of the proposed mitigation on the medical device supply chain. Commenters represented stakeholders from hospitals, the bioscience industry, physicians' organizations, medical device distributors, medical device manufacturers, states, small businesses, and commercial sterilization facilities. Of note, commenters stated that if the mitigation measures were to be adopted as proposed in the PID, this would cause widespread and catastrophic disruption to the medical device supply chain in the U.S. and subsequently limit patient access to medical care, since the U.S. medical device supply chain is already at capacity. Commenters requested the maximum amount of implementation time for mitigation. Finally, commenters reiterated that EtO is often the only suitable sterilization method for a variety of medical devices, and no available alternatives could replace EtO. Commenters cited the following proposed mitigation measures as expected to adversely affect the supply chain of sterilized medical devices:

- A concentration rate limit of 500 mg/L for medical device sterilization would impact the supply chain especially for existing cycles because of the large number of cycles that currently are in place, which number in the thousands. It could take decades or longer

to have the cycles validated anew. Furthermore, a 500 mg/L limit could result in longer processing times and would therefore put a strain on the medical device supply chain.

- All-in-one processing systems take twice as long to process devices, thus reducing the sterilization capacity by 50%.
- Covered conveyor systems would significantly reduce a contract sterilizer's ability to effectively process products at current healthcare market demand, since the linear design of a conveyor system would impact aeration flexibility.[364]

EPA Response:

EPA thanks the submitters for their comments. EPA shares the concerns of the submitters for a stable supply chain of medical devices and uninterrupted access to patient care. For these reasons, EPA has amended several aspects of the PID to refine the Agency's mitigation strategy to allow facilities the flexibility to meet the demand for sterilized medical devices while also reducing worker exposure. It is worth noting that there are several proposed mitigation measures from the PID that remain part of this Interim Decision based on the reductions in worker exposure provided by these measures and the impacts of these measures on the availability of sterile medical devices, which are expected to be low. See Section V.A. for a detailed explanation of all mitigation measures.

Costs of Proposed Mitigation

Comments Summary:

EPA received two public comments with cost information for the proposed mitigation in the PID. The Medical Device Manufacturers Association (MDMA) and AdvaMed, both of whom represent industry, asserted that the cost of the mitigation as proposed would have a significant impact on the medical device supply chain and access to patient care. AdvaMed and MDMA contest that the cost analysis in the PID, which was largely qualitative, should have been quantified.

AdvaMed claimed that EPA failed to undertake the required assessment of the economic, social, and environmental costs and benefits of the use of EtO, asserting that the inelasticity of

[364] EPA-HQ-OPP-2013-0244-0104, EPA-HQ-OPP-2013-0244-0102, EPA-HQ-OPP-2013-0244-0101, EPA-HQ-OPP-2013-0244-0096, EPA-HQ-OPP-2013-0244-0131, EPA-HQ-OPP-2013-0244-0098, EPA-HQ-OPP-2013-0244-0132, EPA-HQ-OPP-2013-0244-0099, EPA-HQ-OPP-2013-0244-0134, EPA-HQ-OPP-2013-0244-0149, EPA-HQ-OPP-2013-0244-0095, EPA-HQ-OPP-2013-0244-0090, EPA-HQ-OPP-2013-0244-0088, EPA-HQ-OPP-2013-0244-0127, EPA-HQ-OPP-2013-0244-0125, EPA-HQ-OPP-2013-0244-0085, EPA-HQ-OPP-2013-0244-0082, EPA-HQ-OPP-2013-0244-0081, EPA-HQ-OPP-2013-0244-0087, EPA-HQ-OPP-2013-0244-0094, EPA-HQ-OPP-2013-0244-0079, EPA-HQ-OPP-2013-0244-0117, EPA-HQ-OPP-2013-0244-0113, EPA-HQ-OPP-2013-0244-0118, EPA-HQ-OPP-2013-0244-0110, EPA-HQ-OPP-2013-0244-0112, EPA-HQ-OPP-2013-0244-0111, EPA-HQ-OPP-2013-0244-0107, EPA-HQ-OPP-2013-0244-0108, EPA-HQ-OPP-2013-0244-0092, EPA-HQ-OPP-2013-0244-0097, EPA-HQ-OPP-2013-0244-0146, EPA-HQ-OPP-2013-0244-0141, EPA-HQ-OPP-2013-0244-0147, EPA-HQ-OPP-2013-0244-0121, EPA-HQ-OPP-2013-0244-0119 at www.regulations.gov.

demand for medical devices means that even modest sized shifts or disruptions in supply will cause medical device shortages that will adversely affect patients. AdvaMed stated that these factors fall into economic, social, and public health costs and benefits that EPA should consider as part of EPA's "unreasonable adverse effects" standard under FIFRA.[365]

MDMA provided an in-depth quantitative cost analysis of the proposed mitigation in the PID. MDMA asserted that the cost analysis for the PID lacks compounding impact, as it does not take into account the requirements under EPA's Office of Air and Radiation's (OAR) NESHAP for EtO Commercial Sterilizers. MDMA stated that their analysis finds that the costs, reduction in medical services, and risks from reduced sterilization capacity are substantial and could have devasting effects on patients.[366]

EPA Response:

EPA thanks MDMA and AdvaMed for their information on the costs of the proposed mitigation in the PID. EPA shares the concerns of the submitters for a stable supply chain of medical devices and uninterrupted access to patient care. For these reasons, EPA has amended several aspects of the PID to refine the Agency's mitigation strategy to allow facilities the flexibility to meet the demand for sterilized medical devices while reducing worker exposure. It is worth noting that there are several proposed mitigation measures from the PID that remain part of this Interim Decision. See Section V.A. for a detailed explanation of all mitigation measures.

Regarding the request to conduct a quantitative cost analysis, there is no statutory requirement to quantify costs of mitigation measures under FIFRA's risk-benefit standard. See 40 C.F.R. § 155.40(a); 7 U.S.C. § 136a(c)(5); see also 7 U.S.C. §§ 136(bb), which defines "unreasonable adverse effects on the environment" as encompassing both "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide" (FIFRA's risk-benefit standard), and "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the [FFDCA safety standard]". In a PID, EPA sets out a proposed interim decision that includes EPA's "proposed findings with respect to the FIFRA standard for registration and describe the basis for such proposed findings."[367] These findings, as is the case with a cost analysis, may be qualitative. While FIFRA requires EPA to evaluate the "economic, social, and environmental costs and benefits of the use of any pesticide," the statute provides discretion to determine how to describe, evaluate, and weigh those factors. Consistent with other EPA and federal government guidance, OPP does not view this evaluation of risks and benefits as requiring a quantitative comparison. EPA guidance advises that "if important costs or benefits categories cannot be expressed quantitatively, they should be discussed qualitatively."

[365] EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.
[366] EPA-HQ-OPP-2013-0244-0092 at www.regulations.gov.
[367] 40 C.F.R. §§ 155.56, 155.58(b)(1).

Regarding the request to conduct a compounding impact analysis of both the OPP FIFRA PID and the OAR NESHAP, EPA does not agree that such an analysis is required under FIFRA. Further, as noted above, there is no statutory requirement to quantify costs of mitigation measures under FIFRA's risk-benefit standard. For information on the OAR NESHAP cost analysis, see the *Regulatory Impact Analysis for the Final National Emission Standards for Hazardous Air Pollutants: Ethylene Oxide Commercial Sterilization and Fumigation Operations*.[368]

Benefits of EtO for Medical Device Sterilization

Comments Summary:

EPA received several comments regarding the benefits of EtO for medical device sterilization. Some key information is highlighted here. In their public comment, Becton Dickinson (BD) stated that approximately 50% of BD products currently can only be sterilized with EtO, including intravenous (IV) catheters, peripherally inserted central (PIC) catheters, surgical prep devices, surgical kits, Foley urinary catheter trays, glass syringes, and chemotherapy ports, among many others.[369] The Medical Device Manufacturers Association (MDMA) stated that common medical devices that are EtO-reliant include but are not limited to the following: heart valves; intravenous (IV) sets; catheters; sutures; gowns and drapes; fiberoptic endoscopes; surgical kits; pacemakers; respirators; tubing sets; plastic tubing; inhalation therapy supplies; surgical telescopes; anesthesia masks and circuits; renal peritoneal dialysis sets; renal hemodialysis sets; surgical drills; uterine monitors; surgical staplers; and diagnostic electrode catheter.[370] Biocom California stated that for products that can be sterilized using other methods, if companies shift away from EtO and begin sterilizing more products using gamma radiation, there could be a strain on gamma resources, which are used for oncology radiotherapy to kill cancer cells, and could in turn delay life-saving oncology treatments.[371] AdvaMed asserted that surgical kits singularly depend upon EtO – 95% of all surgical kits are sterilized using EtO, and about 40 to 50 million surgeries are performed each year in the U.S. (e.g., more than 100,000 surgeries a day).[372] The Ethylene Oxide Task Force (EOTF) and the Ethylene Oxide Sterilization Association (EOSA) stated that a lack of EtO-sterilized medical supplies to operating rooms would result in delayed or even canceled procedures, which would pose grave risk to those in urgent medical need.[373] Terumo Blood and Cell Technologies (BCT) stated that approximately 80% of Terumo BCT products (and 95% of the Terumo BCT products manufactured in the U.S.) currently can only be sterilized with EtO, including the Rika Plasma Donation System, among many others.[374]

[368] EPA-HQ-OAR-2019-0178-1557 at www.regulations.gov.
[369] EPA-HQ-OPP-2013-0244-0121 at www.regulations.gov.
[370] EPA-HQ-OPP-2013-0244-0092 at www.regulations.gov.
[371] EPA-HQ-OPP-2013-0244-0103 at www.regulations.gov.
[372] EPA-HQ-OPP-2013-0244-0097 at www.regulations.gov.
[373] EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[374] EPA-HQ-OPP-2013-0244-0146 at www.regulations.gov.

EPA Response:

EPA thanks the submitters for their comments. As stated in the EtO PID and the document *Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation,* the EPA agrees that there are high benefits for the use of EtO for medical device sterilization. For these reasons, EPA has amended several aspects of the PID to refine the Agency's mitigation strategy to allow facilities the flexibility to meet the demand for sterilized medical devices while reducing worker exposure. It is worth noting that there are several proposed mitigation measures from the PID that remain part of this Interim Decision; however, these measures are not expected to have a significant adverse impact on the medical device supply chain. See Section V.A. for a detailed explanation of all mitigation measures.

Alternatives for Medical Device Sterilization

Comments Summary:

EPA received three comments from two submitters regarding alternatives to EtO for medical device sterilization: Noxilizer and ClorDiSys. Noxilizer provided information on nitrogen dioxide and its advantages as well as limitations for material compatibility. ClorDiSys provided information on chlorine dioxide and its advantages and applicability as a growing sterilization modality.[375]

EPA additionally received several comments urging the use of alternatives where they exist. The community activist group Stop Sterigenics suggested EPA collaborate with FDA to identify simple devices that could use other sterilization modalities, stating, "Some manufacturers choose to use EtO to achieve sterility requirements and other manufacturers offer functionally identical products that they choose to sterilize with other processing methods." Stop Sterigenics further suggested a regulatory requirement to separate kit components by processing modality into two or three smaller bundles to be assembled together after sterilization would reduce the overall excessive and unnecessary product volume moving through EtO sterilization. Finally, Stop Sterigenics suggested a market driven strategy using clear labelling of the sterilization method on finished products.[376]

EPA Response:

EPA thanks Noxilizer and ClorDiSys for their information on nitrogen dioxide and chlorine dioxide as possible alternatives to EtO for medical device sterilization. Under its Reduced Risk Policy, OPP encourages the submission of applications for pesticides which offer a reduced risk alternative and will give priority consideration to the review of such applications. The registration of such a reduced risk alternative pesticide would allow OPP to achieve greater risk

[375] EPA-HQ-OPP-2013-0244-0091, EPA-HQ-OPP-2013-0244-0084, EPA-HQ-OPP-2013-0244-0086 at www.regulations.gov.
[376] EPA-HQ-OPP-2013-0244-0144 at www.regulations.gov.

reduction. Neither nitrogen dioxide nor chlorine dioxide can presently fully replace the medical device sterilization uses of EtO due to limitations on material compatibility, scalability, and capacity; however, EPA encourages the increased use of alternatives to EtO when possible, to reduce EtO exposures to workers and communities. EPA suggests companies reach out directly to FDA regarding medical device sterilization for their modalities, by email at dice@fda.hhs.gov. Direct phone contacts can also be found at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance.

EPA thanks Stop Sterigenics for their suggestion to identify simple devices, such as scalpels and microfuge tubes, that can use sterilization modalities other than EtO. EPA agrees that anytime a device could use a lower risk sterilization modality, that option should be taken. However, EPA also understands that factors such as the need to package devices as part of sterile surgical kits may limit the ability to use EtO alternatives, even for simple devices. EPA also thanks Stop Sterigenics for their suggestion for improved labelling practices for finished devices. EPA suggests Stop Sterigenics reach out directly to FDA regarding surgical kits and labeling of finished devices, by email at dice@fda.hhs.gov. Direct phone contacts can also be found at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance.

Environmental Justice

Comments Summary:

The Attorneys General of New York, Connecticut, Illinois, Maryland, Massachusetts, Michigan, New Jersey, Oregon, Rhode Island, Vermont, and Wisconsin commented that communities of color are disproportionately exposed to EtO emissions, posing significant environmental justice concerns. They cited the Sterigenics facility in Kingsbury, New York which is nearby a community that has several health and socioeconomic vulnerabilities, including high air toxics cancer risk, high percentage of children under age 5, high percent of low-income households, high levels of respiratory-related emergency department visits, and lower levels of formal education. They also cited Long Island Sterilization in Hauppauge, New York which is nearby a community that has several health and socioeconomic vulnerabilities, including high air toxics cancer risk, high levels of respiratory-related emergency department visits, and high rates of diabetes and mental health challenges. Finally, the Attorneys General stated the Steris Applied Sterilization Technologies in Northborough, Massachusetts is near multiple environmental justice areas.[377]

The Environmental Protection Network (EPN) asserted that EPA's environmental justice analysis focused solely on the potential for differential risks based upon differences in exposures; and that while exposure is a key factor, it is not the only one that can lead to differentiated responses. EPN suggested that EPA examine whether or not the exposure-impacted

[377] EPA-HQ-OPP-2013-0244-0106 at www.regulations.gov.

subpopulations also reflected a differential response in cancer rates, especially for lymphopoietic and breast cancer.[378]

One commenter, who is a private citizen, stated that there are health threats to those people living, working, or going to school near sterilization facilities, and that cancer illnesses have significant, disproportionate impacts on their communities. The development of these cancer cases is especially observed in Black, Latino, Indigenous, and less affluent people who do not speak English and have been systematically underserved and overburdened by social and environmental stressors leading to the development of cumulative and carcinogenic illnesses. Further, more than a fourth of the facilities are located where residents are potentially exposed to emissions from more than one facility, and this is often unknown to the community.[379]

EPA Response:

EPA thanks the submitters for their comment. "Environmental justice" means the just treatment and meaningful involvement of all people, regardless of income, race, color, national origin, Tribal affiliation, or disability, in agency decision-making and other Federal activities that affect human health and the environment.[380] EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. Throughout the registration review process, EPA has sought to include all communities and persons, including minority, low-income, and indigenous populations who may be disproportionately overburdened by exposure to EtO. EPA concurs with the submitters that EtO presents environmental justice concerns, as shown in the EPA analysis conducted as part of the OAR NESHAP.[381]

The EPA appreciates commenters sharing information about the local demographics in impacted communities. EPA anticipates that through the implementation of the OAR final rule and adoption of mitigation measures in this ID, including emissions controls and workplace protections which have the added benefit of further reducing air emissions of EtO, associated health risks in nearby communities, including those with environmental justice concerns will be brought down to acceptable levels of risk based on a risk threshold of 100-in-1 million).

As stated in the EPA OAR's Response to Comments on their recently published *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review*: "The final control requirements under the OAR NESHAP reduce the number of individuals exposed to unacceptable cancer risk (i.e., greater than 100-in-1 million) to zero individuals. Thus, the final requirements reduce risk

[378] EPA-HQ-OPP-2013-0244-0142 at www.regulations.gov.
[379] EPA-HQ-OPP-2013-0244-0260 at www.regulations.gov.
[380] See EO 14096 Sec. 2(b) at https://www.federalregister.gov/documents/2023/04/26/2023-08955/revitalizing-our-nations-commitment-to-environmental-justice-for-all#p-11
[381] EPA-HQ-OAR-2019-0178-1591 at www.regulations.gov.

to acceptable levels for all population groups, including groups with potential EJ concerns. EPA recognizes that a disproportionate share of the individuals that would remain at somewhat elevated risk (albeit at risk levels generally considered acceptable) after implementation of the proposed standards are Hispanic or Latino, driven largely by the facilities in Puerto Rico. While absolute risk declines significantly for Hispanic or Latino individuals after implementing the final requirements, the distribution of the remaining risk is more disproportionately concentrated among Hispanic or Latino individuals compared to the baseline."[382] Although EPA OPP and EPA OAR consider different risk thresholds for residential bystander risks (see Appendix F), at this time, OPP has not identified additional mitigation measures necessary to address residential bystander risk which would not compromise the medical device supply chain.

Regarding EPN's suggestion that EPA examine whether or not the exposure-impacted subpopulations also reflected a differential response in cancer rates, the Environmental Justice analysis conducted for the OAR NESHAP final rule is consistent with EPA's commitment to integrating EJ in the Agency's actions, and followed the directives set forth in multiple Executive orders. EPA is not conducting an EJ analysis on compounding and cumulative factors at this time.

Hierarchy of Controls

Comments Summary:

The American Federation of Labor and Congress of Industrial Organizations (AFL-CIO) stated in their public comment that they support EPA's recognition that workplace exposures must be addressed through the hierarchy of controls, and the Agency's primary emphasis on engineering controls to limit workplace exposures. However, AFL-CIO attested that EPA's proposal would freeze current technologies, rather than encourage the development of new, more effective controls farther up the hierarchy, and that too many workers would be forced to use cumbersome and often ineffective respirators. AFL-CIO suggested EPA require each employer to implement all feasible engineering controls and work practices to reduce exposures, and if those mandated controls do not reduce exposures to the action level, the employer be required to determine whether other engineering controls and work practices would provide further protection. AFL-CIO suggested that only if exposures are still above the action level after all feasible controls have been implemented may respirators be used.[383]

The California Division of Occupational Safety and Health (Cal/OSHA) stated that the use of personal protective equipment (PPE) is a "last resort" when implementing controls for worker safety. The National Institute for Occupational Safety and Health (NIOSH) recommends a hierarchy of controls [NIOSH 1990; NIOSH 2019] that, in descending order of priority, calls for

[382] EPA-HQ-OAR-2019-0178-1595 at www.regulations.gov.
[383] EPA-HQ-OPP-2013-0244-0114 at www.regulations.gov.

the use of elimination, substitution, engineering controls, administrative controls, and lastly PPE.[384]

EPA Response:

EPA thanks the American Federation of Labor and Congress of Industrial Organizations (AFL-CIO) and the California Division of Occupational Safety and Health (Cal/OSHA) for their comments. EPA agrees that, for EtO, the most reliable way to reduce worker exposure is through the hierarchy of controls and that personal protective equipment, such as respirators, should only be used once all other feasible control measures have been put in place. In order to reduce EtO exposure, EPA is implementing the hierarchy of controls, in the following order: elimination, substitution, engineering controls, administrative controls, and lastly personal protective equipment (PPE). Firstly, EPA is eliminating uses for which there are limited benefits. Secondly, EPA is driving industry to look for alternatives to EtO for food commodity fumigation by providing deadlines for its use where alternatives are possible. Next, EPA has identified as necessary label language on EtO products requiring facilities to reach an occupational exposure limit lower than the current OSHA PEL. This may be accomplished through elimination or substitution, or to the extent feasible engineering controls and/or administrative controls. Finally, where it is not feasible to meet the exposure limits through elimination, substitution, engineering or administrative controls, EPA has identified as necessary label language on EtO products requiring the use of PPE in situations where the lowered occupational exposure limits are exceeded. EPA has also identified as necessary label language on EtO products requiring the use of PPE for certain high exposure tasks. Please see Section V.A. for more information on EPA's mitigation strategy for reducing worker exposure to EtO.

Monitoring and Capture Technologies

Comments Summary:

EPA received two comments during the public comment period regarding available technologies for monitoring and capturing EtO in indoor workspaces to 10 ppb or less. Picarro, a company that has developed Cavity Ring-Down Spectroscopy Systems (CRDS), stated in their comment that they recommend EPA clearly specify that CRDS based multipoint workplace monitoring systems are a viable technology option. Picarro asserted that their systems are capable of sampling up to 25 different locations, enabling continuous, real-time monitoring of fugitive emissions, leak detection, and process efficiency. CRDS offers advanced sampling with response time in seconds, no cross-port contamination, and delivers accurate EtO concentration readings in real-time. Picarro further stated that their CRDS systems are already installed and operational in sterilization facilities across many countries. Picarro stated that CRDS systems have demonstrated, in field applications, an ability to detect EtO concentrations below 1 ppb in real-time. Finally, based on concerns for the medical device supply chain, Picarro

[384] EPA-HQ-OPP-2013-0244-0138 at www.regulations.gov.

suggested EPA consider providing extended implementation windows to facilities or adopting a phased approach to implementing new workplace limitations, since this would allow sterilization facilities the necessary time to thoroughly evaluate, install, and implement associated process control strategies.[385]

Regarding other available monitoring technologies, EPA received additional information after the official close of the public comment period from Thermo Fisher about their Fourier Transform Infrared (FTIR) monitoring technology. Thermo Fisher provided technical data to support the feasibility of their systems to reliably monitor EtO in real-time at a level of 10 ppb, including a detection limit assessment, measurement error and linearity study, repeatability study, and an interference study.[386]

EPA received another public comment from Sonata Scientific, a company who develops air purification products. Sonata stated that their air purification systems can reduce EtO levels to below 10 ppb in sterilization facilities and warehouses. Sonata further stated that they are in discussion with medical device suppliers who have expressed interest in their product.[387]

EPA Response:

EPA thanks the submitters for their comments on EtO monitoring and capture technologies. As stated in Section V.A., EPA identified as necessary label language on EtO products requiring that all facilities meet an 8-hour time-weighted average (TWA) occupational exposure limit in work areas using personal breathing zone (PBZ) data, as well as mandatory recordkeeping that demonstrates compliance with this limit. Additionally, EPA identified as necessary label language on EtO products requiring facilities to conduct continuous room air monitoring, using monitoring systems that can measure to at least 0.1 ppm. Facilities may choose the type of monitoring system needed to fulfill these requirements. Data from these monitoring devices must be visible to workers.

Regarding air purification products, as is the case with other engineering and process controls described in Section V.A., EPA encourages facilities to implement any technologies to meet the occupational exposure limit in workspaces.

Warehouses

Comments Summary:

EPA received over 100 comments requesting that communities nearby warehouses and workers inside warehouses be protected from the risks presented by EtO use. These comments came from private citizens as well as the community activist group Stop Sterigenics and non-

[385] EPA-HQ-OPP-2013-0244-0123 at www.regulations.gov.
[386] EPA-HQ-OPP-2013-0244-0401 at www.regulations.gov.
[387] EPA-HQ-OPP-2013-0244-0124 at www.regulations.gov.

profit organizations Earthjustice et. al. In their comment, Stop Sterigenics stated that off-site storage of EtO (e.g., standalone warehouses) is currently not included in the NESHAP proposal, and that sterilizers have been reluctant to disclose these locations to EPA. Stop Sterigenics asserted that the public has a right to know where they are most likely to be exposed to air toxics. Stop Sterigenics further stated that approximately 1% of EtO emissions come from EtO that remains in the sterilized products post aeration, and these sources contribute to community risk and must be addressed.[388]

Earthjustice submitted 10 attachments in their public comment, three of which referenced Becton Dickinson and Company's (BD) warehouse in Covington, Georgia: a report titled, "Estimation of Fugitive Ethylene Oxide Emissions. Global Distribution Center, Covington, Georgia," dated December 13, 2019; a Notice of Violation (NOV) from the Georgia Environmental Protection Division (EPD), dated December 18, 2019; and a statement from Georgia EPD, dated December 20, 2019. BD provided estimates of EtO fugitive emissions occurring at offsite warehouses located in Newton County, Georgia on December 15, 2019, and the Georgia EPD subsequently issued an NOV on December 18, 2019. BD agreed to the terms from the Georgia EPD on December 20, 2019, including ceasing operations from December 23, 2019, until January 6, 2020, conducting air monitoring, and submitting additional information to EPD. At the time of data collection, it was estimated that the warehouse emitted 0.65 pounds per hour or 5,600 pounds of EtO per year.[389]

EPA Response:

EPA thanks the submitters for their comments.

Although the comment from Stop Sterigenics addressed EPA's Office of Air and Radiation's (OAR) NESHAP proposal, EPA's Office of Pesticide Programs is responding since under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), EPA considers, as appropriate, risks to workers and nearby communities where pesticides are used during the registration review process. FIFRA mandates the periodic review of existing pesticides. All pesticides distributed or sold in the United States must be registered by EPA based on scientific data showing that they will not cause unreasonable adverse effects to human health or to the environment when used as directed on product labeling.

In addition to the registration review of EtO as a pesticide under FIFRA, the Agency also conducts a periodic review of air emission standards for air pollutants, including EtO, through the National Emission Standards for Hazardous Air Pollutants (NESHAP) under the Clean Air Act. Regarding standalone warehouses, which are not co-located with sterilization facilities, standards for these facilities are not included as part of the 2024 OAR NESHAP final rule. However, EPA is planning to gather information from stand-alone warehouses to understand what the source category looks like and its emission potential, and, if necessary, develop a

[388] EPA-HQ-OPP-2013-0244-0144 at www.regulations.gov.
[389] EPA-HQ-OPP-2013-0244-0122 at www.regulations.gov.

regulatory action that both lists a new source category under the CAA and proposes standards for stand-alone warehouses handling EtO sterilized medical devices.
With respect to residential bystanders, while FIFRA and the Clean Air Act have different statutory standards, EPA may consider compliance with a NESHAP when identifying whether mitigation measures are necessary to address risks of concern from the use of a pesticide, consistent with the requirement under FIFRA that EPA consider whether the use of a pesticide when used "in accordance with widespread and commonly recognized practice," causes unreasonable adverse effects on the environment.[390]

EPA is taking immediate action on data collection to inform risks associated with EtO treated products stored in off-site warehouses. In assessing risks to human health and the environment from the use of a pesticide, OPP often assesses post-application exposure under FIFRA. EPA will be issuing a data call-in for a specific study for monitoring data on fumigated medical devices to better understand worker exposure to EtO from fumigated commodities, including commodities stored in warehouses attached to or co-located with sterilization facilities, as well as those stored in off-site (non-co-located) warehouses. See Sections V.A. and V.E. for a full explanation of the data requirement.

Based on the information received, EPA will consider whether additional mitigation measures are appropriate to address risks from post-application exposure, taking into account the potential reduction of residual concentrations (and associated reduction of post-application exposure) that is expected to result from the limitation of EtO concentration rates to 600 mg/L for new medical device sterilization cycles. EPA also intends to share the information collected with OSHA, which has existing protections for warehouse workers under its Ethylene Oxide Standard at 29 C.F.R. § 1910.1047. OSHA's Ethylene Oxide Standard at 29 C.F.R. § 1910.1047 applies to "all occupational exposures to ethylene oxide." In contrast, EPA has authority under FIFRA to regulate the registration, sale, distribution, and use of ethylene oxide as a pesticide. Upon consideration of the information received, EPA intends to coordinate with OSHA on any additional mitigation measures to address risks from post-application exposures. Finally, the data OPP collects may be able to help inform OAR on emissions estimates as a new source category is being considered.

OSHA Authority and EPA Authority under FIFRA

Comments Summary:

EPA received three public comments regarding the authority under the Occupational Safety and Health Administration (OSHA) from AdvaMed, Terumo, and Sterigenics. Each of the submitters, all of whom represent industry, asserted that EPA does not have the authority to establish

[390] 7 U.S.C. § 136a(c)(5)(D).

worker protection standards under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) in a way that diverges from the worker protections set by OSHA.[391]

EPA Response:

In an interim registration review decision, EPA may lay out interim risk mitigation measures necessary to address risks identified at a certain point in the registration review process, identify data or information required to complete the review, and include schedules for submitting the required data, conducting the new risk assessment, and completing the registration review.

When identifying whether mitigation measures are necessary to address risks identified at a certain point in the registration review process, EPA considers factors including whether (1) the use of the pesticide according to specifications "will not generally cause unreasonable adverse effects on the environment"; and (2) the labeling of the pesticide complies with the requirements of FIFRA, including that the product is not misbranded.[392] FIFRA defines "unreasonable adverse effects" broadly to include "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."[393] Additionally, under FIFRA, a pesticide is considered to be misbranded if, among others, it does not contain directions for use which are "necessary for effecting the purpose for which the product is intended" and are "adequate to protect health and the environment."[394]

As was explained in the EtO Proposed Interim Decision (PID), it is appropriate that EPA conduct risk assessments and, where it finds risks of concern to workers, develop risk mitigation measures to address risks from the pesticidal uses of chemicals that OSHA also regulates, and it is expected that EPA's findings and mitigation strategies may sometimes diverge from OSHA's. FIFRA is a "comprehensive regulatory statute," which governs "the use, as well as the sale and labeling," of pesticides, and as noted above, requires EPA to determine that the use of a pesticide will not cause unreasonable adverse effects on the environment.[395] "FIFRA's legislative history indicates that Congress specifically intended for FIFRA to protect workers and other persons from occupational exposure directly to pesticides or to their residues."[396] Courts

[391] EPA-HQ-OPP-2013-0244-0097, EPA-HQ-OPP-2013-0244-0146, EPA-HQ-OPP-2013-0244-0141 at www.regulations.gov.
[392] 7 U.S.C. § 136a(c)(5).
[393] 7 U.S.C. § 136(bb).
[394] 7 U.S.C. § 136(q)(1)(F).
[395] *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 991-92 (1984).
[396] Pesticides; Agricultural Worker Protection Standard Revisions, 80 Fed. Reg. 67,496, 67,500 (2015); *see also* S. Rep. No. 92-838 (Part I), 92nd Congress at 14 (noting that the committee took the "occasion to emphasize that the bill requires the Administrator to require that the labeling and classification of pesticides be such as to protect farmers, farm workers, and others coming in contact with pesticides or pesticide residues."); S. Rep. No. 92-838 (Part II), 92nd Congress at 43 ("The entire purpose of the bill is to protect man and the environment. There is no

have also recognized EPA's authority to address worker exposure to pesticides, including in some cases EPA's authority to preempt OSHA's regulation of worker exposure to pesticides.[397]

Notably, OSHA has also repeatedly acknowledged EPA's role in protecting workers engaged in pesticide applications. *See, e.g.*, OSHA, "Standard Interpretation 1910.1200(f)(5)(i), 1910.1200(f)(5)(ii), 1910.1200(f)(6) (1986), https://www.osha.gov/laws-regs/standardinterpretations/1986-05-01. "Employers involved in the application of pesticides fall under standards established by the U.S. Environmental Protection Agency (EPA)."); OSHA, "Standard Interpretation 1910.1200, 1910.1200(b)(5)(i), 1910.1200(b)(5)(v), 1910.1200(g) (1986)" (2018), https://www.osha.gov/laws-regs/standardinterpretations/2018-07-30-0. "The [Hazard Communication Standard] exempts pesticides as defined in FIFRA, when they are subject to the labeling requirements of that Act and labeling regulations issued under that Act by the EPA."

When developing mitigation measures to address risks of concern to workers, though, EPA will: 1) strive for consistency with OSHA requirements and industry best practices, including appropriate application of the hierarchy of controls (e.g., elimination, substitution, engineering controls, administrative controls, PPE), when those measures would address risks of concern to workers; 2) ensure the EPA mitigation measures apply to all potentially exposed workers; and 3) develop occupational risk mitigation measures to address any risks of concern identified by EPA. EPA has been meeting with OSHA monthly since the establishment of the EtO Interagency Task Force in February 2020 to discuss worker mitigation. Furthermore, OSHA had provided review and concurrence on both the PID and this ID.

Lastly, EPA regularly identifies protections for workers that go beyond what are included in OSHA standards. For example, per the Creosote ID issued by EPA under FIFRA, EPA identified as necessary language on creosote product labels requiring additional vacuum cycles each time a load of wood is pressure treated, and providing that no personnel without proper PPE may be located within 50 feet prior to the completion of ventilation, which are measures more protective than OSHA standards.[398, 399]

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question but that farmers and others coming in contact with pesticides or residues fall within the category man."), 44 ("It is imperative that no pesticide be certified by the Environmental Protection Agency unless it is absolutely safe for use by those who must work with or around it.") (citation omitted).

[397] *See, e.g.*, *Organized Migrants in Community Action v. Brennan*, 520 F.2d 1161, 1166, 1169 (D.C. Cir. 1975) (noting EPA's "ample statutory authority to promulgate and enforce occupational health and safety standards for farmworkers" exposed to pesticides, and concluding that because "Congress intended" EPA to regulate farmworker exposure to pesticides, and EPA exercised that authority, OSHA was "prohibited from acting."); *Public Citizen Health Research Group v. Auchter*, 554 F. Supp. 242 (D.D.C. 1983) (holding that OSHA is not precluded by 29 U.S.C. § 653(b)(1) from regulating worker exposure to ethylene oxide in areas where "EPA has apparently exercised minimal, if any regulatory authority in an overlapping manner").

[398] See the Creosote Interim Registration Review Decision Case Number 0139 located at www.regulations.gov in docket EPA-HQ-OPP-2014-0823.

[399] OSHA Division D: Manufacturing; Major Group 24: Lumber and Wood Products, Except Furniture; Industry Group 249: Miscellaneous Wood Products.

FDA Authority and EPA Authority under FIFRA

Comments Summary:

EPA received four public comments regarding the authority under the Food and Drug Administration (FDA) from AdvaMed, Terumo, Sterigenics, and a combined comment from the Ethylene Oxide Task Force (EOTF) and the Ethylene Oxide Sterilization Association (EOSA). Each of the submitters, all of whom represent industry, asserted that EPA does not have the authority to enforce requirements on industry on how to apply EtO for medical device sterilization under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA); rather, the submitters of the comments contested that this is FDA's authority alone.[400]

EPA Response:

FDA is responsible for ensuring the safety and effectiveness of medical devices. For the subset of medical devices that need to be sterilized, FDA continually works to oversee sterilization methods to ensure they are effective and used in amounts that are safe for the patients and health care professionals who use the devices. Medical devices are sterilized in a variety of ways including using moist heat (steam), dry heat, radiation, ethylene oxide gas, vaporized hydrogen peroxide, and other sterilization methods (for example, chlorine dioxide gas, vaporized peracetic acid, and nitrogen dioxide).

In contrast, EPA is responsible for regulating pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). FIFRA mandates the continuous review of existing pesticides. All pesticides distributed or sold in the United States must be registered by EPA based on scientific data showing that they will not cause unreasonable adverse effects to human health or to the environment when used as directed on product labeling. FIFRA defines "unreasonable adverse effects" broadly to include "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."[401] Additionally, under FIFRA, a pesticide is considered to be misbranded if, among others, it does not contain directions for use which are "necessary for effecting the purpose for which the product is intended" and are "adequate to protect health and the environment."[402] By periodically re-evaluating pesticides as science, public policy, and pesticide-use practices change, the Agency ensures that the public can continue to use products in the marketplace that do not present unreasonable adverse effects. Stated plainly, pesticide labeling directs the user how to apply the product.

While EPA is not adopting a maximum sterilization concentration for the use of EtO on medical devices for existing cycles at this time, EPA has identified as necessary the inclusion of language

[400] EPA-HQ-OPP-2013-0244-0097, EPA-HQ-OPP-2013-0244-0146, EPA-HQ-OPP-2013-0244-0141, EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[401] 7 U.S.C. § 136(bb).
[402] 7 U.S.C. § 136(q)(1)(F).

on EtO labels establishing a concentration rate limit of 600 mg/L for new cycles, with a 10-year implementation timeline, as part of this ID. The Agency notes that pesticide labels commonly include maximum application rates where such maximum application rates are necessary to ensure that use of the pesticide will not generally cause unreasonable adverse effects on the environment. There are countless examples of EPA-registered pesticide products that have a required maximum application rate: two recent examples of published Interim Decisions for antimicrobial pesticides with a maximum application rate include creosote and polymeric betaine.[403] Additionally, certain FDA-regulated products for sterilizing medical devices are excluded from the definition of pesticide under FIFRA—specifically "liquid chemical sterilant products (including any sterilant or subordinate disinfectant claims on such products) for use on a critical or semi-critical device, as defined in section 321 of title 21."[404] However, EtO products "are not liquid products and are not excluded" from regulation by EPA under FIFRA.[405] Thus, EPA has authority to regulate the pesticidal uses of EtO under FIFRA, including to regulate the pesticidal uses of EtO for the sterilization of medical devices.

Healthcare Facilities

Comment Submitted by the American Veterinary Medical Association (AVMA)

Comment Summary:

AVMA expressed concerns that the mitigation measures proposed by the Agency would be financially and logistically difficult for veterinary facilities to implement, particularly within a two-year timeframe. AVMA provided estimates on how much it would cost veterinary facilities to implement each of the proposed measures as well as provided estimates on the lost revenue that would result from larger installation or construction projects necessitated by the proposed measures.[406]

EPA Response:

The Agency appreciates the informative and detailed comment provided by the AVMA. The cost estimates give helpful context for how facilities of various sizes would be impacted by the proposed measures. The Agency recognizes that potential exposure in healthcare facilities (including veterinary clinics) is likely much lower than exposure from commercial sterilization facilities. Therefore, the Agency is making changes to its proposal for healthcare facilities. Rather than including all of the measures specified in the PID, this ID identifies only the

[403] See the *Creosote Interim Registration Review Decision Case Number 0139* located in docket EPA-HQ-OPP-2014-0823 and the *Polymeric Betaine Registration Review Interim Decision Case Number 5116* located in docket EPA-HQ-OPP-2013-0374 at www.regulations.gov.
[404] 7 U.S.C. § 136(u); see also *id*. § 136(mm)(3) (defining "antimicrobial pesticide" to include "any other chemical sterilant product (other than liquid chemical sterilant products exempt under subsection (u)), [and] any other disinfectant product").
[405] 40 C.F.R. § 152.6(a)(1).
[406] EPA-HQ-OPP-2013-0244-0080 at www.regulations.gov.

following mitigation measures for healthcare facilities: venting exhaust from EtO devices through separate ventilation systems as described in the AAMI standard, installing abatement devices to capture EtO emissions if the facility uses more than 10 lbs (4535 g) per year, lowered occupational exposure limit and associated respirator use, worker training, and recordkeeping.[407]

Comments Submitted by R. Scott Krewson; Maria Tuo-Zink; and William K. Andersen and A.E. "Ted" May Sterilizers on behalf of Andersen Sterilizers, Inc.

The comments submitted by various employees of Andersen Sterilizers, Inc. (Andersen) are largely similar, so the Agency has grouped them together to summarize and respond collectively. Andersen is both a registrant – producing ethylene oxide products – and a manufacturer of small-scale sterilization devices used in healthcare facilities.[408]

Comment Summary:

Andersen urged that, though the technology is readily available, EPA should not require that all healthcare facilities install abatement devices on EtO sterilization devices because healthcare facilities emit a small fraction of the amount of EtO compared to commercial sterilization facilities. Andersen proposed that instead of requiring abatement devices for all healthcare facilities, the Agency should identify an emissions threshold, beyond which abatement devices would be necessary. Andersen gave the example of one pound of emissions per month as a possible threshold.

EPA Response:

The Agency acknowledges that healthcare facilities emit a much smaller quantity of EtO compared to commercial sterilization facilities, though even small amounts of EtO may result in risks of concern for exposed individuals. As a result, EPA has identified as necessary mitigation at this time label language requiring healthcare facilities that use more than 10 pounds of EtO per year to install an abatement device on all EtO sterilization devices that are used within that facility.

Comment Summary:

Andersen indicated that EPA's proposal that EtO sterilizers have a dedicated ventilation system that is vented more than 25 feet away from door and window openings has been part of the AAMI guidelines for EtO sterilization for decades and that Andersen already follows these

[407] ANSI/AAMI, 2018. American National Standard: Ethylene Oxide Sterilization in Health Care Facilities: Safety and Effectiveness. ANSI/AAMI ST41:2008/(R)2018. American National Standards Institute/Association for the Advancement of Medical Instrumentation (ANSI/AAMI). 2018.
[408] EPA-HQ-OPP-2013-0244-0083, EPA-HQ-OPP-2013-0244-0105, EPA-HQ-OPP-2013-0244-0135 at www.regulations.gov.

guidelines. Additionally, Andersen claimed that EPA's proposal that EtO sterilization devices be located in rooms that are physically separate from all other work areas is both unnecessary and overly burdensome to end users. This is because Andersen's sterilization devices utilize an EtO-impervious sterilization bag that is sealed and placed within a negative-pressure sterilization cabinet. Andersen considers these design features to satisfy the need to provide a physically separate containment area.

EPA Response:

The Agency appreciates the information that Andersen provided regarding their sterilization devices and the installation process for those devices. Considering these devices are already designed with dedicated ventilation and a negative pressure chamber, and this would achieve the exposure reduction goals intended by certain of the proposed mitigation measures in the PID, the Agency has determined it is necessary for facilities to maintain a dedicated ventilation system but has not included in this ID mitigation involving the construction of a separate sterilization room for EtO sterilization purposes.

Comment Summary:

Andersen expressed concern about the proposal to include language on pesticide labels that indicates that the Maximum Likelihood Estimation (MLE) of cancer for EtO handlers in healthcare facilities is between 1 in 25 to 1 in 12. They indicated that this is an over-estimation of cancer risk and that healthcare facilities would not choose to use EtO sterilization devices if EtO product labels suggest that the cancer risks are that high.

EPA Response:

Though the quantity of EtO used in healthcare facilities is significantly less than the amount used in commercial sterilization facilities, the Agency still identified risks of concern for occupational handlers in the healthcare setting. As a result, the Agency has engaged with registrants and other stakeholders in order to identify measures that are both effective in reducing exposures to workers and allow healthcare facilities the option of continuing to use EtO to sterilize medical devices and materials.[409] In the PID, EPA proposed worker training to include a statement of risks at 1 in 25 for MLE and 1 in 12 for upper bound for EtO handlers in healthcare facilities. However, EPA asserts in this ID that training that includes information on the acute and chronic health effects from EtO exposure that aligns with information from OSHA is implementable and understandable by workers and would enable continuity with respect to how workers are provided information about risks associated with EtO. Please see Section V.A. for details on training.

[409] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen Sterilizers September – December 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0411 and *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders American Veterinary Medical Association (AVMA) December 7, 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0413.

Comment Summary:

Andersen raised concerns about various additional mitigation measures that were proposed in the EtO PID. These include reducing application rates to 500mg/L, real-time EtO air concentration monitoring down to 10 ppb and use of SCBA or SAR respirators when workers are unloading EtO sterilization devices.

EPA Response:

In the PID, EPA proposed all of these measures for commercial sterilization facilities, but not all of those measures were proposed for healthcare facilities. Please see Section V.A. for details on all of the healthcare facility mitigation measures included in this ID.

The Agency notes that in the PID, EPA requested further information concerning the feasibility of respirator use for healthcare facilities. For this ID, EPA has determined that in order to reduce worker exposure, it is necessary to align occupational exposure limits for both healthcare facilities and commercial sterilization facilities as explained further in Section VI.A. As a result, EPA has identified necessary label changes requiring respirators to be worn by personnel in healthcare facilities where EtO occupational exposure limits are exceeded. Once those facilities address the issues that may have resulted in elevated exposure to EtO and exposure levels have been recorded below the established limits, workers may stop using respirators. Following conversations with the manufacturers of EtO sterilization devices used in healthcare facilities, EPA believes that the design of all-in-one EtO sterilization devices used in healthcare settings, in addition to the minimal amount of EtO used in these devices, will rarely, if ever, result in exceedances of occupational exposure limits when used as directed.[410] Additionally, it is EPA's understanding that it is already common practice for device manufacturers to troubleshoot problems that sterilization device operators experience with their devices, so a respirator requirement on the EtO label is not expected to be overly burdensome on end users.

Comment Submitted by Various Non-Profit Organizations

Alliance of Nurses for Healthy Environments
Citizens 4 Clean Air IL
Comite Dialogo Ambiental, Inc.
Comité Pro Uno Maywood California
Earthjustice
Environmental Justice Health Alliance for Chemical Policy Reform (EJHA)
GreenLatinos
Labor Council for Latin American Advancement (LCLAA)

[410] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen Sterilizers September – December 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0411.

Mallory Heights Community Development Corporation
Rio Grande International Study Center (RGISC)
Sierra Club
Stop Sterigenics
Union of Concerned Scientists[411]

Comment Summary:

The commenters raised concerns about the fact that the Office of Pesticide Programs' (OPP) EtO Risk Assessment Addendum (DRA) does not quantify risks to communities surrounding healthcare facilities that use EtO to sterilize materials on-site. Additionally, the commenters question why OPP references the Office of Air and Radiation's (OAR) NESHAP Review when that has not yet been completed for healthcare facility uses.

EPA Response:

While EPA did not quantify certain risks, or the impact that available mitigation measures would have on those risks, EPA considered the risks identified by commenters, consistent with its obligations under FIFRA to evaluate both the risks of the use of a pesticide and the benefits of such use. For example, with respect to the risks to residential and non-residential bystanders from the use of EtO at healthcare facilities, EPA explained in the PID (page 18) that exposures to these populations are expected to be "minimal" because the amount of EtO used at healthcare facilities is "much smaller" than at commercial sterilization facilities.

The Agency acknowledges that risks to communities surrounding healthcare facilities that use EtO have not been quantified. However, there are important factors that would result in lower exposures and risks for communities surrounding healthcare facilities compared to those near to commercial sterilization facilities. First, the volume of EtO being used in healthcare settings is a small fraction of the amount used in commercial sterilization facilities. This is due to the amount of EtO used in each cycle of a sterilization device, and the number of cycles that a facility can run in one day. Most facilities only use one sterilization device, which is limited to one or two sterilization cycles each day.[412] Second, despite the low anticipated usage of EtO in these settings, EPA has identified necessary label changes to require facilities using more than 10 pounds of EtO in a single year install abatement devices on any EtO sterilization devices in the facility. This will reduce the amount of EtO emitted by those facilities.

[411] EPA-HQ-OPP-2013-0244-0140 at www.regulations.gov.
[412] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen Sterilizers September – December 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0411 and *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders American Veterinary Medical Association (AVMA) December 7, 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0413.

Comment Summary:

The commenters expressed concern that venting EtO out of facilities according to the AAMI standard, as discussed in the PID, will result in higher risks to surrounding communities.[413]

EPA Response:

Following extensive engagement with EtO sterilization device manufacturers, it is EPA's understanding that all EtO sterilization devices are already installed according to the AAMI standards regarding ventilation.[414] As a result, EPA does not agree that this mitigation measure will result in higher exposures for the surrounding communities, but rather serves to standardize label language and clarify requirements for end users. Additionally, this serves to address concerns of AAMI standards not being binding. Finally, the installation of abatement devices in facilities which use more than 10 lbs of EtO in a year will limit the amount of EtO exposure that is possible in any given community, regardless of the ventilation system in the healthcare facility.

Comment Summary:

The commenters point out that EPA is not adhering to "hierarchy of control" when asking if wearing SCBA or SARS respirators is viable for workers who unload sterilization devices. The commenters suggest that: (a) employers be required to perform routine exposure monitoring in areas of potential exposure, including the sterilization space and the area into which the exhaust from that space is being vented; (b) if recorded exposures exceed the action level, employers be required to determine whether additional engineering controls or work practices (including permitting workers to vacate the area) would protect the workforce; and (c) respiratory protection only be used as a last resort and only in addition to more effective control measures.

EPA Response:

EPA acknowledges the commenters' concerns about the use of respirators by workers in healthcare facilities. However, for this ID, EPA has determined that in order to reduce worker exposure, it is necessary to align occupational exposure limits for both healthcare facilities and commercial sterilization facilities, as explained further in Section VI.A. As a result, EPA has identified necessary label changes requiring respirators to be worn by personnel in healthcare facilities where EtO occupational exposure limits are exceeded. Once those facilities address the issues that may have resulted in elevated exposure to EtO (for example, through the

[413] ANSI/AAMI, 2018. American National Standard: Ethylene Oxide Sterilization in Health Care Facilities: Safety and Effectiveness. ANSI/AAMI ST41:2008/(R)2018. American National Standards Institute/Association for the Advancement of Medical Instrumentation (ANSI/AAMI). 2018.
[414] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen Sterilizers September – December 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0411.

implementation of engineering or administrative controls) and exposure levels have been recorded below the established limits, workers may stop using respirators. Following conversations with the manufacturers of EtO sterilization devices used in healthcare facilities, EPA believes that the design of all-in-one EtO sterilization devices used in healthcare settings, in addition to the minimal amount of EtO used in these devices will rarely, if ever, result in exceedances of occupational exposure limits when used as directed.[415] Additionally, it is EPA's understanding that it is already common practice for device manufacturers to troubleshoot problems that sterilization device operators experience with their devices, so a respirator requirement on the EtO label is not expected to be overly burdensome on end users.

Comment Summary:

The commenters urge EPA to expand its proposed training measures to provide any workers potentially exposed to EtO at EPA's action level with information about (a) the methods used to detect the presence of EtO in the workplace; (b) the health hazards of EtO exposure; (c) control measures implemented by the employer; and (d) measures workers can take to protect themselves.

EPA Response:

The commenters cited training standards that are required under 29 C.F.R. § 1910.1047. EPA has updated training measures for end users and has considered this information in those training measures, which include OSHA standards for training. Please see Section V.A. for details on training measures.

Comment Submitted by the Ethylene Oxide Sterilization Association (EOSA) and Ethylene Oxide Task Force (EOTF)

Comment Summary:

EOSA and EOTF claimed that healthcare facilities have been following the AAMI ST41 standard for over 21 years, but some of the new proposals are not feasible for small-scale facilities such as veterinary, dental, plastic surgery, etc. Particularly, they suggested that physical separation or respirators should not be required.[416]

EPA Response:

The Agency appreciates EOSA and EOTF's confirmation that many of the proposed measures are already followed by healthcare facilities. After conferring with industry stakeholders, EPA has chosen to alter some of the proposed mitigation measures for healthcare facilities, as

[415] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen Sterilizers September – December 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0411.
[416] EPA-HQ-OPP-2013-0244-0147.

described in Section V.A.[417] One aspect of these changes is to no longer include physical separation for EtO sterilization facilities. Due to the design of EtO sterilization devices used in healthcare facilities, which already utilize a negative pressure gradient and vent emissions out of facilities, EPA no longer believes that an additional separation is necessary. Additionally, while EPA does not anticipate that healthcare facilities will see exceedances of the EtO occupational exposure limits when all-in-one sterilization devices are used appropriately, the Agency has identified necessary label changes requiring that personnel in those settings use respirators when EtO levels exceed the limits laid out in the ID. Once those facilities address the issues that may have resulted in elevated exposure to EtO and exposure levels have been recorded below the established limits, workers may stop using respirators.

Food Commodity Fumigation Use

Prohibit Unnecessary Uses of EtO Including Food Uses

Comments Summary:

EPA received many comments requesting that the Agency prohibit all unnecessary EtO uses including the use of EtO on food. These comments were submitted by the 11 Attorneys General, Earthjustice on behalf of 13 environmental NGOs, a combined comment from Stop Sterigenics and Citizens 4 Clean Air IL, a comment from 114 business, community, environmental, faith, health, and labor organizations, and a mass mail campaign sponsored by Earthjustice which had 30,254 supporting signatures or submissions.[418] Earthjustice and 114 business, community, environmental, faith, health, and labor organizations further commented that the Agency should prohibit the use of EtO on spices similar to the European Union. State Senator Beidle also commented that EtO is banned in most other countries for use in the fumigation of food and expressed disappointment that EtO is still allowed to sterilize food in the U.S.[419]

EPA Response:

EPA thanks the commenters for sending in their comments. As the Agency stated in the Proposed Interim Decision, there are no dietary risks expected from EtO use on food commodities, and there are benefits expected when EtO controls microbes on the food commodities which may cause foodborne illnesses. However, the Agency is concerned with

[417] See *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders Andersen Sterilizers September – December 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0411 and *EPA Office of Pesticide Programs (OPP) Meeting with Ethylene Oxide (EtO) Stakeholders American Veterinary Medical Association (AVMA) December 7, 2023* at www.regulations.gov document ID EPA-HQ-OPP-2013-0244-0413.
[418] EPA-HQ-OPP-2013-0244-0106, EPA-HQ-OPP-2013-0244-0140, EPA-HQ-OPP-2013-0244-0144, EPA-HQ-OPP-2013-0244-0148, EPA-HQ-OPP-2013-0244-0398 at www.regulations.gov.
[419] EPA-HQ-OPP-0244-0399 at www.regulations.gov.

inhalation risks to workers inside commercial sterilization facilities and the potential inhalation risks to the communities near facilities where EtO is used.

To help address inhalation risk concerns identified at this stage in the registration review process, the Agency has determined that it is necessary to limit the use of EtO to specific food commodities where use of EtO is deemed critical for food safety and where alternative treatment methods currently are limited or unavailable via a phased cancellation. There are 19 food commodities identified for immediate cancellation, and 49 food commodities identified for a phased cancellation. The phased cancellation will allow for alternative sterilization methods to replace EtO over time while maintaining food safety in the U.S. The timing of the phased cancellation varies based on whether viable alternatives are currently available. At this stage in the registration review process, the Agency believes it is appropriate to allow EtO use to continue for reconditioning and retreating certain products contaminated with human health pathogens. The phased cancellation of EtO use on certain food commodities is expected to result in fewer EtO applications overall, and thus less exposure to workers (including handlers and occupational bystanders), non-residential bystanders, and residential bystanders.

EtO is currently the industry standard for sterilizing dried herbs, dried spices, and dried vegetables and preventing *Salmonella* and *Listeria monocytogenes* contamination after products have been milled and/or packaged. Available alternative sterilization methods must be used prior to milling and/or packaging to obtain the same level of efficacy in reducing pathogen load as EtO.[420] Therefore, food manufacturers that transition to alternative treatment methods would need to sterilize herbs and spices earlier in their processing and adjust their current hygiene practices to prevent contamination between sterilization, milling, and packaging. This change requires an overhaul of current manufacturing processes to ensure sterility will be maintained after treatment and will take time to implement.[421] For some manufacturers, this change may require shifting from contract sterilization outside of the processing facility to treating the herbs and spices themselves, requiring the purchase of additional equipment and the hiring and training of additional employees.

To inform the EtO ID, USEPA held discussions with the European Commission Directorate-General for Health & Food Safety and also contacted the European Spice Association (ESA), a non-profit association representing the European spice industry, regarding the European Union's (EU's) policies as well as chemical and non-chemical alternatives to EtO in the EU for treating pathogens on dried herbs and spices. Representatives confirmed that EtO is not used in the EU and indicated that if a shipment for import is found to be contaminated at the border it is returned, destroyed, or in rare circumstances irradiated. Spice commodities within the EU requiring treatment are typically treated with steam sterilization but may also be treated with irradiation (although this is rare due to lack of consumer acceptance). In the EU, the maximum

[420] For additional details, please see Ethylene Oxide (PC# 042301): Use, Usage, Benefits, and Impacts of Cancellation at https://www.regulations.gov/document/EPA-HQ-OPP-2013-0244-0051.
[421] EPA-HQ-OPP-2013-0244-0422 and EPA-HQ-OPP-2013-0244-0432 at www.regulations.gov.

residue level (MRL) is a combination of EtO and its reaction product, ECH, and is set at the analytical limit of quantification (LOQ).

There are differences between how the EU and the U.S. assessed the risk of EtO. The EU regulates chemical substances based on either hazard or risk. A hazard-based approach only considers the toxicity of the chemical. The EU regulates some pesticides, e.g., carcinogens (EtO is a carcinogen), based on hazard.[422] The U.S. on the other hand uses a risk-based approach which considers both the toxicity of the pesticide and the potential for exposure to the pesticide[423] for decision making. Also, in the U.S., companies must comply with FDA's Food Safety Modernization Act (FSMA) and the regulations supporting FSMA. For example, when a manufacturing/processing facility is subject to the requirements for hazard analysis and preventive controls in the Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food (PCHF) regulation in 21 C.F.R. part 117 and is using a certain process for pathogen reduction as a preventive control, it must validate the process to ensure it is adequate for controlling the identified hazards (21 C.F.R. 117.160(a)).[424] Transitioning to EtO alternatives will therefore require the development of validations for the alternatives to comply with FSMA. The validation process is comprised of several phases and testing requirements. The transition to an alternative, which includes developing validations at an industrial scale, often takes seven to ten years.[425, 426] Thus, even where there is potential for treatment of food commodities (e.g., dried herbs and spices) via methods other than EtO, time is required for transition to such alternatives.

Benefits of EtO Food Use

Comments Summary:

EPA received four comments regarding the benefit of EtO to food production in the U.S. and for ensuring food safety. The Environmental Protection Network stated that EtO is key to avoiding illness from foodborne pathogens on dried herbs, spices, and vegetables. EOSA and EOTF jointly commented that there are currently no effective alternatives to EtO for certain spices and spice-related categories. They also stated that the use of EtO is essential until effective alternatives exist.[427]

[422] https://ec.europa.eu/commission/presscorner/detail/en/memo_16_2151. Accessed November 8, 2024.
[423] FIFRA requires that EPA consider the risks of a pesticide, not just the hazards. *See* 7 U.S.C. § 136(i) (defining "unreasonable adverse effects" in relevant part as "unreasonable risk to man or the environment").
[424] *Ethylene Oxide (EtO) Spice Sterilizing Facilities*. Center for Food Safety and Applied Nutrition (CFSAN), Food and Drug Administration (FDA) responses to questions from Office of Pesticide Programs (OPP), Environmental Protection Agency (EPA). December 20, 2022.
[425] EPA-HQ-OPP-2013-0244-0412, EPA-HQ-OPP-2013-0244-0420, EPA-HQ-OPP-2013-0244-0422 at www.regulations.gov.
[426] EPA-HQ-OPP-2013-0244-0432 at www.regulations.gov.
[427] EPA-HQ-OPP-2013-0244-0142, EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.

USDA commented that the benefit of EtO to food safety and food production in the U.S. is high. USDA stated that spices are integral to the U.S. food industry, and EtO is one of the primary methods used to sterilize spices prior to their incorporation into other food products, such as commercially prepared foods in the U.S. Without proper sterilization, there is the potential for increased food loss that could occur due to spoilage of products that contain spices with high levels of bacterial contamination. The impacts to this market could have significant economic consequences. USDA noted that retail sales of commercially prepared food items were $259 billion in 2022. USDA further commented on the need to allow time for industry to conduct research to support a transition to alternatives.[428]

ASTA commented on the importance of EtO treatment of spices and noted that spices or flavorings derived from spices are used in the majority of packaged food products sold at retail stores in the U.S. (e.g., prepared meals, meat products, soups, sauces, beverages). ASTA provided detailed information for 63 specific dried herbs, dried spices, and dried vegetables for which they explained use of EtO is critical for food safety often due to the potential for *Salmonella* contamination and limited viable alternatives to EtO for the treatment of human pathogens. ASTA provided commodity-specific information for each of the 63 commodities and whether each has been associated with pathogens (e.g., there was a recall of 2,700 pounds of peppermint organic tea in 2011 due to potential *Salmonella* contamination, an FDA study in 2010 found 23 out of 233 sesame seed shipments sampled were contaminated with *Salmonella* and approximately 22% of the contaminated shipments were packaged for retail sale in their final packaging). ASTA also detailed the current or potential alternatives available for each of the commodities. ASTA further noted that industry will require time to transition their operations to include alternative technologies if EtO use is phased out.[429]

EPA Response:

EPA thanks the commenters for providing information regarding the benefits of and alternatives to EtO. The information was taken into account in the development of the ID.

At this stage in the registration review process, the Agency has determined that a phased cancellation is needed for specific food uses for which EtO treatment is not considered to be critical for food safety and for those specific food uses that EtO treatment is considered critical for food safety but have potential viable alternative treatments. The Agency expects that alternative sterilization methods will replace the use of EtO for these food uses. The phased cancellation will allow for alternative sterilization methods to replace EtO over time while maintaining food safety in the U.S.

Public comments were submitted for certain commodities that indicate the potential alternatives are extremely limited at this time. These commodities are dried peppermint tops, sesame seed, dried spearmint tops and dried vegetables. For these commodities, PPO

[428] EPA-HQ-OPP-2013-0244-0128 at www.regulations.gov.
[429] EPA-HQ-OPP-2013-0244-0130 at www.regulations.gov.

tolerances do not exist and there are no PPO products registered for use on most of these commodities, and thereby PPO is not an option for treatment of those commodities at this time.[430] Steam treatment negatively affects the color, flavor, and quality parameters of the commodities, potentially rendering them unmarketable. Irradiation does not have consumer acceptance and has potential capacity issues due to the uncertainty of the supply of cobalt. In addition, several emerging technologies cannot fully replace EtO's current capacity, ability to treat pre-packaged commodities, or the ability to treat all forms of dried herbs and spices (e.g., finely ground).[431] Therefore, for those commodities, the Agency has determined that a phased cancellation is not practicable at this time. EPA will re-evaluate the continued need for EtO treatment on these commodities in the next round of registration review or sooner.

During the public comment period, the Agency received public comments that use of EtO is critical for food safety of Mexican oregano (*Lippia graveolens*) and sassafras. Mexican oregano and sassafras are not included in crop group 19, and there are no EtO or ECH tolerances for those commodities. EtO is not currently allowed for use on those commodities.

Alternatives for Food Commodity Fumigation

Comments Summary:

EPA received four comments providing specific information on alternatives to EtO for fumigating dried herbs, spices, and vegetables. Agri-Neo provided information on Neo-Pure, which it characterized as an organic, non-thermal pasteurization process that can be used to treat various herbs, spices, dried vegetables, and nuts. Kreyenborg provided information on their infrared system which can be used to treat herbs, spices, dried vegetables, and nuts by rapidly and gently heating products with infrared lights.[432]

USDA provided information about several alternatives in their comment submission. Specifically, they provided information on the use and limitations of propylene oxide (PPO), irradiation, dry heat, and steam. They also stated that ultraviolet (UV) light irradiation, microwave, and infrared radiation (IR) are other alternatives and noted that they are not used commercially and may not be feasible due to efficacy or scalability. USDA noted that transitioning to alternatives will be challenging but may be possible for some spices currently sterilized with EtO. They further stated that additional data are needed to support such a transition.[433] USDA also requested that EPA define what is meant by a "viable alternative." ASTA provided information about the use and limitations of several alternatives in their

[430] PPO tolerances do not exist for dried peppermint tops, sesame seeds, dried spearmint tops, or the vegetables included in EtO's *Dried vegetable* tolerance (except dried garlic and dried onion). Establishing tolerances and adding new uses to PPO product registrations will take time to complete in addition to the time necessary to develop validations.
[431] EPA-HQ-OPP-2013-0244-0128 and EPA-HQ-OPP-2013-0244-0130 at www.regulations.gov.
[432] EPA-HQ-OPP-2013-0244-0402, EPA-HQ-OPP-2013-0244-0404 at www.regulations.gov.
[433] EPA-HQ-OPP-2013-0244-0128 at www.regulations.gov.

comments. Their comments covered steam, irradiation, PPO, and emerging treatment methods.[434]

Additionally, EPA received a comment from Elite Spice, Inc. that currently there are limitations for viable treatment alternatives to EtO. Elite Spice suggested that a way to expedite a transition from EtO would be to align the label usage of PPO to match that of EtO. ASTA included a similar suggestion in their comments, urging EPA to expand PPO's registration to cover all the commodities allowed for EtO.[435]

The Environmental Protection Network (EPN) and Maryland State Senator, Pamela Beidle, also submitted comments encouraging the Agency to take regulatory action to facilitate a shift to alternatives instead of using EtO for the fumigation of food commodities.[436]

Earthjustice commented that a prohibition on EtO sterilization would increase demand for alternatives and incentivize an increase in steam sterilization capacity. Earthjustice also commented that EPA did not identify any scientific or technological obstacles to the use of irradiation to treat dried herbs and spices. In addition, Earthjustice commented that if EtO sterilization was prohibited and irradiated and steam-treated spices were the primary available options, there is no evidence to suggest that consumers would simply stop using spices.[437]

EPA Response:

EPA thanks Agri-Neo and Kreyenborg for their information on Neo-Pure and infrared technology as possible alternatives to EtO for treating dried herbs, spices, and vegetables as well as various nuts. Neither Neo-Pure nor Kreyenborg's infrared technology can fully replace the use of EtO to treat food commodities at this time due to current product compatibility (e.g., not currently compatible with finely ground food products and pre-packaged foods) and capacity; however, EPA encourages the increased use of alternatives to EtO when possible, to reduce EtO exposures to workers and communities. EPA also thanks USDA and ASTA for the detailed information about various alternative treatment methods in their comments. All of the information regarding alternatives was considered while developing the Agency's Interim Decision.

In response to USDA's question about viable alternatives, the Agency considers an alternative to be viable if it is available, effective in controlling pathogens, and would not cause the treated commodity to be rejected by consumers.

EPA thanks Elite Spice and ASTA for their suggestion for expediting a transition from EtO to the alternative PPO by expanding PPO's registration. Registrants of PPO are welcome to submit

[434] EPA-HQ-OPP-2013-0244-0130 at www.regulations.gov.
[435] EPA-HQ-OPP-2013-0244-0130, EPA-HQ-OPP-2013-0244-0136 at www.regulations.gov.
[436] EPA-HQ-OPP-2013-0244-0142, EPA-HQ-OPP-2013-0244-0399 at www.regulations.gov.
[437] EPA-HQ-OPP-2013-0244-0140 at www.regulations.gov.

applications for new uses of PPO and EPA will consider such applications consistent with the requirements of FIFRA.

The Agency also thanks EPN and State Senator Beidle for their suggestions to facilitate a shift to alternatives, as well as Earthjustice's comments on alternatives. In response to Earthjustice's comments, the Agency agrees that the phased cancellation of EtO is likely to increase the demand for alternative sterilization methods and will likely increase the capacity of various alternatives to EtO for treating food commodities over time. The Agency has identified obstacles to the use of irradiation as an alternative to EtO as discussed in the Benefits of EtO Food Use section of this response to comments above. As for whether consumers would choose to use or reject spices that were treated with irradiation or steam, public comments indicate that consumers are wary of irradiated foods, and steam can affect the color and flavor of certain spices, can cause clumping of powdered ingredients, and may damage packaging which could render it unmarketable or not viable for all EtO uses.[438] At this stage in the registration review process, the Agency has identified as necessary the cancellation of specific food commodities for which EtO treatment is not considered critical for food safety, and phased cancellation for specific food commodities for which EtO treatment is currently considered critical for food safety but for which potential viable alternative treatments to EtO exist. The Agency expects that alternative sterilization methods will replace the use of EtO for these food uses eventually. The phased cancellation approach will allow for alternative sterilization methods to replace EtO over time while maintaining food safety in the U.S.

Aggregate Assessment

Comments Summary:

EPA received two comments regarding the aggregate assessment in the PID. These comments were received from Attorneys General from NY, CT, IL, MD, MA, MI, NJ, OR, RI, VT, and WI (hereafter referred to as the "11 Attorneys General") and Earthjustice.

The 11 Attorneys General asserts that EPA understates the risk of EtO. They comment that EPA must aggregate the EtO exposure of workers who handle EtO and also live in nearby communities when calculating the actual cancer risk for workers under FIFRA. They further assert that EPA failed to determine the exact concentrations and quantitatively assess the risks to the occupational, residential, and non-residential bystander populations at commercial sterilization facilities, healthcare facilities, and warehouses that store sterilized products.[439]

Earthjustice similarly comments that EPA did not consider the aggregate risks to people who are exposed both on and off the job from the air they breathe, the places they work, and other exposure pathways. Earthjustice asserts that the PID's aggregate statement is "inaccurate and grounded in an impermissibly narrow interpretation of aggregate risk." Earthjustice states that

[438] EPA-HQ-OPP-2013-0244-0128 and EPA-HQ-OPP-2013-0244-0130 at www.regulations.gov.
[439] EPA-HQ-OPP-2013-0244-0106 at www.regulations.gov.

EPA must assess aggregate risks to workers that live in areas with increased exposure to EtO in the ambient air.[440]

EPA Response:

EPA thanks the submitters for their comments.

At this time, EPA has not assessed the aggregate risks to workers who handle EtO and also live in nearby communities. EPA found risks of concern to workers based solely on occupational exposures, and EPA expects that occupational exposures are significantly higher than exposures to residential and non-residential bystanders. In this ID, EPA has identified as necessary mitigation measures to reduce risks of concern to workers. Mitigation measures to reduce risks of concern to workers would also reduce any aggregate risks to persons who handle EtO and also live in nearby communities. Furthermore, on April 5, 2024, EPA's Office of Air and Radiation (OAR) published their final rule for EtO commercial sterilizers, *National Emission Standards for Hazardous Air Pollutants (NESHAP): Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review*. Through the final NESHAP rule, OAR is requiring mitigation to reduce EtO emissions from commercial sterilizers to residential populations. Specifically, OAR is requiring that emission sources in existing and new facilities reduce emissions by a certain percentage depending on the emission source and EtO usage per year.[441, 442] The emissions limits required under the NESHAP will further reduce any aggregate risks to persons who handle EtO and also live in nearby communities.

As discussed in the PID and in the response included in Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Food Quality Protection Act (FQPA) Requirements section of this response to comments above, EPA did not conduct an aggregate risk assessment because it does not expect the co-occurrence of potential residential exposures to EtO and exposures to EtO residues. While the commenter identified instances where EtO has been detected in food sold in the European Union, the commenter identified no such instances in the United States. Based on EPA's understanding of the supply chain for treated food commodities in the United States, EPA does not expect residues of EtO to be in or on treated food commodities when consumed[443, 444] and therefore has concluded there is no co-occurrence of residues in or on food with any potential residential exposures.

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[440] EPA-HQ-OPP-2013-0244-0140 at www.regulations.gov.

[441] Emission sources in sterilization facilities include: sterilization chamber vents, aeration room vents, chamber exhaust vents, Group 1 room air emissions (emissions from indoor EtO storage, EtO dispensing, vacuum pump operations, and pre-aeration handling of sterilized material), and Group 2 room air emissions (emissions from post-aeration handling of sterilized material).

[442] Note that existing Group 2 room air emissions for facilities using less than 4 tons per year are only required to implement a management practice to reduce emissions.

[443] MRID 46625301. Magnitude of the Residue of Ethylene Oxide and Ethylene Chlorohydrin in/on Spices. Wright, M. (2005). Study sponsored by American Spice Trade Association. 829 p.

[444] Memorandum. *Ethylene Oxide. Case 2275. Results of Trade Practices Survey on Spices & Anticipated Residues for Dietary Exposure Assessment*. Leung Cheng, Health Effects Division. March 26, 1997.

Further, Congress intended "aggregate risk" as referenced in the FQPA to refer to "the pesticide chemical residue to include dietary exposures under all tolerances for pesticide chemical residue, and exposure from non-occupational sources as well." H.R. Rep. 104-669(II), at 41 (1996) (emphasis added). This intent to limit consideration of aggregate exposure to non-occupational exposures is further reflected in the fact that, when "establishing, modifying, leaving in effect, or revoking a tolerance," EPA shall consider factors including "available information concerning the aggregate exposure levels of consumers (and major identifiable subgroups of consumers) to the pesticide chemical residue and to other related substances, including dietary exposure under the tolerance and all other tolerances in effect for the pesticide chemical residue, and exposure from other non-occupational sources." 21 U.S.C. § 346a(b)(2)(D)(vi) (emphasis added). Thus, the FFDCA, as amended by the FQPA, does not require EPA to aggregate occupational and non-occupational sources when determining whether to establish, modifying, leave in effect, or revoke a tolerance and EPA appropriately did not do so here.

Occupational Risk from Downstream Offgassing of Treated Items

Comments Summary:

EPA received two comments that express concerns about risks to workers downstream from the EtO treatment process that may be exposed to EtO offgassing from the treated items. These comments were submitted by Environmental Law and Science and a combined comment from Stop Sterigenics and Citizens 4 Clean Air IL.

The comment from Environmental Law and Science expresses concerns regarding worker risk from offgassing of imported spices that were treated with EtO outside the U.S. Environmental Law and Science commented that EPA did not determine the level of U.S. workers' exposure to EtO from spices that are treated with EtO outside of the U.S. They also commented that if spices are subject to a phased-out cancellation for EtO use in the U.S., there may be a corresponding increase in spice treatments outside the U.S. Environmental Law and Science asserted that increased spice treatments with EtO outside the U.S. will likely result in increased EtO levels in fugitive emissions from these products after they arrive in the U.S.[445]

Stop Sterigenics and Citizens 4 Clean Air IL commented that the risk to downstream workers that may be exposed to EtO has not been quantified and that it would be prudent to evaluate downstream worker risk (e.g., grocery workers that repeatedly unload recently treated spices, semi-truck drivers transporting sterilized products, dock workers handling sterilized products, medical center workers who continually handle sterilized products).

EPA Response:

[445] EPA-HQ-OPP-2013-0244-0137 at www.regulations.gov.

EPA thanks Environmental Law and Science for their comments. The Agency issued a Data Call-In (DCI) for additional EtO data (GDCI-042301-1428) which includes a non-guideline study for monitoring data on fumigated commodities. That study is intended to evaluate emission rates for EtO from treated commodities/materials and the potential for occupational exposure due to those emissions in the channels of trade after fumigation activities are complete. The Agency is working with the EtO registrants to obtain these data and once received, will use this data to assess this exposure scenario.

Although the Agency does not currently have data to quantify EtO exposures and risks from offgassing of imported spices, these exposures are not expected to be significant based on the available residue data. EtO is a volatile gas. Sterilization studies[446] show that EtO residues dissipate rapidly after sterilization. EtO residues are expected to be present on commodities immediately after the fumigation process (e.g., 24 hours) and may be present as the commodity enters the channels of trade, but those EtO residues are expected to completely dissipate by the time the commodity is available for consumption (e.g., two months). The offgassing of EtO is expected to follow a similar trend as the residues. Offgassing would be expected to be higher immediately after treatment and to dissipate over time. Therefore, the worker exposure from any remaining EtO on the spices once they arrive in the U.S. is expected to be minimal. The required monitoring data on fumigated commodities is expected to allow the Agency to confirm this assumption once it is received.

Tolerance Definition

Comments Summary:

EPA received one comment on the proposed wording change in the PID for the commodity definition from USDA.[447] In the PID, the Agency proposed to change the definition from "Herb and spice, group 19, dried, except basil" to "Herb and spice group 19, dried leaves, except basil." USDA commented that the new definition appears to exclude the commodities included in spice subgroup 19B because it specifies dried leaves. USDA further commented that the spices in Crop Group 19 are not limited to the leaves, and also include the roots, rhizomes, stems, leaves, bark, flowers, fruits, and seeds of the listed plants. USDA suggested that EPA revise the wording to "Herbs and spices group 19, except basil, dried."

EPA Response:

The Agency concurs with the concerns noted by USDA (i.e., the definition includes more than just the leaves). The Agency intends to revise the wording as follows: "Herbs and spices group 19, dried, except basil."

[446] MRID 46625301. Magnitude of the Residue of Ethylene Oxide and Ethylene Chlorohydrin in/on Spices. Wright, M. (2005). Study sponsored by American Spice Trade Association. 829 p.
[447] EPA-HQ-OPP-2013-0244-0128 at www.regulations.gov.

Tolerance Revocation

Comments Summary:

EPA received six comments regarding the proposal in the PID to remove tolerances for those herbs and spices for which uses may be cancelled. These comments were submitted by the United States Department of Agriculture (USDA), American Spice Trade Association (ASTA), a combined comment from CropLife America (CLA) and Responsible Industry for a Sound Environment (RISE), Environmental Law and Science, Environmental Protection Network (EPN), and a combined comment from the Ethylene Oxide Task Force (EOTF) and the Ethylene Oxide Sterilization Association (EOSA).

Comments from USDA, ASTA, CLA-RISE, and EOTF/EOSA assert that if the tolerances were revoked as proposed in the PID, this would cause a disruption to global trade and the supply of spices to the U.S. since the tolerance requirements of section 408 of the FFDCA also apply to EtO-treated commodities imported to the U.S. Commenters stated that this proposal would have critical food safety implications for food commodities that largely depend only on EtO for pathogen control. Commenters also noted that EtO and ECH tolerances should be maintained even if registered uses are voluntarily cancelled. ASTA pointed out that if the tolerances are revoked, the tolerance will be interpreted as zero which would be unachievable. USDA requested that EPA consider converting the currently established tolerances to tolerances for residues in imported commodities if registered uses are voluntarily cancelled.[448]

ASTA and CLA-RISE further noted that tolerance revocations would be unnecessary and inappropriate since EPA has identified no concerns about the safety of the EtO tolerances. CLA-RISE states that EPA "inappropriately combines FIFRA's pesticide product registration standard (under which EPA must consider the effects of a pesticide's use on human health and the environment) with the FFDCA's safety standard for tolerances (under which EPA considers dietary risks resulting from exposure to a pesticide chemical residue)."

The comments from ASTA and CLA-RISE assert that occupational risk is not an appropriate basis for tolerance revocation. CLA-RISE also notes that tolerance revocation should be based upon the statutory factors established under the FFDCA, which focuses on aggregate exposure levels of consumers and not residue exposure from occupational sources. CLA-RISE further asserts that if EPA has determined that use of EtO on walnuts no longer meets the standard for registration under FIFRA, cancellation of that use under FIFRA is a more appropriate mechanism for addressing those concerns.[449]

[448] EPA-HQ-OPP-2013-0244-0128, EPA-HQ-OPP-2013-0244-0130, EPA-HQ-OPP-2013-0244-0133, EPA-HQ-OPP-2013-0244-0147 at www.regulations.gov.
[449] EPA-HQ-OPP-2013-0244-0130, EPA-HQ-OPP-2013-0244-0133 at www.regulations.gov.

Conversely, Environmental Law and Science recommended that EPA cancel the tolerances for any spice that is removed from the approved list for ethylene oxide treatment. Additionally, EPN commented that as commodities transition away from EtO to alternatives in the future and a registrant subsequently voluntarily cancels the use of EtO for that commodity, there may be additional tolerances that can be removed.[450]

EPA Response:

EPA thanks the submitters for their comments.

With respect to the allowable grounds for tolerance revocation, the FFDCA provides that EPA may only establish or leave in effect a tolerance if the Agency determines that it is "safe." 21 U.S.C. 321(b)(2)(A)(i). The FFDCA further provides that, if EPA determines that a tolerance is not safe, EPA must modify or revoke it; however, the statute does not prohibit EPA from modifying or revoking tolerances under other circumstances. *Id.* EPA has consistently considered the necessity of a tolerance a relevant factor in determining whether to revoke a tolerance. *See, e.g.*, 82 Fed. Reg. 42,531, 42,532 (Sept. 8, 2017) ("It is EPA's general practice to propose revocation of those tolerances for residues of pesticide active ingredients on crop uses for which there are no active registrations under FIFRA, unless any person in comments on the proposal indicates a need for the tolerance to cover residues in or on imported commodities or legally treated domestic commodities."). However, because EPA has determined that the EtO and ECH tolerances are safe, and has received comments indicating a need for the EtO and ECH tolerances to cover residues on certain imported commodities and while imported commodities and domestically sterilized commodities are in the channels of trade, EPA does not intend to revoke EtO or ECH tolerances for such commodities even if EtO is no longer registered for use on such commodities in the United States. And, as EPN points out in their comment, there may be opportunities in the future to revoke tolerances if they are no longer necessary for food safety in the U.S.

Walnut Tolerance

Comments Summary:

EPA received one comment regarding the need for a walnut tolerance from Hammons Products Company (Hammons). Hammons commented that they are currently treating black walnuts at their facility in Missouri. Hammons also provided information about the black walnut industry in the midwestern U.S. and lack of available alternatives to EtO for treating pathogens on black walnuts.

Hammons also commented that black walnuts and certain spices previously had been listed with an EtO residue tolerance of 50 ppm in section 180.151 of the Code of Federal Regulations

[450] EPA-HQ-OPP-2013-0244-0137, EPA-HQ-OPP-2013-0244-0142 at www.regulations.gov.

(C.F.R.). However, they note that “Black Walnut” was changed to “Walnut” in C.F.R. section 180.151 and comment that the change from “Black Walnut” to “Walnut” had the potential to expand EtO use to the larger walnut industry. Hammons requested that the tolerance for EtO under 40 C.F.R. section 180.151 be allowed to continue for “Walnut” or amend the tolerance to “Black Walnut”.

EPA Response:

EPA thanks Hammons for their comment. The information about the niche use on black walnuts and lack of alternatives was taken into account in the development of the ID.

The Agency did not receive any comments suggesting that English walnuts are treated with EtO in the U.S., nor that any walnut variety is treated with EtO outside of the U.S. and then imported to the U.S., requiring a tolerance for import purposes. However, the comment from Hammons indicates that EtO is being used to treat black walnuts and therefore EtO and ECH tolerances are necessary for black walnut.

In the Federal Register of December 31, 2008 (73 FR 80317), EPA proposed “to revise commodity terminology to conform to current Agency practice as follows: in 40 C.F.R. 180.151(a)(1), ‘‘walnut, black’’ to ‘‘walnut.’’” This action was finalized in the Federal Register of September 11, 2009 (74 FR 46694).

Given the current need for EtO and ECH tolerances for black walnuts treated with EtO, the Agency intends to allow the EtO tolerance for walnut to remain and to establish a walnut tolerance for ECH. However, the Agency has identified as necessary the phased cancellation for the use of EtO to treat black walnuts.

Reduced application rate for food commodity treatment

Comments Summary:

EPA received two comments regarding a lower application rate for the treatment of dried herbs and spices with EtO. ASTA provided comments that many spice companies have indicated that it is possible and efficacious to treat spices at levels lower than the current 500 mg/L maximum. ASTA expressed an interest in working with the Agency to lower the EtO concentration for spice treatment methods. They also commented that time would be needed for the spice industry to conduct scientific studies to validate the efficacy of treatment on various spice commodities, pursuant to FSMA regulations.

The Environmental Protection Network (EPN) commented that EPA did not propose a firm timeframe for establishing a new upper limit of EtO for spice treatments in the PID. EPN recommended two years for timing. They noted that the registrants should have established the rate(s) needed for their product(s) and new studies would be needed only if current

registrations are dependent upon rates above the 500 mg/L limit. They further commented that if results indicate failure to achieve successful pathogen control at or below 500 mg/L, then alternative methods must be developed, or the product registration canceled. EPN also commented that vigorous efforts must be continued to find EtO alternatives.

EPA Response:

The Agency thanks ASTA and EPN for their comments. EPA understands that current EtO validations for dried herb and spice treatments have been developed using the 500 mg/L labeled rate and acknowledges that new validations would be needed for lower EtO rates to comply with FSMA. Developing validations and transitioning to alternatives can take seven to ten years.[451, 452]

In response to EPN's comments, a lower labeled rate would require industry to develop validations for EtO use on the various food commodities at the lower EtO rate for FSMA compliance.

Taking into account the comments received and the phased cancellation outlined in this ID that will require new validations to be established for the alternative treatment methods, EPA is not pursuing a lower EtO rate at this time. The Agency is prioritizing the shift to alternatives and the establishment of validations for those methods over developing validations for EtO at lower application rates. Establishing a lower rate will be revisited at the next round of registration review for any food commodities with continued EtO use or sooner.

Beekeeping Equipment Fumigation Use

Use of EtO on Beekeeping Equipment in North Carolina

Comments Summary:

EPA received three comments on the proposed cancellation of the use of EtO on beekeeping equipment in North Carolina. The 11 Attorneys General and EPN concurred with terminating the use of EtO on beekeeping equipment.[453]

USDA commented that even though alternatives to EtO (e.g., cultural controls, mechanical/physical controls) are promoted in North Carolina, cases of American Foulbrood (AFB) still exist. USDA also commented that other states' managing of AFB without EtO does not mean that EtO does not provide benefits in North Carolina. USDA notes that the main benefit of using EtO to fumigate beekeeping equipment with AFB is that the equipment hive can be

[451] EPA-HQ-OPP-2013-0244-0412, EPA-HQ-OPP-2013-0244-0420, EPA-HQ-OPP-2013-0244-0422 at www.regulations.gov.
[452] EPA-HQ-OPP-2013-0244-0432 at www.regulations.gov.
[453] EPA-HQ-OPP-2013-0244-0106, EPA-HQ-OPP-2013-0244-0142 at www.regulations.gov.

treated without destroying the frames or the comb. They note that irradiation is the only other option that does not destroy drawn comb, and irradiation is more costly. USDA further commented that there is the potential that the occupational exposure is overestimated in the Agency's risk assessment based on the average number of treatments per year, the use of surrogate air monitoring data from spice facility, that fact that the treatment chamber is located outdoors, and that the operator is not spending 8 hours in a 24-hour time-period in the vicinity of the chamber. USDA requested clarity regarding whether EPA would be willing to assess the occupational and bystander risks using additional monitoring data or if EPA would be willing to allow beekeeping equipment to be a labeled use on current products if risks can be mitigated, if the use is supported by a registrant.[454]

EPA Response:

EPA thanks EPN and the 11 Attorneys General for concurring with the Agency's proposal. EPA also thanks USDA for providing benefits information about the beekeeping equipment use in North Carolina and comments on the assumptions used in the Agency's risk assessment.

The Agency agrees that EtO currently provides benefits to beekeepers in North Carolina as an additional tool to sterilize beekeeping equipment once it is infected with *Paenibacillus larvae* and to manage American Foulbrood (AFB). However, alternative chemical, cultural, and mechanical controls are available and widely used nationally. Alternative sterilization methods offer the same level of AFB control as EtO, but beekeepers in North Carolina may face short term impacts, including increased costs, as they transition from EtO to alternative methods of control.

The Agency acknowledges that the risk assessment for the beekeeping equipment use has conservative assumptions; however, the assessment uses the best available data at this time. The current risk estimates are health protective and do not underestimate anticipated exposures, including occupational and bystander (occupational and non-occupational) exposures.

The Agency maintains that there are adequate chemical, cultural, and mechanical controls available to manage AFB at reasonable cost. Therefore, the Agency has determined that termination of the use of EtO for disinfecting beekeeping equipment is necessary to address identified risks of concern from EtO and indicates in the Interim Decision that the use be terminated.

[454] EPA-HQ-OPP-2013-0244-0128 at www.regulations.gov.

Appendix F: Explanation of Office of Air and Radiation and Office of Pesticide Programs Cancer Risk Decision Frameworks

EPA Clean Air Act (CAA) Residual Risk Assessments

Section 112 of the Clean Air Act (CAA) instructs EPA to regulate hazardous air pollutants (also known as "air toxics") by setting limits on the amount of pollution that industrial sources can emit to the air, rather than by setting ambient standards, which are limits on the amount of a pollutant that is allowed in the outdoor air. CAA section 112 establishes a two-stage regulatory process for setting emission standards for hazardous air pollutants (HAP). The first stage involves EPA establishing technology-based standards, either maximum achievable control technology (MACT) emission standards or generally available control technology standards (GACT). The second stage involves EPA evaluating these standards to determine whether additional requirements are needed to address any remaining risk associated with HAP emissions. This second stage is referred to as the "residual risk review."

EPA conducts residual risk reviews for sources of HAP in each industrial source category (e.g., Petroleum Refineries, Taconite Iron Ore Facilities, Aerospace Manufacturing Facilities, etc.) subject to MACT standards in order to address any remaining or "residual" risk from HAP emissions. Specifically, section 112(f)(2) of the CAA requires the EPA to determine whether promulgation of additional standards or revised standards is needed for a source category to provide an ample margin of safety to protect public health or to prevent an adverse environmental effect.

The approach incorporated into the CAA and used by the EPA to evaluate residual risk and to develop standards under CAA section 112(f)(2) is a peer-reviewed two-step approach.[455,456] In the first step, the EPA determines whether risks are acceptable. This determination ''considers all health information, including risk estimation uncertainty, and includes a presumptive limit on maximum individual lifetime [cancer] risk (MIR) 1 of approximately 1 in 10 thousand.'' (54 FR 38045, September 14, 1989). If risks are unacceptable, the EPA must determine the emissions standards necessary to reduce risk to an acceptable level without considering costs.

In the second step of the residual risk approach, the EPA considers whether the emissions standards provide an ample margin of safety to protect public health ''in consideration of all health information, including the number of persons at risk levels higher than approximately 1 in 1 million, as well as other relevant factors, including costs and economic impacts, technological feasibility, and other factors relevant to each particular decision.'' *Id.* The EPA

[455] U.S. EPA. *Risk and Technology Review (RTR) Risk Assessment Methodologies: For Review by the EPA's Science Advisory Board with Case Studies – MACT I Petroleum Refining Sources and Portland Cement Manufacturing*, June 2009. EPA-452/R-09-006. *https://www3.epa.gov/airtoxics/rrisk/rtrpg.html*.

[456] Recommendations of the SAB Risk and Technology Review Methods Panel are provided in their report, which is available at: *https://yosemite.epa.gov/sab/sabproduct.nsf/4AB3966E263D943A8525771F00668381/$File/EPA-SAB-10-007-unsigned.pdf*.

must promulgate emission standards necessary to provide an ample margin of safety to protect public health or determine that the standards being reviewed provide an ample margin of safety without any revisions. After conducting the ample margin of safety analysis, we consider whether a more stringent standard is necessary to prevent, taking into consideration costs, energy, safety, and other relevant factors, an adverse environmental effect.

The EPA conducts a risk assessment that includes estimates of:

- Maximum individual cancer risk (MIR) posed by the HAP emissions from each source in the source category at residential locations.
- Hazard index (HI) for chronic exposures to HAP with potential to cause chronic (or long-term) noncancer health effects at residential locations, and
- Hazard quotient (HQ) for acute exposures to HAP with the potential to cause noncancer health effects off-site and at locations that may be accessible to the public (*e.g.,* roadways and public buildings).

The MIR is defined as the cancer risk associated with a lifetime of exposure (i.e., 70 years) at the highest concentration of HAP where people are likely to live (i.e., residential locations). The HQ is the ratio of the potential exposure to the HAP to the level at or below which no adverse effects are expected; the HI is the sum of HQs for HAP that affect the same target organ or organ system. The risk assessment also provides estimates of the distribution of cancer risks within the exposed populations, cancer incidence and an evaluation of the potential for adverse environmental effects.

Federal Insecticide, Fungicide, Rodenticide Act (FIFRA) Risk Assessment

For OPP, the level of concern, for a given endpoint, refers to a predetermined quantified level above which OPP believes more detailed consideration of the risks of a pesticide is necessary. When it appears that the use of a pesticide may pose risks greater than the level of concern, OPP will first attempt to refine its risk assessment to obtain a more accurate characterization of the risk. If the level of concern is still exceeded, OPP will consider a variety of measures for reducing the risk to a level at or below the level of concern. In general, OPP will use a tiered approach to reduce risks starting with the quickest and least expensive means. This may be accomplished through discussions with registrants who voluntarily agree to risk reduction measures; through risk reduction measures identified in a Reregistration Eligibility Decision document or Interim or Final Registration Review Decision document; or other means. If OPP believes that these actions will not result in sufficient risk reduction, it may initiate a special review or take regulatory action under FIFRA.

OPP considers dietary and non-dietary cancer risks of 10^{-6} and less to be negligible, and thus it would not typically pursue risk reduction measures for such negligible risks. OPP pursues risk mitigation measures to ensure that dietary risks do not exceed 10^{-6}. OPP also pursues risk mitigation measures where non-dietary risks exceed 10^{-4}, except in those cases where it has

determined that benefits exceed the risks. OPP examines non-dietary risks in the 10^{-5} to 10^{-4} range to determine whether the benefits of use outweigh the risks and will seek ways to mitigate unacceptable risks. OPP's policy allows for the consideration of a wide range of factors in making a risk management decision for non-dietary risks. These factors may include: risk to individuals, number of people exposed, weight of scientific evidence regarding carcinogenicity, lower risk alternatives, and benefits associated with the pesticide under review. In general, OPP tolerates less risk to individuals as the size of the exposed population increases. Therefore, for the largest exposed populations, including residents and pesticide handlers, OPP seeks to reduce the individual risks to the greatest extent feasible, preferably to 10^{-6} or less. The goal is to ensure that there is a minimum level of protection from exposure to pesticides for workers, residents, bystanders, and vulnerable populations, particularly children. OPP strives to ensure that this policy is consistently applied to all pesticide program decisions.

Risks greater than 10^{-4}. It is OPP's intent, generally, not to grant new registrations or allow the continued registrations of existing uses which have non-dietary cancer risks greater than 10^{-4} (e.g., 10^{-3}), because such risks, based on the program's experience, typically outweigh benefits and thus will cause unreasonable adverse effects. If risk reduction measures do not reduce the risk below the level of concern, OPP may initiate Special Review or take regulatory action under FIFRA. As is the case for EtO, OPP recognizes there may be currently registered high risk uses which are very beneficial and have no currently registered alternatives.

Risks Between 10^{-6} and 10^{-4}. OPP evaluates pesticides with risks in this range and seeks ways to reduce individual cancer risks to the greatest extent feasible, preferably to 10^{-6} or less. OPP will require, as appropriate, additional protective clothing or equipment or changes in application methods, taking benefits into account, through the reevaluation and registration processes, as follows:

> Applications for new registrations. In considering applications for new registrations with non-dietary cancer risks, OPP carefully examines those uses with potential risks in the 10^{-6} to 10^{-4} range to seek ways of reducing those risks before registration occurs. Also, OPP recognizes there may be currently registered high risk uses which are very beneficial and have no currently registered alternatives. In such a case, under its Reduced Risk Policy, OPP encourages the submission of applications for pesticides which offer a reduced risk alternative and will give priority consideration to the review of such applications. The registration of such a reduced-risk alternative pesticide might affect the risk/benefit balance for the currently registered higher-risk chemical, allowing OPP to achieve greater risk reduction.
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> Reregistration and Registration Review. For those chemicals subject to reregistration and registration review, OPP carefully examines those uses with estimated risks in the 10^{-6} to 10^{-4} range to seek ways of cost-effectively reducing risks.

Ongoing examination of chemicals through reevaluation. OPP monitors registered pesticides with risks greater than 10^{-6} to look for opportunities to reduce risks further, including requiring technology changes and changes in application methods. For example, advances in technology have had a major effect on reducing exposure to pesticide handlers. Examples include closed-loading systems, enclosed cabs offering respiratory protection, containers which limit spilling, and water-soluble packaging. OPP encourages these technological improvements as they become available and requires them in appropriate cases.

Risks Below 10^{-6}. Generally, OPP does not seek risk reduction below this level unless it is cost-effective.[457]

[457] Memorandum, 1996. *Non-Dietary Cancer Risk Policy*. Daniel M. Barolo, Director Office of Pesticide Programs.

Appendix G: Updated Terms and Conditions of Registration

The Agency has identified necessary changes to the terms of the EtO product registrations for use in commercial sterilization facilities to include the following updated terms:

Collection of Worker Exposure Data

On an annual basis, [Name of EtO Registrant] must collect worker monitoring data from commercial sterilization facilities using any of the following products [Product Names and EPA Registration Numbers of Registrant Products for Use in Commercial Sterilization Facilities]. [Name of EtO Registrant] must require persons purchasing any of the aforementioned products to submit worker monitoring data from the commercial sterilization facilities in which these products are used, for example through a contractually binding term in a purchase agreement. [Name of EtO Registrant] may not sell any of the aforementioned products to persons who are not contractually bound to submit worker monitoring data from the commercial sterilization facilities in which these products are used. Worker exposure data must follow approved exposure monitoring methods.

1) [Name of EtO Registrant] must collect worker monitoring data annually beginning six months after the Interim Decision (ID) label amendments are approved.

2) The information collected by [Name of EtO Registrant] must include:
    a. Time-weighted average personal breathing zone (PBZ) monitoring of the handlers specifically involved in activities related to the sterilization/fumigation (e.g., loading and unloading chambers, routine maintenance, product transfer, etc).
    b. Documentation of the activities each worker performed while monitored.
    c. Whether or not the worker was wearing a respirator, and what type of respirator.
    d. For non-handlers in the facility (e.g., office workers, warehouse workers), the data must include PBZ monitoring data to monitor exposures.
    e. A statement on whether or not the facility has complied with the NESHAP requirements (e.g., not required, started, optimizing, in effect).

3) The information collected by [Name of EtO Registrant] is not required to include identifiable facility or worker information.

4) [Name of EtO Registrant] must maintain raw data submitted by individual facilities. Maintenance of amalgamated facility data in lieu of raw data is not permissible.