US Environmental Protection Agency
Office of Pesticide Programs

Reregistration Eligibility Decision for Ethylene Oxide

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Prevention, Pesticides
and Toxic Substances
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Reregistration Eligibility Decision for Ethylene Oxide

Reregistration Eligibility Decision (RED) Document for Ethylene Oxide

List B

Case Number 2275

Approved by: _____ Date: 3/3/08

Steven Bradbury, Ph.D.
Director
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Glossary of Terms and Abbreviations

ai	Active Ingredient
ARC	ARC Specialty Products, Balchem Corporation
ASTA	American Spice Trade Association
BQA	Baltimore Quality Assurance
CAS	Chemical Abstracts Service
CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
CFSAN	FDA Center for Food Safety and Applied Nutrition
CSF	Confidential Statement of Formulation
DCI	Data Call-In
DNT	Developmental Neurotoxicity
EBH	Ethylene Bromohydrin
ECH	Ethylene Chlorohydrin
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EG	Ethylene Glycol
EOSA	Ethylene Oxide Sterilization Association
EPA	Environmental Protection Agency
ETO	Ethylene Oxide
EUP	End-Use Product
FDA	Food and Drug Administration
FDA/BVM	Food and Drug Administration Bureau of Veterinary Medicine
FDMS	Federal Docket Management System
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA	Food Quality Protection Act
FPLA	Fair Packaging and Labeling Act
FR	Federal Register
GACT	Generally Available Control Technology
GAP	Good Agricultural Practices
GLN	Guideline Number
GMP	Good Manufacturing Practices
HACPP	Hazard Analysis and Critical Control Point
HEC	Human Equivalent Concentration
IARC	International Agency for Research on Cancer
IMIS	Integrated Management Information System
IRIS	Integrated Risk Information System
LOC	Level of Concern
LOAEL	Lowest Observed Adverse Effect Level
MACT	Maximum Achievable Control Technology
µg/g	Micrograms Per Gram
µg/L	Micrograms Per Liter
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligram Per Liter

mg/m	Milligram Per Meter
MOE	Margin of Exposure
MRID	Master Record Identification Number. EPA's system for recording and tracking studies submitted.
MUP	Manufacturing-Use Product
NCDA&CS	North Carolina Department of Agriculture and Consumer Affairs
NIH	National Institute of Health
NOAEL	No Observed Adverse Effect Level
OAR	EPA Office of Air and Radiation
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides, and Toxic Substances
ORD	EPA Office of Research and Development
OSHA	Occupational Safety and Health Administration
PD	Pharmacodynamic
PEL	Permissible Exposure Limit
PK	Pharmacokinetic
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PPO	Propylene Oxide
PVC	Polyvinyl Chloride
RED	Reregistration Eligibility Decision
RfC	Reference Concentration
RfD	Reference Dose
RGDR	Regional Gas Dose Ratio
RQ	Risk Quotient
SAP	Science Advisory Panel
SCBA	Self Contained Breathing Apparatus
SF	Safety Factor
SLN	Special Local Needs
STEL	Short-term Exposure Limit
TGAI	Technical Grade Active Ingredient
TRED	Tolerance Reassessment Decision
UF	Uncertainty Factor
URF	Unit Risk Factor
USDA	United States Department of Agriculture
USDA-ARS	United States Department of Agriculture-Agricultural Research Service
VHP	Vaporized Hydrogen Peroxide
WPS	Worker Protection Standard

Abstract

This document presents the Environmental Protection Agency's (EPA's or the Agency's) decision regarding the reregistration eligibility of the registered uses of the active ingredient ethylene oxide (ETO). The Agency has revised its occupational risk assessments for ETO which incorporate worker exposure monitoring from medical and spice contract sterilization facilities. The Agency has determined that the benefits of ETO use outweigh the occupational risks associated with its use provided that the risk mitigation measures outlined in this document are adopted and label amendments are made to reflect these measures. The Agency has therefore determined that products containing the active ingredient ETO are eligible for reregistration provided that the risk mitigation measures outlined in this document are adopted and label amendments are made to reflect these measures.

EPA has identified potential human health risks of concern associated with the current registered uses of ETO from occupational exposure. To reduce these exposures and to address current risks of concern, the Agency, in agreement with the technical registrants of ETO, will implement label restrictions (single chamber technology for hospitals, and respirator use for beekeeping use in North Carolina) for application of ETO to address occupational exposure concerns. The Agency is also specifying that employee safety and awareness training occur for all employees (including office staff) in contract sterilization facilities to ensure that all employees are aware of the risks associated with ambient levels of ETO from sterilization processes. In addition, the Agency encourages additional aeration of contract sterilization facilities as a Best Management Practice. For contract sterilization facilities, future monitoring efforts should include the entire facility (including monitoring and documenting air concentrations in office space, loading and unloading areas, break areas, etc.) to have accurate information regarding exposure of employees that are not wearing respirators as part of their daily routine on account of the nature of their work.

I. Introduction

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended in 1988 to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act calls for the development and submission of data to support the reregistration of an active ingredient, as well as a review of all data submitted to the Environmental Protection Agency (hereafter referred to as EPA or the Agency). Reregistration involves a thorough review of the scientific database underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of a pesticide, to determine the need for additional data on health and environmental effects, and to determine whether or not the pesticide meets the "no unreasonable adverse effects" standard of FIFRA.

On August 3, 1996, the Food Quality Protection Act (FQPA) was signed into law. This Act amended FIFRA and the Federal Food, Drug, and Cosmetic Act (FFDCA) to require reassessment of all existing tolerances for pesticides in food. EPA decided that, for those chemicals that have tolerances and are undergoing reregistration, tolerance reassessment would be accomplished through the reregistration process. Under FQPA, in reassessing these tolerances, the Agency must consider, among other things, aggregate risks from non-occupational sources of pesticide exposure, whether there is increased susceptibility among infants and children, and the cumulative effects of pesticides that have a common mechanism of toxicity. FQPA requires EPA to consider available information concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity" when considering whether to establish, modify, or revoke a tolerance. Potential cumulative effects of chemicals with a common mechanism of toxicity are considered because low-level exposure to multiple chemicals causing a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any one of these individual chemicals.

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to ETO and any other substances, and ETO does not appear to produce a toxic metabolite produced by other substances. For the purposes of this reregistration eligibility decision, therefore, EPA has not assumed that ETO has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

EPA completed the tolerance reassessment for ETO in 2006. This evaluation considered the aggregate risk from exposure to ETO and its reaction products through food and drinking water and any potential residential or bystander exposure. The Agency concluded in its 2006 Tolerance Reassessment Decision (TRED) for ETO that risks from aggregate exposure to ETO are not of concern. Therefore, the tolerances for ETO and its reaction product ethylene chlorohydrin (ECH) were reassessed as safe after risk mitigation options were adopted. The

TRED is available in the public docket EPA-HQ-OPP-2005-0203 located on-line in the Federal Docket Management System (FDMS) at <http://www.regulations.gov>.

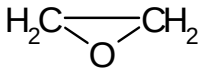
This document addresses the remaining potential risks to workers and as such completes the Agency's Reregistration Eligibility Decision (RED) for ETO. Risks summarized in this document are for ETO only because ETO is the chemical of concern for occupational exposure (not the ETO reaction products).

On August 3, 2005, EPA opened the public docket with the preliminary risk assessments for ETO. Public comment was taken and the risk assessments were revised during phases 3 and 4 of the Public Participation process. The risk assessments were revised to incorporate public comment and new data, and released again on February 22, 2006, for public comment during Phase 5 of the Public Participation process. The TRED was issued July 24, 2006. Based on public comment and incorporation of new information, a second Phase 5 public comment was opened on May 30, 2007.

This document presents EPA's revised occupational risk assessments which incorporate newly available worker exposure monitoring data from medical and spice contract sterilization facilities and the reregistration eligibility decision for ETO. This document consists of six sections. Section I contains the regulatory framework for reregistration. Section II provides a description of the chemical and a profile of the use and usage of the chemical. Section III provides an overview of the revised occupational risk assessments. Section IV presents the Agency's risk management and reregistration eligibility decisions and rationale. Section V outlines specific label changes and language necessary to implement the risk mitigation measures outlined in Section IV. Section VI, the References, provides the sources cited in this document. The appendices provide related information and supporting documents. The preliminary and revised risk assessments for ETO are available in the public docket EPA-HQ-OPP-2005-0203 located on-line in the Federal Docket Management System (FDMS) at <http://www.regulations.gov>.

II. Chemical Overview

A. Chemical Identity

Chemical Structure: 

Molecular Formula: C_2H_4O

Common Name: Ethylene Oxide

CAS Name: Oxirane

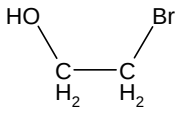
CAS Registry Number: 75-21-8

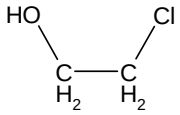
OPP Chemical Code: 042301

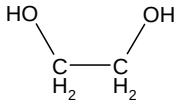
Case Number: 2275

Technical Registrants: Honeywell Corporation and ARC Specialty Products of Balchem Corporation

ETO has three reaction products— ethylene bromohydrin (EBH), ethylene chlorohydrin (ECH), and ethylene glycol (EG).

Ethylene Bromohydrin Chemical Structure: 

Ethylene Chlorohydrin Chemical Structure: 

Ethylene Glycol Chemical Structure: 

EBH and ECH have been shown to result from fumigation of foods with ETO due to interaction with natural bromides and chlorides present in the food items. Residues of EBH and ECH are found in spices. At high sterilization concentrations, ETO reacts with moisture to form EG and, in the presence of sugars, glycol derivatives. Therefore, these reaction products (EBH,

ECH, and EG) were the chemicals of concern for dietary (oral) exposure and were assessed in the 2006 TRED. In the TRED, the Agency determined that dietary risk resulting from exposure to ETO and its reaction products is below the Agency's level of concern after risk mitigation options were adopted.

ETO is the compound of concern for residential non-dietary bystander (inhalation) exposure (i.e., the reaction products mentioned in the previous paragraph do not form during inhalation exposure to bystanders). EPA's Office of Air and Radiation (OAR) conducted a residential risk assessment which estimated cancer as well as acute and chronic non-cancer risk to bystanders (USEPA, 2005). The Agency concluded that potential cancer and non-cancer risks do not indicate any further regulatory action is necessary at this time for residential inhalation exposure.

ETO is also the compound of concern for occupational (inhalation) exposure. While inhalation exposure is the route of most concern, potential exists for dermal exposure to ETO, halohydrin and EG residues during post-sterilization activities (e.g., transportation of treated materials, bagging/containerizing treated spices). However, it is reasonable to assume that handling of the actual treated materials during post-sterilization activities is limited and dermal exposure is negligible. Therefore, this RED addresses risk only from ETO.

B. Regulatory History

ETO was first registered as a pesticide in 1966. It is a FIFRA List B reregistration pesticide. ETO entered EPA's Special Review process in 1978 based on concern for potential developmental toxicity, mutagenicity, and neurotoxic effects in workers. A Position Document 1 (PD1) was published in the Federal Register of January 27, 1978, to announce the initiation of the Special Review. In the early 1980s, the carcinogenicity of ETO became of concern and was added to the Special Review. Based on the reregistration assessments discussed in this RED and the supporting documentation, the Special Review of ETO will be concluded pursuant to the Agency's Special Review regulations and a notice closing out the Special Review will be issued in the near future.

In 1994, the International Agency for Research on Cancer (IARC) reclassified ETO as a known human carcinogen based on epidemiology and mutagenicity effects in humans. EPA's Office of Research and Development (ORD), National Center for Environmental Assessment (NCEA) is in the midst of an Integrated Risk Information System (IRIS) review of ETO. NCEA is conducting its evaluation of the carcinogenicity of ETO based on available human epidemiological data. This analysis is anticipated to be finalized in September 2009. Should this information materially alter EPA's understanding of ETO, the Agency will consider appropriate action.

The Occupational Safety and Health Administration (OSHA) regulates worker exposure to ETO. In 1984, OSHA reduced the permissible exposure limit (PEL) from 50 ppm to 1 ppm. In 1988, OSHA established a short-term exposure limit (STEL) of 5 ppm for exposures up to 15 minutes. In 1996, EPA required pesticide product label improvements to standardize

precautionary statements, specify items to be treated with ETO, and require all users to adopt OSHA's risk reduction measures.

EPA issued a Data Call-In (DCI) Notice for ETO in 1989 requiring submission of product chemistry, residue chemistry, and toxicology studies. Additional DCIs were issued in 1992 to address chemistry data deficiencies. The toxicology database has been reviewed and is considered complete for ETO. A DCI was issued in conjunction with the 2006 TRED requiring submission of toxicology studies for the reaction product ECH.

The Agency's Office of Air and Radiation (OAR) promulgated ETO emission standards for sterilization facilities on December 6, 1994. The rule regulates approximately 65 major commercial sterilization facilities and 35 area sources requiring the application of Maximum Achievable Control Technology (MACT) and/or Generally Available Control Technology (GACT). OAR assessed risks from residual ETO emissions after the application of MACT standards to determine if further control was warranted. After conducting this review, OAR determined that no additional control requirements were warranted. OAR issued a final decision for ETO emissions standards for sterilization facilities on April 7, 2006 (available at <http://www.epa.gov/fedrgstr/EPA-TOX/2006/April/Day-07/t3314.htm>). Recently, OAR analyzed ETO emissions from hospital sterilizers. OAR issued a final rule for hospital emissions on December 28, 2007 (available at <http://www.epa.gov/fedrgstr/EPA-AIR/2007/December/Day-28/a25233.htm>). The final rule required that all hospitals that do not control their emissions of ETO reduce emissions by sterilizing full loads of equipment to the extent possible.

The Food and Drug Administration (FDA) is an important federal partner with respect to ETO regulation. In the case of ETO's medical uses, FDA reviews the efficacy of ETO in the sterilization of a wide variety of medical devices and approves ETO sterilizers for medical use. Sterilization methods available in the United States for the sterilization of medical devices and regulated by FDA fall into two categories. The first category includes sterilization methods used in health care facilities to resterilize devices designed for reuse in patient care. The second general category of sterilization subject to FDA regulation is the sterilization of manufactured medical devices (Murphy, 2006).

With respect to ETO's spice uses, FDA is responsible for ensuring that food, including spices, are not adulterated or misbranded. FDA samples imported spice shipments as well as domestic spice commodities for the presence of pathogens. FDA detains spice shipments when pathogens are found. When a spice shipment is detained, a reconditioning proposal can be submitted by the responsible firm to FDA. ETO is often used to recondition the shipment. After the reconditioning, the shipment is tested again to verify that the contaminant load has been reduced.

The FFDCA prohibits the marketing of adulterated or misbranded cosmetics in interstate commerce and vests FDA with authority in this area. In addition, under the authority of the Fair Packaging and Labeling Act (FPLA), FDA requires an ingredient declaration for finished cosmetic products. ETO and its reaction products (EBH, ECH, and EG) are not considered

cosmetic ingredients. They are not listed in the International Cosmetic Ingredient Dictionary, the primary source of cosmetic ingredient nomenclature.

FDA also regulates finished cosmetic products after they are in commercial distribution and have entered interstate commerce. During the manufacturing of cosmetics, ETO is used as an ethoxylating agent for the synthesis of ethoxylated surfactants that are used in cosmetic products. FDA monitors cosmetic products for levels of 1,4-dioxane, a reaction product of ETO formed during the ethoxylation process. There is a potential for residual ETO to be present in ethoxylated surfactants and cosmetic products containing these ingredients. In addition, there are many cosmetic ingredients that are derivatives of EG. Any unreacted EG present in a cosmetic ingredient, may also be present in a finished cosmetic product (Havery, 2008).

ETO's pesticidal use to reduce microbial loads on cosmetics is minimal (less than 1 percent of total ETO pesticidal use). This RED addresses only the worker exposure from the pesticidal use of ETO on cosmetics.

C. Use and Usage Profile

Ninety percent of ETO use is for non-pesticidal industrial uses that are beyond the scope of FIFRA. The following is information on the currently registered pesticidal uses of ETO. Sections IV and V include information on those currently registered uses which are eligible for reregistration and Appendix A provides a detailed table of those uses which are eligible for reregistration.

Type of Pesticide:	ETO is an antimicrobial and conventional chemical. It is a biocide, fungicide, fumigant, herbicide, insecticide, rodenticide used to control the following pests: American foulbrood disease (*Bacillus* larvae), animal pathogenic bacteria, animal pathogenic fungi, bacteria, bacterial spores, *Candida albicans*, European foulbrood disease (*Streptoccus pluton*), Herpes simplex virus, Hew (FDA/BVM), unspecified microorganisms, *Mycobacterium spp*., *Nosema apis*, *Pseudomonas spp*., Rhinoviruses, storage microorganisms, stored product insects, wax moth.
Formulations:	ETO is formulated and marketed as a gas or a pressurized liquid. The end use formulations are all gas mixtures of ETO and inert gases (e.g., carbon dioxide) in varying concentrations.
Methods of Application:	Sterilization/fumigation with ETO must be performed only in vacuum or gas tight chambers designed for use with ETO. It is applied by commercial applicators only; there are no residential uses of ETO.
Use Sites:	ETO is used to sterilize medical or laboratory equipment, pharmaceuticals, and aseptic packaging (21CFR §201), or to reduce microbial load on musical instruments, cosmetics, whole and ground spices or other seasoning materials (40 CFR §180) and artifacts, archival material or library objects. In North Carolina, ETO is also used to fumigate beehive equipment (e.g., woodenware

	boxes and frames) and wax or plastic combs that are contaminated with the bacteria *Paenibacillus larvae*, the cause of American Foulbrood Disease.
Estimated Usage:	A maximum of approximately 8.2 million pounds of ETO are used annually in the United States for commercial fumigation/sterilization. Approximately 7.4 million pounds are used annually for sterilization of medical and laboratory items/equipment. ETO treatment is the principal method used to reduce bacterial levels in spices/herbs and black walnuts. An estimated maximum of approximately 800,000 pounds are used annually for fumigation of herbs and spices. All other uses combined account for less than 1 percent of the total annual usage.

Approximately 1,900 hospitals have in-house ETO sterilization chambers. Hospitals tend to have small self-contained units for ETO sterilization. Bulk sterilization occurs at contract sterilization facilities that handle multiple pallet sterilizations. The scope of materials potentially sterilized within these types of contract sterilization facilities is assumed to include medical devices (representing the majority of use), musical instruments, library and museum artifacts, and cosmetic ingredients. Approximately 30 contract sterilization facilities exist in the United States; 21 of those facilities represent 90 percent of the contract medical device sterilization capacity in the United States. In addition, many manufacturers of medical devices use ETO in-house to sterilize their products.

There are approximately 9 contract sterilization facilities in the United States that treat both medical devices and spices and 6 contract sterilization facilities in the United States that only treat spices; each facility has 2 to 3 workers that are actively involved in the ETO treatment process in some capacity. Therefore, approximately 45 workers in the United States are exposed to the potential risks from the fumigation of spices.

The beekeeping use of ETO currently is limited to a state-managed facility in North Carolina. The North Carolina Department of Agriculture and Consumer Affairs (NCDA&CS) uses 2 vacuum tight chambers designed for use with ETO. Both chambers are located outdoors. Approximately a half dozen employees in NC currently are involved with the ETO use for sterilization/fumigation of beekeeping equipment.

III. ETO Occupational Risk Assessments

EPA has held three public comment periods for the ETO risk assessments. Based on public comments received during the three public comment periods, worker exposure monitoring data from the medical and spice contract sterilization facilities and new information that the Agency has received, the occupational risk assessments have been revised for ETO. These assessments demonstrate potential human health cancer risks of concern for workers resulting from all uses of ETO. In addition, potential non-cancer health risks have been identified for workers who are exposed to the ambient ETO levels in the facility but not the aeration/unloading rooms. These workers do not wear a respirator at any time during the day. A summary of potential risk concerns is presented below. The revised occupational risk assessments for ETO, dated March 24, 2008 (spice and beekeeping uses), and March 26, 2008 (medical, musical instrument, library and museum artifact, and cosmetics uses), respectively, are available in the public docket EPA-HQ-OPP-2005-0203 located on-line at <http://www.regulations.gov>.

The target occupational margin of exposure (MOE) for ETO is 30. It is based on the uncertainty factor of 30X (3X interspecies factor and 10X intraspecies factor). When conducting inhalation risk assessments, the magnitude of the uncertainty factors applied is dependent on the methodology used to calculate risk. For studies in this risk assessment with inhalation data, uncertainty factors are based on the RfC (reference concentration) methodology developed by the ORD for the derivation of inhalation RfCs and human equivalent concentrations (HECs) for use in MOE calculations. Since the RfC methodology takes into consideration the pharmacokinetic (PK) differences but not the pharmacodynamic (PD) differences, the uncertainty factor for interspecies extrapolation may be reduced to 3X (to account for the PD differences) while the uncertainty factor for intraspecies variation is retained at 10X. Thus, the uncertainty factor when using the RfC methodology is customarily 30X.

Table 1 presents the non-cancer and cancer endpoints. The Agency's ORD is currently analyzing ETO's carcinogenicity based on human epidemiological data. In the interim, the Agency has considered the range of rodent unit risk estimates from 2.22×10^{-2} $(mg/m^3)^{-1}$ to 2.67×10^{-3} $(mg/m^3)^{-1}$ based on lung adenomas/carcinomas in male B6C3F1 mice at the high end and brain tumors in male F344 rats at the low end for risk assessment purposes. This eight-fold selected range of unit risk estimates provides a comparison of both common and rare tumors in both sexes of rats and mice.

Exact information regarding daily/weekly/yearly usage of ETO is only available for the beekeeping use. ETO is used for beekeeping uses in North Carolina for approximately 40 days per year. Therefore it is assumed that there is potential for short- and intermediate-term exposures. Cancer risk calculations for the beekeeping use are based on an exposure frequency of 40 days per year. Occupational exposure duration was assumed to be 35 years over a 70-year lifespan.

Table 1. Summary of Toxicological Doses and Endpoints for Occupational Exposure to ETO.

Exposure Scenario	Dose Used in Risk Assessment, UF	Level of Concern for Risk Assessment	Study and Toxicological Effects
Inhalation Short-Term (1 - 30 days) Intermediate-Term (1 - 6 months)	NOAEL= 50 ppm (37.5 ppm, or 68 mg/m^3 adjusted for occupational exposure)	Occupational MOE = 30	Subchronic Inhalation Toxicity Study in Mice (Snellings et al., 1984) • LOAEL = 100 ppm based on neurological effects (altered gait, decreased motor activity, and abnormal righting reflex) and absolute and relative spleen weight decreases in females.
Inhalation Long-Term (> 6 months)	Occupational Exposure NOAEL = 10 ppm (7.5 ppm, or 13.5 mg/m3 adjusted for occupational exposure)	Occupational MOE = 30	Two Generation Reproduction Study, Inhalation Exposure, Rats (Chun and Neeper-Bradley, 1993) • Systemic LOAEL = 25 ppm (45 mg/m^3) based on decreased mean body weight gains in F0 males and females and F1 males during premating period. • Reproductive LOAEL = 25 ppm based on increased postimplantation loss (two-fold) and decreased live pups per litter in F0 generation were observed. • Offspring LOAEL = 25 ppm based on decreased mean pup body weight gain in both F0 and F1 generations.
Cancer (Inhalation)	High end URF based on lung adenomas/carcinomas in male B6C3F1 mice = 2.22 E-02 $(mg/m^3)^{-1}$ (0.040 $(ppm)^{-1}$). Low end URF based on brain tumors in male F344 rats = 2.67 E-03 $(mg/m^3)^{-1}$ (0.0048 $(ppm)^{-1}$).		

UF = uncertainty factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, MOE = margin of exposure, URF = Unit Risk Factor

Note: Study NOAEL and LOAEL are adjusted to human equivalent doses for occupational scenario only. For example, the animal NOAEL of 10 ppm (6h/day, 5d/week)) is adjusted to human NOAEL of 7.5 ppm (8 h/day, 5d/week), assuming the regional gas dose ratio (RGDR) is similar between animals and humans (10 ppm x 6h/8h =7.5 ppm); In case of any continuous exposures (e.g., RfC), rat NOAEL of 10 ppm would be converted to human equivalent dose of 1.79 ppm [10 ppm x (6h/24h) x (5days in week/7days in week) =1.79 ppm] assuming similar RGDR between animals and humans (USEPA,1994).

For all other uses of ETO, EPA assumed that there is potential for all exposure durations (i.e., short (1-30 days)-term, intermediate (1-6 months)-term, long (> 6 months)-term). For cancer risk calculations it was assumed that exposure frequency (the number of days per year workers are exposed to ETO) was 240 days per year, and occupational exposure duration was 35 years over a 70 year lifespan. Though facilities that use ETO potentially do so year-round (hence the 240 day work-year assumption), it is recognized that these are likely conservative estimates. However, EPA has no additional information for further refinement.

A. Medical Use (Hospitals and Contract Sterilization Facilities)

As discussed in Section 5.0 of the *Review of Calculated Ethylene Oxide Exposures for Ethylene Oxide Sterilization Plant Workers (MRID No. 47331801) Submitted in Support of the Occupational Exposure Assessment of the Antimicrobial Uses of Ethylene Oxide for the Reregistration Eligibility Decision (RED)* (found at <http://www.regulations.gov./>), there are risk estimates that exceed EPA's level of concern from occupational exposure to workers in hospitals and contract sterilization facilities under some exposure scenarios.

For hospital workers that are involved with the ETO sterilization process (e.g., load/unload ETO chamber, change/maintain ETO tanks), short- and intermediate-term MOE estimates are not of concern (MOEs are 77), but long-term non-cancer risks are of concern (MOEs are 15). Using a range of unit risk factors, the potential cancer risks associated with ETO use in hospitals range from 2.6×10^{-4} to 2.1×10^{-3} which exceeds the Agency's level of concern of 1×10^{-6}.

In contract sterilization facilities, the workers who are actually working with ETO and are involved directly with the ETO sterilization process wear respirators at some point during the day (i.e., when performing an activity where the OSHA PEL could be exceeded such as chamber unloading, tank maintenance, etc.). These workers have non-cancer MOE estimates that are not of concern (short- and intermediate-term MOEs are 250 and long-term MOEs are 50) for non-cancer risks. However, based on ambient air monitoring data in facilities, other staff (e.g., workers unloading and loading vehicles and office workers who are not engaged in sterilization activities requiring respirator use) could have long-term non-cancer MOEs of 25 assuming they are in the building 8 hours per day for 240 days each year.

Using a range of unit risk factors, the potential cancer risks associated with the contract sterilization use range from 7.9×10^{-5} to 1.3×10^{-3}, which exceeds the Agency's level of concern of 1×10^{-6}.

B. Musical Instrument Use

Musical instruments are sterilized in contract sterilization facilities. Therefore, risks described above for the medical contract sterilization facilities apply to the musical instrument use.

C. Library and Museum Artifact Use

Library and museum artifacts are sterilized in contract sterilization facilities. Therefore, risks described above for the medical contract sterilization facilities apply to the library and museum artifact use.

D. Cosmetics Use

Cosmetics are sterilized in contract sterilization facilities. Therefore, risks described above for the medical contract sterilization facilities apply to the cosmetics use.

E. Spice Use

As discussed in Section 3.2 of the *Addendum to the Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision (RED) for Ethylene Oxide* (found at <http://www.regulations.gov./>), there are risk estimates that exceed EPA's level of concern from occupational exposure to workers in spice sterilization facilities.

EPA anticipates the following spice industry-related activities to result in potential worker exposure to ETO and its reaction products.

- Inhalation exposure to ETO during sterilization activities;
- Dermal exposure to EG and the halohydrins during post-sterilization activities;
- Inhalation exposure to off-gassed ETO from treated spices during post-sterilization activities.

It is reasonable to assume that handling of the actual treated materials during post-sterilization activities is limited and dermal exposure is negligible. In addition, it is assumed that exposures and risks to off-gassed ETO from residue levels will be no higher than those from chamber re-entry or opening the chamber door. Non-cancer risk estimates for inhalation exposure to ETO during sterilization activities, calculated as MOEs, are not of concern. Workers involved in the ETO sterilization process have short- and intermediate-term MOEs of 380 and long-term MOEs of 190 for non-cancer risks. However, based on ambient air monitoring data in facilities, other staff (e.g., workers unloading and loading vehicles and office workers who are not engaged in sterilization activities requiring respirator use) could have short- and intermediate-term MOEs of 44 and long-term non-cancer MOEs of 40 assuming they are in the building 8 hours per day for 240 days each year. These risk estimates are not of concern. However, potential cancer risks for workers from inhalation of ETO range from 2.1×10^{-5} to 8.4×10^{-4}, which exceeds 1×10^{-6} risk.

F. Beekeeping Use

Exposures and risks associated with fumigation of beekeeping equipment are expected to be similar to those described above for spice fumigation considering the similarities in the fumigation process (e.g., chamber loading, gas introduction).

Based on the limited number of ETO applications (30 to 40 times per year) for the North Carolina beekeeping use, ETO exposure for this use is not of chronic duration. Therefore the short-/intermediate-term endpoint for the non-cancer assessment would apply to this use. Non-cancer risk estimates, calculated as MOEs are not of concern (i.e., short- and intermediate-term MOEs are 69).

Since worker exposures are considered similar to spice fumigation, the beekeeping use information (i.e., 30 to 40 times per year) is applied to recently submitted worker exposure data for spice industry workers. This yields an estimated cancer risk range of 1.1×10^{-5} to 9.2×10^{-5} which exceeds EPA's level of concern.

Table 2 presents a summary of the non-cancer and cancer risk estimates for the various uses of ETO for both the workers that are actively involved with ETO sterilization activities and the workers who are not engaged in sterilization activities requiring respirator use.

Table 2. Summary of Non-cancer and Cancer Risk Estimates for ETO Uses

Use	Non-cancer Risk Estimate[1]	Cancer Risk Estimate[2]
Hospitals (approx. 1,900): (1) Medical Use	Short- and Int-term MOE = 77 **Long-term MOE = 15** (Avg. of 11 SIC codes)	**2.6×10^{-4} to 2.1×10^{-3}** (Avg. of 11 SIC codes)
Contract Sterilization (approx. 30 facilities): (1) Medical Use (2) Musical Instrument Use (3) Library and Museum Artifact Use (4) Cosmetics Use	Workers (respirator): Short- and Int-term MOE = 250 Long-term MOE = 50 Workers (no respirator): Short- and Int-term MOE = 130 **Long-term MOE = 25**	**Workers (respirator):** **7.9×10^{-5} to 6.6×10^{-4}** **Workers (no respirator):** **1.6×10^{-4} to 1.3×10^{-3}**
Contract Sterilization (approx. 15 facilities): (1) Spice Use	Workers (respirator): Short- and Int-term MOE = 380 Long-term MOE = 190 Workers (no respirator): Short- and Int-term MOE = 44 Long-term MOE = 40	**Workers (respirator):** **2.1×10^{-5} to 1.7×10^{-4}** **Workers (no respirator):** **1.0×10^{-4} to 8.4×10^{-4}**
Beekeeping Use (1 facility)	Short-term MOE = 69 Int-term MOE = 69 Long-term – N/A	**1.1×10^{-5} to 9.2×10^{-5}**

[1] Target MOE = 30.

[2] Based on available rodent data. ORD analysis of ETO's carcinogenicity (based on human epidemiological data) due 9/30/09. Cancer slope factor ranges from 0.0048 $(ppm)^{-1}$ to 0.040 $(ppm)^{-1}$.

Note:

Air concentrations needed to obtain 1.0×10^{-4} cancer risk = 0.023 to 0.19 ppm.

Air concentrations needed to obtain 1.0×10^{-6} cancer risk = 0.00023 to 0.0019 ppm.

Air concentration of 0.25 ppm is represented by a range of cancer risks of 1.3×10^{-4} to 1.1×10^{-3}.

Air concentration of 1 ppm is represented by a range of cancer risks of 5.3×10^{-4} to 4.4×10^{-3}.

IV. Risk Management and Reregistration Decisions

A. Determination of Reregistration Eligibility

Section 4(g)(2)(A) of FIFRA calls for the Agency to determine, after submission of relevant data concerning an active ingredient, whether or not products containing the active ingredient are eligible for reregistration. The Agency has previously identified and required the submission of the generic (technical grade) data to support reregistration of products containing ETO as an active ingredient. The Agency has completed its review of generic data that pertain to non-food uses, and has determined that the data are sufficient to support reregistration of all products containing ETO provided the registrations are amended in a manner consistent with this document.

ETO sterilization/fumigation is performed in vacuum or gas tight chambers. Uses of ETO do not include outdoor applications, nor uses on birdseed. The use of ETO for fumigating beekeeping equipment for the control of various honeybee pathogens is expected to benefit the overall health of the hive. Therefore, exposure to terrestrial wildlife, aquatic organisms from the exclusive registration of ETO for indoor food and nonfood uses would be considered negligible. Negligible exposure yields an expectation of negligible risks to non-target terrestrial wildlife, aquatic organisms, and plants. Further, the Agency expects that such indoor uses of ETO will result in insignificant exposure to drinking water resources.

The Agency has completed its review of submitted data and its assessments of the occupational risks associated with the use of pesticide products containing the active ingredient ETO. Based on these data and public comments received on the Agency's assessments for the active ingredient ETO, the Agency has sufficient information on the occupational effects of ETO to make a decision as part of the reregistration process under FIFRA.

Based on its evaluation of ETO, the Agency has determined that products containing the active ingredient ETO, unless labeled and used as specified in this document, would present unacceptable risks under FIFRA. The Agency assessed the benefits of ETO use and made a risk management decision that risks are outweighed by benefits only if certain labeling changes and risk mitigation measures are adopted as part of the product reregistration and labeling. Accordingly, should a registrant fail to implement any of the risk mitigation measures identified in this document, the Agency may take appropriate regulatory action to address unmitigated risk concerns from the use of ETO. Therefore, under FIFRA, if all changes specified in this document are incorporated into the product labels, the Agency concludes that the current uses of ETO are eligible for reregistration.

B. Public Comments and Responses

Through the Agency’s public participation process, EPA worked with stakeholders and the public to reach these regulatory decisions for ETO. The Phase 3 public comment period on the risk assessments, opened on August 3, 2005. Two Phase 5 public comment periods were held. The first opened on February 22, 2006, and requested public comments on the risk assessments and supporting documents for ETO. The Agency also requested additional input to

use/usage information and risk management suggestions for dietary and worker concerns. The ETO TRED was issued July 24, 2006. The second Phase 5 public comment period opened on May 30, 2007. This comment period solicited comments on the risk assessments and risk management suggestions for occupational risks. The Agency received comments from several stakeholders and the technical registrants. A complete listing of these comments can be found at <http://www.regulations.gov./>.

These comments were reviewed and taken into consideration in preparing the revised risk assessments as well as the reregistration eligibility decisions presented in this document. The comments and EPA's responses, are available in their entirety in the public docket EPA-HQ-OPP-2005-0203 located on-line at <http://www.regulations.gov./>.

C. Food Quality Protection Act Findings

1. "Risk Cup" Determination

As described in the 2006 Tolerance Reassessment Eligibility Decision (TRED), EPA has determined that the human health risks from exposures to ETO and its reaction products are within acceptable levels and the tolerances for ETO meet the safety standards under the FQPA amendments to Section 408(b)(2)(C) and 408(b)(2)(D) of the FFDCA after risk mitigation options were adopted. In reaching these determinations, EPA has considered the available information on the special sensitivity of infants and children.

The Agency concluded in its 2006 TRED that risks from aggregate exposure to ETO are not of concern. Therefore, the tolerances for ETO and its reaction product ethylene chlorohydrin (ECH) were reassessed as safe. The TRED is available in the public docket EPA-HQ-OPP-2005-0203 located on-line in the Federal Docket Management System (FDMS) at <http://www.regulations.gov>.

2. Determination of Safety to United States Population (Including Infants and Children)

The Agency has determined that there is a reasonable certainty that no harm will result to the general United States population, infants, children, or other major identifiable subgroups of consumers, from the use of ETO. The safety determination considers factors such as the toxicity, use practices and exposure scenarios, and environmental behavior of ETO. In determining whether or not infants and children are particularly susceptible to toxic effects from exposure to residues of ETO, the Agency considered the completeness of the hazard database for developmental and reproductive effects, the nature of the effects observed, and other information.

3. Endocrine Disruptor Effects

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "*may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.*" Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of the program, androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. When the appropriate screening and/or testing protocols being considered under the Agency's Endocrine Disrupter Screening Program (EDSP) have been developed and vetted, ETO may be subjected to additional screening and/or testing to better characterize possible effects related to endocrine disruption.

4. Cumulative Risks

FFDCA Section 408(b)(2)(D)(v) requires that the Agency consider "available information" concerning cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity" when considering whether to establish, modify, or revoke a tolerance for pesticide residues in food. EPA considers cumulative effects from pesticides and other substances because low-level exposures to multiple chemical substances causing a common effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to each individual substance.

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to ETO and any other substances, and ETO does not appear to produce a toxic metabolite produced by other substances. For the purposes of this reregistration eligibility decision, therefore, EPA has not assumed that ETO has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative/>.

D. Regulatory Rationale

Based on an evaluation of the risks and benefits of ETO's uses, the Agency has determined that products containing the active ingredient ETO are eligible for reregistration provided that the risk mitigation measures specified in this document are adopted and label amendments are made to require those mitigation measures. The following is a summary of the risk mitigation measures and EPA's rationale for the decision for managing risks associated with the use of ETO. Where labeling revisions are warranted, label changes and language are specified in Section V.

1. Occupational Risk Management and Mitigation

As discussed in Section 5.0 of the *Review of Calculated Ethylene Oxide Exposures for Ethylene Oxide Sterilization Plant Workers (MRID No. 47331801) Submitted in Support of the Occupational Exposure Assessment of the Antimicrobial Uses of Ethylene Oxide for the Reregistration Eligibility Decision (RED)* and in Section 3.2 of the *Addendum to the Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision (RED) for Ethylene Oxide* (found at <http://www.regulations.gov./>), there are risk estimates that exceed EPA's level of concern from occupational exposure to ETO.

For hospital workers, long-term non-cancer risks are of concern (MOEs are 15) assuming the workers are in the building 8 hours per day for 240 days each year. Potential cancer risks associated with ETO use in hospitals range from 2.6×10^{-4} to 2.1×10^{-3} which exceeds the Agency's level of concern of 1×10^{-6}. Therefore, in order to mitigate potential non-cancer and cancer risk concerns for workers in hospitals exposed to ETO as a result of medical use, a single chamber process is needed for ETO treatment (sterilization and aeration are to occur in the same chamber). This mitigation measure is expected to lower ambient levels of ETO in hospitals and result in reduced long-term non-cancer and potential cancer risk estimates for hospital workers.

In medical contract sterilization facilities, the workers who are actually working with ETO and are involved directly with the ETO sterilization process wear respirators at some point during the day (i.e., when performing an activity where the OSHA PEL could be exceeded such as chamber unloading, tank maintenance, etc.) and do not have non-cancer risks of concern. However, based on data on ambient levels of ETO in these facilities, other staff (e.g., workers unloading and loading vehicles and office workers who are not engaged in sterilization activities requiring respirator use) could have long-term non-cancer risks of concern assuming they are in the building 8 hours per day for 240 days each year over a 35-year work career. Potential cancer risks for all workers in medical contract sterilization facilities (including workers unloading and loading vehicles and office workers who are not engaged in sterilization activities requiring respirator use) exceeded the Agency target of 1×10^{-6} and range from 7.9×10^{-5} to 1.3×10^{-3}. In spice contract sterilization facilities non-cancer risk estimates are not of concern. However, potential cancer risks for all workers in spice contract sterilization facilities (including office workers not engaged in sterilization activities) range from 2.1×10^{-5} to 8.4×10^{-4}.

Therefore, in order to mitigate potential non-cancer and cancer risk concerns for workers in contract sterilization facilities (including medical and spice contract sterilization facilities), the Agency is specifying that employee safety and awareness training be given to all employees (including office staff). Information and training is to be provided to all employees in the facility at the time of initial assignment and annually thereafter. This training is intended to ensure that all facility employees are aware of the risks associated with ambient levels of ETO from sterilization processes and is to include, at a minimum, the following information:

- The most recent monitored ambient levels of ETO in the facility.
- The potential health effects from the levels of ETO in the facility.
- The emergency response plan and how to respond in an emergency.

- The availability of the Material Safety Data Sheet and other materials related to the health hazards of exposure to ETO.

In addition, the Agency encourages each facility to increase its aeration to reduce ambient levels of ETO. Achieving an ambient level of 0.25 ppm or less (measured as a daily time-weighted average) could eliminate potential long-term non-cancer risks to workers who do not wear respirators as part of their job duties. An ambient level of 0.25 ppm of ETO (measured as a daily time-weighted average) would also be expected to result in potential cancer risks of 1.3×10^{-4} to 1.1×10^{-3}. Achieving ambient ETO levels less than 0.25 ppm would potentially result in lower cancer estimates. Future monitoring efforts at contract sterilization facilities should include the entire facility (including office space, vehicle unloading/loading areas, and break areas) to have accurate information regarding exposure of employees that are not wearing respirators as part of their daily routine.

Non-cancer risk estimates are not of concern for the beekeeping use in North Carolina. However, potential cancer risks exceed the Agency target of 1×10^{-6} and range from 1.1×10^{-5} to 9.2×10^{-5}. Therefore, in order to mitigate potential cancer risk concerns for workers sterilizing beekeeping equipment in North Carolina, respirators are specified to be worn during chamber unloading and tank change/maintenance activities. This risk mitigation measure is expected to lower worker exposure to ETO and result in reduced long-term non-cancer and potential cancer risk estimates for workers.

2. Use-Specific Analyses

The Agency has worked with the technical registrants, Honeywell Corporation (Honeywell) and ARC Specialty Products of Balchem Corporation (ARC), to reduce occupational exposure to ETO. Subsequently, Honeywell and ARC have agreed to the following risk reduction measures and to incorporate them as requirements in their affected product's registration and labeling:

- A single chamber process is required for ETO treatment (sterilization and aeration are to occur in the same chamber) in hospitals. This requirement is expected to lower ambient levels of ETO in hospitals and result in reduced long-term non-cancer and potential cancer risk estimates for hospital workers.

- Employee safety and awareness training is required for all employees (including office staff) in contract sterilization facilities. This requirement ensures that all facility employees are aware of the risks associated with ambient levels of ETO from sterilization processes.

- For the beekeeping use, respirators are required to be worn during chamber opening and unloading and tank change/maintenance activities. This requirement is expected to lower worker exposure to ETO and result in reduced long-term non-cancer and potential cancer risk estimates for workers.

The Agency has determined that the label changes (as specified in Table 4 in Section V), as agreed upon by the technical registrants Honeywell and ARC, are appropriate and needed for reregistration eligibility. Listed below are the specific uses for ETO along with corresponding cancer and non-cancer risk estimates for workers, stakeholder input on use, alternatives/benefits, risk reduction measures in place, and EPA's decision regarding reregistration eligibility. As a general matter, the Agency has determined that there are no short-term or intermediate-term risks of concern to workers from the use of ETO. There is potential, however, for long-term non-cancer and cancer risks to some workers depending upon their specific functions within a facility. The Agency determined that these risks are outweighed by the benefits expected from use of ETO provided the specified risk reduction measures are adopted. The Agency also determined that ETO does not pose risks of concern to the general population or to the environment.

a. Medical Use (Hospitals and Contract Sterilization Facilities)

Current Use Pattern

ETO is used to sterilize new and reusable medical equipment (e.g., surgical instruments, hypodermic needles/syringes, surgical prosthetic parts, hemodialysis machines, heart and lung machines, dental instruments, veterinary instruments, heat labile material, moisture labile material, oral and inhalation equipment, diagnostic instruments, thermometers, surgical dressings, first aid equipment). Approximately 7.4 million pounds are used annually for sterilization of medical and laboratory items/equipment.

Approximately 1,900 hospitals have in-house ETO sterilization chambers. Hospitals tend to have small self-contained units for ETO sterilization. Bulk sterilization occurs at contract sterilization facilities that handle multiple pallet sterilizations. Approximately 30 contract sterilization facilities exist in the United States; 21 of those facilities represent 90 percent of the contract medical device sterilization capacity in the United States. In addition, many manufacturers of medical devices use ETO in-house to sterilize their products. For all of these medical uses, ETO sterilization occurs in vacuum or gas tight chambers designed for use with ETO.

Risks of Concern

As discussed in Section 5.0 of the *Review of Calculated Ethylene Oxide Exposures for Ethylene Oxide Sterilization Plant Workers (MRID No. 47331801) Submitted in Support of the Occupational Exposure Assessment of the Antimicrobial Uses of Ethylene Oxide for the Reregistration Eligibility Decision (RED)* (found at <http://www.regulations.gov./>), there are risk estimates that exceed EPA's level of concern from occupational exposure to workers in hospitals and medical contract sterilization facilities.

The target MOE for ETO is 30. For hospital workers, short- and intermediate-term MOE estimates are not of concern (MOEs are 77), but long-term non-cancer risks are of concern (MOEs are 15) assuming the workers are in the building 8 hours per day for 240 days each year over a 35-year career. Using a range of unit risk factors, the potential cancer risks associated

with ETO use in hospitals range from 2.6×10^{-4} to 2.1×10^{-3} which exceeds the Agency's level of concern of 1×10^{-6}.

In medical contract sterilization facilities, the workers who are actually working with ETO and are involved directly with the ETO sterilization process wear respirators at some point during the day (i.e., when performing an activity where the OSHA PEL could be exceeded such as chamber unloading, tank maintenance, etc.). These workers have non-cancer MOE estimates that are not of concern (short- and intermediate-term MOEs are 130 to 250 and long-term MOEs are 50) for non-cancer risks. However, based on ambient air monitoring data in facilities, other staff (e.g., office workers who are not engaged in sterilization activities) could have long-term non-cancer MOEs of 25 assuming they are in the building 8 hours per day for 240 days each year.

Using a range of unit risk factors, all of the potential cancer risks associated with the contract sterilization use exceeded the Agency target of 1×10^{-6} and range from 7.9×10^{-5} to 1.3×10^{-3}.

Stakeholder Involvement/Input on Medical Use

Since 2005, EPA has been coordinating its ETO risk assessment and management efforts with OSHA. In May 2005, EPA and OSHA staff met to discuss EPA's preliminary occupational exposure analysis and the availability of recent worker exposure data at OSHA. In December 2005, OSHA provided monitoring data for contract sterilization facilities from its Integrated Management Information System (IMIS) to be incorporated into EPA's risk assessment.

In June 2005, EPA staff visited the National Institute of Health (NIH) medical sterilization facility in Bethesda, Maryland. The site visit focused on the use of ETO for medical sterilization. The Agency staff observed the sterilization process and equipment used, saw various medical materials that had been sterilized, and discussed ETO handling occupations in the facility, safety protocols, and emergency procedures.

EPA also participated in a meeting with USDA, ETO registrants, and ETO stakeholders in December 2005. Representatives from Honeywell Inc., ARC, American Chemistry Council, American Spice Trade Association (ASTA), Sterigenics, University of Iowa Hospital, Wake Forest University Baptist Medical Center, and 3M presented their perspectives on the importance of ETO and the potential impacts of the worker exposure analysis in the preliminary risk assessment. Meeting materials and a summary of the meeting can be found in the public docket EPA-HQ-OPP-2005-0203 online at <http://www.regulations.gov./>.

In February 2006, EPA staff held a conference call with representatives from the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) to discuss ETO use in the medical industry from a public health perspective. In summary, FDA and CDC agreed that ETO was a critical sterilant for the health care industry. In their opinion, ETO fills a reprocessing niche for medical equipment that is moisture, temperature, or radiation sensitive.

In October 2007, EPA visited Sterilization Services of Virginia, a contract sterilization facility in Richmond, Virginia. The site visit focused on the use of ETO for sterilization of medical equipment and provided valuable information about the ETO sterilization processes at contract sterilization facilities. Observing existing mitigation measures in place at the facility was another important aspect of the site visit.

In February 2008, EPA staff coordinated with FDA again. FDA staff reiterated their previous statement that ETO was a critical sterilant for the health care industry. In their opinion, ETO continues to fill a niche for sterilizing and reprocessing medical equipment that is moisture, temperature, or radiation sensitive.

During Phases 5 and 6 of the Public Participation Process, in addition to the written comments received from respondents as mentioned in section IV. B. above, the Agency met with ARC, the Ethylene Oxide Sterilization Association (EOSA), STERIS Corporation, Sterigenics International, Inc., and other interested stakeholders with specific knowledge relating to ETO medical use. These stakeholders have provided actual worker exposure monitoring data to refine the risk estimates for contract sterilization facilities. In addition, these stakeholders provided detailed information about the ETO sterilization process and existing mitigation measures that are used in ETO contract sterilization facilities.

Alternatives and Benefits

There are several methods that are available to sterilize medical devices. Depending on the material composition of the device and its sensitivity to different sterilants and the use site (e.g., industrial, hospital, etc.) different sterilizers can be effective, including heat, ETO, gamma radiation, electron beam radiation, x-ray, and hydrogen peroxide plasma. Despite the fact that there are several methods that are available to sterilize medical devices, no currently available sterilization treatment can replace ETO for some uses, including certain heat-sensitive and irradiation-sensitive materials and some instruments and devices that require sterilization on-site in hospitals.

Based on available information, EPA considers ETO critical to sterilization in the medical industry and necessary to protect public health. Currently, there do not appear to be any feasible replacements for its use in sterilizing medical devices.

For additional information, refer to the Agency's *Qualitative Assessment of Alternatives for Ethylene Oxide Uses (DP316692)* and the BEAD response to comments documents which are available in the public docket EPA-HQ-OPP-2005-0203 and located on-line at <http://www.regulations.gov/>.

Risk Reduction Measures in Place

Contract sterilization facilities use a variety of approaches to reduce the risks of ETO exposure to employees. These approaches include facility design, ETO chamber design, ETO treatment cycle protocols, respirator requirements, employee monitoring, employee training, and facility procedures (EOSA, 2007).

Facilities are designed to physically separate areas of ETO-treated materials and non-ETO-treated materials. In addition, the ventilation systems of facilities are designed to keep the ventilation system physically separated from the ETO treatment chambers. Aeration rooms are established at facilities to allow treated materials to aerate in a contained area, where ETO is captured and sent to an emission control device (e.g., wet-scrubber system) thereby minimizing potential exposure. Aeration rooms are kept at an elevated temperature to speed the removal of ETO that is absorbed by the treated materials.

ETO chambers are designed with back vents to pull air into the chamber, especially as the chamber door is opened. Chambers are also designed with an interlock system with direct ETO measurement to reduce potential worker exposure to ETO.

The treatment cycles used in ETO chambers are considered an important tool by the ETO-user industry to reduce worker exposure. A cycle is composed of several steps (e.g., removal of air by vacuum pump; introduction of steam, nitrogen, and ETO; and removal of ETO). Carefully timed cycles with numerous air washes and nitrogen "gas" washes to remove ETO at the end of a treatment cycle reduce the amount of ETO remaining in a chamber before the chamber is opened.

Some facilities use an all-in-one cycle design where materials are preconditioned and/or aerated inside of the sterilization chamber. This all-in-one design is believed to reduce worker exposure because it eliminates the transfer of treated materials to a separate chamber for aeration. Industry claims that the all-in-one cycle "has varying impacts on ETO worker exposure depending on the cycle design and product." Not all medical devices can be processed using the all-in-one cycle design, particularly pressure-sensitive materials (EOSA, 2007).

Respirators are required to be worn during certain tasks such as unloading ETO treatment chambers, entering an aeration room (or cell), performing maintenance tasks on ETO pipes or equipment, sampling or accessing ETO-treatment materials, and changing ETO drums or tanks. Canister masks are the most commonly used respirator. Forced air masks (i.e., supplied air respirators) are used when entering areas with high-ETO concentrations (e.g., aeration rooms). Self Contained Breathing Apparatus (SCBA) is used in emergency situations and for some maintenance activities.

Employee exposure monitoring is required under OSHA regulations. Employees wear monitoring badges at least twice per year to determine their ETO exposure. Continuous ETO monitors are installed throughout many facilities and handheld monitors are used as well.

Contract sterilization facilities have established specific procedures for handling ETO drums/tanks. Employees at contract sterilization facilities receive ETO-specific training to review safety procedures and regulations.

Hospitals use many of the same approaches to reduce the risks of ETO exposure to employees as described above for the contract sterilization facilities. Specifically, hospitals

incorporate facility design, ETO chamber design, ETO treatment cycle protocols, employee monitoring, employee training, and facility procedures to the extent feasible.

Each hospital is unique and its design, equipment, protocols, and procedures may vary depending on the activities of the facility and the materials that are treated. Universally, ETO levels are continuously monitored in the rooms where ETO chambers are located. Visible and audible alarm systems are typically present in the chamber area. Chambers are generally designed with an interlock system with direct ETO measurements to reduce potential worker exposure to ETO. Hospitals combine the aerator and sterilizer into one unit (i.e., all-in-one process design) when possible. Exhaust hoods are often placed over the chambers to aid in capturing any ETO released when opening the chamber for unloading.

Unlike in contract sterilization facilities, workers in hospital settings do not routinely wear respirators. Typically respirators are used only in emergency situations. However, employee exposure monitoring is required under OSHA regulations. Employees wear monitoring badges to determine their ETO exposure. Employees typically receive ETO-specific training to review safety procedures and regulations.

EPA Decision

Based on current worker exposure data and toxicity estimates, ETO has the potential to cause adverse health effects to workers through long-term inhalation exposure (i.e., greater than 6 months of exposure) in both hospitals and medical contract sterilization facilities.

Hospitals. In hospitals, long-term non-cancer risks (MOE of 15 with a target of 30) and potential cancer risks (2.6×10^{-4} to 2.1×10^{-3}) are of concern.

EPA policy for non-dietary risks in the 10^{-5} to 10^{-4} range is to determine whether the benefits of use outweigh the risks and to seek cost effective ways to reduce risks. This policy specifically allows for the consideration of the weight of scientific evidence regarding carcinogenicity and benefits associated with the pesticide under review. The Agency recognizes that the ORD is currently analyzing ETO's carcinogenicity based on human epidemiological data. In the interim, the Agency believes it appropriate to use available rodent data to estimate cancer risks from ETO. The Agency has determined that the health benefits associated with the use of ETO on medical equipment are extremely high.

Given the extremely high health benefits of ETO use and the lack of any feasible replacements for ETO use in sterilizing certain medical equipment/devices, the Agency has determined that ETO use on medical equipment in hospitals is eligible for reregistration with the implementation of the following mitigation.

- A single chamber process is specified for ETO treatment (sterilization and aeration are to occur in the same chamber). This risk mitigation measure is expected to lower ambient levels of ETO in hospitals and result in reduced long-term non-cancer and potential cancer risk estimates for hospital workers.

Medical contract sterilization facilities. In medical contract sterilization facilities, long-term non-cancer risk are of concern for workers that do not wear a respirator at any time during a work day (MOE of 25 with a target of 30). Potential cancer risks for medical contract sterilization facility workers range from 7.9×10^{-5} to 1.3×10^{-3}.

As described above, the EPA policy for non-dietary risks of this nature is to determine whether the benefits of use outweigh the risks and to seek ways to mitigate unacceptable risks. The Agency has determined that the health benefits associated with the use of ETO on medical equipment are extremely high.

Given the extremely high health benefits of ETO use, the lack of any feasible replacements for ETO use in sterilizing certain medical equipment/devices, and the extensive risk reduction measures already in place to protect workers, the Agency has determined that ETO use on medical equipment in contract sterilization facilities is eligible for reregistration with the implementation of the following mitigation.

- Employee safety and awareness training is required for all employees (including office staff). Information and training is to be provided to all employees in the facility at the time of initial assignment and annually thereafter. This training is intended to ensure that all facility employees are aware of the risks associated with ambient levels of ETO from sterilization processes and is to include, at a minimum, the following information:

    - The most recent monitored ambient levels of ETO in the facility.
    - The potential health effects from the levels of ETO in the facility.
    - The emergency response plan and how to respond in an emergency.
    - The availability of the Material Safety Data Sheet and other materials related to the health hazards of exposure to ETO.

- Increased facility aeration is encouraged to reduce ambient levels of ETO. Achieving an ambient level of 0.25 ppm or less (measured as a daily time-weighted average) could eliminate potential long-term non-cancer risks to workers that do not wear respirators as part of their job duties. An ambient level of 0.25 ppm of ETO (measured as a daily time-weighted average) would also be expected to result in potential cancer risks of 1.3×10^{-4} to 1.1×10^{-3}. Achieving ambient ETO levels less than 0.25 ppm would potentially result in lower cancer estimates. Future monitoring efforts at contract sterilization facilities should include the entire facility (including office space, vehicle unloading/loading areas, and break areas) to have accurate information regarding exposure of employees that are not wearing respirators as part of their daily routine.

b. Musical Instrument Use

Current Use Pattern

ETO is used to sterilize musical instruments in a vacuum-sealed treatment chamber, using the same treatment facilities where medical and dental instruments are treated. The application rate of ETO used to treat musical instruments varies based on the type of sterilization chamber used. The sterilization process used by medical device manufacturers and contract sterilizers is largely automated with workers outside the chambers altering temperature and pressures within the chambers as needed. Each of the cycles has been pre-validated by the manufacturer for temperatures, pressures, ETO concentrations, and run times. Afterwards, the medical devices are aerated for up to 12 hours to reduce or eliminate ETO residues. It should be noted that industrial sterilizers frequently utilize hot cells and altered chamber cycles to reduce ETO residuals more effectively.

Typical sterilization chambers to treat musical instruments and used by medical device manufacturers or contract sterilizers are approximately 660 cubic feet and hold 550 cubic feet of medical products (i.e., 6 pallets) (Knee, 2001). The chambers are vacuum-sealed and ETO is injected into the chamber to the desired concentration, where the concentrations can range from 0.02 to 0.080 lbs of ETO per cubic feet of sterilized devices (i.e., 16 to 40 lbs per load).

Risks of Concern

Since musical instruments are treated with ETO in contract sterilization facilities, it is assumed that estimated exposures and risks for the medical contract sterilization facilities cover the musical instrument use.

Stakeholder Involvement

During Phase 5 of the Public Participation Process, the Agency received a total of 31 comments expressing support of the continued ETO registration for use in sterilizing musical instruments. Thirty of these letters were expressing general support for the continued registration of ETO. Additional information supporting the continued registration was submitted by Encore, Etc., the distributor for the ETO musical instrument treatment, EPA Registration number 36736-2. In addition, the Agency met with representatives from Encore, Etc. All comments are available in EPA's public docket <www.regulations.gov> (EPA-HQ-OPP-2005-0203).

Alternatives and Benefits

Every year hundreds of thousands of students receive used musical instruments loaned to them from their schools, rented from local school music dealers, or purchased over the internet. The use of ETO to sterilize musical instruments was developed to eliminate microorganisms from the entire instrument before a new user receives it. Traditionally, only the mouthpiece of an instrument is cleaned with soap, water and possibly alcohol between student rentals.

Information submitted by Encore, Etc., Inc. included a report of a test conducted by Sterigenics, a contract sterilization company. The test compared "sterilization efficacy" of eight treatment methods. The treatments used in this evaluation were: ETO; VHP (vaporized hydrogen peroxide); ozone; alcohol; bleach; boiling; ultrasound with phosphoric acid; and liquid sterilant immersion (unidentified).

The Agency evaluated the submitted information and concluded that bacteria were recovered several weeks after being placed in instruments and mouthpieces. When new and previously used instruments were screened for the presence of microorganisms, none of the numerous species identified were pathogens. However, ETO is an effective antimicrobial treatment that likely will decontaminate musical instruments.

Musical instruments are treated in the same contract facilities that sterilize medical and dental instruments. Because a relatively low volume of instruments are sterilized with ETO, no additional facilities are needed to treat musical instruments at this time. Although there may be benefits associated with using ETO for sterilizing musical instruments, the Agency is unable to quantify them at this time.

Risk Reduction Measures in Place

Since ETO use on musical instruments occurs in contract sterilization facilities, risk reduction measures described above for medical contract sterilization facilities would be the same for this application.

EPA Decision

ETO use has the potential for a slight exceedance for long-term non-cancer inhalation risks for workers (MOE=25, target MOE=30). These potential risks are for workers exposed to background air concentrations within the facility, not wearing respirators. Cancer risks for workers exceed the level of concern for workers in contract facilities (i.e., risks range from 7.9×10^{-5} to 1.3×10^{-3}). For occupational cancer risks between $1x10^{-6}$ and $1x10^{-4}$, EPA carefully evaluates exposure scenarios to seek cost effective ways to reduce cancer risks to the greatest extent feasible, preferably to a risk of $1x10^{-6}$ or less.

Although there is the potential for an exceedance of long-term, non-cancer risks, any increase in air exchanges in the treatment facility should alleviate this concern. In addition, the increased air exchanges will likely decrease the cancer risk for all occupational activities. It should be noted that treatment of musical instruments are not expected to increase worker exposure to ETO in contract treatment facilities since these facilities simultaneously sterilize medical instruments.

Since its inception in 2006, Encore, Etc. has processed four chamber loads of musical instruments, representing approximately 3,000 cubic feet of processing capacity. It is estimated that sterilizing 3,000 cubic feet of musical instruments consumed 0.002 percent of the industry capacity available in 2003. In their comments, Encore Etc. estimated a one hundred fold

increase in instrument sterilization would use approximately 0.197 percent of the total industry capacity.

The Agency does not currently have enough information to quantify the benefits of ETO use to sterilize musical instruments; however, ETO is an effective antimicrobial treatment that likely will decontaminate musical instruments. Because of the low volume of contract treatment capacity needed to treat the musical instruments, the Agency believes there is no appreciable increase in risk to workers beyond what they experience while sterilizing medical instruments.

However, if the demand for sterilization of musical instruments increases significantly (i.e., the number of contract sterilization facilities increases to accommodate the increased demand), the registrant must notify the Agency, initiating further evaluation of the risks associated with the increased ETO use. In addition, the Agency needs data to further document the presence of pathogens in the internal surfaces of musical instruments. The registrant has agreed to submit a study of this nature to the Agency. The Agency finds the sterilization of musical instruments eligible for reregistration.

As stated above, to protect workers who do not perform tasks for which a respirator is required to be worn on a daily basis in a contract sterilization facility, the Agency is specifying an employee safety and awareness training to be given to all employees (including office staff), and encourages each facility to increase its aeration to reduce ambient levels of ETO.

To reduce potential long-term non-cancer and cancer risks to workers who did not enter the aeration rooms (i.e., those who did not wear respirators), the Agency encourages contract facilities to use Best Management Practices to provide additional aeration in treatment facilities.

c. Library and Museum Artifact Use

Current Use Pattern

Library and museum artifacts are treated with ETO to control various pests, such as fungi and insects. Current use of ETO for archival material appears to be infrequent and limited to important preservation needs when alternatives are considered ineffective. This use accounts for less than 1 percent of the total annual usage of ETO for commercial fumigation/sterilization.

ETO treatment of library and museum artifacts generally occurs in contract sterilization facilities located across the United States. Application occurs in vacuum or gas tight chambers designed for use with ETO.

Risks of Concern

Since library and museum artifacts are treated with ETO in contract sterilization facilities, it is assumed that estimated exposures and risks for the medical contract sterilization facilities cover the library and museum artifact uses.

Stakeholder Involvement

In April 2007, EPA staff consulted with the preservation specialist at the Library of Congress to discuss ETO use for library and museum articles. The Library of Congress occasionally sends mold-infested collection items to contract sterilization facilities for ETO fumigation. The Library of Congress also stipulates requirements for aeration of the ETO treated materials. Insect infested materials are treated at a Library of Congress fumigation chamber where infested collections are subjected to a strong vacuum for a few days to kill the insects and their eggs. ETO is not used in this situation.

No written comments were submitted to the Agency regarding ETO use on library and museum artifacts during any phases of the public participation process.

Alternatives and Benefits

Insects and molds are problems for library and museum artifacts. Prevention is the most desirable means of controlling pests. Managing temperature and humidity and light are standard measures. In addition, various non-chemical treatments are often used and chosen depending on the artifacts and pests. Methods include cold treatment, heat treatment, microwave treatment, and natural substances, such as exposure to cedar products. When pesticides are required, usually standard pesticides available to homeowners are used. However, sometimes an artifact is considered to need fumigant treatment. Common fumigants have been methyl bromide, sulfuryl fluoride, carbon dioxide, and ETO. Fumigants are chosen based on the fumigant and artifact characteristics.

The current use of ETO for archival material and museum artifacts appears to be infrequent and limited to important preservation needs where alternatives are considered ineffective. Similarly, museums appear to use ETO only when other treatments are not acceptable. It appears that museum pieces are sent to contract sterilization facilities when ETO is used.

For additional information, refer to the Agency's *Qualitative Assessment of Alternatives for Ethylene Oxide Uses (DP316692)* and the BEAD response to comments documents which are available in the public docket EPA-HQ-OPP-2005-0203 located on-line at <http://www.regulations.gov/>.

Risk Reduction Measures in Place

Since ETO use on library and museum artifacts generally occurs in contract sterilization facilities, risk reduction measures described above for medical contract sterilization facilities would be the same for this application. In addition, the Library of Congress suggests that material designated for ETO-treatment should be conducted by contract sterilization facilities in accordance with EPA and OSHA safety regulations. The National Park Service also recommends to conservation specialists that they ensure safety regulations are followed when ETO is used.

EPA Decision

ETO treatment of library and museum artifacts occurs in contract sterilization facilities with risk reduction measures in place. However, ETO has the potential to cause adverse health effects to workers. Given the infrequent use of ETO for library and museum artifacts and its very minor contribution to the total annual usage of ETO for commercial fumigation/sterilization (less than 1 percent), EPA believes that the benefit to society of preserving historical artifacts for future generations outweighs potential risks of ETO for this use. Given that, the Agency has determined that ETO use on library and museum artifacts in contract sterilization facilities is eligible for reregistration.

As stated above, to protect workers who do not perform tasks for which a respirator is required to be worn on a daily basis in a contract sterilization facility, the Agency is specifying an employee safety and awareness training to be given to all employees (including office staff), and encourages each facility to increase its aeration to reduce ambient levels of ETO.

To reduce potential long-term non-cancer and cancer risks to workers who did not enter the aeration rooms (i.e., those who did not wear respirators), the Agency encourages contract facilities to use Best Management Practices to provide additional aeration in treatment facilities.

d. Cosmetics Use

Current Use Pattern

ETO is used during the processing of some gums and dyes in manufacturing cosmetics to reduce microbial activity of organisms that can contaminate ingredients. In addition, other associated products such as packaging material for cosmetics may be treated with ETO. Ingredients that are treated with ETO are sent to contract sterilizing facilities for the fumigation treatment (Czerkowicz et al., 1996). This use accounts for less than 1 percent of the total annual usage of ETO for commercial fumigation/sterilization.

Risks of Concern

Since cosmetic ingredients are treated with ETO in contract sterilization facilities, it is assumed that estimated exposures and risks for the medical contract sterilization facilities cover the cosmetics uses.

Stakeholder Involvement

In February 2008, EPA staff coordinated with FDA on ETO's use in the cosmetics industry. FDA provided information on the role of ETO as an ethoxylating agent for the synthesis of ethoxylated surfactants that are used in cosmetic products. FDA is aware of the potential for residual ETO to be present in ethoxylated surfactants and cosmetic products containing these ingredients. FDA is developing an analytical method to measure ETO and 1,4-dioxane (a reaction product of ETO formed during the ethoxylation process in cosmetics). In addition, there are many cosmetic ingredients that are derivatives of EG. Some unreacted EG

present in a cosmetic ingredient may also be present in a finished cosmetic product (e.g., polyethylene glycol ingredients that are commonly found in cosmetics may have some unreacted EG present).

No written comments were submitted to the Agency regarding ETO's use in the cosmetics industry during any phase of the public participation process.

Alternatives and Benefits

Previous OPP analyses from 1996 suggested that while some ingredients in cosmetics are treated with ETO, effective alternatives exist for at least some ingredients. These alternatives include irradiation and dry heat.

In a survey of 12 cosmetic companies conducted by Mitre Corporation nearly 30 years ago, 58 percent rated ETO "essential" to reducing microbial contamination, while 33 percent said ETO was "moderately essential" (referenced in Czerkowicz et al., 1996). It is not known whether the survey results reflect the current attitude towards ETO use in the cosmetics industry. No updated information is available.

Risk Reduction Measures in Place

Since ETO use on cosmetic ingredients generally occurs in contract sterilization facilities, risk reduction measures described above for medical contract sterilization facilities would be the same for this application.

EPA Decision

ETO treatment of cosmetics occurs in contract sterilization facilities with risk reduction measures in place. However, ETO has the potential to cause adverse health effects to workers. Given the minor contribution to the total annual usage of ETO for commercial fumigation/sterilization (less than 1 percent) from cosmetics treatment, EPA believes that the benefit to society of reducing potential infection from the application of cosmetic products outweighs potential risks of ETO for this use. Given that, the Agency has determined that ETO use on cosmetics in contract sterilization facilities is eligible for reregistration.

As stated above, to protect workers who do not perform tasks for which a respirator is required to be worn on a daily basis in a contract sterilization facility, the Agency is specifying employee safety and awareness training to be given to all employees (including office staff), and encourages each facility to increase its aeration to reduce ambient levels of ETO.

To reduce potential long-term non-cancer and cancer risks to workers who did not enter the aeration rooms (i.e., those who did not wear respirators), the Agency encourages contract facilities to use Best Management Practices to provide additional aeration in treatment facilities.

e. Spice Use

Current Use Pattern

ETO is used in the United States during the processing of spices to reduce microbial and insect activity. Several pathogens have been identified as contaminants of herbs and spices, most commonly: *Bacillus* spp., *Clostridium perfringens, Escherichia coli, Salmonella* spp., *Klebsiella pneumoniae*, and *Staphylococcus aureus* (e.g., CDC, 2001; ANZFA, 2002; Vij et al., 2006). Most prominent for concern in spices is contamination by *Salmonella*, especially when spices are applied to uncooked food or applied to food after the food has been cooked.

Each year in the United States approximately 32 percent of whole spices (including herbs) are treated with ETO. ETO treatment primarily depends on whether microbial or insect contamination has been found above acceptable levels and specific spice characteristics. Treatment includes spices grown domestically as well as those imported into the United States. An estimated maximum of approximately 800,000 pounds are used annually for fumigation of herbs and spices. This represents about 10 percent of the total ETO sterilization market.

The ETO fumigation process for spices is essentially identical to the sterilization process used for medical equipment/devices. Despite the fact that the sterilization process is so similar, the same chamber cannot be used for both medical equipment/devices and spice fumigation. Chambers used to treat spices retain the odors associated with these commodities and these odors are often transferred to materials treated subsequently in the same chamber. In addition, if the packaging for herbs and spices is damaged, herbs and spices can spill in the treatment chamber. Contract sterilizers avoid having residual herbs and spices and medical devices in the same area. For these reasons, the treatment of spices and medical equipment/devices are distinct and separate (Abt, 2006).

Spice treatments generally occur in bulk at contract sterilization facilities that handle multiple pallet sterilizations located across the United States. The American Spice Trade Association (ASTA) has stated that there are approximately 9 contract sterilization facilities in the United States that treat both medical devices and spices and 6 contract sterilization facilities in the United States that only treat spices. ETO treatment occurs in vacuum or gas tight chambers designed for use with ETO.

Risks of Concern

As discussed in Section 3.2 of the *Addendum to the Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision (RED) for Ethylene Oxide*, non-cancer risk estimates, calculated as MOEs are not of concern (i.e., short-/intermediate- and long-term MOEs > 30). However, ETO has the potential to cause adverse health effects to workers. Potential cancer risks for workers range from 2.1×10^{-5} to 8.4×10^{-4}.

Stakeholder Involvement

In March 2005, EPA conducted a site visit of the Baltimore Quality Assurance (BQA) spice sterilization facility in Baltimore, Maryland. The site visit focused on the use of ETO for spice sterilization. Agency staff observed ETO sterilization equipment, the loading of a sterilizer, spice packaging materials and various spice handling occupations in the facility. Safety protocols, emergency procedures, and alternative sterilization options were discussed.

In December 2005, OSHA provided monitoring data for spice treatment facilities from its IMIS to be incorporated into EPA's risk assessment.

EPA also participated in a meeting with USDA, ETO registrants and ETO stakeholders in December 2005. Representatives from Honeywell Inc., ARC, American Chemistry Council, ASTA , and medical interests presented their perspectives on the importance of ETO and the potential impacts of the worker exposure analysis in the preliminary risk assessment.

In March 2008, EPA staff coordinated with FDA on ETO's use in the spice industry from a public health perspective. In summary, FDA representatives agreed that ETO was an important tool for controlling *Salmonella* on spices although FDA representatives discussed the relatively low risk of public outbreak associated with contaminated spices because spices are not consumed in large quantities and spices are usually cooked prior to consumption.

During Phases 5 and 6 of the Public Participation Process, in addition to the written comments received from respondents as mentioned in section IV. B. above, the Agency met with and received comments from the ASTA with specific knowledge relating to ETO use on spices. In particular, these stakeholders have provided actual worker exposure monitoring data to refine the risk estimates for spice sterilization facilities and a description of existing mitigation measures that are used in ETO contract sterilization facilities.

Alternatives and Benefits

Methods of treating spices depend on the particular characteristics of the spice and whether the spice can withstand a particular treatment without significant degradation in quality. In the United States, various methods are available to reduce microbial and insect activity in spices including heat, irradiation, good agricultural practices, ETO, and propylene oxide.

- *Heat*. Spices require intact volatile compounds, which can be destroyed by heat. There must be a balance between managing pathogens with heat and maximizing flavor. Depending on the spice, heat may or may not be an effective treatment.

- *Irradiation*. According to the Food and Agricultural Organization of the United Nations, approximately 80,000 metric tons of spices were irradiated worldwide in 2000. However, while registered for use on spices in most of Europe, Australia, and the United States, irradiation currently appears to be an underused technology, due primarily to consumer perceptions of adverse health side-effects. Organic certification standards in

the United States (NOP, 2002) do not allow the use of irradiation for herbs and spices. McCormick, the largest United States spice dealer, does not irradiate its products.

- *Good Agricultural Practices (GAPs)*. Procedures such as GAP, Good Manufacturing Practices (GMP) and principles of Hazard Analysis and Critical Control Point (HACPP) for food safety are used by many food industries throughout the world and are generally accepted by the spice industry in the United States. GAP, GMP and HACPP standards are well-established in the meat, poultry, dairy, and egg industries and in production of fresh fruits and vegetables to ensure food safety for particularly susceptible products. These procedures serve to meet FDA and industry requirements. GAP, GMP, and HACPP practices, which include high standards for clean production and harvesting practices, clean post-harvest practices, appropriate drying and storage facilities, are the first line of defense against contaminated products. Spices are routinely cleaned mechanically to remove unacceptable and contaminating material.

- *Propylene Oxide (PPO)*. Another fumigant used on spices, PPO, may be effective against some insect infestations, but is not regarded as effective in reducing microbial contamination. Further PPO has been banned for use on spices in the European Union.

Many countries have banned the use of ETO on spices and other food due to concerns for public exposure to ETO and its reaction products. Countries have banned the food use of ETO due to its classification as a known human carcinogen and genotoxic agent. According to the Decision Guidance Document on Ethylene Oxide for the Operation of the Interim Prior Informed Consent (PIC) Procedure for Banned or Severely Restricted Chemicals in International Trade (FAO/UNEP, 2001), some of the countries that have banned the use of ETO on spices (and other foods) include: Belize, China, the European Union (EU, currently numbering 25 countries), Australia, and Japan. EPA assessed ETO and its reaction products (EBH, ECH, and EG) for dietary (oral) exposure and risk in the 2006 TRED. In the TRED, the Agency determined that dietary risk to ETO and its reaction products are below the Agency's level of concern after risk mitigation options were adopted. In addition, the Agency concluded that risks from aggregate exposure to ETO are not of concern and the tolerances for ETO and its reaction product, ECH, were reassessed as safe.

Because a single end-product decontamination treatment is not sufficient to address both microbial contamination and preservation of spice quality, "[A] combination of preventative hygiene control measures at the production level, and end-product treatments is needed" (ANZFA, 2002). Since most countries no longer allow the use of ETO, or the import of spices that have been treated with ETO, the most commonly used alternatives to ETO for spices are non-chemical, including improved agricultural practices, product selection, and with some commodities, heat. Irradiation can be an effective treatment, and is permitted by numerous countries, but has not been universally adopted primarily due to consumer questions of the process.

The threat of food-borne contamination and the potential for serious illness is a concern for government agencies, food manufacturers, and the general public. Most reported cases of microbial contamination of foods occur on fresh and processed fruits and vegetables, meats,

seafood, dairy, and eggs (CDC, 2001). Few foods recalls in the United States have involved spices. It is not known if the recalled spices were, or were not, treated with ETO. The United States imports spices from more than 6,100 manufacturers in 129 countries. Of the few recalled spices most were contaminated with *Salmonella* serotypes (Vij et al., 2006). A review was recently conducted of spice recalls that were recorded by the FDA Center for Food Safety and Applied Nutrition (CFSAN) from 1969 through 2003. A total of 21 recalls were reported, five recalls occurred between 1971 and 1996, and 16 recalls occurred between 2001 and 2003. Twelve spices (including sesame seeds) were involved in the recalls (Vij et al., 2006). One contaminated spice batch (bay leaves) was infested with *Listeria monocytogenes*, 20 batches of various spices were infested with nine *Salmonella* serotypes. Of the known origin of 15 of the recalled spices, 12 were imported to the United States and three were grown domestically. It is not known if any illnesses were associated with the contaminated spices, although these spices could have caused illnesses that were not reported. The CDC estimates that for every case of Salmonella that is diagnosed there are 38 cases undiagnosed or reported (Mead, et al., 1999). Consequently, it is difficult to estimate the extent to which ETO prevents potential food-borne illness associated with untreated herbs and spices.

For additional information, refer to the Agency's *Qualitative Assessment of Alternatives for Ethylene Oxide Uses (DP316692)* and the BEAD response to comments documents which are available in the public docket EPA-HQ-OPP-2005-0203 located on-line at <http://www.regulations.gov/>.

Risk Reduction Measures in Place

As described above, the ETO fumigation process for spices is essentially identical to the sterilization process used for medical equipment/devices and occurs in contract sterilization facilities. As such, most of the risk reduction measures discussed for medical contract sterilization facilities are used in spice only contract sterilization facilities. In addition, spice only contract sterilization facilities typically use single chamber technology as specified in the 2006 TRED. As such, the treatment cycles are designed to use more air or nitrogen washes than many facilities using conventional ETO treatment processes.

Other measures typically in place in spice sterilization facilities includes a ventilation design that moves air from areas of low potential risk toward areas of potentially higher risk. Offices in the spice sterilization facilities are generally positively pressurized to prevent airborne concentrations from entering the office work areas. Facilities also establish clearly signed "restricted areas" to prevent workers or visitors from entering areas where they are not authorized and could be exposed to a higher risk for sterilization activities (Ruckert, 2008).

EPA Decision

Based on current worker exposure data and toxicity estimates, ETO has the potential to cause adverse health effects to workers through long-term exposure. Potential cancer risks for spice workers range from 2.1×10^{-5} to 8.4×10^{-4}.

EPA policy for non-dietary risks in the 10^{-5} to 10^{-4} range is to determine whether the benefits of use outweigh the risks and to seek ways to mitigate unacceptable risks. This policy

specifically allows for the consideration of the weight of scientific evidence regarding carcinogenicity, number of people exposed, and benefits associated with the pesticide under review.

In the case of the use of ETO on herbs and spices, this use makes up 10 percent of total ETO use for pesticidal purposes.

Although many countries have banned the use of ETO on spices and other food due to dietary concerns for public exposure to ETO and its reaction products, EPA believes that use of ETO on spices is safe. The Agency analyzed the dietary risks associated with ETO and its reaction products as part of the 2006 TRED. These risks were considered not of concern after risk mitigation options were adopted. One of the risk mitigation options adopted in the TRED is the transition of the spice industry to single chamber fumigation facilities that have demonstrated to result in residue levels which are lower than those that result from sterilization using conventional sterilization methods. It is also believed that single chamber fumigation has the potential to reduce worker exposure to ETO.

Food-borne illness is a concern of the Agency. As stated above, there were 21 spice recalls reported between 1969 and 2003, five recalls occurred between 1971 and 1996, and 16 recalls occurred between 2001 and 2003. Most of the recalled spices were contaminated with *Salmonella* serotypes. The CDC estimates that for every case of Salmonella that is diagnosed there are 38 cases undiagnosed or reported (Mead, et al., 1999). Consequently, it is difficult to estimate the extent to which ETO prevents potential food-borne illness associated with untreated herbs and spices. The Agency has not received information that identifies ETO as primarily responsible for the relatively low contamination rates attributed to spices. However, since ETO treatment of herbs and spices is effective in reducing microbial activity, it is assumed that it also reduces the potential of food-borne illness.

Alternatives to ETO exist for antimicrobial treatment of spices (e.g., heat, irradiation, PPO), although none of the alternatives can be considered a single replacement for ETO for all spices and pests currently treated by ETO.

Given the range of potential risk following worker exposures that require 35 years of ETO exposure and in light of the benefit of reducing potential food-borne illness, the lack of a single replacement for ETO, and risk reduction measures already in place, the Agency has determined that ETO use on herbs and spices is eligible for reregistration with the implementation of the following mitigation.

- Employee safety and awareness training is required for all employees (including office staff). Information and training is to be provided to all employees in the facility at the time of initial assignment and annually thereafter. This training is intended to ensure that all facility employees are aware of the risks associated with ambient levels of ETO from sterilization processes and is to include, at a minimum, the following information:

    - The most recent monitored ambient levels of ETO in the facility.
    - The potential health effects from the levels of ETO in the facility.

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

- Increased facility aeration is encouraged to reduce ambient levels of ETO. Achieving an ambient level of 0.25 ppm or less (measured as a daily time-weighted average) could eliminate potential long-term non-cancer risks to workers that do not wear respirators as part of their job duties. An ambient level of 0.25 ppm of ETO (measured as a daily time-weighted average) would also be expected to result in potential cancer risks of 1.3×10^{-4} to 1.1×10^{-3}. Achieving ambient ETO levels less than 0.25 ppm would potentially result in lower cancer estimates. Future monitoring efforts at contract sterilization facilities should include the entire facility (including office space, break areas) to have accurate information regarding exposure of employees who are not wearing respirators as part of their daily routine.

f. Beekeeping Use

Current Use Pattern

The use of ETO for beehive material currently is limited to a state-managed facility in North Carolina via a Special Local Needs (SLN) registration. It is used to fumigate beehive equipment (e.g., woodenware boxes and frames) and wax or plastic combs that are contaminated with the bacteria *Paenibacillus larvae*, the cause of American Foulbrood Disease. The beekeeping use accounts for less than 1 percent of the total annual usage of ETO for commercial fumigation/sterilization.

The North Carolina Department of Agriculture and Consumer Affairs (NCDA&CS) uses 2 vacuum tight chambers designed for use with ETO. One chamber (48" x 54" x 84") is located outside on a covered concrete pad. A second chamber, 1/3 the size of the larger chamber, also is located outside.

Beekeeping equipment is treated 30 to 40 times per year in North Carolina. Most of the treatments are done between December and March. The larger chamber is loaded manually by one licensed state employee and occasionally assisted by one of four associates. A different licensed state employee is the primary operator of the smaller chamber. A total of 6 employees in NC are involved with the ETO use for sterilization/fumigation of beekeeping equipment.

Risks of Concern

Exposures and risks associated with fumigation of beekeeping equipment are expected to be similar to those described above for spice fumigation considering the similarities in the fumigation process (e.g., chamber loading, gas introduction).

Based on the limited number of ETO applications (30 to 40 times per year) for the North Carolina beekeeping use, ETO exposure for this use is not of chronic duration. Therefore the short-/intermediate-term endpoint for the non-cancer assessment would apply to this use. Non-

cancer risk estimates, calculated as MOEs are not of concern (i.e., short- and intermediate-term MOEs > 30).

Since worker exposures are considered similar to spice fumigation, the beekeeping use information (i.e., 30 to 40 times per year) is applied to the recently submitted worker exposure data for spice industry workers. This yields an estimated cancer risk range of 1.1×10^{-5} to 9.2×10^{-5}.

Stakeholder Involvement

In April 2007, EPA staff consulted with the state apiarists in Maryland and Maine to get information about their previous ETO use, and with the NCDA&CS to learn more about the current use of ETO in North Carolina. State representatives described specifically what is treated (or was historically treated in the case of Maryland and Maine) with ETO, when treatments occur, how treatments typically occur, and alternatives to ETO when disease is present.

EPA has also coordinated with the United States Department of Agriculture – Agricultural Research Service (USDA-ARS), Bee Research Laboratory. In July 2007, the USDA-ARS Bee Research Laboratory provided information on methods used to control and decontaminate infected bee equipment, including the use of ETO. The USDA-ARS Bee Research Laboratory views ETO as a useful tool to the beekeeping industry for fumigating beekeeping equipment contaminated with American Foulbrood disease.

During Phases 5 and 6 of the Public Participation Process, the Agency received comments from the Maryland Department of Agriculture, NCDA&CS, and the North Carolina State Beekeepers Association, with specific knowledge relating to ETO use on beekeeping equipment. In particular, the North Carolina Department of Agriculture and Consumer Affairs provided detailed information on the ETO treatment process used in North to refine the risk estimates for the beekeeping use.

Alternatives and Benefits

Alternatives are available to manage the American Foulbrood Disease effectively, and are used throughout the United States. The alternatives to ETO consist of scorching the supers, tops, and bottoms with a portable propane torch. Contaminated frames and combs are burned. Another method is to boil all hive material, including frames, combs, and supers in a lye solution. To retain the use of hive material, some choose to fumigate with ETO, where available.

Cost saving is a major reason for beekeepers to use ETO, because some hive material may have to be destroyed in severe cases of American Foulbrood Disease. The use of ETO for beehive material may be useful for severely infested hives where destruction of frames, as an alternative, would be costly. However, alternatives are clearly available to manage the disease effectively, as shown by the small use of ETO for beekeeping purposes in the United States.

For additional information, refer to the Agency's *Qualitative Assessment of Alternatives for Ethylene Oxide Uses (DP316692)* and the BEAD response to comments documents which are available in the public docket EPA-HQ-OPP-2005-0203 located on-line at <http://www.regulations.gov/>.

Risk Reduction Measures in Place

NCDA&CS vents the ETO treatment chamber prior to unloading. A vacuum is drawn on the chamber and fresh air is released into the chamber 3 times. It is vented through an 80 foot PVC pipe stack 80 feet from the valve and approximately 20 feet above the ground. During the unloading process, the chamber door is always located between the employee and the chamber opening. The door serves as a partial barrier between the employee and any ETO remaining in the chamber.

NCDA&CS allows the beehives to aerate in the ETO chamber for 60 minutes after the chamber door is opened. This delay allows ETO to dissipate from the wood and the honey combs. In addition, after the beehives are removed from the chamber, they are further aerated before they are returned to their owner.

No respirators or other personal protective equipment are worn during the ETO treatment process.

EPA Decision

ETO has the potential to cause adverse health effects to workers. Potential cancer risks for workers associated with the beekeeping use in North Carolina range from 1.1×10^{-5} to 9.2×10^{-5}.

EPA policy for non-dietary risks in the 10^{-5} to 10^{-4} range is to determine whether the benefits of use outweigh the risks and to seek ways to mitigate unacceptable risks. This policy specifically allows for the consideration of the weight of scientific evidence regarding carcinogenicity, number of people exposed, and benefits associated with the pesticide under review.

In the case of the use of ETO on beekeeping equipment, this use makes up less than 1 percent of total ETO use for pesticidal purposes. There are 2 chambers currently used to treat beekeeping equipment in North Carolina.

The Agency has determined that there are economic benefits of ETO use on beekeeping equipment and, as specified above, losing its use would involve additional costs to beekeepers in North Carolina, some of which can be quantified. Given the infrequent use of ETO for beekeeping, its very minor contribution to the total annual usage of ETO for commercial fumigation/sterilization (less than 1 percent), and the cost savings seen in North Carolina, the Agency has determined that ETO use on beekeeping equipment is eligible for reregistration with the implementation of the following mitigation.

- Respirators to be worn during chamber opening and unloading and tank change/maintenance activities. This risk mitigation measure is expected to lower worker exposure to ETO and result in reduced long-term non-cancer and potential cancer risk estimates for workers.

It should be noted that in the future if additional states receive SLN registrations for the use of ETO on beekeeping equipment, the Agency will require any such registrations to include the mitigation measures stated above.

V. What Registrants Need to Do

The Agency has determined that products containing the active ingredient ETO are eligible for reregistration provided that the risk mitigation measures outlined in this document are adopted and label amendments are made to reflect these measures. The Agency intends to issue DCIs for generic (technical grade) data and product-specific data. Generally, registrants will have 90 days from receipt of a generic DCI to complete and submit response forms or request time extension and/or waiver requests with a full written justification. The DCIs will include specific requirements and instructions on how to respond. Table 3 below presents the additional generic data the Agency intends to require for ETO to confirm the decision that products containing the active ingredient ETO are eligible for reregistration. For product-specific DCIs, registrants will have eight months from receipt of the DCI to submit data and to submit amended labels. In order for products containing the active ingredient ETO to be eligible for reregistration, all product labels must be amended to incorporate the specific changes and language presented in Table 4 below. Table 4 also describes how the required language should be incorporated.

A. Manufacturing-Use Products

1. Additional Generic Data Requirements

The generic database supporting the reregistration of ETO has been reviewed and determined to be substantially complete. However, EPA is requiring the following additional data to confirm the decisions presented in this RED. The Agency intends to issue a generic DCI for these data.

Documentation of the presence of pathogens will provide useful information to the Agency to determine the types of pathogens that would remain and flourish inside of a musical instrument. The presence of these pathogens inside the instrument would make them potentially available for a musician to inhale into their lungs, possibly causing an illness. These data will be used to further refine the benefits analysis, allowing the Agency to understand the types of pathogens present inside of the musical instruments.

After review and evaluation of the data, the Agency will be able to further refine the benefits analysis for ETO use to sterilize musical instruments. These data will inform the Agency about the types of pathogens that would remain inside the instrument without the ETO sterilization treatment. Although a DCI will be sent to the technical registrant, Encore, Etc., the distributor for the ETO musical instrument treatment, has agreed to conduct and submit the results of this study to the Agency.

Table 3. Data Requirement for the Reregistration of ETO.

Data Requirement	New OPPTS Guideline Number (GLN)
Documentation of Presence of Pathogens in Internal Surfaces of Musical Instruments	Special Study

2. Labeling for Manufacturing-Use Products

To ensure compliance with FIFRA, labeling for all manufacturing-use products (MUPs) should be revised to comply with all current EPA regulations, PR Notices, and applicable policies. The MUP labeling should bear the specific language presented in Table 4 below.

B. End-Use Products

1. Additional Product-Specific Data Requirements

Section 4(g)(2)(B) of FIFRA calls for the Agency to obtain any needed product-specific data regarding the pesticide after a determination of eligibility has been made. The registrant must review previous data submissions to ensure they meet current EPA acceptance criteria and if not, commit to conduct new studies. If a registrant believes that previously submitted data meet current testing standards, then the study MRID numbers can be cited according to the instructions in the Requirement Status and Registrations Response Form provided for each product. The Agency intends to issue a separate product-specific DCI outlining specific data requirements.

2. Labeling for End-Use Products

To be eligible for reregistration, labeling changes are necessary to implement measures outlined in Section IV above. The specific changes and language are presented in Table 4 below. Generally, conditions for the distribution and sale of products bearing old labels/labeling will be established when the label changes are approved. However, specific existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes, and other factors.

In order to be eligible for reregistration, amend all product labels to incorporate the risk mitigation measures outlined in Section IV. The following table describes how language on the labels should be amended.

Table 4. Summary of Labeling Changes for ETO

Description	Amended Labeling Language for Manufacturing Use Products	Placement on Label
Manufacturing Use Products		
For all Manufacturing Use Products	"Only for formulation into a biocide, fungicide, fumigant, herbicide, insecticide, or rodenticide for the following use(s) [fill blank only with those uses that are being supported by MP registrant]."	Directions for Use
One of these statements may be added to a label to allow reformulation of the product for a specific use or all additional uses supported by a formulator or user group	"This product may be used to formulate products for specific use(s) not listed on the MP label if the formulator or user group has complied with U.S. EPA submission requirements regarding support of such use(s)." "This product may be used to formulate products for any additional use(s) not listed on the MP label if the formulator or user group has complied with U.S. EPA submission requirements regarding support of such use(s)."	Directions for Use
Environmental Hazards Statements Required by the RED and Agency Label Policies	"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollution Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."	Precautionary Statements
End Use Products Intended for Occupational Use		
PPE Requirements for **all products**	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are" (*registrant inserts correct chemical-resistant material*). "If you want more options, follow the instructions for category" *[registrant inserts A,B,C,D,E,F,G,or H]* "on an EPA chemical-resistance category selection chart."	Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals

	"All handlers must wear at a minimum: > Long-sleeved shirt and long pants, > Shoes plus socks, > Chemical-resistant gloves, and > when the ambient ETO concentration is 1 to 50 ppm, full-facepiece respirator with ETO approved canister, front or back mounted, > when the ambient ETO concentration is 50 to 2,000 ppm, (1) positive-pressure supplied-air respirator equipped with full-facepiece, hood, or helmet; or (2) continuous-flow supplied-air respirator (positive-pressure) equipped with hood, helmet, or suit, > when the ambient ETO concentration is >2,000 ppm or unknown (e.g., emergency situations), (1) positive-pressure self-contained breathing apparatus equipped with full-facepiece; or (2) positive-pressure full-facepiece supplied-air respirator equipped with an auxiliary positive-pressure self-contained breathing apparatus. When handlers could have eye or skin contact with ETO or ETO solutions, such as during maintenance and repair, vessel cleaning, or cleaning up spills, they must wear: > Chemical-resistant attire, such as an apron, protective suit, or footwear that protects the area of the body that might contact ETO or ETO solutions, and >Face-sealing goggles, a full face shield, or a full-face respirator."	
PPE Requirements for **beekeeping use**	"Personal Protective Equipment (PPE)" "Some materials that are chemical-resistant to this product are" (*registrant inserts correct chemical-resistant material*). "If you want more options, follow the instructions for category" *[registrant inserts A,B,C,D,E,F,G,or H*] "on an EPA chemical-resistance category selection chart." "All handlers must wear at a minimum:	In the PPE section of the label

	> Long-sleeved shirt and long pants, > Shoes plus socks, and > Chemical-resistant gloves. > When opening and unloading a chamber and during tank change/maintenance activities, a full-facepiece respirator with ETO approved canister that is front or back mounted is required.	
User Safety Requirements	1. Follow the respirator manufacturer's user's instructions for changing canisters. 2. Respirators must be fit-tested and fit-checked using a program that conforms to OSHA's requirements (see 29CFR Part 1910.134). 3. Respirator users must be trained using a program that confirms to OSHA's requirements (see 29CFR Part 1910.134). 4. Respirator users must be examined by a qualified medical practitioner to ensure physical ability to safely wear the style of respirator to be worn. A qualified medical practitioner is a physician or other licensed health care professional (PLHCP) who will evaluate the ability of a worker to wear a respirator. The initial evaluation consists of a questionnaire that asks about medical conditions (such as a heart condition) that would be problematic for respirator use. If concerns are identified, then additional evaluations, such as a physical exam, might be necessary. The initial evaluation must be done before respirator use begins. It does not need to be repeated unless the health status or respirator use conditions change (see 29CFR Part 1910.134).	In the PPE section of the label
User Safety Recommendations	"Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables exist, use detergent and hot water. Keep and wash PPE separately from other laundry."	Precautionary Statements: Hazards to Humans and Domestic Animals immediately following the PPE requirements
User Safety	"User Safety Recommendations	Precautionary Statements under:

Recommendations	Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet. Users should remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing. Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."	Hazards to Humans and Domestic Animals immediately following Engineering Controls (Must be placed in a box.)
Environmental Hazards	"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollution Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."	Precautionary Statements immediately following the User Safety Recommendations
Other Application Restrictions for products with directions for use in **hospitals and healthcare facilities** (Risk Mitigation)	"In hospitals and healthcare facilities, Sterilization/fumigation with ETO must be performed only in vacuum or gas tight chambers designed for use with ETO. After February 28, 2010, a single chamber process is required for ETO treatment (sterilization and aeration are to occur in the same chamber) in hospitals and healthcare facilities."	Directions for Use
Other Application Restrictions for products with directions for use in **contract sterilization facilities (including medical, musical instruments,**	"In contract sterilization facilities, including facilities treating medical equipment and supplies, musical instruments, library/museum artifacts, cosmetics, and spices the following requirements must be followed: Sterilization/fumigation with ETO must be performed only in vacuum or gas tight chambers designed for use with ETO.	Directions for Use

library/museum artifacts, cosmetics, and spice use) (Risk Mitigation)	Safety and awareness training is required for all employees including office staff. Information and training must be provided to all employees in the facility at the time of initial assignment and annually thereafter. The safety training must include, at a minimum, the following information: 1. the most recent monitored ambient levels of ETO in the facility; 2. the potential health effects from the levels of ETO in the facility; 3. the emergency response plan and how to respond in an emergency; 4. the availability of the Material Safety Data Sheet and other materials related to the health hazards of exposure to ETO. In order to reduce ambient levels of ETO, lengthy facility aeration is encouraged. Achieving an ambient level of 0.25 ppm (measured as a daily time-weighted average) greatly reduces potential long-term risks to employees not directly involved in the ETO applications. Air monitoring should include the entire facility including office space, break areas, and loading/unloading areas."	
Other Application Restrictions for products with directions for use in **contract sterilization facilities: spice use** (Risk Mitigation)	"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 pre-condition 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 ETO and air is compatible with the chamber design, then, introduce into the chamber a concentration of ETO 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	Directions for Use

	evacuations) between 1.5 PSIA (27” Hg) and 5.0 PSIA (20” Hg) while maintaining a minimum chamber temperature of 115° F.”	
Other Application Restrictions for products with directions for use in **beekeeping** (Risk Mitigation)	“Do not treat combs containing honey.”	Directions for Use
Other Application Restrictions Currently required in the 29 CFR	Employers in facilities that use ETO must comply with all of the requirements for ETO use specified in 29 CFR 1910.1047.	Directions for Use

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Appendix A. ETO Uses and Use-Patterns Eligible for Reregistration

Use Pattern	LIMITATIONS
Medical	ETO may be used only to sterilize medical or laboratory items, pharmaceuticals, and aseptic packaging. or to reduce microbial load on cosmetics, whole and ground spices or other seasoning materials, artifacts, archival material or library objects. ETO may be used only in facilities that meet the requirements of 29 CRF 1910.1047 in non-portable vacuum or gas-tight chambers designed for use with ETO and carbon dioxide. ETO may only be used by persons who have been trained in accordance with 29 CRF 1910.1047. When used by healthcare providers to sterilize health care items, ETO must be used in non-portable ethylene oxide gas sterilizers that meet FDA regulatory requirements and in accordance with directions supplied by the sterilizer manufacturer.
Musical Instruments	
Library and Museum Artifacts	
Cosmetic	
Spice	
Beekeeping	

Appendix B. Table of Generic Data Requirements and Studies Used to Make the ETO Reregistration Decision

Guide to Appendix B

Appendix B contains listing of data requirements which support the reregistration for active ingredients covered by the ETO RED. It contains generic data requirements that apply to ETO in all products, including data requirements for which a "typical formulation" is the test substance.

The data table is organized in the following formats:

1. Data Requirement (Column 1). The data requirements are listed in the order in which they appear in 40 CFR part 158. The reference numbers accompanying each test refer to the test protocols set in the Pesticide Assessment Guidance, which are available from the National technical Information Service, 5285 Port Royal Road, Springfield, VA 22161 (703) 487-4650.

2. Use Pattern (Column 2). This column indicates the use patterns for which the data requirements apply. The following letter designations are used for the given use patterns.

    A. Terrestrial food
    B. Terrestrial feed
    C. Terrestrial non-food
    D. Aquatic food
    E. Aquatic non-food outdoor
    F. Aquatic non-food industrial
    G. Aquatic non-food residential
    H. Greenhouse food
    I. Greenhouse non-food
    J. Forestry
    K. Residential
    L. Indoor food
    M. Indoor non-food
    N. Indoor medical
    O. Indoor residential

3. Bibliographic Citation (Column 3). If the Agency has acceptable data in its files, this column list the identify number of each study. This normally is the Master Record Identification (MIRD) number, but may be a "GS" number if no MRID number has been assigned. Refer to the Bibliography appendix (Appendix C) for a complete citation of the study.

Guideline Number	Requirement	Use Pattern	Bibliographic Citation(s) (MRID)
Occupational/Residue Exposure			
Special Study	ETO Specific Worker Monitoring Study to Support the Medical Sterilization Uses	L,M,N	47331801
Special Study	ETO Specific Worker Monitoring Study To Support the Spice Sterilization Use	L,M,N	47338301
Toxicology			
830.7800	2-Generation Reproduction – Rat	L,M,N	42788101

Appendix C. Technical Documents to Support the ETO RED

Additional documentation in support of this RED is maintained in the OPP docket EPA-HQ-OPP-2005-0203. This docket may be accessed in the OPP docket room located at Room S-4900, One Potomac Yard, 2777 S. Crystal Drive, Arlington, VA. It is open Monday through Friday, excluding Federal holidays, from 8:30 a.m. to 4:00 p.m. All documents may be viewed in the OPP docket room or downloaded or viewed via the Internet at the following site: <http://www.regulations.gov>.

The docket initially contained preliminary risk assessments, supporting documents, and technical (or manufacturing-use) registrant error comments for ETO as of August 3, 2005. After a sixty-day public comment period, EPA considered the public comments that were submitted to the docket and revised the risk assessments as necessary. The revised risk assessments, any supporting documents that needed to be revised, impact assessments, and memos describing the Biological and Economic Assessment Division (BEAD), the Antimicrobials Division (AD), and Health Effects Division (HED) response to public comments will be added to the docket when the RED is posted in April 2008.

The Agency documents in the docket will include:

1. Review of Calculated Ethylene Oxide Exposures for Ethylene Oxide Sterilization Plant Workers (MRID No. 47331801) Submitted in Support of the Occupational Exposure Assessment of the Antimicrobial Uses of Ethylene Oxide for Reregistration Eligibility Decision (RED). PC Code 042301. DP Barcode 348868. March 26, 2008.

2. Ethylene Oxide: Addendum to the Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision (RED) for Ethylene Oxide. March 24, 2008.

Appendix D. Generic Data Call-In (GDCI)

Note that a complete generic DCI, with all pertinent instructions, will be sent to registrants under separate cover.

Appendix E. Product-Specific Data Call-In (PDCI)

Note that a complete product-specific DCI, with all pertinent instructions, will be sent to registrants under separate cover.

Appendix F. EPA's Batching of ETO Products for Meeting Data Requirements for Reregistration

In an effort to reduce the time, resources and number of animals needed to fulfill the acute toxicity data requirements for reregistration of products containing ETO as the active ingredient, the Agency has batched products which can be considered similar for purposes of acute toxicity. Factors considered in the sorting process include each product's active and inert ingredients (identity, percent composition and biological activity), type of formulation (e.g., emulsifiable concentrate, aerosol, wettable powder, granular, etc.), and labeling (e.g., signal word, use classification, precautionary labeling, etc.). Note that the Agency is not describing batched products as "substantially similar" since some products within a batch may not be considered chemically similar or have identical use patterns.

Note: A complete batching index will be sent to registrants under separate cover.

Appendix G. List of Available Related Documents and Electronically Available Forms

Pesticide Registration Forms are available at the following EPA internet site:
<http://www.epa.gov/opprd001/forms/>.

Pesticide Registration Forms (These forms are in PDF format and require the Acrobat reader)

Instructions:

1. Print out and complete the forms. (Note: Form numbers that are bolded can be filled out on your computer then printed.)

2. The completed form(s) should be submitted in hardcopy in accord with the existing policy.

3. Mail the forms, along with any additional documents necessary to comply with EPA regulations covering your request, to the following address for the Document Processing Desk:

    Document Processing Desk (distribution code)*
    Office of Pesticide Programs (7504P)
    Environmental Protection Agency
    1200 Pennsylvania Ave, NW
    Washington, DC 20460-0001

    * Distribution Codes are as follows:
    (APPL) Application for product registration
    (AMEND) Amendment to existing registration
    (CAN) Voluntary Cancellation
    (EUP) Experimental Use Permit
    (DIST) Supplemental Distributor Registration
    (SLN) Special Local Need
    (NEWCO) Request for new company number
    (NOTIF) Notification
    (PETN) Petition for Tolerance
    (XFER) Product Transfer

DO NOT fax or e-mail any form containing "Confidential Business Information" or "Sensitive Information."

If you have any problems accessing these forms, please contact Nicole Williams at (703) 308-5551 or by e-mail at *williams.nicole@epamail.epa.gov*. If you want these forms mailed or faxed to you, please contact Lois White, *white.lois@epa.gov* or Floyd Gayles, *gayles.floyd@epa.gov*.

If you have any questions concerning how to complete these forms, please contact OPP's ombudsperson for conventional pesticide products: Linda Arrington, (703) 305-5446.

The following Agency Pesticide Registration Forms are currently available via the Internet at the following locations:

8570-1	Application for Pesticide Registration/Amendment	http://www.epa.gov/opprd001/forms/8570-1.pdf
8570-4	Confidential Statement of Formula	http://www.epa.gov/opprd001/forms/8570-4.pdf
8570-5	Notice of Supplemental Registration of Distribution of a Registered Pesticide Product	http://www.epa.gov/opprd001/forms/8570-5.pdf
8570-17	Application for an Experimental Use Permit	http://www.epa.gov/opprd001/forms/8570-17.pdf
8570-25	Application for/Notification of State Registration of a Pesticide To Meet a Special Local Need	http://www.epa.gov/opprd001/forms/8570-25.pdf
8570-27	Formulator's Exemption Statement	http://www.epa.gov/opprd001/forms/8570-27.pdf
8570-28	Certification of Compliance with Data Gap Procedures	http://www.epa.gov/opprd001/forms/8570-28.pdf
8570-30	Pesticide Registration Maintenance Fee Filing	http://www.epa.gov/opprd001/forms/8570-30.pdf
8570-32	Certification of Attempt to Enter into an Agreement with other Registrants for Development of Data	http://www.epa.gov/opprd001/forms/8570-32.pdf
8570-34	Certification with Respect to Citations of Data (in PR Notice 98-5)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-5.pdf
8570-35	Data Matrix (in PR Notice 98-5)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-5.pdf
8570-36	Summary of the Physical/Chemical Properties (in PR Notice 98-1)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-1.pdf
8570-37	Self-Certification Statement for the Physical/Chemical Properties (in PR Notice 98-1)	http://www.epa.gov/opppmsd1/PR_Notices/pr98-1.pdf

Pesticide Registration Kit available at <http://www.epa.gov/pesticides/registrationkit/>.

Dear Registrant:

For your convenience, we have assembled an on-line registration kit which contains the following pertinent forms and information needed to register a pesticide product with the U.S. Environmental Protection Agency's Office of Pesticide Programs (OPP):

1. The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA) as Amended by the Food Quality Protection Act (FQPA) of 1996.

2. Pesticide Registration (PR) Notices

    a. 83-3 Label Improvement Program-Storage and Disposal Statements
    b. 84-1 Clarification of Label Improvement Program
    c. 86-5 Standard Format for Data Submitted under FIFRA
    d. 87-1 Label Improvement Program for Pesticides Applied through Irrigation Systems (Chemigation)
    e. 87-6 Inert Ingredients in Pesticide Products Policy Statement
    f. 90-1 Inert Ingredients in Pesticide Products; Revised Policy Statement
    g. 95-2 Notifications, Non-notifications, and Minor Formulation Amendments
    h. 98-1 Self Certification of Product Chemistry Data with Attachments (This document is in PDF format and requires the Acrobat reader.)

    Other PR Notices can be found at <http://www.epa.gov/opppmsd1/PR_Notices.>

3. Pesticide Product Registration Application Forms (These forms are in PDF format and will require the Acrobat reader.)

    a. EPA Form No. 8570-1, Application for Pesticide Registration/Amendment
    b. EPA Form No. 8570-4, Confidential Statement of Formula
    c. EPA Form No. 8570-27, Formulator's Exemption Statement
    d. EPA Form No. 8570-34, Certification with Respect to Citations of Data
    e. EPA Form No. 8570-35, Data Matrix

4. General Pesticide Information (Some of these forms are in PDF format and will require the Acrobat reader.)

    a. Registration Division Personnel Contact List
    b. Biopesticides and Pollution Prevention Division (BPPD) Contacts
    c. Antimicrobials Division Organizational Structure/Contact List
    d. 53 F.R. 15952, Pesticide Registration Procedures; Pesticide Data Requirements (PDF format)
    e. 40 CFR Part 156, Labeling Requirements for Pesticides and Devices (PDF format)
    f. 40 CFR Part 158, Data Requirements for Registration (PDF format)
    g. 50 F.R. 48833, Disclosure of Reviews of Pesticide Data (November 27, 1985)

Before submitting your application for registration, you may wish to consult some additional sources of information. These include:

1. The Office of Pesticide Programs' Web Site.

2. The booklet "General Information on Applying for Registration of Pesticides in the United States", PB92-221811, available through the National Technical Information Service (NTIS) at the following address:

   National Technical Information Service (NTIS)
   5285 Port Royal Road
   Springfield, VA 22161

   The telephone number for NTIS is (703) 605-6000. Please note that EPA is currently in the process of updating this booklet to reflect the changes in the registration program resulting from the passage of the FQPA and the reorganization of the Office of Pesticide Programs.

3. The National Pesticide Information Retrieval System (NPIRS) of Purdue University's Center for Environmental and Regulatory Information Systems. This service does charge a fee for subscriptions and custom searches. You can contact NPIRS by telephone at (765) 494-6614 or through their website.

4. The National Pesticide Telecommunications Network (NPTN) can provide information on active ingredients, uses, toxicology, and chemistry of pesticides. You can contact NPTN by telephone at (800) 858-7378 or through their website: <http://npic.orst.edu>.

   The Agency will return a notice of receipt of an application for registration or amended registration, experimental use permit, or amendment to a petition if the applicant or petitioner encloses with his submission a stamped, self-addressed postcard. The postcard must contain the following entries to be completed by OPP:

   - Date of receipt
   - EPA identifying number
   - Product Manager assignment

   Other identifying information may be included by the applicant to link the acknowledgment of receipt to the specific application submitted. EPA will stamp the date of receipt and provide the EPA identifying File Symbol or petition number for the new submission. The identifying number should be used whenever you contact the Agency concerning an application for registration, experimental use permit, or tolerance petition.

To assist us in ensuring that all data you have submitted for the chemical are properly coded and assigned to your company, please include a list of all synonyms, common and trade names, company experimental codes, and other names which identify the chemical (including "blind" codes used when a sample was submitted for testing by commercial or academic facilities). Please provide a CAS number if one has been assigned.