Proposed Re-evaluation Decision PRVD2010-21

Ethylene Oxide

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Overview

What is the Proposed Re-evaluation Decision?

After a re-evaluation of the pesticide uses of ethylene oxide, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing ethylene oxide in Canada.

The purpose of this Proposed Re-evaluation Decision is to notify registrants, pesticide regulatory officials, and the Canadian public of proposed interim mitigation measures and label amendments for the product containing ethylene oxide. Additional data are also being requested as a result of this re-evaluation. The PMRA will assess the data and any new information that becomes available, and will communicate the results and provide a further update at a later date.

This proposal affects the current end-use product containing ethylene oxide registered in Canada. Once the re-evaluation decision is made, the registrant will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the preliminary science evaluation for ethylene oxide and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of ethylene oxide.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health *and* the environment. Regulatory Directive DIR2001-03, *Pest Management Regulatory Agency Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act.*

Ethylene oxide, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA also takes into account the Canadian use pattern and issues (for example, the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in the 2008 RED, the USEPA concluded that ethylene oxide was eligible for re-registration provided that risk-reduction measures were adopted. Further, the USEPA is currently evaluating ethylene oxide's carcinogenicity classification and will determine whether additional actions are warranted in the future based on the results of this assessment. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED relevant to the Canadian situation.

Based on a review of the currently available information, the PMRA is proposing that interim mitigation measures be implemented to further protect workers and bystanders. The implementation of these interim measures is considered a first step in the re-evaluation of the Canadian pesticide uses of products containing ethylene oxide. Additional data are also required to determine the effectiveness of the mitigation measures. In the long-term, the PMRA is proposing to work with registrants and stakeholders to develop and implement a guidance document on Fumigation Management Plans. It is also recommended that the registrant and/or users work towards improving the technologies to further reduce human exposure.

The PMRA is aware that the USEPA carcinogenicity assessment of ethylene oxide is ongoing. Therefore, the status of ethylene oxide as a pest control product in Canada may be revised.

For more details on the information presented in this overview, please refer to the Science Evaluation of this consultation document.

What is Ethylene Oxide?

Ethylene oxide is a fumigant gas registered in Canada to control microorganisms and stored-product insects. It is applied indoors using specialized chambers that are designed for use with ethylene oxide. The application rates and methods vary depending on the type and quantity of material to be treated, how the material is packed, the types of organisms to be killed, as well as the chamber size, temperature and relative humidity.

Currently, ethylene oxide is registered for use on whole or ground spices and processed natural seasonings to control bacteria and stored product insects, and is regulated under the *Pest Control Products Act*. It is also an approved food additive for for fumigation of whole and ground spices under Division 16 of the *Food and Drugs Regulations*. Finally, it is used to sterilize medical and laboratory equipment, pharmaceuticals, cosmetics and aseptic packaging. In Canada, these uses are regulated under the authority of the Canadian *Food and Drugs Act*. The present Proposed Re-evaluation Decision only addresses the use of ethylene oxide as a pest control product under the *Pest Control Products Act*.

Health Considerations

Can Approved Uses of Ethylene Oxide Affect Human Health?

Ethylene oxide may have potential human health risks of concern from occupational exposure. Additional risk-reduction measures are required.

People could be exposed to ethylene oxide or its reaction products (for example, ethylene chlorohydrin or ethylene glycol) by working inside sterilization facilities or by consuming treated food. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that ethylene oxide may have potential human health risks of concern from occupational exposure, and additional risk-reduction measures were required. The USEPA concluded that ethylene oxide or its reaction products were unlikely to affect human health as a result of food consumption, provided additional label amendments were adopted. These conclusions apply to the Canadian situation and equivalent risk-reduction measures are required.

Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue at the established MRL does not pose an unacceptable health risk.

Ethylene oxide is currently registered in Canada for use on spices and processed natural seasonings and could be used in other countries on food that is imported into Canada. Ethlene oxide is also currently approved as a food additive under Division 16 of the *Food and Drugs Regulations.* Under Division 16, ethylene oxide may be used as a fumigant on whole or ground spices (excluding those containing salt) at levels consistent with Good manufacturing Practices.[2]

Environmental Considerations

What Happens When Ethylene Oxide Is Introduced Into the Environment?

Ethylene oxide is unlikely to affect non-target organisms when used according to the label directions.

The USEPA concluded that the reregistration of ethylene oxide was acceptable provided risk-reduction measures to further protect the environment were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of ethylene oxide, the PMRA is proposing interim risk-reduction measures for the ethylene oxide product label. These interim measures are designed to further protect human health and the environment. The following is proposed:

- Safety and awareness training for all employees in the sterilization facility
- Sterilization/fumigation only to be performed in vacuum or gas-tight chambers
- A reduction of the occupational exposure limit to 0.1 ppm ethylene oxide
- Increased aeration and air monitoring of the entire facility
- Additional personal protective equipment for handlers
- A reduction of the maximum application rate on spices and natural seasonings

[2] "Good Manufacturing Practice" is defined in the F&DR (B.01.044) as: "where the limit prescribed for a food additive in a Table to section B.16.001 is stated to be "Good Manufacturing Practice", the amount of the food additive added to a food in manufacturing and processing shall not exceed the amount required to accomplish the purpose for which the additive is permitted to be added to that food."

- Use of an improved method for sterilization of spices that uses a single chamber process
- Prohibition for the use in/on basil
- Additional advisory and precautionary statements

What Additional Scientific Information Is Required?

Data are required as a condition of continued registration under Section 12 and Section 19 of the *Pest Control Products Act*. The registrant of this active ingredient must provide these data or an acceptable scientific rationale for a waiver to the PMRA within the timeline specified in the decision letter. Appendix I lists all data requirements.

Next Steps

Before making the re-evaluation decision on ethylene oxide, the PMRA will consider all comments received from the public in response to this consultation document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document). The PMRA will then publish a Re-evaluation Decision[3] document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

[3] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

Ethylene oxide is an antimicrobial and insecticide used to control microorganisms and stored-product insects in dried spices and natural seasonings, and is regulated under the *Pest Control Products Act* and as a fumigant for whole and dried spices under the *Food and Drugs Regulations*. It is also used to sterilize medical and laboratory equipment, pharmaceuticals, cosmetics and aseptic packaging. In Canada, these uses are regulated under the authority of the Canadian *Food and Drugs Act*, and were not included in the current assessment.

Following the re-evaluation announcement for ethylene oxide, the registrant of the ethylene oxide product in Canada indicated that they intended to provide continued support for all uses currently registered in Canada.

The PMRA used recent assessments of ethylene oxide from the United States Environmental Protection Agency (USEPA), and additional information currently available. The USEPA Reregistration Eligibility Decision (RED) document for ethylene oxide, dated 2008, and the USEPA TRED (USEPA, 2006) as well as other information on the regulatory status of ethylene oxide in the United States can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

In Canada, non-pesticide uses of ethylene oxide were previously assessed under the *Canadian Environmental Protection Act, 1999* and the results were published in the 2001 Second Priority Substances List (PSL2) Assessment Report. It was concluded that non-pesticide use of ethylene oxide constitutes or may constitute a danger in Canada to human life or health, but does not have harmful effects on the environment or its biological diversity. Therefore, ethylene oxide is considered to be "toxic" as defined under Section 64 (*c*) of the *Canadian Environmental Protection Act, 1999*. Environment Canada and Health Canada's PSL2 Assessment Report for ethylene oxide is available on the Chemical Substances website at www.chemicalsubstances.gc.ca.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Ethylene Oxide
Function	Antimicrobial, Insecticide, Fumigant
Chemical family	Epoxide
Chemical name	Ethylene Oxide
1 International Union of Pure and Applied Chemistry (IUPAC)	1,2-Epoxyethane
2 Chemical Abstracts Service (CAS)	Oxirane
CAS Registry Number	75-21-8
Molecular formula	C_2H_4O
Structural formula	
Molecular weight	44.05 amu
Purity of the technical grade active ingredient	Not available (No registered TGAI)
Registration Number	22965 (Restricted)

The product will be assessed for impurities of human health or environmental concern when the full Part 2 Product Chemistry is provided as requested.

2.2 Physical and Chemical Properties

Property	Result
Vapour pressure at 20°C	1095 mmHg
Henry's law constant	19.86 $Pa \bullet m^3 \bullet mol^{-1}$
UV–visible spectrum	No UV absorbing chromophore
Solubility in water	>100 ppm
***n*-Octanol–water partition coefficient**	Log K_{ow} = -0.30
Conversion Factors	1 ppm in air = 1.83 mg/m^3 or 1 mg/m^3 = 0.55 ppm

2.3 Comparison of Use Patterns in Canada and the United States

Ethylene oxide is a fumigant gas registered in Canada to control microorganisms and stored-product insects in whole and ground spices and processed natural seasonings (except mixtures containing salt). It interacts directly with genetic material and indirectly affects protein synthesis. Currently, there is one restricted ethylene oxide product registered as of 9 May 2010, under the authority of the *Pest Control Products Act* (Appendix II).

The end-use product is applied indoors using gas-tight vaults or chambers which are designed for use with ethylene oxide, and can be applied either alone or in combination with carbon dioxide or dichlorodifluoromethane. The maximum application rate is 1500 mg a.i./L (milligrams active ingredient per litre chamber volume). Exposure times vary between 45 minutes to 20 hours depending on the type and quantity of material, how the material is packed, the types of organisms to be killed, as well as the chamber size, temperature and relative humidity.

The American and Canadian use patterns were compared. In the United States, ethylene oxide is registered as a pesticide to control microorganisms and stored-product insects on spices, natural seasonings and black walnuts. Ethylene oxide is also registered for non-pesticide uses on medical/laboratory items, pharmaceuticals, cosmetics, aseptic packaging, musical instruments, artifacts, archival equipment, library items and beehive equipment. Overall, the formulation, guarantee, application rates and methods for pesticide uses described in the USEPA RED encompass the Canadian use patterns. Based on this comparison of use patterns, it was concluded that the USEPA RED for ethylene oxide is relevant to the Canadian situation.

All current pesticide uses are being supported by the registrant and were, therefore, considered in the re-evaluation of ethylene oxide.

3.0 Impact on Human Health and the Environment

In their 2008 RED, the USEPA concluded that the current use of products containing ethylene oxide registered at the time of the RED publication may have potential human health risks of concern from occupational exposure. However, it was determined that the benefits of ethylene oxide use outweigh the occupational risks provided that the risk mitigation measures and product label amendments are adopted. It was also determined that the use of ethylene oxide does not pose unreasonable risks or adverse effects to the general population or the environment, and is therefore eligible for reregistration. The USEPA also published a TRED in 2006 that includes a dietary (food) risk assessment that met the *Food Quality Protection Act* requirements. In addition, the USEPA is currently evaluating ethylene oxide's carcinogenicity classification through the *Integrated Risk Information System* program based on human epidemiological data. When this evaluation is finalized, the USEPA will determine whether further actions are warranted.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed.

Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Occupational exposure to ethylene oxide and/or its reaction products may occur while working in a sterilization facility either as a handler (for example, operating the chamber and wearing a respirator) and/or a non-handler (for example, working in the office, warehouse or receiving area and not wearing a respirator). Residential exposure is not expected as there are no residential uses registered.

Dietary exposure may occur as a result of residues on treated food. When used to sterilize food (such as spices and natural seasonings), ethylene oxide reacts to form three major by-products: ethylene chlorohydrin, ethylene bromohydrin and ethylene glycol. Based on detected levels in foodstuffs, ethylene chlorohydrin and ethylene glycol are the two reaction products of toxicological concern. Since ethylene oxide use for the sterilization of spices only occurs indoors, exposure to drinking water is not expected. The USEPA's human health risk assessments for pesticide uses are summarized below.

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

In the case where evidence of carcinogenicity is identified for the active ingredient, a cancer potency factor (Q_1*) is generated and used to estimate cancer risk. The product of the expected exposure and the cancer potency factor (Q_1*) estimates the lifetime cancer risk as a probability. A lifetime cancer risk in the range of 1 in 10^{-5} to 1 in 10^{-6} in worker populations is generally considered acceptable.

Workers can be exposed to ethylene oxide through handling material that has been treated with ethylene oxide or through inhalation during sterilization and/or post-sterilization activities.

The USEPA considered the potential for occupational dermal exposure to ethylene oxide and the reaction products ethylene chlorohydrin and ethylene glycol (via post-sterilization activities for spices) was expected to be minimal since actual handling of the treated materials was limited (material is placed on pallets). Therefore, a quantitative dermal exposure and risk assessment was not conducted.

To determine inhalation exposure and risk in sterilization facilities, refined occupational assessments were conducted by the PMRA based on ethylene oxide-specific worker and air monitoring data. Exposure analyses were based on worker activity information (for example, loading/unloading and cleaning the chamber, working in the office, etc.), time spent wearing or not wearing respirators, and individual sampling badges and/or air monitoring. These assessments therefore covered exposure for both sterilization and post-sterilization activities.

It was concluded that short- and intermediate-term inhalation MOEs for all workers were above the target MOE, and therefore, below the level of concern. Long-term inhalation exposure for non-handlers resulted in an MOE below the target MOE. Further, cancer risks as a result of inhalation exposure for all workers exceeded the level of concern.

Based on these quantitative assessments, the following mitigation measures were required: safety and awareness training for all employees in the fumigation facility (including office staff); increased aeration and air monitoring of the entire facility; additional personal protective equipment for workers involved in sterilization activities (such as respiratory protection under certain conditions); and, specific directions for use indicating that sterilization/fumigation is only to be performed in vacuum or gas-tight chambers designed for use with ethylene oxide.

3.1.2 Dietary (Food) Exposure and Risk Assessment

For ethylene oxide, no dietary end-points of concern were identified since residues decline rapidly after sterilization and are unlikely to be found in spices at the time of consumption. For ethylene chlorohydrin, both acute and chronic dietary endpoints of concern were identified. For ethylene glycol, only a chronic dietary endpoint of concern was identified.

Refined acute and non-cancer chronic dietary assessments were performed by the USEPA for treated food based on residue data from ethylene oxide fumigation studies on spices, herbs and dried vegetables. The dietary risk assessments for the reaction products, ethylene chlorohydrin and ethylene glycol, resulted in risk estimates below 100% of the reference doses for acute and non-cancer chronic exposures for children aged 1 to 2 years (the most sensitive subpopulation). It was concluded that dietary (food) risks from ethylene chlorohydrin and ethylene glycol were below the level of concern with the implementation of the following mitigation measures: the use of an approved application method which uses single chamber technology for the sterilization of spices, dried vegetables or seasonings; a rate reduction (maximum ethylene oxide concentration of 500 mg/L); and, the prohibition of ethylene oxide use in/on basil. Further, based on data gaps identified for ethylene chlorohydrin, additional data were required (such as chronic toxicity/oncogenicity studies, developmental toxicity and reproduction toxicity studies).

3.1.3 Aggregate Risk Assessment and Cumulative Effects

Aggregate risk combines the different routes of exposure to ethylene oxide (for example, from food, water and residential/bystander exposures). It was concluded that aggregate risk from exposure to ethylene oxide and its reaction products were not of concern after the risk mitigation measures were adopted.

The USEPA has not determined whether ethylene oxide has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that ethylene oxide does not share a common mechanism of toxicity with other substances and a cumulative risk assessment was not required.

3.2 Environment

The USEPA did not conduct a quantitative ecological risk assessment. It was concluded that indoor uses of ethylene oxide were not likely to result in unacceptable ecological risk to non-target organisms based on minimal exposure potential. Overall, advisory statements to protect the environment from effluent discharge were required.

3.3 Relevance to the Canadian Situation

The pesticide use patterns and exposure scenarios described in the USEPA RED for ethylene oxide sterilization are considered relevant to the Canadian situation. Based on the available information at this time, the USEPA conclusions for the pesticide uses of ethylene oxide are applicable to Canada. Therefore, the PMRA is proposing the following interim measures and label amendments to mitigate potential risks from exposure to ethylene oxide and its reaction products:

- Annual safety and awareness training for all employees in the facility, including office staff. The training is to include information regarding ambient levels of ethylene oxide in the facility, the health hazards and an emergency response plan.

- Sterilization/fumigation is only to be performed in vacuum or gas-tight chambers designed for use with ethylene oxide.

- Increased aeration and air monitoring of the entire facility including office space, break areas and loading/unloading areas in order to achieve levels of ethylene oxide below 0.1 ppm.

- Additional personal protective equipment for workers involved in the handling and/or application of ethylene oxide, including additional respiratory protection under certain conditions (for example, if ethylene oxide concentrations are elevated).

- A reduction of the maximum application rate for sterilization of whole and ground spices and other processed natural seasonings (except mixtures to which salt has been added). The concentration of ethylene oxide must not exceed 500 mg a.i./L in the chamber.

- The use of the improved ethylene oxide sterilization method for spices that uses a single sterilization chamber to pre-condition and aerate with an alternating vacuum and aeration purging procedure.

- Prohibition for use of ethylene oxide in/on any form of basil.

The PMRA is proposing the following additional measures:

- A reduction of the occupational exposure limit (threshold limit value) to 0.1 ppm ethylene oxide based on the recommended exposure limit set by the National Institute for Occupational Safety and Health (NIOSH).
- An update of the current label to include additional standard statements regarding restricted use, basic hygiene and general precautionary statements.

The PMRA also requires additional data for the reaction product ethylene chlorohydrin (such as chronic toxicity/oncogenicity, developmental toxicity, reproduction toxicity and short-term oral toxicity). In addition, a confirmatory study is required under Section 19 of the *Pest Control Products Act*, to determine the effectiveness of the interim mitigation measures (monitoring data for ambient (indoor) air levels of ethylene oxide in sterilization facilities).

It should be noted that the registration status of ethylene oxide as a pest control product in Canada may change based on the PMRA's evaluation of the additional data and/or the USEPA carcinogenicity assessment. The PMRA will provide a further update as applicable in the future.

3.4 Pest Control Product Policy Considerations

3.4.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, for example, persistent (in air, soil, water and/or sediment), bioaccumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the re-evaluation process, ethylene oxide was assessed in accordance with the PMRA Regulatory Directive DIR99-03[4] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Ethylene oxide is associated with an octanol-water partition coefficient (log K_{ow}) of -0.30 which is below the Track 1 criterion of ≥ 5.0, and therefore is not expected to be bioaccumulative. On this basis, ethylene oxide does not meet Track 1 criteria, and is not considered a Track 1 substance.

4.0 Incident reports

Starting 26 April 2007, registrants are required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame.

[4] DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

There were no incident reports submitted for ethylene oxide as of 21 March 2010.

5.0 Organization for Economic Co-operation and Development Status of Ethylene Oxide

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 33 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies. They compare experiences, share information and analyses, seek answers to common problems, and work to co-ordinate domestic and international policies to allow for consistency in practices across nations.

Based on the current available information, the use of ethylene oxide as a plant protection product (for example, fumigation of plants or plant products in storage) has been prohibited in the European Union since 1991 due to potential residue concerns. Pesticide use for control of wool and fur pests and industrial uses are permitted. The use of ethylene oxide as a sterilant for medicinal products is permitted if no other method of sterilization is available.

In Australia, ethylene oxide is not permitted for use on food products, children's toys, food/drink containers, kitchen utensils used in food preparation, items intended for use in the mouth (for example, toothbrushes, toothpicks) or on skin (for example, cosmetics), or clothing that may have skin contact (for example, undergarments). Pesticide uses of ethylene oxide may include quarantine treatments of imported non-food commodities, such as plant fibre materials, wood products, certain fabrics and apparel, ceramics, glassware and metal materials. Ethylene oxide is registered for sterilization of medical devices.

As described earlier in this document, the United States, also an OECD member assessed the registration of all uses of ethylene oxide in their 2008 RED. The USEPA concluded that the current use of products containing ethylene oxide may have potential human health risks of concern from occupational exposure. However, the USEPA determined that the benefits of ethylene oxide use outweigh the occupational risks provided that the risk-reduction measures recommended in the RED document were implemented.

The OECD status of ethylene oxide has been taken into consideration in the proposed Canadian re-evaluation decision.

6.0 Proposed Re-evaluation Decision

The PMRA is proposing continued registration for the sale and use of the end-use product containing ethylene oxide in Canada with the implementation of the proposed interim mitigation measures. The implementation of these interim measures is considered a first step in the re-evaluation of the Canadian pesticide uses of the product containing ethylene oxide. As a condition of the continued registration of the product containing ethylene oxide, new risk-reduction measures must be included on the label. These measures are required to further protect human health and the environment. The label of the Canadian end-use product must be amended to include the label statements listed in Appendix III. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrant of the ethylene oxide product is required to submit data as a condition of continued registration under Section 12 and Section 19 of the *Pest Control Products Act*. Appendix I lists data requirements.

7.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, *Pest Management Regulatory Agency Re-evaluation Program,* and DACO tables can be found on the Pesticides and Pest Management portion of Health Canada's website at www.healthcanada.gc.ca/pmra. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxiques-toxics/.

The USEPA RED document for ethylene oxide is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

List of Abbreviations

a.i.	active ingredient
amu	atomic mass unit
aPAD	acute population adjusted dose
^{o}C	degree Celcius
CAS	Chemical Abstracts Service
DACO	data code
DNA	deoxyribonucleic acid
g	gram(s)
″Hg	inch mercury
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
m	metre(s)
m^3	metre(s) cubed
mg	milligram(s)
mm	millimetre(s)
mm Hg	millimetre mercury
MOE	margin of exposure
mol	mole
MRL	maximum residue limit
MSHA	Mine Safety and Health Administration
NIOSH	National Institute for Occupational Safety and Health
OECD	Organisation for Economic Co-operation and Development
OEL	Occupational Exposure Limit
OPPTS	Office of Prevention, Pesticides and Toxic Substances
Pa	Pascal
PMRA	Pest Management Regulatory Agency
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
Q_1*	cancer potency factor
RED	Reregistration Eligibility Decision
RNA	ribonucleic acid
RVD	Re-evaluation Decision
TGAI	technical grade active ingredient
TRED	Tolerance Reregistration Eligibility Decision
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Additional Data Requirements

The following data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrant of the ethylene oxide product is required to provide these data or an acceptable scientific rationale for a waiver within the timeline specified in the decision letter the PMRA will send.

1) An application to register a technical source for ethylene oxide, including:

- DACO 2 - Chemistry requirements for the registration of a technical grade active ingredient (TGAI) or an integrated system product.

2) Toxicology data for ethylene chlorohydrin:

- DACO 4.3.1 - Short-term oral (90 day rodent)
- DACO 4.3.2 - Short-term oral (6-12 month dog)
- DACOs 4.4.1 to 4.4.3 - Chronic/Oncogenicity (2 rodent species)
- DACO 4.5.1 - Multi-generation Reproductive Toxicity (rodent)
- DACO 4.5.3 - Developmental Toxicity/Teratogenicity (non-rodent)

These studies must be conducted with the reaction product, ethylene chlorohydrin, which is of suitable quality and purity and be conducted according to the appropriate USEPA Office of Prevention, Pesticides and Toxic Substances or OECD guidelines.

In addition, confirmatory data for ethylene oxide are required as a condition of continued registration under Section 19 of the *Pest Control Products Act*, in order to determine the effectiveness of the proposed mitigation measures (for example, increased facility aeration, etc.). The registrant of the ethylene oxide product is required to provide these data or an acceptable scientific rationale for a waiver within the timeline specified in the decision letter the PMRA will send.

- DACO 5.10 – Ambient Air Samples, Indoor

The study for DACO 5.10 must be representative of typical sterilization activities in Canada; it is recommended that the applicant consult with the PMRA on the protocol to be used for the air monitoring study because the protocol must be approved by the PMRA prior to study initiation.

Appendix II Registered Product Containing Ethylene Oxide as of 9 May 2010

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
22965	Restricted	Praxair Canada Inc.	Ethylene oxide	Gas	100

Appendix III Label Amendments Required for the Product Containing Ethylene Oxide

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, storage and disposal statements, precautionary statements and supplementary protective equipment. Additional information on the label of the currently registered product should not be removed unless it contradicts the above label statements.

The label of the ethylene oxide end-use product in Canada must be amended to include the following statements to further protect workers, bystanders and the environment.

1. Restricted Classification

The following statement must be included on the primary display panel of the label:

> **RESTRICTED PRODUCT**
>
> This product is only to be used by individuals holding an appropriate pesticide applicator certificate or license recognized by the provincial/territorial pesticide regulatory agency where the pesticide application is to occur.
>
> Before any sterilization or fumigation begins, handlers must be familiar with and comply with all local/provincial/territorial/federal laws and regulations.

2. Label amendments pertaining to basic hygiene for all end-use products

Add to PRECAUTIONS:

> Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet.
>
> Remove clothing immediately if pesticide comes in contact with skin through soaked clothing or spills. Then wash skin thoroughly and put on clean clothing. Wash contaminated clothing separately from other clothes before reuse.
>
> Remove personal protective equipment immediately after handling this product. Remove personal protective equipment in a pre-determined area separate from living or working areas.
>
> Wash the outside of the gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.

Avoid touching eyes and face until you have washed your hands.

Respirators should be stored in a sealed plastic bag until the next use, to preserve the life of the filter. Regularly change respirator cartridge filters.

Repair/replace torn or broken personal protective equipment.

Treat all clothing worn during pesticide use as contaminated, and handle with chemical resistant gloves.

Use hot water, heavy-duty liquid detergent, the highest water level setting, and the longest wash cycle. Keep and wash personal protective equipment separately from other laundry.

Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers must be in the area during application.

3. Label amendments and user safety requirements to further protect workers and bystanders

Add to **PRECAUTIONS**:

Wear a long-sleeved shirt, long pants, shoes plus socks, and chemical-resistant gloves during mixing, loading, transfer, application or any other handling activities. A NIOSH/MSHA-approved respirator must also be worn under the following conditions:

- when the ambient ethylene oxide concentration is **1 to 50 ppm** – wear a full-facepiece respirator with ethylene oxide approved canister, front or back mounted;
- when the ambient ethylene oxide concentration is **50 to 2,000 ppm** – wear (1) a positive-pressure supplied-air respirator equipped with full-facepiece, hood, or helmet; or (2) a continuous-flow supplied-air respirator (positive-pressure) equipped with hood, helmet, or suit;
- when the ambient ethylene oxide concentration is **greater than 2,000 ppm or unknown** (e.g., emergency situations) – wear (1) a positive-pressure self-contained breathing apparatus equipped with full-facepiece; or (2) a positive-pressure full-facepiece supplied-air respirator equipped with an auxiliary positive-pressure self-contained breathing apparatus (SCBA).

The respiratory protection must fit properly, any obstruction to a proper fit should be removed (e.g., beard, long sideburns).

When handlers could have eye or skin contact with ethylene oxide or ethylene oxide 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 ethylene oxide or ethylene oxide solutions, and,
- face-sealing goggles, a full face shield, or a full-face NIOSH/MSHA-approved respirator.

Add to **DIRECTIONS FOR USE**:

Sterilization/fumigation with ethylene oxide must be performed only in vacuum or gas tight chambers designed for use with ethylene oxide.

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:

- the most recent monitored ambient levels of ethylene oxide in the facility;
- the potential health effects from the levels of ethylene oxide 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 ethylene oxide.

The occupational exposure limit (OEL) for ethylene oxide is 0.1 ppm (8 hour time-weighted average concentration) based on the National Institute for Occupational Safety and Health (NIOSH) standard.

In order to reduce ambient levels of ethylene oxide, lengthy facility aeration is encouraged. Achieving an ambient level of less than 0.1 ppm ethylene oxide (measured as a daily time-weighted average) greatly reduces potential long-term risks to employees not directly involved in the ethylene oxide applications.

Air monitoring must include the entire facility including office space, break areas, and loading/unloading areas.

For sterilization/fumigation of spices and natural seasonings:

DO NOT use in or on any form of basil.

This product may only be applied to or on whole or ground spices and other processed natural seasonings (except mixtures to which salt has been added) utilizing an ethylene oxide 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 Pest Management Regulatory Agency (PMRA) of Health Canada for instruction on how to receive authorization.

Place spices in the treatment chamber. Assure that the mixture of ethylene oxide and air is compatible with the chamber design, then, introduce into the chamber a concentration of ethylene oxide not to exceed 500 mg/L, with a dwell time not to exceed 6 hours. Then evacuate the gas from the chamber using a sequence of not less than 21 steam washes (injections and evacuations) between 1.5 pounds per square inch absolute (PSIA) (27 ″Hg or 686 mmHg) and 5.0 PSIA (20 ″Hg or 508 mmHg) while maintaining a minimum chamber temperature of 46°C.

4. Additional label amendments

The following statement must be removed from the label of the ethylene oxide end-use product: "*restricted 3.00 kg.100 m*^{3}".

The label of the ethylene oxide end-use product must differentiate between the application rate for spices/natural seasonings and the application rate for other materials. The maximum application rate for spices and natural seasonings (except mixtures to which salt has been added) is 500 mg a.i./L. The application rate for other materials (such as medical instruments) ranges between 250 to 1500 mg a.i./L.

References

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

Not available.

B. ADDITIONAL INFORMATION CONSIDERED

Published Information

Environment Canada and Health Canada. 2001. *Canadian Environmental Protection Act, 1999*. Priority Substances List Assessment Report: Ethylene Oxide.

National Institute for Occupational Safety and Health. 2007. *NIOSH Pocket Guide to Chemical Hazards*. Department of Health and Human Services, Centers for Disease Control and Prevention. DHHS (NIOSH) Publication No. 2005-149.