Proposed Registration Decision PRD2010-06

# Liquid Carbon Dioxide: Cryonite

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# Overview

## Registration Decision for Cryonite

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing to grant full registration for the sale and use of Carbon Dioxide Technical and Cryonite, containing the technical grade active ingredient (TGAI) liquid carbon dioxide, to control flour beetles, cockroaches and bed bugs.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of liquid carbon dioxide and Cryonite.

## What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

Before making a final registration decision on liquid carbon dioxide and Cryonite, the PMRA will consider all comments received from the public in response to this consultation document[3]. The PMRA will then publish a Registration Decision[4] on liquid carbon dioxide and Cryonite, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act.*

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

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

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

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

## What Is Cryonite?

The Cryonite system consists of a device and liquid carbon dioxide ($CO_2$). The device releases liquid carbon dioxide as very cold dry-ice particles (referred to as "snow") which, when applied directly to infested sites, rapidly freeze flour beetles, cockroaches and bed bugs. This rapid freezing kills the target insect on contact.

## Health Considerations

### Can Approved Uses of Cryonite Affect Human Health?

**Cryonite is unlikely to affect your health when used according to label directions.**

The technical grade active ingredient contained in Cryonite, liquid carbon dioxide, is maintained at extremely low temperature and high pressure. Aside from severe burns and frostbite occurring on contact, the overall toxicity of carbon dioxide in its liquid form could not be determined. As a solid (dry ice), carbon dioxide's effects due to exposure mirror those of the liquid form. The carbon dioxide snow sublimates into the gaseous form of carbon dioxide at room temperature. As a gas, carbon dioxide can affect the cardiovascular, respiratory, and neurological systems.

The health risks associated with the use of Cryonite have been assessed and are acceptable. There is a concern with users and bystanders coming into direct contact with the carbon dioxide snow or entering an area where the levels of carbon dioxide gas could exceed safe levels. Accordingly, appropriate handling and use of Cryonite must be observed and precautionary label statements followed. When the levels of carbon dioxide gas exceed 5000 ppm, persons without proper respiratory protection should not be permitted to enter the area being treated.

### Residues in Water and Food

**Dietary risks from food and water are not of concern.**

Cryonite is not for use on food or feed, thus dietary risks from food and water are not of concern.

### Occupational Risks from Handling Cryonite

**Occupational risks are not of concern when Cryonite is used according to label directions, which include protective measures.**

Applicators applying Cryonite and other personnel entering a treatment site can come in contact with carbon dioxide as a solid or a gas. Therefore, the label specifies the proper use of Cryonite and provides safety measures to be followed by applicators and personnel entering a treatment site to ensure a negligible risk due to exposure.

### Bystander Exposure and Risk

For bystanders and pets, exposure is expected to be negligible if the label instructions and precautionary statements are followed.

## Environmental Considerations

### What Happens When Liquid Carbon Dioxide Is Introduced into the Environment?

**Carbon dioxide is a substance that is naturally occurring in the environment. It is necessary in the respiratory cycle of humans and animals, and required by plants for photosynthesis. The use of liquid carbon dioxide and Cryonite is not expected to cause any adverse environmental effects to non-target organisms.**

Under ambient conditions, carbon dioxide is found in a stable gaseous state. Under high pressure and extremely low temperature, it can convert to liquid or solid state, which sublimes into the gaseous state when submitted to lower pressure and higher ambient temperature.

Once the liquid carbon dioxide is released from the Cryonite device as solid snow, it sublimes to gaseous carbon dioxide and disperses in the air. The use of Cryonite is not expected to significantly increase the occurrrence of carbon dioxide in the atmosphere.

## Value Considerations

### What Is the Value of Cryonite?

The value of Cryonite was assessed and it was determined that Cryonite kills flour beetles, cockroaches and bed bugs in structures, furniture, machinery and electrical equipment by rapidly freezing the target insect on contact when applied according to the directions for use. Cryonite can be used in areas where some conventional pest control products cannot be used, such as mattresses, and is compatible with current pest management practices including sanitation (e.g., vacuuming) and other pest control products (e.g., diatomaceous earth).

## 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.

The key risk-reduction measures being proposed on the label of Cryonite to address the potential risks identified in this assessment are as follows.

### Key Risk-Reduction Measures

### Human Health

There is a concern for users and bystanders coming into direct contact with solid carbon dioxide or entering an area where the levels of carbon dioxide gas could exceed safe levels. Accordingly, appropriate handling and use of Cryonite must be observed and precautionary label statements followed. When the levels of carbon dioxide gas exceed 5000 ppm, persons without proper respiratory protection should not be permitted to enter the area being treated.

### Environment

No additional risk mitigation measures or label statements are required.

## Next Steps

Before making a final registration decision on liquid carbon dioxide and Cryonite, the PMRA will consider all comments received from the public in response to this consultation document. 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 (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency’s response to these comments.

## Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on liquid carbon dioxide and Cryonite (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

# Science Evaluation

## 1.0 The Active Ingredient, Its Properties and Uses

### 1.1 Identity of the Active Ingredient

| | |
|---|---|
| **Active substance** | Liquid Carbon Dioxide |
| **Function** | Insecticide |
| **Chemical name** | |
| **1. International Union of Pure and Applied Chemistry (IUPAC)** | Carbon Dioxide |
| **2. Chemical Abstracts Service (CAS)** | Carbon Dioxide |
| **CAS number** | 124-38-9 |
| **Molecular formula** | $CO_2$ |
| **Molecular weight** | 44.01 |
| **Structural formula** | O═ C═ O |
| **Purity of the active ingredient** | 99.8% (Limits 96.8–100%) |

### 1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product

**Technical Product— Carbon Dioxide Technical**

| Property | Result |
|---|---|
| Colour and physical state | Clear Liquid |
| Odour | None |
| Melting range | Not applicable |
| Boiling point or range | -56.6 degrees at 1 atm |
| Density | 0.77 g/mL (liquid at 56 atm and 20°C)<br>849.6 g/L (supercritical fluid at 150 atm and 30°C) |
| Vapour pressure at 20°C | Not available |
| Henry’s law constant at 20°C | Not available |

| Property | Result |
|---|---|
| Ultraviolet (UV)-visible spectrum | Not applicable |
| Solubility in water at 20°C | 1.45 g/L at 25°C, 100 kPa |
| Solubility in organic solvents at 20°C (g/100 mL) | Solvent — Solubility<br>Acetic acid — 10.5<br>Acetone — 7.9<br>Chloroform — 14.9<br>Amyl acetate — 8.8<br>Toluene — 8.7<br>Xylene — 8.8<br>Amyl bromide — 12.2<br>Glycerol — 12.0 |
| *n*-Octanol–water partition coefficient ($K_{ow}$) | Not applicable |
| Dissociation constant (p$K_a$) | Not applicable |
| Stability (temperature, metal) | Not available |

**End-Use Product— Cryonite**

| Property | Result |
|---|---|
| Colour | Clear |
| Odour | None |
| Physical state | Liquid |
| Formulation type | Liquid |
| Guarantee | 99.8% (Limits 96.8–100%) |
| Container material and description | Gas cylinder with steel reinforced high pressure hose |
| Density | 0.77 g/mL (liquid at 56 atm and 20°C)<br>849.6 g/L (supercritical fluid at 150 atm and 30°C) |
| pH of 1% dispersion in water | Not applicable (not required) |
| Oxidizing or reducing action | Not applicable |
| Storage stability | Not provided (not required) |
| Corrosion characteristics | Not applicable |
| Explodability | Not applicable. |

### 1.3 Directions for Use

Cryonite is to be used to kill flour beetles, cockroaches and bed bugs in structures such as food manufacturing facilities, factories, health care facilities (e.g., hospitals), educational institutions (e.g., universities, colleges), transport vehicles (e.g., boats, trucks, trains, airplanes), hospitality facilities (e.g,. hotels, motels, inns, bed and breakfasts, hostels), commercial buildings (e.g., restaurants, malls, movie theatres, stores, offices) and residential buildings (e.g., shelters, houses, apartments). The product may also be used on furniture, machinery and electrical equipment.

The layer of snow should be applied so that it lasts 20–30 seconds with two or three applications applied immediately one after the other. The ideal spraying distance is 10-20 cm from the target site but this can be varied depending on the individual characteristics of the environment being treated. The jet nozzle can be used in confined and hard-to-reach spaces.

### 1.4 Mode of Action

Cryonite kills flour beetles, cockroaches and bed bugs by rapid freezing.

## 2.0 Methods of Analysis

### 2.1 Methods for Analysis of the Active Ingredient

The methods on file for the analysis of the impurities in Carbon Dioxide Technical have been validated and assessed to be acceptable. The active ingredient, carbon dioxide, is a commodity.

### 2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

### 2.3 Methods for Residue Analysis

Methods for Residue Analysis were not required.

# 3.0 Impact on Human and Animal Health

## 3.1 Toxicology Summary

A critical review of the toxicological database for liquid carbon dioxide was conducted. The database consisted of foreign reviews (United States Environmental Protection Agency and European Union) and published scientific literature to support the data requirements for acute oral, dermal, and inhalation toxicity, dermal and eye irritation, skin sensitization, short-term toxicity, genotoxicity, and prenatal developmental toxicity. The scientific quality of the data is high and the database is considered adequate to define the potential toxic effects that may result from exposure to this chemical pest control product.

Liquid carbon dioxide's acute toxicity could not be determined because of the extremely low temperature and high pressure required for the liquid state to be maintained. Oral or dermal exposure to liquid carbon dioxide would result in severe burns and frostbite, but determination of the $LD_{50}$ values, skin and eye irritation, and dermal sensitization was not possible. Likewise, the short-term toxicity, prenatal developmental toxicity, and genotoxicity could not be determined for liquid carbon dioxide.

Liquid carbon dioxide is expected to be expelled from the applicator nozzle as a solid, which will then sublimate into the gaseous form of carbon dioxide. In the solid form, acute effects due to dermal, ocular, or oral exposure to carbon dioxide will result in severe burns and frostbite, but excessive inhalation of the gas may result in cardiovascular, respiratory, and neurological effects. Symptoms of exposure to carbon dioxide as a gas may range from headaches and dizziness at 20 000–50 000 ppm to coma and death at concentrations exceeding 170 000 ppm. Fetotoxicity in pregnant rats exposed to 60 000 ppm of carbon dioxide gas for 24 hours has been reported. Developmental effects included hypoplasia of the vertebral column and an increased incidence of cardiac and skeletal malformations.

## 3.2 Determination of Acute Reference Dose

A No Observed Adverse Effect Level (NOAEL) could not be determined for liquid carbon dioxide, regardless of the route of exposure. Therefore, setting an acute reference dose was not possible.

## 3.3 Determination of Acceptable Daily Intake

Cryonite is not for use on food. A value for an acceptable daily intake was not necessary.

## 3.4 Occupational and Residential Risk Assessment

### 3.4.1 Toxicological Endpoints

Occupational exposure to Cryonite is expected to be short-term in duration and predominantly by the inhalation route upon sublimation. A NOAEL could not be identified for liquid carbon dioxide, therefore, persons without respiratory protection should not be permitted access to the treated area until the carbon dioxide levels drop below 5000 ppm.

#### 3.4.1.1 Dermal Absorption

Not applicable.

### 3.4.2 Occupational Exposure and Risk

#### 3.4.2.1 Exposure and Risk Assessment for Mixer/Loader/Applicator and for Workers Entering Treated Areas

All persons working with liquid carbon dioxide should be knowledgeable of this chemical's hazards, and trained in the use of required respirator equipment and detector devices, in emergency procedures and in the use of the product. When used for treatment of enclosed spaces, two persons familiar with the use of this product must be present during introduction of the pesticide, initiation of aeration and after aeration when testing for re-entry.

Mitigative statements, such as the need for appropriate personal protective equipment (long-sleeved shirt, long pants, shoes and socks, chemical-resistant gloves, and full face shield), have been included on the label. In addition, if Cryonite is to be applied in enclosed or poorly ventilated areas, and if carbon dioxide levels are between 5000 and 30 000 ppm, persons may re-enter the treated area without respiratory protection for 15 minutes or less. For periods longer than 15 minutes, use of either a NIOSH approved supplied-air respirator or a NIOSH/MSHA approved self-contained breathing apparatus (SCBA) with a full face shield is required. If carbon dioxide levels are over 30 000 ppm or are unknown, workers are not permitted entry into the treated area.

A self-contained breathing apparatus should always be available for emergency use.

A significant risk due to exposure of the worker is not anticipated.

#### 3.4.2.2 Bystander Exposure and Risk

Significant risk due to exposure of bystanders and pets to the gas is not anticipated because mitigative measures have been included on the label, such as limiting non-worker personnel access to the treated area when the concentration of carbon dioxide exceeds 5000 ppm.

### 3.5 Food Residues Exposure Assessment

Cryonite is intended for non-food/feed uses. No dietary exposure is anticipated.

## 4.0 Impact on the Environment

Carbon dioxide is present in the atmosphere at a concentration of 0.04%. Carbon dioxide is necessary to sustain all aerobic life on earth. It is taken up by plants during photosynthesis, and is a by-product of all aerobic respiration by living organisms. The potential increased environmental exposure of non-target organisms to liquid (or gaseous) carbon dioxide under operational conditions of the use of Cryonite is considered to be negligible. No additional mitigating measures are required.

### 4.1 Fate and Behaviour in the Environment

Carbon dioxide is a substance that is naturally occurring in the environment and its fate and behaviour are well understood. Under ambient atmospheric conditions, carbon dioxide occurs as a stable gas. The use of Cryonite will result in direct exposure of targeted pests to low temperatures as a result of contact with the “snow” (solid state of carbon dioxide) produced by the release of liquid carbon dioxide through this device. The “snow” will rapidly sublime to a gaseous state and disperse in the air.

### 4.2 Effects on Non-Target Species

Carbon dioxide is taken up by plants in the presence of light and converted into energy and oxygen via photosynthesis. Carbon dioxide is a by-product of all aerobic respiration by living organisms.

The potential toxicity of carbon dioxide is well understood. Based on the use pattern of liquid carbon dioxide in Cryonite, exposure of non-target terrestrial and aquatic organisms to carbon dioxide is expected to be minimal.

## 5.0 Value

### 5.1 Effectiveness against Pests

The Cryonite system consists of a device and liquid carbon dioxide. The device releases liquid carbon dioxide as very cold dry-ice particles. Dry ice has a freezing temperature of -78°C. However, the actual temperatures at the site of application can be higher, depending on where it is applied (e.g., -20 to -62°C). The dry ice rapidly freezes the target insect on contact, resulting in death.

Four efficacy trials were used to support the use of Cryonite to kill flour beetles, bed bugs and cockroaches.

An operational trial demonstrated that higher levels of *Tribolium confusum* adult beetle mortality were found post-treatment with Cryonite (78%) compared to vacuuming alone (36%). In addition, the applicant submitted a study on the temperatures required to kill various stored product pests, including flour beetle species. The study demonstrated that the temperatures generated by Cryonite kills flour beetles.

A laboratory trial demonstrated almost 100% control of bed bugs using Cryonite. In addition, the temperatures generated by Cryonite are expected to kill bed bugs in realistic settings.

A laboratory trial was conducted against German cockroaches. Treatment with the Cryonite system resulted in 100% German cockroach mortality at 24 hours post application. Although some egg hatched in the Cryonite treatment during the 7 days post treatment, the number of 1$^{st}$ instar nymphs was lower compared to the untreated control. The data from the submitted efficacy trial were extrapolated to other species of cockroaches because the temperatures reached by Cryonite are lower than the temperatures required to kill various cockroach species. However, adults of larger cockroach species may not be killed by Cryonite and this is indicated on the label.

### 5.1.1 Acceptable Efficacy Claims

Cryonite is to be used to kill flour beetles, cockroaches and bed bugs in structures such as food manufacturing facilities, factories, health care facilities (e.g., hospitals), educational institutions (e.g., universities, colleges), transport vehicles (e.g., boats, trucks, trains, airplanes), hospitality facilities (e.g,. hotels, motels, inns, bed and breakfasts, hostels), commercial buildings (e.g., restaurants, malls, movie theatres, stores, offices) and residential buildings (e.g., shelters, houses, apartments). The product may also be used on furniture, machinery and electrical equipment.

## 5.2 Adverse affects

Although Cryonite is not expected to damage most substrates, it is recommended that it be tested in a small, inconspicuous area prior to treating an entire area.

The pressures produced by the Cryonite device may result in target insects being pushed out of the treatment area prior to receiving a lethal freezing. To reduce this from happening, the speed at which Cryonite snow is released from the nozzle can be adjusted by putting less pressure on the trigger mechanism of the device.

## 5.3 Economics

No market analysis was done for this application.

## 5.4 Sustainability

### 5.4.1 Survey of Alternatives

**Flour beetles:**
Active ingredients in pest control products registered to control flour beetles include: aluminium phosphide, boric acid, carbon dioxide, diatomaceous earth, d-trans allethrin, imiprothrin, magnesium phosphide, methyl bromide, malathion, permethrin, phosphine, propoxur, pyrethrins and sulfuryl fluoride. Other control methods for flour beetles include prevention of the infestation, good sanitation practices and temperature (hot or cold) treatments.

**Bed bugs:**
Active ingredients in pest control products registered to control bed bugs include: bendiocarb, boric acid, carbaryl, cyfluthrin, diatomaceous earth, d-trans allethrin, permethrin, phenothrin, pyrethrins, resmethrin and tetramethrin. Resistance to many of these active ingredients has been identified in bed bug populations. Other control methods for bed bugs include prevention of the infestation, reducing clutter, mattress encasements, vacuuming, heat, steam and laundering.

**Cockroaches:**
Active ingredients in pest control products registered to control cockroaches include: aluminum phosphide, abamectin, boric acid, chlorpyrifos, cyfluthrin, diatomaceous earth, dichlorvos, d-trans allethrin, d-phenothrin, disodium octaborate tetrahydrate, german cockroach extract, hydramethylnon, imidacloprid, imiprothrin, lamda-cyhalothrin, magnesium phosphide, propetamphos, malathion, methyl bromide, permethrin, propoxur, pyrethrins, resmethrin, silica aerogel and tetramethrin. Other control methods for cockroaches include prevention of the infestation, reducing clutter, good sanitation practices, vacuuming, trapping and cold treatments.

### 5.4.2 Compatibility with Current Management Practices Including Integrated Pest Management

Cryonite is compatible with current management practices such as sanitation (e.g., vacuuming) and other pest control products (e.g., diatomaceous earth).

### 5.4.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

Resistance is unlikely to occur because the mode of action for Cryonite is rapid freezing.

### 5.4.4 Contribution to Risk Reduction and Sustainability

Cryonite rapidly freezes the target insect (i.e., flour beetles, bed bugs and cockroaches). For this reason, these insects are unlikely to develop resistance to Cryonite. This product can be used in areas where some conventional pest control products cannot be used, such as mattresses.

# 6.0 Pest Control Product Policy Considerations

## 6.1 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, i.e., persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, liquid carbon dioxide and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

Liquid carbon dioxide does not meet the Track 1 criteria and will not form any transformation products which meet the Track 1 criteria. Liquid carbon dioxide is a naturally occurring substance and is not expected to be persistent or bioaccumulative in the environment.

## 6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[6]. The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[8], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

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

6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*.

8 DIR2006-02, PMRA Formulants Policy.

Technical grade liquid carbon dioxide and the end-use product Cryonite do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02[9].

# 7.0 Summary

## 7.1 Human Health and Safety

The available information for liquid carbon dioxide is adequate to qualitatively define the effects associated with exposure to this compound. Oral, ocular and dermal exposure to liquid carbon dioxide can result in severe burns and frostbite. Dermal sensitization, short-term toxicity, and genotoxicity could not be determined for carbon dioxide in its liquid form. Fetotoxicity was observed in pregnant rats exposed to 60 000 ppm of carbon dioxide gas for 24 hours. The developmental effects to rats exposed to carbon dioxide gas included hypoplasia of the vertebral column and an increased incidence of cardiac and skeletal malformations. Exposure to solid carbon dioxide is expected to mirror the effects noted for liquid carbon dioxide and excessive exposure to carbon dioxide as a gas by inhalation may result in cardiovascular, respiratory, and neurological effects. Symptoms of exposure to carbon dioxide as a gas may range from headaches and dizziness at 20 000–50 000 ppm to coma and death at concentrations exceeding 170 000 ppm.

The health risks associated with the use of Cryonite have been assessed and are acceptable. Risk mitigation measures are imposed on the product label. Significant risk due to exposure of workers, bystanders and pets to Cryonite is not anticipated if the mitigative measures required are followed.

## 7.2 Environmental Risk

Carbon Dioxide is a substance that is naturally occurring in the environment. The exposure of non-target organisms to liquid carbon dioxide in Cryonite under operational conditions is considered to be negligible, and the use of Cryonite is not expected to cause any adverse effects to the environment.

[9] DIR2006-02, PMRA Formulants Policy.

### 7.3 Value

Cryonite kills flour beetles, cockroaches and bed bugs in structures, furniture, machinery and electrical equipment by rapidly freezing the target insect on contact when applied according to the directions for use. Cryonite can be used in areas where some conventional pest control products cannot be used, such as mattresses, and is compatible with current pest management practices including sanitation (e.g., vacuuming) and other pest control products (e.g., diatomaceous earth).

### 7.4 Unsupported Uses

All uses have been supported.

## 8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Carbon Dioxide Technical and Cryonite, containing the technical grade active ingredient liquid carbon dioxide, to control flour beetles, cockroaches and bed bugs.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

# List of Abbreviations

| | |
|---|---|
| Atm | atmosphere |
| CAS | Chemical Abstracts Service |
| cm | centimetres |
| $CO_2$ | carbon dioxide |
| g | gram |
| IUPAC | International Union of Pure and Applied Chemistry |
| kg | kilogram |
| $K_{ow}$ | *n*-octanol–water partition coefficient |
| L | litre |
| $LD_{50}$ | lethal dose 50% |
| mg | milligram |
| mL | millilitre |
| N/A | not applicable |
| NOAEL | no observed adverse effect level |
| p*K*a | dissociation constant |
| PMRA | Pest Management Regulatory Agency |
| ppm | parts per million |
| SCBA | self-contained breathing apparatus |
| TGAI | technical grade active ingredient |
| TSMP | Toxic Substances Management Policy |
| UV | ultraviolet |

# Appendix I Tables and Figures

## Table 1 Acute Toxicity of Carbon Dioxide Technical and Its Associated End-use Product Cryonite

| Study Type | Species | Result | Comment | Reference |
|---|---|---|---|---|
| **Acute Toxicity of Liquid Carbon Dioxide (Technical)** | | | | |
| Oral<br>Dermal | Because of the extremely low temperature required to maintain the liquid nature of carbon dioxide, severe burns and frostbite are likely to be the predominant symptom of oral and/or dermal exposure. A value for the oral and dermal $LD_{50}$ was not available, nor expected, from the publicly available information. | | | N/A |
| Inhalation | Because the TGAI is a liquid, the acute inhalation toxicity could not be determined. | | | N/A |
| Skin irritation<br>Eye irritation | Skin and eye irritation could not be determined, but it is expected that burns and frostbite would result from dermal and ocular exposure to liquid carbon dioxide. | | | N/A |
| Skin sensitization | Dermal sensitization to liquid carbon dioxide could not be determined. | | | N/A |
| **Acute Toxicity of End-Use Product - Cryonite** | | | | |
| Oral<br>Dermal | As with the active ingredient, liquid carbon dioxide, frostbite is likely to be the predominant symptom of any initial exposure. On application, the liquid carbon dioxide is converted to carbon dioxide snow (solid $CO_2$). The effects of exposure to solid carbon dioxide is expected to be the same as with liquid carbon dioxide. A value for the oral and dermal $LD_{50}$ was not available from the publicly available information.<br><br>Shortly after application, the solid carbon dioxide will undergo sublimation resulting in exposure to carbon dioxide in its gaseous form. The physical form is such that the acute toxicity by either the oral and/or the dermal routes could not be determined.<br><br>Mitigative label statements are required to ensure that risk due to oral and/or dermal exposure to solid and liquid forms of carbon dioxide is negligible. | | | N/A |
| Inhalation | Although an assessment of the acute toxicity of solid or liquid carbon dioxide by inhalation is not possible, the effects of inhaling the gaseous form on sublimation is well documented.<br><br>Symptoms of exposure to carbon dioxide as a gas is subject to the concentration and time of exposure. At 20 000–50 000 ppm concentrations, symptoms of carbon dioxide exposure include headaches, dizziness, sweating, and dyspnoea; at 60 000–100 000 ppm, symptoms include hyperventilation, tachycardia, and worsening dizziness; at 110 000–170 000 ppm, drowsiness, muscle twitching, loss of consciousness; at concentrations >170 000 ppm, convulsions, coma, and death. | | | N/A |
| Skin irritation<br>Eye irritation | Burns and frostbite will result from dermal and ocular exposure to liquid or solid carbon dioxide. In gaseous form, the eye and skin irritation could not be determined. | | | N/A |

| Study Type | Species | Result | Comment | Reference |
|---|---|---|---|---|
| Skin sensitization | There is no publicly available information that supports the likelihood of dermal sensitization to the liquid or solid forms of carbon dioxide. In the gaseous form, carbon dioxide cannot be tested for dermal sensitization by conventional means. | | | N/A |

## Table 2 Toxicity Profile of Carbon Dioxide Technical

| Study Type | Species | Results[a] (mg/kg/day in M/F ) | Reference |
|---|---|---|---|
| 90-day dietary | Repeated exposure to liquid carbon dioxide is expected to result in burns and frostbite for the oral or the dermal route. | | N/A |
| Prenatal Developmental toxicity | Fetotoxicity was noted in pregnant rats after exposure to 60,000 ppm of carbon dioxide gas for 24 hours. Developmental effects included hypoplasia of the vertebral column and an increased incidence of cadiac and skeletal malformations. | | N/A |
| Reverse gene mutation assay | No data was available on the potential mutagenic and genotoxic effects of liquid carbon dioxide. | | N/A |
| Gene mutations in mammalian cells *in vitro* | | | |

[a] Effects observed in males as well as females unless otherwise reported

# References

## A. List of Studies/Information Submitted by Registrant

### 1.0 Chemistry


1801044 1997, COZ-PXR/PXA/IPB-MULTIPLE Response to Regulatory Directive 93-02 Items, DACO: 2.1,2.11.1,2.11.4,2.13,2.14.8,2.3,2.4,2.5,2.6,2.8,2.9 **CBI**

1801054 1997, COZ-PXR/PXA/IPB-MULTIPLE Product Specifications - Praxair QA Program Document P-15-085 Excerpts, DACO: 2.12 **CBI**

1801055 1997, COZ-PXR/PXA/IPB-MULTIPLE Praxair $C0_2$ Production Plants Supplying the Canadian Market, DACO: 2.11 **CBI**

1801062 1997, COZ-PXR/PXA/IPB-MULTIPLE Plants and Lab $CO_2$ Test Results Plant and Lab % $C0_2$ Test Results 1997, DACO: 2.11 **CBI**

1801071 1997, COZ-PXR/PXA/IPB-MULTIPLE Batch Test Logs - Production Plants, DACO: 2.13 **CBI**

1801073 1997, COZ-PXR/PXA/IPB-MULTIPLE Lab Test Results - Plant No. 580. $CO_2$ Analysis, DACO: 2.13 **CBI**

1801074 1997, COZ-PXR/PXA/IPB-MULTIPLE Analytical Equipment Technology Center. Instrumentation and Methodology for Gas Analysis., DACO: 2.13.1 **CBI**

1801077 1997, COZ-PXR/PXA/IPB-MULTIPLE Quantitative Lab Test Chromatograms – Plant No. 580 (May 28, 1997), DACO: 2.13 **CBI**

1801082 COZ-PXR/PXA/IPB-MULTIPLE Quantitative Plant Chromatograms – Plant No.712 (August 6 and 7, 1997), DACO: 2.13 **CBI.**

1801087 1997, COZ-PXR/PXA/IPB-MULTIPLE $CO_2$ Solubility Data and Graphs $CO_2$ Solubility in Various Solvents Technical Sales Bulleting 734 Figures 14, 15, 16, 17 and 18, DACO: 2.14.8 **CBI.**


### 2.0 Human and Animal Health


1778074 Acute Studies - EP, DACO: 4.6

1778075 Short Term Studies - EP, DACO: 4.7

1778076 Use Description/Scenario (Application and Post Application), DACO: 5.2

1786346 2005, Cooling Different Geometries, DACO: 5.2

1786347 Cryonite Video Chapters - paper, DACO: 5.2


### 3.0 Value


1786335 2005, Use of the Cryonite system for the control of stored product pests, DACO: 10.2.3

1786336 2006, Field trial to assess the efficacy of a combined Cryonite/diatomaceous earth treatment against bed bugs, *Cimex lectularius*, DACO: 10.2.3

1786337 2006, Laboratory bioassay to assess the efficacy of the Cryonite system against bed bug adult, nymph and egg stages, DACO: 10.2.3

1786339 2006, Laboratory bioassay to assess the efficacy of the Cryonite system against German cockroaches and Indian meal moths, DACO: 10.2.3
1786344 1993, Combatting pests_by_freezing, DACO: 10.2
1786346 2005, Cooling Different Geometries, DACO: 5.2

## B. Additional Information Considered

### i) Published Information

#### 1.0 Environment

1811587 European Commission, 2008, Review report for the active substance carbon dioxide. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 28 October 2008 in view of the inclusion of carbon dioxide in Annex I of Directive
1811592 The Health and Safety Executive, 2002, Advisory Committee On Pesticides Food and Environment Protection Act 1985, PART III. Control of Pesticides Regulations 1986. Evaluation of Fully Approved or Provisionally Approved Products. Evaluation on: Carbon Dioxide
1811595 Environmental Protection Agency, 1991, Reregistration Eligibility Document (RED) Carbon and Carbon Dioxide, DACO: 12.5.8,12.5.9
1811599 Environmental Protection Agency, 1991, R.E.D. FACTS Carbon, DACO: 12.5.8,12.5.9
1811602 2007, Competent Authority Report. Carbon Dioxide CAS No. 124-38-9 for use as insecticide (Product type 18) Document I, DACO: 12.5.8,12.5.9
1811604 2007, Directive 98/8/EC concerning the placing biocidal products on the market Inclusion of active substances in Annex I or IA to Directive 98/8/EC Assessment Report CARBON DIOXIDE PT 14 (Rodenticides) Annex I&IA - France, DACO: 12.5.8,12.5.9

#### 2.0 Value

1796733 Stored Product Integrated Pest Management With Extreme Temperatures, DACO: 10.2.1
1796736 Use of Extreme Temperatures in Urban Insect Pest Management, DACO: 10.2.1,10.3.2
1796744 2006, Armed Forces Pest Management Board TECHNICAL GUIDE NO. 44 Bed Bugs - Importance, Biology, and Control Strategies, DACO: 10.2.2
1810545 Integrated Pest Management for Cockroaches, University of Connecticut, DACO: 10.2.2
1810551 1993, Cold-tolerance of the oriental cockroach Blatta orientalis, Entomol. Exp. Appl. 68: 257-263, 1993., DACO: 10.2.2
1810552 1997, American Cockroach, Handbook of Pest Control, 8th ed., 144-147, DACO: 10.2.2

### ii) Unpublished Information

None.