

カナダにおけるエチレン登録の現状

PMRA (農薬管理規制局)による資料

2001 年10月5日

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エチレン (商品名 Eco Sprout Guard)



Proposed Regulatory Decision Document PRDD2001-04

Ethylene Eco Sprout Guard

The active ingredient ethylene, as Eco Sprout Guard technical grade active ingredient (TGAI) and the associated end-use product Eco Sprout Guard EP containing 2–100% ethylene in compressed gas cylinders for the control of sprouting in stored “Russet Burbank” processing potatoes, are proposed for registration under Section 13 of the Pest Control Products Regulations.

This proposed regulatory decision document (PRDD) provides a summary of data reviewed and the rationale for the proposed full registration of these products. The Pest Management Regulatory Agency (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 the Publications Coordinator at the address listed below.

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Foreword

The submissions for registration of Eco Sprout Guard TGAI (ethylene) and its end-use product Eco Sprout Guard EP, supplied by Praxair Inc. and marketed by McCain Foods Limited, have been reviewed by the Pest Management Regulatory Agency (PMRA).

Eco Sprout Guard EP, containing 2–100% ethylene in compressed gas cylinders, was investigated as an alternative product to conventional pesticides for the inhibition of sprouting in stored processing potato tubers. Ethylene occurs ubiquitously in the natural environment and is a natural plant hormone. Ethylene is relatively nontoxic and has a long history of use as a clinical anaesthetic at high concentrations (up to 80–90% in oxygen). At the recommended concentration of 4 ppm, ethylene inhibits excessive sprout growth by reducing apical dominance. Levels of ethylene and its major metabolites in treated potatoes are similar to those in untreated potatoes.

The PMRA has carried out an assessment of available information in accordance with Section 9 of the Pest Control Products (PCP) Regulations and has found it sufficient, pursuant to Section 18.b, to allow a determination of the safety, merit and value of *Eco Sprout Guard TGAI (ethylene) and its end-use product Eco Sprout Guard EP*. The Agency has concluded that the use of *Eco Sprout Guard TGAI (ethylene) and its end-use product Eco Sprout Guard EP* in accordance with the label has merit and value consistent with section 18.c of the PCP Regulations and does not entail an unacceptable risk of harm pursuant to Section 18.d. Therefore, based on the considerations outlined above, the use of *Eco Sprout Guard TGAI (ethylene) and its end-use product Eco Sprout Guard EP* is proposed for full registration, pursuant to Section 13 of the Pest Control Products Regulations.

The PMRA is proposing to grant full registration to this product. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed registration decision for this product.

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1.0 The active substance, its properties, and uses

1.1 Identity of the active substance and preparation containing it

Active substance	Ethylene
Function	Sprout inhibitor
Chemical name	
1. International Union of Pure and Applied Chemistry	Ethene
2. Chemical Abstract Services (CAS)	Ethene
CAS Number	74-85-1
Molecular formula	C ₂ H ₄
Molecular weight	28.06
Structural formula	CH ₂ =CH ₂
Nominal purity of active	Pure ethylene gas, 100%
Identity of relevant impurities of toxicological, environmental, and other significance	The product contains carbon monoxide at a maximum level of <0.1%. Impurities of toxicological concern as identified in Section 2.13.4 of DIR98-04 <i>Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product</i> or Toxic Substances Management Policy (TSMP) Track-1 materials as identified in Appendix II of DIR99-03 <i>The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy</i> are not expected to be present or formed in the product.

1.2 Physical and chemical properties of the active substance and end-use product

Technical product: Eco Sprout Guard TGAI

Property	Result	Comment
Colour and physical state	Colourless compressed gas	
Odour	Sweet odour	
Melting point/range	N/A	
Boiling point/range	–103EC	
Specific gravity	0.978 at 0EC (air = 1)	
Vapour density (g/mL)	0.001 26 at 0EC	
Ultraviolet (UV) / visible spectrum	Not expected to absorb UV at wavelengths >300 nm	Photolysis will not be expected
Solubility in water at 20EC	Slightly	
<i>n</i> -Octanol/water partition coefficient (K_{ow})	$\log K_{ow} = 1.16$	Bioaccumulation is not expected
Dissociation constant	Does not dissociate	
Stability (temperature, metal)	The flash point is –136EC. Avoid impact and high temperature at cylinder pressure; incompatible with oxidizing agents, halogens, acid, aluminum chloride and halocarbons	

End-use product: Eco Sprout Guard EP

Property	Result
Colour	Colourless
Odour	Sweet

Property	Result
Physical state	Gas
Formulation type	Compressed gas
Guarantee	2–100%, nominal
Formulants	The product does not contain any EPA List 1 formulants or formulants known to be TSMP Track-1 substances.
Container material and description	Compressed gas cylinders
Oxidizing or reducing action	Incompatible with oxidizing agents, halogens, acids, aluminum chloride and halocarbons
Storage stability	Expected to be stable when stored in the cylinders
Explosibility	Spontaneously explosive in sunlight with chlorine. Forms explosive mixture with air and oxidizing agents. Containers may rupture due to heat or fire. Avoid impacts against containers.

1.3 Details of uses

Ethylene is a growth regulator. In potato tubers, ethylene has been documented to shorten the post-harvest rest period, often resulting in earlier sprouting but inhibiting the elongation of sprouts by reducing apical dominance.

Eco Sprout Guard EP, containing from 2 to 100% ethylene in pressurized cylinders, is recommended for application to “Russet Burbank” processing potato tubers in commercial potato storages. Eco Sprout Guard EP is recommended for daily application into the ventilation airstream of the storage facility to attain an ethylene concentration of up to 4 ppm.

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

The active was determined using two gas chromatographic (GC) methods.

2.2 Method for formulation analysis

The active was determined using two GC methods.

3.0 Impact on human and animal health

3.1 Integrated toxicological summary

Ethylene is a naturally occurring gaseous chemical produced by all plant tissues in significant amounts and acts as an endogenous plant growth regulator. Ethylene is also a naturally occurring endogenous chemical in humans and laboratory animals and has been identified in the air exhaled by unexposed rats and humans. Possible sources of endogenous ethylene in humans and laboratory animals include lipid peroxidation of unsaturated fats, oxidation of free methionine, oxidation of hemin in haemoglobin and metabolism of intestinal bacteria. In humans, the concentration of ethylene in the blood resulting from its endogenous production is approximately 0.097 nmol/L.

Under environmental conditions, ethylene is a gas; therefore, the most probable route of human exposure to ethylene is by inhalation. Ethylene at high concentrations (up to 80–90% in oxygen) has a long history of use as a clinical anaesthetic, with little concomitant toxicity. Anaesthesia is complete within 20–30 min with 90% in oxygen. Ethylene is more advantageous than ether as an anaesthetic because of safer induction and more rapid recovery. Ethylene has been classified as an asphyxiant in Canada because its presence at high concentrations in air lowers the available oxygen concentration.

The uptake, exhalation and metabolism of ethylene can be described by first-order kinetics. Uptake of ethylene into the body is low due to its low solubility in blood. For rats it is estimated that approximately 15–17% of inhaled ethylene reaches the alveolar blood. In humans, it is estimated that approximately 21% of inhaled ethylene reaches the alveolar blood using a physiological toxicokinetic model which is similar to values obtained for rats. Inhalation of ethylene in human volunteers at atmospheric concentrations of up to 50 ppm by gas uptake in a closed spirometer system indicates that at an alveolar ventilation rate of 150 L/h, approximately 5.6% of inhaled ethylene reaches the alveolar blood with the majority, 94.4%, being exhaled again without becoming systemically available via the blood system. At steady state the estimated alveolar retention in humans is approximately 2–3%. Due to its low blood/gas solubility, ethylene is rapidly excreted and does not appear to accumulate in the body. Ethylene from both endogenous and exogenous sources is metabolized to ethylene oxide *in vivo* in rats, mice and humans. Studies in healthy volunteers suggest that approximately 2–3% of ethylene absorbed is metabolized to ethylene oxide, whereas up to 98% of ethylene is exhaled unchanged. The data also suggest that the metabolism of ethylene can be stimulated by an inducer of the mixed-function oxidase system.

Ethylene has low acute toxicity via the inhalation route of exposure in mice. There is some acute hazard of dermal and ocular frost burns and of flammability posed by the compressed gas. In a subchronic inhalation study with Sprague-Dawley rats, there were no toxic effects at concentrations up to and including 10 000 ppm, the highest dose tested. In a chronic toxicity/oncogenicity inhalation study with Fischer 344 rats, no significant treatment-related findings or evidence of oncogenicity were observed at ethylene

concentrations up to and including 3000 ppm, the highest dose tested. The weight of evidence suggests that ethylene is not genotoxic. There is inadequate evidence in humans and experimental animals for carcinogenicity of ethylene. Overall, ethylene is not classifiable as to its carcinogenicity to humans (International Agency for Research on Cancer (IARC) classification - Group 3). Ethylene is not listed as a carcinogen by the National Toxicology Program (NTP) or Occupational Safety and Health Association (OSHA).

The toxicological concerns regarding ethylene are related primarily to its metabolites, specifically the initial metabolite, ethylene oxide. Ethylene oxide is a direct alkylating agent that is genotoxic in numerous in vitro and in vivo test systems and is carcinogenic in mice and rats. Positive results have been obtained using the mouse lung tumour bioassay (\$70 ppm) and the standard 2-year bioassays in mice and rats at concentrations \$100 ppm. Based on these findings, ethylene oxide is classified as carcinogenic to humans by IARC (IARC classification - Group 1) and NTP (*Report on Carcinogens*, 9th edition “known carcinogen”). However, published literature indicates that exposures to 1000 and 40 ppm ethylene in closed inhalation chambers are equivalent to ethylene oxide exposures of 5.6 and 1 ppm, respectively, in rats. When exposure data was combined with previously obtained rat tumour induction data for ethylene oxide, extrapolation of the tumour data to the highest possible ethylene oxide equivalent, 5.6 ppm, indicated that high ethylene exposures would not result in tumour incidence more than 2% above the tumour background level. It was concluded that the body burden of ethylene oxide resulting from such low ethylene oxide exposures (i.e., 5.6 ppm) is too small to lead to a significant increase in tumours in ethylene exposed rats. Published literature also indicates that above concentrations of approximately 1000 ppm ethylene, the $V_{\max}$ for ethylene is reached, thus, higher exposures would not yield greater conversion of ethylene to ethylene oxide. Published literature suggest that it would be difficult to obtain statistically significant positive tumour results for ethylene regardless of the dose. In humans, using a physiological model, predicted blood levels resulting from one 8-h exposure to 1 ppm ethylene oxide would be equivalent ethylene oxide levels expected following an 8-h exposure to 45 ppm ethylene assuming bioavailability of 100% for the metabolically formed ethylene oxide (there is some evidence that at low ethylene exposure concentrations the bioavailability of metabolically formed ethylene oxide may be 100%). Based on measurements of haemoglobin adduct levels in humans exposed to up to 5 ppm ethylene, it is estimated that an average of 2–3% of absorbed ethylene is metabolized to ethylene oxide. The current threshold for ethylene oxide of 1 ppm [current OSHA standard for ethylene oxide, i.e., 8-h time-weighted average (TWA) per 40-h work week] is toxicologically equivalent to an ethylene concentration of 37 ppm. Published literature indicates that long-term human occupational exposure to low airborne concentration of ethylene oxide, at or below current occupational exposure limits of 1 ppm (1.83 mg/m³) would not produce unacceptable increased genotoxic or carcinogenic risk.

Based on these findings and on the proposed conditions of use for ethylene (the ethylene concentration will be a maximum of 4 ppm until the end of the storage period), it is unlikely that ethylene oxide concentrations would reach levels that would produce unacceptable genotoxic or carcinogenic risks.

There is sufficient information from published literature to make a risk assessment for the proposed use of ethylene. Based on information from published literature, ethylene has low toxicity concerns and has been used extensively as an anaesthetic with little concomitant toxicity. Based on the proposed low levels of ethylene exposure, the low absorption rate for ethylene and the low conversion rate of ethylene to ethylene oxide, it is unlikely that ethylene oxide levels would reach unacceptable levels (i.e., >1.0 ppm). It can be concluded that ethylene will be nontoxic to humans under the conditions of use as a plant growth regulator for suppression of sprout growth on stored potatoes, provided that it is used as indicated on the product label; therefore, under the proposed conditions of use as indicated on the product label, it is unlikely that ethylene will present a risk.

3.2 Determination of acceptable daily intake

As indicated by the Health Protection Branch of Health Canada in the “Health and Safety Status Report” for ethylene (May 1994), an acceptable daily intake (ADI) is not required for ethylene, since it is a naturally occurring chemical produced by fruits and vegetables, including potatoes, during senescence. Ethylene is also a naturally occurring endogenous chemical in humans and laboratory animals and has been identified in the air exhaled by unexposed rats and humans. Potential ethylene metabolites have also been shown to occur naturally. Analytical data for these metabolites in treated potatoes showed that residue levels were either nondetectable or were at levels similar to any measurable residues found in controls.

3.3 Acute reference dose

An acute reference dose (ARfD) was not established, since ethylene was considered unlikely to present an acute hazard. The available literature suggests that there are no significant treatment-related findings to indicate a concern in acute dietary risk assessment. The potential risks to humans from exposure to ethylene are considered negligible due to low toxicity concerns and the widespread use of ethylene as an anaesthetic with little concomitant toxicity.

3.4 Toxicology end-point selection—occupational and bystander risk assessment

The primary route of exposure is inhalation. Ethylene has low acute toxicity via the inhalation route. Ethylene is considered a simple asphyxiant. In a subchronic inhalation study from the published literature, there were no toxic effects in Sprague-Dawley rats at concentrations up to and including 10 000 ppm, the highest dose tested. In a published chronic toxicity/oncogenicity inhalation study with Fischer 344 rats, no significant treatment-related findings or evidence of oncogenicity were observed at ethylene

concentrations up to and including 3000 ppm, the highest dose tested. Contact with ethylene as a compressed gas can cause dermal and ocular frost burns and present a hazard due to its flammability. Potential for this type of exposure can be mitigated through labelling. This was considered to be the most appropriate regulatory approach for this active ingredient and a qualitative assessment of exposure and risk for the proposed use of ethylene was conducted.

3.5 Impact on human and animal health arising from exposure to the active substance or to its impurities

3.5.1 Operator exposure assessment

Application to stored potatoes

Eco Sprout Guard consists of compressed ethylene gas contained in pressurized cylinders of varying concentrations (ranging from 2 to 100% ethylene), the balance being made up with nitrogen. Eco Sprout Guard would be applied by releasing the gas in the ventilation system of the potato storage facility at a specific rate up to 4 ppm for the duration of the storage period. The proposed label indicates that for best results application must begin at 1–7 days after the potatoes are harvested and continue until 1–7 days before processing. Typically storage operators would have gas cylinders containing concentrations of ethylene to be used. The concentration in the storage facility would be determined by the delivery rate and the percent concentration of ethylene in Eco Sprout Guard. The concentration of ethylene in the storage building would be monitored, continuously and remotely, to ensure that it remains near the target level throughout the storage period. Typically, the ethylene gas delivery system uses programmable controls to operate valves in response to ventilation conditions in the building. The system is self contained and requires human intervention to review and adjust parameters, to connect or disconnect cylinders to replace empty ones or in the event of a leak in the system.

Operator exposure

Potential occupational exposure to ethylene may occur when entering the storage building or its ventilation duct work (e.g., for repair) during application of ethylene or when standing near the ventilation exhaust. The primary route of exposure would be inhalation.

Ethylene is a naturally occurring gaseous chemical produced by both plants and animals. It has had a long history of use as a clinical anaesthetic (anaesthesia is obtained with exposure to concentrations of 80–90% in oxygen) with little concomitant toxicity. It is generally recognized as safe (GRAS) in the U.S. No exposure limits have been established for ethylene by the American Conference of Governmental Industrial Hygienists (ACGIH). The ACGIH classifies ethylene as a “simple asphyxiant.” Respiratory protection is not normally required for simple asphyxiants except in emergency or planned entry into unknown concentration or in areas of oxygen deficiency. In a published subchronic inhalation study with Sprague-Dawley rats, there were no toxic effects at concentrations up to and including 10 000 ppm, the highest dose tested. A 2-year chronic rat inhalation study from the published literature showed no effects in rats

exposed to 3000 ppm ethylene (6 h/day, 5 days/week). Based on this, it is concluded that the potential risk of workers from exposure to ethylene via inhalation, when used under the proposed conditions, is considered negligible.

Potential exposure to high concentrations of ethylene may occur in the event of a leak in an enclosed space. The proposed label includes precautionary statements regarding proper handling of cylinders and gas release system to avoid leaks; as well, the registrant would provide the user with access to information on proper equipment to use for releasing and monitoring ethylene gas. Respiratory protection for entry into an area of unknown ethylene concentration is recommended on the draft label. These precautionary statements are considered adequate.

Handling cylinders of compressed gas or any equipment under pressure represents a hazard due to its flammability and a potential for acute dermal or ocular exposure to the liquefied gas (i.e., it may cause frost burns if in contact with skin or eyes). This risk can be adequately mitigated with use of appropriate protective equipment; long sleeves, long pants, goggles or faceshield and appropriate gloves are considered adequate.

3.5.2 Bystanders

Based on the nature of the proposed use pattern of Eco Sprout Guard, there would be negligible potential for exposure of bystanders.

3.5.3 Workers

Workers may enter a storage area (e.g., for potato inspection) during or after treatment with ethylene before ventilation is complete (see section 3.5.1 for an assessment of worker potential exposure).

4.0 Residues

No residue data were submitted with this petition. However, previously submitted data and information in support of a former petition to register use of ethylene as a potato sprout inhibitor were summarized by the Health Protection Branch of Health Canada in May 1994 in the “Health and Safety Status Report” for ethylene. Information excerpted from this report is presented in this chapter.

Data provided indicate that the metabolism of ethylene, while not specifically elucidated in potatoes, is similar and probably identical to those metabolic pathways determined for ethylene metabolism in many plants. Potato tubers, as senescent tissues, exhibit low basal metabolic rates such that ethylene is metabolized very slowly, if at all. Endogenous concentrations of ethylene range between 0.0007–0.15 ppm for nonsprouting tubers and 0.1–3 ppm for sprouted tubers. These low concentrations of ethylene, combined with the low diffusion rates suggest that low concentrations of ethylene metabolites would be expected in stored tubers.

Ethylene and its potential metabolites were not identified in treated potatoes at levels exceeding those found in control potatoes, and therefore, animal metabolism and livestock feeding studies were not considered necessary for evaluation.

Residue data was provided for potatoes treated with 4 ppm ethylene for up to 150 days of storage. Residues of chloroethanol, dichloroethane, bromoethanol, ethylene oxide, and ethylene glycol (including its glucoside) residues were in total less than 0.1 ppm. Residues for the metabolite of greatest toxicological concern, ethylene oxide, were <2 ppm (the lower limit of quantitation (LLQ) of the analytical method employed). In addition, the processing or cooking of tubers is expected to result in a reduction of volatile residues (ethylene oxide) by up to 90%. This dissipation of residues would occur by diffusion out of potato tissues during processing of the tubers and by heat-assisted volatilization during cooking.

The partition coefficient for ethylene into potato tuber tissue is very low (0.207), indicating that there is little if any metabolism, compartmentalization of ¹⁴C-ethylene by potato tubers or both. Typical soil atmospheres contain about 10 ppm endogenous ethylene levels that can increase as the moisture status of the soil increases. This indicates that developing potato tubers, which are metabolically active, might be expected to metabolize and bioaccumulate ethylene residues. This level of background exposure is 2.5 times greater than that proposed for supplementation of ambient storage bin atmospheres. No residues of ethylene metabolites (after correction for some measurable residues of ethylene glycol and its glucoside) were determined above LLQs in mature tubers for any treated potato tubers in the 1993 and 1994 research trial residue studies.

Evidence was presented that elucidated the impermeability of ethylene into potato tubers. Potato tubers have a high resistance to diffusion because the periderm of the tuber presents a barrier to gaseous diffusion and the bulk of the diffusion occurs through a very small area of the tuber, up to 2% of its volume. This condition effectively blocks movement of exogenous ethylene into the tuber (even against a concentration gradient) thereby maintaining internal concentrations of ethylene in the tuber at endogenous levels.

Processing studies were not performed for ethylene-treated potatoes. However, the processing of treated tubers into french fries, powdered potatoes, potato flour or cooking of raw potato tubers would reduce the residue of most concern, ethylene oxide, if it were present at levels above background. Ethylene oxide is a gas at room temperature and a liquid below 12EC. It would be expected to volatilize out of potatoes during cooking.

Based on the data submitted, residues in potatoes treated according to the proposed label directions will not result in residues of ethylene or its probable major metabolites above levels found in untreated potatoes. Therefore, no dietary risk assessment is considered necessary, and no MRLs are proposed.

5.0 Fate and behaviour in the environment

5.1 Physical and chemical properties relevant to the environment

The physicochemical properties of ethylene, summarized in Table 5.1, are based on a review conducted by the Laboratory Services Subdivision and other information gathered from various sources. Active ingredient purity was >98.5% in the reviewed studies.

Table 5.1 Physical and chemical properties relevant to the environment

Property	Value	Comments
Water solubility	22.6 mL/100 mL at 0EC; 12.2 mL/100 mL at 20EC	Sparingly soluble
Vapour pressure	4100 kPa at 0EC; 1063 kPa at 50EC	Product is a gas
log K_{ow} (25EC)	1.16	Bioaccumulation is not expected
Dissociation constant (pKa at 20EC)	Not applicable	No dissociable groups present in the active ingredient (a.i.)
UV / visible spectrum	Not expected to absorb UV at wavelength >300 nm	Photolysis is not expected to be route of dissipation in the environment

Summary of environmental chemistry and fate studies

No data were submitted or requested on the environmental fate of ethylene because this gas occurs naturally in the environment and the contribution from the proposed use will not be significant.

Expected environmental concentrations

Ethylene use in storage will only impact the expected environmental concentrations (EEC) of ethylene in the atmosphere; however, the contribution of ethylene from the proposed use site to atmospheric concentrations is considered to be negligible.

It is estimated that 89% of natural and anthropogenically produced ethylene gas is destroyed in the troposphere by OH⁻ radicals, and 8% is destroyed in reactions with ozone. Approximately 3% is transported into the stratosphere. Estimated lifetime in the atmosphere is approximately 2–4 days.

6.0 Effects on non-target species

No data were submitted or requested on effects to nontarget organisms because the contributions from the proposed use will not be significant. Adverse effects on nontarget organisms from the proposed use of ethylene, therefore, are not expected.

7.0 Efficacy

7.1 Effectiveness

7.1.1 Intended use

Eco Sprout Guard EP is intended for use on “Russet Burbank” potatoes in commercial storage facilities to inhibit sprout growth.

7.1.2 Mode of action

Ethylene is a plant growth regulator. In potatoes, ethylene has been documented to shorten the post-harvest rest period, resulting in earlier sprouting but inhibiting the elongation of sprouts by reducing apical dominance. Ethylene also enhances the abscission of sprouts.

7.1.3 Crops

Eco Sprout Guard EP is intended for use on stored “Russet Burbank” potatoes for processing.

7.1.4 Effectiveness against sprouting

Laboratory and commercial scale trials were conducted in which the efficacy of Eco Sprout Guard EP was assessed for the inhibition of sprouting in “Russet Burbank” processing potato tubers. In laboratory trials conducted from 1991–1992 to 1995–1996, Eco Sprout Guard EP was applied to tubers in barrels or steel cabinets to abruptly raise the concentration to 4 ppm once tubers had been permitted to cure (suberize) and cool to the final storage temperature of 9°C, about 8 weeks after the beginning of storage. A commercial standard treatment of chlorpropham (CIPC) was applied to tubers (dipped in 1% emulsion) in each trial.

No sprouting was observed in the CIPC treatment. In the ethylene treatment, the weight of large sprouts (>5 mm) was minimal or absent and ranged from 0 to 0.01 and from 0 to 0.5 g·kg⁻¹ tuber fresh weight at 20 and 25 weeks after the initiation of application, respectively. In contrast, large sprout weight in the untreated control at 20 and 25 weeks ranged from 2.2 to 17.4, and from 8.5 to 38.5 g·kg⁻¹ tuber fresh weight, respectively.

Sprout length increased over time but was always less for ethylene-treated tubers than untreated control tubers. Sprout length averaged 9 mm after 25 weeks of ethylene treatment whereas that in the untreated control averaged 204 mm.

Ethylene often increased number of small sprouts (2–5 mm) relative to the untreated control. At the biochemical and cellular level, continual ethylene exposure may have terminated rest (dormancy) in tuber eyes, possibly leading to an increase in sprout initiation while preventing excessive growth of these sprouts through the inhibition of cell differentiation and elongation. The force required to remove sprouts on ethylene treated potatoes was quantitatively assessed in the 1993–1994 trial and was determined to be significantly less than on untreated tubers.

In a laboratory trial conducted in 1997–1998, ethylene applied in accordance with the proposed application method resulted in sprouts that were less than 5 mm long at 33 weeks after the beginning of treatment. No sprouting was observed in the CIPC control treatment.

In commercial-scale trials conducted from 1992–1993 to 1994–1995, ethylene was applied to potato tubers to abruptly raise the ethylene concentration in the storage building to 4 ppm once tubers had been permitted to cure and cool to the final storage temperature of 9EC. In each trial, a commercial standard treatment of CIPC was applied once to cured tubers in a neighbouring storage building as an aerosol (Stanchem Sprout Nip 840). Ethylene reduced sprout number, sprout weight and sprout length. In 1992–1993, the longest sprout observed after 4 months of ethylene treatment was 2 mm, and total sprout weight averaged less than 0.01 g per tuber. No sprouting was observed in the CIPC treatment in this trial. In the trial conducted in 1993–1994, ethylene-treated tubers had higher sprout weight and sprout number than CIPC-treated tubers up until 22 weeks of storage. After this time, CIPC-treated tubers had large increases in sprout length and weight, such that by week 29, CIPC-treated tubers had about five times the sprout weight that ethylene-treated tubers had. CIPC residues are known to gradually decline over time, such that retreatment is often required to maintain sprout inhibition following 4–6 months of storage. In 1994–1995, it was stated in the trial report that a similar degree of sprout control was achieved with ethylene as in the previous 2 years and that sprout control was less than that achieved with CIPC. In the latter two trials, some sprouting was observed in CIPC treatment along the wall of the storage building, where it was likely CIPC did not reach the tubers. Ethylene is a lighter gas than CIPC applied as an aerosol, and therefore, ethylene is distributed more evenly throughout the storage pile than CIPC. The percentage of tubers with internal sprouts was lower for the ethylene treatment (0.01–0.05%) than for the CIPC treatment (0.5–0.7%).

In an additional commercial-scale trial conducted in 1998–1999, the degree of sprout inhibition was observed to be greater for the treatment of ethylene, applied in accordance with the proposed method, than for the CIPC treatment after 6 months of storage probably due to decreasing CIPC residues on tubers. At 6 months after the beginning of storage, about 17 and 48% of tubers treated with ethylene and CIPC had at least one sprout,

respectively. By the final removal at 8 months, 37 and 56% of tubers treated with ethylene and CIPC, respectively, had at least one sprout. After 6 months of ethylene treatment, weight of small and large sprouts each averaged less than 1 g in tuber samples of approximately 35 kg, whereas the weight of small and large sprouts in CIPC-treated tubers averaged 3 and 7 g in similar-sized samples. After 8 months of ethylene treatment, the mean weight of small and large sprouts was about 17 and 42 g per 35 kg sample, respectively, whereas the mean weight of small and large sprouts of tubers treated with CIPC averaged 16 and 167 g, respectively. The mean maximum sprout length observed in ethylene-treated tubers was 6.5 and 27.5 mm at 6 and 8 months of storage, respectively, much shorter than the 45 and 122 mm observed for the CIPC treatment at these two evaluation times.

In each of the commercial trials, sprouts of ethylene-treated tubers were typically stunted, often branched and very brittle, such that these club-shaped sprouts easily fell off when the tubers were removed from storage.

7.2 Undesirable or unintended side effects on treated plant products

Potato tuber fry colour, as measured on an Agtron reflectance colorimeter (range of 0 = black to 100 = white), was assessed in the same laboratory trials in which efficacy was evaluated. In trials conducted from 1991–1992 to 1995–1996, fry colour generally improved (higher Agtron scale value) with storage time for all treatments. Tubers treated daily with 4 ppm ethylene were usually darker upon frying than either the untreated control or the CIPC treatment, which was related to higher reducing sugar levels in ethylene-treated tubers. At the 25-week evaluation date, relative fry colour among treatments was variable over years. Fry colour of ethylene-treated tubers was darker than untreated control tubers in two trials and darker than CIPC-treated tubers in three trials, was similar to that of CIPC-treated tubers in one trial and was lighter than CIPC-treated tubers in one trial. When averaged over the 5 years, ethylene-treated tubers had a lower Agtron value (by 7–10 points) than CIPC-treated tubers when assessed from 5 to 25 weeks. In the trial conducted in 1997–1998, ethylene was applied in accordance with the proposed application method to attain a maximum ethylene concentration of 4 ppm in the storage facility. The treatment evaluated in earlier trials was included for comparison along with a CIPC control. Fry colour of tubers treated with ethylene according to the proposed application method was 6–7 Agtron units darker than CIPC-treated potatoes from 18 to 33 weeks after the beginning of storage. In contrast, potato tubers treated with ethylene beginning at the end of the cooling period resulted in fry colour that was 19–25 Agtron units darker than that treated with CIPC. In an additional trial conducted in 1996–1997, ethylene applied in accordance with the proposed application method resulted in fry colour that was 15–22 Agtron units higher (lighter) than where ethylene had been applied at the end of the cooling period.

Fry colour was assessed in the same commercial-scale trials in which efficacy was evaluated. Fry colour of potato tubers randomly selected from the storage pile was assessed weekly in each of the trials conducted in 1992–1993, 1993–1994 and

1994–1995. Fry colour was generally darker in ethylene-treated tubers than in CIPC-treated tubers in all 3 years, regardless of when data were collected. Unlike the laboratory trials conducted from 1991–1992 until 1995–1996, fry colour did not improve over storage time for either of these treatments. Over the 26 weeks following the initiation of ethylene treatment, U.S. Department of Agriculture fry colour grade ratings (range of 1=light to 7=dark) for ethylene- and CIPC-treated tubers were 3.0 and 2.6 in 1992–1993, 3.4 and 2.8 in 1993–1994, and 2.5 and 1.7 in 1994–1995, respectively.

In the commercial-scale trial conducted in 1998–1999, potato tubers treated with ethylene applied in accordance with the proposed application method resulted in darker fry colour than CIPC after 3 and 6 months of storage. After 3 and 6 months of storage, the fry colour of tubers treated with ethylene were, respectively, 5 and 6 Agtron points lower on average than tubers treated with CIPC. Fry colour of ethylene-treated tubers and CIPC-treated tubers were similar after 8 months of storage.

7.3 Observations on undesirable or unintended side effects

Eco Sprout Guard EP is proposed for post-harvest use only on stored “Russet Burbank” potato tubers for processing in closed-system commercial storage facilities. It would not be expected to impact other crops. It would not be used on or near seed potatoes.

7.4 Economics

In 1998–1999, 4 292 000 t of potatoes were produced in Canada on 156 000 ha. Since 1992–1993, potato production has increased by 2–3% per year. In 1998, 620 000 t of potatoes were exported, mainly to the U.S. In that year, 30% of fresh exports were seed potatoes, and 70% were table stock potatoes and potatoes for processing. Approximately 50% of all potatoes grown in Canada are processed, much of which is exported as frozen french fries. In 1998, 483 436 t of frozen french fries valued at \$461 million were exported, mainly to the U.S., but also to more than 90 countries worldwide. Between 1995 and 1998, the quantity and value of exported frozen french fries more than doubled. The importance of processed potato products to the Canadian economy is expected to continue to increase.

7.5 Sustainability

7.5.1 Survey of alternatives

7.5.1.1 Nonchemical control practices

Storage at very low temperatures (3 or 4°C) may be used to delay sprouting of potato tubers; however, these temperatures may induce high levels of reducing sugars, thereby resulting in fry colour of the processed product that is too dark to command top grades and prices.

7.5.1.2 Chemical control practices

Products containing maleic hydrazide or chlorpropham, listed in Table 7.5, are registered for control of sprouting in potatoes. There are two types of chlorpropham products: those that are applied as aerosols in the ventilation system of the potato storage building and those that are applied as emulsions to potatoes in the packing line. Products of the latter type are not typically used for processing potatoes and are not shown in Table 7.5.

Table 7.5 Alternative products for control of sprouting of stored processing potatoes

Active ingredient	End-use products	Mode of action	Application timing	Application rate
Maleic hydrazide	Royal MH 60SG (Reg. No. 18143)	Inhibits cell division	Applied in the field between 2–3 weeks past full bloom and 2 weeks before expected date of topkill or first frost, and when tubers are at least 4–5 cm in diameter	3.4 kg a.i./ha
Chlorpropham	Sprout Nip 840 (Reg. No. 18833)	Inhibits cell division	After harvesting, potatoes are allowed to cure (suberize) for at least 2 weeks before application	Sufficient product applied to achieve deposit of 6–12 ppm on potatoes
	Decco 273 Aerosol Potato Sprout Inhibitor (Reg. No. 24007)			For <4 months storage: 1 kg a.i./60 t potatoes; For 4–6 months storage: 2 kg a.i./50 t potatoes
	Clean Crop Spud-Nic Aerosol Grade (Reg. No. 24691)			For 3 months storage: 1.5–2 kg a.i./100 t potatoes; For 4–6 months storage: 3–3.75 kg a.i./100 t potatoes
	Ag-Services Potato Sprout Inhibitor (Fogging Grade) (Reg. No. 11848)			For 3 months storage: 1.5–2 kg a.i./100 t potatoes; For 4–6 months storage: 3–3.75 kg a.i./100 t potatoes
	Ag-Services 750A Potato Sprout Inhibitor (Fogging Grade) (Reg. No. 25834)			For 3 months storage: 1.5–2 kg a.i./100 t potatoes; For 4–6 months storage: 3–3.75 kg a.i./100 t potatoes

7.6 Conclusions

7.6.1 Summary

Data generated in laboratory and commercial-scale trials demonstrated that Eco Sprout Guard EP, when applied in accordance with the proposed method, can be expected to effectively inhibit sprouting of stored “Russet Burbank” processing potatoes while having minimal impact on processed product quality, such as fry colour. The accepted uses summarized in Table 7.6 are based on the value assessment.

Table 7.6 Summary of accepted use for Eco Sprout Guard EP

Crop	Potatoes (<i>Solanum tuberosum</i>)
Cultivar	Russet Burbank (for processing only)
Application timing	Throughout the storage period (up to 10 months)
Frequency of application	Daily during ventilation cycles
Application method	Applied from a pressurized gas cylinder into the ventilation airstream of the storage building to attain an ethylene concentration of up to 4 ppm.
Pest controlled	Sprouting

8.0 Toxic Substances Management Policy

Ethylene occurs naturally in the environment. The contribution from this use will not be significant. The technical grade ethylene does not contain any impurities or microcontaminants known to be Toxic Substances Management Policy (TSMP) Track-1 substances. The end-use product, Eco Sprout Guard EP does not contain any U.S. Environmental Protection Agency List 1 formulants or formulants known to be TSMP Track-1 substances.

9.0 Proposed regulatory decision

The Pest Management Regulatory Agency (PMRA) has carried out an assessment of available information in accordance with Section 9 of the Pest Control Products (PCP) Regulations and has found it sufficient, pursuant to Section 18.b, to allow a determination of the safety, merit, and value of Eco Sprout Guard TGAI and Eco Sprout Guard EP, proposed for registration by McCain Foods Ltd. The PMRA has concluded that the use of Eco Sprout Guard TGAI and Eco Sprout Guard EP in accordance with the label has merit and value consistent with Section 18.c of the PCP Regulations and does not entail an unacceptable risk of harm pursuant to Section 18.d. Therefore, based on the considerations outlined above, the use of Eco Sprout Guard TGAI and Eco Sprout Guard EP for the control of sprouting on stored “Russet Burbank” potatoes for processing is proposed for full registration, pursuant to Section 13 of the PCP Regulations.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed registration decision for this product.

List of abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
a.i.	active ingredient
ADI	acceptable daily intake
ARfD	acute reference dose
bw	body weight
CIPC	chlorpropham
d	day(s)
DNA	deoxyribonucleic acid
EEC	expected environmental concentration
EP	end-use product
EPA	U.S. Environmental Protection Agency
g	gram(s)
GC	gas chromatography
GRAS	generally recognized as safe
h	hour(s)
ha	hectare(s)
IARC	International Agency for Research on Cancer
K_{ow}	<i>n</i> -octanol/water partition coefficient
kg	kilogram(s)
kPa	kilo-Pascal(s)
L	litre(s)
LLQ	lower limit of quantitation
m	metre(s)
mL	millilitre(s)
mm	millimetre(s)
nm	nanometre(s)
nmol	nanomoles(s)
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
PMRA	Pest Management Regulatory Agency
PRDD	proposed regulatory decision document
ppm	parts per million
t	tonnes
TGAI	technical grade active ingredient
TS	test substance
TSMP	Toxic Substances Management Policy
TWA	time-weighted average
UV	ultraviolet
FL	microlitre



Regulatory Decision Document

RDD2001-07

Ethylene Eco Sprout Guard

The active ingredient ethylene, as Eco Sprout Guard TGAI, and the associated end-use product Eco Sprout Guard EP containing 2–100% ethylene in compressed gas cylinders for the control of sprouting in stored “Russet Burbank” processing potatoes, are eligible for full registration under Section 13 of the Pest Control Products Regulations.

This Decision Document outlines this stage of the Pest Management Regulatory Agency’s regulatory decision-making process concerning the use of ethylene and the end-use product Eco Sprout Guard EP for the control of sprouting in stored “Russet Burbank” processing potatoes.

(publié aussi en français)

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1.0 Introduction

This Decision Document outlines the Pest Management Regulatory Agency's (PMRA) regulatory decision-making process concerning the use of Eco Sprout Guard EP containing ethylene, for the control of sprouting in stored "Russet Burbank" processing potatoes.

2.0 Background

The PMRA carried out an assessment of available information in accordance with Section 9 of the Pest Control Products (PCP) Regulations. The assessment found that there was sufficient information, pursuant to Section 18.b, to allow a determination of the safety, merit, and value of ethylene and the end-use product Eco Sprout Guard EP marketed by McCain Foods Ltd. The PMRA concluded that the use of Eco Sprout Guard EP in accordance with the label accompanying the product has merit and value consistent with Section 18.c of the PCP Regulations and does not entail an unacceptable risk of harm under Section 18.d.

These products were proposed for registration in Proposed Regulatory Decision Document [PRDD2001-04](#). No comments were received by the PMRA concerning [PRDD2001-04](#).

3.0 Regulatory Decision

Based on the considerations outlined above, ethylene and the associated end-use product Eco Sprout Guard EP, for the control of sprouting in stored "Russet Burbank" processing potatoes, are eligible for full registration, pursuant to Section 13 of the PCP Regulations.

(参考資料) カナダにおけるエチレン登録の現状

PMRA (農薬管理規制局)による資料

2001 年10月5日

申請規則決定書(案)PRDD2001-04

エチレン(商品名 Eco Sprout Guard)

活性物質エチレン、Eco Sprout Guard TGAI および Eco Sprout Guard EP (2-100%圧縮ガスシリンダー)は、加工用貯蔵”Russet Burbank”ジャガイモの萌芽抑制に使用するために、PCP 規則の第 13 条のもとに登録が提案される。

登録申請書には、データの要約とこの製品の完全登録のための理論的根拠が示されている。PMRA(農薬管理規制局)は、この書類の提出日付から45日以内にこの提案について文書でコメントする予定である。下記に示した住所に Publications Coordinators に対して意見を期待している。

はじめに

PMRA (農薬管理規制局)は、Eco Sprout Guard TGAI (エチレン)とその商品 Eco Sprout Guard EP (Praxian 会社によって製造、McCain Foods 会社によって販売)の登録出願書を審査する。

Eco Sprout Guard EP は、2-100%圧縮ガスシリンダー状容器、加工用貯蔵ジャガイモでの萌芽抑制のための代替農薬として実験された。エチレンは、自然環境ではどこにでも存在する自然植物ホルモンである。エチレンは毒性がなく、高濃度(大気中 80-90%)では臨床用の麻酔剤として使用された歴史がある。4ppm の濃度のエチレンは、頂芽優性を抑えることによりジャガイモ塊茎の萌芽を抑制する。エチレンを処理したジャガイモのエチレンレベルとその主要代謝産物は、無処理のものと同一である。

PMRI は、PCP Regulations(害虫駆除製剤規則)の第9条の規定に従って提出案件の評価を行い、第 18.b 条によって Eco Sprout Guard TGAI (エチレン)およびその最終商品 Eco Sprout Guard EP の安全性、利点、価値について決定を下した。当局は、表示に基づいた Eco Sprout Guard TGAI (エチレン)およびその最終商品 Eco Sprout Guard の使用が、PCP 規則の第 18.c 条に合致してメリットと価値があり、第 18d 条によって危害の認容できない危険性も引き起こさないと結論した。それ故に、上記に概略した事項に基づき、Eco Sprout Guard TGAI(エチレン)およびその最終産物 Eco Sprout Guard EPの使用について、PCP 規則の第 13 条によって完全登録を提案する。

PMRAは、この商品の完全登録を取得するための提案を行っている。この製品が提案された規則決定に関係機関が加わるための機会を与えるために、PMRA は、この提出日付から45日以内に この申請書について文書によってコメントを受理する予定である。

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1 活性物質、特性および使用

1.1 活性物質の同定とそれを含む製剤

活性物質:エチレン

機能:萌芽抑制

化学名:

- 1、 国際純正応用化学連合、エチレン
- 2、 化学情報検索サービス機関 (CAS)、エチレン

CAS 番号:74-85-1

分子式:C₂H₄

分子量:28.06

構造式:CH₂=CH₂

純度:純粋エチレンガス、100%

毒性、環境、その他意味のある関連不純物の同定:製品は最大 0.1%以下の1酸化炭素を含む。毒性関連不純物は、下記に示す。(省略)

1.2 活性物質の物理化学的性質と最終用途製品

工業製品:Eco Sprout Guard TGAI

特性	結果	コメント
色と物理的状況	無色で圧縮ガス	
匂い	甘い	
融点／範囲	なし	
沸点／範囲	マイナス 103 C	
比重	0.978 (0 C) (大気=1)	
蒸気密度 (g/mL)	0.00126 (0 C)	
紫外線／可視スペクトル	波長>300nm, UV 吸収なし	光分解は可能性がない
溶解性 (20C)	わずか	
オクタノール/水分係数(<i>K</i> _{OW})	log <i>K</i> _{OW} =1.16	生物濃縮は可能性がない
解離定数	解離しない	
安定性(温度、金属)	引火点はマイナス 136 C 圧縮状態では衝撃と高温はさける;酸化物、ハロゲン、酸、塩化アルミニウムおよびハロカーボンとは不親和性である	

最終用途製品:Eco Sprout Guard EP

特性	結果
色	無色
匂い	甘い
物理的状态	ガス
製剤のタイプ	圧縮ガス
保証	2-100%, 公称
製剤	生産物はどのような EPA List 1 製剤や TSMP-1 物質として知られている製剤も含まない。
容器材料と表示	圧縮ガスシリンダー容器
酸化および還元作用	酸化物、ハロゲン、酸、塩化アルミニウムおよびハロカーボンとは不親和性である
貯蔵安定性	シリンダー状容器で貯蔵する場合は安定である。
爆発性	自然では塩素を含む日光のもとでは爆発性である。大気と酸化剤と爆発性混合の型になっている。熱を火災によって容器が破裂することがある。容器に対する衝撃を防ぐこと。

1.2 使用詳細

エチレンは成長調節剤である。ジャガイモ塊茎では、エチレンは収穫後の休眠期間を短縮させ、時に早期萌芽を生じるが、しかし頂芽優性を抑制することによって萌芽伸長を阻害する。

Eco Sprout Guard EP は、2-100%エチレンの圧縮円筒型容器に充填され、貯蔵中の加工用ジャガイモ”Russet Burbank”の使用に適用される。Eco Sprout Guard EP は、4ppm のエチレン濃度に調節できる貯蔵施設の循環換気システムに連続処理される。

2 分析方法

2.1 工場における活性物質の分析方法

活性は、2種のガスクロマトグラフィー法によって測定された。

2.2 製剤の分析方法

活性は2種のガスクロマトグラフィー法によって測定された。

3 ヒトと動物に対する影響

3.1 総合的な毒性についての要約

エチレンは、すべての植物組織から生産されるガス状の化学物質として自然に存在し、植物成長調節作用として機能する。エチレンはまたヒトおよび家畜の内生の化学物質として自然に存在し、未暴露のラットやヒトによって吐き出された大気中からも検出される。ヒトや家畜のもつ内生エチレンの発生源は、不飽和脂肪の過酸化、フリーのメチオニンの酸化、ヘモグロビンのヘミンの酸化および腸内細菌の代謝などが考えられる。ヒトでは、内生生産から生じる血液中のエチレン濃度は、約 0.097 nmol/L である。

環境条件のもとでは、エチレンはガス状である。そのためエチレンによるヒトへの汚染のルートは吸入による。高濃度のエチレン(酸素中 80-90%まで)は、臨床的な麻酔剤として使用された歴史的な経緯があるが、ほとんど合併毒性はないとされている。酸素中に 90%エチレンが含まれると、20-30 分以内に完全に麻酔がかかる。麻酔剤としてのエチレンは、吸入に安全性が高く、回復性が早いことから、エーテルより利点が多いとされている。エチレンはカナダでは、大気中に高濃度で存在すると酸素濃度を低下させるため窒息剤として分類されている。

エチレンの摂取、発散および代謝は、一時速度式によって表現することができる。体内へのエチレンの摂取は、血液中では低溶解性のために低い。ラットでは、摂取されたエチレンの 15-17%が肺胞血液に達すると算出されている。ヒトでは、21%のエチレンが肺胞血液に達する(生理的毒性カイネテックシステムを用いて)。密閉条件では、50 ppm の濃度のエチレンをヒトの体内に取り込ませると、150L/H の割合で約 5.6%のエチレンが肺胞血液中に達し、94.4%が血液システムを通じて全身に利用されずに排出される。定常状態では、ヒトで算出された肺胞保持割合は、約 2-3%である。血液中ではガス溶解性が低いいため、エチレンは敏速に排泄され、体内には蓄積されない。内部また外部から供給されたエチレンは、ラット、マウス、ヒトにおいても生体内で酸化エチレンに代謝される。健全なヒトでの実験から、吸収された約 2-3%のエチレンは酸化エチレンに代謝されるが、それに対して 98%のエチレンは変化せず放出される。またエチレンの代謝は混合機能オキシダーゼ系の誘導因子によって活性化されるというデータもある。

マウスを用いた暴露実験から、エチレンは低急性毒性であるとされている。圧縮ガスに接触すると、皮膚、目の霜、やけどなどいくつかの急性的な危険がある。Sprague-Dawley ラットを用いた摂取実験では、10000 ppm 摂取(試験中最高濃度)でも毒性の影響は認められなかった。Fischer 344 ラットを用いた慢性毒性/発がん性吸入実験では、エチレン濃度 3000 ppm(試験中の最高濃度)でも、処理区における有意な違いや発がん性の証拠は観察されなかった。重要な証拠はエチレンが遺伝毒性でないことである。ヒトと動物実験からエチレンは発がん性がないとされている。総括すると、エチレンは、ヒトに対する発がん性としては分類されていない(IARC 国際癌研究機関の分類、グループ3)。エチレンは、NTP(国家毒性プログラム)および OSHA (職業安全衛生管理局)でも発がん物質としてリストされていない。

エチレンの毒性について重要なことは、基本的にはその代謝産物、特に初期代謝産物である酸化エチレンとの関係である。酸化エチレンは直接アルキル化剤である。それは多くの生体内、生体外実験例から遺伝毒性があり、マウスやラットに発がん性があるとされている。マウス肺がん生物検定(70ppm)と標準2年間マウスとラット生物検定(100ppm 濃度)から陽性の結果を得ている。これらの実験に基づき、IARC(IRAC 分類、グループ1)とNTP(発ガン物質報告, 9版、“既知の発がん物質“)は、酸化エチレンがヒトに対して発がん性であると分類している。しかしながら、文献上では、ラットを用いた密閉容器内吸入実験、1000 および 40ppm エチレンの暴露は、それぞれ 5.6 および 1ppm の酸化エチレンに匹敵する。この暴露結果をすでに得られた酸化エチレンに対するラットガン誘因結果と加味して考えると、酸化エチレンが発がん性を示す推定値、5.6 ppm は、発ガン発生率2%を超えるレベルに至っていない。そのような低い酸化エチレン暴露(5.6ppm)から生じる酸化エチレンの身体負荷量(体内蓄積物)は、エチレンを暴露したラットにおいて発ガン性を誘因するにはあまりにも低すぎると結論された。また、文献上では、約 1000ppm のエチレン濃度は、すでにエチレンの Vmax に達している。すなわち、より高い濃度のエチレン暴露は、必ずしも高濃度の酸化エチレンへの変換を伴っていないことを意味している。文献によると、エチレンの濃度に関わらず、統計的に有意な発がん性を示す数値を得るのは困難である。生理的モデルを用いたヒト実験では、1 ppm 酸化エチレンを8時間暴露で生じる予測血液レベルは、45 ppm エチレンを8時間暴露後に生じる予測レベルと同等であることが示された。5 ppm エチレンを暴露したヒトにおけるヘモグロビン付加物レベルの測定から、吸収されたエチレンの平均 2-3%は、酸化エチレンに代謝されると算出されている。最新の基準(酸化エチレンの最新 OSHA 基準、週 40 時間就業、8 時間加重平均)によると、1 ppm の酸化エチレンは毒性的には 37 ppm のエチレン濃度と同等である。文献上、酸化エチレンの低大気濃度での長時間職業上の暴露は、その限界濃度は 1ppm (1.83 mg/m³)かそれ以下では、遺伝毒性や発がん性の危険はないとされている。

これらの事実およびエチレンの使用条件(エチレン濃度が貯蔵期間の最終まで最大 4 ppm であること)から、酸化エチレン濃度が許容できない遺伝毒性および発がん性の危険を起こすレベルに達することはあり得ないと考えられる。

文献上、エチレンの使用についてリスクアセスメントのための十分な情報がある。その情報に基づくと、エチレンは低毒性であり、低毒性麻酔剤として広く用いられていた。低レベルのエチレン暴露、エチレンの低吸収率およびエチレンの酸化エチレンへの低変換に基づいて、酸化エチレン濃度が認容できないレベル(>1.0 ppm)に達するとは考えられない。エチレンは、貯蔵ジャガイモの萌芽抑制のための植物成長調節剤としての使用条件のもとでヒトに対して無害であると結論できる。製品ラベルの表示に基づいて提案された使用条件を厳守すれば、エチレンの危険性はないと考えられる。

3.2 一日摂取許容量の決定

HPBHC(カナダ健康省、健康保護支局)発刊の”健康・安全状況報告”(1994 年5月)には、エチレンの ADI (一日摂取許容量)は要求されていない。それは、エチレンが果物やジャガイモを含む野菜類の老化とともに自然に生じるからである。エチレンはまたヒトや室内家畜において自然に生じる内生化学

物質であり、暴露していないラットやヒトの呼吸によっても放出されるため大気中からも検出される。潜在的なエチレン代謝は自然にも存在している。処理ジャガイモにおける代謝産物の分析データには、残留レベルが検出限界レベル以下または対照区とほぼ同じレベルであると示されている。

3.3 急性参照用量

エチレンが急性危険性でないことから、急性参照用量(ARfD)は算定されていない。文献では、急性食事危険評価の事項に関して有意な処理証拠はないとされている。低毒性であることそして麻酔剤として広く使用されていたことから、エチレン暴露によるヒトの潜在的危険性は無視してもよいと考えられている。

3.4 毒性エンドポイント選抜:業務従事者および第三者危険評価

暴露の一次的ルートは吸入である。エチレンは吸入ルートを通して低急性毒性である。エチレンは単純な麻酔剤と考えられている。文献上から、Sprague-Dawley ラットを用いた亜慢性吸入実験では 10000 ppm(試験中最高量)でも毒性効果はみられなかった。Fischer 344 ラットを用いた毒性/発ガン性吸入実験では、処理区に有意な結果は見られず、また 3000 ppm の濃度(試験中最高濃度)でも発がん性の証拠はみられなかった。圧縮ガスとしてエチレンに接触すると皮膚と目にやけどを起こすことがあり、可燃性による危険性がある。このタイプの暴露の可能性は表示(注意事項)を厳守することによって軽減することができる。このような表示はこの活性成分の最も適切な規制アプローチと考えられ、エチレン使用上の暴露と危険性の質的評価が実施されている。

3.5 活性物質またはその不純物暴露によるヒトと動物の健康に対する影響

3.5.1 オペレーターの暴露評価

貯蔵ジャガイモへの適用

Eco Sprout Guard は、種々の濃度(2から 100%)の圧縮エチレンガスからなり、シリンダー容器に充填されている。窒素ガスを補充することでバランスをとっている。Eco Sprout Guard は、ジャガイモ貯蔵施設の空調システムで貯蔵期間中 4 ppm の濃度でエチレンガスを放出することによって効果が得られる。最もよい結果を得るためには、ジャガイモを収穫後1-7日で処理を開始し、加工前1-7日まで処理を継続することである。貯蔵業務従事者は、規定のガス濃度を示す濃縮エチレンガス容器を管理しなければならない。貯蔵施設内のガス濃度は注入速度とエチレン濃度(%)によって決定される。貯蔵建物内のエチレン濃度はモニターされ、継続的に遠方からでも貯蔵期間を通して目標レベルに近い値であることを確認しなければならない。一般的には、エチレンガス注入システムは、建物内で空調条件に応じてバルブを操作するためのプログラム制御法を用いている。システム自身は自動的に組み込まれているが、パラメーターの設定、容器の連結と取り外し、使用済み容器やシステムの欠陥箇所の取り替えの場合には人の介入が必要である。

オペレーターへの暴露

作業従事者へのエチレンの暴露は、エチレン処理中に貯蔵建物に入室時、循環ダクト工事中(例え

ば修理のため)あるいはベンチレーションの排出口の近くにいる時におこる可能性がある。暴露の基本的ルートは吸入である。

エチレンは、植物と動物によって作られる自然発生ガス状化学物質である。ほとんど付随毒性なしに麻酔剤(麻酔剤は酸素中 80-90%のエチレンを暴露することで使用される)として使用された長い歴史がある。一般に米国では安全性であることの確認(GRAS)がなされている。ACGIH(米国産業衛生専門家会議)では、エチレンの暴露限界は示されていない。ACGIH はエチレンを“単純な窒息剤”として分類している。単純な窒息剤使用の場合、緊急時または未知の濃度の施設に意図的に入室する場合または酸素欠乏の場所を除いて、呼吸保護は必要とされていない。文献上、亜急性吸入毒性実験では、Sprague-Dawley ラットで 10000 ppm(試験中最高量)まで、毒性効果はみられなかった。ラットを用いた2年間の長期吸入実験でも 3000 ppm(1 日6時間、週5日間)の暴露で影響がないことが示された。このことから、指定された条件で用いる場合、吸入によってエチレンに暴露された従事者の危険性の可能性は無視できると結論される。

高濃度のエチレンの暴露は、密閉施設でリークしたときに生じる可能性がある。予防説明書には、ガス容器の適切な取り扱いとリークを防ぐためのガス放出システムについて示されている。同じように登録者は使用者に対して、エチレンガスの放出と監視を代行する設備についての情報を提供している。未知の濃度のエチレンガス使用施設に入室する場合、呼吸保護は図面表示に従うことが大切である。これらの予備説明は適切であると考えている。

圧縮ガス容器の取り扱いや圧力のかかった設備では、その可燃性による危険性、液体ガスによる急性皮膚または目への暴露の可能性(皮膚や目に接触した場合にやけどを起こす)が示されている。この危険性は適切な保護設備の使用によって適切に軽減することができる。長めのスリーブ、長めのズボン、ゴーグルまたはフェイス・シールド、適切なグローブの着用を勧める。

3.5.2 第三者

Eco Sprout Guard の適切な使用形態に特性から第三者への暴露の可能性は無視できる。

3.5.3 作業員

作業員は、ベンチレーションが終了する前にエチレン処理中または処理後に貯蔵場所(例えば点検のため)に入ることができる(3.5.1を参照)

4 残留

本申請では、残留についてのデータは提出されていない。しかし、ジャガイモ萌芽抑制剤としてエチレンを登録するためにすでにデータが提出されている。その情報は 1994 年5月にエチレンのための“健康・安全状況報告”の中のカナダ健康省健康保護支局によって要約されている。この報告から抜粋した情報をこの章に記載する。

エチレンの代謝作用は、ジャガイモでは特別に調べられていないが、多くの植物で調べられているエチレン代謝および代謝経路と類似しているかほとんど同じである。老化組織としてのジャガイモ塊茎では、エチレンはもしあったとしても非常にゆっくり代謝されるため、基本的には低いエチレン代謝速度である。内生濃度は、未萌芽塊茎で 0.0007-0.15 ppm、萌芽塊茎で 0.1-3ppm の範囲である。エチレンが低浸透性であることを加味すると貯蔵塊茎中のエチレン代謝は低濃度であると予想される。

エチレンとその可能な代謝産物について、処理ジャガイモと対照の無処理のジャガイモの間には検出レベルに有意な差はみられない。それ故に評価として動物代謝と家畜の飼料の研究は必要がないと考えられる。

4 ppm のエチレンを 150 日間処理したジャガイモについてエチレン残留のデータがある。クロロエタノール、ジクロロエタン、ブromoエタノール、酸化エチレンおよびエチレングリコール(そのグルコサイドを含む)の残留は全体で 0.1 ppm 以下であった。最も毒性の高い代謝産物、酸化エチレンの残留は 2 ppm 以下であった。さらに、揮発性の残留物(酸化エチレン)は塊茎の加工や調理の過程で 90%まで低下すると予想される。この残留の散逸は、加工中のジャガイモ組織の拡散と調理中の加熱による揮発によって生じる。

ジャガイモ塊茎組織内のエチレンの分配係数は非常に低い(0.207)、このことは、もし代謝しているとしてもジャガイモ塊茎における ^{14}C -エチレンの 区別がほとんどできないことを示している。一般に土壌中には約 10 ppm レベルの内生エチレンを含む、そのレベルは土壌の湿度が高くなるにつれて増加する。代謝的に活性のある発達中のジャガイモ塊茎では、エチレン残留を代謝して生物濃縮すると予想される。1993 年と 1994 年の実験で処理したジャガイモ塊茎の成熟塊茎について調べられたエチレン代謝産物の残留は LLQ 以上には至らなかった。

ジャガイモ塊茎内ではエチレンの不浸透性が証明されている。ジャガイモ塊茎は拡散に対して高い抵抗性をもつ。それは塊茎の表皮がガス状物質の拡散のバリアーになることと塊茎全体の約2%を占める非常に小さな組織を通して拡散されるためである。この状態が塊茎内における外生エチレンの移行を効率的にブロックしている(濃度こう配に対しても)。それによって塊茎内のエチレンの内部濃度は内生レベルで維持されている。

エチレンを処理したジャガイモについて加工実験は行われていない。しかしながら、処理した塊茎をフレンチフライ、パウダーポテト、ポテトフラワーまたは生のジャガイモ料理に加工すると、最も注目される酸化エチレンの残留がもしバックグラウンド以上のレベルにあったとしても非常に減少する。酸化エチレンは室温ではガスであり、12C 以下では液体である。調理中にジャガイモから蒸発されることが考えられる。

提出データによると、常法によって処理されたジャガイモでは、エチレンまたその主要な代謝物は無処

理レベル以上には残留しない。それ故に、食物としての危険評価の必要性がなく、MRL は提案されていない。

5 環境における運命と性質

5.1 環境に関係のある物理化学的性質

エチレンの物理化学的性質は表 5.1(省略)に要約する。LSS とその他の種々のソースから集めた情報によって行われたレビューに基づいている。活性成分は 98.5%以上である。

環境化学と運命実験の要約

エチレンの環境運命についてのデータは、このガスは自然に存在するため、要求されていない。

予想される環境濃度

貯蔵でのエチレンの使用は大気中におけるエチレンの EEC(予想される環境濃度)に影響をあたえる。しかし、使用場所から大気濃度へのエチレンの貢献は無視してもよいと考えられる。

自然および人為的に発生されるエチレンガスの 89%は、対流圏では OH-ラディカルによって分解され、8%はオゾンと反応して破壊される。約3%は成層圏に運ばれる。大気中に放出されたエチレンの寿命は約2-4日である。

6 非標的種に対する影響

(省略)

7 有効性

(省略)

8 毒性物質管理方針

(省略)

9 提案された規則決定 (PRD)

(省略)