Proposed Registration Decision PRD2013-12

# 3-decen-2-one

*(publié aussi en français)*

**24 May 2013**

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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ISSN: 1925-0878 (print)
1925-0886 (online)

Catalogue number: H113-9/2013-12E (print version)
H113-9/2013-12E-PDF (PDF version)

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# Overview

## Proposed Registration Decision for 3-decen-2-one.

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of AMV-1018 Technical and AMV-1018 (98% Liquid Concentrate) for use on potatoes in storage to control sprouting once the dormancy period has ended.

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 AMV-1018 Technical and AMV-1018 (98% Liquid Concentrate).

## 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.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at healthcanada.gc.ca/pmra.

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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."

Before making a final registration decision on 3-decen-2-one, 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 3-decen-2-one, 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.

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

## What is 3-decen-2-one?

3-decen-2-one is a plant growth regulator that belongs to the chemical family of the alpha-beta unsaturated aliphatic ketones. AMV-1018 (98% Liquid Concentrate), containing 98% 3-decen-2-one, is applied as an aerosol to potatoes in storage once there is evidence of sprouting. While the mode of action is not fully understood, 3-decen-2-one acts to damage or destroy the meristematic tissue of sprouts and actively growing terminal and axillary buds.

## Health Considerations

- **Can Approved Uses of 3-decen-2-one Affect Human Health?**

**3-decen-2-one is unlikely to affect human health when it is used according to label directions.**

Exposure to 3-decen-2-one may occur when handling the end-use product, AMV-1018 (98% Liquid Concentrate), which has a proposed commercial use as a sprout inhibitor for potatoes in commercial storage. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

The technical grade active ingredient, 3-decen-2-one, is of low acute toxicity by the oral and dermal routes, and is slightly acutely toxic by the inhalation route. It is mildly irritating to the eyes, severely irritating to the skin, and is not a dermal sensitizer. It is considered to be non-mutagenic, and not a reproductive toxicant. Cautionary statements alerting users to the potential for respiratory toxicity and eye and skin irritation are required on product labels.

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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*.

Dermal and inhalation exposure is possible for workers handling the end-use product, AMV-1018 (98% Liquid Concentrate), and for workers engaged in post-application clean-up and maintenance activities. Therefore, personal protective equipment and other risk-reduction measures are required on the end-use product label to mitigate such exposure concerns. Entry will not be allowed into treated areas prior to complete ventilation of the potato storage facility. The potential for bystander exposure is expected to be minimal as non-workers are prohibited from entering potato storage facilities during treatment.

Waivers and additional information obtained from the public domain were deemed adequate to address the potential for short-term toxicity.

- **Residues in Water and Food**

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

3-decen-2-one is used as an additive to flavour certain foods and it also occurs naturally in certain foods. The end-use product, AMV-1018 (98% Liquid Concentrate), will be applied as a fog directly to potatoes; however, food residue exposure is not expected to be of concern as exposure estimates indicate that use of AMV-1018 (98% Liquid Concentrate) will not appreciably increase the dietary exposure to 3-decen-2-one above what is currently expected from its presence in food. In addition, as the end-use product is to be applied inside a closed potato storage facility, exposure to 3-decen-2-one in drinking water is not expected to occur. The PMRA has also determined that a maximum residue limit (MRL) is not required for 3-decen-2-one.

- **Occupational Risks From Handling AMV-1018 (98% Liquid Concentrate)**

**Occupational risks are not of concern when AMV-1018 (98% Liquid Concentrate) is used according to label directions, which include protective measures.**

Occupational exposure to individuals handling AMV-1018 (98% Liquid Concentrate) is not expected to result in unacceptable risk when the product is used according to label directions.

Precautionary and hygiene statements on the label (for example, wearing of personal protective equipment (PPE)) are considered adequate to protect individuals from any unnecessary risk due to occupational exposure.

## Environmental Considerations

- **What Happens When 3-decen-2-one Is Introduced Into the Environment?**

3-decen-2-one is a chemical substance that occurs naturally in some food and is currently used as a flavouring agent in food industry. 3-decen-2-one is highly volatile and has a high solubility in water. It is expected to degrade rapidly in the environment through photochemical reactions (with hydroxyl radicals) or microbial activity. Environmental exposure from the indoor use of this product is expected to be limited.

There is no concern about inhalation risk to wild birds nesting or roosting in the vicinity of storage facilities. No or very limited exposure of aquatic ecosystem is expected.

## Value Considerations

- **What Is the Value of AMV-1018 (98% Liquid Concentrate)?**

AMV-1018 (98% Liquid Concentrate) is applied to potatoes in storage to control sprouting once the dormancy period has ended thereby extending the storage period. AMV-1018 (98% Liquid Concentrate) is an alternative option with a different mode of action to products containing chlorpropham (CIPC), which are commonly used to extend the dormancy period of potatoes thereby delaying sprouting. The active ingredient, 3-decen-2-one, is classified as a biopesticide by the U.S. EPA and is acceptable for use by the U.S. FDA as a food additive (flavouring agent), and has a GRAS designation.

## 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 AMV-1018 (98% Liquid Concentraye) to address the potential risks identified in this assessment are as follows.

### Key Risk-Reduction Measures

### Human Health

The signal words “CAUTION – POISON, EYE IRRITANT”, and “DANGER – SKIN IRRITANT” are required on the principal display panels of both the technical and end-use product labels. The statements “Harmful if inhaled”, “May irritate eyes”, and “Severely irritating to skin” are required on the secondary display panel of the technical and end-use product labels.

The personal protective equipment for all loading, handling, clean-up and maintenance activities required on the end-use product label includes a long-sleeved shirt, long pants, shoes, socks,

respirator with a NIOSH/MSHA approved organic vapour-removing cartridge with a pre-filter approved for pesticides, goggles, and chemical resistant gloves. Storage areas must be ventilated for at least 24 hours or until ventilation is complete before allowing workers to enter for normal activities. If entering storage area before full ventilation, workers must wear coveralls over long-sleeved shirt, long pants, shoes, socks, chemical resistant gloves, and a self-contained breathing apparatus or full-face respirator with a NIOSH/MSHA approved organic vapour-removing cartridge with a pre-filter approved for pesticides.

## Next Steps

Before making a final registration decision on 3-decen-2-one, 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

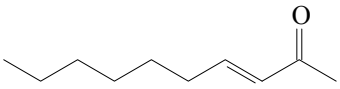
When the PMRA makes its registration decision, it will publish a Registration Decision on 3-decen-2-one (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

# Science Evaluation

## 3-decen-2-one

## 1.0 The Active Ingredient, Its Properties and Uses

### 1.1 Identity of the Active Ingredient

| | |
|---|---|
| **Active substance** | |
| **Function** | |
| **Chemical name** | |
| **1. International Union of Pure and Applied Chemistry (IUPAC)** | 3-decen-2-one |
| **2. Chemical Abstracts Service (CAS)** | 3-decen-2-one |
| **CAS number** | 10519-33-2 |
| **Molecular formula** | $C_{10}H_{18}O$ |
| **Molecular weight** | 154.25 |
| **Structural formula** |  |
| **Purity of the active ingredient** | 98% |

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

### Technical Product—AMV-1018 Technical

| Property | Result |
|---|---|
| Colour and physical state | Colourless to pale yellow liquid |
| Odour | Pleasant |
| Melting range | N/A |
| Boiling point or range | 224.0°C |
| Density | 0.845 g/mL |
| Vapour pressure at 25°C | 430 Pa |
| Ultraviolet (UV)-visible spectrum | pH $\lambda_{max}$ (nm) ε (L/mol*cm)<br>Neutral 229.0 14408.1<br>Acidic 229.0 16464.7<br>Alkaline 229.0 9330.6 |
| Solubility in water at 24°C | 0.140 g/L |
| Solubility in organic solvents at 20°C (g/100 mL) | Soluble in methanol, ethanol and acetone. |
| *n*-Octanol-water partition coefficient ($K_{OW}$) | log $K_{ow}$ = 3.45 |
| Dissociation constant (p$K_a$) | N/A |
| Stability (temperature, metal) | A significant decrease in the concentration of the active ingredient was observed at elevated temperatures (54°C) for the untreated test substance and in presence of metals and metal ions. A decrease of concentration was also observed at ambient temperature for the samples treated with iron acetate. |

### End-Use Product—AMV-1018 (98% Liquid Concentrate)

| Property | Result |
|---|---|
| Colour | Colourless to pale yellow |
| Odour | Pleasant |
| Physical state | Liquid |
| Formulation type | Liquid |
| Guarantee | 98% |
| Container material and description | Plastic 946 mL – 208 L, bottles, barrels or totes |
| Density | 0.845 g/mL |
| pH of 1% dispersion in water | 4.33 |

| | |
|---|---|
| Oxidizing or reducing action | N/A |
| Storage stability | Stable when stored for 12 months at ambient temperature in commercial packaging |
| Corrosion characteristics | No corrosion of the storage container was observed. |
| Explodability | Not explosive |

## 1.3 Directions for Use

AMV-1018 (98% Liquid Concentrate) is a plant growth regulator applied to potatoes (except seed potatoes) in storage to control sprouting. AMV-1018 (98% Liquid Concentrate) is applied at 137.5 ml/tonne (115 g a.i./tonne) of potatoes and up to four applications may be made to any one lot of potatoes for example, cumulative maximum of 550 ml/tonne potatoes. The use pattern is summarized in Table 1.3.1.

**Table 1.3.1 Use Pattern for AMV-1018 (98% Liquid Concentrate)**

| Rate | Application Details/Timing |
|---|---|
| 115 g a.i./tonne | Application by means of standard aerosol (fogging) equipment.<br>Application is made when ~75% of tubers show visible signs of sprouting or 'peeping' and may be reapplied when tubers show visible signs of resprouting, normally 1 to 3 months after initial or previous application, depending on potato cultivar and storage conditions (for example, temperature).<br>May also be applied as a "rescue" treatment when potatoes in storage have developed sprouts of up to 2.5 cm in length.<br>May also be applied to potatoes undergoing reconditioning or prior to packaging and shipment (when sprouts are up to 2.5 cm in length).<br>Immediately prior to commencing application, the ventilation system must be closed and the recirculation system operated for a minimum of 24 hours to recirculate the aerosolized product throughout the potato storage unit.<br>A maximum of four applications may be made to any one lot of potatoes. |

## 1.4 Mode of Action

3-decen-2-one is a plant growth regulator which belongs to the class of alpha-beta unsaturated aliphatic ketones and that while the mode of action is not fully understood, it appears that shortly following application of AMV-1018 (98% Liquid Concentrate), the meristematic tissue of sprouts and terminal and axillary buds, also known as "peeps", is damaged or destroyed, such that they have a burnt appearance.

# 2.0 Methods of Analysis

## 2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in AMV-1018 Technical have been assessed to be acceptable for the determinations.

## 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.

# 3.0 Impact on Human and Animal Health

## 3.1 Toxicology Summary

A detailed review of the toxicological database for 3-decen-2-one consisting of toxicity studies and waiver rationales was conducted. The scientific quality of the data is acceptable and the database is sufficiently complete to define the majority of the toxic effects that may result from exposure resulting from the intended use of this pest control product.

The applicant submitted acute toxicity (oral, dermal and inhalation), irritation (ocular and dermal), sensitization, mutagenicity, and prenatal developmental toxicity studies on 3-decen-2-one. Although the PMRA requires toxicity and irritation studies to be conducted with both the technical grade active ingredient and the end-use product, given that the end-use product is a repack of the technical grade active ingredient, and contains no formulants of toxicological concern, no testing with the end-use product was required to support registration.

3-decen-2-one was of low acute toxicity by the oral and dermal routes in rats, and slightly acutely toxic by the inhalation route. It was mildly irritating to the eyes and severely irritating to the skin of rabbits, and did not induce sensitization in guinea pigs in a Buehler test. 3-decen-2-one was considered to be non-mutagenic in a bacterial reverse mutation assay and in a mouse erythrocyte micronucleus test.

Information from the published literature was provided and accepted as a data waiver rationale to address the short-term oral toxicity of 3-decen-2-one. A weight of evidence approach was used to estimate the likelihood of potential toxicity from repeated short-term oral exposure to 3-decen-2-one based on available toxicological and metabolism data for 3-decen-2-one, combined with its natural occurrence and use as a food additive in certain foods and exposure estimates from the use of the end-use product.

A data waiver rationale was also submitted and accepted for the short-term inhalation toxicity of 3-decen-2-one, based on the fact that workers do not typically enter the storage facility during potato treatment; 3-decen-2-one is rapidly removed from the storage facility after treatment; 3-decen-2-one released from the storage facility vents will be diluted and quickly dissipate in outdoor air; and repeated inhalation exposure to significant levels of the end-use product is not expected based on the proposed use pattern.

A prenatal developmental toxicity study was submitted for 3-decen-2-one, in which the test substance was administered to 24 female Crl:CD (SD) rats by gavage at dose levels of 0, 100, 300, or 1000 mg/kg bw/day from days six through 19 of gestation. There were no treatment-related effects on maternal mortality or caesarean parameters. Lower food consumption, lower bodyweight gain, and excessive salivation in the high dose group were attributed to potential gastric irritation from the test substance. Consequently, the maternal LOAEL is > 1000 mg/kg bw/day, and the maternal NOAEL is 1000 mg/kg bw/day. There were no treatment-related effects in developmental parameters. The developmental LOAEL in this study is > 1000 mg/kg bw/day and the developmental NOAEL is 1000 mg/kg bw/day.

## 3.2 Food Residue Exposure Assessment

### 3.2.1. Food and Drinking Water

Dietary exposure to 3-decen-2-one may occur through consumption of treated potatoes, however it is not expected to be of concern. Available toxicology data indicates that 3-decen-2-one is of low acute oral toxicity, unlikely to be toxic via repeated oral exposure, and is not a developmental toxicant or a mutagenic substance. Metabolism data suggests that 3-decen-2-one will be converted to innocuous compounds such as its corresponding alcohol, which can then be conjugated with glucuronic acid and excreted. In addition, humans are already exposed to the compound in food as an additive to flavour certain foods such as baked goods, gelatins and puddings, candy, alcoholic and non-alcoholic beverages, and it also occurs naturally in certain foods including skipjack tuna, yogurt, and porcini mushrooms.

Residue studies provided by the applicant demonstrated that residues in potato tissue declined throughout the study period following application. It is also expected that residues of 3-decen-2-one and its metabolites will further decrease in potato tissue as a result of washing, peeling, and cooking. An additional study provided by the applicant measured residues of 3-decen-2-one on potatoes that were subsequently steamed or baked, which showed that residues were reduced when potatoes were cooked. Furthermore, exposure estimates using residue data provided by the applicant indicate that food residue exposure to 3-decen-2-one from consumption of treated potatoes will not appreciably increase the dietary exposure to 3-decen-2-one above what is currently expected from its presence in food.

In addition, as the end-use product is to be applied inside a closed potato storage facility, exposure to 3-decen-2-one in drinking water is not expected to occur. Therefore, the use of AMV-1018 (98% Liquid Concentrate) is not expected to result in unacceptable dietary risks when the product is used according to label instructions.

### 3.2.2 Maximum Residue Limits (MRLs)

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine that the consumption of the maximum amount of residues that are expected to remain on food products when a pesticide is used according to label directions will not be a concern to human health. This maximum amount of residues expected is then legally established as a maximum residue limit (MRL) under the *Pest Control Products Act* (PCPA) for the purposes of adulteration provision of the *Food and Drugs Act* (FDA). Health Canada sets science-based MRLs to ensure the food Canadians eat is safe.

As the proposed use of AMV-1018 (98% Liquid Concentrate) at the maximum application rate as a sprout inhibitor on stored potatoes is not expected to appreciably increase the dietary exposure to 3-decen-2-one above the levels which are currently expected from its presence in food, the PMRA has not required the establishment of a maximum residue limit (MRL) for 3-decen-2-one.

## 3.3 Occupational and Bystander Risk Assessment

### 3.3.1 Use Description/Exposure Scenario

The proposed commercial use of AMV-1018 (98% Liquid Concentrate) is as a sprout inhibitor for potatoes in commercial storage facilities. The product is to be applied through standard fogging equipment (thermal or cold) in a closed potato warehouse, and is pumped from the container to the fogger through a hose that is attached to the product container. The product is introduced into the warehouse by inserting the dispenser end of the fogger through a port into the plenum (passageway that contains openings into the ventilation ducts that run along the floor perpendicular to the plenum and under the stored potatoes) or the air mixing chamber of the facility. The fog is then introduced into the storage area by way of the ducts and allowed to rise through the piles of potatoes. Once all of the product is introduced, the ventilation system will re-circulate the air in the closed warehouse for 24 hours. Personnel will remain outside of the warehouse during application. Following the 24 hour re-circulation of product inside the warehouse, the ventilation louvers will be opened and the total volume of air would be evacuated within minutes.

The rate of application for AMV-1018 (98% Liquid Concentrate) is 137.5 mL (115 g a.i.) per 1000 kg of potatoes. The rate of application should not exceed a total of 550 mL (460 g a.i.) per 1000 kg of potatoes per storage season, which would equate to four applications of the product.

### 3.3.2 Mixer, Loader and Applicator Exposure and Risk Assessment

Occupational exposure to 3-decen-2-one in AMV-1018 (98% Liquid Concentrate) is expected to be mainly by the dermal and inhalation routes which is possible during handling and clean-up activities. Since no mixing is required, there is no potential occupational exposure from this activity. Personal protective equipment that will be required on the label include a long-sleeved shirt, long pants, shoes, socks, respirator with a NIOSH/MSHA approved organic vapour removing cartridge with a prefilter approved for pesticides, goggles, and chemical resistant gloves, as 3-decen-2-one is severely irritating to the skin and slightly acutely toxic by the inhalation route. Occupational exposure is not expected during application of AMV-1018 (98% Liquid Concentrate) as workers will not be present in the warehouse once the end-use product is introduced into the closed system. Should entry or re-entry into treated areas during application and prior to thorough ventilation be necessary in an emergency situation only, workers must wear coveralls over a long-sleeved shirt, long pants, shoes, socks, chemical resistant gloves, and a self-contained breathing apparatus or full-face respirator with a NIOSH/MSHA approved organic vapour removing cartridge with a prefilter approved for pesticides. Other precautionary statements on the label will require the user to avoid contact with skin, eyes or clothing, to avoid inhaling vapours or fog, and to wash hands thoroughly with soap and water after handling.

Consequently, when label directions are followed, significant risk from exposure to AMV-1018 (98% Liquid Concentrate) for workers during loading, application, clean-up and maintenance activities is not anticipated.

### 3.3.3 Bystander Exposure and Risk Assessment

Bystander exposure is expected to be negligible as the commercial application of AMV-1018 (98% Liquid Concentrate) is expected to involve authorized personnel only, and potato warehouses are typically located where bystanders cannot accidentally enter. The product is to be applied by professional applicators, and the storage facilities are to be closed and sealed from all entry during application, with warning signs posted on the doors indicating that entry is not permitted during treatment. In addition, when the product is vented from the warehouse after fogging application and recirculation of air, it will be diluted in the outdoor air. The potential for bystander exposure is therefore expected to be minimal.

### 3.3.4 Post-Application Exposure

Post-application activities are limited to handling and shipping the treated potatoes, which would occur after normal ventilation has been resumed in the warehouse, at which time the end-use product would have been vented out of the warehouse, and fresh air would fill the warehouse. Therefore, inhalation exposure would not be a concern at this time.

Although the air containing AMV-1018 (98% Liquid Concentrate) will begin to be evacuated within minutes of opening the ventilation louvers following the fogging application, label directions will state that the treated area must be ventilated for at least 24 hours or until ventilation is complete (a minimum of 5 air exchanges for facilities that are equipped with an air

exchange system), before allowing workers to enter for normal activities to prevent the possibility of exposure to higher levels of 3-decen-2-one.

### 3.3.5 Incident Reports Related to Human and Animal Health

Since April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the Health Canada website. As 3-decen-2-one is not registered for pesticidal use in Canada, there are no incidents reported. Incidents from the United States were searched and reviewed for products containing 3-decen-2-one for use as pesticides. As of October 27, 2011, there were no health-related incident reports reported by the U.S. EPA or the California Department of Pesticide Regulation (CalDPR) for end-use products containing this active ingredient.

## 4.0 Impact on the Environment

### 4.1 Fate and Behaviour in the Environment

As per *PRO2010-06, Guidelines for the Registration of Low-Risk Biochemicals and Other Non-Conventional Pesticides,* no environmental fate data are required for 3-decen-2-one (TGAI and end-use product). 3-decen-2-one is an organic volatile compound that occurs naturally in food such as porcini mushrooms. In the terrestrial environment, 3-decen-2-one is expected to volatilize from dry, wet or moist surfaces. When applied to potatoes, 3-decen-2-one is expected to be gradually metabolized in the presence of potatoes. After dissipation into the atmosphere, 3-decen-2-one is expected to be degraded through photochemical reactions with hydroxyl (OH) radicals with half-lives of 1.9 – 2.2 hours. Accumulation of 3-decen-2-one in soil is unlikely due to its rapid microbial degradation. Based on the use pattern, no or very limited exposure of aquatic ecosystem is expected.

### 4.2 Risks to Non-Target Species

As per *DIR2012-01, Guidelines for the Registration of Non-Conventional Pest Control Products,* no toxicity data are required under Tier I for indoor use (storage facility). Use of the end use product AMV-1018 (98.0% Liquid Concentrate) on storage potatoes at the maximum application at rate of 137.5 ml product/tonne of potatoes, is not expected to result in any significant inhalation exposure of wild birds nesting or roosting in the vicinity of storage facilities. The degradation of 3-decen-2-one inside the storage room during treatment and the absorption of some product by potatoes are expected to lessen the amount of substance that is released when the enclosed storage facilities are opened or vented. Furthermore, dilution in the air once venting occurs will be rapid. Thus, negligible risk to birds is expected. Given the use pattern, no or very limited exposure of aquatic ecosystem is expected; therefore an aquatic risk assessment was not conducted.

# 5.0 Value

## 5.1 Effectiveness Against Pests

### 5.1.1 Acceptable Efficacy Claims

The efficacy of AMV-1018 (98% Liquid Concentrate) applied non-thermally was evaluated in five studies. In these trials, AMV-1018 (98% Liquid Concentrate) was applied to filter paper in 3.9 L glass jars (that would contain several tubers) or to filter paper in 190 L plastic barrels (that would contain about 33 kg of tubers), fitted with a fan at the bottom to distribute the vapour containing 3-decen-2-one. Containers were then sealed for 24 or 48 hours.

The efficacy of AMV-1018 (98% Liquid Concentrate) applied thermally was evaluated in five studies. In these trials, thermal fogger application devices and contraptions were used to vaporize the product at 160 to 180$^{o}$C. In one of these studies, a Swingfog thermal fogger was used for product application to half-tonne samples of tubers in a sealed shipping container. In the remaining trials that were conducted in Idaho, application apparatuses that were fitted with a hot plate or a cook top with element as the heat source were used to vaporize the product prior to delivery to enclosed treatment boxes containing tuber samples in mesh bags.

The data generated in these trials collectively support the claims and use directions in Table 5.1.1.

**Table 5.1.1. Summary of use pattern and efficacy claims for AMV-1018 (98% Liquid Concentrate)**

| Rate | Timings | Use Directions | Claims |
|---|---|---|---|
| 115 g a.i./tonne (137.5 ml/tonne) potatoes;<br><br>Maximum storage season rate per any one lot of potatoes: 460 g a.i./tonne (550 ml/tonne) for a maximum of 4 applications of 115 g a.i./tonne. | - First application when ~75% of tubers show visible signs of 'peeping' and reapplied when tubers show visible signs of resprouting;<br>- Applied as a rescue treatment when potatoes in storage have developed sprouts of up to 2.5 cm in length;<br>- Applied to potatoes in storage undergoing reconditioning or prior to packaging and shipment (when sprouts are up to 2.5 cm in length). | - Application by standard aerosol generating (fogging) equipment.<br>- Recirculation of for a minimum of 24 hours to continuously recirculate the fog before ventilation with outside air. | - Control of sprouting for 1-3 months per application, with duration of control being dependant on cultivar and storage conditions. (for example, temperature)<br>- Damages or destroys growing eye or sprout meristems tissue, visibly apparent as necrosis or blackening of same in 3-5 days following application. |

### 5.1.2 Combinations with other Pest Control Products

The submitted information indicates that AMV-1018 (98% Liquid Concentrate) is compatible for use with other products that are registered for the inhibition of sprouting in stored potatoes provided that potatoes are showing signs of sprouting or have developed sprouts at the time AMV-1018 (98% Liquid Concentrate) is applied. These other products may be applied in sequence with AMV-1018 (98% Liquid Concentrate) and for products containing chlorpropham (CIPC) or ethylene gas, may be co-injected into the fogging equipment with AMV-1018 (98% Liquid Concentrate).

## 5.2 Adverse Effects to Target Plant Products

In five studies, four in which AMV-1018 (98% Liquid Concentrate) was applied thermally and one in which it was applied non-thermally, one or more of the following non-safety adverse effects parameters was assessed: reducing sugars (% glucose and sucrose), fry quality characteristics (bud and stem end reflectance, sugar ends, off colour, mottling), and taste characteristics of baked potatoes, including colour, flavour and texture.

AMV-1018 (98% Liquid Concentrate) applied at the rate of 115 g a.i./tonne potatoes did not affect potato quality, assessed as reducing sugar concentrations, fry quality or taste characteristics of baked potatoes. Furthermore, there was no evidence for any increased incidence of physiological disorders. A strong spearmint-like odour may emanate from the treated potatoes shortly after treatment, but dissipates quickly.

## 5.3 Impact on succeeding Crops

Not Applicable.

## 5.4 Economics

No market analysis was done for this submission.

## 5.5 Sustainability

### 5.5.1 Survey of Alternatives

<u>Nonchemical control practices</u>

Potatoes may be stored at low temperatures to maintain dormancy and delay sprouting, with the ideal storage temperature being dependant on crop condition, cultivar and intended use (for example, table stock versus processing, such as for fries).

Chemical control practices

Plant growth regulator products containing chlorpropham (CIPC), ethylene or 1,4-dimethylnaphthalene are currently registered for use on potatoes in storage for sprout inhibition. Products containing maleic hydrazide are registered for pre-harvest use to inhibit sprouting in storage.

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

Under ideal storage conditions tubers can be stored up to 10 months. Ideal storage conditions include maintaining appropriate temperatures, maintaining a high relative humidity, providing oxygen for respiration and removing carbon dioxide. The use of AMV-1018 (98% Liquid Concentrate) is compatible with such practices as well as with registered potato sprout inhibitors used in potato storage management. For example, products containing CIPC can be used early in the storage season to extend the dormancy period followed by application of AMV-1018 (98% Liquid Concentrate) once the CIPC-treated potatoes emerge from dormancy and show signs of sprouting. This will burn the 'peeping' sprouts thereby extending the storage period, and may result in lower CIPC residues as compared to where a second CIPC application had been made.

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

Potatoes are unlikely to develop resistance to 3-decen-2-one as this active ingredient acts to damage or destroy the cell structure of sprouts or exposed actively growing terminal and axillary buds; it does not target a specific metabolic pathway or enzyme.

### 5.5.4 Contribution to Risk Reduction and Sustainability

AMV-1018 (98% Liquid Concentrate) is an alternative product with a different mode of action to the commonly used CIPC to combat the sprouting of potatoes in storage. The active ingredient, 3-decen-2-one, is classified as a biopesticide by the U.S. EPA and is acceptable for use by the U.S. FDA as a food additive (flavouring agent), and has a GRAS designation.

## 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*].

AMV-1018 Technical and AMV-1018 (98% Liquid Concentrate) were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5]:

- 3-decen-2-one does not meet the Track 1 criteria as the active ingredient is not highly toxic, is not expected to form any transformation products that are Track 1 substances and is not expected to be persistent in the environment or to bioaccumulate.

- There are also no formulants, contaminants or impurities present in the end-use product AMV-1018 (98% Liquid Concentrate) that would meet the TSMP Track 1 criteria.

## 6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the EP 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:

- AMV-1018 Technical and AMV-1018 (98% Liquid Concentrate) 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 DIR2006-02.

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5 Regulatory Directive 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/2005-11-30) 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 I 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 Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*

8 Regulatory Directive DIR2006-02, *PMRA Formulants Policy*

# 7.0 Summary

## 7.1 Human Health and Safety

The available information for 3-decen-2-one is adequate to qualitatively identify the toxicological hazards that may result from human exposure to 3-decen-2-one. 3-decen-2-one is of low acute toxicity by the oral and dermal routes, and is slightly acutely toxic by the inhalation route. It is mildly irritating to the eyes, severely irritating to the skin, is not a dermal sensitizer, and is considered to be non-mutagenic.

Occupational exposure to AMV-1018 (98% Liquid Concentrate) is expected to be minimal if the precautionary statements and recommended personal protective equipment on the product label, which are intended to minimize worker exposure, are observed. Bystander exposure is likely to be negligible. Post-application exposure can be minimized if the required restricted-entry interval is observed by workers and bystanders.

Dietary exposure to 3-decen-2-one from the use of the proposed end-use product is not expected to result in unacceptable dietary risks when the product is used according to label instructions. The Pest management Regulatory Agency did not establish a maximum residue limit (MRL) for 3-decen-2-one.

## 7.2 Environmental Risk

Based on the use pattern for 3-decen-2-one and the end-use product AMV-1018 (98% Liquid Concentrate), which includes direct application as an aerosol into enclosed storage space filled with potatoes, 3-decen-2-one presents a limited risk to wild birds nesting or roosting in the vicinity of storage facilities.

## 7.3 Value

The value data submitted in support of AMV-1018 (98% Liquid Concentrate) are adequate to describe its efficacy for controlling sprouting of potatoes in storage. A single application of 115 g a.i./tonne potatoes when 75% of tubers show visible signs of sprouting can be expected to extend the period of storability by 1 to 3 months. The storage period may be extended further with additional applications. Application of this rate when potatoes have developed sprouts of up to 2.5 cm in length can be made as a rescue treatment or for potatoes undergoing reconditioning prior to processing. AMV-1018 (98% Liquid Concentrate) may be used alone or with other pest control products that are registered for the inhibition of sprouting in stored potatoes provided that potatoes are showing signs of sprouting or have developed sprouts at the time of AMV-1018 (98% Liquid Concentrate) application. A maximum of four applications of AMV-1018 (98% Liquid Concentrate) may be made to any one lot of potatoes.

AMV-1018 (98% Liquid Concentrate) is unlikely to increase incidence of physiological disorders of stored potatoes or to negatively impact potato quality, such as fry quality or taste characteristics of baked potatoes.

The registration of AMV-1018 (98% Liquid Concentrate) provides an alternative sprout inhibitor option and mode of action to the commonly used chlorpropham (CIPC).

### 7.4 Unsupported Uses

Certain claims originally proposed by the applicant were not supported by the PMRA because the value was not adequately demonstrated. These claims included:

- long term sprout control where sprouting is prevented for 2-3 months.

## 8.0 Proposed Regulatory Decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of AMV-1018 Technical and AMV-1018 (98% Liquid Concentrate) for use on potatoes in storage to control sprouting once the dormancy period has ended.

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.

**Human Health**

The signal words "CAUTION – POISON, EYE IRRITANT", and "DANGER – SKIN IRRITANT" are required on the principal display panels of both the technical and end-use product labels. The statements "Harmful if inhaled", "May irritate eyes", and "Severely irritating to skin" are required on the secondary display panel of the technical and end-use product labels.

The personal protective equipment for all loading, handling, clean-up and maintenance activities required on the end-use product label includes a long-sleeved shirt, long pants, shoes, socks, respirator with a NIOSH/MSHA approved organic vapour-removing cartridge with a pre-filter approved for pesticides, goggles, and chemical resistant gloves. Storage areas must be ventilated for at least 24 hours or until ventilation is complete before allowing workers to enter for normal activities. If entering storage area before full ventilation, workers must wear coveralls over long-sleeved shirt, long pants, shoes, socks, chemical resistant gloves, and a self-contained breathing apparatus or full-face respirator with a NIOSH/MSHA approved organic vapour-removing cartridge with a pre-filter approved for pesticides.

# List of Abbreviations

| | |
|---|---|
| µg | micrograms |
| a.i. | active ingredient |
| ADI | acceptable daily intake |
| bw | body weight |
| $^{o}$C: | degrees centigrade |
| CAS | Chemical Abstracts Service |
| cm | centimetres |
| CIPC: | Isopropyl-m-chloro-carbonilate (chlorpropham) |
| cm: | centimetres |
| g: | grams |
| GRAS: | Generally Recognized As Safe |
| ha | hectare(s) |
| kg | kilogram |
| L: | litres |
| $LC_{50}$ | lethal concentration 50% |
| $LD_{50}$ | lethal dose 50% |
| LOAEL | lowest observed adverse effect level |
| LOEC | low observed effect concentration |
| mg | milligram |
| mL | millilitre |
| MRL | maximum residue limit |
| NOAEL | no observed adverse effect level |
| NOEL | no observed effect level |
| PMRA | Pest Management Regulatory Agency |
| TGAI | technical grade active ingredient |
| TSMP | Toxic Substances Management Policy |
| U.S. FDA | United States Food and Drug Administration |
| U.S. EPA: | United States Environmental Protection Agency |
| v/v | volume per volume dilution |

# Appendix I

## Tables and Figures

### Table 1 Summary of acute toxicity, irritative effects, sensitization and mutagenicity information for 3-decen-2-one

| STUDY | SPECIES/STRAIN AND DOSES | RESULT | TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS | REFERENCE |
|---|---|---|---|---|
| Oral toxicity (Limit test)<br><br>Exposure by gavage | Rat – Sprague Dawley<br>(4 females) | $LD_{50}$ (♀) > 5000 mg/kg bw<br><br>**Low acute toxicity.** | One mortality occurred within two days of test substance administration. | 1845944 |
| Dermal<br><br>24 hour exposure period | Rat – Sprague Dawley<br>(5/sex) | $LD_{50}$ (♀) > 5000 mg/kg bw<br>$LD_{50}$ (♂) > 5000 mg/kg bw<br><br>**Low acute toxicity.** | One mortality occurred within two days of test substance administration. Dermal irritation occurred at dose sites of all surviving animals between Days 1 and 14. | 1845945 |
| Inhalation<br><br>Nose-only exposure chamber | Rat – Sprague Dawley<br>(10 males, 5 females) | $LC_{50}$ (♀) > 2.04 mg/L<br>$LC_{50}$ (♂) 0.52 – 2.04 mg/L<br><br>**Slightly acutely toxic.** | One male died immediately following exposure to 2.04 mg/L. Two males died within two days of exposure to 2.04 mg/L. One male died within one day of exposure to 0.52 mg/L. | 1845947 |
| Eye Irritation<br><br>Draize method | Rabbit – New Zealand White<br>(3 females)<br><br>Dose: 0.1 mL of test substance. Eyes were left unwashed. | MIS = 24.3/110<br><br>**Mildly irritating.** | Conjunctivitis, iritis, and corneal opacity cleared by Day 10. | 1845948 |

| STUDY | SPECIES/STRAIN AND DOSES | RESULT | TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS | REFERENCE |
|---|---|---|---|---|
| Dermal Irritation<br><br>Draize method | Rabbit – New Zealand White<br>(3 males)<br><br>Dose: 0.5 mL of test substance applied for 4 hours. | MIS = 6/8<br><br>**Severely irritating.** | Severe irritation was observed through 72 hours post patch removal. Well-defined to severe erythema and moderate edema cleared by Day 14. | 1845949 |
| Dermal Sensitization<br><br>Buehler test | Guinea pig – Hartley Albino<br>(males and females)<br><br>Test group = 20<br>Naïve control group = 10 | Negative results. Not a dermal sensitizer. | No positive reactions were observed following challenge in any test or control animals. | 1845950 |
| Bacterial reverse mutation assay<br><br>Plate incorporation test and pre-incubation test | *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 102<br><br>Test concentrations: 0.0136, 0.100, 0.316, 1.0, 2.5 and 5.0 µL/plate | Non-mutagenic. | No biologically relevant increases in revertant colony numbers of any of the tester strains were observed at any concentration, in the presence or absence of metabolic activation, in either experiment. | 1845952 |
| Mammalian erythrocyte micronucleus test | Mouse – NMRI<br>(5 males, 5 females per dose group)<br><br>Doses: 1 MTD, 0.5 MTD, 0.2 MTD (1 MTD was equivalent to application of 10 mL/kg bw of 5 % v/v test item solution in cottonseed oil) | Non-mutagenic. | All mean values of micronuclei for the treatment groups were within the range of, or decreased compared to, the corresponding negative controls. | 2027863 |

# References

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

### 1.0 Chemistry


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1845936 2009, Production Process for AMV-1018 Technical, DACO: 2.11.1,2.11.3,2.11.4,830.1620 CBI

1845939 2009, Formation of Impurities of AMV-1018 Technical, DACO: 2.11.1,2.11.3,2.11.4,3.2.3,830.1670 CBI

1845940 2009, Preliminary Analysis, DACO: 2.13.1,2.13.2,2.13.3,830.1700 CBI

1845942 2009, Physical and Chemical Characteristics of AMV-1018 Technical, DACO: 2.14.1,2.14.11,2.14.12,2.14.13,2.14.14,2.14.2,2.14.3,2.14.5,2.14.6,2.14.7,2.14.8,3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.6,3.5.7,830.6302,830.6303,830.6304,830.6313,830.6317,830.6320,830

1845943 2009, Product Properties - Vapour Pressure, DACO: 2.14.9,830.7950 CBI

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1845976 2009, Physical and Chemical Characteristics of AMV-1018 Technical, DACO: 2.14.1,2.14.11,2.14.12,2.14.13,2.14.14,2.14.2,2.14.3,2.14.5,2.14.6,2.14.7,2.14.8,3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.6,3.5.7,830.6302,830.6303,830.6304,830.6313,830.6317,830.6320,830

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2243607 2010, Storage Stability and Corrosion Characteristics, DACO: 2.14.14,3.5.10 CBI


### 2.0 Human and Animal Health


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1845945 2009, Acute Dermal Toxicity in Rats – Limit Test of AMV-1018 Technical, DACO 4.2.2.

1845947 2009, Acute Inhalation Toxicity in Rats of AMV-1018 Technical, DACO 4.2.3.

1845948 2009, Primary Eye Irritation in Rabbits of AMV-1018 Technical, DACO 4.2.4.

1845949 2009, Primary Skin Irritation in Rabbits, DACO 4.2.5.

1845950 2009, Dermal Sensitization in Guinea Pigs of AMV-1018 Technical, DACO 4.2.6, 4.6.6.

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2027860 2011, Short-term Inhalation Request for Waiver DACO 4.3.6.

2027861 2011, Prenatal Developmental Toxicity Request for Waiver DACO 4.5.2.

2243609 2012, AMV-1018: Study for Effects on Embryo-Fetal Development in the CD Rat by Oral Gavage Administration, DACO: 4.5.2

1845952 2009, Reverse Mutation Assay using Salmonella typhimurium of AMV-1018 Technical, DACO: 4.5.4,870.5100

1845951 2009, In vitro Mammalian Cell Gene Mutatnion Assay of AMV-1018 Technical, DACO: 4.5.5,870.5300

2027863 2009, Mammalian Micronucleus Test Murine Peripheral Blood Cells, DACO: 4.7.5

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1862565 2009, Comprehensive Data Summaries, DACO: 12.7

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1846071 AMV-2, DACO: 10.2.3.3

1846075 AMV-3, DACO: 10.2.3.2

1846077 AMV-4, DACO: 10.2.3.2

1846078 AMV-5, DACO: 10.2.3.2

1846080 AMV-6, DACO: 10.2.3.2

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