



Proposed Registration Decision

PRD2023-03

1-Aminocyclopropanecarb oxylic acid, VBC-30452 SG Plant Growth Regulator, Accede SG Plant Growth Regulator

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Overview

Proposed registration decision for 1-Aminocyclopropanecarboxylic acid

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the [Pest Control Products Act](#), is proposing registration for the sale and use of ACC Technical Powder, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, containing the technical grade active ingredient 1-aminocyclopropanecarboxylic acid, for commercial fruit tree thinning for apple trees.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

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 1-aminocyclopropanecarboxylic acid, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator.

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 acceptable¹ 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 value² when used according to the label directions. Conditions of registration may include 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. 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 Health Canada regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides portion of Canada.ca.

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 1-aminocyclopropanecarboxylic acid, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, Health Canada's PMRA will consider any comments received from the public in response to this consultation document.³ Health Canada will then publish a Registration Decision⁴ on 1-aminocyclopropanecarboxylic acid, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada'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 1-aminocyclopropanecarboxylic acid?

1-Aminocyclopropanecarboxylic acid is a naturally occurring amino acid found in many higher plants. It is a potent plant growth regulator and is a precursor for ethylene production in plant tissues. Ethylene affects plant processes such as flower development, fruit set, fruit maturation, fruit ripening, and fruit abscission.

Health considerations

Can approved uses of 1-aminocyclopropanecarboxylic acid affect human health?

1-Aminocyclopropanecarboxylic acid is unlikely to affect your health when used according to label directions.

Potential exposure to 1-aminocyclopropanecarboxylic acid may occur through the diet (food and water) or when handling or applying the product. 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 levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed.

In laboratory animals, 1-aminocyclopropanecarboxylic acid was of low acute toxicity by the oral, dermal and inhalation routes, minimally irritating to the eyes, slightly irritating to the skin, and not a dermal sensitizer.

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*.

Short-term oral and dermal toxicity, prenatal developmental toxicity, reproductive toxicity, and genotoxicity/mutagenicity testing of 1-aminocyclopropanecarboxylic acid was also assessed. Animals given repeated high doses of 1-aminocyclopropanecarboxylic acid in the diet or dermally did not exhibit treatment-related adverse effects. There was no indication that the young were more sensitive than the adult animals. 1-Aminocyclopropanecarboxylic acid is not considered to be genotoxic.

In laboratory animals, the end-use product, VBC-30452 SG Plant Growth Regulator, was of low toxicity by the oral, dermal and inhalation routes, non-irritating to the eye and skin, and not a dermal sensitizer. The toxicological profile of Accede SG Plant Growth Regulator is the same as the toxicological profile of VBC-30452 SG Plant Growth Regulator. The labels for VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator also require a milk allergen warning statement.

The risk assessment protects against the findings noted above as well as any other potential effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occur in animal studies.

Residues in water and food

Dietary risks from food and water are acceptable.

1-Aminocyclopropanecarboxylic acid is a plant amino acid and is the direct precursor in the biosynthesis of ethylene (a plant hormone regulating a variety of plant developmental processes) in plant tissues. Humans are exposed to 1-aminocyclopropanecarboxylic acid through fruit and vegetable consumption. Due to its low toxicity profile and the proposed use pattern (applied only twice per season and before mature fruit have formed), 1-aminocyclopropanecarboxylic acid present in VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator is not expected to pose a health risk when the end-use products are applied as directed by the label. In addition, the likelihood of residues of 1-aminocyclopropanecarboxylic acid in drinking water will be very low. Consequently, health risks are acceptable for all segments of the population, including infants, children, adults and seniors.

Risks in residential and other non-occupational environments

Estimated risk for residential and other non-occupational exposure is acceptable.

VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator are commercial products for use in apple orchards and there are no residential uses proposed. In the interest of promoting best management practices, the labels have a standard spray drift statement to protect against drift to residential areas.

Residential and non-occupational exposure to VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator is expected to be low when label directions are followed. Consequently, the risk to residents and the general public is acceptable.

Occupational risks from handling VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator

Occupational risks are acceptable when VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator are used according to the label directions, which include protective measures.

Workers handling VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator can come into direct contact with 1-aminocyclopropanecarboxylic acid through inhalation and contact with skin during mixing, loading, application, clean-up and repair. Eye exposure is also possible, but expected to be minimal. To limit worker exposure to VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, the proposed labels require workers to wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during mixing, loading, application, clean-up and repair.

The labels also require that workers not enter treated areas for twelve (12) hours after application.

The occupational risks are acceptable when the label directions are followed.

Environmental considerations

What happens when 1-aminocyclopropanecarboxylic acid is introduced into the environment?

1-Aminocyclopropanecarboxylic acid can enter the environment when VBC-30452 SG Plant Growth Regulator or Accede SG Plant Growth Regulator are applied to apples for fruit thinning and enhanced return bloom. 1-Aminocyclopropanecarboxylic acid is a naturally occurring non-protein amino acid produced by many plants and microorganisms. It is non-persistent in the environment as it is rapidly transformed in higher plants and microbes. 1-Aminocyclopropanecarboxylic acid is not bound tightly to soil following application. It is not expected to accumulate in organisms.

1-Aminocyclopropanecarboxylic acid does not exhibit toxicity to most terrestrial or aquatic organisms. However, as a plant growth regulator, 1-aminocyclopropanecarboxylic acid may pose risks to algae and non-target terrestrial plants. Precautionary label statements to inform users of the toxicity to non-target aquatic and terrestrial plants and spray buffer zones to reduce exposure to aquatic and terrestrial habitats will be required to mitigate these risks. When 1-aminocyclopropanecarboxylic acid is used in accordance with the label and required precautions, the resulting environmental risk is considered to be acceptable.

Value considerations

What is the value of VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator?

VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator are proposed for use in apple orchards for the purposes of fruit thinning and enhanced return bloom.

The registration of VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator will provide apple growers with a new active ingredient and end-use products for the purposes of fruit thinning and enhanced return bloom.

VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator provide effective thinning of apple fruitlets measuring up to 18-20 mm at the time of application, which is a later stage than for currently available fruit thinners. Fruitlet thinning is important in order to increase apple size, ensure more consistent blooming in the following year (return bloom) and to help maintain harvest size from year to year.

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 labels of ACC Technical Powder, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Key risk-reduction measures - Human Health

- The allergen warning statement “WARNING: Contains the allergen milk” is required on the principal display panel of the label for VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator.
- To protect workers from exposure to VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, workers must wear long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during mixing, loading, application, clean-up and repair.
- There is a restricted-entry interval of twelve (12) hours.
- A standard precautionary drift statement is present to mitigate exposure to residential areas.

Key risk-reduction measures - Environment

- Label statements to indicate toxicity to non-target terrestrial and aquatic plants
- Spray buffer zones to protect sensitive terrestrial and aquatic habitats

Next steps

Before making a final registration decision on 1-aminocyclopropanecarboxylic acid, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, Health Canada's PMRA will consider any comments received from the public in response to this consultation document. Health Canada will accept written comments on this proposal up to 45 days from the date of publication of this document. Health Canada will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and Health Canada's response to these comments.

Other information

When the Health Canada makes its registration decision, it will publish a Registration Decision on 1-aminocyclopropanecarboxylic acid, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator (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. For more information, please contact the PMRA's [Pest Management Information Service](#).

Science evaluation

ACC Technical Powder

1.0 The active ingredient, Its properties and uses

1.1 Identity of the active ingredient

Active substance 1-aminocyclopropanecarboxylic acid

Function Plant Growth Regulator

Chemical name

1. International Union of Pure and Applied Chemistry (IUPAC) 1-aminocyclopropanecarboxylic acid

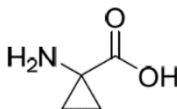
2. Chemical Abstracts Service (CAS) 1-aminocyclopropanecarboxylic acid

CAS number 22059-21-8

Molecular formula C₄H₇NO₂

Molecular weight 101.10

Structural formula



Purity of the active ingredient 98.56%

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

Technical product—ACC Technical Powder

Property	Result
Colour and physical state	Off-white fine powder with some agglomerates
Odour	Faint and unpleasant
Melting range	Decomposes on melting
Boiling point or range	Not determined as decomposes on melting
Density	1.26 (relative density)
Vapour pressure	3.6×10^{-5} mPa at 25°C

Property	Result														
Ultraviolet (UV)-visible spectrum	λ (nm) log ϵ 235.0 3.572 257.1 3.636 313.0 3.162 350.1 3.504 Absorbance = 0.8121 at λ = 203 nm, ϵ = 41.74 L·mol ⁻¹ ·cm ⁻¹ ; no significant absorbance at wavelength greater than 290 nm.														
Solubility in water at 20°C	<table border="1"> <thead> <tr> <th>pH</th> <th>Solubility (g/L)</th> </tr> </thead> <tbody> <tr> <td>pure</td> <td>68</td> </tr> <tr> <td>5</td> <td>70</td> </tr> <tr> <td>7</td> <td>72</td> </tr> <tr> <td>9</td> <td>149</td> </tr> </tbody> </table>	pH	Solubility (g/L)	pure	68	5	70	7	72	9	149				
pH	Solubility (g/L)														
pure	68														
5	70														
7	72														
9	149														
Solubility in organic solvents at 20°C	<table border="1"> <thead> <tr> <th>Solvent</th> <th>Solubility (mg/L)</th> </tr> </thead> <tbody> <tr> <td>Hexane</td> <td>< 0.2</td> </tr> <tr> <td>Xylene</td> <td>< 0.2</td> </tr> <tr> <td>Dichloromethane</td> <td>< 0.2</td> </tr> <tr> <td>Acetone</td> <td>300</td> </tr> <tr> <td>Methanol</td> <td>3500</td> </tr> <tr> <td>Ethyl acetate</td> <td>< 1</td> </tr> </tbody> </table>	Solvent	Solubility (mg/L)	Hexane	< 0.2	Xylene	< 0.2	Dichloromethane	< 0.2	Acetone	300	Methanol	3500	Ethyl acetate	< 1
Solvent	Solubility (mg/L)														
Hexane	< 0.2														
Xylene	< 0.2														
Dichloromethane	< 0.2														
Acetone	300														
Methanol	3500														
Ethyl acetate	< 1														
<i>n</i> -Octanol-water partition coefficient (K_{ow})	<p>pH 5; log K_{ow} = -2.8</p> <p>pH 7; log K_{ow} = -2.9</p> <p>pH 9; log K_{ow} = < -3.0</p>														
Dissociation constant (pK_a)	8.8														
Stability (temperature, metal)	Stable in contact with aluminum, aluminium acetate, iron, iron acetate, zinc and zinc acetate and at elevated temperature when stored at 54°C for 14 days														

End-use products—VBC-30452 SG Plant Growth Regulator, Accede SG Plant Growth Regulator

Property	Result
Colour	Off-white
Odour	No discernible odour
Physical state	Soft and friable extruded granule
Formulation type	WG (Wettable granule)
Label concentration	40.0 %
Container material and description	100 g – bulk plastic (HDPE) bottle or jug
Density	0.5 g/mL
pH of 1% dispersion in water	5.2

Property	Result
Oxidizing or reducing action	Incompatible with any hydrogen peroxide based compound, goethite, copper sulfate, iron sulfide, iron chloride, iron citrate (all metal ions; with NaOCl). Methyl bromide can alkylate the product.
Storage stability	The product is chemically and physically stable when stored in commercial packaging (HDPE) at 54°C for 14 days
Corrosion characteristics	No sign of corrosive characteristics (packaging material HDPE) when stored at 54°C for 14 days
Explosibility	No explosive characteristics

1.3 Directions for use

Either VBC-30452 SG Plant Growth Regulator or Accede SG Plant Growth Regulator is to be applied at a rate of 200–400 g a.i./ha in a water volume of 1000 L/ha. Adequate water volume is critical to ensure successful application and water volumes should be adjusted based on plant size and spacing. Excessive spray volume can result in run-off and reduced efficacy. A non-ionic surfactant can be included in the spray to improve consistency of performance and response. Application may be made via airblast sprayer where 80% of the spray is directed into the upper 2/3 of the canopy. A maximum of two applications of 1-aminocyclopropanecarboxylic acid can be made per season with an interval of 7–10 days between applications. VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator may be employed in a program with other registered apple thinners.

1.4 Mode of action

The active ingredient 1-aminocyclopropanecarboxylic acid is a naturally occurring aliphatic amino acid found in higher plants and is a member of the non-protein amino acids group. 1-Aminocyclopropanecarboxylic acid is the immediate precursor to ethylene, an important plant hormone, and therefore may be directly or indirectly involved in many of the major events of plant growth and development regulated by ethylene. Ethylene is a well-researched and understood phytohormone that affects the growth and development of plants as well as their senescence. It plays a key role in the flowering of many plants and the development of fruits and has been broadly used for decades in orchards and greenhouses as a plant growth regulator. 1-Aminocyclopropanecarboxylic acid can be used to achieve ethylene responses, such as induction of fruitlet abscission, and is considered to mirror the mode of action and activity of ethylene.

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 impurities in the technical product have been validated and assessed to be acceptable.

2.2 Method for formulation analysis

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

2.3 Methods for residue analysis

No methods are required to quantify residues of 1-aminocyclopropanecarboxylic acid due to its low toxicity. Furthermore, 1-aminocyclopropanecarboxylic acid is naturally present in fruit (see Section 3.0).

3.0 Impact on human and animal health

3.1 Toxicology summary

A detailed review of toxicology information was conducted in support of the technical grade active ingredient, ACC Technical Powder, and the end-use products, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator. The data package for ACC Technical Powder, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator is considered acceptable (Appendix I, Tables 1–2) to assess the toxic effects that may result from exposure to 1-aminocyclopropanecarboxylic acid.

The data package consisted of acute toxicity studies (acute oral, dermal, and inhalation toxicity, eye and skin irritation, and dermal sensitization testing), short-term oral (dietary) and dermal toxicity, prenatal developmental toxicity, an extended one-generation reproductive toxicity, and in vitro genotoxicity and mammalian cell mutagenicity studies in support of the technical grade active ingredient. The test substances in all of the technical grade active ingredient studies contained the active ingredient 1-aminocyclopropanecarboxylic acid at concentrations ranging from 94.5–96.68% w/w (see Appendix I, Table 1). The test substances were all considered acceptable as surrogates to the technical grade active ingredient, ACC Technical Powder containing 1-aminocyclopropanecarboxylic acid at 98.5% w/w.

ACC Technical Powder was of low acute toxicity by the oral, dermal and inhalation routes, minimally irritating to the eyes, slightly irritating to the skin, and not a dermal sensitizer.

In a 28 day dermal toxicity study in rats, there were no signs of irritation and no clinical signs of toxicity. The no observable adverse effects level (NOAEL) was greater than 1000 mg/kg bw/d.

In a 90 day oral toxicity study in mice by dietary administration, there were no treatment-related adverse effects. The NOAEL was greater than 882.8 mg/kg bw/d for males and greater than 1071.2 mg/kg bw/day for females, the highest dose tested.

In an oral prenatal developmental toxicity study in rats by the dietary route, there were no treatment-related effects and no evidence of sensitivity of the young. The maternal and developmental NOAEL was >982 mg/kg/day, the highest dose tested.

In an extended one-generation dietary reproductive toxicity study in rats, parental males exhibited decreased body weight at the mid dose, and decreased mean body weights and body weight gains at the highest dose tested; for parental males, the systemic NOAEL was 136 mg/kg bw/day. There were no adverse effects in female parental animals, therefore the systemic NOAEL was greater than the highest dose tested (647 mg/kg/day prior to mating). Treatment-related adverse effects in male offspring included decreased body weight and body weight gain, increased liver weight and elevated aspartate aminotransferase at the high dose; the NOAEL for male offspring was 348 mg/kg bw/day. In female offspring, there were no treatment-related adverse effects (NOAEL greater than 763 mg/kg bw/day). There was no evidence of reproductive toxicity in the parental animals nor in offspring, and no evidence of sensitivity of the young.

1-aminocyclopropanecarboxylic acid was not mutagenic in a reverse gene mutation assay in bacteria and was not clastogenic in an in vitro mammalian cell gene mutation assay.

To address the data requirements for the end-use products, acute toxicity studies (acute oral, dermal, inhalation toxicity, eye and skin irritation and dermal sensitization) with VBC-30452 Plant Growth Regulator were submitted. VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator are of low acute toxicity by the oral, dermal, and inhalation routes, non-irritating to the eyes and skin and are not dermal sensitizers. The toxicological profile of Accede SG Plant Growth Regulator is equivalent to the toxicological profile of VBC-30452 SG Plant Growth Regulator (see Appendix I, Table 2).

3.2 Occupational, residential and bystander exposure and risk assessment

3.2.1 Dermal absorption

An in vitro dermal absorption study investigating absorption of radiolabelled 1-aminocyclopropanecarboxylic acid using excised human skin was reviewed. The dermal absorption values after 24 hours (8 hour skin wash) were 0.07% at the high dose and 0.81% at the low dose. Dermal absorption values included all residues in the tape strips. The tested doses are representative of expected exposure scenarios.

1-aminocyclopropanecarboxylic acid is a non-protein amino acid with high water solubility (72 ± 1.4 g/L) and low partition coefficient ($\text{Log } K_{ow} = -2.9$). Although the compound is small (<500 g/mol), the physicochemical properties of 1-aminocyclopropanecarboxylic acid indicate that it is likely to have low dermal absorption.

Based on the results of the in vitro study, as well as the physicochemical properties, absorption of 1-aminocyclopropanecarboxylic acid through human skin is expected to be low for all scenarios.

3.2.2 Use description

VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator are proposed for use in commercial apple production for early season blossom and fruitlet thinning. The end-use products are not intended for use in or around residential areas.

The end-use products are to be applied by airblast sprayers only. The maximum application rate is 400 g a.i./ha in 1000 L spray volume (400 ppm) with a maximum of two applications per year and a minimum spray interval of 7 days.

3.2.3 Mixer, loader, and applicator exposure and risk assessment

When VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator are used according to label directions, occupational exposure is characterized as short- to intermediate-term in duration and is primarily by the dermal and inhalation routes when workers are exposed to the dust generated from handling water soluble granules during mixing, or during exposure to diluted spray solution while spraying, or from the spray drift. Ocular exposure is possible but expected to be minimal.

To limit worker exposure to the end-use products, workers must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, during mixing, loading, application, clean-up and repair.

Precautionary statements on the end-use product labels, such as the wearing of personal protective equipment (PPE), aimed at mitigating exposure are adequate to protect individuals from any risk due to occupational exposure. Overall, occupational risks to workers are acceptable when the precautionary statements on the label are followed which include PPE.

3.2.4 Postapplication exposure and risk assessment

There is the potential for postapplication exposure to workers re-entering areas treated with VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator. Given the nature of the post-application activities typically performed (for example, scouting treated areas), dermal contact with treated plants, soil, and surfaces is possible. Inhalation of suspended spray droplets is also possible if re-entry occurs immediately after application. The label has a restricted-entry interval (REI) of twelve (12) hours following application, which restricts workers from entering treated sites.

Precautionary statements on the end-use product labels aimed at mitigating exposure are considered adequate to protect workers from risk due to postapplication exposure.

3.2.5 Residential and bystander exposure and risk assessment

VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator are commercial products for use in apple orchards and there are no residential uses proposed. The potential for drift is expected to be minimal based on the label directions.

Residential and bystander exposure to VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator is expected to be low when label directions are observed. Consequently, the risk to residents and the general public is acceptable.

3.3 Food residue exposure assessment

3.3.1 Food

1-Aminocyclopropanecarboxylic acid is a naturally occurring non-protein amino acid, which acts as the direct precursor in the biosynthesis of ethylene (a plant hormone regulating a variety of developmental processes) in plant tissues. Humans have long been exposed to 1-aminocyclopropanecarboxylic acid as part of the typical human diet from consumption of fruit and vegetables. Due to the proposed use pattern of VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator (applied only twice per season before fruit maturation) and the likely biodegradability of 1-aminocyclopropanecarboxylic acid, residues remaining on apples at harvest are anticipated to be negligible. Furthermore, 1-aminocyclopropanecarboxylic acid has a low toxicity profile. Consequently, the health risk is acceptable for the general population, including infants and children, and domestic animals.

3.3.2 Drinking water

Exposure to residues of 1-aminocyclopropanecarboxylic acid from drinking water is expected to be negligible because of the use pattern, anticipated low mobility in soil, and their likely biodegradability in nature. Furthermore, the labels have the necessary mitigation measures to limit contamination of drinking water from the proposed uses of 1-aminocyclopropanecarboxylic acid. Health risks from residues of 1-aminocyclopropanecarboxylic acid in drinking water are acceptable due to the low toxicity profile and limited exposure following applications of VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator.

3.3.3 Acute and chronic dietary risks for sensitive subpopulations

As noted above, when the end-use products are applied as directed by the labels, the health risk is acceptable for the general population, including infants and children, and domestic animals.

3.3.4 Aggregate exposure and risk

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation).

In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential exposure pathways is assessed. A major consideration is the likelihood of co-occurrence of exposures. Additionally, only exposures from routes that share common toxicological endpoints can be aggregated.

1-aminocyclopropanecarboxylic acid is of low acute oral, dermal, and inhalation toxicity, minimally irritating to the eyes, slightly irritating to skin, and is not a skin sensitizer. Based on available information, there is reasonable certainty that no harm will result from aggregate exposure of residues of 1-aminocyclopropanecarboxylic acid to the general population in Canada, including infants and children, when VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator are used as labelled. This includes anticipated dietary (food and drinking water) exposures only, since residential exposure is not expected to occur.

3.3.5 Cumulative assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. Accordingly, an assessment of potential common mechanisms of toxicity with other pesticides was undertaken.

For the current evaluation, PMRA did not identify information indicating that 1-aminocyclopropanecarboxylic acid shares a common mechanism of toxicity with other registered pest control products. While 1-aminocyclopropanecarboxylic acid is the precursor for the biosynthesis of ethylene, which is also a pesticide active ingredient (or a derivative thereof), both ethylene and 1-aminocyclopropanecarboxylic acid are naturally present in fruit and vegetables. Furthermore, as both ethylene and 1-aminocyclopropanecarboxylic acid are of low toxicity, a qualitative approach was taken for the health assessment. No health concerns were identified, and thus cumulative risks are acceptable.

3.3.6 Maximum residue limits

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether dietary risks are acceptable from the consumption of foods treated with the pesticide when used according to the supported label directions. If acceptable, this means food containing that amount of residue is safe to eat, and maximum residue limits (MRLs) may be proposed. MRLs are the maximum amount of pesticide residue legally permitted to remain in/on food sold in Canada and are specified under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act*.

Dietary risk from the proposed use of 1-aminocyclopropanecarboxylic acid on apple orchards is acceptable, given the history of human dietary exposure to 1-aminocyclopropanecarboxylic acid from fruits and vegetables, the low toxicity profile of 1-aminocyclopropanecarboxylic acid, and the proposed use-pattern of VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator (applied only twice per season and before mature fruit have formed) in apple orchards, which will result in negligible residues on the fruit. Consequently, the specification of MRLs, under the *Pest Control Products Act*, will not be required.

3.4 Health incident reports

1-Aminocyclopropanecarboxylic acid is a new active ingredient pending registration for use in Canada, and as of 24 August 2022, no incident reports had been submitted to the PMRA.

4.0 Impact on the environment

ACC Technical Powder and its associated end-use products, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, are considered for registration as non-conventional products according to PMRA Regulatory Directive DIR2012-01, *Guidelines for Registration of Non-Conventional Pest Control Products*.

4.1 Fate and behaviour in the environment

1-Aminocyclopropanecarboxylic acid is a naturally occurring non-protein amino acid found in plants. 1-Aminocyclopropanecarboxylic acid is very soluble in water. It is not likely to volatilize from water and moist soils based on the low vapour pressure and Henry's Law Constant. 1-Aminocyclopropanecarboxylic acid has low potential for direct phototransformation, based on the UV/Visible absorption spectra indicating no wavelength absorption maxima above 203 nm.

Based on laboratory studies, 1-aminocyclopropanecarboxylic acid will be rapidly broken down by microorganisms. Run-off and leaching of 1-aminocyclopropanecarboxylic acid from treated areas are not expected due to the non-persistent nature of this compound in the environment. Thus, surface and ground water sources are not expected to be contaminated as a result of foliar application. 1-Aminocyclopropanecarboxylic acid is not likely to bioaccumulate in organisms.

In the atmosphere, 1-aminocyclopropanecarboxylic acid will not be subject to long-range transport as it is expected to undergo rapid degradation by reactions with hydroxyl radicals.

Data on the fate and behaviour of 1-aminocyclopropanecarboxylic acid are summarized in Appendix I, Table 3.

4.2 Environmental risk characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e., protection at the community, population, or individual level). A summary of the terrestrial and aquatic endpoints available and the effects metrics used in the risk assessment are presented in Appendix I, Tables 4 and 5, respectively.

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value ($RQ = \text{exposure}/\text{toxicity}$), and the risk quotient is then compared to the level of concern ($LOC = 1$). If the screening level risk quotient is below the LOC, the risk is considered acceptable, and no further risk characterization is necessary. If the screening level RQ is equal to or greater than the LOC, further characterization of the risk is conducted by taking into consideration more realistic exposure scenarios and effects metrics.

4.2.1 Risks to terrestrial organisms

Terrestrial organisms, such as honeybees, wild birds and terrestrial non-target vascular plants can be exposed to 1-aminocyclopropanecarboxylic acid through direct contact with spray, spray drift, contact with sprayed surfaces, or from ingestion of contaminated food. A risk assessment of 1-aminocyclopropanecarboxylic acid and the associated end-use products, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, was undertaken based on available toxicity data for these organisms. The most sensitive terrestrial endpoints used in the risk assessment are provided in Appendix I, Table 5. The screening-level and refined risk results are presented in Appendix I, Tables 6–7.

4.2.1.1 Risk to bees

At the screening level, the pollinator LOC was not exceeded for acute contact and oral exposure of adult honeybees to 1-aminocyclopropanecarboxylic acid ($RQs < 0.266$). Overall, the risks associated with the application of 1-aminocyclopropanecarboxylic acid are considered acceptable.

4.2.1.2 Risk to wild birds

At the screening level, the RQs for small and medium wild birds marginally exceeded the LOC of 1 ($RQs: 1.1–1.5$) for insectivores, on an acute oral basis; the LOC was not exceeded for all birds on a dietary basis ($RQs: 0.0–0.4$). These acute oral RQs are very low and were not exceeded for all birds when taking account the mean nomogram residues off site. Considering the conservative assumptions noted above for the screening level assessment, the acute risk to small and medium sized birds are acceptable and do not require risk mitigation.

4.2.1.3 Risk to non-target terrestrial plants

At the screening level, the LOC was exceeded for effects of 1-aminocyclopropanecarboxylic acid on non-target vascular plants for both vegetative vigour ($RQ < 1.07$) and seedling emergence (RQ of 506, based on tomato shoot dry weight).

Based on off-field exposure from spray drift (airblast application), the LOC was not exceeded for vegetative vigour (RQ: <0.63 – <0.8), but was still exceeded for seedling emergence with RQs of 374 (early season) and 298.5 (late season). A spray buffer zone will be required to mitigate the risk to non-target plants adjacent to the application site.

4.2.2 Risks to aquatic organisms

Aquatic organisms, such as invertebrates, fish, amphibians and aquatic plants may be exposed to 1-aminocyclopropanecarboxylic acid via spray drift or runoff entering aquatic habitats. The most sensitive aquatic endpoints used in the risk assessment are provided in Appendix I, Table 5. The screening-level and refined risk results are presented in Appendix I, Table 8.

4.2.2.1 Risk to aquatic invertebrates

At the screening level, RQs for freshwater invertebrates did not exceed the LOC (RQs ≤ 0.0088). Therefore, the risks to aquatic invertebrates from the use of 1-aminocyclopropanecarboxylic acid are acceptable.

4.2.2.2 Risk to fish and amphibians

At the screening level, RQs for freshwater fish and amphibians did not exceed the LOC (RQs <0.045). Therefore, the risks to aquatic vertebrates from the use of 1-aminocyclopropanecarboxylic acid are acceptable.

4.2.2.3 Risk to algae and aquatic vascular plants

At the screening level, the LOC was not exceeded for aquatic vascular plants (RQ of 0.156); however, it was exceeded for freshwater algae (RQ of 5.4). The potential risk to algae was further characterized. Based on exposure from spray drift (airblast application), the LOC was exceeded for freshwater algae with RQs of 4 (early season) and 3.18 (late season). A spray buffer zone will be required to mitigate the risk to non-target aquatic plants. Risk to aquatic organisms from runoff was not required due to natural occurrence and rapid breakdown of 1-aminocyclopropanecarboxylic acid in the terrestrial environment. Therefore, the risks to algae are acceptable with spray drift buffer zones.

4.3 Environment incident reports

1-Aminocyclopropanecarboxylic acid is a new active ingredient pending registration for use in Canada, and as of 24 August 2022, no incident reports had been submitted to the PMRA.

5.0 Value

Thinning of tree fruit is critical to increasing fruit size and therefore marketability and maximizing financial returns due to higher grading of fruits. Thinning is primarily accomplished via pruning, hand thinning or chemical thinning.

Information in support of the value of VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator consisted of data from thirteen field trials conducted in the United States (Oregon, Washington, Michigan, Pennsylvania, Maryland and New York), Canada (Ontario, BC and Nova Scotia), and Europe and included several popular varieties of apples. Various rates were tested as well as different application timings. The data suggest that VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator are effective at thinning apples relative to the control treatments, and are more effective than certain commercial standards, both alone and when used sequentially with other thinners. The data further demonstrated efficacy on larger fruitlets measuring 18-20 mm at the time of application, as well as acceptable thinning at different application timings. While presently registered thinning agents are applied at 10 mm fruitlet diameter, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator maintain effectiveness on larger fruitlet sizes up to 25 mm in diameter. The information provided also supports a claim of enhanced return bloom as well as the use of a non-ionic surfactant.

The registration of VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator will provide apple growers with a new active ingredient and end-use products for the purposes of fruit thinning and enhanced return bloom.

6.0 Pest control product policy considerations

6.1 Assessment of the active ingredient under the toxic substances management policy

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, i.e., those that meet all four criteria outlined in the policy: 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*. The *Pest Control Products Act* requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, 1-aminocyclopropanecarboxylic acid was assessed in accordance with the PMRA Regulatory Directive DIR99-03⁵ and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that 1-aminocyclopropanecarboxylic acid is a naturally occurring substance and does not meet all of the TSMP Track 1 criteria.

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

6.2 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.⁶ The list is used as described in the PMRA Science Policy Note SPN2020-01⁷ and is based on existing policies and regulations, including the *Toxic Substance Management Policy and Formulants Policy*,⁸ and taking into consideration the *Ozone-depleting Substances and Halocarbon Alternatives Regulations* under the *Canadian Environmental Protection Act, 1999*, (substances designated under the *Montreal Protocol*).

The PMRA has reached the conclusion that 1-aminocyclopropanecarboxylic acid and its end-use products VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator do not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*. The end-use products, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, contain the allergen, milk, which is on the *List of Pest Control Product Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions*.

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

7.0 Proposed regulatory decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of ACC Technical Powder, VBC-30452 SG Plant Growth Regulator and Accede SG Plant Growth Regulator, containing the technical grade active ingredient 1-aminocyclopropanecarboxylic acid, for commercial fruit tree thinning for apple trees.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

⁶ SI/2005-114, last amended on June 24, 2020. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

⁷ PMRA's Science Policy Note SPN2020-01, *Policy on the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under paragraph 43(5)(b) of the Pest Control Products Act*

⁸ DIR2006-02, *Formulants Policy and Implementation Guidance Document*

Additional information being requested

Since this technical product is manufactured only at pilot scale before registration, five-batch data representing commercial-scale production will be required as post-market information after registration.

List of abbreviations

µg	micrograms
µL	Microlitres
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
AOP WIN	Windows based atmospheric oxidation program
ARfD	acute reference dose
atm	atmosphere
bw, BW	body weight
BWG	body weight gain
CAS	Chemical Abstracts Service
cm	Centimetre(s)/centimeter(s)
d	Day(s)
DF	dry flowable
DIR	(Regulatory) Directive
DNA	deoxyribonucleic acid
DT ₅₀	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT ₉₀	dissipation time 90% (the dose required to observe a 90% decline in concentration)
dw	Dry weight
EAD	Environmental Assessment Directorate
EC ₂₅	effective concentration on 25% of the population
EC ₅₀	effective concentration on 50% of the population
EDE	Estimated dietary exposure
EEC	Estimated environmental concentration
EIIS	Ecological Incident Information System
EPA	Environmental Protection Agency
ER ₂₅	Effective rate 25%
ER ₅₀	Effective rate 50%
FIR	Food ingestion rate
g	gram
h	Hour(s)
ha	hectare(s)
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography

IUPAC	International Union of Pure and Applied Chemistry
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
kg	kilogram
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{oc}	Adsorption quotient normalized to organic carbon
KOCWIN	Windows based program model that estimates the K_{oc} for soil and sediment
K_{ow}	<i>n</i> -octanol-water partition coefficient
L	litre
LC ₅₀	lethal concentration 50%
LD ₅₀	lethal dose 50%
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOC	Level of concern
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR ₅₀	lethal rate 50%
MAS	maximum average score
MAS	maximum average score (at 24, 48 and 72-hrs)
mg	milligram
MIS	maximum irritation score (at a specified timepoint)
mL	millilitre
MMAD	mass median aerodynamic diameter
MOE	margin of exposure
mol.	Mole(s)
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
N/R	not required
nm	Nanometers
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content

Pa	Pascal
PBI	plantback interval
PHI	preharvest interval
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency
PND	postnatal days
PPE	personal protective equipment
ppm	parts per million
REI	restricted-entry interval
RQ	Risk quotient
RSD	relative standard deviation
SC	soluble concentrate
SD	standard deviation
SMILES	Simplified molecular-input line-entry system
SPN	Science Policy Note
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TGAI	technical grade active ingredient
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
US	United States
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and figures

Table 1 Toxicity profile of ACC Technical Powder

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons)

Study Type/Animal/PMRA#	Study Results
Acute toxicity studies ¹	
Acute oral toxicity (Acute Toxic Class Method) Rat, Sprague-Dawley (♀) PMRA# 3226811	LD ₅₀ > 4973.6 mg/kg bw/day) Low Toxicity
Acute dermal toxicity Rat, Sprague-Dawley PMRA# 3226813	LD ₅₀ > 3000 mg/kg bw (combined) Low toxicity
Acute inhalation toxicity (Nose-only exposure) Rat, Sprague-Dawley PMRA# 3226815	LC ₅₀ (combined) > 5.10 mg/L MMAD = 2.87 µm Low toxicity
Eye irritation Rabbit, New Zealand (♀) PMRA# 3226817	MAS = 0.2/110 (at 24, 48 and 72 hrs) MIS = 6.0/110 (1 h) No signs of irritation at 48 hrs. Minimally irritating
Skin Irritation Rabbit, New Zealand (♂) PMRA# 3226819	MAS = 0.78/8 (at 24, 48 and 72 hrs) MIS = 2/8 (24 hr) All signs of irritation resolved by 72 hours. Slightly irritating
Skin Sensitization (Local lymph node assay) CBA/J mice (♀) PMRA# 3226821	Negative Not a dermal sensitizer

Study Type/Animal/PMRA#	Study Results
Short-term toxicity studies ²	
90-Day oral (dietary) Mice - CRL CD PMRA# 3226823	NOAEL > 882.8 mg/kg bw/day (♂); 1071.2 mg/kg bw/day (♀)
28-Day dermal Rat, Sprague-Dawley PMRA# 3226831	NOAEL > 1000 mg/kg bw/day (combined)
Developmental/Reproductive Toxicity Studies ²	
Prenatal Developmental Toxicity Rat, Sprague-Dawley PMRA# 3226838	<p>Maternal NOAEL > 982 mg/kg bw/day, HTD</p> <p>Developmental NOAEL > 982 mg/kg bw/day, HTD</p> <p>No evidence of sensitivity of the young.</p>
Extended one-generation reproductive toxicity (dietary) Rat- CRL Sprague-Dawley CD PMRA# 3226834	<p>Parental Toxicity : NOAEL ♂=136 mg/kg bw/day</p> <p>≥ 271 mg/kg bw/day: ↓ BWG (♂)</p> <p>≥ 543 mg/kg bw/day: ↓ BW (♂)</p> <p>NOAEL ♀ > 647 mg/kg/d prior to mating, HTD</p> <p>Offspring Toxicity: NOAEL ♂ = 348 mg/kg/day</p> <p>≥ 701 mg/kg bw/day: ↓ BW (PND98, PND119), ↓ BWG (PND21-119), ↑ liver wt, ↑ AST (♂)</p> <p>NOAEL ♀ > 763 mg/kg bw/day, HTD</p> <p>Reproductive Toxicity: NOAEL > HTD, 701 mg/kg bw/day ♂; 763 mg/kg bw/day ♀</p> <p>No treatment-related effects.</p>

Study Type/Animal/PMRA#	Study Results
	No evidence of sensitivity of young.
Genotoxicity Studies	
Bacterial Reverse Mutation Assay ³ S. typhimurium (TA98, TA100, TA1535, TA1537) Escherichia coli WP2uvrA PMRA# 3226840	Negative
Chromosome aberration assay ⁴ Chinese hamster ovary K-1 (CHO K-1) cells PMRA# 3347687	Negative

¹ The test substance for all acute toxicity studies was 1-aminocyclopropanecarboxylic acid (96.68% w/w; solid). This test substances is considered equivalent to the TGAI, ACC Technical Powder containing 1-Aminocyclopropane-1-carboxylic acid at 98.5% w/w.

² The test substance for the 90-d dietary toxicity study, the 28-d dermal toxicity study, the prenatal developmental toxicity study and the extended one-generation reproductive toxicity study was VBC-30449, containing 1-aminocyclopropane-1-carboxylic acid at 94.5-96.68%. This test substances is considered equivalent to the TGAI, ACC Technical Powder containing 1-Aminocyclopropane-1-carboxylic acid at 98.5% w/w.

³ The test substance for in vitro bacterial genotoxicity testing was 1-Aminocyclopropane-1-carboxylic acid (96.68% w/w; solid). This test substances is considered equivalent to the TGAI, ACC Technical Powder containing 1-Aminocyclopropane-1-carboxylic acid at 98.5% w/w.

⁴ The test substance for the chromosome aberration assay was VCB-30449, containing 1-Aminocyclopropane-1-carboxylic acid at 95.1%. This test substances is considered equivalent to the TGAI, ACC Technical Powder containing 1-Aminocyclopropane-1-carboxylic acid at 98.5% w/w.

Table 2 Toxicity profile of VBC-30452 Plant Growth Regulator and Accede SG Plant Growth Regulator

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons)

Study Type/Animal/PMRA # ¹	Study Results
Acute Oral Toxicity Rat, Sprague Dawley (♀) PMRA# 3226901	LD ₅₀ > 5000 mg/kg bw/day Low toxicity
Acute Dermal Toxicity Rat, Sprague Dawley	LD ₅₀ > 5050 mg/kg bw No signs of irritation

Study Type/Animal/PMRA # ¹	Study Results
PMRA# 3226903	Low toxicity
Acute Inhalation Toxicity Rat, Sprague Dawley	LC ₅₀ > 5.10 mg/L
PMRA# 3226905	Low toxicity
Eye Irritation Rabbit, New Zealand White (♀)	MAS (at 24, 48, and 72 hrs)= 0/110 MIS (1h)=0/110 Non-irritating
PMRA# 3226907	
Primary Skin Irritation Rabbit, New Zealand White (♀)	MAS (at 24, 48, and 72-hrs)= 0/8 MIS (1h)= 0/8 Non-irritating
PMRA# 3226907	
Skin Sensitization (Local lymph node assay) Mouse, CBA/J (♀)	Negative Not a dermal sensitizer
PMRA# 3226911	

¹ The test substance for all acute toxicity testing for the EP was VBC-30452 Plant Growth Regulator, containing 1-aminocyclopropanecarboxylic acid, 40% w/w.

Table 3 Fate and behaviour in the environment

Property	Value	Comments	PMRA #
Abiotic Transformation			
Atmospheric hydroxylation half-life	5.9 h	Rapid transformation in the atmosphere. Estimated using AOP WIN v1.92	3226806
Biotransformation			
Aerobic soil biotransformation DT _{50s} (Conducted in darkness at 20°C)	0.814 d (Sandy Clay Loam) 1.18 d (Loamy Sand) 2.55 d (Clay Loam) 3.4 d (Sandy Loam)	Rapid biotransformation in aerobic soil. Both major TPs (CO ₂ , 2-ketobutyric acid) are naturally occurring. Study not reviewed in full (only summary provided).	3226844

Property	Value	Comments	PMRA #
Bioconcentration factor (BCF)	3.162	Low potential for bioaccumulation Estimated using BCFBAF v3.01	3136539
Mobility			
Adsorption coefficient	$K_{oc} = 1 \text{ L/kg}$	Not bound tightly to soil. Estimated using KOCWIN v2.00	3226844
Volatility	Vapour pressure : $3.64 \times 10^{-5} \text{ Pa}$ at 25°C $1.78 \times 10^{-5} \text{ Pa}$ (estimated) at 20°C Henry's law constant: $2.7 \times 10^{-8} \text{ Pa m}^3 \text{ mol}^{-1}$ at 20°C	Non-volatile under field conditions. Not likely to volatilize from surface waters and moist soils.	3226806

Table 4 Toxicity to non-target species

Organism	Exposure	Test Substance (purity)	Toxicity Endpoint	Degree of Toxicity ¹	PMRA #
Terrestrial Organisms					
Honeybee (<i>Apis mellifera</i> L.)	48 h	VBC-30449 (96.68%)	Oral LD ₅₀ > 254.4 µg a.i./bee Contact LD ₅₀ > 120.9 µg a.i./bee	Relatively non-toxic	3226846
Honeybee (<i>Apis mellifera</i> L.)	48 h	VBC-30452 (39.99%)	Oral LD ₅₀ > 43.0 µg a.i./bee Contact LD ₅₀ > 60.0 µg a.i./bee	Relatively non-toxic	3226848
Northern Bobwhite (<i>Colinus virginianus</i>)	14 d	VBC-30108 (101.1%)	Oral LD ₅₀ = 343 mg a.i./kg bw	Moderately toxic	3226856
Northern Bobwhite (<i>Colinus virginianus</i>)	5 d	VBC-30449 (96.68%)	Dietary LC ₅₀ = 5106 mg a.i./kg diet (1712 mg a.i./kg bw/day)	Practically non-toxic	3226858

Organism	Exposure	Test Substance (purity)	Toxicity Endpoint	Degree of Toxicity ¹	PMRA #
Terrestrial plants (10 species)	21 d (vegetative vigour)	VBC-30445 (10.1%)	ER ₂₅ (all species % survival, shoot length, shoot dw) > 600 g a.i./ha	N/A	3226868
Terrestrial plants (10 species)	14 d (seedling emergence)	VBC-30445 (10.1%)	ER ₂₅ (tomato shoot dw) = 0.98 g a.i./ha ER ₂₅ (other species shoot length, % survival) > 600 g a.i./ha	N/A	3226866
Aquatic Organisms					
Daphnid (<i>Daphnia magna</i>)	48 h (static)	VBC-30449 (94.9%)	EC ₅₀ (signs of toxicity) > 105 mg a.i./L (mean-measured)	Practically non-toxic	3226850
Daphnid (<i>Daphnia magna</i>)	21 d (semi-static)	VBC-30449 (94.9%)	NOEC (reproduction) = 11.3 mg a.i./L (mean-measured)	N/A	3226852
Rainbow trout (<i>Oncorhynchus mykiss</i>)	96 h (static)	VBC-30108 (101.1%)	LC ₅₀ > 117 mg a.i./L (mean-measured)	Practically non-toxic	3226854
Freshwater green alga (<i>Pseudokirchneriella subcapitata</i>)	96 h (static)	VBC-30449 (94.9%)	EC ₅₀ (area under growth curve) = 0.037 mg a.i./L (mean-measured)	Very highly toxic	3226860
Freshwater aquatic plant (<i>Myriophyllum spicatum</i>)	14 d (semi-static)	VBC-30449 (95.1%)	EC ₅₀ (fresh weight yield) = 1.28 mg a.i./L	Moderately toxic	3226862

¹ USEPA classification for others, where applicable; N/A=not applicable

Table 5 Endpoints and uncertainty factors used to establish effects metrics for the risk assessment

Organism	Test Substance	Exposure	Endpoint Value	UF ¹ applied	Effects Metrics	LOC ²
Terrestrial Organisms						
Pollinators: Honeybee (<i>Apis mellifera</i> L.)	VBC-30452 (39.99%)	Acute contact adult	48-h LD ₅₀ > 60.0 µg a.i./bee	1	> 60.0 µg a.i./bee	0.4
		Acute oral adult	48-h LD ₅₀ > 43.0 µg a.i./bee	1	> 43.0 µg a.i./bee	0.4
Birds: Northern Bobwhite (<i>Colinus virginianus</i>)	VBC-30108 (101.1%)	Acute oral	LD ₅₀ = 343 mg a.i./kg bw	10	34.3 mg a.i./kg bw	1
	VBC-30449 (96.68%)	Acute dietary	5-d LD ₅₀ = 5106 mg a.i./kg diet (1712 mg/kg bw/day)	10	171.2 mg a.i./kg bw/day	1
Terrestrial Plants: Standard Test Species	VBC-30445 (10.1%)	Vegetative vigour	ER ₂₅ > 600 g a.i./ha	1	> 600 g a.i./ha	1
Terrestrial Plants: Standard Test Species	VBC-30445 (10.1%)	Seedling emergence	ER ₂₅ = 0.98 g a.i./ha (tomato shoot length, dw)	1	0.98 g a.i./ha	1
Aquatic Organisms (Freshwater)						
Invertebrates: Water flea (<i>Daphnia magna</i>)	VBC-30449 (94.9%)	Acute	48-h EC ₅₀ > 105 mg a.i./L (signs of toxicity)	2	> 52.5 mg a.i./L	1
	VBC-30449 (94.9%)	Chronic	21-d NOEC = 11.3 mg a.i./L (reproduction)	1	11.3 mg a.i./L	1
Fish: Rainbow trout (<i>Oncorhynchus mykiss</i>)	VBC-30108 (101.1%)	Acute	96-h LC ₅₀ > 117 mg a.i./L	10	> 11.7 mg a.i./L	1
Amphibians: Rainbow trout (<i>Oncorhynchus mykiss</i>) ³	VBC-30108 (101.1%)	Acute	96-h LC ₅₀ > 117 mg a.i./L	10	> 11.7 mg a.i./L	1
Green algae (<i>Pseudokirchneriella</i>)	VBC-30449	Acute	96-h EC ₅₀ = 0.037 mg	2	0.0185 mg a.i./L	1

Organism	Test Substance	Exposure	Endpoint Value	UF ¹ applied	Effects Metrics	LOC ²
Terrestrial Organisms						
<i>subcapitata</i>)	(94.9%)		a.i./L (area under growth curve)			
Aquatic vascular plant (<i>Myriophyllum spicatum</i>)	VBC-30449 (95.1%)	Acute	14-d EC ₅₀ = 1.28 mg a.i./L (fresh weight yield)	2	0.64 mg a.i./L	1

¹ UF = uncertainty factor; as per the Guidance Manual; ²LOC = Level of Concern; ³used as a surrogate for amphibians.

Table 6 Screening level and refined risk to bees and non-target terrestrial plants

Organism Class (Species)	Exposure	Endpoint Value	EEC ¹	RQ ²	LOC ³	LOC Exceeded
Honeybee (<i>Apis mellifera</i> L.)	Adult contact acute	LD ₅₀ > 60.0 µg a.i./bee	0.960 µg a.i./bee	< 0.0160	0.4	No
	Adult oral acute	LD ₅₀ > 43.0 µg a.i./bee	11.5 µg a.i./bee	< 0.266	0.4	No
Vascular plants	Vegetative vigour	ER ₂₅ > 600 g a.i./ha	<i>In-field</i> : 646 g a.i./ha ⁴	< 1.07	1	Yes
			<i>Off-field</i> : Airblast application, early season (74%): 478 g a.i./ha Airblast application, late season (59%): 381 g a.i./ha	< 0.8 < 0.63		No
	Seedling emergence	ER ₂₅ = 0.98 g a.i./ha	<i>In-field</i> : 496 g a.i./ha ⁵	506	1	Yes
			<i>Off-field</i> : Airblast application, early season (74%): 367 g a.i./ha Airblast application, late season (59%): 293 g a.i./ha	374 298.5	1 1	Yes

¹EEC = Estimated Environmental concentration.

- The pollinator EECs were calculated using the maximum single proposed rate of 400 g a.i./ha, as follows:
Estimated contact exposure = 2.4 µg a.i./bee × 0.400 kg a.i./ha; and
Estimated dietary exposure = 29 µg a.i./bee × 0.400 kg a.i./ha.

²RQ = Risk Quotient. The RQ is calculated by dividing the EEC by the endpoint value (RQ = EEC/endpoint value)

³LOC = Level of Concern. The RQ is compared to the LOC.

⁴maximum cumulative seasonal rate of 1-aminocyclopropanecarboxylic acid (multiple application rates of 400 + 400 g a.i./ha, 7-day interval and

considering a default 10- day foliar half- life)

⁵ maximum cumulative seasonal rate of 1-aminocyclopropanecarboxylic acid (multiple application rates of 400 + 400 g a.i./ha, 7-day interval and considering a soil half- life of 3.4 days)

Table 7 Screening level and refined risks to birds exposed to 1-Aminocyclopropanecarboxylic Acid

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg ai/kg bw/d)	Food Guild (food item) ¹	EDE (mg ai/kg bw) ²	RQ ³	EDE (mg ai/kg bw)	RQ	EDE (mg ai/kg bw)	RQ	EDE (mg ai/kg bw)	RQ
Small Bird (0.02 kg)										
Acute	34.30	Insectivore	52.60	1.5	38.93	1.1	36.32	1.06	26.88	0.78
	34.30	Granivore (grain and seeds)	8.14	0.2	6.02	0.2	3.88	0.11	2.87	0.08
	34.30	Frugivore (fruit)	16.28	0.5	12.05	0.4	7.77	0.23	5.75	0.17
Dietary	171.20	Insectivore	52.60	0.3	38.93	0.2	36.32	0.21	26.88	0.16
	171.20	Granivore (grain and seeds)	8.14	0.0	6.02	0.0	3.88	0.02	2.87	0.02
	171.20	Frugivore (fruit)	16.28	0.1	12.05	0.1	7.77	0.05	5.75	0.03
Medium Sized Bird (0.1 kg)										
Acute	34.30	Insectivore	41.05	1.2	30.38	0.9	28.34	0.83	20.97	0.61
	34.30	Granivore (grain and seeds)	6.35	0.2	4.70	0.1	3.03	0.09	2.24	0.07
	34.30	Frugivore (fruit)	12.71	0.4	9.40	0.3	6.06	0.18	4.48	0.13
Dietary	171.20	Insectivore	41.05	0.2	30.38	0.2	28.34	0.17	20.97	0.12
	171.20	Granivore (grain and seeds)	6.35	0.0	4.70	0.0	3.03	0.02	2.24	0.01
	171.20	Frugivore (fruit)	12.71	0.1	9.40	0.1	6.06	0.04	4.48	0.03
Large Sized Bird (1 kg)										
Acute	34.30	Insectivore	11.99	0.3	8.87	0.3	8.28	0.24	6.12	0.18
	34.30	Granivore (grain and seeds)	1.85	0.1	1.37	0.0	0.88	0.03	0.65	0.02
	34.30	Frugivore (fruit)	3.71	0.1	2.75	0.1	1.77	0.05	1.31	0.04
	34.30	Herbivore (short grass)	26.52	0.8	19.62	0.6	9.42	0.27	6.97	0.20
	34.30	Herbivore (long grass)	16.19	0.5	11.98	0.3	5.29	0.15	3.91	0.11
	34.30	Herbivore (Broadleaf plants)	24.53	0.7	18.15	0.5	8.11	0.24	6.00	0.17

¹Specialized feeding guilds are considered for each category of animal weights to help determine exposure (herbivore, frugivore, insectivore and granivore).
²EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/BW) × EEC, where: FIR: Food Ingestion Rate, BW: Body Weight, EEC: Estimated Environmental Concentration. For generic birds with body weight less than or equal to 200 g, the “passerine” equation was used; for generic birds with body weight greater than 200 g, the “all birds” equation was used: Passerine Equation (BW < or = 200 g): FIR (g dry weight/day) = 0.398(BW in g)^{0.850}
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(BW in g)^{0.651}.
³RQ = Risk Quotient. The RQ is calculated by dividing the EDE by the endpoint value (RQ = EDE/endpoint value).

Table 8 Screening level and refined risks to aquatic organisms exposed to 1-Aminocyclopropanecarboxylic Acid

Organism Class (Species)	Exposure	Endpoint and Uncertainty Factor Applied	Effects Metrics	Direct Overspray EEC ¹	RQ ²	LOC ³	LOC Exceeded	
				(mg a.i./L)				
Freshwater species								
Water flea (<i>Daphnia magna</i>)	Acute	LC ₅₀ /2	> 52.5	0.1	< 0.0019	1	No	
	Chronic	NOEC	11.3	0.1	0.0088	1	No	
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Acute	LC ₅₀ /10	> 11.7	0.1	< 0.0085	1	No	
Aquatic-phase amphibians (Rainbow trout as surrogate)	Acute	LC ₅₀ /10	> 11.7	0.53	< 0.045	1	No	
Green algae (<i>Pseudokirchneriella subcapitata</i>)	Acute	EC ₅₀ /2	0.0185	0.1	5.4	1	Yes	
				Airblast drift ⁴	E. season: 0.074			4.00
					L. season: 0.059			3.18
Aquatic vascular plant (<i>Myriophyllum spicatum</i>)	Acute	EC ₅₀ /2	0.64	0.1	0.156	1	No	

¹EEC = Estimated Environmental Concentration. Calculated assuming a maximum cumulative application of 400 × 2 g a.i./ha to water bodies of 80 cm depth (aquatic invertebrates, fish, and aquatic plants) and 15 cm depth (amphibian).
²RQ = Risk quotient. The RQ is calculated by dividing the EEC by the endpoint value (RQ = EEC/endpoint value).
³LOC = Level of concern. The RQ is compared to the LOC. If the screening level risk quotient is below the level of concern, the risk is considered acceptable and no further risk characterization is necessary.
⁴Further characterisation based on spray drift for airblast application: 74 % drift (early season) and 59% drift (late season).

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