Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Note REG2006-03

Potassium Bicarbonate

The reduced risk active ingredient potassium bicarbonate and associated end-use product MilStop Foliar Fungicide (containing 85% by weight of the active ingredient) have been granted temporary registrations under the Pest Control Products Regulations for the control/suppression of powdery mildew on tomatoes, sweet peppers, cucumbers, pumpkins, flowering dogwood, bee balm, African daisy, hydrangea, phlox and poinsettia in greenhouses.

This Regulatory Note provides a summary of data reviewed and the rationale for the regulatory decision for these reduced risk products.

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Foreword

Health Canada's Pest Management Regulatory Agency (PMRA) has issued temporary registrations for the reduced risk technical grade active ingredient potassium bicarbonate and the associated end-use product MilStop Foliar Fungicide for the control/suppression of powdery mildew on tomatoes, sweet peppers, cucumbers, pumpkins, flowering dogwood, bee balm, African daisy, hydrangea, phlox and poinsettia in greenhouses.

The PMRA has carried out an assessment of available information in accordance with the Pest Control Products Regulations and has found it sufficient to allow a determination of the safety, merit and value of these reduced risk products. The Agency has concluded that the use of potassium bicarbonate and the end-use product MilStop Foliar Fungicide for control/suppression of powdery mildew on tomatoes, sweet peppers, cucumbers, pumpkins, flowering dogwood, bee balm, African daisy, hydrangea, phlox and poinsettia in greenhouses in accordance with the label has merit and value consistent with the Pest Control Regulations and does not entail an unacceptable risk of harm. Therefore, based on the considerations outlined above, potassium bicarbonate and the associated end-use product MilStop Foliar Fungicide have been granted temporary registration under the Pest Control Products Regulations.

BioWorks, Inc. will be carrying out confirmatory studies as a condition of this temporary registration. Following the review of this information, the PMRA will publish a proposed regulatory decision document and request comments from interested parties before proceeding with a final regulatory decision.

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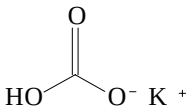
1.0 The Active Substance, its Properties and Uses

1.1 Identity of the Active Substance and Impurities

Identification of the Technical Grade Active Ingredient

Active substance	Potassium bicarbonate
Function	Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry	Potassium bicarbonate
2. Chemical Abstracts Service (CAS)	Potassium acid carbonate
CAS number	298-14-6
Molecular formula	$KHCO_3$
Molecular weight	100.11
Structural formula	
Nominal purity of active	99.9%
Identity of relevant impurities of toxicological, environmental or other significance	The technical grade potassium bicarbonate does not contain any microcontaminants known to be Toxic Substances Management Policy (TSMP) Track 1 substances.

1.2 Physical and Chemical Properties of Active Substances and End-use Product

Technical Product—Potassium Bicarbonate

Property	Result
Colour and physical state	Colourless solid
Odour	Odourless
Melting point or range	Melts with decomposition between 100°C and 200°C
Boiling point or range	N/A

Property	Result
Specific gravity	2.17
Vapour pressure at 20°C	Negligible
Henry's law constant at 20°C	N/A
Ultraviolet (UV)–visible spectrum	Does not absorb UV
Solubility in water	22.4 g in 100 mL cold water
Solubility in organic solvents	Insoluble in ethanol and acetone
n-Octanol–water partition coefficient (K_{ow})	N/A
Dissociation constant (pK_a)	pK_{a1} = 6.37 for carbonic acid (dissociating to form the bicarbonate ion) pK_{a2} = 10.25 for carbonic acid (bicarbonate ion dissociating to form the carbonate ion)
Stability (temperature, metal)	Stable to most metals. The compound decomposes when it is heated, first forming potassium carbonate by loss of water and then potassium oxide, by loss of carbon dioxide. Reacts with acids.

End-use Product—MilStop Foliar Fungicide

Property	Result
Colour	White to off-white
Odour	Mild, characteristic odour
Physical state	Solid
Formulation type	Dust or powder
Nominal guarantee	85%
Formulants	The product does not contain any United States Environmental Protection Agency (USEPA) or PMRA List 1 or List 2 formulants or formulants known to be TSMP Track 1 substances.
Container material and description	5 lb polyethylene bags
Density	0.76–0.86 g/cm^3
pH of 1% dispersion in water	8.0–8.4

Property	Result
Oxidizing or reducing action	N/A
Storage stability	Stable for 12 months when stored at ambient temperature in commercial packaging
Explodability	N/A

1.3 Details of Uses

The end-use product MilStop Foliar Fungicide contains 85% potassium bicarbonate. Potassium bicarbonate is toxic to fungal cells through the combined actions of pH, osmotic pressure and specific carbonate/bicarbonate interactions. Although it has protectant and mild curative properties, preventive applications prior to the spread of disease symptoms or just at the beginning of the disease will provide better protection of crops.

MilStop Foliar Fungicide is to be used for the control/suppression of powdery mildew on vegetable crops (tomato, sweet pepper, cucumber and pumpkin) and on ornamental plants (flowering dogwood, bee balm, African daisy, hydrangea, phlox and poinsettia) grown in greenhouses.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Substance as Manufactured

The technical product meets the requirements for food grade material specified for potassium bicarbonate in the Food Chemicals Codex. The same analytical methods referenced by the Codex were used to confirm the food quality. The methods are from XII USP XXII - NF XVII (United States Pharmacopea XII edition, National Formulary XVII edition, 1993) and are well established analytical methods.

2.2 Method for Formulation Analysis

A titration method was provided for the determination of the active ingredient in the formulation. A sample of the product is dissolved in water and titrated to the methyl orange endpoint with standard hydrochloric acid. The level of potassium bicarbonate in the material is calculated from the concentration and volume of titrant used.

The method was assessed to be acceptable for use as an enforcement analytical method.

3.0 Impact on Human and Animal Health

3.1 Integrated Toxicological Summary

Potassium bicarbonate was of low acute oral (lethal dose 50% [LD_{50}] 2064 mg/kg bw), dermal (LD_{50} > 2000 mg/kg bw) and inhalation (lethal concentration 50% [LC_{50}] > 4.88 ± 0.06 mg/L) toxicity. It was, however, minimally irritating to the skin and mildly irritating to the eyes. Potassium bicarbonate is not a skin sensitizer.

An evaluation of available literature indicates that potassium bicarbonate is not a developmental, reproductive or nervous system toxicant, a carcinogen or a genotoxicant.

A survey of the publically available literature has demonstrated that one component in one of the formulants that comprises MilStop Foliar Fungicide is a moderate skin irritant and mild eye irritant. The acute toxicity of the end-use product is expected to remain low and MilStop Foliar Fungicide is not expected to be a dermal sensitizer.

3.2 Determination of Acceptable Daily Intake

Potassium bicarbonate is food grade, as per Food Chemicals Codex; thus, an acceptable daily intake was not necessary.

3.3 Acute Reference Dose

No acute effects were observed from administration of a single dose of potassium bicarbonate. Therefore, setting an acute reference dose was not necessary.

3.4 Toxicological Endpoint Selection—Occupational and Bystander Risk Assessment

The qualitative risk assessment anticipates exposure to the applicator and worker. An unlimited number of applications of MilStop Foliar Fungicide per growing season is assumed; thus, exposure of the affected personnel should be considered continuous throughout the growing season. Bystanders are not expected to enter the treated area; therefore, they were not considered for the risk assessment. The primary routes of exposure are by the dermal and inhalation routes.

Evaluation of acute studies and available literature of potassium bicarbonate and the formulants in MilStop Foliar Fungicide did not yield any concerns based on acute oral, dermal and inhalation toxicity. One component in a formulant in MilStop Foliar Fungicide did, however, cause moderate skin and eye irritation in test animals. The component was tested at concentrations at or below those found in MilStop Foliar Fungicide. There was no apparent potential for skin sensitization associated with potassium bicarbonate or MilStop Foliar Fungicide.

An examination of available literature supported the position that potassium bicarbonate was not a developmental, reproductive or nervous system toxicant, a carcinogen or a genotoxicant. In general, the effects observed from the analysis of submitted and publically available literature for potassium bicarbonate and the formulants in MilStop Foliar Fungicide were primarily eye and skin irritation.

Dermal absorption was not evaluated; therefore, adequate personal protective equipment, hygiene and ventilation have been recommended to mitigate the need for such a study.

3.5 Impact on Human and Animal Health Arising from Exposure to the Active Substance or to its Impurities

3.5.1 Operator Exposure Assessment

There is a potential for exposure to the applicator when applying MilStop Foliar Fungicide to greenhouse crops. Application is by foliar spray, using a calibrated sprayer. Exposure estimates were not evaluated for mixers, loaders or applicators, but it is anticipated that the use of appropriate eyewear, waterproof gloves, long-sleeved shirt and pants or coveralls, footwear with socks as well as adequate ventilation should be sufficient to minimize the risk due to exposure of MilStop Foliar Fungicide.

There is a potential for postapplication exposure to the crops treated with MilStop Foliar Fungicide but a dislodgeable foliar residue study was not requested. A precautionary statement on the secondary label advises that a four-hour re-entry interval be observed prior to entering the treated area. If re-entry is sooner and contact is expected with anything that has been treated, such as plants, soil or water, a long-sleeved shirt and pants or coveralls, waterproof gloves, and shoes plus socks are required. Because a foliar residue analysis was not performed and the number of applications per growing season has not been limited, it is recommended that gloves, long-sleeved shirt and pants or coveralls as well as shoes and socks be worn for any postapplication activities, even after the four-hour re-entry interval.

3.5.2 Bystanders

It is expected that only applicators and workers will be permitted access to the treated crops. Thus, an exposure assessment of bystanders is not necessary.

3.5.3 Workers

An exposure assessment of the workers was not evaluated; thus, as a precautionary measure, it is recommended that gloves, a long-sleeved shirt and pants or coveralls as well as footwear and socks be worn for any postapplication activity.

4.0 Residues

4.1 Residue Summary

Food grade potassium bicarbonate is exempted from the requirements for establishing a maximum residue limit in food or feed crops.

5.0 Fate and Behaviour in the Environment

Potassium and bicarbonate are naturally occurring ions. Due to their ubiquitous nature, the addition of potassium bicarbonate to the environment based on greenhouse uses (as MilStop) is not expected to be a concern. Furthermore, the environmental fate and behaviour of potassium bicarbonate are well documented and understood. The chemical is highly soluble (22 g/100 mL cold water) and the primary route of exposure to the environment from greenhouses would be through discharge of dissolved forms in effluent water. Potassium bicarbonate is an inorganic salt that rapidly dissociates at environmentally relevant pHs (pKa 6.37) to the potassium and bicarbonate ions. Neither the potassium bicarbonate molecule nor its dissociated ions are volatile. Dissociation in the presence of water to potassium and bicarbonate ions is the primary fate of potassium bicarbonate, and no hydrolysis or phototransformation occurs. Potassium does not transform further, and the primary route of transformation of bicarbonate in the environment occurs by the molecule becoming incorporated into the carbon cycle. Because of the high water solubility, potassium and bicarbonate are naturally mobile in soil and will leach, but this would be limited to the unbound form of the ions only.

Potassium is not found as an element in the environment, but is found either dissolved or in compound form. The bicarbonate ion, under natural conditions in the absence of water, is present in compound forms that are stable. In the presence of water, these compounds dissociate and the bicarbonate component will reach equilibrium with the carbon dioxide, water and carbonate ion cycling that is occurring normally.

Natural levels of potassium in soil can exceed 20 000 mg/kg; however, much of this is chemically bound, insoluble and only slowly available for plant growth (through weathering processes of the soil causing release of bound potassium). Potassium is found in seawater at concentrations of approximately 385 mg/L. Natural levels in freshwater are lower; registrant-submitted data indicated that potassium in Oregon streams ranged from 0.3 to 1.1 mg/L, and the level was approximately 14 mg/L in a lake.

Bicarbonate is naturally present in surface waters due to the equilibrium between dissolved carbon dioxide and carbonic acid, carbonic acid and bicarbonate, and bicarbonate and carbonate. The major source of bicarbonate in ocean waters is weathering and erosion of continental rocks, which contributes enormous amounts. In soil, bicarbonate is present primarily through contributions from weathering rocks containing carbonate.

Environmental concentrations of potassium bicarbonate based on the use pattern are expected to be low. Assuming no degradation, direct application and an application frequency of 6 times per season (considered standard) at the maximum rate, soil concentrations are conservatively estimated to be 12.7 mg a.i./kg and water to be 9.5 mg a.i./L. The actual values of potassium bicarbonate in soil and water, particularly due to greenhouse uses, would likely be considerably lower.

6.0 Effects and Risk on Non-target Species

Potassium and bicarbonate are used in the physiological processes of all living cells. Therefore, due to the ubiquitous occurrence of potassium and bicarbonate in the environment, the requirement of these chemicals for physiological processes and the anticipated low environmental input, the potential risk posed to terrestrial organisms in the environment due to the greenhouse use of potassium bicarbonate is considered low. Standard label statements for greenhouse uses are required (Section 6.1).

The PMRA promotes the use of products that are compatible with integrated pest management (IPM) practices in greenhouses. Data or information were not submitted by the applicant addressing the potential effects of potassium bicarbonate used in greenhouses on beneficial invertebrate species (predators and parasites) used in coincident IPM programs. The PMRA is asking that the registrant provides further clarification regarding their request for waivers concerning effects of potassium bicarbonate on terrestrial invertebrates, with an emphasis on how the proposed application in greenhouses will affect beneficial invertebrate species typically used for IPM purposes. In addition, the PMRA is requiring that the applicant monitor the effects of potassium bicarbonate on beneficial invertebrates in greenhouses once the product is in use in these operations.

6.1 Risk Mitigation

Changes and additions are required to the current label statements related to the environment on the proposed end-use product label.

Under the **DIRECTIONS FOR USE** heading, add the following text.

> DO NOT allow effluent or runoff from greenhouses or mushroom houses containing this product to enter lakes, streams, ponds or other waters.

Remove all current text under the **STORAGE AND DISPOSAL** heading. Replace this heading with a separate **STORAGE** heading and **DISPOSAL** heading. Under the new **STORAGE** heading add the following text.

> To prevent contamination, store this product away from food or feed.

Under the new **DISPOSAL** heading add the following text.

> DO NOT reuse this container for any purpose. This container is recyclable and is to be disposed of at a container collection site. Contact your local distributor/dealer or municipality for the location of the nearest collection site. Before taking the container to the collection site:
>
> 1. Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.
>
> 2. Make the empty, rinsed container unsuitable for further use.
>
> If there is no container collection site in your area, dispose of the container in accordance with provincial requirements.

7.0 Efficacy

7.1 Mode of Action

MilStop is a contact fungicide. The active ingredient, potassium bicarbonate serves both as a protectant and as a mild curative fungicide. The toxic effects of potassium bicarbonate to mildew fungi are thought to be the combined action of osmotic pressure, pH, and specific bicarbonate/carbonate interactions. Preventive applications of Milstop fungicide when environmental conditions are favourable for disease development or applications just at the beginning of the disease infestation will provide better protection of crops.

7.2 Efficacy Summary

MilStop Foliar Fungicide (potassium bicarbonate 85%) at 2.8 to 5.6 kg product/ha has been proposed for the control of powdery mildew on tomato, sweet pepper, cucumber, pumpkin, flowering dogwood, bee balm, African daisy, hydrangea, phlox, gerber daisy and poinsettia grown in greenhouses. Results of 18 efficacy trials conducted in Israel, the Netherlands and the United States were submitted in support of the claims. MilStop Fungicide was applied as a foliar spray to complete coverage of foliage and stems using conventional ground application equipment.

Efficacy data showed that MilStop Fungicide at a rate of 0.28 kg/1000 m^2 to 0.56 kg/1000 m^2 or 1/10 hectare in greenhouse and at 2.8 kg/ha to 5.6 kg/ha in field after 1 to 8 applications significantly controlled or suppressed powdery mildew on vegetable crops (tomato, sweet pepper, cucumber and pumpkin) and on ornamental plants (flowering dogwood, bee balm, African daisy, hydrangea, phlox and poinsettia) (Table in Section 7.5). Results showed that one application of potassium bicarbonate provided control up to 7 to 8 days on vegetables and up to 14 days on ornamentals. Therefore,

multiple applications of MilStop will be needed for season long control of powdery mildew in greenhouses.

No phytotoxic effects were observed on any of the tested plants except the gerber daisy. Water volume plays a significant role in the development of phytotoxicity as it determines the concentration of spray solution and the amount of MilStop Fungicide being sprayed. Results suggest that the amount of water volume should be different for different plant species and in general, water volumes of 1000 to 2000 L/ha are recommended.

7.3 Resistance Management

No evidence of development of resistance to MilStop Fungicide has been recorded. Based on the mode of action, the development of resistance to potassium bicarbonate is unlikely in powdery mildew populations. This low resistance development risk allows the use of multiple applications of MilStop per season. MilStop Fungicide will provide a low risk alternative to registered products and help in the prevention of resistance build-up to registered fungicides.

7.4 Sustainability

Biological pest management practices, such as the inundative release of predatory insects, are a key part of an Integrated Pest Management programs widely used in greenhouse vegetable production. Reduced risk alternatives to conventional chemical pest control products that are compatible with current biological methods are necessary to maintain a sustainable greenhouse vegetable sector. Confirmatory data on its effects on beneficial invertebrates used within an IPM program is still needed. Nonetheless, MilStop is a reduced risk product with low risks to workers, consumers and the environment as well as an effective product in controlling mildew in a variety of greenhouse crops.

7.5 Summary of Supported Uses

Supported Uses of Milstop Foliar Fungicide for the Control/Suppression of Powdery Mildew on Vegetable and Ornamental Plants

Crops	Use Sites	Pathogens	Rate (kg/ha)	Days Between Applications	Spray Volume (L/ha)	Control/ Suppression
Vegetables	Greenhouse					
Cucumber, sweet pepper, tomato		*Podosphaera xanthii*, *Leveillula taurica*, *Oidium lycopersicon*	5.6	7	2 000	Control
Pumpkin		*Podosphaera xanthi*	5.6	7	1 000	Suppression*
Ornamentals	Greenhouse					
Flowering dogwood, bee balm		*Microsphaera* sp., *Erysiphe cichoracearum*	5.6	7–14	1 000	Control
African daisy		*Oidium* sp.	2.8–5.6	7–14	1 000	Control
Hydrangea, poinsettia		*Erysiphe polygoni*, *Oidium* sp.	5.6	7–14	2 000	Control
Phlox		*Erysiphe cichoracearum*	2.8–5.6	7–14	1 000	Suppression*

* Suppression is defined as consistent control at a level that is not optimal but is still of commercial benefit.

NOTE: Use the high rate (5.6 kg product/ha) and short application interval (7 days) when conditions favour the development of powdery mildew.

8.0 Toxic Substances Management Policy Considerations

During the review of potassium bicarbonate, the PMRA has taken into account the federal Toxic Substances Management Policy[1] and has followed its Regulatory Directive DIR99-03[2]. It has been determined that this active ingredient and product do not meet TSMP Track 1 criteria for the following reasons.

- Potassium bicarbonate does not meet the criterion for bioaccumulation.

- Potassium bicarbonate technical grade active ingredient does not contain any impurities of toxicological concern as identified in Section 2.14 of Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade Active Ingredient or an Integrated System Product*, nor any TSMP substances as listed in Appendix II of Regulatory Directive DIR99-03.

The formulated product is not known to contain any USEPA inert List 1 or 2 formulants or any known TSMP Track 1 substances.

9.0 Regulatory Decision

The reduced risk active ingredient potassium bicarbonate and the end-use product MilStop Foliar Fungicide have been granted temporary registrations for the control/suppression of powdery mildew on tomatoes, sweet peppers, cucumbers, pumpkins, flowering dogwood, bee balm, African daisy, hydrangea, phlox and poinsettia in greenhouses, pursuant to the Pest Control Products Regulations, subject to the following conditions:

- clarification and monitoring regarding the effects of potassium bicarbonate on beneficial invertebrates.

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1 The federal Toxic Substances Management Policy is available through Environment Canada's website at www.ec.gc.ca/toxics.

2 Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, is available through the Pest Management Information Service. Phone 1 800 267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); Fax (613) 736-3798; E-Mail pmra_infoserv@hc-sc.gc.ca or through our website at www.pmra-arla.gc.ca.

List of Abbreviations

bw	body weight
CAS	Chemical Abstracts Service
cm	centimetre(s)
DNCB	dinitrochlorobenzene
g	gram(s)
ha	hectare
IPM	integrated pest management
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
lb	pound
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
m	metre(s)
MAS	maximum average score
mg	milligram(s)
MIS	maximum irritation score
mL	millilitre(s)
N/A	not applicable
NOAEL	no observed adverse effect level
PMRA	Pest Management Regulatory Agency
pK_a	dissociation constant
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume-to-volume ratio
w/v	weight-to-volume ratio

Appendix I Toxicology

Study	Species, Strain and Doses	NOAEL and LOAEL mg/kg bw/day	Target Organ, Significant Effects, Comments
ACUTE STUDIES—TECHNICAL			
Oral	Rats—Cr1:CD BR; 5/sex/dose; 1500, 2500, 3500 and 5000 mg/kg bw	LD_{50} 3706 mg/kg bw (males); 2064 mg/kg bw (females); 2825 mg/kg bw (combined)	**Low toxicity**
Dermal	Rabbits—New Zealand White; 5/sex; 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw (males, females, and combined)	**Low toxicity**
Inhalation	Rats—Sprague-Dawley; 5/sex; Nominal: 61.09 mg/L; Analytical: 4.88 ± 0.60 mg/L	LC_{50} > 4.88 ± 0.60 mg/L (males, females, and combined)	**Low toxicity**
Skin Irritation	Rabbits—New Zealand White; 6 males; 0.5 g moistened with 0.9 % saline solution.	MIS: 0.5 at 4 hours MAS: 0.06 (24, 48 and 72 hour)	**Minimally irritating**
Eye Irritation	Rabbits—New Zealand White; 6 females; 0.1 g	Unwashed MIS: 15.8 at 1 hour MAS: 5.7 (24, 48 and 72 hour)	**Mildly irritating**

Study	Species, Strain and Doses	NOAEL and LOAEL mg/kg bw/day	Target Organ, Significant Effects, Comments
Skin Sensitization (Buehler test method)	Guinea Pigs—Albino Cr1: (HA)BR; 10 males in the test group, 10 males in the naive control group and 4 males in the positive control group; 0.2 g moistened with deionized water in the test group (induction and challenge), deionized water (induction) and 0.2 g moistened with deionized water (challenge) in the naive control, and 0.4 mL positive control (induction and challenge)	Positive control (0.3 % w/v 2,4-DNCB in 80% v/v ethanol in deionized water) There was no indication of sensitization in either the test group or the positive control.	**Not a dermal sensitizer**
ACUTE STUDIES—FORMULATION (MilStop Foliar Fungicide)			
Oral	Rats—Cr1:CD BR; 5/sex/dose; 1500, 2500, 3500 and 5000 mg/kg bw	LD_{50} 3706 mg/kg bw (males); 2064 mg/kg bw (females); 2825 mg/kg bw (combined)	**Low toxicity**
Dermal	Rabbits—New Zealand white; 5/sex; 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw (males, females and combined)	**Low toxicity**
Inhalation	Rats—Sprague-Dawley; 5/sex; Nominal: 61.09 mg/L; Analytical: 4.88 ± 0.60 mg/L	LC_{50} > 4.88 ± 0.60 mg/L (males, females and combined)	**Low toxicity**
Skin Irritation	Rabbits—3 of unknown sex; 0.5 mL	MIS: 7.0 at 72 hours MAS: 3.7 (24 and 72 hour)	**Moderately irritating**
Eye Irritation	Rabbits—New Zealand White; 6 females; 0.1 g	Unwashed MIS: 15.8 at 1 hour MAS: 5.7 (24, 48 and 72 hour)	**Mildly irritating**

Study	Species, Strain and Doses	NOAEL and LOAEL mg/kg bw/day	Target Organ, Significant Effects, Comments
Skin Sensitization (Buehler test method)	Guinea Pigs—Albino Cr1: (HA)BR; 10 males in the test group, 10 males in the naive control group, and 4 males in the positive control group; 0.2 g moistened with deionized water in the test group (induction and challenge), deionized water (induction) and 0.2 g moistened with deionized water (challenge) in the naive control, and 0.4 mL positive control (induction and challenge)	Positive control (0.3 % w/v 2,4-DNCB in 80% v/v ethanol in deionized water) There was no indication of sensitization in either the test group or the positive control.	**Not a dermal sensitizer**