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Registration Decision

Pantoea agglomerans Strain C9-1

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Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6605C
Ottawa, Ontario
K1A 0K9

Internet: pmra_publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra_infoserv@hc-sc.gc.ca

Canada

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Registration Decision for *Pantoea agglomerans* Strain C9-1

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of *Pantoea agglomerans* strain C9-1 Technical and BlightBan C9-1, containing the microbial pest control agent *Pantoea agglomerans* strain C9-1, for the suppression of fire blight (*Erwinia amylovora*) on apple and pear trees, saskatoonberries, caneberries and non-bearing pome fruit nursery stock.

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

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2008-16, *Pantoea agglomerans strain C9-1*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for *Pantoea agglomerans* strain C9-1 and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of the comment received during the consultation process as well as the PMRA's response to the comment. This decision is consistent with the proposed registration decision stated in PRD2008-16.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2008-16, *Pantoea agglomerans strain C9-1,* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] 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 conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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

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

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

4 "Value" as defined by subsection 2(1) of *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".

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 (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at healthcanada.gc.ca/pmra.

What is *Pantoea agglomerans* Strain C9-1?

Pantoea agglomerans is a bacterium that is ubiquitous in nature and occurs naturally on fruit trees. As the active ingredient in BlightBan C9-1, it colonizes flowers and other parts of fruit trees and occupies sites that would otherwise be colonized by the fireblight pathogen, *Erwinia amylovora*. BlightBan C9-1 will suppress fireblight on fruit trees and shrubs when applied during flowering.

Health Considerations

Can Approved Uses of *Pantoea agglomerans* Strain C9-1 Affect Human Health?

Pantoea agglomerans strain C9-1 is unlikely to affect your heath, when BlightBan C9-1 is used according to label directions

Exposure to *Pantoea agglomerans* strain C9-1 may occur during handling and application of BlightBan C9-1. When assessing health risks, several key factors are considered: the microorganism's biological properties (e.g. production of toxic by-products); reports of any adverse incidents; its potential to cause disease or toxicity as determined in toxicological studies; and the levels to which people may be exposed, relative to exposures already encountered in nature to other isolates of the microorganism.

Toxicology studies in laboratory animals describe potential health effects from large doses in an effort to identify any potential to cause disease or toxicity. When *Pantoea agglomerans* strain C9-1 was tested on laboratory animals there were no signs that it caused any significant toxicity or disease.

Other strains of *Pantoea agglomerans* found in nature have been associated with minor wound infections involving punctured skin; however, there is no indication that infection would arise if healthy skin is penetrated. This species of microorganisms does not cause disease in humans and is not known to produce byproducts that are harmful to humans or other animals.

Pantoea agglomerans strains of bacteria contain a substance in their cell walls called lipopolysaccharide that can shed from the cells as tiny “pockets”. If inhaled in large amounts, the lipopolysaccharide can cause inflammation in the respiratory system. Upon repeated exposure to this product, people, such as farm workers and applicators, could develop a condition know as respiratory hypersensitivity. Like all bacteria, *Pantoea agglomerans* strain C9-1 contains other substances that can cause allergic reactions in people who are repeatedly exposed to it at high concentrations. However, these reactions can be avoided if farm workers and applicators follow label recommendations to minimize exposure to BlightBan C9-1, including wearing a dust mask

Residues in Water and Food

Dietary risks from food and water are not of concern

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Strains of *Pantoea agglomerans* are common in nature and the use of BlightBan C9-1 in orchards to suppress fireblight on apple and pear trees is not expected to significantly increase the natural environmental background levels of this microorganism. Furthermore, when *Pantoea agglomerans* strain C9-1 was administered orally to rats, no signs of toxicity or diseases were observed. Other than the cell wall lipopolysaccharide that can cause inflammation in the respiratory system upon repeated exposure, strains of *Pantoea agglomerans* are not known to produce toxicologically significant secondary metabolites. Consequently, the risks from secondary metabolites for the general population, including infants and children or animals, are negligible. Therefore, the establishment of a MRL is not required for *Pantoea agglomerans* strain C9-1. As well, the likelihood of residues of *Pantoea agglomerans* strain C9-1 contaminating drinking water supplies is negligible to non-existent. Consequently, dietary exposure and risk are minimal to non-existent.

Occupational Risks from Handling BlightBan C9-1

Occupational risks are not of concern when BlightBan C9-1 is used according to label directions, which include protective measures.

Growers handling BlightBan C9-1 can come into direct contact with *Pantoea agglomerans* strain C9-1 on the skin, in the eyes, or by inhalation. For this reason, the label specifies that growers exposed to BlightBan C9-1, during handling, mixing/loading, application or clean- up/repair activities, must wear water proof gloves, long-sleeved

shirts, long pants, shoes plus socks, and a National Institute of Occupational Safety and Health (NIOSH) approved respirator with any N-95, R-95, P-95 or HE filter. Furthermore, early entry workers are restricted from entering areas where BlightBan C9-1 has been applied as a foliar spray for a period of four hours unless wearing the above mentioned personal protective equipment.

Bystander exposure is expected to be much less than that of applicators, handlers and mixer/loaders and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When BlightBan C9-1 Is Introduced into the Environment?

Studies designed to examine the effects of *Pantoea agglomerans* strain C9-1 on various non-target organisms were evaluated. Few adverse effects were observed in birds, terrestrial arthropods (honeybees), freshwater fish and freshwater arthropods.

Pantoea agglomerans strain C9-1 is not generally considered a disease-causing agent. Therefore, BlightBan C9-1 is expected to present negligible risk to non-target organisms.

Value Considerations

What Is the Value of BlightBan C9-1?

BlightBan C9-1 is registered to suppress fireblight on apples, pears, saskatoonberries, caneberries and non-bearing pome fruit nursery stock.

BlightBan C9-1 is an alternative product to Streptomycin 17, a bactericide currently registered for fireblight control. Suppression of the fireblight pathogen (*Erwinia amylovora*) with BlightBan C9-1 will reduce grower reliance on streptomycin.

Measures to Minimize Risk

Registered pesticide product labels 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 on the label of BlightBan C9-1 to address the potential risks identified in this assessment are as follows.

Human Health

As there are concerns with users developing allergic reactions through repeated high exposures to *Pantoea agglomerans* strain C9-1, anyone handling, mixing/loading, applying or involved in clean-up/repair activities of BlightBan C9-1 must wear water proof gloves, long-sleeved shirts, long pants, and a NIOSH approved respirator with any N-95, R-95, P-95 or HE filter. Furthermore, early entry workers are restricted from entering areas where BlightBan C9-1 has been applied as a foliar spray for a period of four hours unless wearing the indicated personal protective equipment.

Environment

As a general precaution, handlers are asked not to contaminate irrigation or drinking water or aquatic habitats through equipment cleaning or waste disposal. In addition, growers must not allow effluent or runoff containing this product to enter lakes, streams, ponds or other water bodies.

Precautionary labelling indicating that handlers must avoid application of BlightBan C9-1 on orchards abutting newly-planted conifer forestry blocks will mitigate the risk of gall formation by the microbial pest control agent in potentially susceptible seedlings.

Other Information

The relevant test data on which the decision is based (as referenced in this document) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the PMRA's website, Request a Reconsideration of Decision, or contact the PMRA's Pest Management Information Service).

[5] As per subsection 35(1) of the *Pest Control Products Act.*

Appendix I Comment and Response

The following comment was received on the health concern of *Pantoea agglomerans* strain C9-1

While the toxicological studies indicated the risks from *Pantoea agglomerans* strain C9-1 to human health were acceptable, there is a possibility that *Pantoea agglomerans* strain C9-1 may mutate into a virulent strain that could pose risks to humans, animals, or plants. This is supported by evidence of virulent forms of *Pantoea agglomerans* in the published literature (Kratz et al. 2003; Aly et al. 2008). Factors such as high population pressure (i.e. at 10^6 CFU/mL), and exposure to UV radiation and agricultural chemicals or the plant's organic compounds are known to promote bacterial mutation. Any of these scenarios may be encountered during use of Blightban C9-1.

PMRA Response

The assessment of risk of *Pantoea agglomerans* strain C9-1 on human and animal health did take into account published reports of adverse effects from *Pantoea agglomerans* which included a few clinical cases related to *Pantoea agglomerans*. It is unlikely that field conditions would result in a high enough population pressure to encourage mutation in *Pantoea agglomerans*. Exposure to UV radiation has been shown to considerably reduce phyllosphere bacteria populations. Therefore, exposure to UV radiation is more likely to lead to reduced population levels of *Pantoea agglomerans* strain C9-1 rather than instigate a mutation to render this avirulent strain virulent. Moreover, exposure to *Pantoea agglomerans* strain C9-1 is minimized in workers by wearing personal protective equipment, including long sleeved shirt, long pants, shoes plus socks, waterproof gloves as well as a NIOSH approved respirator (with any N-95 R-95, P-95 or HE filter for biological products) for all mixing/loading and application activities. Workers are also restricted from entering treated areas for four hours unless wearing the prescribed personal protective equipment.

References

Kratz, A., D. Greenberg, Y. Barki, E. Cohen and M. Lifshitz. 2003. *Pantoea agglomerans* as a cause of septic arthritis after palm tree thorn injury; case report and literature review. *Archives of Disease in Childhood*. 88: 542–544.

Aly, N.Y. A, H. N. Salmeen, R. A. Abo Lila, and P. A. Nagaraja. 2008. *Pantoea agglomerans* bloodstream infections in preterm neonates. *Medical Principles and Practices*. 17: 500–503.

References

A. List of Studies/Information Submitted by Registrant

Chemistry

PMRA Document Number 1460063
Reference 2007, *Pantoea agglomerans* Strain C9-1: A Strain Specific Method of Identification, PAG-VS-150107, DACO: M2.7.1 CBI

PMRA Document Number 1460083
Reference 2007, Certificate of Analysis: *Pantoea agglomerans* C9-1, PAG-Osprey-180407, DACO: M2.10 CBI

PMRA Document Number 1617899
Reference 2008, Assessment of Viability, 08Ea297, DACO: 2.14.14 CBI

PMRA Document Number 1625789
Reference 2008, Clarification Response 01 August 2008, DACO: 0.8.23

PMRA Document Number 1625790
Reference 2008, Pseudomonas Plate Count Procedure, DACO: 3.4 CBI

B. Additional Information Considered

Value

PMRA Document Number 1563403
Reference 2008, Submission No. 2008-0898: Evaluation Report for Category C, Subcategory 6.3 (URMULE) Application