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RD2007-10

Registration Decision

Streptomyces lydicus **strain WYEC 108**

Actinovate SP

(publié aussi en français)

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Overview

Registration Decision for *Streptomyces lydicus* strain WYEC 108

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the [Pest Control Products Act](#), is granting full registration for the sale and use of the technical grade active ingredient *Streptomyces lydicus* WYEC 108 and the end-use product Actinovate SP for the suppression of Botrytis fruit rot and powdery mildew on field and greenhouse grown strawberries and powdery mildew on field and greenhouse peppers and Gerber daisies.

Current scientific data from the registrant, scientific reports and information from other regulatory agencies were evaluated to determine if, under the proposed 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 document¹: *Proposed Registration Decision—Streptomyces lydicus* strain WYEC 108 ([PRD2007-10](#)). This Registration Decision² describes this stage of the PMRA's regulatory process for *S. lydicus* strain WYEC 108 and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on *Proposed Registration Decision—Streptomyces lydicus* strain WYEC 108 (PRD2007-10). This decision is consistent with the proposed registration decision stated in *Proposed Registration Decision—Streptomyces lydicus* strain WYEC 108 (PRD2007-10).

For more details on the information presented in this Registration Decision, please refer to the Science Evaluation section of the related Proposed Registration Decision *Streptomyces lydicus* strain WYEC 108 (PRD2007-10).

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 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 or proposed conditions of registration³. The Act also requires that products have

¹ "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act* (<http://laws.justice.gc.ca/en/P-9.01/92455.html>)

² "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act* (<http://laws.justice.gc.ca/en/P-9.01/92455.html>)

³ "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act* (<http://laws.justice.gc.ca/en/P-9.01/92455.html>)

value⁴ when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies hazard and risk assessment methods as well as policies that are rigorous and modern. These methods consider the unique characteristics of sensitive subpopulations in both humans (e.g. children) and 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 present 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 www.pmra-arla.gc.ca.

What is Actinovate SP?

Actinovate SP is a biological fungicide containing the bacterium, *Streptomyces lydicus* strain WYEC 108, for the suppression of fungal diseases on field and greenhouse strawberries, peppers and Gerber daisies.

S. lydicus strain WYEC 108 works by invading and growing within the fungal pathogens, where it releases enzymes that break down the cell wall of fungi. It also readily grows on the tip of plant roots, which protects the plant's roots from plant pathogens by competing with and displacing fungi that may cause disease and by excreting metabolites that target disease fungi.

Health Considerations

Can Approved Uses of *S. lydicus* strain WYEC 108 Affect Human Health?

***S. lydicus* strain WYEC 108 is unlikely to affect your health when used according to label directions.**

Exposure to *S. lydicus* strain WYEC 108 may occur during handling and applying of the product. 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 for pathogenicity, infectivity and toxicity as determined in toxicological studies and the likely levels to which people may be exposed to this strain relative to exposures already encountered in nature to other strains of the microorganism.

Toxicology studies in laboratory animals describe potential health effects from large doses in hopes of identifying any potential pathogenicity, infectivity and toxicity concerns.

⁴ "Value" as defined by subsection 2(1) of *Pest Control Products Act* (<http://laws.justice.gc.ca/en/P-9.01/92455.html>): "...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".

An alternate formulation of Actinovate SP was mildly irritating to the eyes of test animals. Consequently, the signal words “CAUTION: Eye Irritant” and “May irritate eyes. Avoid contact with eyes” are required on the label.

No other significant toxicity and no signs of pathogenicity or infectivity were observed when *S. lydicus* strain WYEC 108 was tested on laboratory animals.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Pesticide maximum residue limits (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. The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established MRL.

S. lydicus strains are common in soil and application of Actinovate SP to strawberry, pepper and Gerber daisy in fields and commercial greenhouses is not expected to significantly increase the natural environmental background levels of this microorganism. No adverse effects have been attributed to dietary exposure from natural populations of *S. lydicus* and none were observed during acute oral toxicity testing. The establishment of a MRL is, therefore, not required for *S. lydicus* strain WYEC 108. Furthermore, the likelihood of residues of *S. lydicus* strain WYEC 108 contaminating drinking water supplies is negligible to non-existent. Consequently, dietary exposure and risk are minimal to non-existent.

Occupational Risks From Handling Actinovate SP

Occupational risks are not of concern when Actinovate SP is used according to label directions, which include protective measures.

Potential exposure to workers and pesticide handlers from *S. lydicus* strain WYEC 108 is not expected to pose any undue risk. Pesticide applicators handling or applying Actinovate SP and field workers re-entering fields where crops were sprayed, can come into direct contact with *S. lydicus* strain WYEC 108 on the skin, in the eyes or by inhalation. For this reason, the label will specify that applicators and other handlers of Actinovate SP must wear personal protective equipment including water proof gloves, long-sleeved shirts, long pants and shoes and socks. Mixer/loaders and applicators must additionally wear a dust/mist filtering mask. Furthermore, early entry workers will be restricted from entering fields or greenhouses treated with Actinovate SP for up to one hour after spraying or until the solution has dried, unless they are wearing the appropriate personal protective equipment.

S. lydicus strain WYEC 108 may cause hypersensitivity, especially in people exposed repeatedly to high concentrations of this microbe. The signal words “POTENTIAL SENSITIZER” and precautionary statement “May cause sensitization” are required on the product label to warn workers of this potential hazard. Personal protective equipment and the restricted entry interval will further mitigate any potential risks to workers and handlers.

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Actinovate SP is Introduced Into the Environment?

Environmental risks are not of concern.

There are no published reports of disease associated with *S. lydicus* in wild mammals, birds, earthworms, bees and other arthropods, aquatic invertebrates, fish, algae and aquatic plants. Furthermore, a study designed to examine the effects of *S. lydicus* strain WYEC 108 on fish reported no adverse effects. Therefore, *S. lydicus* strain WYEC 108 is expected to present a negligible risk to these non-target organisms.

While there were no reports in published literature of plant disease caused by *S. lydicus*, literature indicated that certain *Streptomyces* species, such as *S. scabies*, *S. acidiscabies* and *S. turgidiscabies* which cause “potato scab” on potato, are known plant pathogens. The applicant referred to growth chamber studies and small scale field trials conducted with this microbial pest control agent (MPCA) that demonstrated that there were no deleterious effects on potato. Based on the lack of phytotoxicity reported in efficacy trials conducted with Actinovate SP on strawberry, Gerber daisy and bell pepper (see Section 5.2) there is reasonable certainty that no deleterious effects are anticipated on nontarget plants.

Value Considerations

What is the Value of Actinovate SP?

The registration of Actinovate SP would result in an additional non-chemical fungicide for Canadian growers, in particular the greenhouse industry. It could be used as a resistance management tool since the active ingredient has a multiple-site mode of action. Actinovate SP could also be used as an alternative fungicide in organic fruit production.

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 being proposed on the label of Actinovate SP to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

As a standard precaution anyone handling or applying Actinovate SP must wear waterproof gloves, long-sleeved shirt, long pants and shoes plus socks. In addition, a dust/mist filtering mask must be worn by mixers/loaders and applicators. Furthermore, early-entry workers will be restricted from entering fields and greenhouses treated with Actinovate SP for up to 1 hour after spraying or until solution has dried, unless the appropriate personal protective equipment is worn.

Environment

As a general precaution, handlers are advised not to contaminate irrigation or drinking water or aquatic habitats while cleaning equipment or disposing of waste.

Other Information

1. 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 by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).
2. Any person may file a notice of objection⁵ regarding this registration decision on *S. lydicus* strain WYEC 108 within 60 days from the date of publication of this Registration Decision Document. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the PMRA's website (Requesting a Reconsideration of Decision, www.pmra-arla.gc.ca/english/pubreg/reconsideration-e.html) or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

⁵ As per subsection 35(1) of the *Pest Control Products Act* (<http://laws.justice.gc.ca/en/P-9.01/92455.html>)

List of References

A. List of Studies Submitted by Registrant

1.0 The Active Ingredient Its Properties and Uses

PMRA Number	Reference
PMRA 1164650	Product chemistry of Actinovate SP. Project No. 04-059. April 24, 2000. 28 pages. DACO 2.1-2.11
PMRA 1360736	University of Idaho. 1998. Thesis: Mechanism of biocontrol of fungal root pathogens in the rhizosphere by <i>Streptomyces lydicus</i> WYEC 108. Ph. D. Microbiology. Moscow, ID. 81 pages.
PMRA 1360737	University of Idaho. 2002. Plant growth promotion and siderophore production by selected root-colonizing nonpathogenic <i>Streptomyces</i> species. M. Sc.
PMRA 1348803	University of Idaho. 2006. Thesis: Characterization of novel members of the <i>Streptomyces violaceusniger</i> clade and characterization of antibiotic biosynthesis gene of <i>Streptomyces lydicus</i> WYEC 108. Ph. D. Microbiology. Moscow, ID. 113 pages.
PMRA 1348801	Locci, R. 1989. <i>Streptomyces</i> and related genera. In: Bergey's Manual of Systematic Bacteriology. Vol. 4. 2451-2492.
PMRA 1164646	Biopesticide Regulatory Action Document. <i>Streptomyces lydicus</i> WYEC 108. U.S. EPA. April 27, 2004. 41 pages.

2.0 Methods of Analysis

PMRA Number	Reference
PMRA 1164650	Product chemistry of Actionovate SP. Project No. 04-059. April 24, 2000. 28 pages. DACO 2.1-2.11
PMRA 1348800	Response to Clarifax. Dec. 20, 2000. 5 pages.
PMRA 1360731	Natural Industries Inc.: Summary of storage stability information. Jan. 18, 2007.
PMRA 1348805	Summary of physical and chemical properties: Actinovate SP (EP) and <i>Streptomyces lydicus</i> WYEC 108 (TGAI). 1 page.
PMRA 1360734	Goodfellow, M. And K. E. Simpson. 1987. Ecology of <i>Streptomyces</i> . <i>Frontiers Applied Microbiology</i> . 2: 97-125.

- PMRA 1360735 University of Idaho. 1992. *Streptomyces lydicus* WYEC 108 as a biocontrol agent against *Pythium* seed rot and emergence damping-off. Ph. D. Dissertation. Moscow, ID.
- PMRA 1348804 University of Idaho. 2006a. 16S rDNA sequence of *Streptomyces lydicus* WYEC 108. Department of Microbiology, Molecular Biology, and Biochemistry. Moscow, ID.
- PMRA 1348803 University of Idaho. 2006b. Characterization of novel members of the *Streptomyces violaceuniger* clade and characterization of antibiotic biosynthesis genes from *Streptomyces lydicus* WYEC 108. Ph. D. Dissertation. Department of Microbiology, Molecular Biology, and Biochemistry. Moscow, ID. May 2006.

3.0 Impact on Human and Animal Health

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| PMRA 1164643 | Final Report: Acute Pulmonary Toxicity/Pathogenicity study in Rats with a Microbial Pest Control Agent (MPCA). Laboratory Study No. 5202-99. March 1, 2000. Unpublished. |
| PMRA 1164641 | Final Report: Acute injection toxicity/pathogenicity in rats with a microbial pest control agent (MPCA). Laboratory Report No. 5203-99. March 1, 2000. 45 pages. Unpublished. |
| PMRA 1164649 | Final Report: Primary Eye Irritation Study in the Rabbit. Laboratory Study No. 5200-99. September 2, 1999. 16 pages. Unpublished. |
| PMRA 1164640 | Final Report: Acute Dermal Irritation Study in Rabbit Laboratory Study No. 5201-99. September 2, 2000. 13 pages. Unpublished. |
| PMRA 1164644 | Administrative Volumes EPA Cover Letters. April 20, 2000. 14 pages. |

4.0 Impact on the Environment

- | PMRA Number | Reference |
|--------------|---|
| PMRA 1164644 | Administrative Volumes EPA Cover Letters. April 20, 2000. 14 pages. |

- PMRA 1161653 Final Report: WYEC 108 (*Streptomyces lydicus*): A 96-hour acute toxicity study with rainbow trout (*Oncorhynchus mykiss*). Project No. 506A-101. March 22, 2000. 23 pages.
- PMRA 1164646 Biopesticide Regulatory Action Document. *Streptomyces lydicus* WYEC 108. U.S. EPA. April 27, 2004. 41 pages.
- PMRA 1360735 University of Idaho. 1992. *Streptomyces lydicus* WYEC 108 as a biocontrol agent against *Pythium* seed rot and emergence damping-off. Ph. D. Dissertation. Moscow, ID.
- PMRA 1360737 University of Idaho. 2002. Plant growth promotion and siderophore production by selected root-colonizing nonpathogenic *Streptomyces* species. M. Sc. 102 pages.
- PMRA 1164650 Product chemistry of Actionovate SP. Project No. 04-059. April 24, 2000. 28 pages. DACO 2.1-2.11
- PMRA 1360734 Goodfellow, M. and K. E. Simpson. 1987. Ecology of Streptomycetes. *Frontiers Applied Microbiology*. 2: 97-125.

5.0 Value

- | | |
|--------------|---|
| PMRA Number | Reference |
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B. Additional Information Considered

i) Published Information

1.0 The Active Ingredient, Its Properties and Uses

- | | |
|--------------|---|
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| PMRA 1371714 | Yuan, W. M. and D. L. Crawford. 1995. Characterization of <i>Streptomyces lydicus</i> WYEC 108 as a potential biocontrol agent against fungal root and seed rots. <i>Appl. Environ. Microbiol.</i> 61(8):3119-3128. |

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- PMRA 1377257 Mahadevan, B. and D. L. Crawford. 1997. Properties of the chitinase of the antifungal biocontrol agent *Streptomyces lydicus* WYEC 108. *Enz. Microb. Technol.* 20: 489-493.
- PMRA 1371711 McManus, P. S. 2004. Strawberry Disorder:Black root rot. [on-line] <http://cecommerce.uwex.edu/OrderPubLookup.asp>

2.0 Methods of Analysis

- | PMRA Number | Reference |
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3.0 Impact on Human and Animal Health

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- PMRA 1377261 Che, D., S. Liu, and X. Huang. 1989. Pathogenesis of extrinsic allergic alveolitis and pulmonary fibrosis induced by *Streptomyces thermohygroscopicus*. *Chin. Med. J. (Engl)*. 102(7):563-567.
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4.0 Impact on the Environment

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