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Registration Decision

RD2010-10

***Lactobacillus casei* strain LPT-111,
Lactobacillus rhamnosus strain LPT-21,
Lactococcus lactis ssp. *lactis* strain LL64/CSL,
Lactococcus lactis ssp. *lactis* strain LL102/CSL,
Lactococcus lactis ssp. *cremoris* strain M11/CSL**

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Registration Decision for for *Lactobacillus casei* strain LPT-111, *Lactobacillus rhamnosus* strain LPT-21, *Lactococcus lactis* ssp. *lactis* strain LL64/CSL, *Lactococcus lactis* ssp. *lactis* strains LL102/CSL and *Lactococcus lactis* ssp. *cremoris* strain M11/CSL

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 *Lactobacillus casei* Technical, *Lactobacillus rhamnosus* Technical, *Lactococcus lactis* ssp. *lactis* Technical and *Lactococcus lactis* ssp. *cremoris* Technical, DOM Manufacturing Concentrate and the end-use product Organo-Sol, containing the microbial pest control agents *Lactobacillus casei* strain LPT-111, *Lactobacillus rhamnosus* strain LPT-21, *Lactococcus lactis* ssp. *lactis* strain LL64/CSL, *Lactococcus lactis* ssp. *lactis* strain LL102/CSL and *Lactococcus lactis* ssp. *cremoris* strain M11/CSL, for the partial suppression of clovers, black medick, bird's-foot trefoil, and wood sorrel in established lawns.

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 document¹ Proposed Registration Decision PRD2010-09, *Lactobacillus casei* strain LPT-111, *Lactobacillus rhamnosus* strain LPT-21, *Lactococcus lactis* ssp. *lactis* strain LL64/CSL, *Lactococcus lactis* ssp. *lactis* strain LL102/CSL *Lactococcus lactis* ssp. *cremoris* strain M11/CSL. This Registration Decision² describes this stage of the PMRA's regulatory process for *Lactobacillus casei* Technical, *Lactobacillus rhamnosus* Technical, *Lactococcus lactis* ssp. *lactis* Technical and *Lactococcus lactis* ssp. *cremoris* Technical, DOM Manufacturing Concentrate and Organo-Sol and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2010-09. This decision is consistent with the proposed registration decision stated in PRD2010-09.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2010-09 that contains a detailed evaluation of the information submitted in support of this registration.

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*.

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 acceptable³ 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 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 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 Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What is *Lactobacillus casei* strain LPT-111, *Lactobacillus rhamnosus* strain LPT-21, *Lactococcus lactis* ssp. *lactis* strains LL64/CSL and LL102/CSL and *Lactococcus lactis* ssp. *cremoris* strain M11/CSL?

Lactobacillus casei strain LPT-111, *Lactobacillus rhamnosus* strain LPT-21, *Lactococcus lactis* ssp. *lactis* strains LL64/CSL and LL102/CSL, and *Lactococcus lactis* ssp. *cremoris* strain M11/CSL are lactic acid bacteria that produce the fermentation products citric acid and lactic acid. Due to the presence of citric acid and lactic acid in the end-use product Organo-Sol, it has a low pH (~3.5) that allows for penetration of plant cells causing tissue necrosis and suppression of plant growth. Plant species most susceptible to Organo-Sol are those with a thin leaf cuticle. Organo-Sol is a commercial herbicide used for the partial suppression of clovers, black medick, bird's-foot trefoil, and wood sorrel in established lawns.

³ "Acceptable risks" as defined by subsection 2(2) of the *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".

Health Considerations

Can Approved Uses of *Lactococcus lactis* ssp. *lactis* strains LL64/CSL and LL102/CSL, *Lactococcus lactis* ssp. *cremoris* strain M11/CSL, *Lactobacillus rhamnosus* strain LPT-21, and *Lactobacillus casei* strain LPT-111 and Their Fermentation Products, Citric Acid and Lactic Acid, Affect Human Health?

***Lactococcus lactis* ssp. *lactis* strains LL64/CSL and LL102/CSL, *Lactococcus lactis* ssp. *cremoris* strain M11/CSL, *Lactobacillus rhamnosus* strain LPT-21, and *Lactobacillus casei* strain LPT-111 and their fermentation products, citric acid and lactic acid, are unlikely to affect your health when Organo-Sol is used according to the label directions.**

Exposure to *Lactococcus lactis* ssp. *lactis* strains LL64/CSL and LL102/CSL, *Lactococcus lactis* ssp. *cremoris* strain M11/CSL, *Lactobacillus rhamnosus* strain LPT-21, and *Lactobacillus casei* strain LPT-111 and their fermentation products, citric acid and lactic acid, may occur during handling of Organo-Sol.

When assessing the health risks associated with microbial active ingredients, several key factors are considered: a microorganism's biological properties (e.g. production of toxic byproducts), reports of any adverse incidents, potential to cause disease or toxicity as determined in toxicological studies and the level to which people may be exposed relative to exposures already encountered in nature to other isolates of this microorganism.

For biochemical actives, the levels where no health effects occur and the levels to which people may be exposed are considered. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

The lactic acid bacteria used in the manufacture of Organo-Sol and their organic acids are already occurring in the food chain for human consumption at similar levels to those found in Organo-Sol and there have been relatively few reports of infection or adverse effects despite their ubiquity.

The fermentation products, citric acid and lactic acid, are of low acute toxicity by the oral route. Lactic acid is of low acute toxicity via the dermal route while both lactic and citric acid are slightly irritating to the skin. Eye irritation studies indicated that, at the concentrations found in Organo-Sol, lactic acid and citric acid are capable of producing moderate to severe injury to the eye, particularly with repeated or prolonged exposure. Appropriate label statements and requirements for basic personal protective equipment will minimize exposure.

Residues in Water and Food

Dietary risks from food and water are not of concern.

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

As there are no direct applications to food and no significant adverse effects were reported in Tier I acute toxicity/pathogenicity studies, the establishment of maximum residue limits are not required for *Lactococcus lactis* ssp. *lactis* strains LL64/CSL and LL102/CSL, *Lactococcus lactis* ssp. *cremoris* strain M11/CSL, *Lactobacillus rhamnosus* strain LPT-21, *Lactobacillus casei* strain LPT-111 and their fermentation products, citric acid and lactic acid. In addition, the likelihood of residues of *Lactococcus lactis* ssp. *lactis* strains LL64/CSL and LL102/CSL, *Lactococcus lactis* ssp. *cremoris* strain M11/CSL, *Lactobacillus rhamnosus* strain LPT-21, *Lactobacillus casei* strain LPT-111, citric acid or lactic acid contaminating drinking water supplies is negligible. Consequently, dietary exposure and risk are minimal to non-existent.

Occupational Risks From Handling Organo-Sol

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

Users of Organo-Sol can come into direct contact with *Lactococcus lactis* ssp. *lactis* strains LL64/CSL and LL102/CSL, *Lactococcus lactis* ssp. *cremoris* strain M11/CSL, *Lactobacillus rhamnosus* strain LPT-21, *Lactobacillus casei* strain LPT-111, citric acid or lactic acid primarily via the skin or eyes. As a standard requirement intended to minimize exposure, the label specifies that users of Organo-Sol must wear water-proof gloves, long-sleeved shirts, long pants, shoes and socks and eye-goggles. Users are also directed to avoid inhaling the product and its mists.

As the end-use product may contain the allergen, unmodified milk protein (whey), the Organo-Sol label restricts entry and re-entry into treated areas until the spray is dried.

Environmental Considerations

What Happens When Organo-Sol Is Introduced Into the Environment?

Environmental risks are not of concern.

Lactic acid bacteria are considered widespread in nature and can be recovered from water, soil, manure, sewage, and silage as well as from a variety of plant material such as fruit, vegetables, grass, and clover. Lactic acid bacteria are also part of the commensal microflora of humans and animals as part of the gastrointestinal tract, oral cavity, and vagina. Published literature indicates that although lactic acid bacteria can survive outside of the dairy environment they are unlikely to thrive. As well, the number of lactic acid bacteria contained in Organo-Sol is relatively low. Since the use of Organo-Sol is not likely to result in an increase of the number of lactic acid bacteria in the environment, the risk to terrestrial and aquatic non-target organisms from lactic acid bacteria is negligible.

Citric acid and lactic acid readily undergo biotransformation in terrestrial and aquatic environments. Given the ubiquitous nature of citric acid and lactic acid in animals, plants, edible food commodities and industrial chemicals, the proposed uses of Organo-Sol on lawns is not expected to result in a considerable increase in exposure to non-target terrestrial and aquatic organisms. Furthermore, reports in published literature of cases of adverse effects, as well as published toxicological endpoints, do not suggest that exposure of non-target terrestrial and aquatic organisms to the levels of citric acid and lactic acid in Organo-Sol will pose a concern with respect to toxicity. Based on the available data, citric acid and lactic acid are expected to pose negligible risk to terrestrial and aquatic organisms under the conditions of use.

Value Considerations

What Is the Value of Organo-Sol?

Acids in Organo-Sol produced by living lactic acid bacteria cause cell necrosis and suppression of plant growth after penetrating into plant cells.

Application of Organo-Sol provides partial suppression of white clover, red clover, bird's-foot trefoil, black medick, and wood sorrel in established lawns. Based on the mode of action of Organo-Sol, development of herbicide resistance is unlikely. The availability of Organo-Sol contributes to an integrated and sustainable pest management program in turf.

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 are required by law to be followed.

The key risk-reduction measures on the label of Organo-Sol to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

To minimize exposure to *Lactococcus lactis* ssp. *lactis* strains LL64/CSL and LL102/CSL, *Lactococcus lactis* ssp. *cremoris* strain M11/CSL, *Lactobacillus rhamnosus* strain LPT-21, and *Lactobacillus casei* strain LPT-111 and their fermentation products, citric acid and lactic acid, all applicators, mixer-loaders and handlers must wear water-proof gloves, long-sleeved shirts, long pants, shoes and socks and eye goggles. A label statement directing users to avoid inhaling the product and its mists is also included.

As the end-use product may contain the allergen, unmodified milk protein (whey), the Organo-Sol label restricts entry and re-entry into treated areas until the spray is dried.

Environment

As a general precaution, statements will be added to the label to prevent handlers from contaminating aquatic habitats and systems, and to prevent the accidental treatment of desirable plants with Organo-Sol.

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 by phone (1-800-267-6315) or by e-mail (pmra.inforserv@hc-sc.gc.ca).

Any person may file a notice of objection⁵ 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 Pesticides and Pest Management portion of Health Canada's website (Request a Reconsideration of Decision, healthcanada.gc.ca/pmra) or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.inforserv@hc-sc.gc.ca).

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

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B. Additional Information Considered - Published Information

1.0	Environment
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1766317	1997, Lactobacillus Bacteremia and Endocarditis: Review of 45 Cases, DACO: 2.7,M9.3
1766323	1995, Journal of Infection, Lactobacillus rhamnosus Infection in a Child Following Bone Marrow Transplant, DACO: 2.7,M9.3
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1766363	2005, Journal of Infection, Lactobacillus endocarditis: Case report and review of cases reported since 1992, DACO: 2.7,M9.3
1766365	2008, Journal of Medical Case Reports, Diagnostic difficulties of Lactobacillus casei bacteraemia in immunocompetent patients: A case report, DACO: 2.7,M9.3
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- 1766385 CCOHS Chemical Name: Lactic Acid , DACO: 2.7,9.3,9.4,9.5,9.6,9.7,9.8,M9.2
- 1766386 RTECS Lactic acid, DACO: 2.7,9.3,9.4,9.5,9.6,9.7,9.8,M9.2
- 1766619 RTECS Citric acid, DACO: 2.7,9.3,9.4,9.5,9.6,9.7,9.8,M9.2
- 1767451 Farina, C., et al, *Lactobacillus casei* subsp. *rhamnosus* sepsis in a patient with ulcerative colitis, CAT.INIST - Journal of clinical gastroenterology, vol. 33, no 3, pp 251-252, DACO: M2.7.2,M9.3
- 1767455 Sloss, J.M., Cumberland, N.S., Deep Seated Infection due to *Lactobacillus casei* - case report, JR Army Med Corps, 1993; 139: 25-26, DACO: M2.7.2,M9.3
- 1779127 Nogales, R. et al., Nogales, R., Elvira, C., Benítez, E., Thompson, R. and Gomez, M.(1999)'Feasibility of vermicomposting dairy, Feasibility of Vermicomposting Dairy Biosolids Using A Modified System to Avoid Earthworm Mortality. J.Environ.Sci. Health, B3

2.0 Value

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