

Evaluation Report for Category B, Subcategory 2.1, 2.3, 2.4, 3.1, 3.11, 3.12, and 3.4 Application

Application Number: 2010-4096
Application: B.2.1-New EP Product Chemistry-Guaranteee
B.2.3-New EP Product Chemistry-Identity of Formulants
B.2.4-New EP Product Chemistry-Proportion of Formulants
B.3.1-New EP Product Labels-Application Rate Increase
B.3.11-New EP Product Labels-New Pests
B.3.12-New EP Product Labels-New site
B.3.4-New EP Product Labels-Application Method
Product: Tackle
Registration Number: 30054
Active ingredients (a.i.): *Bacillus subtilis* strain MBI 600 (BSM)
PMRA Document Number English PDF: 2034203

Purpose of Application

The purpose of this application was to register Tackle, a microbial end-use product for suppression of damping-off and root diseases caused by *Fusarium*, *Rhizoctonia* and *Pythium* spp. on ornamentals and vegetables.

Chemistry Assessment

The applicant submitted the required information on the manufacturing process that included appropriate measures for quality assurance, and the limiting of microbial contaminants and unintentional ingredients. The data submitted supports the label guarantee of at least 5.5×10^{10} viable spores/g and storage stability of 16 months at 25°C. The product characterization database for Tackle is complete.

Health Assessments

Scientific rationales were submitted to address the requirement for dermal toxicity and dermal irritation studies with the end-use product. The rationale was based on the lack of toxicity of *Bacillus subtilis* strain MBI 600 observed in the dermal toxicity study, as well as the low toxicity and lack of pathogenicity of *B. subtilis* strain MBI 600 via the acute oral, pulmonary, and intravenous routes of exposure. It was also based on the absence of adverse effects reported for workers involved in the manufacture and use of the end-use product in the United States since 2005. Furthermore, use pattern is limited to the application to plant growing media in commercial facilities and the formulants do not pose a concern with respect to dermal toxicity and irritation. Therefore, dermal toxicity and irritation testing with the end-use product was not required.

Occupational/Bystander Assessment

When handled according to the label instructions, the potential for dermal, inhalation and to some extent, ocular exposure for applicators and handlers exists, with the primary source of exposure to workers being dermal.

Since unbroken skin is a natural barrier to microbial invasion of the human body, dermal absorption could only occur if the skin were cut, if the microbe were a pathogen equipped with mechanisms for entry through the skin or infection of the skin, or if metabolites were produced that could be dermally absorbed. *B. subtilis* strain MBI 600 has not been identified as a wound pathogen, and there is no indication that it could penetrate intact skin of healthy individuals. Furthermore, *B. subtilis* strain MBI 600 demonstrated low toxicity and minimal irritation in the dermal toxicity/irritation studies.

The risk of toxicity exists in individuals exposed to large quantities of spores of *B. subtilis* strain MBI 600 by inhalation. In addition, respiratory hypersensitivity could be expected to develop upon repeated exposure to the product. Specific label wording to minimize exposure to dusts generated while handling the dry product is required. To mitigate the risk of pulmonary exposure to *B. subtilis* strain MBI 600, applicators who apply Tackle to the plant growing media (eg. soil) will be required to wear a dust mask as they are most likely to be exposed via inhalation.

Furthermore, the PMRA assumes that all microorganisms contain substances that can elicit positive hypersensitivity reactions, regardless of the outcome of sensitization testing. Label statements (i.e., Potential Sensitizer) and risk mitigation measures such as personal protective equipment, including waterproof gloves, long-sleeved shirt, long pants, shoes and socks and a dust/mist filtering respirator/mask (NIOSH approval number prefix TC-21 or NIOSH approved respirators with any N-95, P-95, R-95 or HE filter) are required to minimize exposure and protect applicators and handlers that are likely to be primarily exposed.

Based on the use pattern, the potential for ocular exposure is expected to be minimal. Based on the low toxicity profile of *B. subtilis* strain MBI 600 and on the nature of the end-use product formulation, ocular exposure is not expected to pose an unacceptable risk to workers. Also, the label for Tackle requires the use of eye goggles that would further mitigate ocular exposure.

Inhalation or dermal exposure to the general public is expected to be low based on the indoor application of Tackle to plant growing media (eg. soil) in commercial nurseries, garden centres, greenhouses and planting media manufacturers. Overall, the PMRA does not expect that bystander exposures will pose an undue risk on the basis of the low toxicity/pathogenicity profile for *B. subtilis* strain MBI 600 and the related end-use product formulation.

The label states that applications to turf, residential or recreational areas are not allowed. Therefore, non-occupational dermal exposure and risk to adults, infants and children are low. Because the use sites are agricultural and horticultural, exposure to infants and children in school, residential and daycare facilities is likely to be minimal to non-existent. Consequently, the health risk to infants and children is expected to be negligible.

Dietary Exposure and Risk Assessment

Food: Based on the indoor use pattern of Tackle as a direct application to plant growing media prior to planting, dietary exposure to residues of *B. subtilis* strain MBI 600 on food commodities grown in plant-growing media treated with *B. subtilis* strain MBI 600 are expected to be very low. Furthermore, no adverse effects were observed at maximum hazard dose levels in the Tier I acute oral toxicity study with the Technical Grade Active Ingredient. Moreover, *B. subtilis* strain MBI 600 is a ubiquitous organism found in most terrestrial environments. Therefore, negligible to no risk is expected for the general population, including infants, children, or animals.

Higher-tier subchronic and chronic toxicity studies were not required based on the toxicity profile of the test animals in the Tier I acute oral, pulmonary, toxicity/infectivity and intravenous injection infectivity studies. Therefore, there are no concerns for chronic risks posed by dietary exposure of the general population and sensitive subpopulations, such as infants and children.

Drinking water: The likelihood that *B. subtilis* strain MBI 600 could potentially enter neighbouring aquatic environments as a result of the greenhouse use of Tackle is minimal. Risks from exposure to residues of *B. subtilis* strain MBI 600 via drinking water are not of concern because exposure will be minimal and because the Microbial Pest Control Agent (MPCA) showed no harmful effects on animals that were exposed orally in Tier I acute oral toxicity and infectivity testing. Also, the label for Tackle will instruct users not to contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes. Users are also advised not to allow effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other waters. Furthermore, municipal treatment of drinking water will likely reduce the transfer of residues to drinking water. Therefore, potential exposure to *B. subtilis* strain MBI 600 in surface and drinking water is negligible.

Maximum Residue Limits

As part of the assessment process prior to the registration of a pesticide, Health Canada 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 (MRL) under the Pest Control Products Act (PCPA) for the purposes of the adulteration provision of the Food and Drugs Act (FDA). Health Canada sets science-based MRLs to ensure the food Canadians eat is safe.

Although the United States Food and Drug Administration has noted that some strains of *B. subtilis* have been isolated from food implicated in food poisoning, these strains demonstrated the ability to produce a highly heat-stable toxin that was not reported in *B. subtilis* strain MBI 600. No such illnesses were reported for this MPCA in the United States where it has been registered for use on crops since 1994. Also, in Canada where the MPCA has been registered since 2007, no such illnesses have been reported. Therefore the establishment of an MRL is not required for *B. subtilis* strain MBI 600 under PCPA.

Aggregate Exposure

Based on the toxicity and infectivity test data previously submitted, waiver rationales submitted for the end-use product, and other relevant information in the PMRA's files, there is reasonable certainty no harm will result from aggregate exposure of residues of *B. subtilis* strain MBI 600 to the general Canadian population, including infants and children, when the microbial pest control product is used as an application to plant growing media as labelled. This includes all anticipated dietary (food and drinking water) exposures and all other non-occupational exposures (dermal and inhalation) for which there is reliable information. Even if there is an increase in exposure to this microorganism from the use of Tackle there should not be any increase in potential human health risk.

Cumulative Effects

The PMRA has considered the available information on the cumulative effects of such residues and other substances that have a common mechanism of toxicity. These considerations included the cumulative effects on infants and children of such residues and other substances with a common mechanism of toxicity. Besides naturally occurring strains of *B. subtilis* in the environment, and the biological fungicide products, Subtilex Biological Fungicide, ProMix with Biofungicide, Integral Liquid Biological Fungicide which also contain *B. subtilis* strain MBI 600 as the active ingredient, the PMRA is not aware of any other microorganisms, or other substances that share a common mechanism of toxicity with this active ingredient. No cumulative effects are anticipated if the residues of *B. subtilis* strain MBI 600 interact with related strains of this microbial species.

The health assessment for this end-use product is complete.

Environmental Assessment

The end-use product, Tackle does not contain formulants that present an unacceptable risk to terrestrial or aquatic environments.

Value Assessment

The data package contained a total of 30 greenhouse trials. For each of the tested pathogens, i.e. *Fusarium solani*, *Rhizoctonia solani* and *Pythium ultimum*, nine trials were conducted on tomatoes (3) cucumbers (3) and peppers (3). Three additional tomato trials were inoculated with *F. oxysporum* f. sp. *lycopersici*. Tackle effectively suppressed damping-off and root rot symptoms caused by these pathogens on tomatoes, peppers and cucumbers in all 30 greenhouse trials, as evidenced by the significantly higher final stand counts as well as the significant reductions in disease incidence and severity obtained with the rate of 400 g/175 m³.

Extrapolation from tomatoes, peppers and cucumbers to their respective crop groups, i.e. fruiting vegetables and cucurbit vegetables, can be safely supported based on substantial similarities in pest and crop biology among these crops. As no trials were conducted under field conditions, the use of Tackle is supported for suppression of damping-off and root diseases caused by *Fusarium* spp., *R. solani* and *Pythium* spp. on greenhouse fruiting vegetables and greenhouse cucurbits.

No efficacy data were provided to support the claims on ornamentals. Since *Pythium* spp. are non-host specific pathogens with comparable biology, the dispersal and infection processes among greenhouse crops, and the levels of protection achieved with Tackle on greenhouse vegetable seedlings, therefore, provide supplementary evidence in support of the claims on greenhouse ornamentals. Moreover, Subtilex has the same guarantee and use pattern as Tackle, and is registered for suppression of damping-off and root rot diseases caused by *Pythium* spp. on greenhouse ornamentals. The use of Tackle is accepted for conditional registration for suppression of damping-off and root diseases caused by *Fusarium* spp., *R. solani* and *Pythium* spp. on greenhouse ornamentals. Additional data are required for this use to be accepted for full registration.

Conclusion

The Pest Management Regulatory Agency has completed an assessment of the information provided in support of the product, Tackle, and has found the information sufficient to grant conditional registration for the microbial end-use product.

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