

Evaluation Report for Category B, Subcategory 1.1, 2.1 Application

Application Number: 2019-2122 / QST 713 Technical 2 and
2019-2123 / QST 713 SC

Application: New Technical Grade Active Ingredient (TGAI):
New End-Use Product (EP)

Product: QST 713 Technical 2 / QST 713 SC

Registration Number: 33650 (QST 713 Technical 2)
33651 (QST 713 SC)

Active ingredients (a.i.): *Bacillus subtilis* strain QST 713

PMRA Document Number: 3068821

Purpose of Application

The purpose of these applications was to register a new biofungicide, QST 713 Technical 2, and the associated end-use product, QST 713 SC, containing *Bacillus subtilis* strain QST 713, for suppression of listed crop diseases.

Product Characterization and Analysis

The manufacturing and formulating processes and the quality assurance associated with the production of QST 713 Technical 2 and QST 713 SC were described in sufficient detail and determined to be appropriate. Acceptable representative potency and microbial contaminant screening data were also submitted to demonstrate that all batches of the TGAI and EP meet the required acceptance criteria for microbial contamination. All batches of TGAI must conform to the limits outlined in the OECD Issue Paper on Microbial Contaminants for Microbial Pest Control Products.

The potential production of secondary metabolites was adequately addressed using acceptable analytical methods.

An acceptable rationale for QST 713 SC was provided to support a storage period of up to 3 years when stored at room temperature.

Health Assessment

Previous assessments of the active ingredient concluded that *Bacillus subtilis* strain QST 713 is non-infective via the oral, pulmonary (intratracheal) and intravenous routes of exposure (see ERC 2007-06¹). In the current applications, studies conducted with toxicologically equivalent

¹ ERC2007-06 – *Bacillus subtilis* strain QST 713, Serenade MAX, Serenade ASO, Rhapsody ASO, Serenade Garden Concentrate, Serenade Garden Ready To Use

test substances indicated that QST 713 Technical 2 and QST 713 SC are of low toxicity by the oral and pulmonary (inhalation) routes. Although dermal toxicity testing was not conducted on either the technical grade active ingredient (TGAI) or the end-use product (EP), the results of the available toxicity studies and the lack of metabolites of concern indicate that the EP will be of low toxicity via the dermal route. Both the TGAI and the EP are slightly irritating to the skin and minimally irritating to the eye. As is the case with all microbial pest control agents (MPCAs), *B. subtilis* strain QST 713 is considered to be a potential sensitizer.

Although the colony forming unit (CFU)/ha rate is higher for QST 713 SC than other registered EPs containing *B. subtilis* strain QST 713, there are no additional occupational, bystander, dietary or drinking water exposure concerns given the low toxicological and irritation profile of QST 713 SC and the lack of infectivity associated with the active ingredient. The label for QST 713 SC contains appropriate hazard signal words, precaution statements and personal protective equipment aimed at reducing occupational, residential and bystander and drinking water exposure. Furthermore, the active ingredient is present in a number of other registered EPs for which there are few reports of adverse effects.

Maximum Residue Limit

Bacillus subtilis strain QST 713 is currently registered in Canada for food uses. The Pest Management Regulatory Agency (PMRA) has determined that specification of a maximum residue limit (MRL) under the *Pest Control Products Act* (PCPA) is not required for *B. subtilis* strain QST 713 (see ERC 2007-06²).

Incident Reports Related to Human and Animal Health

There was one human incident involving *B. subtilis* QST 713. In this incident, a person reported minor symptoms of rash and cough when applying a product containing *B. subtilis* strain QST 713. The label of QST 713 SC contains appropriate hazard signal words, precaution statements and personal protective equipment aimed at reducing pesticide exposure when mixing, loading or applying the product. Hence, no additional mitigation measures are required based on the incident report review.

Environmental Assessment

The risk posed by *B. subtilis* strain QST 713 to non-target species was previously assessed and found to be acceptable (see ERC 2007-06³). Although the CFU/ha rate is higher for QST 713 SC than other registered EPs containing *B. subtilis* strain QST 713, there are no additional environmental concerns given the low toxicological profile of QST 713 SC (as demonstrated in the available acute toxicity studies in laboratory animals) and the lack of metabolites of concern.

² ERC2007-06 – *Bacillus subtilis* strain QST 713, Serenade MAX, Serenade ASO, Rhapsody ASO, Serenade Garden Concentrate, Serenade Garden Ready To Use

³ Ibid.

The label for QST 713 SC contains appropriate statements to minimize exposure to non-target organisms. Furthermore, the active ingredient is present in a number of other registered EPs for which there are no reports of adverse effects on non-target organisms.

Incident Reports Related to the Environment

As of October 1, 2019, there was one environment incident involving *B. subtilis* (strain unspecified). Mortality was reported in spinach plants following aerial application of a product containing *B. subtilis*. The incident was assigned a certainty index of unlikely. Since the causality of the incident does not meet the criteria of highly probable, probable and possible, the incident was not considered in this review. No additional risk mitigation measures are recommended for *B. subtilis* strain QST 713.

Value Assessment

A scientific rationale was provided to support the registration of QST 713 SC based on the registered soil use patterns of a precedent product. When applied via soil applications, the rate of active ingredient applied per hectare for the precedent product and QST 713 SC is similar. However, the product rates for the same use are largely reduced for QST 713 SC as it is approximately 5x more concentrated in terms of the active ingredient in cfu/g than that in the precedent product. The change in the product rates would not likely have negative impact on the product performance as the application solutions should contain the same concentrations of the active ingredient from both the precedent product and QST 713 SC.

Results from bridging efficacy trials on potato in Manitoba also demonstrated that low product rates of QST 713 SC performed similarly as the registered rates of the precedent product since the spore concentration of the active ingredient is the same in the spraying solutions for both products.

Conclusion

The Pest Management Regulatory Agency has completed an assessment of the information provided, and has found the information sufficient to support the registration of QST 713 Technical 2 and QST 713 SC.

References

PMRA

Document

Number	Reference
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2994552	2018, <i>Bacillus subtilis</i> QST713 FS: Total Spore Number and Viable Spore Count Validation (GLP) - Final Report -, DACO: M2.10.1,M2.10.2 CBI
2994553	2017, Method for determination of aerobic colony forming units in QST 713 HiCFU samples, DACO: M2.10.1,M2.10.2 CBI
2994554	2017, Procedure for determination of cell and spore counts in bacterial samples, DACO: M2.10.1,M2.10.2 CBI
2994555	2017, The characterization of <i>Bacillus subtilis</i> QST713 whole broth, batch number 2017-006359, DACO: M2.12 CBI
2994556	2018, Waiver for certain physical and chemical characteristics of QST 713 MUP, DACO: M2.12 CBI
2994557	2018, Manufacturing process overview for QST 713 MUP for USA, DACO: M2.8 CBI
2994558	2018, Product chemistry of QST 713 MUP, DACO: M2.10.1,M2.10.2,M2.10.3,M2.9.2 CBI
2994582	2018, Amendment No. 1 to Final Report - Material Accountability of <i>Bacillus subtilis</i> QST713 FS: - 5 Batch analysis (GLP), DACO: M2.10.1,M2.10.2 CBI
2994584	2018, <i>Bacillus subtilis</i> QST713 FS: Total Spore Number and Viable Spore Count Validation (GLP) - Final Report -, DACO: M2.10.1,M2.10.2 CBI
2994586	2018, Waiver for storage stability and stability to normal and elevated temperatures, metals, and metal ions of QST 713 FS, DACO: M2.11 CBI
2994587	2018, Physical and chemical properties of <i>Bacillus subtilis</i> QST713 FS, DACO: M2.12 CBI
2994588	2018, Manufacturing process overview for QST 713 FS end use product - For USA, DACO: M2.8 CBI
2994589	2018, Product chemistry of QST 713 FS, DACO: M2.10.1,M2.10.2,M2.10.3,M2.9.2 CBI
3026534	2019, Response to PMRA Deficiency Letter for Submission No. 2019-2122; DACO: M2.10.2 -Analysis for Microbial Contaminants, DACO: M2.10.2 CBI
3026535	2019, The Genetic Capacity for the Production of Secondary Metabolites by <i>B. amyloliquefaciens</i> QST 713 - Final Report, DACO: M2.10.3 CBI
3026536	2019, Evaluation of biological chemistry in Serenade ASO - Final Report, DACO: M2.10.3 CBI
3059756	2019, Response to PMRA clarification request from 01Nov2019, DACO: M2.7.1
2994561	2017, <i>Bacillus subtilis</i> QST713 WB TK: Acute oral toxicity - Up-and-down procedure in rats, DACO: M4.2.2
2994562	2017, <i>Bacillus subtilis</i> QST713 WB TK: Acute inhalation toxicity in rats, DACO: M4.2.3
2994564	2017, <i>Bacillus subtilis</i> QST713 WB TK: Primary skin irritation in rabbits, DACO: M4.5.2

- 2994565 2017, *Bacillus subtilis* QST713 WB TK: Primary eye irritation in rabbits, DACO: M4.9
- 2994594 2017, *Bacillus subtilis* QST713 FS: Acute oral toxicity - Up-and-down procedure in rats, DACO: M4.2.2
- 2994595 2017, *Bacillus subtilis* QST713 FS: Acute inhalation toxicity in rats, DACO: M4.2.3
- 2994598 2017, *Bacillus subtilis* QST713 FS: Primary skin irritation in rabbits, DACO: M4.5.2
- 2994599 2017, *Bacillus subtilis* QST713 FS: Primary eye irritation in rabbits, DACO: M4.9
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- 2918021 2010, Root colonization visualization of serenade, DACO: M10.2.1
- 2994581 2019, Bridging Rationale to support Extrapolation of Soil Application Uses from Precedent to QST 713 SC (syn. HiCFU), DACO: M10.1, M10.2, M10.2.2, M10.3, M10.3.1, M10.3.2, M10.3.2.1, M10.3.2.2, M10.4, M10.4.2, M10.4.3, M10.4.4

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