Health Canada Santé Canada

Evaluation Report for Category B, Subcategory 2.3 and 2.4 Application

Application Number: 2016-6201
Application: Changes to end-use product chemistry – Identity and proportion of formulants
Product: Bioprotec HP
Registration Number: 27099
Active ingredients (a.i.): *Bacillus thuringiensis* subsp. *kurstaki*
PMRA Document Number: 2657781

Background

Bacillus thuringiensis ssp. *kurstaki* strain EVB113-19 has been registered in Canada since 2000. A slurry formulation of Bioprotec Technical (Registration Number 26425; containing *Bacillus thuringiensis* ssp. *kurstaki* strain EVB113-19) is currently registered and used in the manufacture of the commercial and restricted class end-use product, Bioprotec HP (Registration Number 27099), which is an insecticides used to control certain species of lepidopteran larvae in forests, woodlands, residential and other treed areas.

Purpose of Application

The purpose of this application was to change the formulation of Bioprotec HP. This product is to be manufactured with a new powder formulated technical grade active ingredient, Bioprotec Technical Powder, reviewed concurrently under application 2015-6180.

Five other Bioprotec Technical Powder containing end-use products are being reviewed concurrently under applications 2015-6189, 2015-6194, 2015-6200, 2015-6203 and 2015-6219.

Product Characterization and Analysis

A review of the submitted information/data indicated that the end-use products produced using Bioprotec Technical Powder are chemically equivalent to those produced using Bioprotec Technical (slurry formulation).

An updated description of the manufacturing process was submitted for the end-use product.

Data were submitted in support of the guarantee being expressed as potency units [cabbage looper units (CLU)/mg and billion CLU (BCLU)/L]. The guarantee is as follows:

Canada

End-Use Product	Potency	
	CLU/mg	BCLU/L
Bioprotec HP	17500	20.1

Analyses were conducted on batches of Bioprotec HP for unintentional ingredients and microbial contaminants and the results were acceptable.

Storage stability was assessed. Bioprotec HP is stable for up to one year from the date of manufacture at temperatures of between 4°C and 20°C.

Health Assessments

The active ingredient, *Bacillus thuringiensis* ssp. *kurstaki* strain EVB-113-19, is considered to be equivalent to currently registered strains of *Bacillus thuringiensis* ssp. *kurstaki*. The toxicology database for *B. thuringiensis* ssp. *kurstaki* strain EVB-113-19 along with the data submitted in support of the present applications for Bioprotec Technical Powder, Bioprotec Aqueous Biological Insecticide, Bioprotec CAF Aqueous Biological Insecticide, Bioproec ECO, Bioprotec HP, Bioprotec XHP Aqueous Biological Insecticide and AEF 13-03 are adequate to define the toxic effects that may result from exposure to the active ingredient. Bioprotec Technical Powder and the end-use products formulated from it are expected to be of low acute toxicity and not infective via the oral, inhalation and dermal routes of exposure.

The oral LD_{50} of Bioprotec Technical Powder was found to be $>3.5 \times 10^8$ CFU/animal and a pattern of clearance was established.

Dermal toxicity was not observed following treatment with 2 g/kg bw of a Bioprotec Technical (slurry form) containing end-use product. A maximum average score (MAS) of 2.7/8.0 was observed on Day 2 (day of unwrapping), thus, indicating mild irritation. Considering that the test animals were exposed to high doses of the test material for 24 hours (as opposed to the norm of four hours for acute dermal irritation studies) and that the observations on the day following unwrapping (Day 3) were only very slight erythema and edema, the label wording "CAUTION SKIN IRRITANT" is not required.

A primary eye irritation study indicated that a Bioprotec Technical containing end-use product was minimally irritating to the eyes of rabbits.

The dermal toxicity/irritation and primary eye irritation studies, conducted using Bioprotec Technical containing end-use products, are considered acceptable for assessing the dermal toxicity/irritation and eye irritation potential of Bioprotec Aqueous Biological Insecticide, Bioprotec CAF Aqueous Biological Insecticide, Bioproec ECO, Bioprotec HP, Bioprotec XHP Aqueous Biological Insecticide and AEF 13-03 formulated using Bioprotec Technical Powder. Many of the formulation constituents in slurry and powder containing end-use products are the same, and are present at similar or at lower levels in the powder containing end-use products. Any new formulation ingredients present in the Bioprotec Technical Powder containing end-use products are either List 4A or 4B.

The only List 3 ingredient is present at a lower concentration in the end-use products produced using the Bioprotec Technical Powder. Therefore, the dermal toxicity/irritation and eye irritation potentials of the Bioprotec Technical Powder containing end-use products are not expected to exceed that of Bioprotec Technical containing end-use products.

The List 3 ingredient is a preservative that contains low levels of polychlorinated dibenzo-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) as microcontaminants that have been identified Track 1 substances. The presence of these microcontaminants in Bioprotec Technical Powder and its associated end-use products was assessed and found to be acceptable because their levels are low/being managed as outlined in the PMRA Regulatory Directive DIR99-03 for the implementation of the Toxic Substances Management Policy.

As all microbial-based pest control products are considered to contain substances that could elicit a hypersensitivity reaction in animals, the signal words "POTENTIAL SENSITIZER" are required on the principal display panel of all Bioprotec labels.

Environmental Assessment

The environmental toxicology database for *B. thuringiensis* ssp. *kurstaki* strain EVB-113-19 was found to be adequate to define the toxic effects to non-target organisms that may result from exposure to the active ingredient. A previous review of the environmental toxicology studies cited for the current submissions found that *B. thuringiensis* ssp. *kurstaki* strain EVB-113-19 is not expected to pose a risk to non-target organisms when used in accordance with the label directions.

The end-use products formulated with Bioprotec Technical Powder are considered to be equivalent to those formulated with Bioprotec Technical in that the guarantees and many of the formulation ingredients are the same. The uses, rates and application methods of both the Bioprotec Technical Powder and Bioprotec Technical containing end-use products are identical.

Therefore, based on the results of non-target testing conducted for Bioprotec Technical and the similarities in formulation and proposed use scenarios, the risk to non-targets associated with the Bioprotec Technical Powder containing end-use products is not expected to exceed that of the Bioprotec Technical containing end-use products.

Value Assessment

The formulation was supported based on bioassay data demonstrating equivalent potency of the previously registered and new formulations.

Conclusion

The PMRA has completed a review of all available information in support of Bioprotec HP and found it sufficient to support the change in technical source to a powder formulation.

References

PMRA Document Number	Reference
1698843	Technical Chemistry BTB-AGA-1 Appendix Protocol: Subcutaneous Toxicity Test on Mice, DACO: M2.8
1698930	Technical Chemistry BTB-AGA-1 Analysis for Microbial Contaminants, DACO: M2.10.2 CBI
1698937	Technical Chemistry BTB-AGA-1 Method for Detection and Enumeration of Total Coliforms, DACO: M2.10.2 CBI
1698939	Technical Chemistry BTB-AGA-1 Method for Detection and Enumeration of Faecal Coliforms, DACO: M2.10.2 CBI
1698941	Technical Chemistry BTB-AGA-1 Method for Detection and Enumeration of *Faecal Streptococci*, DACO: M2.10.2 CBI
1698942	Technical Chemistry BTB-AGA-1 Method for Detection and Enumeration of *Pseudomonas aeruginosa*, DACO: M2.10.2 CBI
1698943	Technical Chemistry BTB-AGA-1 Method for Detection and Enumeration of *Staphylococcus aureus*, DACO: M2.10.2 CBI
1698945	Technical Chemistry BTB-AGA-1 Method for Detection and Enumeration of Yeasts and Fungi, DACO: M2.10.2 CBI
1698946	Technical Chemistry BTB-AGA-1 Method for Detection of Salmonella, DACO: M2.10.2 CBI
2582318	2014, Method Product Guarantee, DACO: M2.9.2 CBI
2582330	2015, Physical and Chemical Properties, DACO: M2.12 CBI
2582436	2015, Physical and Chemical Properties, DACO: M2.12 CBI
2582558	2015, Physical and Chemical Properties, DACO: M2.12 CBI
2582608	2015, Physical and Chemical Properties, DACO: M2.12 CBI
2582704	2015, Physical and Chemical Properties, DACO: M2.12 CBI
2583115	2015, DACOs M2.1-2.6, DACO: M2.1, M2.2, M2.3, M2.4, M2.5, M2.6 CBI
2583117	2015, Manufacturing Process, DACO: M2.8 CBI
2583119	2015, Manufacturing Process M8.1-3, DACO: M2.8 CBI
2583121	2015, Potency Estimation and Product Guarantee, DACO: M2.9.2 CBI
2583122	2015, Unintentional Ingredients, DACO: M2.9.3 CBI
2583123	2015, Results of Exotoxin Presence in B.t. Product, DACO: M2.9.3 CBI
2583129	2015, Physical and Chemical Properties, DACO: M2.12 CBI
2583186	2015, Physical and Chemical Properties, DACO: M2.12 CBI
2624559	2016, Manufacturing Process AEF 13-03, DACO: M2.8 CBI
2624587	2016, Manufacturing Process Bioprotec, DACO: M2.8 CBI
2624601	2016, Storage Stability, DACO: M2.11 CBI
2624602	2016, Storage Stability Report, DACO: M2.11 CBI
2624624	2016, Storage Stability, DACO: M2.11 CBI
2624631	2016, Manufacturing Process ECO, DACO: M2.8 CBI

2624650 2016, Storage Stability, DACO: M2.11 CBI
2624657 2016, Manufacturing Process Bioprotec HP, DACO: M2.8 CBI
2624671 2016, Storage Stability, DACO: M2.11 CBI
2624679 2016, Manufacturing Process Bioprotec XHP, DACO: M2.8 CBI
2624691 2016, Storage Stability, DACO: M2.11 CBI
2624712 2016, Unintentional Ingredient, DACO: M2.9.3 CBI
2624713 2016, Unintentional Ingredient, DACO: M2.9.3 CBI
2624714 2016, Unintentional Ingredient, DACO: M2.9.3 CBI
2637593 2016, Potency Estimation, DACO: M2.9.2 CBI
2637594 2016, Potency Estimation, DACO: M2.9.2 CBI
1371542 2001, Bioprotec Technical Material (*Bacillus thuringiensis* ssp. *kurstaki*) Dietary Toxicity and Pathogenicity Test with Honey Bees (*Apis mellifera*), DACO: M9.5.1
1371544 2001, Bioprotec Technical Material (*Bacillus thuringiensis* ssp. *kurstaki*): A Dietary Pathogenicity and Toxicity Study with Green Lacewing Larvae (*Chrysoperla carnea*), DACO: M9.5.1
1371547 2000, Bioprotec Technical Material (*Bacillus thuringiensis* ssp. *kurstaki*): An Avian Oral Pathogenicity and Toxicity Study in the Northern Bobwhite, DACO: M9.2.1
1371548 2001, Bioprotec Technical Material (*Bacillus thuringiensis* ssp. *kurstaki*) - Infectivity and Pathogenicity to Rainbow Trout (*Oncorhynchus Mykiss*) During a 30-Day Static-Renewal Test, DACO: M9.4.1
1371550 2000, Bioprotec Technical Material (*Bacillus thuringiensis* ssp. *kurstaki*): A Dietary Pathogenicity and Toxicity Study with the Ladybird Beetle (*Hippodamia Convergens*), DACO: M9.5.1
1371552 2001, Bioprotec Technical Material (*Bacillus thuringiensis* ssp. *kurstaki*) - Toxicity, Infectivity and Pathogenicity to Daphnids (*Daphnia Magna*) During a 21-Day Static-Renewal Test, DACO: M9.5.2
1191866 1999, Acute Dermal Toxicity/Pathology Study of Bioprotec, *Bacillus thuringiensis* ssp. *kurstaki* Strain HD-1, Biopesticide in Rabbits (Final Report), DACO: M4.4
1191869 1999, Primary Eye Irritation Study of Bioprotec End-Use Product Containing *Bacillus thuringiensis* ssp. *kurstaki* Strain HD-1 in Rabbits, DACO: M4.9
2583135 2015, Acute Oral Toxicity/Pathogenicity Study in Rats, DACO: M4.2.2
2583138 2015, Reporting of Hypersensitivity Incidence, DACO: M4.6

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