Health Canada Santé Canada

Evaluation Report for Category B, Subcategory 2.6 Application

Application Number: 2022-1352
Application: New End-Use Product Chemistry-New combination of Technical Grade Active Ingredients
Product: Ilevo Duo Seed Treatment
Registration Number: 35227
Active ingredients (a.i.): Fluopyram and *Bacillus firmus* strain I-1582
PMRA Document Number: 3601947

Purpose of Application

The purpose of this application was to register a new commercial seed treatment product, Ilevo Duo Seed Treatment, which contains a new combination of active ingredients, for use on soybeans as a fungicide and nematicide.

Chemistry Assessment / Product Characterization and Analysis

Ilevo Duo Seed Treatment is formulated as a suspension containing fluopyram at a concentration of 360 g/L and *Bacillus firmus* strain I-1582 at a minimum of 4×109 CFU/mL. This end-use product has a density of 1.201-1.241 g/mL and a pH of 6.0-7.0. The described manufacturing and quality control processes, and representative batch data for Ilevo Duo Seed Treatment were acceptable to support the new seed treatment product. Acceptable potency and storage stability testing supports the guarantee of the microbial pest control agent (MPCA) and storage period on the end-use product label. The required chemistry data for Ilevo Duo Seed Treatment have been provided, reviewed and found to be acceptable.

Health Assessments

Ilevo Duo Seed Treatment was moderately acutely toxic via the oral route, and of low acute toxicity via the dermal and inhalation routes. Ilevo Duo Seed Treatment was minimally irritating to the eye and non-irritating to the skin. Ilevo Duo Seed Treatment was not a dermal sensitizer.

The MPCA, *Bacillus firmus* strain I-1582, is currently registered (Proposed Registration Decision PRD2011-24, Registration Decision RD2012-20 - *Bacillus firmus* strain I-1582). When *Bacillus firmus* strain I-1582 was tested on laboratory animals, there were no signs that it caused any toxicity or disease from oral, pulmonary (inhalation and instillation), dermal and intravenous routes of exposure. PMRA considers all microbial pest control agents (MPCAs) as potential sensitizers since most microorganisms contain substances that could elicit a positive reaction in test animals. Consequently, the statements, “POTENTIAL SENSITIZER” and “May cause sensitization,” are required on the principal display panel, and on the secondary display panel of the end-use product label under the “PRECAUTIONS” section, respectively.

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Quantitative occupational exposure risk assessments on file for fluopyram are adequate to demonstrate that the use of Ilevo Duo Seed Treatment for seed treatment on soybeans fits within the registered seed treatment use pattern of fluopyram. No health risks of concern are anticipated for workers involved in commercial seed treatment facilities and mobile treaters, or for individuals handling treated seed while planting, provided all label use directions, precautions and restrictions are adhered to.

No new residue data for fluopyram in soybeans were submitted or were required to support the registration of Ilevo Duo Seed Treatment. Previously reviewed residue data for fluopyram from field trials conducted in/on soybeans were reassessed in the framework of this application and were deemed acceptable. Based on this assessment, residues are not expected to be greater than from the currently registered uses and will be covered by the established Maximum Residue Limits (MRLs). Consequently, dietary exposure to residues of fluopyram is not expected to increase with the registration of Ilevo Duo Seed Treatment. No health risks of concern are expected for acute or chronic dietary exposure (food and drinking water) for fluopyram to any segment of the population, including infants, children, adults, and seniors.

Based on the seed treatment use of Ilevo Duo Seed Treatment, the likelihood of *Bacillus firmus* strain I-1582 to remain as residues on the soybeans at harvest is very low. Furthermore, since *Bacillus firmus* strains are common in nature, a seed treatment use is not expected to result in a sustained increase of the natural environmental background levels of this microorganism. No adverse effects have been attributed to dietary exposure from natural populations of *Bacillus firmus* strain I-1582, and when *Bacillus firmus* strain I-1582 was administered orally to rats, there was no significant toxicity and no signs of disease were observed.

For the same reasons, risks from exposure to this microorganism via drinking water are acceptable. The Ilevo Duo Seed Treatment label instructs users not to contaminate irrigation or drinking water supplies or aquatic habitats through equipment cleaning or waste disposal, and municipal treatment of drinking water is expected to further remove the transfer of residues to drinking water.

The health risks are acceptable from the use of Ilevo Duo Seed Treatment, when label directions are followed.

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

The specification of a maximum residue limit is not required for *Bacillus firmus* strain I-1582.

Environmental Assessment

The environmental risks associated with the use of Ilevo Duo Seed Treatment are acceptable when used according to label directions. Environmental concerns have been mitigated through adequate statements on the product label.

No new environmental studies were submitted. The database including non-target studies, scientific rationales and supporting published scientific literature previously submitted in support of *Bacillus firmus* strain I-1582 (for details see Proposed Registration Decision PRD2011-24, *Bacillus firmus* strain I-1582) was determined to be sufficiently complete. The use of Ilevo Duo Seed Treatment as a seed treatment is not expected to pose an unacceptable risk to birds, mammals, arthropods, fish and plants.

Value Assessment

To support claims against sudden death syndrome and soybean cyst nematodes on soybean, the applicant submitted results from eight field efficacy trials. The results from five greenhouse efficacy trials were submitted to support the claims against soybean cyst nematodes, root lesion nematodes and root knot nematodes on soybean. The applicant also submitted information in the form of use history information for a US-registered product as well as scientific rationales. The data demonstrated that application of Ilevo Duo Seed Treatment at labelled rates managed sudden death syndrome, soybean cyst nematodes, root lesion nematodes and root knot nematodes effectively on soybean.

Sudden death syndrome has become one of the leading yield-limiting soybean diseases in North America and soybean cyst nematodes are highly associated with sudden death syndrome development in a field. Soybean cyst nematodes, root lesion nematodes and root knot nematodes are very common in soybean fields and are yield-limiting factors. As a pre-mixture of two active ingredients, Ilevo Duo Seed Treatment will provide soybean growers with a new combination of fungicides and nematicides for use in managing sudden death syndrome and labelled nematodes.

Conclusion

The Pest Management Regulatory Agency has completed an assessment of the information provided, and has found the information acceptable to support the registration of Ilevo Duo Seed Treatment.

References

PMRA Document Number	Reference
3337137	2019, BAS 494 ST (BAS 494 00 I): Group A - Product Identity, Composition and Analysis, DACO: 3.2.1,3.2.2,3.2.3,3.3.1,3.4.2 CBI
3337138	2019, BAS 780F: GLP Validation of Analytical Method AFR0157/01: Determination of Fluopyram (Reg No. 5203319) content in BAS 494 00 I by HPLC, DACO: 3.4.1 CBI
3337140	2019, Determination of physico-chemical properties according to UN Transport Regulation and Directive 94/37/EC (Regulation (EC) No. 440/2008), DACO: 3.5.11,3.5.12,3.5.2,3.5.4,3.5.6,3.5.8
3337141	2019, BAS 494 00 I: Determination of Oxidation/Reduction, Chemical Incompatibility, DACO: 3.5.8
3337142	2022, DACO 3.5 - Chemical and Physical Properties, DACO: 3.5.13,3.5.15,3.5.16
3337143	2022, Determination of Physical/Chemical Properties of BAS 494 00 I: Long Term Storage Stability and Corrosion Characteristics in Commercial Type Containers, DACO: 3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.5,3.5.6,3.5.7,3.5.9
3496833	2023, Additional information regarding storage stability, DACO: 3.5.10
3496834	2023, Storage stability of BAS 494 00 I: Determination of Fluopyram contents, DACO: 3.5.10 CBI
3337132	2006, SOP: Application of test compounds to seed, DACO: 10.1
3337133	2022, Petition for Application: BAS 494 ST for use in soybean for the control of *Fusarium virguliforme* the causal agent of Sudden Death Syndrome and the suppression of nematodes, DACO: 10.1, 10.2.1, 10.2.2,10.3, 10.3.1, 10.3.2, 10.4, 10.5.1, 10.5.2, 10.5.3, 10.5.4, 10.5.5
3337135	2022, Trial reports in support of the petition to register BAS 494 ST as a fungicide and nematicide seed treatment for use in soybean, DACO: 10.2.3.3
3409695	2022, DACO 10 - Value Additional information to address deficiencies, DACO: 10.2.3.3
3409696	2022, Use History of ILEVO on soybean in the United States, DACO: 10.2.4
3409697	2021, Fluopyram ST, DACO: 10.2.4
3337145	2019, BAS 494 AA I: Acute Oral Toxicity: Acute Toxic Class Method in Rats, DACO: 4.6.1
3337146	2019, BAS 494 AA I: Acute Dermal Toxicity in Rats, DACO: 4.6.2
3337147	2019, BAS 494 AA I: Acute Inhalation Toxicity in Rats, DACO: 4.6.3
3337148	2019, BAS 494 AA I: Primary Eye Irritation in Rabbits, DACO: 4.6.4
3337149	2019, BAS 494 AA I: Primary Skin Irritation in Rabbits, DACO: 4.6.5
3337150	2019, BAS 494 AA I: Dermal Sensitization Test in Guinea Pigs - Buehler Method, DACO: 4.6.6
3337151	2022, Dusting Off Study, Soybean, DACO 5.15
3337139	2019, BFI-1582 (*Bacillus firmus*) bacterial spores in Fluopyram + Bacillus Firmus FS 500: Viable count method validation, DACO: 3.4.1 CBI
3337144	2022, BFI-1582 (*Bacillus firmus*) bacterial spores in Fluopyram + Bacillus Firmus FS 500: 2 year Storage Stability, DACO: 3.5.10