Health Canada / Santé Canada

Pest Management Regulatory Agency / Agence de réglementation de la lutte antiparasitaire

Date Received - Date de réception :
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Notice of Objection to a Registration Decision under Subsection 35(1) of the *Pest Control Products Act*

Avis d'opposition à une décision d'homologation en vertu du paragraphe 35(1) de la *Loi sur les produits antiparasitaires*

1. Objector information - Information sur l'opposant

Name - Nom / Corporation - société / Organization - organisation			
MANITOBA CONSERVATION			
Postal Address - Adresse postale			
200 SAULTEAUX CRES,			BOX 70
City/Town - Ville	Province/State - Province/État	Country - Pays	Postal Code/ZIP - Code postal/Zip
WINNIPEG	MB	CANADA	R3J 3W3
Phone - Téléphone	Fax - Télécopieur	E-mail - Adresse électronique	
(204) 945-7846	942-2641	Keith.Knowles@gov.mb.ca	

2. Product information - Information sur le produit

Name of active ingredient to which decision relates: / Nom de la matière active à laquelle la décision se rapporte :	Bacillus thuringiensis Kurstaki
Name of end-use product to which decision relates: / Nom de la préparation commerciale à laquelle la décision se rapporte :	

3. Registration decision to which objection relates - Décision d'homologation pour laquelle vous déposez un avis d'opposition

Decisions on application - Décision concernant la demande

- ☐ Granting registration - Homologation accordée
- ☐ Denying registration - Homologation rejetée
- ☐ Granting an amendment of a registration - Modification à l'homologation accordée
- ☐ Denying an amendment of a registration - Modification à l'homologation rejetée

Decisions on re-evaluation or special review - Décision concernant la réévaluation ou l'examen spécial

- ☐ Confirming registration - Homologation confirmée
- ☐ Cancelling registration - Homologation annulée
- ☒ Amending registration - Modification à une homologation

4. Date the decision statement was made public: / Date de la publication de l'énoncé de décision :

5. Area of scientific evaluation to which the objection relates - Volet de l'évaluation scientifique touché par l'avis d'opposition

- ☒ Health risk assessment (toxicology, food residue, occupational exposure) - Évaluation des risques pour la santé (toxicologie, résidus dans les aliments, exposition professionnelle)
- ☒ Environmental risk assessment (environmental fate, environmental toxicology) - Évaluation des risques pour l'environnement (devenir dans l'environnement, écotoxicologie)
- ☐ Value and efficacy assessments (tolerance, value) - Évaluation de la valeur et de l'efficacité (tolérance des cultures, valeur)

6. Scientific basis for the objection - Fondement scientifique de l'opposition

Attachment included: ☒ Yes ☐ No / *Pièce jointe incluse :* ☐ Oui ☐ Non

SEE ATTACHED ENVIRONMENTAL HAZARD CRITERIA 217 PERTAINING TO HEALTH HAZARD AND SAFETY IN AQUATIC ENVIRONMENTS.

7. Signature of objector or representative - Signature de l'opposant ou de son représentant

K Knowles

KEITH KNOWLES

Printed Name - en lettres moulées

Objectors who submit confidential information which is part of their submission (i.e., confidential business information, confidential test data) are responsible for identifying this information.

Information required to process the notice of objection may include some personal information as defined in the *Privacy Act*. In accordance with that Act, such personal information may be made public as authorized by the *Pest Control Products Act* and its regulations. Under the *Privacy Act*, individuals have the right to their personal information. For more information on how the PMRA manages personal information, contact the PMRA Information Services 1-800-267-6315 within Canada and 1-613-736-3799 outside Canada or via e-mail at pmra_infoserv@hc-sc.gc.ca.

Les opposants qui soumettent des renseignements confidentiels (c.-à-d. des renseignements commerciaux confidentiels, des données d'essai confidentielles) sont responsables de leur identification comme tels dans leur envoi.

L'information requise pour traiter cet avis d'opposition peut comprendre certains renseignements personnels tels que définis dans la *Loi sur la protection des renseignements personnels*. Conformément à cette Loi, ces renseignements peuvent être rendus publics, ce qui est permis par la *Loi sur les produits antiparasitaires* et son Règlement. En vertu de la *Loi sur la protection des renseignements personnels*, tous les individus ont le droit de consulter leurs renseignements personnels. On peut obtenir des précisions sur la gestion des renseignements personnels auprès de l'Agence de réglementation de la lutte antiparasitaire (ARLA) en communiquant avec le Service de renseignements au 1-800-267-6315 au Canada, ou au 1-613-736-3799 de l'extérieur du Canada, ou par courrier électronique à pmra_infoserv@hc-sc.gc.ca.

Canada

Manitoba

Conservation

June 26, 2008

Manitoba Conservation
Forestry Branch
200 Saulteaux Crescent
Winnipeg, Manitoba
R3J 3W3

Health Canada Pest Management Regulatory Agency
Address Locator: 6606E
2720 Riverside Drive
Ottawa, Ontario K1A 0K9

On behalf of Manitoba Conservation, enclosed is a Notice of Objection to a Registration Decision under Subsection 35(1) of the Pest Control Products Act, pertaining to the May 6, 2008 reevaluation of *Bacillus thuringiensis* (*Bt*).

This objection pertains to the restrictive nature of wording on the *Bt* label with regard to product handling and aerial application. This wording is contrary to scientific documentation stating that *Bt* products have been demonstrated to have no adverse health effects after occupational exposure and have been deemed safe for use in controlling insect pests in forest environments containing aquatic habitats.

Keith Knowles
Forest Health Biologist

UNITED NATIONS ENVIRONMENT PROGRAMME
INTERNATIONAL LABOUR ORGANISATION
WORLD HEALTH ORGANIZATION

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

ENVIRONMENTAL HEALTH CRITERIA 217

BACILLUS THURINGIENSIS

Environmental Health Criteria 217

Microbial Pest Control Agent

BACILLUS THURINGIENSIS

Published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization, and produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals.

World Health Organization
Geneva, 1999

1. SUMMARY

This monograph deals with microbial pest control agents (MCPAs) based on *Bacillus thuringiensis* (Bt). This bacterium is also a key source of genes for transgenic expression to provide pest resistance in plants and microorganisms as pest control agents in so-called genetically modified organisms (GMOs). The potential effects on human health and the environment of GMOs involve several aspects that are only remotely or not at all related to Bt products, and they are therefore outside the scope of this monograph.

1.1 Identity, biological characteristics and analytical methods

Bt is a facultative anaerobic, gram-positive bacterium that forms characteristic protein inclusions adjacent to the endospore. Bt subspecies can synthesize more than one parasporal inclusion. Bt is genetically indistinguishable from Bc, except for the ability of Bt to produce parasporal crystalline inclusions, which are toxic for certain invertebrates, especially species of insect larvae belonging to the insect orders *Coleoptera, Diptera* and *Lepidoptera.* The parasporal inclusions are formed by different insecticidal crystal proteins (ICP). The crystals have various shapes (bipyramidal, cuboidal, flat rhomboid, spherical or composite with two crystal types), depending on their ICP composition. A partial correlation between crystal morphology, ICP composition, and bioactivity against target insects has been established.

The basic phenotypic taxon is the subspecies, identified by the flagellar (H) serotype. By 1998, 67 subspecies had been described. The genes that encode the ICPs are mostly on plasmids. Each ICP is the product of a single gene. Most plasmids with ICP genes are readily transferred by conjugation between Bt strains and may be transferred to related species of bacteria. The phenotypic classification has now been complemented by molecular biological characterization, based on the sequence of the crystal *(cry* and *cyt)* genes rather than target organism specificity. Different domains of the ICP are responsible for host susceptibility (receptor recognition) and toxicity (pore formation).

Techniques commonly used to characterize Bt strains or the ICP itself include cell wall fatty acid analysis, monoclonal antibodies, oligonucleotide DNA probes, plasmid profiles, polymerase chain reaction (PCR) analysis, DNA fingerprinting and SDS-PAGE profiles.

Beta-exotoxin, a heat-stable nucleotide, is produced by some Bt subspecies during vegetative growth and may contaminate the products. Beta-exotoxin is toxic for almost all forms of life including humans and the target insect orders. During vegetative growth, various Bt strains produce an assortment of antibiotics, enzymes, metabolites and toxins, including Bc toxins, that may have detrimental effects on both target organisms and non-target organisms (NTOs). Spore counts do not accurately reflect the insecticidal activity of a Bt strain or Bt product. The potency (ITU/mg) of each Bt product is bioassayed using an international standard that uses a specific test insect.

1.2 Mode of action on target insects

The sporulated Bt with ICP or spore-ICP complexes must be ingested by a susceptible insect larva. The efficacy of the ICP depends on the solubilization in the midgut, the conversion of the protoxin to the biologically active toxin by proteolytic enzymes, specific membrane receptor binding by the C-terminal domain of the active toxin, and pore formation by the N-terminal domain with subsequent lysis of the epithelial cells. Spore germination and proliferation of the vegetative cells into the haemocoel may result in a septicaemia, contributing to the cause of death. Receptor binding by the ICP is the major determinant of host specificity by the different Bt ICPs.

1.3 Habitats

Many different Bt subspecies have been isolated from dead or dying insects mostly from the orders *Coleoptera, Diptera* and *Lepidoptera,* but many subspecies have also been isolated from soil, leaf surfaces and other habitats. The carcasses of dead insects often contain large quantities of spores and ICPs that may enter the environment. The coleopteran-active and lepidopteran-active Bt subspecies are primarily associated with the soil and phylloplane (leaf surfaces), whereas the dipteran-active Bt subspecies are commonly found in aquatic environments. In the environment, the spores persist and vegetative growth may occur when conditions are favourable and nutrients are available.

1.4 Commercial products, production and application

Conventional Bt products, which utilize naturally-occurring Bt strains, account for approximately 90% of the world MPCA market. Most Bt products contain ICP and viable spores, but in some Bti products the spores are inactivated. Each year some 13 000 tonnes are produced using aerobic fermentation technology. Conventional Bt products have been targeted primarily against lepidopteran pests of agricultural and forestry crops; however in recent years, Bt strains active against coleopteran pests have also been marketed. Strains of Bti active against dipteran vectors of parasitic and viral diseases are being used in public health programmes.

Commercial Bt formulations may be applied as an insecticide to foliage, soil, water environments or food storage facilities. After the application of a Bt subspecies to an ecosystem, the vegetative cells and spores may persist at gradually decreasing concentrations for weeks, months or years as a component of the natural microflora. The ICPs, however, are rendered biologically inactive within hours or days.

1.5 Effects of Bt on non-target organisms

Studies on mammals, particularly those on laboratory animals, have evaluated possible infectivity and toxicity of various Bt preparations, which include the ICPs, vegetative cells and spores. The ICPs, spores and vegetative cells of the Bt subspecies, which were administered by different routes, were mostly non-pathogenic and non-toxic to the various animal species tested. The vegetative cells and/or spores of Bt were demonstrated to persist for weeks without causing adverse effects. Bt has not been observed to adversely affect birds, fish or many other non-target aquatic vertebrates tested in a large number of laboratory and field studies. Relatively few species of aquatic invertebrates are susceptible to Bt under either laboratory or field conditions. Bt does not adversely affect earthworms.

The Bt subspecies have generally been shown to be highly specific in their insecticidal activity for *Coleoptera, Diptera* and *Lepidoptera* and have demonstrated little, if any, direct toxicity to non-target arthropods. Most of the existing safety data on non-target arthropods has been generated using the Bt subspecies with activity against *Diptera* and *Lepidoptera.*

Studies of Bti formulations free of toxic contaminants have not demonstrated deleterious effects on the vast majority of non-target arthropods. Some midges *(Diptera*: *Chironomidae),* which are closely related to mosquitoes, have been shown to be susceptible to high dosages of Bti, but are not affected by mosquito larvicidal dosages. In field studies, transient decreases or increases in populations of some non-target arthropods have been reported.

Many insect orders have been tested in either the laboratory or field, most of which have shown no effect from Btk.

Mortality has been observed in honey-bees *(Apis mellifera)* after exposure to vegetatively growing Btt and Btk, but the effect does not seem to be related to spores or ICPs. In laboratory and field studies Btg demonstrated no adverse effect on honey-bees.
Bte strains that produce beta-exotoxin have been shown to have adverse effects on non-target arthropods.

1.6 Exposure and effects of Bt on humans

The field application of Bt products can result in considerable aerosol and dermal exposure of workers. Agricultural uses of Bt can result in Bt contamination of potable water and food. With the exception of case reports on ocular and dermal irritation, no adverse health effects have been documented after occupational exposure to Bt products. Human volunteers ingested and inhaled large quantities of a Btk formulation but experienced no adverse health effects. Antibody titres to the vegetative cells, spores and spore-crystal complexes have been demonstrated in workers who spray Bt products; however, no adverse health effects were reported. There have been some case reports on the occurrence of Bt in patients with different infectious diseases. However, none of these studies unequivocally demonstrates an actual risk to human health from the use of Bt. Bt has not been reported to cause adverse effects on human health when present in drinking-water or food.

1.7 Conclusions

Owing to their specific mode of action, Bt products are unlikely to pose any hazard to humans or other vertebrates or to the great majority of non-target invertebrates provided that they are free from non-Bt microorganisms and biologically active products other than the ICPs. Bt products may be safely used for the control of insect pests of agricultural and horticultural crops as well as forests. They are also safe for use in aquatic environments including drinking-water reservoirs for the control of mosquito, black fly and nuisance insect larvae. However, it should be noted that vegetative Bt has the potential for the production of Bc-like toxins, the significance of which as a cause of human disease is not known.