Health Canada / Santé Canada

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

2008-2570

DEC 16 2009

Jennifer Burleigh
British Columbia Ministry of Forests and Range
PO Box 9513 Stn. Prov. Govt.
Victoria, BC V8W 9C2

Dear Ms. Burleigh:

Re: Notice of Objection – RVD2008-18 *Bacillus thuringiensis*

We have carefully reviewed your Notice of Objection, filed in July of 2008, regarding the Health Canada Pest Management Regulatory Agency (PMRA) decision to continue the registration of *Bacillus thuringiensis* (RVD2008-18). We are aware of your long-standing interest in *Bacillus thuringiensis*, and continue to make every effort to answer your questions and address your concerns.

Under the *Pest Control Products Act*, any person who believes there is a scientific basis for reconsideration of a decision to which subsection 28(1) applies can file a Notice of Objection within 60 days of the publication of the decision. Objections are expected to focus on the scientific basis of the decision related to health and environmental risks, the value of the pesticide and the need for this decision to be taken to an external panel of experts for consideration of the scientific argument presented in the Notice and to obtain advice to the Minister in that regard.

When a notice of objection is filed, a team of PMRA scientists, who were not involved in the original decision, is established. The team considers the scientific basis for the objection and determines if the criteria for the establishment of a review panel have been met.

Criteria for establishing a review panel include:

a. whether the information in the notice raises scientifically founded doubt as to the validity of the evaluation or re-evaluation of the health and environmental risks and the value of the pesticide; and
b. whether the advice of a panel of expert scientists would assist in addressing the objection.

.../2

The concern you raised in your objection was addressed during the extensive review and consultation process for the re-evaluation of *Bacillus thuringiensis*, and in our previous communications with you previously. Our team of PMRA scientists has carefully and extensively reviewed your question and concern, and has responded to in the attached document with information that was considered in the re-evaluation decision of *Bacillus thuringiensis*. The team did not identify any scientifically founded doubt with respect to the validity of the PMRA re-evaluation decision in the information you provided in your objection. As a result this notice of objection does not fulfill the criteria to establish a review panel to reconsider the decision for continued registration of *Bacillus thuringiensis*. . However, some statements will be amended on the product labels, as outlined in the attached detailed response.

We trust that the information provided in the attached detailed response provides some clarity to the issues you raised. The PMRA continues to put human health and the environment at the forefront of our regulatory activities, and will only register products for which there is reasonable certainty that no harm will result from their use as directed, including *Bacillus thuringiensis*.

Sincerely,

Marion Law
Chief Registrar
PEST MANAGEMENT REGULATORY AGENCY

Attachment:
Detailed Response to Notice of Objection

Attachment: A
Sub. No. 2008-2570

Detailed Response to Notice of Objection – RVD2008-18 *Bacillus thuringiensis*

The notice of objection, filed under subsection 35(1) of the *Pest Control Products Act* (PCPA), by Ms. Jennifer Burleigh regarding the re-evaluation decision for *Bacillus thuringiensis* has now been reviewed and assessed in accordance with the Act and Regulations.

The following information was received and reviewed in support of the notice of objection:

- Attachment to notice of objection (rationale)

Issues raised in the Notice of Objection are **bolded**, PMRA responses are not.

1) Personal Protective Equipment

"We are filing this Notice of Objection in regards to the recommended requirements of Personal Protective Equipment (PPE) by applicators and mixers of *Bacillus thuringiensis* (Bt). Our objection to these new requirements is based on science, specifically on the lack of studies that have shown any potential for sensitization or any study the results of which would warrant the requirement of NIOSH-approved respirators with an N-95 filter in the application and mixing of Bt.

In 1999, The World Health Organization's International Programme on Chemical Safety characterised the exposure and effects specifically of Btk on humans as follows:

'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.'
(http://www.inchem.org/documents/ehc/ehc/ehc217.htm)

Within the PACR2006-09 document, PMRA makes several statements on the lack of risk posed by Bt products including:

'Products containing Bacillus thuringiensis do not present unacceptable risks to human health or the environment when used according to label direction'

'The risk from occupational exposure, however, was determined to be low given the lack of mammalian toxicity.'

'*B. thuringiensis* has a long history of safe use as a pesticide'

If there is a long history of safe use, low risk from occupational exposure and no present unacceptable risk, then, why is there a need to impose additional risk reduction measures? PMRA provides no science to support the new measures.

When comments were submitted to PMRA on PACR2006-09 regarding our concerns on these requirements, PMRA's responses in RVD2008-18 is not based on science. Instead, PMRA dealt with potential sensitization, to which no evidence was presented, and that the required PPE was no more intrusive or threatening in appearance than disposable masks.

The label, as it appears on a product, is a legal document. It is not subject to interpretation by different groups as to intent. When people read the label for a product we are about to spray on their houses, playgrounds and parks requires applicators to a -95 NIOSH-approved respirator, which are used by health officials during infectious disease outbreaks such as SARS, tuberculosis and Avian Flu, we will be swamped with environmental appeals, will face outraged citizens at public protest, and will be vilified in the press over the perceived threat implied by the PPE requirements over what is stated as reduced risk, safe insecticide. The following statement, contained within the RVD2008-18 in response to our concerns over the new PPE requirements shows a complete lack of understanding of the very real public relations issues faced by land managers.

' .. . the required NIOSH-approved respirators are not any more intrusive or threatening in appearance than disposable dust masks and other PPE. These protective measures are unlikely to raise public concern.'

The increased requirements from PPE for applicators and mixers of these products indicate that Bt presents an unacceptable risk without a high level of protective equipment and this increased risk would also be perceived to extend to the general public. This is an important consideration given that Bt-based products are the only category of pesticides that are frequently applied aerially to residential areas including homes, playgrounds, and public spaces. The very high level of public scrutiny that occurs during these programs will result in the belief that Bt-based products are inherently dangerous, requiring respirators equivalent to those used to protect health officials during the SARS outbreak.

The BC Ministry of Forests and Range is strongly committed to a safe work environment for all our employees and contractors. If there was any scientific evidence to support the use of the PPE equipment recommended within the PACR, we would endorse its use and would seriously reconsider the use of this product in urban environments. However, there is no scientific evidence to support these changes, and in fact the science reinforces the safety of this product for the approved uses in Canada. Based on the scientific evidence that shows no adverse health risk, we recommend that the cautionary notes regarding potential sensitization and the requirement for '-95' NIOSH respirators should be deleted."

The current PMRA policy on the requirement of a dust/mist filtering respirator mask (MSH/NIOSH approval number prefix TC-21C) or a NIOSH-approved respirator with any N-95, R-95, P-95 or HE filter for biological products was largely adopted due to hygienic/sensitization concerns associated with the use of large concentrations of micoorganisms as well as harmonization activities such as joint reviews under North American Free Trade Agreement (NAFTA). In some cases, masks/respirators may also be required as a result of acute mammalian testing (i.e., pulmonary studies).

Microbial pest control products contain numerous biological macromolecules associated with not only the microbial pest control agent, but those associated with possible microbial contaminants, and growth medium constituents as well. Many of these biological materials could, in theory, induce allergies in susceptible individuals via a number of possible routes of exposure. PMRA is aware of standard OECD and U.S. EPA test methods for evaluating the sensitization potential of products, however, these methods only measure the sensitization potential of compounds on a small number of test animals via the dermal/intradermal route. Since these studies do not include a larger number of animals to account for natural variation in any given population and only measure the sensitization potential of samples via the dermal/intradermal route (e.g., not inhalation or intranasal routes), they do not entirely address PMRA's concerns with these types of product. PMRA is also aware of growing evidence that, at certain exposure and/or at certain periods of life, exposure to some microorganisms may be beneficial and may even reduce the risk for allergies. These findings, however, are not definitive meaning that some individuals can still develop allergies despite early exposure to bacteria. In addition, some researchers noted that, if the immune system was already primed to produce allergies, microbial antigens could still exacerbate existing allergic conditions. Also, positive sensitization reactions were reported in several dermal sensitization studies conducted on previously registered and currently registered products (see "Dermal sensitization studies" below) despite the limitations noted above.

The PMRA would like to add that the requirement for a NIOSH-approved respirator/mask is also justified by findings in acute pulmonary studies. Acute pulmonary studies conducted on various *B. thuringiensis*-based products have demonstrated severe effects at high doses (i.e., $\geq 10^8$ colony forming units per animal; see "Pulmonary studies" below). Although these effects are not expected to occur following a single operational exposure, the observed persistence of *B. thuringiensis* in the lungs could lead to an accumulation of spores in the lungs of applicators, and handlers/mixers through repeated exposure during an entire use season. The above-noted respirators/masks can significantly reduce the accumulation of this microorganism in the lungs of workers in situations where inhalation exposure is likely. Please note, however, that the PMRA has recently made changes to the aerial application instructions *B. thuringiensis*-based products. The changes are summarized as follows:

- the handler requirement for a NIOSH-approved respirator/mask and eye goggles may be waived when handlers use closed systems to load *B. thuringiensis*-based products onto aircrafts;

- when reduced personal protective equipment is worn, the respirator/mask and eye goggles must be immediately available for use in the event of an emergency such as a spill or equipment breakdown; and

- as noted in the Re-evaluation Decision Document, RVD2008-18, the requirement for eye goggles may be waived entirely if indicated by eye irritation test data or an acceptable rationale.

As a result, the following aerial application instructions and precautions will be required on all *B. thuringiensis*-based products that have aerial applications:

> "**Aerial Application Instructions:**
> Apply only by fixed-wing or rotary aircraft equipment that has been functionally and operationally calibrated for the atmospheric conditions of the area and the application rates and conditions of this label.
>
> Label rates, conditions and precautions are product-specific. Apply only at the rate recommended for aerial application on this label. Where no

rate for aerial application appears for the specific use, this product cannot be applied by any type of aerial equipment.

Ensure uniform application by using appropriate marking devices and/or electronic guidance equipment.

Use Precautions:
Apply only when meteorological conditions at the treatment site allow for complete and even coverage. Apply only when meteorological conditions are in compliance with local and/or provincial authorities.

Operator Precautions:
DO NOT allow the pilot to mix product to be loaded onto the aircraft. However, loading of premixed product with a closed system is permitted. It is desirable that the pilot have communication capabilities at each treatment site at the time of application.

The field crew and the mixer/loaders must wear the personal protective equipment described in the PRECAUTIONS section of this label. When handlers/loaders use closed systems to load the product onto the aircraft, the handler requirement for eye goggles and a NIOSH-approved respirator/mask with any N-95, R-95, or P-95 filter for biological products may be waived. When reduced personal protective equipment is worn, the respirator/mask and eye goggles must be immediately available for use in an emergency such as a spill or equipment breakdown.

All personnel on the job site must wash hands and face thoroughly before eating and drinking. Protective clothing must be washed before reuse. Decontaminate aircraft cockpits and vehicle cabs if contamination occurs.

Product Precautions:
Read and understand the entire label before opening this product. If you have questions, call the manufacturer at [insert toll free number] or obtain technical advice from the distributor or from your provincial agricultural or forestry representative. Application of this specific product must meet and/or conform to the aerial uses and rates on this label."

For *B. thuringiensis* subsp. *israelensis* (Bti)-based products, handlers, mixers and loaders of commercial and restricted use products are required to wear the listed personal protective equipment. As noted in Re-evaluation Decision Document, RVD2008-18, *Bacillus thuringiensis* subsp. *israelensis* applicators may remove gloves, eye goggles and respirators/masks if the design and delivery of the application apparatus reduces exposure to a negligible level.

With regards to concerns with the cost and the public perception of NIOSH-approved respirators/masks, PMRA is aware of these concerns and would like to note that the Agency's primary concern on this matter is the health and safety of all handlers, mixers/loaders, and applicators. The PMRA would also like to clarify its response to this

concern in RVD2008-18 by adding that some NIOSH-approved N-95 masks look almost identical to regular dust masks which are often requested as a replacement for the requirement of a NIOSH-approved respirator/mask. These NIOSH-approved N-95 masks are thus not any more intrusive or threatening in appearance.

Dermal sensitization studies

PMRA 1381470	2000. Skin Sensitization Study in Guinea Pigs, DACO: M4.6.
PMRA 1193164	Human Health and Safety Testing, Reporting of Hypersensitivity Incidents, Dermal Sensitization Study in Guinea Pigs, Final Report, Completed December 8, 1997
PMRA 1208220	Dermal Sensitization Study of Dipel R6AF in Guinea Pigs (L08151-B), DACO: 4.6.6.
PMRA 1247735	Hypersensitivity Study on Teknar in the Guinea Pig, DACO: 4.6.6.
PMRA1169441	Dermal Sensitization – Guinea Pig, DACO: 4.2.6

Pulmonary studies

PMRA 1174032	Acute Pulmonary Toxicity/Pathogenicity Study of Dipel Technical Material (Bacillus thuringiensis var Kurstaki) in Rats, Final Report, DACO: M4.2.3.
PMRA 1174179	Four-Week Subacute Inhalation Toxicity Study in Guinea Pigs. Dipel. Final Report. Ocotber 17, 1973. DACO: M4.2.3.
PMRA 1381464	1988, Murine Pulmonary Toxicity of Bacillus thuringiensis sp. Microbial Pesticides, DACO: M4.2.3.
PMRA 1465204	1990, Acute Pulmonary Toxicity / Pathogenicity Study of Vectobac Technical Material (Bacillus thuringiensis var. israelensis) in Rats, Document 5, DACO: M4.2.3.
PMRA 1174389	Acute Pulmonary/Pathogenicity Study in Rats, DACO: M4.2.3.
PMRA 1225754	Acute Pulmonary Toxicity and Infectivity to Rats, DACO: 4.2.3, 4.6.3.

Note: These study reports are available in the PMRA Reading Room.