

B. Product Identity and Chemistry

The Cry34Ab1 and Cry35Ab1 genes were isolated from *Bacillus thuringiensis* strain PS149B1 and modified before insertion into corn plants. The Cry34/35Ab1 ICP has been adequately characterized. Several safety studies were conducted using microbially produced test substances that contained 54% of the Cry34Ab1 (14 kDa) protein and 37% of the Cry35Ab1 (44 kDa) protein. Studies conducted to establish the equivalence of the Cry34/35Ab1 ICP obtained from corn or from a microbial source demonstrate that the materials are similar with respect to molecular weight, immunoreactivity, lack of post-translational modification (glycosylation) N-terminal amino acid sequence, and spectrum of bioactivity.

A qualitative analytical method (lateral flow immunoassay) for the detection of the Cry34Ab1 (14 kDa) protein has been submitted (MRID #45383401).

C. Mammalian Toxicity Profile

Cry proteins have been deployed as safe and effective pest control agents in microbial *Bacillus thuringiensis* formulations for almost 40 years. There are currently 180 registered microbial *Bacillus thuringiensis* products in the United States for use in agriculture, forestry, and vector control. The numerous toxicology studies conducted with these microbial products show no significant adverse effects, and demonstrate that the products are practically non-toxic to mammals. An exemption from the requirement of a tolerance has been in place for these products since at least 1971 (40 CFR 180.1011).

Toxicology studies conducted to determine the toxicity of Cry34/35Ab1 ICP demonstrated that the proteins have very low toxicity. The acute oral LD₅₀ of Cry34Ab1 (14 kDa) is greater than 5,000 milligrams/kilogram (mg/kg), and at 54% purity, the acute LD₅₀ for pure protein is greater than 2,700 mg/kg. The acute oral LD₅₀ of Cry35Ab1 (44 kDa) is greater than 5,000 mg/kg, and at 37% purity, the acute LD₅₀ for pure protein is greater than 1,850 mg/kg in male mice when the proteins were tested individually. When tested as a mixture (1:3 molar ratio of Cry34Ab1:Cry35Ab1 proteins), the acute oral LD₅₀ of PS149B1 Cry34/35Ab1 proteins in male and female mice is greater than 5,000 mg/kg, and greater than 2,000 mg/kg of an equimolar (1:3) mixture of pure proteins.

In *in vitro* studies, Cry34/35Ab1 ICP exhibited a high rate of digestibility under simulated gastric conditions

(referred to as SGF) in the presence of pepsin. The Cry34Ab1 (14 kDa protein) was greater than 90% digested in SGF 6.2 minutes. The Cry35Ab1 (44 kDa protein) was greater than 97% digested in less than 5 minutes. Also, thermolability testing results showed that the ICP was deactivated following exposure to 60 °C, 75 °C, and 90 °C for 30 minutes. A search of relevant data bases indicated that the amino acid sequences of the Cry34/35Ab1 ICP exhibit no significant homology to the sequences of known protein allergens. Thus, Cry34/35Ab1 ICP is highly unlikely to exhibit an allergic response.

The genetic material necessary for the production of the Cry34/35Ab1 ICP is nucleic acid (DNA) which is common to all forms of plant and animal life. There are no known instances where nucleic acids have caused toxic effects as a result of dietary exposure.

Collectively, the available data on Cry34/35Ab1 ICP along with the safe use history of microbial *Bacillus thuringiensis* products establishes the safety of the plant-incorporated protectant *B.t.* Cry34/35Ab1 ICP and the genetic material necessary for its production in all raw agricultural commodities.

D. Aggregate Exposure

Because *B.t.* Cry34/35Ab1 ICP is expressed in minute quantities and is retained within the plant, there is virtually no potential for dermal or inhalation exposure to the protein. Significant dietary exposure to Cry34/35Ab1 ICP is unlikely to occur. Dietary exposures at very low levels, via ingestion of processed commodities, although, they may occur, are unlikely to be problematic because of the low toxicity and the high degree of digestibility of the protein. In addition, the protein is not likely to be present in drinking water because the protein is deployed in minute quantities within the plant, and studies demonstrate that Cry34/35Ab1 ICP is rapidly degraded in soil. In summary, the potential for significant aggregate exposure to Cry34/35Ab1 is highly unlikely.

E. Cumulative Exposure

Common modes of toxicity are not relevant to consideration of the cumulative exposure to *B.t.* Cry34/35Ab1 ICP. The product has demonstrated low toxicity, and these effects do not appear to be cumulative with any other known compounds.

F. Safety Determination

1. *U.S. population.* The deployment of the product in minute quantities within the plant, the very low toxicity of the

product, the lack of allergenic potential, and the high degree of digestibility of the proteins, are all factors in support of Mycogen/Dow AgroSciences' assertion that no significant risk is posed by exposure of the U.S. population to *B.t.* Cry34/35Ab1 ICP.

2. *Infants and children.* Non-dietary exposure to infants and children is not anticipated, due to the proposed use pattern of the product. Due to the very low toxicity of the product, the lack of allergenic potential, and the high degree of digestibility of the proteins, dietary exposure is anticipated to be at very low levels and is not anticipated to pose any harm to infants and children.

G. Effects on the Immune and Endocrine System

Given the high degree of digestibility of the Cry34/35Ab1 ICP, no chronic effects are expected. Cry34/35Ab1 ICP, or metabolites of the ICP are not known to, or are expected to have any effect on the immune or endocrine systems. Proteins in general are not carcinogenic, therefore, no carcinogenic risk is associated with the Cry34/35Ab1 ICP.

H. Existing Tolerances or Exemptions from Tolerance

There are no existing tolerances or exemptions from tolerance for *B.t.* Cry34/35Ab1 ICP.

[FR Doc. 03-5620 Filed 3-7-03; 2:17 pm]

BILLING CODE 6560-50-S

ENVIRONMENTAL PROTECTION AGENCY

[OPP-2003-0016; FRL-7289-3]

Experimental Use Permit; Receipt of Application

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This notice announces receipt of an application 68467-EUP-4 from Mycogen Seeds/Dow Agrosciences LLC requesting an experimental use permit (EUP) amendment/extension for *Bacillus thuringiensis* moCry1F protein and the genetic material necessary for its production (plasmid insert PHP 12537) in corn. The Agency has determined that the application may be of regional and national significance. Therefore, in accordance with 40 CFR 172.11(a), the Agency is soliciting comments on this application.

DATES: Comments, identified by docket ID number OPP-2003-0016, must be received on or before April 7, 2003.

ADDRESSES: Comments may be submitted electronically, by mail, or