

Draize method 1, 24, 48 and 72 hours after test material instillation. The 24 hour examination also included a fluorescein staining examination for corneal effects. All rabbits survived the study. All rabbits developed slight conjunctival irritation that cleared within 48 hours of treatment. No corneal opacity or iritis were noted. GB 34 Concentrate was minimally irritating to the eye and is placed in Toxicity Category IV.

ii. *Primary eye irritation—GB 34 Technical.* (OPPTS 870.2400; OPP 152.35; MRID 454335-02, corrected as 457225-02). Three male and three female young adult New Zealand white rabbits were, prior to test, treated in both eyes with 2% fluorescein and then examined under UV light for ocular abnormalities. The test material, in the amount of 0.1 mL, was instilled into the everted lower lid of the right eye and the upper and lower lids were held closed for 1 second. The contralateral eye served as control. The eyes were examined and scored according to the Draize method 1, 24, 48 and 72 hours after test material instillation. The 24 hour examination also included a fluorescein staining examination for corneal effects. All rabbits developed moderate conjunctival irritation that cleared up within 72 hours of treatment. No corneal opacity or iritis or non-ocular effects were noted. The GB technical test substance was mildly irritating to the eye and is placed in Toxicity Category III.

6. *Primary dermal irritation—i. GB 34 Concentrate.* (Submitted to determine the adequacy of data to support an EUP for GB 34 Concentrate, and here, bridged to support a section 3 registration of the microbial product) (OPPTS 870.2500; OPP 152.34; MRID 452940-03). Three male and three female young adult New Zealand white rabbits were received for the study. The fur on the dorso-lumbar area of each rabbit was clipped. The rabbits were given a single 0.5 g dose of test material applied under a 1 inch x 1 inch 4-ply gauze pad on a 6 cm² clipped site. The gauze pad is then secured and Elizabethan collars were placed on the animals. Four hours later these were removed and the sites wiped with a moistened towel. The application sites were observed for dermal irritation 1, 24, 48, and 72 hours after patch removal. In addition the rabbits were observed at least daily for clinical signs of toxicity during the 72-hour study period. All rabbits survived the study. No dermal irritation was observed on any rabbit at any site. Based on the study GB 34 Concentrate is non-irritating to the New Zealand white

rabbit and is placed in Toxicity Category IV.

ii. *Primary dermal irritation—GB 34 Technical.* (OPPTS 870.2500; OPP 152.34; MRID 454335-03 corrected as MRID 457225-03). Three male and three female New Zealand albino rabbits were prepared by clipping the dorsal area and the trunk. Only healthy animals without preexisting skin irritation had been selected for the test. The test substance in the amount of 0.5 g was placed on a 1 inch x 1 inch, 4-ply gauze pad which was applied and secured on each rabbit. After 4 hours exposure to the test substance, the pads were removed and the test sites gently wiped with water and towel to remove any residual test substance. Individual dose sites were scored according to the Draize scoring system at approximately 1, 24, 48 and 72 hours after patch removal. The animals were observed for signs of gross toxicity and behavioral changes at least once daily during the test period. All animals appeared active and healthy. There were no signs of gross toxicity, adverse pharmacologic effects or abnormal behavior. No dermal irritation was noted at any test site during the study. Under the conditions of the study, the GB 34 Technical is classified as non-irritating to the skin and placed in Toxicity Category IV.

7. *Acute injection toxicity/Pathogenicity—GB 34 Technical.* (Submitted to determine the adequacy of data to support an EUP for GB 34, and here, bridged to support a section 3 registration of the microbial product) (OPPTS 885.3200; OPP 152.33; MRID 453416-01). A total of 39 male and 39 female rats were used in the tests. The results showed:

i. *Mortality.* No deaths were observed in any of the dosed or control groups prior to scheduled sacrifice.

ii. *Body and organ weights.* Overall, both male and female rats gained weight for the duration of the study, demonstrating the continued health of the animals.

iii. *Clinical Observation.* Overall, both male and female rats showed no abnormal clinical signs.

iv. *Gross necropsy.* No significant signs of abnormalities were seen except for a laceration on the left shoulder of a test substance treated male rat. An enlarged spleen was seen in one test substance treated male rat on day

The conclusion in the Data Evaluation report was that *Bacillus pumilus* GB 34 does not appear to be toxic, infective, and/or pathogenic in rats, when dosed at 1×10^7 cfu/animal. This test supports the requirements for both the TGAI (the technical) and the end use product (the concentrate).

A hypersensitivity study, or dermal sensitization study (OPP 152.36) is not required for registration of this product since the routes of use will not result "in repeated human contact by inhalation or dermal routes" as specified in footnote iii of the table in 40 CFR 158.740(c). Use of the product is limited to that of a seed treatment which takes place in a commercial facility using mechanical seed treatment equipment.

An Immune response study is not required for registration of this product because the Acute I.V., I. C., or I. P. Injection toxicity/Pathogenicity study, (OPPTS guideline 885.3200/OPP 153.33) submitted to determine the adequacy of data to support an EUP for GB 34, and here bridged support a section 3 registration of the microbial product, serves to address the endpoint of immune response. This injection study examines the normal functioning of the immune system when faced with the potentially most challenging exposure to this microbial pesticide active ingredient: Direct injection into the bloodstream. If the test animal is able to withstand and survive the introduction of such a large number of microbes, bypassing the normal protective barriers of the skin, the pulmonary macrophages and the gastrointestinal lymphoid tissues, then the immune system is functioning normally. The normal functioning of the immune system implies that it can recognize the introduced microbes as foreign and can clear them from the blood and other exposed organs. After the active ingredient, *Bacillus pumilus* GB 34 was intravenously injected into the test animals (rats), no deaths, adverse clinical signs or significant findings upon necropsy were seen 35 days after the injection. (See item 7).

The requirement for Tier II and Tier III data was not triggered because of the results of Tier I data which had been submitted or waived.

V. Aggregate Exposures

Section 408(b)(2)(D)(vi) of the FFDCA directs EPA to consider available information concerning aggregate exposures to consumers (and major identifiable subgroups of consumers) from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

A. Dietary Exposure

Bacillus pumilus GB 34 is a naturally occurring soil microorganism which