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BRIEFING MEMORANDUM

SUBJECT: Registration of New Chemical (Biological Fungicide) Streptomyces sp. strain K61

FROM: Lawrence E. Culleen
Acting Director
Registration Division

TO: Douglas D. Campt
Director
Office of Pesticide Programs

BACKGROUND

Kemira Oy submitted, on February 15, 1991, a petition for an exemption from the requirement of a tolerance for residues of the biological fungicide Streptomyces sp. strain K61 in or on all raw agricultural commodities when used as a fungicide for the treatment of seeds, cuttings, transplants and plants of agricultural crops in accordance with good agricultural practices. Concurrently, applications for registration of a repackaging-use product and end-use products for field use on agronomic crops, for greenhouse and field use on ornamental crops and for greenhouse and field use on vegetable crops were submitted. All products contain 30% active ingredient consisting of dried spores and mycelium of ray fungus (Streptomyces sp. strain K61) which is equivalent to 10^8 colony forming units (cfu) per gram.

The product Mycostop Biofungicide for Repackaging Only is intended for repackaging of end-use products. Mycostop Biofungicide for Agronomic Crops is for seed or soil application to field crops such as cotton, corn, soybeans, wheat, sorghum, beans and peas. Mycostop Biofungicide for Ornamental Crops and Mycostop Biofungicide for Vegetable Crops are intended for both greenhouse and field use and may be applied as a seed treatment, soil treatment, transplant application or foliar spray on numerous crops. These treatments are intended to control seed rot, root and stem rot and wilt diseases caused by Fusarium and Alternaria and to control Botrytis on lettuce and ornamentals. Dosage rates range from 2-4 oz/20 lbs of seed for ornamental and vegetable crops to 4-8 oz/100 lbs of field crop seed. Band, in-furrow and side-dress applications to soil require dosage rates of 0.5-1.0 lb/treated acre. Seedling and transplant applications to ornamentals and

vegetables are made as a root dip, soil spray or drench with a 0.01-0.1% suspension of the product. Foliar sprays are made with a 0.1% suspension.

The active ingredient in these products is a strain of Streptomyces which was isolated from Sphagnum peat in Finland. Streptomyces species are distributed worldwide. Although this strain most closely resembles Streptomyces griseoviridis, morphologically and physiologically, the strain could not be completely characterized to the species level.

SCIENCE FINDINGS

Summary Science Statement

The results of the toxicity/pathogenicity studies submitted indicated that the active ingredient was not pathogenic or infective to treated animals in any of the studies. Streptomyces sp. strain K61 was not toxic when administered orally or dermally. Moderate skin sensitization in treated guinea pigs was observed at 24 and 48 hours following treatment. Mild conjunctival irritation was elicited in rabbits in the Primary Eye Irritation Study. There have been two reports of hypersensitivity related to biological dust exposure but in these instances, no protective measures had been taken.

Mortality to treated rats was observed in the Acute Pulmonary Toxicity/Pathogenicity Test and to treated mice in the Acute Intraperitoneal Toxicity/Pathogenicity Test. The large size of the organism and the large quantity of material given to the animals in the intraperitoneal test was a strong influence on the toxicity of the organism. However, size of the organism did not appear to be the main factor in animal deaths in the pulmonary test. The necropsy and histopathological observations indicated a severe pulmonary reaction to the presence of the live organism. The high death rate observed was sufficient to provoke concern about pulmonary exposure to significant amounts of the organism. Consequently, product labeling must advise the user that a dust/mist filter respirator (MSHA/NIOSH approval number prefix TC-21C) must be worn when handling the product. The maximum human exposure to the products would be so far below those levels causing mortality in rats that there should be no adverse human health risk from the use of the organism. The pulmonary toxicity/mortality effects on rats is no different than those observed from high acute exposures to currently registered Bacillus thuringiensis varieties.

The environmental effects studies submitted indicated that the products are practically nontoxic to terrestrial and aquatic avian species, aquatic invertebrates and to honey bees. Requests for waiver of data requirements for non-target insect and non-target plant testing were acceptable. Due to the lack of toxicity in the acute oral testing, the products should not pose a risk to wild

mammalian species. Effects of the product on fish was not adequately determined and a test on rainbow trout must be repeated.

The need for data on environmental fate was not triggered under current requirements for the proposed products since the organism is naturally occurring and results of initial Tier I tests did not meet the criteria which would require additional testing.

Toxicological characteristics

Acute oral toxicity/pathogenicity test: Streptomyces sp. strain K61 was neither pathogenic nor infective to rats when orally dosed with 3×10^9 cfu/animal. No signs of toxicity or disease were present and clearance through the caecum was established.

Acute dermal toxicity test: The test organism was not toxic to rabbits when a single 2 g/kg dose was administered dermally.

Acute pulmonary toxicity/pathogenicity test: The test organism was found to be somewhat toxic to rats at a dosage of 3×10^9 cfu/g/animal. The test substance caused death in 54% of treated male and 48% treated female rats. The organism was not pathogenic or infective.

Acute intraperitoneal toxicity/pathogenicity test: The LD_{50} value for the organism was determined to be 1,306 mg/kg and 870 mg/kg in male and female mice respectively. Since all clinical signs were resolved by day 3 of the test, the organism was not considered infective. Toxicity was possibly due to the excessive quantity of test material and large size of the organism.

Primary eye irritation study: A mild conjunctival irritation was elicited due to the administration of the organism to the eyes of rabbits. No infectivity was noted.

Skin sensitization study: An overall moderate skin sensitization reaction was noted in treated guinea pigs 24 and 48 hours after treatment.

Hypersensitivity: Two cases of allergic reaction, possibly initiated from exposure to the product, have been reported. Recommended protective measures were not followed. The product has been used in Finland and other countries for about 10 years with no reports of adverse effects.

Ecological Characteristics

Avian studies: In avian oral pathogenicity/toxicity studies, the acute oral LD_{50} value for both northern bobwhite quail and mallard ducks exposed to Streptomyces sp. strain K61 was greater than $2,500$ mg/kg (2.45×10^9 cfu/kg) which indicates that the product is practically nontoxic, on an acute basis, to birds.

Aquatic invertebrate studies: An EC_{50} of 190 ppm was established in a 21-day static renewal toxicity/pathogenicity evaluation of the effects of Streptomyces sp. strain K61 on Daphnia magna which indicates that the organism is practically nontoxic to aquatic invertebrate species.

Fish studies: Data submitted evaluating effects of the organism on rainbow trout indicated slight toxicity but a definitive LC_{50} could not be determined since a dose response trend was not established. The study is being repeated.

Honey bee study: The dietary LC_{50} for honey bees was determined to be 2,400 ppm which indicates that the product is practically non-toxic to honey bees.

Non-target insect studies: Data requirements for testing of non-target insects were waived based on the fact that no adverse effects have been observed in insects exposed to this organism during field testing. Additionally, the product was found to be practically non-toxic to aquatic invertebrates and had a low probability of causing adverse effects to honey bees which indicates that this organism should not cause significant adverse effects to non-target insects.

Non-target plant studies: Non-target plant testing requirements were waived based upon the lack of pathogenicity to a wide variety of crop plant types. There was a slight reduction in germination in certain crop plants when the product was applied as a seed treatment but since non-target plants would not be exposed in this manner, additional testing was considered unnecessary.

Mammalian wildlife considerations: Toxicological studies indicated that there is no significant toxicity to rodents from acute oral testing at the maximum hazard dose so risk to mammalian wildlife is expected to be minimal to non-existent.

Endangered species considerations: It was concluded from the data submitted that there would not be a "may effect" situation for endangered species from the proposed use of this organism.

BENEFITS

This microbial fungicide, when used as directed will protect a variety of field, vegetable and ornamental plants from Fusarium and Alternaria caused diseases and protect certain vegetables and ornamental crops from diseases caused by Botrytis. These diseases can cause considerable economic losses to crops. The causal organisms are difficult to control with currently available fungicides. This biological pesticide may be an effective alternative to chemical control measures and may result in a decrease in the use of more hazardous products.

TOLERANCE ASSESSMENT

An exemption from the requirement of a tolerance is proposed to be established for the residues of Streptomyces sp. strain K61 in or on all raw agricultural commodities when used as a fungicide for the treatment of seeds, cuttings, transplants and plants of agricultural crops in accordance with good agricultural practices. Based upon the low level of toxicity of this organism in the Tier I mammalian toxicity/pathogenicity studies, an exemption from tolerance requirements is warranted.

SUMMARY OF MAJOR DATA GAPS

The only remaining data gap for this biological fungicide is the requirement to repeat the test of the product to determine effects on rainbow trout. The study which was submitted indicated that the organism may be slightly toxic to rainbow trout but a definitive LC_{50} value could not be determined. Exposure of aquatic organisms to this microbial fungicide is expected to be unlikely since the main methods of application are as a seed or soil treatment where the organism will be covered by soil. Based on the lack of exposure potential and the low toxicity demonstrated in the submitted test, conditional registration would be justified while the repeat study is being conducted.

RECOMMENDATION

I recommend that you concur with this section 3(c)(7)(C) registration for Streptomyces sp. strain K61.

Concur: _____

Do not concur: _____

Date: _____

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