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Australia

[8F8697]

EPA has received a pesticide petition **([8F8697])** from AgBiTech Pty Ltd, 8 Rocla Court; Glenvale, Queensland, 4350 Australia proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180.

(Options (pick one)

2. to establish an exemption from the requirement of a tolerance for

(Options (pick one)

1. microbial pesticide *Autographa californica Multiple* Nucleopolyhedrovirus, isolate R3 [SD-7095]

Pursuant to section 408(d)(2)(A)(i) of FFDCA, as amended, AgBiTech Pty Ltd has submitted the following summary of information, data, and arguments in support of their pesticide petition. This summary was prepared by AgBiTech Pty Ltd and EPA has not fully evaluated the merits of the pesticide petition. The summary may have been edited by EPA if the terminology used was unclear, the summary contained extraneous material, or the summary unintentionally made the reader conclude that the findings reflected EPA's position and not the position of the petitioner.

I. AgBiTech Pty Ltd **Petition Summary**

[8F8697]

A. Product Name and Proposed Use Practices

Autographa californica Multiple Nucleopolyhedrovirus (AcMNPV) is a baculovirus characterized by rod-like nucleocapsids contained within a viral envelope. *Baculoviridae* genomes are supercoiled circular double stranded DNA ranging from 80-180 kbp in size. Virons consist of one or more nucleocapsids enclosed within a single envelope. Virons are embedded in protein bodies called occlusion bodies (OBs). These OBs are approximately 1 to 10 µm in diameter and visible through a light microscope, appearing as translucent irregular crystals.

Baculoviruses are ancient organisms, likely discovered as early as 5000 years ago as a disease impacting the silk industry in Asia. They have been exclusively isolated from arthropods, specifically from Lepidoptera, Hymenoptera and Diptera, and usually identified by the species that they infect along with the type of occlusion body that they form.

Most nucleopolyhedrovirus' infect one or a few host species, with the exception of AcMNPV, *Anagrapha falcifera* NPV and MbMNPV, which have a broader host range infecting up to 10 different Lepidopteran families. *Autograpaha californica* Multiple Nucleopolyhedrovirus (AcMNPV; formerly known as *Angrapha falcifera MNPV* (AfMNPV) and *Rachiplusia ou* MNPV (RoMNPV)), the subject of this regulatory application has an narrow host range specific for Noctuidae Lepidoptera. The target pests are *Helicoverpa zea* (corn earworm, cotton bollworm, tomato fruitworm), *Heliothis virescens* (tobacco budworm), *Chrysodeixis includens* (soybean looper) and *Trichoplusia ni* (cabbage looper).

AcMNPV and NPVs in general are ubiquitous in nature, found in nearly every location where investigated. This natural product will be an excellent addition to growers' options for *H. zea*, *H virescens*, *C. includens* and *T. ni* control that reduces or eliminates the need for chemical inputs and fits well within an integrated pest management program for organic or conventional production.

B. Product Identity/Chemistry

1. *Identity of the pesticide and corresponding residues.* The insect viral strain, *Autographa californica Multiple* Nucleopolyhedrovirus – R3 [SD-7095] was isolated from *Autographa biloba* larvae collected in Rolla, Missouri in 2001. The strain is a natural insect viral strain that has not been modified in any way and is identical to AcMNPV that are ubiquitous in nature. NPVs are known for their ability to control their hosts and have been shown to reduce larval damage below economic levels leading to improved crop production.

2. *Magnitude of residues at the time of harvest and method used to determine the residue.* **[**NA remove – see 1. above**]**

3. *A statement of why an analytical method of detecting and measuring the levels of the pesticide residue are not needed.* No analytical method is included since this petition requests an exemption from the requirement of a tolerance.

C. Mammalian Toxicological Profile

Baculoviruses in general have a long history of safe use as microbial pesticides in the USA. Baculoviruses have narrow host ranges and virtually no adverse effects in people, wildlife, or non-target insects. The active ingredient for all baculoviruses, including AcMNPV, is the occlusion bodies (OBs) that are formed in the nuclei of infected cells. Target larvae ingest OBs and until about day 4 post-infection, no symptoms are observed. From 4-6 days post-infection, the larvae begin to appear diseased and typically stop eating at day 6-7 with death occurring between 7-10 days post-infection. This mode-of-action occurs across all baculoviruses demonstrating the similarity of this group of insect control viruses.

The body of toxicology data is quite extensive for NPVs, addressing different routes of exposure – oral, pulmonary, dermal and injection – with many different species, rodents, dogs, monkeys and even humans for *Helicoverpa zea* NPV (EPA, 1990). Since the reregistration actions completed in 1990, other NPV and GV strains have been registered, beet armyworm, Indian Meal Moth, etc. In addition, a full set of toxicology results are available from other less related NPVs (e.g., OpNPV, LdNPV) addressing the same routes of exposure but limited to rodent and a dog study.

The last re-registration documents prepared by EPA that provide detailed historical regulatory data and extensive review of health and safety data on NPVs were published in 1990s (EPA, 1990; EPA, 1996). The full body of toxicology data regardless of the baculovirus species is important to cite given the close relatedness of all baculoviruses and their common mode of action (see Figure 2, Harrison et al., 2008). What makes each strain unique is the pest complex that they control, which is typically very narrow.

Perhaps one of the best description of the lack of human toxicity is provided in by OECD (2002):

> *'Baculoviruses are naturally occurring pathogens of arthropods. Their host range is exclusively restricted to arthropods. No member of this virus family is infective to plants or vertebrates. Baculoviruses are ubiquitously resent in the environment and have been used for biological insect control for more than 100 years. Circumstantial evidence for the safety of baculoviruses emerges from the history of contact between baculoviruses and humans without any detrimental effect.'*

As part of the scientific rationale, a bridging study was conducted using mammalian cell lines to characterize any mammalian cell effects from AcMNPV. Non-occluded AcMNPV isolates, control insect medium (NPV control), spent medium, inactivated virus as appropriate and a commercial NPV product were included in the tests.

In this study, no cytopathic effects or replication of AcMNPV exposed to any of the mammalian cell lines were observed. If NPV nucleic acid had been detected in the cells, then viral antigen would have been assayed; and, the presence of infectious virus in the supernatant at the same days of incubation would also have been assayed in a sensitive insect bioassay. However, since no AcMNPV nucleic acid was detected, no further testing was necessary.

The results of this cell culture study, demonstrating a total lack of infectivity or toxicity of AcMNPV to mammalian cells, allows for a bridge to the many different types of mammalian toxicology studies conducted with commercial NPV strains. The common mode of action shared by all NPV adds to the weight of evidence that NPVs as a group, and specifically AcMNPV, will not cause mammalian toxicity. Therefore, AcMNPV should be considered as safe as any baculovirus used in past and current commercial end products.

D. Aggregate Exposure

1. *Dietary exposure.* Since AcMNPV is applied to the crop, there will be negligible to non-existent dietary, dermal or inhalation exposure. Use of this baculovirus in pesticide products will not increase the exposure of humans beyond normal background levels.

i. *Food.* There will be no accumulation of the insect virus or this AcMNPV product in any plant tissues or food.

ii. *Drinking water.* Drinking water is unlikely to be contaminated with AcMNPV, because AcMNPV only grows and replicates within the *C. includens* host, which are limited to plant and soil habitats and do not live in water environments.

2. *Non-dietary exposure.* Non-dietary exposure of infants, children or the US population in general, to AcMNPV are not expected due to the uses of this product within agricultural settings.

E. Cumulative Effects

The unique mode-of-action and narrow host range AcMNPV, and of NPV occlusion bodies in general, coupled with the lack of mammalian toxicity provides no basis for the expectation of cumulative exposure with other compounds.

F. Safety Determination

1. *U.S. population.* The lack of mammalian toxicity to the insect virus AcMNPV provides support for our request of an exemption from the requirement of a tolerance set forth in this petition, including infants and children.

2. *Infants and children*. (See F.1. above)

G. Effects on the Immune and Endocrine Systems

The unique mode-of-action and narrow host range AcMNPV, and of NPV occlusion bodies in general, coupled with the lack of mammalian toxicity provides no basis for the expectation of effects on the immune or endocrine systems.

H. Existing Tolerances

No tolerances or tolerance exemptions have been granted for AcMNPV. However, these naturally occurring insect viruses have all been granted exemptions from the requirement of a tolerance; *Spodoptera frugiperda* NPV (§180.1339), *Heliocoverpa zea* NPV (§180.1027), *Spodoptera exigua* NPV (§180.1118), *Anagrapha falcifera* MNPV (§180.1149) and *Cydia pomonella* GV (§180.1148) and Indian Meal Moth GV (§180.1218). The first registered product was based on *H. zea* NPV under the brand name Elcar in 1975 for use on cotton and tobacco. And as of 2002, the EPA had registered10 products from five NPVs and from two granuloviruses (EPA, 1990).

I. International Tolerances

No international tolerances or tolerance exemptions have been granted for AcMNPV.