

providing a higher exposure scenario (for exposure of body tissues, organs and systems). Cell culture studies which demonstrate no toxicity to mammalian cell lines upon inoculation with the viral pest control agent can therefore be used as an indicator in determining the probability of toxicity to the viral pest control agent via other routes of exposure (oral, dermal, inhalation). Therefore, this evaluation criteria along with the data submitted (referenced above) and the long history of safe use of baculoviruses provided the Agency with a scientific rationale to waive the requirement for an acute dermal toxicity study. In addition, the IMMGV is a characteristically large molecular entity and is therefore unable to penetrate intact skin. However, in the unlikely event that viral penetration does occur through contact with broken skin, the studies submitted by the registrant have demonstrated a lack of toxicity/pathogenicity and infectivity associated with IMMGV.

ii. *Acute inhalation toxicity.* This study was waived based upon the lack of toxicity in animals dosed orally (453070-01) and, more importantly cells inoculated with the viral pest control agent (450662-07 and 450662-08). Cell culture infectivity and cytotoxicity assays demonstrated that there were no toxic effects to mammalian cell lines (human lung, human endothelial and primate renal cell lines) when infected with doses of IMMGV. Cell culture assays provide valuable information on the ability of the viral pest control agent to infect, replicate in, transform or cause toxicity in mammalian cell lines. Thus, this assay is the most likely indicator of evaluating the toxicity of a viral pest control agent. Unlike the oral, dermal and inhalation routes of exposure, these barriers (exposure conditions) do not exist in cell culture assays as the host cell is completely exposed thus providing a higher exposure scenario (for exposure of body tissues, organs and systems). Cell culture studies which demonstrate no toxicity to mammalian cell lines upon infection with the viral pest control agent can therefore be used as an indicator in determining the probability of toxicity to the viral pest control agent via other routes of exposure (oral, dermal and inhalation). Therefore, this evaluation criteria along with the data submitted (referenced above) and the long history of safe use of baculoviruses provided the Agency with a scientific rationale to waive the requirement for an acute inhalation toxicity study. In addition, the product labeling includes precautionary language for the pesticide handler to use

a dust mask as a further measure of safety.

iii. *Primary dermal irritation.* This study was waived based upon the lack of toxicity in animals dosed orally (453070-01) and, more importantly cells inoculated with viral pest control agent (450662-07 and 450662-08). Cell culture infectivity and cytotoxicity assays demonstrated that there were no toxic effects to mammalian cell lines (human lung, human endothelial and primate renal cell lines) when infected with doses of IMMGV. Cell culture assays provide valuable information on the ability of the viral pest control agent to infect, replicate in, transform or cause toxicity in mammalian cell lines. Thus, this assay is the most likely indicator of evaluating the toxicity of a viral pest control agent. Unlike the oral, dermal and inhalation routes of exposure, these barriers (exposure conditions) do not exist in cell culture assays as the host cell is completely exposed thus providing a higher exposure potential (for exposure of body tissues, organs and systems). Cell culture studies which demonstrate no toxicity to mammalian cell lines upon infection with the viral pest control agent can therefore be used as an indicator in determining the probability of toxicity to the viral pest control agent via other routes of exposure (oral, dermal and inhalation). Therefore, this evaluation criteria along with the data submitted (referenced above) and the long history of safe use of baculoviruses provided the Agency with a scientific rationale to waive the requirement for an acute dermal toxicity study. In addition, the product labeling includes precautionary language for the pesticide handler to wear gloves as a further measure of safety.

iv. *Literature citations (450662-06).* Information from the open scientific literature has been cited in support of the relative safety and lack of mammalian toxicity associated with baculoviruses, including the IMMGV. The IMMGV is very host-specific, it does not infect any host other than the Indian meal moth larvae and does not cross-infect any Lepidopteran or other insect. The range for the insect host is worldwide. Studies listed in the literature review provide information on the life cycle and mode of action of IMMGV such that it acts by pathogenicity, not a toxic mechanism. It presents no hazard potential to mammals and non-target species.

V. Aggregate Exposures

In examining aggregate exposure, section 408 of the FFDCA directs EPA to consider available information concerning exposures 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

1. *Food.* Because baculoviruses are naturally occurring organisms, there is a great likelihood for previous exposure for most, if not all individuals. To date, there have been no reports of any hypersensitivity incidents or reports of any known adverse reactions resulting from exposure to IMMGV. The amount of product used will result in a negligible increase, if any, of virus exposure. In addition, even if there is a significant increase in exposure to the virus, the toxicity studies submitted by the registrant along with the extensive reports in the scientific literature indicating the safety of the viruses, suggest that there should not be any additional risk of adverse effects due to exposure to IMMGV.

2. *Drinking water exposure.* Because of the use site and amount of product that will be applied, potential non-occupational exposures in drinking water is negligible. Currently, there are no reports which show that IMMGV has been found in any drinking water. Baculoviruses occur naturally in soil and there is a low likelihood that they would survive passage through the soil to reach underground water (Ref. 1, MRID 450662-06). Even if the virus is able to reach ground water, it is highly unlikely that the viruses would survive municipal water treatment due to its inability to survive outside its host. Therefore, it is not likely there will be an increase of IMMGV in drinking water. In addition, because the virus host range is limited to the Indian meal moth, the results of the acute oral toxicity studies using a high dose of the virus, suggest that there will not be any adverse effects upon human consumption in the unlikely event any virus found its way into drinking water, therefore, the Agency has no drinking water exposure concerns.

B. Other Non-Occupational Exposure

Baculoviruses are naturally occurring viruses that have been described in the scientific literature for approximately 40 years. In addition to scientific research, there has been a long history of safe use of baculoviruses to control arthropods. Because the amount of virus which will be applied is small, it is not likely that there will be a significant increase in potential exposure. Any increase in virus titer is likely to be negligible at