UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

816A

MEMORANDUM **6(A)(2) RESPONSE**

Subject: **Sulfuryl Fluoride. ID# 078003.** Response to 6(a)(2) Submission for Chronic Toxicity/Neurotoxicity/Carcinogenicity Data.

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CONCLUSIONS

Following a preliminary review of three long-term inhalation studies in rat, dog and mouse on sulfuryl fluoride, no imminent hazard was identified. The new data would not alter the risk assessment for short-term or intermediate-term applicator and residential exposure. A detailed review of these studies will be provided at a later time.

ACTION REQUESTED

TB-I received for review several studies on sulfuryl fluoride submitted by DowElanco (1) a 1-year inhalation study in the dog (MRID 433549-01), (2) 2-year inhalation chronic toxicity/neurotoxicity/carcinogenicity study in rat (MRIDs 432167-02 and 433549-02) and (3) an 18-month inhalation carcinogenicity study in mice (MRID 433549-03). The data were received flagged as 6(a)(2) data.

DISCUSSION

TB-I notes that these studies were required by California Department of Pesticide Regulation, but not by U.S. EPA, with the exception of the chronic neurotoxicity study. The

neurotoxicity data were submitted to provide additional information for upgrading a previously conducted 90-day inhalation neurotoxicity study in rat, in which some parameters were not examined (MRID 408399-02 and -03; Core-supplementary).

TB-I does not consider the submitted data to represent an imminent hazard, nor to significantly affect the risk assessment for sulfuryl fluoride exposure, for the following reasons:

1. The submitted studies are chronic toxicity studies, but subchronic (90-day) studies are considered more appropriate for repeated exposure to applicators, which is expected to be intermittent. The Reregistration Eligibility Document for sulfuryl fluoride states that the primary toxicologic concern is for neurotoxicity and that the 90-day neurotoxicity study in rat (MRID 408399-01; HED Doc. no. 009479) will be used for applicator repeated exposure risk assessment upon submission of the additional information required to upgrade this study. The toxicity endpoint for repeated applicator exposure risk assessment, which has not been performed pending review of additional subchronic/chronic neurotoxicity data, will not be affected.

2. The NOELs/LELs for neurotoxicity and systemic toxicity in rat in the new 2-year study are not less than those already identified in earlier studies. The NOEL for subchronic neurotoxicity in rat was previously determined to be 30 ppm, based on electrophysiologic effects, compared to a NOEL of 80 ppm (highest dose tested) for the additional neurotoxicity-related parameters tested in the 2-year study. The lowest NOEL for any systemic effect was 5 ppm in both the 2-generation reproductive toxicity study in rat (increased accumulation of alveolar macrophages in lungs at 20 ppm) (MRID 421798-01; HED Doc. no. 009479) and the new 2-year study (slight fluorosis of teeth at 20 ppm).

3. The NOELs/LELs in mice for subchronic toxicity (MRID 431294-01; in review) and chronic inhalation toxicity are similar (30 ppm/100 ppm, 90-day study vs 20 ppm/80 ppm, 18-month carcinogenicity study).

4. Although the NOEL of 20 ppm in the new 1-year dog inhalation study is lower than the NOEL of 100 ppm in an earlier 90-day study (MRID 422566-01; HED doc. no. 009506), toxicity observed at 80 ppm in the 1-year study was minimal (very slight fluorosis of teeth, very slight increase in aggregates of macrophages in the lung) and probably not appropriate endpoints for risk assessment to applicators. The LELs for significant toxicity including neurotoxicity were 200 ppm in both the 90-day and 1-year dog inhalation studies.

5. The chronic rat and mouse studies do not demonstrate carcinogenicity of sulfuryl fluoride from long-term exposure.

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