



MEMORANDUM

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DATE: May 25, 2020

SUBJECT: Response to comments by US EPA on DPR's draft Addendum to the 2006 Sulfuryl Fluoride Risk Characterization Document dated December 2018

I. Background

At the request of the Human Health Assessment (HHA) Branch of the California Department of Pesticide Regulation (DPR), the Health Effects Division of United States Environmental Protection Agency's (US EPA) Office of Pesticide Programs reviewed the draft Addendum to the 2006 Risk Characterization Document (RCD) for Sulfuryl Fluoride (December, 2018) and provided comments in letter submitted to HHA on March 26, 2019.

DPR sincerely appreciates the HED's review. We consider comments by other regulatory agencies to be helpful in the development of technically complex, science-based regulatory documents. When appropriate, HED's comments were incorporated in to the final Sulfuryl Fluoride Addendum. The final Addendum referenced throughout this response refers to DPR's final May 2020 Addendum to the Sulfuryl Fluoride Risk Characterization Document. Responses to specific comments are detailed below.

II. Response to Comments

HED comment 1: HED notes that the exposure duration in the two-day study used to derive the RfCs is appropriate for assessing acute exposure. As the study was conducted with adult animals, there is uncertainty with using the results to assess risk to infants and children. HED also acknowledges that CA DPR proposed that in this study, fluoride may enter the brain directly

through the nasal cavity, bypassing the blood-brain barrier; however, no definitive data are available to support this hypothesis.

DPR response: DPR agrees with HED's opinion on the uncertainty associated with using the two-day study to derive acute reference concentrations (RfCs), acknowledging this in Section V.A.1 of the final Addendum. DPR also accounted for this uncertainty by retaining the database uncertainty factor (UF_{DB}) of 3. DPR agrees with HED that there are no definitive data to support a direct path from nose to the brain. This is acknowledged in Appendix E of the final Addendum.

HED comment 2: The study being considered by CA DPR is of acute duration and shows no apparent effects at the highest concentration tested, but it is not protective of neurological effects that occurred at a much lower concentration in the inhalation DNT study. Although the DNT study is of somewhat longer duration, the kinetics associated with fluoride clearance and the lack of accumulation indicate that the observed effects occurred within a duration of exposure that is appropriate for assessing acute risk. Therefore, HED recommends that CA DPR consider this study when deriving points of departure for acute assessment.

DPR response: The increased motor activity observed in pups on postnatal day (PND) 22 in the developmental neurotoxicity (DNT) study cannot be considered an acute effect, since the observation was made after 11 days of repeated exposure to sulfuryl fluoride. Although the sulfuryl fluoride database in rats does not suggest significant fluoride accumulation in the brain with repeated exposure, this does not in any way infer an equivalent susceptibility of brain tissues after acute (one time) versus repeated short-term (11 days) exposure. In other words, the available pharmacokinetic data do not account for brain tissue's changing susceptibility. Consequently, DPR did not use neurological effects observed in the short-term DNT study to derive an acute point of departure.