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DATE: February 9, 2022

SUBJECT: Response to Comments by the US Environmental Protection Agency regarding DPR's 2020 Allyl Isothiocyanate Draft Risk Characterization Document

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Background

At the request of the Department of Pesticide Regulation (DPR), the Health Effects Division (HED) of US Environmental Protection Agency's (US EPA) Office of Pesticide Programs reviewed the July 2020 Draft Risk Characterization Document (RCD) for Allyl Isothiocyanate (AITC). HED was asked to comment on a series of charge questions covering the hazard identification, exposure assessment, risk characterization, and worker and bystander margins of exposure. Their comments appeared in a letter submitted to DPR on October 8, 2020.

DPR's responses to the comments specific to the hazard identification and risk characterization sections of the draft RCD are provided in this document. Responses to the charge questions relating to the exposure assessment appear in a separate memorandum. HED noted that their comments concerning worker and bystander margins of exposure (Charge Questions 8 and 9) were included as part of their answers to the exposure assessment charge questions. Consequently, those comments are not addressed here.

DPR sincerely appreciates HED's review. Comments from other regulatory agencies can be helpful in the development of technically complex, science-based regulatory documents.

Responses to Hazard Identification Charge Questions

DPR Charge Question 1: Acute POD: A default 10x LOEL-to-NOEL extrapolation factor was used to establish the critical acute POD of 2.5 ppm.

HED Comment: HED has not reviewed the cited acute inhalation study and cannot comment on the NOEL/LOEL established by DPR. Selection of an acute inhalation study for an acute inhalation POD is appropriate because it is route-specific and reflects effects observed following a single exposure. In cases where BMD modeling is not recommended, the use of a 10x factor for the lack of a NOAEL in a study is appropriate. Note that HED uses NOAELs (no observed adverse effect levels) and LOAELs (lowest observed adverse effect levels) rather than the NOELs/LOELs used by the DPR. When HED reviews the AITC toxicity database, the NOAEL/LOAEL selected by HED may be different than the NOEL/LOEL established by DPR.

DPR Response: No response necessary.

DPR Charge Question 2: The critical chronic inhalation POD was estimated from the subchronic critical POD by applying a default duration extrapolation factor of 10. This was necessitated by the lack of chronic inhalation studies.

HED Comment: HED has not yet reviewed the cited 13-week inhalation study and cannot confirm the NOEL/LOEL established by DPR. Since the 13-week inhalation study was the only repeat dose inhalation study available, the use of this study for the chronic inhalation POD appears to be supported; however, HED has not yet evaluated the entire database. Generally, a default extrapolation factor of 10x is appropriate to extrapolate a chronic inhalation POD from a subchronic inhalation study.

DPR Response: No response necessary.

DPR Charge Question 3: PODs from oral studies were not used to establish critical PODs.

HED Response: The scope of the DPR risk characterization document stated that the assessment is focused on the inhalation toxicity of AITC to align with its proposed use as a chemical fumigant. However, HED has not evaluated the cited oral toxicity studies and cannot comment on whether the use of a POD selected from an inhalation toxicity study for inhalation risk assessment is appropriate.

DPR Response: No response necessary.

DPR Charge Question 4: This RCD did not include a cancer risk estimate for AITC

HED Response: The scope of the DPR risk characterization document stated that this assessment is focused on the inhalation toxicity of AITC to align with its proposed use as a chemical fumigant. Risks to workers, occupational bystanders, and residential bystanders, including vulnerable subpopulations, were estimated for acute exposures. Risks to workers were also estimated for subchronic (seasonal) and chronic (annual, lifetime) exposures. HED agrees that there is potential for chronic (annual, lifetime) exposure. However, HED cannot comment on the DPR cancer risk assessment since HED has not yet evaluated the carcinogenic potential of AITC.

DPR Response: No response necessary.

Responses to Risk Characterization Charge Questions

DPR Charge Question 7: Dosimetric adjustments of air concentrations to account for pharmacokinetic differences between laboratory animals and humans were used to calculate reference concentrations (RfCs) and risk targets (i.e., target Margins of Exposure).

HED Response: The inhalation PODs were converted to human equivalent concentration (HEC) with a target MOE of 30 which is consistent with current HED practice.

DPR Response: No response necessary.