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[1F8942]

Valent U.S.A. LLC

Summary of Petition

EPA has received a pesticide petition (1F8942) from Valent U.S.A. LLC, 4600 Norris Canyon Road, San Ramon, CA 94583, 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 by establishing a tolerance for residues of inpyrfluxam (3-(difluoromethyl)-*N*-[(*R*)-2,3-dihydro-1,1,3-trimethyl-1*H*-inden-4-yl]-1-methyl-1*H*-pyrazole-4-carboxamide) in or on the raw agricultural commodity Rapeseed subgroup 20A at 0.01 mg/kg (ppm) and Rapeseed, forage at 0.02 mg/kg (ppm). EPA has determined that the petition contains data or information regarding the elements set forth in section 408 (d)(2) of FDDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism.*

A complete dataset of plant metabolism studies for inpyrfluxam has been conducted on apple, soybean, rice, and potato, to support the proposed uses. Metabolic pathways were similar across all crops tested. The residues definition for both monitoring and risk assessment is parent inpyrfluxam.

2. *Analytical method.*

An independently validated analytical method RM-50C-1 has been submitted for analyzing parent inpyrfluxam residues with appropriate sensitivity in all crop commodities for which tolerances are being requested.

3. *Magnitude of residues.*

No inpyrfluxam residue study has been done at the proposed maximum application rate of 10 g ai/100kg seed for Rapeseed subgroup 20A. But, given that the rate is ≤ 10 gai/100 kg seeds, this submission qualified under the EPA Reduced Residue Chemistry Data Requirements for Seed Treatment Uses (Memo 26 Jan 2018), therefore, a tolerance at the LOQ of 0.01 mg/kg is proposed for Rapeseed subgroup 20A and 0.02 mg/kg for Rapeseed, forage https://www.epa.gov/pesticides/reduced-residue-chemistry-data-requirements-seed-treatment-uses. An enforcement analytical method that was included in an ILV study (MRID 49706487)

has been submitted with the initial petition. Canada MRL has been set at 0.01 ppm for Rapeseeds, Crop Subgroup 20A (MRID 50312815; PMRL2020-23).

B. Toxicological Profile

A complete, valid and reliable database of mammalian and genetic toxicology studies has been submitted to EPA that supports the proposed tolerances for Rapeseed subgroup 20A and Rapeseed, forage. The full Revised Human Health Risk Assessment can be found in docket ID number EPA-HQ-OPP-2018-0038-0037 at www.regulations.gov. The toxicological profile summary for inpyrfluxam was published in the Final Rule for inpyrfluxam tolerances in the Federal Register on August 26, 2020 (85 FR 52483). https://www.federalregister.gov/documents/2020/08/26/2020-18661/inpyrfluxam-pesticide-tolerances.

C. Aggregate Exposure

1. *Dietary exposure*. A partially refined dietary exposure assessment from food and water were conducted by EPA to evaluate the potential risk due to chronic dietary exposure of the U.S. population and various subpopulations to residues of inpyrfluxam. Residues from use of inpyrfluxam on rapeseed were not included in the current assessment because the contribution to the overall aggregate exposure is considered negligible.

The inpyrfluxam Acute Dietary (All Populations) NOAEL is 30 mg/kg/day, derived from an acute neurotoxicity study in the rat. The inpyrfluxam Chronic Dietary (All Populations) NOAEL is 26 mg/kg/day, derived from a Two- Generation Reproduction study in the rat. An uncertainty factor of 100 was applied to account for intra- and inter-species variation. No additional uncertainty factor for FQPA was necessary. The acute and chronic population adjusted dose is 0.3 mg/kg body wt/day.

The acute dietary (food and drinking water) exposure and risk estimates do not exceed the Agency's level of concern (< 100% of the acute population-adjusted dose [aPAD]) at the 95th exposure percentile for the general U.S. population (2.3% of the aPAD) and all population subgroups. The most highly exposed population subgroup is all infants (<1 yr. old) at 6.3% of the aPAD. The chronic dietary (food and drinking water) exposure and risk estimates for the general U.S. population and all population subgroups are below the Agency's level of concern (LOC). The chronic dietary exposure estimate to the general U.S. population is <1% of the chronic population-adjusted dose (cPAD). Children 1-2 years old, the most highly exposed population subgroup, is 1.6% of the cPAD.

i. *Food*. The potential chronic dietary risk from exposure of the U.S. population and various subgroups to inpyrfluxam residues in food commodities was assessed using a partially refined dietary risk assessment, which used anticipated residues to account for the metabolites of concern, 100 percent crop treated (% CT), and incorporated the Agency's 2018 default processing factors.

ii. *Drinking water*. Modeling for residues in drinking water included parent inpyrfluxam, and four additional residues: 3'-OH-S-2840, 1'-COOH-S-2840, 1'keto-S-2840, and N-des-Me-S-2840. Drinking water was incorporated directly into the dietary assessment and used the ground water concentration generated by the Pesticide Root Zone Model Groundwater (PRZM-GW). Seed treatments uses were classified as nonfood and were not included in the dietary assessment.

2. *Non-dietary exposure*. No non-dietary residential or turf exposures are expected with the petitioned use pattern.

D. Cumulative Effects

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to inpyrfluxam and any other substances; and inpyrfluxam does not appear to produce a toxic metabolite produced by other substances.

E. Safety Determination

FFDCA section 408 provides that EPA shall apply an additional margin of safety, up to ten-fold, for added protection for infants and children in the case of threshold effects, unless EPA determines that a different margin of safety will be safe for infants and children. A clear no-observed adverse-effect level (NOAEL) and lowest-observed adverse-effect level (LOAEL) was established, and the points of departure (PODs) selected for risk assessment purposes are protective of the developmental or offspring effects. The FQPA SF has been reduced to 1X because: (1) the toxicity database is adequate to characterize potential pre- and post-natal risk for infants and children; (2) decreased motor activity was observed in females in the acute neurotoxicity study; however, no neurotoxicity was observed in the subchronic neurotoxicity or in any other studies in the inpyrfluxam database; (3) in the 2-generation reproduction study in rats, no reproductive effects were observed, offspring toxicity (decreased pup weights in F1 and F2 generations) was observed in the presence of parental toxicity (thyroid weight changes and histopathology in P and F1 generations); (4) although there were developmental effects (decreased fetal weights) in the developmental study in rats in the absence of maternal toxicity, a clear NOAEL and LOAEL were identified; and (5) the PODs selected for risk assessment purposes are protective of the developmental effects seen in the database.

1. *U.S. population.* The acute dietary (food and drinking water) exposure and risk estimates do not exceed the Agency's level of concern (< 100% of the acute population-adjusted dose [aPAD]) at the 95th exposure percentile for the general U.S. population (2.3% of the aPAD) and all population subgroups. The chronic dietary (food and drinking water) exposure and risk estimates for the general U.S. population and all population subgroups are below the Agency's level of concern (LOC). The chronic dietary exposure estimate to the general U.S. population is <1% of the chronic population-adjusted dose (cPAD). Based on a highly conservative risk assessment, Valent U.S.A. LLC concludes that there is a reasonable certainty that no harm will result to the general population from the aggregate exposure to inpyrfluxam from the proposed uses.

2. *Infants and children.* For acute exposures, the most highly exposed population subgroup is all infants (<1 yr. old) at 6.3% of the aPAD. The chronic dietary exposure estimate to children 1-2 years old, the most highly exposed population subgroup, is 1.6% of the cPAD. Based on a highly conservative risk assessment, Valent U.S.A. LLC concludes that there is a reasonable certainty that no harm will result to infants and children from the aggregate exposure to inpyrfluxam from the proposed uses.

F. International Tolerances

There are no CODEX maximum residue levels (MRLs) established or proposed for residues of inpyrfluxam in or on Rapeseed subgroup 20A. Currently, an MRL for residues of inpyrfluxam on Rapeseeds (crop Subgroup 20A) is set at 0.01 ppm in Canada. No MRL has been established in Mexico.