UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: **02/06/2023**

SUBJECT: **Azoxystrobin.** Human Health Risk Assessment for the Establishment of Tolerances for Residues in/on Mango and Papaya and Establishment of a Tolerance for Residues in/on Imported Palm Oil.

PC Code: 128810
Decision No.: 578208
Petition No.: IE8946
Risk Assessment Type: Single Chemical/Aggregate
TXR No.: NA
MRID No.: NA

DP Barcode: D463678
Registration No.: 100-1120
Regulatory Action: Section 3
Case No.: NA
CAS No.: 131860-33-8
40 CFR: §180.507

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The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The Registration Division (RD) of OPP has requested that HED evaluate hazard and exposure data and conduct dietary, occupational, residential, and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from the proposed domestic tolerances for azoxystrobin in/on mango and papaya, and proposed tolerance without U.S. registration for azoxystrobin in/on palm oil. A summary of the findings and an assessment of human health risk resulting from the proposed domestic tolerances of azoxystrobin are provided in this document. While this risk assessment considers the proposed domestic tolerances, the domestic uses were not updated. This risk assessment includes dietary assessment, hazard characterization and aggregate assessment. There are currently registered domestic agricultural and residential uses and several tolerances without U.S. registration for azoxystrobin. Drinking water exposure is expected. However, as the petition does not include proposed residential uses, neither occupational nor residential exposure assessments were conducted for azoxystrobin at this time. Additionally, as this petition does not include antimicrobial uses, exposure assessments were not conducted for antimicrobial uses. HED's draft risk assessment (DRA) in support of registration review for azoxystrobin was completed in 2015 and revised again in 2018; the interim decision was made public on March 18, 2019 (Case No. 7020, EPA-HQ-OPP-2009-0835-0040, 84 FR 9778).

Table of Contents

1.0 Executive Summary

The active ingredient (ai) azoxystrobin [methyl (*αE*)-2-[[6-(2-cyanophenoxy)-4-pyrimidinyl]oxy]-*α*-(methoxymethylene)benzeneacetate], is a β-methoxyacrylate fungicide used to control mold and fungus on agricultural crops, agricultural seeds, residential areas, and on indoor surfaces. Tolerances are established (40 CFR §180.507) for residues of the fungicide azoxystrobin and its Z-isomer. Tolerances range from 0.04 ppm (asparagus) to 420 ppm (aspirated grain factions). Current tolerances are established for residues at 2 ppm on mango and papaya.

Use Profile
Syngenta is seeking a tolerance without U.S. registration (in/on palm oil) and proposing amendments to domestic tolerances (in/on mango, papaya) for azoxystrobin. To support the tolerances on these commodities, Syngenta has submitted English translations of approved foreign labels for end-use products (EPs) Amistar Top®, Uniform®, and Graduate A+ for use on mango, papaya, or palm oil. Both Amistar Top® and Graduate A+ are formulated as soluble concentrates (SCs) containing 200 and 239 g ai/L, respectively. Uniform® is formulated as a suspoemulsion (SE) containing 321 g ai/L. These EPs are not registered in the U.S., nor are for domestic use.

Exposure Profile
For the proposed tolerances without U.S. registration, exposures are limited to dietary (food and water).

Hazard Characterization
The azoxystrobin database is complete for risk assessment. The 90-day inhalation toxicity study and immunotoxicity study were previously recommended to be waived by the Hazard and Science Policy Council (HASPOC) (TXR 0050756, M. Lewis, 09/12/2017; TXR 0057071, J. Leshin, 11/13/2014). In repeat-dose oral studies, the liver and bile ducts were consistently the target organs of azoxystrobin toxicity. Developmental effects were not seen in rabbit or rat developmental toxicity studies. In the rat reproduction study, offspring and parental effects (decreased body weight and increased adjusted liver weight) were observed at the same dose in both offspring and parental animals. Therefore, the azoxystrobin toxicity data show no increased susceptibility in the young. The dietary and incidental oral points of departure (PODs) and levels of concern (LOCs) have not changed since the previous risk assessment. A dermal POD has not been selected because there was no dermal or systemic toxicity seen up to the limit dose in a route-specific dermal toxicity study, and no developmental or reproductive effects were seen in the azoxystrobin database. However, for short- and intermediate-term inhalation exposure assessment, the POD was selected based on a route-specific inhalation toxicity study in rats with the soluble concentrate (SC) formulation of azoxystrobin (8% ai). For inhalation exposures, the standard interspecies extrapolation uncertainty factor (UF) can be reduced from 10X to 3X.

Azoxystrobin is characterized as "Not Likely to be Carcinogenic to Humans." For assessing acute risk, EPA is retaining a Food Quality Protection Act (FQPA) Safety Factor (SF) of 3X to account for the use of a lowest-observed adverse-effect level (LOAEL) from the acute neurotoxicity study to derive an acute reference dose. For assessing chronic dietary, incidental