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Interregional Research Project Number 4 (IR-4)
PP# 7E7218

EPA has received a pesticide petition (PP 7E7218) from Interregional Research Project Number 4 (IR-4), 681 U.S. Highway #1 South, North Brunswick, NJ 08902-3390 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 methoxyfenozide in or on the raw agricultural commodites avocado, black-sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple at 0.6 parts per million (ppm); guava, feijoa, jaboticaba, wax jambu, starfruit, passion fruit, and acerola at 0.4 parts per million (ppm); green onion, fresh chive leaves, fresh Chinese chive leaves, Elegans Hosta, Fritillaria leaves, kurrat, Lady's leek, leek, wild leek, Beltsville bunching onion, fresh onion, macrostem onion, tree onion tops, Welsh onion tops, and fresh shallot leaves at 5.0 parts per million (ppm). EPA has determined that the petition contains data or information regarding the elements set forth in section 408 (d)(2) of the 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.* The qualitative nature of methoxyfenozide residues in plants and animals is adequately understood. Residues in plants, meat and fat are defined in terms of parent compound only. Residues in eggs, liver and meat by-products (mbyp) are defined in terms of combined residues of parent and its glucuronide metabolite, expressed as parent. More details have been previously published in the Federal Register of July 5, 2000 (65 FR 41355) (FRL-6497-5).

2. *Analytical method.* Adequate enforcement methods are available for determination of methoxyfenozide residues in plant commodities, based on the Rohm and Haas Company Technical Report No. 34-98-87, "Tolerance Enforcement Method for Parent RH-2485 in Pome Fruit". The available Analytical Enforcement Methodology was previously reviewed in the Federal Register of September 20, 2002 (67 FR 59193).

3. *Magnitude of residues.* Complete residue data for methoxyfenozide on avocado; guava; and green onions have been submitted by IR-4. The requested tolerances are adequately supported.

B. Toxicological Profile

1. *Acute toxicity.* The toxicological profile and endpoints for methoxyfenozide which supports this petition to establish tolerances were previously published in the Federal Register of August 31, 2005 (70 FRL-7732-3).

1. *Acute toxicity*. NA

2. *Genotoxicty*. NA

3. *Reproductive and developmental toxicity*. NA

4. *Subchronic toxicity*. NA

5. *Chronic toxicity*. NA

6. *Animal metabolism*. NA

7. *Metabolite toxicology*. NA

8. *Endocrine disruption*. NA

C. Aggregate Exposure

1. *Dietary exposure.* Assessments were conducted to evaluate potential risks due to chronic and acute dietary exposure of the U.S. population subgroups to residues of methoxyfenozide. These analyses cover all registered crops, as well as, uses pending with the Agency, active and proposed section 18 uses, and newly proposed IR-4 minor uses. There are no registered residential nonfood uses of methoxyfenozide.

i. Food. a. Acute risk. No appropriate toxicological endpoint attributable to a single exposure was identified in the available toxicology studies on methoxyfenozide including the acute neurotoxicity study in rats, the developmental toxicity study in rats and the developmental toxicity study in rabbits. Since no acute toxicological endpoints were established, the acute aggregate risk is expected to be negligible.

b. Chronic assessments were conducted to evaluate potential risks due to chronic dietary exposure of the U.S. population and sensitive population subgroups to residues of methoxyfenozide. The tier-1 assessment used the Dietary Exposure Evaluation Model™ (DEEM-FCID, ver. 2.14, Exponent, Inc., Washington, DC-20036) software for conducting the chronic dietary (food) risk analysis. DEEM is a dietary exposure analysis system that is used to estimate exposure to a pesticide chemical in foods comprising the diets of the U.S. population, including population subgroups. DEEM contains food consumption data as reported by respondents in the USDA Continuing Surveys of Food Intake by Individuals (CSFII) conducted in 1994-1996 and 1998 and food translation to

RACs, as indicated by EPA/USDA FCID recipe set as of August, 2002.

None of the currently proposed uses are involving crops commonly used as feed for livestock. Therefore, an estimated animal dietary burden is not needed.

The chronic tox-endpoint is the cRfD = 0.1 mg/kg-bw/day, published in the Federal Register of August 31, 2005 (70 FRL-7732-3). The published FQPA SF = 1x for methoxyfenozide and therefore the cPAD = 0.1 mg/kg/day. The tier-I exposure was found to occupy up to 19.5% of the chronic population adjusted dose (PAD) for US-general population and 42.8% of PAD for the most highly exposed population subgroup, children 1 to 2 years old. These results should be viewed as conservative (health protective) risk estimates. Refinements such as use of percent crop-treated information and/or anticipated residue values would yield lower estimates of chronic dietary exposure.

ii. Drinking water. There are no water-related exposure data from monitoring to complete a quantitative drinking water exposure analysis and risk assessment for methoxyfenozide. Screening level exposure levels to water were estimated from EPA's water models. Index Drinking Water Reservoir model (FIRST) was used to calculate estimated the environmental concentrations (EECs) for surface water. The screening concentration in ground water was estimated by using the model Screening Concentrations in GROund Water (SCI-GROW), an empirical model based upon actual monitoring data collected for a number of pesticides that serve as benchmarks. These models take into account the use patterns and the environmental profile of a pesticide, but do not include consideration of the impact that processing raw water for distribution as drinking water would likely have on the removal of pesticides from the source water. The primary use of these models at this stage is to provide a coarse screen for assessing whether a pesticide likely to be present in drinking water at concentrations which would exceed human health levels of concern.

A drinking water level of comparison (DWLOC) is the concentration of a pesticide in drinking water that would be acceptable as a theoretical upper limit in light of total aggregate exposure to that pesticide from food, water, and residential uses. HED uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. In the absence of monitoring data for a pesticide, the DWLOC is used as a point of comparison against the conservative EECs provided by computer modeling (SCI-GROW, FIRST, GENEEC, PRZM/EXAMS). The DWLOCs for assessing chronic aggregate dietary risk can be back-calculated by subtracting from the cRfD the amount of the estimated dietary exposure. The methoxyfenozide's DWLOC calculated for different sub-population groups ranged between 0.6 to 2.8 ppm and it is much higher than the highest EEC's estimated by conservative tier-1 water models.

a. Acute exposure and risk. Because no acute dietary endpoint was established, Dow AgroSciences concludes that there is a reasonable certainty of no harm from acute exposure from drinking water.

b. Chronic exposure and risk. Tier I screening-level exposure assessments was conducted using the simulation models SCI-GROW and FIRST to generate EECs for ground and surface water, respectively. The modeling was conducted based on the environmental profile and the maximum seasonal application rate proposed across current and proposed labels The concentration used for chronic exposure from drinking-water was estimated by the screening model FIRST as an annual average concentration EEC = 15.8 parts per billion (ppb).

2. Non-dietary exposure. Methoxyfenozide is not currently registered for use on any residential non-food sites. Therefore, there is no non-dietary acute, chronic, short- or intermediate-term exposure.

D. Cumulative Effects

Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA does not have, at this time, available data to determine whether methoxyfenozide has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, methoxyfenozide does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, it is assumed that methoxyfenozide does not have a common mechanism of toxicity with other substances.

E. Safety Determination

1. *U.S. Population*. Using the DEEM exposure assumptions described in this unit, Dow AgroSciences has concluded that the aggregate exposure to methoxyfenozide from the current and proposed new tolerances will utilize 19.5% of the chronic PAD for the U.S. population. If potable water is aggregated to the dietary exposure, at the maximum residue level estimated by EPA's model FIRST (0.016 ppm), the aggregate exposure to US-population is slightly increasing from to 19.8% PAD. EPA generally has no concern for exposures below 100% of the chronic PAD because the chronic PAD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Despite the potential for exposure to methoxyfenozide in drinking water, the aggregate exposure is not expected to exceed 100% of the chronic PAD. Therefore, it can be concluded with a reasonable certainty that no harm will result to US-general population from aggregate exposure to methoxyfenozide residues.

2. *Infants and children*. In assessing the potential for additional sensitivity of infants and children to residues of methoxyfenozide, EPA considered data from developmental

toxicity studies in the rat and rabbit and a 2-generation reproduction study in the rat. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure during gestation. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity.

FFDCA section 408 provides that EPA shall apply an additional ten-fold safety factor for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a margin of exposure (MOE) analysis, or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. EPA believes that reliable data support using the standard uncertainty factor (UF = 100 for combined interspecies and intraspecies variability) and no additional safety factor is required for the calculation of MOE for any population sub-group.

The toxicology data base available for methoxyfenozide included acceptable developmental toxicity studies in both rats and rabbits as well as a 2-generation reproductive toxicity study in rats. The data provided no indication of increased sensitivity of rats or rabbits to *in utero* and/or postnatal exposure to methoxyfenozide. There is a complete toxicity data base for methoxyfenozide and the exposure data are complete or are estimated based on data/assumptions that reasonably accounts for potential exposures. Based on the completeness of the data base and the lack of prenatal and postnatal toxicity, EPA determined that an additional safety factor was not needed for the protection of infants and children (FQPA SF = 1x).

Since no acute toxicological endpoints were established, the acute aggregate risk is considered to be negligible. Using the exposure assumptions described in this report, Dow AgroSciences has concluded that chronic dietary exposure to methoxyfenozide from the existing and proposed new tolerances will utilize at the most 42.8% of the cPAD for infants and children. If exposure from drinking water is aggregated to the dietary exposure, at the maximum residue level estimated by EPA's model FIRST (0.016 ppm), the aggregate exposure to children 1-6 is slightly increasing to 43.3 % PAD. EPA generally has no concern for exposures below 100% of the cPAD because the cPAD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Short and intermediate term risks are judged to be negligible due to the lack of significant toxicological effects observed. Based on these risk assessments, Dow AgroSciences concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to methoxyfenozide residues.

F. International Tolerances

There are several countries around the globe that have established tolerances/ MRLs for methoxyfenozide. The most extensive list has been published by

Codex (25 food commodities). Among others countries, Canada, Australia, Brazil, United Kingdom, and several other European countries have MRL's established for residues of methoxyfenozide. A comparative assessment of MRLs from leading countries has concluded that the MRLs established by different agencies are incompatible. The difference may be originated by diverse good agricultural practices used for efficacious pest control, different guidelines for conducting field crop residue studies and different calculation methods to propose tolerances. Based on the current situation, the U.S. tolerance levels cannot be re-considered in order to harmonize with MRLs from other countries, and therefore the incompatibility will persist.