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Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Flumiclorac pentyl

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Approved By:

_____/s/_____
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Date

I. Regulatory Determination

The Federal Food, Drug and Cosmetic Act (FFDCA), as amended by FQPA, requires EPA to reassess all the tolerances for registered chemicals in effect on the day before enactment of the FQPA on August 3, 1996. In reassessing these tolerances, the Agency must consider, among other things, aggregate risks from non-occupational sources of pesticide exposure, whether there is increased susceptibility to infants and children, and the cumulative effects of pesticides with a common mechanism of toxicity. When a safety finding has been made that aggregate risks are not of concern, the tolerances are considered reassessed. Existing tolerances associated with flumiclorac pentyl must be reassessed in accordance with FFDCA, as amended by FQPA. Ecological and occupational assessments were originally conducted when flumiclorac pentyl was first registered in 1994. Therefore, no further ecological or occupational assessments were conducted as part of this Report of the FQPA Tolerance Reassessment Progress and Risk Management Decision for Flumiclorac pentyl (also referred to as a TRED).

Flumiclorac pentyl (active ingredient number 128724) is a postemergence herbicide used on field corn, soybeans and non-crop areas, such as: industrial sites, airports, military installations, roadsides and associated rights-of-way, and other similar areas to control a selected group of broadleaf weeds, specifically morning-glory and velvet leaf. Although there are no labeled residential homeowner uses, there is potential risk for non-occupational exposure from other treated areas, such as golf courses, athletic fields, recreational areas, schools, apartment buildings, etc.

The Agency has evaluated the human health risks associated with all currently registered uses of flumiclorac pentyl and has determined that there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue. In making this determination, EPA has considered dietary exposure from food and drinking water and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, the five (5) tolerances established for residues of flumiclorac pentyl in/on raw agricultural commodities are now considered reassessed as safe under section 408(q) of FFDCA, as amended by FQPA.

The Agency also included in the risk assessments supporting this TRED petitions for establishment of a new use and associated tolerances of flumiclorac pentyl on cotton. To evaluate the tolerance petition and determine if new tolerances should be established, EPA considered all of the criteria described above to ensure that the FQPA safety standard was met. For the proposed new use of flumiclorac pentyl on cotton, the Agency has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to flumiclorac pentyl. However, because the TRED pertains only to the reassessment of tolerances in effect before FQPA, the determination regarding the establishment of the new use and associated tolerances is outside the scope of this TRED and will be made by the Agency in a separate decision.

The Agency's human health and drinking water findings for the pesticide flumiclorac pentyl are summarized in the following risk assessments: *Flumiclorac pentyl: HED Chapter of the Tolerance Reassessment Eligibility Decision Document (TRED),* dated June 28, 2005 and *Tier 1 Drinking Water Assessment for Flumiclorac pentyl on Corn and Soybeans (TRED) and Cotton (New*

Use), dated March 17, 2005. For further details, please refer to these risk assessments and other technical documents pertaining to the flumiclorac pentyl TRED, which are available on the Internet at http://www.epa.gov/e-dockets and in the public docket for viewing.

The Agency is issuing this TRED document for flumiclorac pentyl as announced in a Notice of Availability published in the ***Federal Register***. The Agency is providing a 30-day comment period for stakeholders to respond to this risk management decision. If substantive information is received during the comment period that indicates a need to refine any of EPA's assumptions or a need for risk mitigation, then this decision will be modified as appropriate through an amendment to the TRED.

II. Tolerance Reassessment

A. FQPA Assessment Supporting Tolerance Reassessment Decision

The Agency has conducted risk assessments to ensure that the flumiclorac pentyl tolerances meet the new safety standards established by FFDCA, as amended by FQPA. These recent risk assessments for flumiclorac pentyl include evaluation of potential susceptibility to infants and children; dietary, drinking water, and residential exposure of adults and children; and aggregate risk from these various exposure pathways. EPA also considered potential cumulative risks for flumiclorac pentyl and other substances sharing a common mechanism of toxicity, as well as potential endocrine effects associated with flumiclorac pentyl.

EPA has determined that risk from exposure to flumiclorac pentyl is within its own "risk cup." In other words, EPA is able to conclude today that the tolerances for flumiclorac pentyl meet the FQPA safety standards. In reaching this determination, the Agency has considered the available information on the potential sensitivity of infants and children, as well as the chronic and acute food exposure. However, an endpoint of concern attributable to a single dose was not identified for this chemical; therefore, an acute reference dose (RfD) was not established and an acute dietary assessment was not conducted. An aggregate assessment was conducted for exposures through food, residential uses, and drinking water. Results of this aggregate assessment indicate that the human health risks from these combined exposures are considered to be within acceptable levels; that is, combined risks from all exposures to flumiclorac pentyl "fit" within the individual risk cup for this chemical. The Agency's risk assessment conclusions are summarized below.

FQPA Safety Factor Considerations. The FFDCA, as amended by the FQPA, directs the Agency to use an additional tenfold (10X) safety factor to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children. FFDCA authorizes the Agency to modify the tenfold safety factor only if reliable data demonstrates that the resulting level of exposure would be safe for infants and children.

Flumiclorac pentyl did not cause developmental toxicity in rat or rabbit fetuses and did not adversely affect reproductive parameters in rats in a two-generation study. There is no quantitative or qualitative evidence of increased susceptibility of rat or rabbit fetuses after *in utero* and/or post-natal exposure to flumiclorac pentyl in the developmental and reproduction studies. Dose-response

relationships are well-characterized and clear No/Lowest Observable Adverse Effect Levels (NOAELs/LOAELs) have been identified for the critical effects. Therefore, the Special FQPA Safety Factor can be reduced to 1X, since the degree of concern is low and there are no residual uncertainties for pre- and/or post-natal toxicity.

Further, no evidence of neurotoxicity was observed in any study. Based on the weight of evidence, a developmental neurotoxicity (DNT) study is not required for flumiclorac pentyl.

Dietary Risks from Food and Drinking Water. Because an endpoint attributable to a single dose was not identified from the available toxicity database for flumiclorac pentyl, an acute dietary assessment was not conducted. A chronic dietary risk assessment was conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™),Version 2.00, and the Lifeline Model Version 2.0, which use food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The Tier 1 chronic analysis assumed 100% crop treated and tolerance-level residues for all foods. Drinking water exposure was incorporated directly in the DEEM-FCID and Lifeline chronic dietary assessments. Chronic estimated drinking water concentrations (EDWC) for surface water and ground water were generated by the Tier 1 FIRST and SCI-GROW models, respectively.

EPA's Tier 1 chronic dietary risk assessment indicates that dietary risk from flumiclorac pentyl residues in food and drinking water are low and not of concern. The resulting chronic dietary exposure estimates using the DEEM-FCID model were less than 0.01% of the chronic Population Adjusted Dose (cPAD) for the U.S. general population and all population subgroups; including the most highly exposed population subgroup (Children, 3 to 5 years old). Estimated chronic exposures using the Lifeline model were consistent with the DEEM-FCID results (<0.01% of the cPAD for the U.S. general population and all population subgroups). Therefore, no mitigation measures are necessary to address dietary risks from food and drinking water.

Residential Risks. Residential or non-occupational risks from potential post-application exposure were assessed because of flumiclorac pentyl use on golf courses, parks, recreation areas, schools, apartment buildings, etc. Children were identified as the most sensitive of potentially exposed subpopulations to residential post-application exposures to flumiclorac pentyl. Since a dermal endpoint of concern was not selected, because no systemic effects were observed in the dermal rat toxicity study, dermal risks were not assessed. Therefore, the only exposure assessed was for incidental oral exposure to infants and children, which includes: hand to mouth, object to mouth, and soil ingestion activities. Margins of Exposure (MOEs) ranged from >58,000 to 1.75×10^7, which are well above the target MOE of 100. Therefore, no mitigation measures are necessary to address residential risks.

Aggregate Risk. Short- and long-term (chronic) aggregate risk assessments were conducted for flumiclorac pentyl and are not of concern. An acute aggregate assessment was not conducted because an acute endpoint was not selected. The short-term assessment considered both dietary (food + drinking water) and residential exposures. The long-term (chronic) assessment considered dietary exposure only, since the current uses of flumiclorac pentyl are not expected to result in long-term

residential exposure. Intermediate-term residential exposures are not anticipated, and therefore an intermediate-term aggregate risk assessment was not conducted.

The results of the long-term (chronic) aggregate assessment indicate that the combined exposure to flumiclorac pentyl from food and drinking water is well below the Agency's level of concern, with estimated exposures representing <0.01% of the cPAD for the U.S. population and all population subgroups, including infants and children. When the chronic dietary exposure is combined with short-term residential exposure, the resulting short-term aggregate risks for children are also below Agency's level of concern. The MOE of concern for short-term aggregate risk is 100. Since the estimated short-term aggregate MOE for children (toddlers) is 46,000, short-term aggregate risk is not considered to be of concern for flumiclorac pentyl. Therefore, no mitigation measures are necessary to address aggregate risks.

B. Cumulative Assessment

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 flumiclorac pentyl and any other substances, and flumiclorac pentyl does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that flumiclorac pentyl has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

C. Endocrine Disruptor Effects

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

In the available toxicity studies on flumiclorac pentyl, there was no estrogen, androgen, and/or thyroid mediated toxicity. When additional appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, flumiclorac pentyl may be

subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

D. Tolerance Summary

Tolerances Listed in 40 CFR § 180.477

Permanent tolerances are established for residues of flumiclorac pentyl, including all the metabolites of flumiclorac pentyl. The tolerance level is expressed in terms of the parent only, in/on field corn grain, forage, and fodder at 0.01 ppm; soybean seed at 0.01 ppm, and soybean hulls at 0.02 ppm [40 CFR §180.477]. The Agency recommends that the tolerance expression be revised to only include residues of flumiclorac pentyl *per se*. There are currently no tolerances for flumiclorac pentyl residues in livestock commodities or for inadvertent residues in rotational crops.

Adequate magnitude of the residue data are available to reassess the tolerances listed in 40 CFR §180.477. The available data indicate that residues of flumiclorac pentyl were consistently below the LOQ of 0.01 ppm in/on samples of soybean seed and field corn grain, forage, and stover treated according to the maximum use patterns for each crop. The tolerances for soybean seed and hulls are reassessed at 0.01 and 0.02 ppm, respectively. The tolerances for field corn raw agricultural commodities (RACs) are reassessed at 0.01 ppm each.

Although the available residue data for soybean hay and forage indicate that flumiclorac pentyl residues were detected above the LOQ, no tolerances are needed for these soybean RACs, because the registered end-use products contain adequate label restrictions which prohibit the feeding and grazing of livestock animals on treated soybean fields.

The requirements for residue data on the aspirated grain fractions may be waived since residues in/on samples of field corn grain and soybean seed, following treatment at 1x, were below the LOQ. In addition, one field corn trial conducted at an exaggerated rate of 5x also showed flumiclorac pentyl residue levels below LOQ in corn grain. Based on these findings, a tolerance for aspirated grain fractions need not be established. A summary of flumiclorac pentyl tolerance reassessment is presented in Table 1.

Tolerances Proposed in PP#3F6767

Valent U.S.A. has submitted an amended registration application and a tolerance petition (PP#3F6767) for the use of flumiclorac pentyl on cotton as a harvest aid (desiccant). The petitioner proposes the establishment of tolerances for residues of flumiclorac pentyl *per se* in/on undelinted cottonseed at 0.1 ppm and cotton gin byproducts at 2.0 ppm.

Adequate residue data have been submitted to support the proposed uses on cotton pending submission of a revised Section F to reflect appropriate tolerance levels. The petitioner needs to submit a revised Section F to increase the proposed tolerance levels on: (i) undelinted cottonseed from 0.1 to 0.20 ppm; and (ii) cotton gin byproducts from 2.0 to 3.0 ppm.

Table 1. Tolerance Reassessment Summary for Flumiclorac Pentyl.			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comments
Tolerances Listed in 40 CFR §180.477			
Corn, field, grain	0.01	0.01	
Corn, field, forage	0.01	0.01	
Corn, field, stover	0.01	0.01	
Soybean, hulls	0.02	0.02	
Soybean, seed	0.01	0.01	
Tolerances Proposed in PP#3F6767			
Cotton, seed undelinted	0.1 (proposed)	0.20	Cotton, undelinted seed
Cotton gin byproducts	2.0 (proposed)	3.0	Cotton, gin byproducts

As previously mentioned, the Agency has considered a petition for new use on cotton in the risk assessments supporting this TRED, but the determination regarding the establishment of new tolerances will be made separately by the Agency. The residue chemistry data for cotton has been reviewed and included in the dietary risk assessment for this TRED.

III. Data Gaps and Confirmatory Data Requirements

The Agency has concluded that the database for flumiclorac pentyl is complete and no data gaps have been identified. However, there are data that must be submitted to support the continuing registration of flumiclorac pentyl. These data are not expected to change the regulatory conclusions for flumiclorac pentyl described in this document. The following is the list of required data:

Product and Residue Chemistry

- The submitted poultry metabolism studies (MRIDs 46082805 and 46082806) have been deemed unacceptable because information pertaining to sample storage conditions and intervals was not provided. The studies may be upgraded if the petitioner submits the dates of hen sacrifice as well as the dates of initial and final analyses. Storage stability data in support of metabolism studies are not routinely required for samples analyzed within 4 to 6 months of collection. However, longer sample storage periods should be supported with storage stability data.

- The petitioner is required to submit a revised Section F to increase the proposed tolerance levels on: (i) undelinted cottonseed from 0.1 ppm to 0.20 ppm; and (ii) cotton gin byproducts from 2.0 ppm to 3.0 ppm.

- Additional data are required for the UV/Visible absorption spectrum for the Valent USA Corporation 98.6% flumiclorac pentyl Technical (EPA Reg. No. 59639-81) [Guideline #

830.7050]. Note: This is a new data requirement and will be required in a Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) section 3(c)(2)(B) Data Call-In (DCI) to be sent under separate cover.

Occupational and Residential Exposure

- The registrant is required to submit revised product labeling (EPA Reg. No. 59632-92) to reflect the proposed maximum application rate of 0.115 lbs. ai/A for non-agricultural use sites.

Environmental

- An aquatic phototoxicity study is being required for light-dependent peroxidizing herbicides, including flumiclorac pentyl. Note: This is a new data requirement and will be required under a group DCI for Light-Dependent Peroxidizing Herbicides to be sent under separate cover.