Notice of Filing: Pesticide Petition 7E7287

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Interregional Research Project #4

Pesticide Petition #7E7287

EPA has received a pesticide petition (PP#7E7287) from Interregional Research Project #4 (IR-4), Rutgers, The State University of New Jersey, 500 College Road East, Suite 201 W, Princeton, NJ 08540 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 180.438 by establishing tolerances for residues of gamma-cyhalothrin ((S)-[alpha]-cyano-3-phenoxybenzyl (Z)-(1R,3R)-3-(2-chloro-3,3,3-trifluoripropenyl)-2,2-dimethylcyclopropanecarboxylate) in or on the raw agricultural commodity pistachio at 0.05 parts per million (ppm) and okra at 0.2 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 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.* Gamma-cyhalothrin relies on the metabolism data conducted on lambda-cyhalothrin, which has been thoroughly tested and is adequately understood. Gamma-cyhalothrin is a resolved isomer of the lambda-cyhalothrin mixture.

2. *Analytical method.* An adequate analytical method is available for enforcement purposes. Per the Federal Register of April 8, 2004 (69 FRL-7353-4), the ICI method 81 for lamda-cyhalothrin has been validated by EPA. Given the enantiomeric relation of gamma-cyhalothrin to lambda-cyhalothrin and the fact that the method does not provide chiral resolution, the method is also applicable to gamma-cyhalothrin.

3. *Magnitude of residues.* This petition is based on existing IR-4 proposals (previously reviewed by HED) regarding crop groupings with rational for the addition of okra to “Vegetables, fruiting, group 8 (except cucurbits)” and the additional of pistachio to “Nut, tree, group 14”. Gamma-cyhalothrin has tolerances established in these related crop groupings per Federal Register of April 8, 2004 (69 FRL-7353-4). A tolerance of 0.05 ppm is established for the “Nut, tree, group 14” and a tolerance of 0.2 ppm is established for the “Vegetables, fruiting, group 8 (except cucurbits)”. For okra, the currently-labeled use pattern for the fruiting vegetables will be adopted. For pistachio, the currently-labeled use pattern for tree nuts will be used. Because the proposed use patterns are the same, the residues should not exceed those of currently approved uses and the tolerances are supported.

B. Toxicological Profile Per the Federal Register of April 8, 2004 (69 FRL-7353-4), EPA has determined the toxicological profile and endpoints for gamma-cyhalothrin which support this petition. The toxicological evaluation is accomplished by studies with gamma-cyhalothrin as well as by studies on lambda-cyhalothrin and/or cyhalothrin. Because gamma-cyhalothrin is a resolved component (single isomer) of the registered isomer mixtures of both lambda-cyhalothrin and cyhalothrin, much of the toxicological testing has been accomplished through existing tests on the previous cyhalothrin mixtures (as discussed in further detail within the Federal Register of September 27, 2002 (67 FR 60902).

1. *Acute toxicity.* Per the Federal Register of April 8, 2004 (69 FRL-7353-4), an acute reference dose (aRfD) of 0.0025 mg/kg for gamma-cyhalothrin is established. This value is based on: 1) an UF=100; 2) the NOEL of 0.5 mg/kg/day for the 1 and 2 day timeframe within the chronic oral study in the dog with lambda-cyhalothrin with clinical signs of neurotoxicity observed from day 2, 3 to 6 hour post-dose; and 3) multiplication of ½ factor based on the purity of the lambda isomer compared to the enriched isomer gamma cyhalothrin. Given the FQPA SF=1X, the aRfD = aPAD = 0.0025 mg/kg/day for gamma-cyhalothrin.

2. *Genotoxicty.* Per Federal Register of February 13, 1998 (63 Number 30), genotoxicity tests for lambda-cyhalothrin were all negative: a gene mutation assay (Ames), a mouse micronucleus assay, an in-vitro cytogenetics assay and a gene mutation study in mouse lymphoma cells.

3. *Reproductive and developmental toxicity.* Per Federal Register of April 8, 2004 (69 FRL-7353-4) and Federal Register of August 15, 2007 (72 FRL-8143-1, no quantitative or qualitative evidence of increased susceptibility of rat or rabbit fetuses to *in utero* exposure in the developmental studies was observed. For both species, the Developmental NOAEL = Maternal LOAEL and the values were 15 mg/kg/day in the rat and 30 mg/kg/day in the rabbit.

A 3-generation reproduction test in the rat covering cyhalothrin, lambda-cyhalothrin and gamma-cyhalothrin indicated a reproductive NOAEL of 5 mg/kg/day, the reproductive LOAEL was not established and the Offspring NOAEL/LOAEL was 1.5 mg/kg/day. Offspring toxicity (decreased body weight and body weight gain) was observed in the reproduction study at the same dose level as parental toxicity; these effect are not considered to be more several than the effects in the parent.

4. *Subchronic toxicity.* Per the Federal Register of April 8, 2004 (69 FRL-7353-4), the short-term incidental oral exposure scenario is to be evaluated against a NOAEL of 0.1 mg/kg/day with a residential MOE of 100; this was based on observations with the chronic oral study in the dog for lambda-cyhalothrin. However for this tolerance petition for food use on okra and pistachios, this endpoint is not applicable.

5. *Chronic toxicity.* Per the Federal Register of April 8, 2004 (69 FRL-7353-4), a chronic reference dose (cRfD) of 0.001 mg/kg for gamma-cyhalothrin is established. This value is based on: 1) an UF=100; 2) the NOAEL of 0.1 mg/kg/day from the chronic oral study in the dog with lambda-cyhalothrin; and 3) and no adjustment for the relative amounts of the lambda isomer compared to the gamma-cyhalothrin. Given the FQPA SF=1X, the cRfD = cPAD = 0.001 mg/kg/day for gamma-cyhalothrin. For all routes (oral, dermal and inhalation), gamma-cyhalothrin has been classified as "not likely to be Carcinogenic to Humans"; no cancer assessment is needed.

6. *Animal metabolism.* Per the Federal Register of April 8, 2004 (69 FRL-7353-4), the rat model indicates 55% of the oral dose is absorbed and then extensively metabolized. The ester is cleaved to the cyclopropylcarboxylic acid and a phenoxybenzyl derivative. Comparison of multi and single dose studies indicates distribution and excretion rates are similar. With the exception of accumulation of unchanged compound in the fat with chronic dosing, cyhalothrin is rapidly metabolized and excreted.

7. *Metabolite toxicology*. Per Federal Register of February 13, 1998 (63 Number 30), the metabolism of lambda-cyhalothrin in livestock was studied in the goat, chicken and cow; only unchanged parent is the major residue component of toxicological concern in meat and milk.

8. *Endocrine disruption*. No studies have been conducted to investigate the potential of gamma-cyhalothrin to induce estrogenic or other endocrine effects. However, no evidence of such effects has been noted in the battery of toxicity studies which have been conducted on cyhalothrin/lambda-cyhalothrin.

C. Aggregate Exposure

1. *Dietary exposure.* The agency has conducted an extensive assessment of the aggregate exposure for lambda-cyhalothrin reported in the Federal Register of September 27, 2002 (FR 65 60902) (FRL-7200-1). The EPA recently conducted a refined exposure assessment to cover new uses for lambda-cyhalothrin per Federal Register of August 15, 2007 (72 FRL-8143-1). In the Federal Register of April 8, 2004 (69 FRL-7353-4), the EPA concluded that risk assessments on lambda-cyhalothrin sufficiently covers gamma-cyhalothrin and "no new aggregate risk assessment is needed for gamma-cyhalothrin". Their conclusion is based on the following: 1) gamma-cyhalothrin is the isolated active of lambda-cyhalothrin, 2) the residue data from comparison studies showed that residues "from the gamma uses are, on average , no more than half of those of lambda-cyhalothrin" and 3) the toxicological endpoints selected for gamma-cyhalothrin are not less than half those selected for lambda-cyhalothrin.

i. *Food.* The lambda-cyhalothrin assessment in the Federal Register of August 15, 2007 (72 FRL-8143-1) includes Tier I worse-case assumptions of 100 PCT and tolerance level values for residues on pistachio and okra. Dietary exposure for the resolved isomer

gamma-cyhalothrin has already been implicitly assessed; there is no new data and the assessment need not be repeated.

ii. *Drinking water.* The lambda-cyhalothrin assessment in the Federal Register of August 15, 2007 (72 FRL-8143-1) includes a modeled estimate for acute water exposure of 5.35 ppb and a modeled estimate for chronic water exposure of 0.130 ppb. Exposure to the resolved isomer gamma-cyhalothrin has already been implicitly assessed; there is no new data and no new assessment is needed.

2. *Non-dietary exposure*. The newly proposed tolerances for gamma-cyhalothrin on pistachios and okra are dietary uses and there is no increase in the non-dietary exposure potential previously included in the recent exposure assessment Federal Register of August 15, 2007 (72 FRL-8143-1). The existing residential uses were assessed by the agency via a screening-level approach to address the risks associated with the use of the aerosol can product of lambda-cyhalothrin purchased by homeowners. This use is assumed to have the highest exposure potential of all the residential uses. No new assessment is needed for gamma-cyhalothrin.

D. Cumulative Effects

For the purpose of this request, it has been assumed that the cyhalothrins (i. e., cyhalothrin, gamma-cyhalothrin and lambda-cyhalothrin) do not have a common mechanism of toxicity with other substances.

E. Safety Determination In a recent exposure assessment Federal Register of August 15, 2007 (72 FRL-8143-1), the proposed uses of gamma-cyhalothrin on okra and pistachios was implicitly covered by the assessment for lambda-cyhalothrin, which already assumed 100 percent crop treated (PCT) for okra and pistachios. EPA concluded there is a reasonable certainly that no harm will result to the general population of infants and children for lambda-cyhalothrin. Because gamma-cyhalothrin is a resolved isomer of lambda-cyhalothrin, the risk has already been implicitly assessed and no new assessment is needed.

1. *U.S. population.* In a recent exposure assessment Federal Register of August 15, 2007 (72 FRL-8143-1), the agency determined the acute dietary exposure from food and water to lambda-cyhalothrin to occupy 46% of the aPAD and 17% of cPAD for the general US population. EPA concluded that food, water and residential exposures result in aggregate MOEs of 140 to 490. Because the MOEs are greater than 100, there were no concerns for aggregate exposure. There is no additional new exposure to be added to this model; gamma-cyhalothrin has already been implicitly assessed through the use of 100 PCT for lambda-cyhalothrin and no new assessment is needed.

2. *Infants and children*. Per Federal Register of August 15, 2007 (72 FRL-8143-1), EPA has reviewed a DNT for lambda-cyhalothrin (MRID 46449102); while the study has been deemed technically unacceptable, the EPA is not requiring a repeat of the study. Instead a 10X factor has been applied to the NOAEL of 4 mg/kg bw/day to arrive at a 0.4

mg/kg bw/day. This value is similar to the acute and chronic NOAELs. EPA concluded that use of the NOAELs from the dog study is protective of infants and children and the FQPA SF=1.

In the exposure assessment of Federal Register of August 15, 2007 (72 FRL-8143-1), the agency determined the acute dietary exposure from food and water to lambda-cyhalothrin to occupy 61% of the aPAD for all infants as the most highly exposed populations subgroup. The chronic assessment for children indicated that children (1-2 years old) were the most highly exposed subpopulation with potential exposure at 50% of cPAD. Because the projected exposures are less than 100% of the PAD, there is a reasonable certainty of no harm.

F. International Tolerances

A review of national websites and the Homologa MRL database reveals that for nuts and fruiting vegetables there are no MRLs outside the US which have been specifically established for gamma cyhalothrin. MRLS are fairly harmonized for the related isomers of lambda-cyhalothrin per the table below. In addition, there are Codex maximum residue levels pending for residues of cyhalothrin, as the sum of all isomers, in or tree nuts (shelled and unshelled) at 0.05 ppm. For Canada, treenuts including pistachios are covered based on the "negligible" residue clause of Canadian Food and Drug Act Regulations (B.15.002(1).

Active	Country	Commodity	Value	Unit
Lambda-cyhalothrin	US, Canada, EU, Mexico	Tomatoes	0.1	ppm
Gamma-cyhalothrin	US	Tomato	0.1	ppm
Lambda-cyhalothrin	Mexico	Peppers	0.2	ppm
Lambda-cyhalothrin	EU	Peppers	0.1	ppm
Lambda-cyhalothrin and Gamma-cyhalothrin	US	Peppers	0.2	ppm
Gamma-cyhalothrin	US	Treenuts	0.05	ppm
Lambda-cyhalothrin	EU, US	Treenuts and Pistachio	0.05	ppm

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