

Dated: July 3, 2003.

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Pesticide Programs.

### Summary of Petition

The petitioner's summary of the pesticide petition is printed below as required by FFDCA section 408(d)(3). The summary of the petition was prepared by the petitioner and represents the view of the petitioner. The petition summary announces the availability of a description of the analytical methods available to EPA for the detection and measurement of the pesticide chemical residues or an explanation of why no such method is needed.

### FMC Corporation

PP 3F6577

EPA has received pesticide petition (3F6577) from FMC Corporation, 1735 Market Street, Philadelphia, PA 19103, proposing pursuant to section 408(d) of the FFDCA, 21 U.S.C. 346a(d), to amend 40 CFR 180.418 by establishing a tolerance for residues of the insecticide zeta-cypermethrin ( $\pm$ - $\alpha$ -cyano(3-phenoxyphenyl)methyl ( $\pm$ ) *cis*, *trans* 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate) and its inactive isomers in or on the raw agricultural commodity fruit, pome, group 11, at 0.6 ppm and fruit, stone, group 12, at 0.9 ppm. EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data support granting of the petition. Additional data may be needed before EPA rules on the petition.

### A. Residue Chemistry

1. *Plant metabolism.* The metabolism of cypermethrin in plants is adequately understood. Studies have been conducted to delineate the metabolism of radiolabeled cypermethrin in various crops all showing similar results. The residue of concern is the parent compound only.

2. *Analytical method.* There is a practical analytical method for detecting and measuring levels of cypermethrin in or on food with a limit of detection (LOD) that allows monitoring of food with residues at or above the levels set in these tolerances (gas chromatography with electron capture detection (GC/ECD)).

3. *Magnitude of residues.* Crop field trial residue data from studies conducted at the maximum label rates

for representative commodities for pome fruit and stone fruit crop groups root, show that the proposed zeta-cypermethrin tolerances on fruit, pome, group 11, at 0.6 ppm and fruit, stone, group 12, at 0.9 ppm; will not be exceeded when the zeta-cypermethrin products labeled for these uses are used as directed.

### B. Toxicological Profile

1. *Acute toxicity.* For the purposes of assessing acute dietary risk, FMC Corporation has used the no observed adverse effect level (NOAEL) of 10.0 milligrams/kilogram/day (mg/kg/day) from the zeta-cypermethrin acute neurotoxicity study in rats. The lowest observed adverse effect level (LOAEL) of 50.0 mg/kg/day was based on clinical signs. This acute dietary endpoint is used to determine acute dietary risks to all population subgroups.

2. *Genotoxicity.* The following genotoxicity tests were all negative: *In vivo* chromosomal aberration in rat bone marrow cells; *in vitro* cytogenic chromosome aberration; unscheduled DNA synthesis (UDS); Chinese Hamster Ovary/Hypoxanthine Guanine Phosphoribosyl Transferase (CHO/HGPRT) mutagen assay; weakly mutagenic; gene mutation (Ames).

3. *Reproductive and developmental toxicity.* No evidence of additional sensitivity to young rats was observed following prenatal or postnatal exposure to zeta-cypermethrin.

i. A 2-generation reproductive toxicity study with zeta-cypermethrin in rats demonstrated a NOAEL of 7.0 mg/kg/day and a LOAEL of 27.0 mg/kg/day for parental/systemic toxicity based on body weight, organ weight, and clinical signs. There were no adverse effects in reproductive performance. The NOAEL for reproductive toxicity was considered to be >45.0 mg/kg/day (the highest dose tested (HDT)).

ii. A developmental study with zeta-cypermethrin in rats demonstrated a maternal NOAEL of 12.5 mg/kg/day and a LOAEL of 25 mg/kg/day based on decreased maternal body weight gain, food consumption, and clinical signs. There were no signs of developmental toxicity at 35.0 mg/kg/day, the HDT level.

iii. A developmental study with cypermethrin in rabbits demonstrated a maternal NOAEL of 100 mg/kg/day and a LOAEL of 450 mg/kg/day based on decreased body weight gain. There were no signs of developmental toxicity at 700 mg/kg/day, the HDT level.

4. *Subchronic toxicity.* Short-term and intermediate-term toxicity (incidental oral exposure). The NOAEL of 10.0 mg/kg/day based on clinical signs at the

lowest effect level (LEL) of 50.0 mg/kg/day in the zeta-cypermethrin acute neurotoxicity study in rats would also be used for short-term percent acute population adjusted dose (PAD) and margin of exposure (MOE) calculations (as well as acute, discussed in (1) above), and the NOAEL of 5.0 mg/kg/day based on decreased motor activity in the zeta-cypermethrin subchronic neurotoxicity study in rats, would be used for intermediate-term MOE calculations.

5. *Chronic toxicity*—i. The chronic reference dose (RfD) of 0.06 mg/kg/day for zeta-cypermethrin is based on a NOAEL of 6.0 mg/kg/day from a cypermethrin chronic feeding study in dogs and an uncertainty factor (UF) of 100. The endpoint effect of concern was based on clinical signs.

ii. Cypermethrin is classified as a Group C chemical (possible human carcinogen with limited evidence of carcinogenicity in animals) based upon limited evidence for carcinogenicity in female mice; assignment of a Q\* has not been recommended.

6. *Animal metabolism.* The metabolism of cypermethrin in animals is adequately understood. Cypermethrin has been shown to be rapidly absorbed, distributed, and excreted in rats when administered orally. Cypermethrin is metabolized by hydrolysis and oxidation.

7. *Metabolite toxicology.* The Agency has previously determined that the metabolites of cypermethrin are not of toxicological concern and need not be included in the tolerance expression nor in the risk exposure assessments.

8. *Endocrine disruption.* No special studies investigating potential estrogenic or other endocrine effects of cypermethrin have been conducted. However, no evidence of such effects were reported in the standard battery of required toxicology studies which have been completed and found acceptable. Based on these studies, there is no evidence to suggest that cypermethrin has an adverse effect on the endocrine system.

### C. Aggregate Exposure

1. *Dietary exposure*—i. *Food.* Permanent tolerances, in support of registrations, currently exist for residues of zeta-cypermethrin on: Alfalfa hay, alfalfa forage, alfalfa seed, aspirated grain fractions, sugar beets (roots and tops), head, stem and leafy brassica vegetables, cabbage, field corn grain, pop corn grain, field corn forage, field corn stover, pop corn stover, sweet corn (K+CWHR), sweet corn forage, sweet corn stover, cottonseed, dried shelled peas and beans, edible podded legume