

## List of Subjects

Environmental protection, Agricultural commodities, Feed additives, Food additives, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: May 13, 2003.

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## 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 ISK Bioscience Corporation, 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.

## ISK Biosciences Corporation

PP 3F6552

EPA has received a pesticide petition [3F6552] from ISK Biosciences Corporation, 7470 Auburn Road, Suite A, Concord, Ohio, 44077, 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 tolerances for the combined residues of the insecticide flonicamid, (N-cyanomethyl-4-trifluoromethylnicotinamide) and its metabolites, TFNA, (4-trifluoromethylnicotinic acid), TFNA-AM, (4-trifluoromethylnicotinamide) and TFNG, (N-(4-trifluoromethylnicotinoyl)-glycine) in or on the raw agricultural commodities: Celery, at 1.2 parts per million (ppm); cotton, at 0.5 ppm; cotton, gin trash, at 6.0 ppm; cotton, hulls, at 1.0 ppm; cotton, meal, at 1.0 ppm; fruit, pome, group 11, at 0.2 ppm; fruit, stone, group 12, except plum and fresh prune plum, at 0.7 ppm; lettuce, head, at 1.0 ppm; lettuce, leaf, at 4.0 ppm; plum, at 0.1 ppm; potato, at 0.2 ppm; potato, flakes, at 0.4 ppm; prune, fresh, at 0.1; spinach, at 9.0 ppm; tomato, paste, at 2.0 ppm; tomato, puree, at 0.5 ppm; vegetable, cucurbit, group 9, at 0.4 ppm; vegetable, fruiting, group 8, at 0.4 ppm; by establishing tolerances for the combined residues of the insecticide flonicamid, (N-cyanomethyl-4-trifluoromethylnicotinamide) and its metabolite TFNA-AM, (4-trifluoromethylnicotinamide) in animal tissues and poultry meat byproducts: Cattle, fat, at 0.01 ppm; cattle, meat, at 0.04 ppm; eggs, at 0.02 ppm; goat, fat,

at 0.01 ppm; goat, meat, at 0.04 ppm; hog, fat, at 0.01; hog, meat, at 0.01 ppm; horse, fat, at 0.01 ppm; horse, meat, at 0.04 ppm; milk, at 0.02 ppm; poultry, fat, at 0.01 ppm; poultry, meat, at 0.01 ppm; poultry, meat byproducts, at 0.01 ppm; sheep, fat, at 0.01 ppm; sheep, meat, at 0.04 ppm; by establishing tolerances for the combined residues of the insecticide flonicamid, (N-cyanomethyl-4-trifluoromethylnicotinamide) and its metabolites TFNA, (4-trifluoromethylnicotinic acid) and TFNA-AM, (4-trifluoromethylnicotinamide) in the animal meat byproducts: cattle, meat byproducts, at 0.06 ppm; goat, meat byproducts, at 0.06 ppm; hog, meat byproducts, at 0.01 ppm; horse, meat byproducts, at 0.06 ppm; and sheep, meat byproducts, at 0.06 ppm.

## A. Residue Chemistry

1. *Plant metabolism.* Wheat, potato and peach metabolism studies were conducted using [14C]-pyridyl-flonicamid. The metabolic profile was similar for all three matrices. The major metabolites for the various crops were: TFNA in peach, TFNA and TFNG in potato, and TFNG in wheat. The metabolism of flonicamid in plants shows, the main pathway of metabolism involves hydrolysis of -CN and CONH<sub>2</sub> functional groups in the molecule. The metabolism of flonicamid in plants is well understood.

2. *Analytical method.* Analytical methodology has been developed to determine the residues of flonicamid and its three major plant metabolites, TFNA, TFNG, and TFNA-AM in various crops. The residue analytical method for the majority of crops includes an initial extraction with acetonitrile (ACN)/deionized (DI) water, followed by a liquid-liquid partition with ethyl acetate. The residue method for wheat straw is similar, except that a C<sub>18</sub> solid phase extraction (SPE) is added prior to the liquid-liquid partition. The final sample solution is quantitated using a liquid chromatograph (LC) equipped with a reverse phase column and a triple quadrupole mass spectrometer (MS/MS).

3. *Magnitude of residues.* Residue data were collected on various crops and crop groups during field trials. Maximum total residues for cucurbits (total of 17 field trials) ranged from 0.164 (summer squash) to 0.333 ppm (cucumber). Maximum total residues for stone fruits (total of 21 field trials) ranged from 0.092 (plum) to 0.520 ppm (cherry). Maximum total residues for pome fruits (total of 18 field trials) ranged from 0.054 (pears) to 0.169 ppm

(apples). Maximum total residues for fruiting vegetables (total of 21 field trials) ranged from 0.195 (bell pepper) to 0.290 ppm (non-bell pepper). Maximum total residues for leafy vegetables (total of 24 field trials) ranged from 0.049 (head lettuce without wrappers) to 7.978 ppm (spinach). Maximum total residues for cottonseed with linters (12 field trials) were 0.343 and for gin trash were 5.001 ppm. Maximum total residues for potatoes (total of 17 field trials) were 0.119 ppm.

## B. Toxicological Profile

1. *Acute toxicity.* A battery of acute toxicity studies was conducted which placed flonicamid technical in Toxicity Category III for oral lethal dose (LD)<sub>50</sub>, Category IV for dermal LD<sub>50</sub>, inhalation LC<sub>50</sub>, dermal irritation, and eye irritation. Flonicamid technical is not a dermal sensitizer. In an acute neurotoxicity study, the no observed adverse effect levels (NOAELs) for neurotoxicity were 600 milligrams/kilogram (mg/kg) in males and 1,000 mg/kg in female (highest doses tested). The systemic NOAELs were 600 mg/kg in males and 300 mg/kg in females.

2. *Genotoxicity.* Flonicamid technical did not cause mutations in the bacterial reverse mutation or mouse lymphoma tests with or without metabolic activation, chromosome damage in the mouse micronucleus or cytogenetics tests with and without metabolic activation, an increase in DNA damage in the comet assay or in an *in vivo* rat unscheduled DNA synthesis (UDS) study. Based on the weight of evidence, it is concluded that, flonicamid technical is not genotoxic.

3. *Reproductive and developmental toxicity.* A developmental toxicity study in rats resulted in the maternal and developmental no observed adverse effect levels (NOAELs) of 100 mg/kg/day. The maternal lowest observed adverse effect level (LOAEL) was 500 mg/kg/day based on the treatment-related effects observed on the liver and kidney of the dams in the highest dose group. The developmental LOAEL was 500 mg/kg/day based on the increases in placental weights and incidences of fetal skeletal variations seen only at maternally toxic doses of 500 mg/kg/day.

In the rabbit developmental toxicity study, the maternal and developmental NOAELs were 7.5 mg/kg/day and 25 mg/kg/day highest dose tested (HDT), respectively. The maternal LOAEL was 25 mg/kg/day based on decreased body weights and food consumption. No adverse effects on the fetuses were observed at the highest dose.