

ISK Biosciences Corporation

PP 1F6305

EPA has received a pesticide petition [1F6305] from ISK Biosciences Corporation, 7470 Auburn Road, Suite A, Concord OH 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 a tolerance for residues of the fungicide cyazofamid, 4-chloro-2-cyano-N, N-dimethyl-5-(4-methylphenyl)-1H-imidazole-1-sulfonamide (CA), in or on the raw agricultural commodity (RAC) potatoes at 0.01 parts per million (ppm) and cucurbits at 0.1 ppm and the fungicide cyazofamid and the metabolite CCIM, 4-chloro-5-(4-methylphenyl)-1H-imidazole-2-carbonitrile (CA) in or on the RAC tomatoes at 0.2 ppm and wine grapes at 1.0 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 plant metabolism studies in potatoes and tomatoes, together with the magnitude of the residue studies in potatoes, tomatoes and cucurbits, suggest that the tolerance for potatoes, tomatoes, and cucurbits should be based only on parent cyazofamid. However, magnitude of the residue studies on processed tomatoes indicate that both cyazofamid and CCIM are identifiable residues in tomato puree and paste. The nature and magnitude of the residue studies for potatoes showed that there were no detectable residues of cyazofamid or any of its metabolites in the RACs or processed commodities. Similar studies on fresh tomatoes indicated that the major identifiable and quantifiable residue is cyazofamid. Magnitude of the residue studies conducted on cucurbits (cucumber, summer squash and melon) also confirmed that the major residue is cyazofamid. Nature of the residue studies showed that no single identifiable residue represents more than about 7% of the total radioactive residue. The nature and magnitude of the residue studies on grapes showed that cyazofamid was the major identifiable residue with low levels of CCIM. The residue in wine made from cyazofamid treated grapes is CCIM. The tolerance expression for potatoes and cucurbits will include parent

cyazofamid only. The tolerance expression for wine grapes and tomatoes will include parent, cyazofamid, and the metabolite CCIM.

2. *Analytical method.* An analytical enforcement method is available for determining cyazofamid plant residues in or on potatoes, cucurbits, tomatoes and wine grapes. Samples are chopped in a food chopper and a 20-g sub-sample is removed for extraction with 100 milliliter (mL) of acetonitrile (twice). The combined extracts are partitioned with hexane and then are reduced to 10 mL with a rotary evaporator. The sample is then partitioned between 100 mL of 2% aqueous sodium sulfate solution and 50 mL of methylene chloride (twice). The residue is dissolved and passed through a 2 gram (g) Florisil column followed by quantification by ultraviolet-high performance liquid chromatography (UV-HPLC).

3. *Magnitude of residues.* Residue data from 31 field trials (0- and 7-day pre-harvest intervals (PHIs)) on cucurbits [11 sites for cucumbers, 11 sites for muskmelons and 9 sites for summer squash] conducted from 1999-2001 showed that mean cyazofamid residues were 0.02 ppm for 0-day PHI and <0.01 ppm for 7-day PHI on the RAC commodities. The highest mean cyazofamid residue was 0.07 ppm at 0-day PHI on muskmelon. The highest 7-day PHI cyazofamid residue was 0.04 ppm on cucumbers. At both PHI's CCIM residues were <0.01 ppm except for 3 samples (2 sites, both 0-day PHI) which were at the 0.01 ppm LOQ. The sample with the highest total residue had 0.08 ppm (0.07 ppm cyazofamid + 0.01 ppm CCIM). The studies had a target of 6 applications of 0.071 lb. of active ingredient per acre (0.42 lb acre (a.i./acre) total) of the Cyazofamid 400SC formulation each at 7-day intervals.

Data from 18 field trials in potatoes conducted in 1999-2000 showed that no residues of cyazofamid or CCIM were observed in any of the RAC commodity at any location (7-day PHI). There were up to 10 applications of 0.071 lb. of active ingredient per acre (0.70 lb a.i./acre total) of the Cyazofamid 400SC formulation at 7-day intervals. The PHI for most trials was 7-days; however, residue dissipation studies with PHIs of 0-, 1-, 3- and 7-days were run at 2 locations. Maximum residues of 0.01 ppm of cyazofamid were seen at 0- and 1-day PHIs at one location and no residues were found at the other location. The results of a processing study in which the final application was at a 3X application rate showed that for samples taken with a 3-day PHI no detectable residues of cyazofamid or

CCIM were found in potato flakes, chips or wet peels. Therefore, no concentration of residues occurred during processing.

For tomatoes, residues of cyazofamid were determined in the treated samples from 35 RAC trials (0- and 7-day PHI) conducted from 1999-2001. The mean per site residues ranged from non-detected (<0.01 ppm) to 0.15 ppm cyazofamid. CCIM residues of 0.01-0.02 ppm were found in samples from four of the sites. The sample with the maximum residue had 0.16 ppm cyazofamid and no detectable CCIM. The studies had a target of six applications of 0.071 lb of active ingredient per acre (0.42 lb a.i./acre total) of the Cyazofamid 400SC formulation each at 7-day intervals.

The results of a tomato processing study in which the final application was at a 3X application rate showed that for samples taken with a 3-day PHI, cyazofamid was <0.01 ppm in both tomato paste and puree. Tomato paste had 0.02 ppm CCIM and tomato puree had 0.01 ppm CCIM. Therefore, there is no concentration of residues during tomato processing.

Data from 15 field trials in grapes conducted from 1999-2001 in the United States, Argentina, Mexico and Europe showed that mean cyazofamid residues ranged from <0.01 to 0.34 ppm and mean CCIM residues ranged from <0.01 to 0.02 ppm in the RAC commodity (21-day PHI) following eight applications of 0.081 to 0.089 lb. of active ingredient per acre (0.65 to 0.71 lb a.i./acre total) of the Cyazofamid 25SC formulation each at 10- to 16-day intervals.

Grapes from six of the sites were processed into must and wine. Most samples had cyazofamid residues ranging from 0.01 to 0.09 ppm. The CCIM residues in must ranged from <0.01 to 0.01 ppm. Cyazofamid residues in wine were all <0.01 ppm. CCIM residues in wine ranged from <0.01 ppm to 0.02 ppm.

B. Toxicological Profile

1. *Acute toxicity.* Results from a battery of acute toxicity studies place technical cyazofamid in Toxicity Category IV for oral LD₅₀, inhalation LC₅₀ and dermal and eye irritation, and Category III for dermal LD₅₀. Technical cyazofamid is not a dermal sensitizer. In an acute neurotoxicity study, no treatment related effects were observed at any dose. The no observed effect level (NOEL) was 2,000 milligrams/kilogram (mg/kg) bodyweight (bwt).

2. *Genotoxicity.* A battery of five tests has been conducted to assess the genotoxic potential of technical