UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Date: 11/19/07

Subject: Fluopicolide. PP#5F7016. Petition for Establishment of Tolerances for Use on Tuberous and Corm Vegetables, Leafy Vegetables (except *Brassica*), Fruiting Vegetables, Cucurbit Vegetables, and Grapes and for Indirect or Inadvertent Residues on the Rotational Crop Wheat. Summary of Analytical Chemistry and Residue Data.

DP Numbers:	326080, 327026, 339155	Decision Number:	362973
PC Code:	027412	MRID Nos.:	46708418, 46708514, 46708515, 46708516, 46708517, 46708518, 46708519, 46708520, 46708521, 46708522, 46708523, 46708524, 46708525, 46708526, 46708527, 46708528, 46708529, 46708530, 46708531, 46708532, 46708533, 46708534, 46708535, 46708536, 46708537, 46708538, 46708539, 46708540, 46708541, 46708542, 46708543, 46708544, 46708545, 46708546, 46708547, 47073701
40 CFR 180.	627		
Chemical Class:	Benzamide/Pyridine Fungicide		

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Registration Action Branch 3/Health Effects Division (7509P)

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This document was originally prepared under contract by Dynamac Corporation (2275 Research Blvd, Suite 300; Rockville, MD 20850; submitted 3/9/2007). The document has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

Executive Summary

Valent U.S.A. Corporation has submitted a petition, PP#5F7016, proposing the establishment of tolerances for residues of the fungicide fluopicolide [2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]benzamide] in/on the following raw agricultural commodities (RACs):

Commodity	ppm
Tuberous and corm vegetables subgroup 1C	0.02
Vegetable, leafy, except *Brassica*, group 4	20
Vegetable, fruiting, group 8	0.8
Vegetable, cucurbit, group 9	0.4
Grape	2
Raisins	6
Wheat forage	0.2
Wheat grain	0.02
Wheat hay	0.5
Wheat straw	0.5

HED notes that the petitioner actually proposed separate tolerances for the individual crops in the tuberous and corm vegetable, leafy vegetable, fruiting vegetable, and cucurbit vegetable crop groups (see Table 9 for a full list of proposed crops).

HED also notes that some crops in Crop Group 1C (bitter and sweet cassava, dasheen, tanier, and true yam) are also in Group 2: Leaves of Root and Tuber Vegetables (Human Food or Animal Feed) Group in 40 CFR §180.41; however, tolerances are not needed for the leaves of these crops since the leaves of these crops are not significant food/feed items based on Agency guidelines (OPPTS 860.1000, Table 1; and Table 1 Feedstuffs, October 2006).

The petitioner is not proposing use of fluopicolide on wheat as a primary crop; the proposed tolerances are for indirect or inadvertent residues in rotational wheat commodities.

In conjunction with this petition, Valent U.S.A. has submitted a FIFRA Section 3 request to register two end-use products, V-10161 4 SC, a 4 lb ai/gal flowable concentrate (FlC) formulation with EPA File Symbol No. 59639-RUN; and V-10162 Premix, a FlC formulation containing 0.52 lb/gal of fluopicolide and 5.2 lb/gal of propamocarb hydrochloride, with EPA File Symbol No. 59639-RUE. The products are proposed for use on grapes, potatoes, sweet potatoes, the cucurbit vegetable crop group, the fruiting vegetable crop group, and the leafy vegetable (except *Brassica*) crop group, as multiple foliar applications at up to 0.125 lb ai/A/application with a maximum seasonal rate of 0.375 lb ai/A. The petitioner has proposed preharvest intervals (PHIs) of 2 days for cucurbit vegetables, fruiting vegetables, and leafy vegetables, 7 days for potato and sweet potato, and 21 days for grape, and minimum retreatment intervals (RTIs) of 7 days for fruiting vegetables, 10 days for cucurbit vegetables, leafy vegetables, potato, and sweet potato, and 12 days for grape. The 4 lb/gal FlC formulation (V-10161 4 SC) may be applied in a tank mix with fungicides that are registered for the same use.

Tolerances have been established (40 CFR §180.627) for residues of fluopicolide, 2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl] benzamide, on *grape* at 2.0 ppm and *grape, raisin* at 6.0 ppm for use on imported crops (see PP#5E6903; DP Number 321209, 1/23/2007, A.

Acierto). No livestock tolerances have been established. There are currently no registered uses of fluopicolide in the U.S. No Codex, Canadian, or Mexican Maximum Residue Limits (MRLs) or tolerances have been established for fluopicolide.

HED notes that one of the proposed products, V-10162 Premix (EPA File Symbol No. 59639-RUE), is a multiple active ingredient (MAI) FlC formulation containing propamocarb hydrochloride. The proposed uses of propamocarb hydrochloride on cucurbit vegetables, fruiting vegetables, head and leaf lettuce, and potato are not evaluated in this document. Tolerances do exist for residues of propamocarb hydrochloride on cucurbit vegetables, fruiting vegetables, head and leaf lettuce, and potato [40 CFR §180.499(a)]. The adequacy of the proposed use directions for propamocarb hydrochloride and the availability of adequate supporting residue data will be addressed in a separate review for propamocarb hydrochloride.

The qualitative nature of the residues in primary plants is adequately understood for the purposes of this petition based on acceptable grape, lettuce, and potato metabolism studies. HED has determined that the tolerance expression for all primary crops is fluopicolide *per se* as an indicator of combined residues of fluopicolide and its metabolite, 2,6-dichlorobenzamide (BAM). For risk assessment purposes, the residue of concern for the tuberous and corm vegetables includes the parent compound, fluopicolide, and its metabolites, 3-chloro-5-trifluoromethylpyridine-2-carboxylic acid (PCA) and BAM. For all other primary crops, the residue of concern for risk assessment purposes includes the parent compound and the metabolite, BAM.

The metabolism of fluopicolide in rotational crops has been adequately delineated for the purpose of this petition. HED has concluded that the tolerance expression for inadvertent residues of fluopicolide in rotational crops should be expressed as fluopicolide *per* se as an indicator of combined residues of parent and its metabolite, BAM. For risk assessment purposes, the residue of concern in grain for human food includes the parent compound, fluopicolide and its metabolites BAM, PCA and 3-methylsulfinyl-5-trifluoromethylpyridine-2-carboxylic acid (P1X). The residue of concern in forage/hay/straw and grain for livestock feed is parent compound and the metabolite, BAM. The residue of concern for risk assessment purposes for all other rotational crops includes fluopicolide (parent) and its metabolite, BAM.

There are livestock feed items associated with the requested new uses of fluopicolide. Additional information is needed to support the submitted fluopicolide ruminant and poultry metabolism studies. In ruminants, the studies indicate that a large portion of the dosed radioactivity (75-84%) was excreted. Fluopicolide was the major residue identified in milk (29% TRR) and fat (64-76%); it was found at low levels in muscle, liver, and kidney (<3% TRR). Fluopicolide appears to be metabolized in ruminants via hydroxylation of the chlorophenyl ring in two positions to form AE 0712556 and AE C643890; these metabolites were found in liver and kidney at <7% TRR each. Each of these metabolites is then conjugated with sulfate or glucuronic acid, or hydroxylated in a second position and then conjugated with sulfate or glucuronic acid. Finite residues of fluopicolide are not expected in ruminant commodities. A small amount of BAM was found in milk (4% TRR), and no PCA was found in any cattle matrix. In poultry, based on the study conducted with fluopicolide radiolabeled in the phenyl ring, a large portion of the dosed radioactivity was excreted (up to 95%). Fluopicolide was identified at low levels in egg white, egg yolk, and fat (≤11% TRR); it was not identified in liver or skin. The major metabolite identified in egg white and fat was Metabolite 1, a methyl

sulfone metabolite of fluopicolide, at 51% TRR in egg white and 38% TRR in fat. The major residue identified in liver was BAM, at 37% TRR; this metabolite was not found in any other matrix. Finite residues of fluopicolide are not expected to occur in livestock commodities. Pending submission of the required additional data, HED has tentatively determined that the tolerance expression for livestock commodities should include residues of the metabolite BAM only. For risk assessment purposes, the residue of concern for risk assessment purposes is fluopicolide and its metabolite, BAM.

Acceptable data collection methods were used in the storage stability, field trial, processing, and field rotational crop studies associated with this petition. The LC/MS/MS Method, RM-43C-1, which determines residues of fluopicolide *per se* in plant commodities has been validated and is adequate for enforcement purposes.

An adequate data collection method, LC/MS/MS Method 303-02, which determines residues of fluopicolide and BAM, was submitted for cattle commodities. HED has determined that tolerances are not required for poultry and swine; however, tolerances are required for ruminant commodities. Method 303-02 has been reviewed and is not acceptable as an enforcement method. A confirmatory procedure is required for the LC/MS/MS Method 303-02 to be considered an adequate enforcement method for ruminant commodities.

Multiresidue methods testing data have been submitted. These data indicate that the multiresidue methods are not appropriate for determining residues of fluopicolide.

Adequate feeding study data for parent fluopicolide have been submitted. However, since measurable residues of the fluopicolid metabolite, BAM are likely in cattle feed items, a ruminant feeding study conducted with BAM must be submitted or referenced and tolerances for ruminant commodities, at the limit of quantitation of the method, must be proposed. Tolerances for ruminant commodities were not proposed in the registrant's submission.

No poultry feeding study is required for fluopicolide based on the poultry metabolism studies and the calculated dietary burden. HED has calculated a dietary burden to poultry based on BAM residues in feedstuff items. Given the very low dietary burden, a poultry feeding study with BAM is not required at this time. No tolerances are required for poultry commodities.

Adequate field trial data for tuberous and corm vegetables, leafy vegetables (except *Brassica*), fruiting vegetables, cucurbit vegetables, and grapes are available, pending submission of additional storage stability data/information for leafy vegetables and wheat. An adequate number of geographically representative field trials were conducted at 1x the proposed maximum seasonal rate for each crop. The available field trial data indicate that the proposed tolerances for tuberous and corm vegetables and grapes are adequate, but that increased tolerances are needed for the leafy vegetable, fruiting vegetable crop group 8, and cucurbit vegetables crop group 9, at 25 ppm, 1.6 ppm, and 0.50 ppm, respectively.

Adequate processing data for grapes, potatoes, tomatoes, and rotated wheat are available pending submission of additional storage stability data/information on wheat. The available processing data indicate that residues of fluopicolide are not likely to concentrate in grape juice, potato chips and flakes, or wheat flour. Residues of fluopicolide were found to concentrate in raisins, processed potato waste (wet peels), tomato paste and puree, and wheat milled byproducts (bran,

germ, middlings, and shorts). The processing data indicate that the proposed tolerance of 6 ppm for raisins is appropriate. In addition, a tolerance for processed potato waste must be proposed at 0.05 ppm, and tolerances for wheat milled byproducts and aspirated grain fractions (AGF) must be proposed at 0.07 ppm. Since residues concentrate in wheat milled byproducts, residue data and a tolerance are required for aspirated grain fractions. HED recommends setting the AGF tolerance at 0.07 ppm based on the wheat processing data and requiring confirmatory residue data on AGF. Separate tolerances for tomato processed commodities are not needed, as residues in these commodities are not expected to exceed the recommended tolerance of 1.6 ppm for the fruiting vegetable group.

Pending submission of storage stability data/information, adequate field rotational crop data have been submitted to support the proposed 30-day plantback interval (PBI) for wheat. The data indicate that rotational crop tolerances are needed for wheat forage, hay, grain, and straw. The petitioner has proposed a PBI of one year for all crops other than cucurbit vegetables, fruiting vegetables, grapes, leafy vegetables, tuber vegetables, and wheat. Because the confined rotational crop data indicated the potential for quantifiable residues of fluopicolide in/on rotated crops at a one-year PBI, additional field rotational crop data must be submitted. Until the data are submitted and livestock tolerances are established, rotation should be restricted only to crops listed on the label.

Regulatory Recommendations and Residue Chemistry Deficiencies

HED has examined the residue chemistry database for fluopicolide. Pending submission of a revised Section B and a revised Section F (see requirements under Direction for Use and Proposed Tolerances), there are no residue chemistry issues that would preclude granting a registration for the requested uses of fluopicolide excluding wheat and potato and establishment of tolerances for fluopicolide as stated below. The remaining deficiency regarding storage stability (see requirement under Storage Stability) must be resolved as a condition of registration.

Provided the forthcoming Human Health Risk Assessment does not identify any risks of concern, HED recommends establishment of tolerances as follows.

Tolerances to be established under 180. 627(a) General. (1)
Tolerances are established for residues of the fungicide fluopicolide [2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]benzamide] as an indicator of combined residues of fluopicolide and its metabolite, 2,6-dichlorobenzamide in/on the following raw agricultural commodities (RACs):

Grape …….	2.0 ppm
Grape, raisin ……...	6.0 ppm
Vegetable, cucurbit, group 9 ……...	0.50 ppm
Vegetable, fruiting, group 8 ……	1.6 ppm
Vegetable, leafy, except *Brassica*, group 4 ……	25 ppm
Vegetable, tuberous and corm, except potato, subgroup 1D …….	0.02 ppm

Note to RD: HED is recommending a revision of the tolerance expression for fluopicolide in/on RACs under (a) (1) to address issues of quantifiable residues 2,6-dichlorobenzamide (BAM) in/on RACs resulting from fluopicolide application.

DEFICIENCIES

860.1200 Directions for Use

- Sufficient rotational crop data is not available to support the proposed rotational crop restrictions. The Section B/label must be modified to state that rotation is limited only to those crops on the current label.

- A revised Section B/label must be submitted to delete the proposed use on potato.

860.1550 Proposed Tolerances

- The petitioner should submit a revised Section F which reflects the crop groups, tolerance levels and commodity definitions specified above and in Table 9 of this document.

860.1380 Storage Stability

- Additional storage stability data are needed for celery and spinach reflecting a storage interval of 38 months. One study should be conducted on any representative leafy vegetable.

At this time, HED is unable to recommend in favor of the establishment of tolerances on potato and wheat (inadvertent) due to the deficiencies listed below.

Deficiencies

860.1200 Directions for Use

- Until all field rotational crop data requirements have been satisfied, the proposed rotational crop restrictions must be modified to state that rotation is limited only to those crops on the current label: cucurbit vegetables, fruiting vegetables, grapes, leafy vegetables, tuberous and corm vegetables, and wheat. A 0-day PBI for cucurbit vegetables, fruiting vegetables, grapes, leafy vegetables, and tuberous and corm vegetables, and a 30-day PBI for wheat are supported by the available data.

860.1340 Residue Analytical Methods

- HED has determined that tolerances are required for ruminant commodities. Method 303-02 has been reviewed and is not acceptable as an enforcement method. A confirmatory procedure is required for the LC/MS/MS Method 303-02 to be considered an adequate enforcement method for ruminant commodities.

- An analytical reference standard for the metabolite 2,6-dichlorobenzamide (BAM) must be sent to USEPA, National Pesticide Standards Repository/Analytical Chemistry Branch/OPP, 710 Mapes Road, Fort George G. Meade, MD 20755-5350.

860.1550 Proposed Tolerances

- The petitioner should submit a revised Section F which reflects the crop groups, tolerance levels and commodity definitions specified in Table 10 of this document.

860.1300 Nature of the Residue - Livestock

- For the fluopicolide phenyl-^{14}C-labeled cow metabolism study (MRID 46708514), the petitioner should provide complete sample history information for samples from the study, including not only dates of collection, but also dates of storage, radioassay, extraction, and analysis. If sample analyses were not completed within 6 months of sample collection, the petitioner must provide data demonstrating that the metabolic profile was stable in the affected matrices during storage.

- For the fluopicolid pyridinyl-^{14}C-labeled cow metabolism study (MRID 46708518):
  - Storage stability data are required to support the study. If samples were stored for greater than 6 months, the petitioner should provide data showing stability of the metabolic profile of the affected matrices for the duration of the storage period and under the conditions that the samples were stored.
  - The petitioner must clarify the identification of two peaks in liver methanol/water extract (retention times of 43 and 47 minutes) to state whether the text on page 65 (which states that the metabolites are sulfate conjugates) or the results reported in Table 10 of MRID 46708518 (which indicate that one is a sulfate conjugate and one is a glucuronide conjugate) are correct, and to further explain how the retention times for these metabolites were correlated with the identified metabolites in urine and kidney.
  - The petitioner should correct the flowchart for omental fat (Figure 10) to include the correct TRR value for this matrix (0.039 ppm).
  - The petitioner should recalculate the radioactivity levels and/or clarify the results for the HPLC analysis of any extract in which the calculated LOQ was too high to allow meaningful interpretation of the chromatogram.

- For the hen metabolism study reported in MRID 46708515:
  - The petitioner should provide complete sample history information for samples from the study, including not only dates of collection but also dates of storage, radioassay, extraction, and analysis. If sample analyses were not completed within 6 months of sample collection, the petitioner should provide data demonstrating that the metabolic profile was stable in the affected matrices during the storage period and under the conditions that the samples were stored.
  - The petitioner should submit copies of the LC/MS chromatograms of metabolite AE C653711 (BAM) in liver as well as the corresponding chromatogram of the reference standard. These chromatograms were referenced in the submission (MRID 46708515, page 113) but were not included.

- The hen metabolism study conducted with [2,6-^{14}C-pyridinyl]fluopicolide (MRID 46708519) is incomplete but upgradeable. The samples from this study were not extracted until >6 months after sample collection. The petitioner should provide data showing stability of the metabolic profile for the duration of the storage period and under the conditions that the samples were stored.

860.1380 Storage Stability

- To support the wheat field rotational crop study, storage stability data are needed reflecting the stability of P1X in wheat grain for 21 months and of fluopicolide and BAM in wheat forage and straw for 24 months. The additional storage stability data for residues of P1X in wheat grain is also required to support the wheat processing study.

860.1480 Meat, Milk, Poultry and Eggs

- Since BAM may occur in livestock feed items and livestock (ruminant) commodities, a BAM ruminant feeding study must be submitted or referenced and livestock tolerances at the limit of quantitation of the method must be proposed.

860.1520 Processed Food & Feed

- No data have been submitted on aspirated grain fractions. Since data indicate that residues of fluopicolide concentrate in wheat milled byproducts, HED concludes that residue data and a tolerance for AGF is required. HED will base the tolerance for AGF on the available wheat process data, but requires confirmatory residue data on AGF as a condition of registration.

860.1900 Field Accumulation in Rotational Crops

- In the confined rotational crop study, residues of fluopicolide >0.01 ppm were observed in/on all rotational crop commodities at all PBIs, with the exception of wheat grain at the 133- and 365-day PBIs. Based on these results and the proposed rotational crop restrictions, limited field rotational crop studies should be conducted at 1, 4, and 12-month PBIs with any representative leafy vegetable, root vegetable, and cereal grain crops. Although the petitioner is proposing a 30-day PBI for wheat and has submitted supporting field rotational crop data, limited field rotational crop data for wheat as a representative cereal grain are also needed at 4- and 12-month PBIs. If the results of the limited field rotational crop study indicate the potential for quantifiable fluopicolide residues of concern in/on rotational crops at the desired PBI, then extensive field rotational crop studies will be required for all crops. Residues of parent, BAM, PCA and P1X should be determined in the field rotational crop studies.

If the deficiencies cited above are resolved in full, the available data support the following tolerances of fluopicolide:

Tolerances to be established under 180. 627(a) General. (1)
Tolerances for residues of the fungicide fluopicolide [2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]benzamide] as an indicator of combined residues of

fluopicolide and its metabolite, 2,6-dichlorobenzamide in/on the following raw agricultural commodities (RACs):

Potato, processed potato waste	……0.05 ppm
Vegetable, tuberous and corm, subgroup 1C	……0.02 ppm

Tolerances to be established under 180. 627(a) General. (2*)*
Tolerances for residues of 2,6-dichlorobenzamide in/on the following food commodities:

Cattle, fat…….	0.05 ppm
Cattle, meat……..	0.02 ppm
Cattle, meat byproducts……	0.05 ppm
Goat, fat……	0.05 ppm
Goat, meat…….	0.02 ppm
Goat, meat byproducts……..	0.05 ppm
Horse, fat……..	0.05 ppm
Horse, meat……..	0.02 ppm
Horse, meat byproducts……	0.05 ppm
Milk……..	0.01 ppm
Sheep, fat……..	0.05 ppm
Sheep, meat……..	0.02 ppm
Sheep, meat byproducts……	0.05 ppm

Tolerances to be established under 180.627 "(d) *Indirect or inadvertent residues*":
Tolerances for indirect or inadvertent residues of the fungicide fluopicolide [2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]benzamide] as an indicator of combined residues of fluopicolide and its metabolite, 2,6-dichlorobenzamide in/on the following raw agricultural commodities (RACs):

Wheat, forage…….	0.20 ppm
Wheat, grain……..	0.02 ppm
Wheat, hay……	0.50 ppm
Wheat, milled byproducts ……..	..0.07 ppm
Wheat, straw ……..	0.50 ppm
Wheat, aspirated grain fractions ……	0.07 ppm

Background

Fluopicolide is a benzamide/pyridine fungicide intended for the control of plant diseases caused by *Oomycetes*. Valent U.S.A. has applied for registration of fluopicolide in the U.S. for use on cucurbit vegetables, fruiting vegetables, grapes, leafy vegetables (except *Brassica*), potato, and sweet potato.

The nomenclature of fluopicolide is summarized in Table 1, and the physicochemical properties are summarized in Table 2. The chemical names and structures of fluopicolide and its transformation products are presented in Appendix 1.

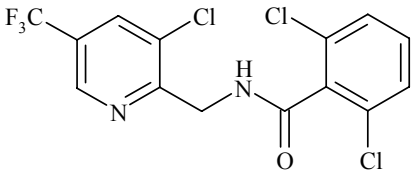
Table 1. Fluopicolide Nomenclature.	
Chemical structure	
Common name	Fluopicolide
Company experimental name	AE C638206
IUPAC name	2,6-dichloro-*N*-[3-chloro-5-(trifluoromethyl)-2-pyridylmethyl]benzamide
CAS name	2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]benzamide
CAS registry number	239110-15-7
End-use products (EPs)	V-10161 4SC Fungicide (39.5% fluopicolide; EPA File Symbol No. 59639-RUN) V-10161 Premix Fungicide (5.54% fluopicolide and 55.4% propamocarb; EPA File Symbol No. 59639–RUE)

Table 2. Physicochemical Properties of Fluopicolide.		
Parameter	Value	Reference
Melting point/range	149 °C	MRID 46474015[1]
pH	6.5 at 22.0 °C (1% suspension)	MRID 46474013[1]
Density	1.65 g/cm^3 (30 °C)	MRID 46474016[1]
Water solubility (20 °C)	2.86 mg/L at pH 4 2.80 mg/L at pH 7 2.80 mg/L at pH 9	MRID 46474021[1]
Solvent solubility (g/L at 20 °C)	n-Hexane: 0.20 Ethanol: 19.2 Toluene: 20.5 Ethyl acetate: 37.7 Acetone: 74.7 Dichloromethane: 126 Dimethyl sulfoxide: 183	MRID 46474022[1]
Vapor pressure at 25 °C	8.03 x 10^{-7} Pa	MRID 46474023[1]
Dissociation constant (pKa)	No evidence of ionization in the pH range of 1.9 to 9.8	MRID 46474017[1]
Octanol/water partition coefficient Log(K_{OW})	Log P_{OW} = 3.26 at pH 7.8 and 22 ± 1 °C	MRID 46474018[1]
	Log P_{OW} = 2.9 at pH 4.0, 7.3 and 9.1 and 40 °C	MRID 46474019[1]
UV/visible absorption spectrum	Absorption maxima wavelengths (nm): In methanol: 203 and 271 In methanol/HCl: 202 and 270 In methanol/NaOH: 219 and 271	MRID 46474014[1]

[1] DP Number 318332, 10/17/2006, S. Mathur.

HED notes that methods, field trial, storage stability and processing data on residues of 3-OH-BAM were provided as part of this submission. The HED RARC has determined that 3-OH-BAM should not be included in the tolerance expression or risk assessment due to aspects of its structure/nature (it's a phenol, as a result of ring hydroxylation) which increase its solubility, make it more readily conjugated and more readily excreted. References to 3-OH-BAM are included throughout this document for completeness of information only.

The proposed uses of propamocarb hydrochloride on cucurbit vegetables, fruiting vegetables, head and leaf lettuce, and potato are not evaluated in this document; the adequacy of the proposed use directions and the availability of adequate supporting residue data will be addressed in a separate review**.**

860.1200 Directions for Use

Valent submitted proposed labels for two products to be used on food/feed crops: V-10161 4 SC (suspendable concentrate), a 4 lb ai/gal FlC (an aqueous flowable concentrate) formulation with EPA File Symbol No. 59639-RUN; and V-10162 Premix, a FlC (an aqueous flowable concentrate) formulation containing 0.52 lb/gal of fluopicolide and 5.2 lb/gal of propamocarb hydrochloride, with EPA File Symbol No. 59639-RUE.

The proposed use directions for fluopicolide are presented in Table 3.

Table 3. Summary of Directions for Use of Fluopicolide.

Trade Name	Application Timing	Application Rate (lb ai/A)	Max. No. Applic. per Season	RTI[1] (days)	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and other Limitations
Cucurbit Vegetables [Acorn Squash; Balsam Apple; Balsam Pear; Bittermelon; Butternut Squash; Calabaza; Cantaloupe; Chayote, Fruit; Chinese Cucumber; Chinese Okra; Chinese Preserving Melon; Chinese Waxgourd; Citron Melon; Cucumber; Cucuzza; Gherkin; Gourd, Edible; Hechima; Hubbard Squash; Hyotan; *Momordica* spp; Muskmelon; Pumpkin; Spaghetti Squash; Summer Squash; Watermelon; Winter Squash]							
V-10161 4 SC	Postemergence	0.09-0.125	4	10	0.375	2	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.
V-10162 Premix	Postemergence	0.09-0.11	4	10	0.34	2	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.
Fruiting Vegetables [Bell Pepper; Chili Pepper; Cooking Pepper; Eggplant; Groundcherry (*Physalis* spp.); Pepino; Pimento, Sweet Pepper; Tomatillo; Tomato]							
V-10161 4 SC	Postemergence	0.09-0.125	4	7	0.375	2	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.
V-10162 Premix	Postemergence	0.09-0.11	4	7	0.34	2	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.
Grapes							
V-10161 4 SC	Postemergence	0.09-0.125	4	12	0.375	21	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.
Leafy Vegetables (except *Brassica* Vegetables) [Amaranth, Chinese Spinach; Arugula, Roquette; Cardoon; Celery; Celtuce; Chinese Celery; Chervil; Chrysanthemum, Edible-leaved; Chrysanthemum, Garland; Corn Salad; Cress, Garden; Cress, Upland; Dandelion; Dock, Sorrel; Endive, Escarole; Fennel; Florence; Lettuce, Head and Leaf; Orach; Parsley; Purslane, Garden; Purslane, Winter; Radicchio, Red Chicory; Rhubarb; Spinach; Spinach, New Zealand; Spinach, Vine; Swiss Chard]							
V-10161 4 SC	Postemergence	0.09-0.125	4	10	0.375	21	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.

Table 3. Summary of Directions for Use of Fluopicolide.							
Trade Name	Application Timing	Application Rate (lb ai/A)	Max. No. Applic. per Season	RTI[1] (days)	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and other Limitations
Lettuce, Head and Leaf							
V-10162 Premix	Postemergence	0.09-0.11	4	10	0.34	2	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.
Potato							
V-10161 4 SC	Postemergence	0.09-0.125	4	10	0.375	7	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.
V-10162 Premix	Postemergence	0.09-0.11	4	10	0.34	7	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.
Sweet Potato							
V-10161 4 SC	Postemergence	0.09-0.125	4	10	0.375	7	Application to be made in a minimum of 20 gal/A using ground equipment or 5 gal/A using aerial equipment.

[1] RTI = Retreatment interval

The proposed label for the 4 lb ai/gal FlC formulation (V-10161 4 SC) specifies that the product should always be applied in a tank mix with fungicides from different target site of action groups that are registered for the same use and that are effective against the pathogens of concern. The label specifies that the minimum labeled rate of each fungicide in the tank mix should be used. The label for the 0.52 lb/gal FlC formulation, which also contains propamocarb hydrochloride, states that the product may be used in tank mixtures with fungicides from different target site of action groups that are registered for the same use. The label specifies that the minimum labeled recommended rate of each fungicide in the tank mix should be used.

Applications are to begin when crop and/or environmental conditions favor disease development. A maximum of two sequential fluopicolide applications are to be made before alternating with an effective fungicide from a different resistance management group.

The following tank mixes are recommended on the label for the 4 lb ai/gal FlC formulation: mefenoxam or other labeled product with activity on downy mildew and *Phytophthora* for cucurbit and fruiting vegetables; Flint® (trifloxystrobin), Pristine® (pyraclostrobin and boscalid), or Procure® (triflumizole), or other labeled products with activity on downy mildew for grapes; strobilurin (Group 11 fungicides) or Aliette® (fosetyl-Al), or other products listed on the label with activity on downy mildew for leafy vegetables; and mefenoxam or other products listed on the label with activity on *Phytophthora* for potato and sweet potato. The label specifies that all use directions specified on each label should be followed for any product to be tank mixed with V-10161 4 SC.

The 0.52 lb/gal FlC formulation allows tank-mixing with other labeled pesticides although no specific tank mixes were recommended.

A restricted entry interval of 12 hours has been proposed. The following rotational crop restrictions are proposed for the 4 lb/gal FlC formulation: a 0-day PBI for cucurbit vegetables, fruiting vegetables, grapes, leafy vegetables, and tuber vegetables; a 30-day PBI for wheat; and a 12-month PBI for all other crops. The 0.52 lb/gal FlC formulation specifies the same rotational crop restrictions except that a 120-day PBI is proposed for wheat.

***Conclusions*:** The submitted use directions are sufficient to allow evaluation of the available residue data relative to the proposed uses.

The available data, which reflect three foliar applications of a FlC (aqueous flowable concentrate) formulation at ~0.12 lb ai/A/application for a total of ~0.36 lb ai/A/season, will support the proposed four applications with a maximum of 0.34-0.37 lb ai/A/season to grapes, the tuberous and corm vegetable subgroup 1C, leafy vegetable (except *Brassica*) group 4, fruiting vegetable group 8, and cucurbit vegetable group 9. The data will also support: a minimum retreatment interval of 5 days for all crops on the label; a PHI of 2 days for the leafy vegetable (except *Brassica*) group 4, fruiting vegetable group 8, and cucurbit vegetable group 9; a PHI of 7 days for the tuberous and corm vegetable subgroup 1C; and a PHI of 21 days for grape. The proposed use directions for each crop are adequate.

Until all field rotational crop data requirements have been satisfied, the proposed rotational crop restrictions should be modified to state that rotation is permitted only to crops on the label. A 0-day PBI for cucurbit vegetables, fruiting vegetables, grapes, leafy vegetables, and tuberous and corm vegetables, and a 30-day PBI for wheat are supported by the available data.

Since data on potato satisfies the data requirements for all commodities in the tuberous and corm vegetable subgroup 1C, the petitioner may wish to modify the proposed Section B/label to expand uses on potato and sweet potato to include all members of the tuberous and corm crop subgroup.

860.1300 Nature of the Residue - Plants

DER Reference: 46708520.der.doc (Lettuce)
46708521.der.doc (Potato)
Residue Chemistry Memo DP Number 321209, 1/23/2007, A. Acierto (PP#5E6903)

Valent U.S.A. submitted metabolism studies with lettuce and potato in conjunction with this petition. A metabolism study with grape had been submitted previously.

Grape

A grape metabolism study with [2,6-^{14}C-pyridinyl]fluopicolide and [U-^{14}C-phenyl]fluopicolide (specific activity 22 and 20 μCi/mg, respectively) was submitted in conjunction with the grape import petition. The radiolabeled test substances were formulated as suspension concentrates and applied to grape vines as three sequential foliar treatments at a total application rates of 0.357 lb ai/A (~1x the proposed maximum seasonal rate) and 3.56 lb ai/A (~10x the proposed maximum seasonal rate). In the grape metabolism study, the majority of radioactivity was found to be on the surface of fruit and foliage samples; surface washes with ACN released ~97-99% of the total radioactive residues (TRR) from foliage samples collected immediately after

application, ~73-93% TRR from foliage samples collected 26-28 days after application, ~50-75% TRR from mature foliage samples, and ~46-79% TRR from mature fruit samples. Fluopicolide was the primary residue identified in fruit, accounting for ~87-91% TRR. The metabolites BAM and PCA were found in fruit at <3% TRR each. One additional metabolite, AE C643890 (2,6-dichloro-*N*-[(3-chloro-5-trifluoromethylpyridin-2-yl)methyl]-3-hydroxybenzamide), was identified at ≤0.2% TRR. Fluopicolide appeared to be metabolized slowly in grape vines to BAM and PCA, via cleavage of the bond between the carbon attached to the pyridine ring and the amide nitrogen of the parent compound, and AE C643890 is produced by the hydroxylation of the phenyl ring in the parent compound.

Lettuce

Valent U.S.A. Corporation has submitted a study investigating the metabolism of [2,6-^{14}C-pyridinyl]fluopicolide (specific activity 40.1-40.2 µCi/mg) and [U-^{14}C-phenyl]fluopicolide (specific activity 39.4-39.7 µCi/mg) in lettuce. The radiolabeled test substances were formulated as suspension concentrate formulations and diluted with water, then applied to lettuce plants as two sequential foliar treatments at 0.180-0.181 lb ai/A/application for a total of 0.361 lb ai/A (~1x the proposed rate). Total application rates for the pyridinyl and phenyl labels were 0.360 and 0.362 lb ai/A, respectively. A spray adjuvant (Crodamol PC) was added to the spray mixtures at 0.05%. The first application was made 41 days after planting, and the second application was made 21 days later. A separate group of lettuce plants received a single in-furrow soil drench application of the phenyl-labeled formulation at 0.181 lb ai/A (203 g ai/ha) made 41 days after planting (at the same time as the first foliar application).

Samples of immature lettuce were harvested immediately following the first application (foliar applications only) and 21 days after the first application (just prior to the second foliar application); samples of mature lettuce were harvested 14 days after the second foliar application (35 days after the first foliar application or soil-drench application). Samples from the foliar applications were surface washed with acetonitrile (ACN) on the day of collection. The in-life and analytical phases of the study were conducted by AgrEvo USA Company (Pikeville, NC).

The petitioner collected and analyzed two samples at each sampling interval for all samples. The values for total radioactive residues (TRR) reported below reflect the range of values recovered for the individual samples. Because results for extraction and analysis were similar for the duplicate samples, values for distribution, characterization, and identification of residues reflect average values.

TRR in samples of immature lettuce following foliar application were calculated by summing radioactivity in the surface wash, ACN extract, and nonextractable residues. TRR in samples of mature lettuce following foliar application were calculated by adding radioactivity in the surface wash to the radioactivity in the washed sample, determined by combustion/LSC, and TRR in samples following soil drench application were determined by combustion/LSC. TRR were similar in samples following foliar applications of pyridinyl- and phenyl-labeled fluopicolide, but significantly different in foliar-treated and soil-treated samples. Following a single foliar application of the test substances at ~0.180 lb ai/A, TRR were 9.583-15.640 ppm in samples harvested immediately following application (0 day) and 1.143-1.470 ppm in samples harvested 21 days after application. In samples of mature lettuce harvested 14 days following the second foliar application (35 days following the first foliar application; total application rate of ~0.360 lb ai/A), TRR were 12.647-14.821 ppm. TRR were 0.075-0.076 ppm in samples of immature

lettuce harvested 21 days following a single soil drench application of phenyl-labeled fluopicolide at 0.181 lb ai/A, and 0.142-0.208 ppm in mature lettuce harvested 35 days after soil application.

The ACN surface wash released the majority of the radioactivity from all foliar-treated samples: 95.4-96.6% TRR from 0-day immature lettuce harvested immediately following the first application; 61.0-66.6% TRR from immature lettuce harvested 21 days following the first application (21-day samples); and 84.0-84.6% TRR from mature lettuce harvested 14 days following the second application (35-day samples). Solvent extraction with ACN released the majority of the remaining radioactivity: 3.4-4.6% TRR from 0-day samples; 32.5-37.6% TRR from 21-day samples; and 14.8-15.1% TRR from 35-day samples. ACN extraction of unwashed lettuce harvested following the soil drench application released 97.2% TRR from 21-day samples and 95.9% TRR from 35-day samples. Remaining nonextractable residues were ≤1.5% TRR (≤0.140 ppm) in lettuce samples following foliar applications and ≤4.1% TRR (≤0.007 ppm) in lettuce samples following soil drench application. These procedures adequately extracted the majority of the residues from lettuce matrices; accountabilities were ~100%.

Residues were identified and confirmed using normal and reverse phase TLC. The petitioner did not report separate TLC results for surface washes and extracts, although these fractions were analyzed separately (based on representative chromatograms). The petitioner should note for future submissions that quantitative data for individual chromatograms should be provided. All analyses were completed within 2 months of harvest; therefore, no supporting storage stability data are needed.

Fluopicolide was the primary residue identified in lettuce following all treatments at all sampling intervals, accounting for 92.5-97.5% TRR (1.227-13.979 ppm) in immature and mature lettuce harvested following foliar applications and for 71.7-74.5% TRR (0.057-0.128 ppm) in immature and mature lettuce harvested following soil drench application. The metabolites AE C653711 (BAM; phenyl label only) and AE C657188 (PCA; pyridinyl label only) were found in foliar-treated lettuce at 0.1-3.9% and 0.6-1.5% TRR, respectively; BAM was identified at higher percentage (16.5-19.8% TRR, 0.013-0.034 ppm) in lettuce following a soil drench application of phenyl-labeled fluopicolide. A third metabolite, AE C643890, was also identified in 21-day foliar-treated lettuce (both labels) at 1.0-1.4% TRR and mature (35-day) soil-treated lettuce (phenyl label) at 2.8% TRR. The petitioner stated that no other single metabolite comprised more than 1% of the TRR in any sample.

Based on the results of the lettuce metabolism study, the petitioner proposed that fluopicolide is metabolized slowly in lettuce to BAM, PCA, and AE C643890. BAM and PCA result from the cleavage of the bond between the carbon attached to the pyridine ring and the amide nitrogen of the parent compound, and AE C643890 is produced by the hydroxylation of the phenyl ring in the parent compound. Fluopicolide is metabolized in soil to BAM, which is then taken up by the lettuce plant.

Potato

Valent U.S.A. Corporation has submitted a study investigating the metabolism of [2,6-^{14}C-pyridinyl]fluopicolide (specific activity 40.0-40.08 µCi/mg) and [U-^{14}C-phenyl]fluopicolide (specific activity 39.92-40.0 µCi/mg) in potato foliage and tubers. The radiolabeled test substances were formulated as suspension concentrate formulations and diluted with water, then

applied to potato plants as two sequential foliar treatments at 0.179-0.182 lb ai/A/application (200-204 g ai/ha/application) or 1.70-1.81 lb ai/A/application (1909-2029 g ai/ha/application)... Total application rates for the phenyl and pyridinyl labels were 0.363 and 0.360 lb ai/A, respectively, for the ~1x rate, and 3.60 and 3.51 lb ai/A, respectively, for the ~10x rate. A spray adjuvant (Crodamol PC) was added to the spray mixtures at 0.05%. The first application was made 69 days before harvest at BBCH 31-35, and the second application was made 49 days later (20 days before harvest).

Samples of immature potato foliage were harvested immediately following the first application (0-day) and 40-41 days after the first application (8-9 days prior to the second application). Samples of mature potato foliage and tubers were harvested 20 days after the second application. Samples were surface washed with acetonitrile (ACN) on the day of collection. The in-life and analytical phases of the study were conducted by AgrEvo USA Company (Pikeville, NC).

The petitioner collected and analyzed two samples at each sampling interval for all samples except foliage harvested 0 and 41 days following ~10x treatment with the pyridinyl label, for which four samples were collected. The values for total radioactive residues (TRR) reported below reflect the range of values recovered for the individual samples. Because results for extraction and analysis were similar for the duplicate/quadruplicate samples, values for distribution, characterization and identification of residues reflect average values.

TRR in 0-day samples were calculated by summing radioactivity in the surface wash, ACN extract, and nonextractable residues, and TRR in 40/41-day and mature potato samples were calculated by adding radioactivity in the surface wash to the radioactivity in the washed sample, determined by combustion/LSC. TRR were similar in samples following foliar applications of pyridinyl- and phenyl-labeled fluopicolide for all samples except immature foliage harvested 40-41 days after the first application of the ~10x treatment, where the mean TRR was ~3x higher in pyridinyl-treated samples than in phenyl-treated samples.

Following treatment at the ~1x rate, TRR were 42.69-55.48 ppm in samples of immature foliage harvested immediately following the first application (0 day), and 7.08-11.39 ppm in foliage samples harvested 40-41 days after the first application. In mature samples harvested 20 days following the second foliar application at the ~1x rate, TRR were 9.37 -12.57 ppm in foliage and 0.05-0.09 ppm in tubers. Following treatment at the ~10x rate, TRR were 395.65-567.51 ppm in 0-day foliage samples. In foliage samples harvested 40-41 days after the first application, TRR were 55.87-175.70 ppm following treatment with the pyridinyl label and 29.90-47.96 ppm following treatment with the phenyl label. In mature samples harvested 20 days following the second foliar application at the ~10x rate, TRR were 75.17-382.07 ppm in foliage and 0.43-0.86 ppm in tubers.

The ACN surface wash released the majority of the radioactivity from all foliage samples at both treatment rates: 98.0-99.4% TRR from 0-day foliage; 65.2-78.7% TRR from immature foliage harvested 40-41 days following first application; and 59.2-79.5% TRR from mature foliage. In tubers, the ACN surface wash released 10.7-16.7% TRR. Solvent extraction with ACN released the majority of the remaining radioactivity for all samples: 0.6-1.9% TRR from 0-day foliage samples; 19.1-30.2% TRR from 40/41-day foliage samples; 33.9-37.1% TRR from mature foliage samples (~1x treatment only; ~10x samples were not extracted), and 71.9-79.4% TRR from tubers. The nonextractable residues of 1x tubers following ACN extraction were also

subjected to acid hydrolysis with 1 N HCl, which released 5.9-8.7% TRR. These procedures adequately extracted the majority of residues from potato matrices; accountabilities were ~100%. Remaining nonextractable residues were ≤4.7% TRR in immature foliage samples from both harvest intervals, 3.8-3.9% TRR in ~1x mature foliage samples and 4.9-6.9% TRR in ~1x tuber samples. In ~10x tubers, which were not subjected to acid hydrolysis, nonextractable residues were 7.8-10.1% TRR.

Residues were identified and confirmed using normal and reverse phase TLC. For 0-day foliage, only the ACN surface wash was analyzed. For all remaining samples, although both the surface wash and extracts were analyzed, the petitioner only reported separate results for immature foliage harvested 40-41 days following first application. The petitioner should note for future submissions that quantitative data for individual chromatograms should be provided. The petitioner stated that preliminary chromatographic analysis of the principal extracts of the RACs was completed within 2 months of final harvest, and analysis for the entire study was completed within 3 months of final harvest; no data were included in the submission to support this statement. However, based on the completion date of the study, all analyses were completed within 6 months of collection; therefore, supporting storage stability data are not needed.

Fluopicolide was the primary residue identified in potato matrices following all treatments at all sampling intervals, accounting for 97.0-98.3% TRR (45.97-53.09 ppm for ~1x samples) in 0-day foliage, 88.8-94.6% TRR (6.78-9.03 ppm for ~1x samples) in 40/41-day foliage, 89.8-91.0% TRR (8.64-11.14 ppm) in ~1x mature foliage, and 51.1-70.2% TRR (~0.041 ppm for ~1x samples) in tubers. The metabolites PCA (pyridinyl label only) and BAM (phenyl label only) were found in mature foliage at 0.8% TRR and 1.9% TRR, respectively, and metabolite AE C643890 was found in mature foliage from both labels at 0.6-0.7% TRR. PCA and BAM were identified at higher percentage in ~1x and ~10x tubers, at 12.0% and 26.1% TRR (0.01 and 0.19 ppm), respectively, for PCA and 25.4% and 22.2% TRR (0.021 and 0.116 ppm), respectively, for BAM. In tubers (both labels), metabolite AE C643890 accounted for 1.7-2.4% TRR (0.001-0.003 ppm) following ~1x treatment, and was not identified following ~10x treatment. The petitioner stated that no other single metabolite comprised more than 2% of the TRR in any sample.

Based on the results of the potato metabolism study, the petitioner proposed that fluopicolide is metabolized in potato to BAM, PCA, and minor amounts of AE C643890. BAM and PCA result from the cleavage of the bond between the carbon attached to the pyridine ring and the amide nitrogen of the parent compound, and AE C643890 is produced via the hydroxylation of the phenyl ring in the parent compound.

***Conclusions*:** The grape, lettuce, and potato metabolism data are adequate to satisfy nature of the residue data requirements in support of the proposed uses on cucurbit vegetables, fruiting vegetables, grapes, leafy vegetables (except *Brassica*), and tuberous and corm vegetables. The metabolism of fluopicolide was found to be similar in the test crops. Fluopicolide appears to be metabolized slowly to BAM and PCA, via cleavage of the bond between the carbon attached to the pyridine ring and the amide nitrogen of the parent compound, and AE C643890 is produced by hydroxylation of the phenyl ring in the parent compound. Based on the results of the soil drench applications in lettuce, it appears that fluopicolide is metabolized in soil to BAM, which is then taken up by the lettuce plant. HED notes that because of the radiolabel of the test

substance used for the soil drench applications, the metabolite PCA would not have been observed.

The nature of the residue in primary crop plants is adequately understood. In HED's RARC1 meeting held on 7/19/07, HED determined that the tolerance for all primary crops should be expressed in terms of fluopicolide *per se*. However, since there are quantifiable residues of the metabolite, BAM in some primary crops, and this metabolite is a regulated metabolite of the registered pesticide, diclobenil, the Fluopicolide Team recommends that the numerical value for the tolerance be expressed in terms of the parent compound as a marker or indicator of total residue. The Team recommends that the tolerance expression read "Tolerances are established for residues of the fungicide fluopicolide [2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]benzamide] as an indicator of combined residues of fluopicolide and its metabolite, 2,6-dichlorobenzamide in/on the following raw agricultural commodities (RACs):"

For risk assessment purposes, the residue of concern in tuberous and corm vegetables treated directly with fluopicolide is parent compound and its PCA and BAM metabolites. For all other primary crops, the residue of concern for risk assessment purposes is the parent compound and its BAM metabolite (*BAM and Fluopicolide. Report of the Risk Assessment Review Committee (RARC1)*, Sarah Winfield, 7/19/07).

860.1300 Nature of the Residue - Livestock

DER Reference: 46708514.der.doc (Cow; phenyl label)
46708515.der.doc (Hen; phenyl label)
46708518.der.doc (Cow; pyridinyl label)
46708519.der.doc (Hen; pyridinyl label)

Ruminant (phenyl label)

Valent U.S.A. Corporation has submitted a study investigating the metabolism of [U-^{14}C-phenyl]fluopicolide (specific activity 5.572 MBq/mg) in lactating cows. The test substance was orally administered twice daily to two cows for 7 consecutive days, one at 1.1 ppm and one at 10.6 ppm in the diet. The 1.1 ppm dosing level corresponds to 5.2x and 3.8x the dietary burden for beef cattle and dairy cattle, respectively. The 10.6 ppm dosing level corresponds to 50x and 37x the dietary burden for beef cattle and dairy cattle, respectively. Milk was collected twice daily throughout the study, and tissues (muscle, fat, liver, and kidney) were collected at sacrifice, 23.25-23.75 hours after the final dose. The in-life and analytical phases of the study were conducted at Covance Laboratories, Ltd. (Harrogate, England).

Total radioactive residues (TRR) following dosing at 1.1 ppm were 0.9-1.8 ppb in milk, 5.1-5.7 ppb in fat, 3.4-4.3 ppb in muscle, 90 ppb in liver, and 26 ppb in kidney. TRR following dosing at 10.6 ppm were 3.5-19 ppb in milk, 40-43 ppb in fat, 23-25 ppb in muscle, 644 ppb in liver, and 302 ppb in kidney. Radioactivity was highest in liver and appeared to plateau in milk after 5 days of dosing. The majority of the administered dose was excreted, with urine, feces, and cage wash accounting for a total of ~75% of the administered dose.

Metabolic profiling was conducted on milk and tissues from the high-dose cow. The majority of the radioactivity (85-86% TRR) was extracted from milk and fat using acetonitrile (ACN); ACN extracted 14% of the TRR from muscle. In liver and kidney, the majority of the radioactivity

(89-91% TRR) was extracted using water. Separate aliquots of the water extracts of liver and kidney were subjected to solvent extraction, acid hydrolysis, base hydrolysis, and enzyme hydrolysis. Nonextractable residues accounted for ≤0.03 ppm in fat, muscle, and kidney, and 11% TRR (72 ppb) in liver.

These procedures adequately extracted the majority of the residues from cow matrices. Residues were identified and quantitated by HPLC. Milk samples were assayed fresh prior to sub-sampling and storage. Animal tissues were processed on the day of collection and stored frozen (<-10^{0}C) prior to analysis.

Approximately 76% TRR was identified in fat, and ~3-33% TRR was identified in milk, muscle, liver, and kidney. Fluopicolide was the major residue identified in milk at 29% TRR (5 ppb) and fat at 76% TRR (31 ppb); fluopicolide was also identified in muscle, liver, and kidney at 0.9-2.9% TRR (0.7-5.5 ppb). Metabolite AE C653711 (BAM) was identified in milk at 3.9% TRR, and metabolites AE C643890 and AE 0712556 were identified in liver and kidney at 1.2-6.8% TRR each (7.6-21 ppb). In milk, fat, and muscle, the remainder of the extractable radioactivity consisted of unknowns and polar material totaling <8 ppb in each matrix. In liver and kidney, HPLC unknowns accounted for 6-11% TRR (32-41 ppb) and polar material accounted for 17-19% TRR (57-108 ppb). A large portion of the radioactivity in these tissues appeared to have been lost, or distributed into fractions that were not HPLC analyzed; accountability in terms of total identified/characterized plus total nonextractable was 38% for liver and 50% for kidney.

Enzyme hydrolysis of liver and kidney indicated that radioactivity in the water-extractable fraction was not associated with glucuronide conjugates. Protease digestion of liver and kidney yielded mostly polar material which did not match any reference standards. Cellular fractionation of these tissues indicated that portions of radioactivity were associated with low molecular weight proteins, amino acids, and peptides (33% TRR in kidney, 16.9% in liver); lipids (11.8% TRR in kidney, 15.4% TRR in liver); RNA (0.9% TRR in kidney, 0.5%TRR in liver); sulfurated glucosaminoglycans (13.6% TRR in kidney, 15.2% in liver); carbohydrates (2.4% TRR in kidney, 3.0% TRR in liver); DNA (1.7% in kidney, 2.1% in liver); and the final nonextractable radioactivity was associated with protein (36.0% TRR in kidney, 46.4% in liver).

The petitioner suggested that the metabolic pathway in the cow may be similar to that in the hen (Covance Study 2014/004) and rat (Bayer Report No. TOX/00283-24), where one of the main metabolite residues was the S-methyl analogue probably produced via glutathione conjugation. The glutathione metabolites produced could then undergo cleavage by β-lyase leaving a product that could bind to proteins.

Ruminant (pyridinyl label)

Valent U.S.A. Corporation has submitted a study investigating the metabolism of [2,6-^{14}C-pyridinyl]fluopicolide (specific activity 49.12 µCi/mg for the low-dose dose cow and 24.76 µCi/mg for the high-dose cow) in lactating cows. The test substance was administered orally to two cows, one at 1 ppm and one at 10 ppm in the diet. The 1 ppm dosing level corresponds to 4.8x and 3.4x the dietary burden for beef cattle and dairy cattle, respectively. The 10 ppm dosing level corresponds to 48x and 34x the dietary burden for beef cattle and dairy cattle, respectively. The cows were dosed twice daily for 7 consecutive days. Milk was collected twice daily throughout the study, and tissues (muscle, fat, liver, and kidney) were collected at sacrifice,

23 hours after the final dose. The in-life and analytical phases of the study were conducted at Inveresk Research (Tranent, Scotland).

Total radioactive residues (TRR) following dosing at 1 ppm were 0.001 ppm in milk, 0.005 ppm in fat, 0.001 ppm in muscle, 0.058 ppm in liver, and 0.033 ppm in kidney. TRR following dosing at 10 ppm were 0.004-0.010 ppm in milk, 0.039-0.042 ppm in fat, 0.012 ppm in muscle, 0.449 ppm in liver, and 0.196 ppm in kidney. Radioactivity was highest in liver and kidney, and lowest in milk and muscle; residues in milk appeared to reach a plateau after 1 day of dosing. The majority of the administered dose was excreted, with urine, feces, and cage wash accounting for a total of ~80-84% of the administered dose.

Metabolic profiling was conducted on liver, kidney, and renal fat from the low-dose cow and on milk and tissues from the high-dose cow. The majority of the radioactivity (78-89% TRR) was extracted from milk and fat using methanol (MeOH)/water. MeOH/water extracted 15-36% of the TRR from liver, kidney, and muscle. A large portion of radioactivity was extracted from liver and kidney using pepsin and protease hydrolysis (total of 7-38% TRR) and strong acid hydrolysis (5-40% TRR). Nonextractable residues accounted for ≤0.02 ppm in liver, kidney, and renal fat from the low-dose cow, and milk, renal and omental fat, muscle, and kidney from the high-dose cow; nonextractable residues remaining following strong acid hydrolysis were 32% TRR (0.142 ppm) in liver from the high-dose cow.

These procedures adequately extracted the majority of residues from cow matrices. Although nonextractable residues in liver accounted for a significant portion of the radioactivity, the petitioner made sufficient attempts to release residues (pepsin and protease hydrolysis, and hydrolysis in 6 N HCl at reflux). Because the petitioner normalized extraction results, accountabilities were generally 100%. Residues were identified and quantitated by HPLC and confirmed by LC/MS/MS. Samples were stored up to 12.5 months prior to analysis; no supporting storage stability data were submitted.

The extracts of milk, omental fat, and muscle from the high-dose cow, and the extracts of kidney from the low-dose cow were not analyzed due to low radioactivity levels.

In tissues from the high-dose cow, approximately 73% TRR was identified in renal fat, and 14% and 24% TRR was identified in liver and kidney, respectively. Fluopicolide was the only residue identified in fat at 73% TRR (0.034 ppm); fluopicolide was also identified in liver and kidney at <3% TRR (<0.02 ppm). A dihydroxy glucuronide of fluopicolide was identified in kidney at 10% TRR (0.019 ppm); this metabolite was not found in liver. All other metabolites identified in liver and kidney accounted for <6% TRR each (<0.03 ppm). Identified metabolites included a hydroxy glucuronide of fluopicolide, a hydroxy sulfate of fluopicolide, a dihydroxy sulfate of fluopicolide, AE C643890, and AE 0712556.

In renal fat from the low-dose cow, fluopicolide was the only identified metabolite, at 64.4% TRR. No metabolites were identified in liver or kidney from the low-dose cow.

The combined enzyme hydrolysates of liver from the low- and high-dose cow, comprising 33.2% and 38.2% TRR, respectively, were analyzed by HPLC, which resolved a number of unknown peaks, each below the LOQ (low-dose cow) or <0.04 ppm (high-dose cow); similar results were observed for the combined enzyme hydrolysates of kidney from the high-dose cow (17.6%

TRR). The acid hydrolysate of liver from the high-dose cow was analyzed by HPLC which yielded four components, each <2% TRR. The petitioner reported that HPLC analysis of the acid hydrolysate of kidney from the high-dose cow yielded a single peak, accounting for 37.9% TRR (0.074 ppm); however, the HPLC chromatogram of this fraction showed several peaks.

Based on the results of the study, the petitioner proposed that fluopicolide is metabolized in ruminants via hydroxylation of the chlorophenyl ring in two positions to form AE 0712556 and AE C643890. Each of these metabolites is then conjugated with sulfate or glucuronic acid, or hydroxylated in a second position and then conjugated with sulfate or glucuronic acid.

Poultry (phenyl label)

Valent U.S.A. Corporation has submitted a study investigating the metabolism of [U-^{14}C-phenyl]fluopicolide (specific activity 5.81 MBq/mg) in laying hens. Two dose formulations (low and high) were prepared in capsule form to allow daily dose administration of 0.15 mg/day (specific activity equivalent to 0.857 MBq/day) and 1.5 mg/day (specific activity equivalent to 5 MBq/day). Two groups of five hens each were dosed daily for 14 consecutive days, one group at 1.2 ppm and one group at 10.7 ppm in the diet. The 1.2 ppm dosing level corresponds to 34x the dietary burden for poultry. The 10.7 ppm dosing level corresponds to 306x the dietary burden for poultry. Eggs were collected twice daily throughout the study, and tissues (fat, liver, skin with subcutaneous fat, and muscle) were collected at sacrifice, 23-24 hours after the final dose. The in-life and analytical phases of the study were conducted at Covance Laboratories, Ltd. (Harrogate, England).

Total radioactive residues (TRR) following dosing at 1.2 ppm were 0.002-0.018 ppm in egg white, 0.001-0.024 ppm in egg yolk, 0.004-0.007 ppm in fat, 0.086-0.224 ppm in liver, 0.004-0.011 ppm in skin (including subcutaneous fat), and 0.003-0.006 ppm in muscle. TRR following dosing at 10.7 ppm were 0.005-0.072 ppm in egg white, 0.003-0.224 ppm in egg yolk, 0.042-0.099 ppm in fat, 0.602-1.69 ppm in liver, 0.060-0.087 ppm in skin, and 0.031-0.047 ppm in muscle. Radioactivity was highest in liver and appeared to plateau in eggs after 10-11 days of dosing. The majority of the administered dose was excreted; with excreta and cage wash accounting for an average total of ~83% of the administered dose in the low-dose hens and ~95% of the administered dose in the high-dose hens.

Metabolic profiling was conducted on eggs and tissues from the high-dose hens. The majority of the radioactivity (56-98% TRR) was extracted from egg yolk, egg white, skin, fat, and muscle using acetonitrile (ACN). In liver, the majority of the radioactivity (78% TRR) was extracted using protease hydrolysis followed by ACN and methanol/water extraction. Nonextractable residues accounted for ≤0.05 ppm in egg white, egg yolk, skin, fat, and muscle, and 22% TRR (0.214 ppm) in liver. Residues were identified and quantitated by HPLC. Samples were stored frozen prior to analysis, but no information pertaining to storage intervals was provided.

Approximately 11-54% TRR was identified in egg white, egg yolk, liver, skin, and fat; no compounds were identified in muscle. Fluopicolide was identified at low levels in egg white, egg yolk, and fat (2.5-11% TRR; 0.001-0.017 ppm); it was not identified in liver or skin. The major metabolite identified in egg white and fat was Metabolite 1, a methyl sulfone conjugate of fluopicolide, at 51% TRR (0.022 ppm) in egg white and 38% TRR (0.023 ppm) in fat; Metabolite 1 was also identified in skin, at 10% TRR (0.007 ppm). The major residue identified in liver was AE C653711 (BAM), at 37% TRR (0.361 ppm); this metabolite was not found in

any other matrix. Metabolite AE C643890 was the major metabolite found in skin, at 15% TRR (0.010 ppm). This metabolite and/or AE 0608000 was found in liver at 3.1% TRR (0.030 ppm). The remainder of the radioactivity consisted of unknowns (each present at ≤0.06 ppm) and polar compounds.

Although metabolite AE C653711 was found in liver following enzyme hydrolysis, comparative analysis of an extract of liver with or without glucuronidase hydrolysis indicated that metabolite AE C653711 was not present in liver as a glucuronide conjugate. Additional characterization procedures with liver indicated that the largest portion of radioactivity (≥90% TRR) could be extracted with water; however, only ~40% TRR was organosoluble. The remainder was assumed to be associated with polar material. Cellular fractionation of liver indicated that the largest portions of radioactivity were associated with low molecular weight proteins, amino acids, and peptides (23% TRR), sulfurated glucosaminoglycans (29% TRR), and protein (26% TRR; released upon base hydrolysis).

The procedures of the study adequately extracted the majority of residues from hen matrices. The petitioner proposed that fluopicolide is metabolized in hens via ring hydroxylation to form AE C643890, cleavage of the pyridinyl ring moiety to form AE C653711, or formation of Metabolite 1.

Poultry (pyridinyl label)

Valent U.S.A. has submitted a study investigating the metabolism of [2,6-^{14}C-pyridinyl]fluopicolide (specific activity 183 μCi/mg) in laying hens. The test substance was administered orally to two groups of five hens each, one at 1 ppm and one at 10 ppm in the diet. The dosing levels correspond to 29x and 286x the dietary burden to poultry. The hens were dosed daily for 14 consecutive days. Eggs were collected daily throughout the study, and tissues (fat, liver, skin with fat, and muscle) were collected at sacrifice, 23 hours after the final dose.

TRR following dosing at 1 ppm were 0.001-0.004 ppm in egg white, 0.001-0.018 ppm in egg yolk, 0.002-0.004 ppm in fat, 0.031-0.052 ppm in liver, 0.002-0.003 ppm in skin (with fat), and 0.001-0.002 ppm in muscle. TRR following dosing at 10 ppm were 0.004-0.023 ppm in egg white, 0.004-0.104 ppm in egg yolk, 0.014-0.044 ppm in fat, 0.237-0.357 ppm in liver, 0.013-0.039 ppm in skin, and 0.007-0.015 ppm in muscle. Radioactivity was highest in liver and appeared to plateau in eggs after 11-12 days of dosing. The majority of the administered dose was excreted, with excreta and cage wash accounting for an average total of ~94-95% of the administered dose.

Metabolic profiling was conducted on egg yolk and liver from the low-dose hens and egg white, egg yolk, and tissues from the high-dose hens. The majority of the radioactivity (62-95% TRR) was extracted from egg white, egg yolk, fat and skin using MeOH/water; MeOH/water extracted 18-24% TRR from muscle and liver. A large portion of radioactivity was extracted from liver using pepsin and protease hydrolysis (total of 51-52% TRR) and strong acid hydrolysis (10-17% TRR); pepsin and protease hydrolysis released a total of 29-37% TRR from egg yolk. Nonextractable residues accounted for ≤0.01 ppm in egg white, egg yolk, skin, fat, muscle, and liver (low-dose hens), and 20% TRR (0.06 ppm) in liver from high-dose hens.

These procedures adequately extracted the majority of residues from hen matrices. Although nonextractable residues in liver accounted for a significant portion of the radioactivity, the

petitioner made sufficient attempts to release residues (pepsin and protease hydrolysis, and hydrolysis in 6 N HCl at reflux). Because the petitioner normalized extraction results, accountabilities, in terms of extractable plus nonextractable residues, were generally 100%. However, some radioactivity appeared to be "lost" in the various extraction steps; accountabilities in terms of total identified/characterized residues plus nonextractable residues ranged from 52-103%. The petitioner should note for future submissions that attempts should be made to account for all radioactivity during extraction procedures.

Residues were identified and quantitated by HPLC and confirmed by LC/MS/MS. Samples were stored frozen for 6.2-6.7 months prior to extraction and for a total of 7.8-13.1 months prior to completion of analysis. No supporting storage stability data were provided.

Approximately 10-64% TRR was identified in egg white, egg yolk, liver, skin, and fat; no compounds were identified in muscle. Fluopicolide was identified at low levels in egg yolk, fat, and skin (3.3-16% TRR; 0.003-0.005 ppm); it was not identified in liver or egg white. The major metabolite identified in egg white, fat, and skin was AE 0712556, at 41% TRR (0.005 ppm) in egg white, 47% TRR (0.012 ppm) in fat, and 30% TRR (0.007 ppm) in skin; this metabolite was also identified in egg yolk at 10-16% TRR (0.004-0.014 ppm) and in liver at 6% TRR (0.016 ppm). A metabolite determined to be a dihydroxy sulfate of fluopicolide, or two metabolites that were both dihydroxy sulfates of fluopicolide, was a major portion of the residue in egg white (23% TRR, 0.003 ppm) and egg yolk (15-34% TRR, 0.013-0.015 ppm); it was also found in liver at 2% TRR. A hydroxy sulfate of fluopicolide was observed in egg yolk and liver at low levels (1.0-7.1% TRR), and a second hydroxy sulfate of fluopicolide was observed as a minor metabolite in liver (1.4% TRR). The remainder of the radioactivity consisted of unknowns (each present at <0.03 ppm). The majority of the radioactivity in liver (51-52% TRR) was released upon pepsin and protease hydrolysis, with an additional 10-17% released via strong acid hydrolysis; the hydrolysates were found to consist of several unknowns, each <0.03 ppm.

The petitioner proposed that fluopicolide is metabolized in hens via hydroxylation of the chlorophenyl ring in two positions to form AE 0712556 and AE C643890 (AE C643890 was only observed in excreta). Each of these metabolites is then conjugated with sulfate or hydroxylated in a second position, to form a proposed dihydroxy intermediate, which is conjugated with sulfate.

***Conclusions*:** The submitted livestock metabolism studies are incomplete but upgradeable. Additional information is required for three of the studies; the required additional information is detailed below.

If sample analyses of any of the ruminant and poultry metabolism studies were not completed within 6 months of sample collection, the petitioner should provide data demonstrating that the metabolic profile was stable in the affected matrices during storage.

For the phenyl-^{14}C-labeled cow metabolism study (MRID 46708514), the petitioner should provide complete sample history information for samples from the study, including not only dates of collection but also dates of storage, radioassay, extraction, and analysis.

For the pyridinyl-^{14}C-labeled cow metabolism study (MRID 46708518), additional information should be submitted to address storage stability requirements and to correct errors and

inconsistencies in the study submission. Storage stability data are required to support the study. In addition, the petitioner should clarify the identification of two peaks in the liver MeOH/water extract (retention times of 43 and 47 minutes) to state whether the text on page 65 (which states that the metabolites are sulfate conjugates) or the results reported in Table 10 (which indicate that one is a sulfate conjugate and one is a glucuronide conjugate) are correct, and to further explain how the retention times for these metabolites were correlated with the identified metabolites in urine and kidney. The petitioner should correct the flowchart for omental fat (Figure 10) to include the correct TRR value for this matrix (0.039 ppm). Finally, the petitioner should recalculate the radioactivity levels and/or clarify the results for the HPLC analysis of any extract in which the calculated LOQ was too high to allow meaningful interpretation of the chromatogram. For example, the HPLC analysis of the acid hydrolysate of kidney, Figure 24, showed diffuse radioactivity over the entire chromatogram (based on the dpm results in each collected fraction). The petitioner's calculated results for this chromatogram showed only one spot in which the radioactivity was above the LOQ (fraction 24) and so the petitioner reported that HPLC analysis yielded one peak, comprising the entire analyzed fraction. This reported result is misleading.

The hen metabolism study conducted with [2,6-^{14}C-pyridinyl]fluopicolide (MRID 46708519) and U-^{14}C-phenyl]fluopicolide (MRID 46708515) are incomplete but upgradeable. In addition to the data demonstrating the stability of the metabolic profile, the petitioner should provide complete sample history information for samples from the study conducted with [U-^{14}C-phenyl]fluopicolide including not only dates of collection but also dates of storage, radioassay, extraction, and analysis. In addition, the petitioner should submit copies of the LC/MS chromatograms of metabolite AE C653711 (BAM) in liver as well as the corresponding chromatogram of the reference standard. These chromatograms were referenced in the submission (MRID 46708515, page 113) but were not included.

Provided the requested information to support the fluopicolid metabolism studies noted above are submitted, HED tentatively concludes that the nature of the residue in livestock has been adequately delineated for the purpose of this petition. The Fluopicolide Risk Assessment Team has concluded that tolerance expression in livestock should include the metabolite, 2,6-dichlorobenzamide (BAM) only. For risk assessment purposes, the residue of concern is parent compound and BAM.

860.1340 Residue Analytical Methods

Plant commodities

DER Reference: 46708522.der.doc (includes review of MRIDs 46708523 and 46708524)
Residue Chemistry Memo DP Number 321209, 1/23/2007, A. Acierto (PP#5E6903)
Residue Chemistry Memo DP Number 329686, A. Acierto, 6/8/2006

Enforcement method: Valent U.S.A. has submitted an LC/MS/MS method, Method RM-43C-1, for the determination of residues of fluopicolide *per se* in/on crops. The petitioner has noted that this method is based on Bayer CropScience Method 00782, and three modified versions of the method: Method 00782/M001, Method 00782/M002, and Method 00782/M003. HED notes that the method most closely follows Method 00782/M002, with modifications made to incorporate

some of the changes recommended during the independent laboratory validation (ILV). Adequate method validation data have been submitted for Method 00782/M002 (46474027.der.doc, 11/29/06, A. Acierto).

Radiovalidation data have been submitted previously for Method 00782/M003; these data indicate that the extraction procedures of Method 00782/M003 adequately extract aged residues of fluopicolide, BAM, and PCA, as well as P1X and 3-OH-BAM (rotational crop metabolites), from grape and wheat straw samples (46474027.der.doc, 11/29/06, A. Acierto).

Adequate ILV data for fluopicolide have been submitted for Methods 00782/M002 and 00782/M003 using samples of wheat forage; adequate data were also submitted for fluopicolide metabolites BAM and 3-OH-BAM using samples of wheat forage. Adequate ILV data for fluopicolide, BAM, and PCA have been submitted previously for Method 00782/M002 using samples of tomato. HED notes that the ILV laboratory did not validate Methods 00782/M002 and 00782/M003 in wheat forage for fluopicolide metabolites PCA and P1X.

In Method RM-43C-1, chopped plant commodities are mixed with acetone/water, and the mixture is acidified to pH <2 with 2 M sulfuric acid. An aqueous solution of L-cysteine hydrochloride is added, and the sample is extracted by blending, shaking, or vortexing. The extract is isolated by gravity filtration and diluted to volume with acetone and water. An aliquot of the extract is concentrated to remove the acetone, and the concentrated extract is partitioned twice with methyl *t*-butyl ether (MTBE). The MTBE phases are combined, and an aliquot is evaporated to dryness, redissolved in acetonitrile/water, and then filtered for LC/MS/MS analysis. Fluopicolide is detected and quantified using the daughter ion. The validated LOQ is 0.01 ppm for crop matrices.

The ACB/BEAD reviewed the proposed enforcement method, Method RM-43C-1, and reported that the method was not considered specific enough to positively confirm analyte identity since the tandem mass spectrometric analysis only monitored a single ion transition. ACB recommended that the petitioner provide information for a second ion transition to provide confirmation of analyte identities, or provide an alternate chromatographic column and/or mobile phase combination to add an additional degree of specificity. (Memo, Charles Stafford, 3/1/07).

In response to the ACB/BEAD review of Method RM-43C-1, the petitioner has now submitted a revised enforcement method (Method RM-43C-2; MRID 47073701) in which the primary analytical column is a reversed-phase C18 packing while the alternative column is a mixed phase of C18 plus a strong cation exchange packing material. The difference of polarity between the primary and alternate columns provides an additional degree of method selectivity which satisfies the guideline requirement for a confirmatory method (Memo, DP #339155, Charles Stafford, 3/14/07).

Data collection methods: Samples of crop commodities from the storage stability, crop field trial, processing, and field rotational studies associated with this petition were analyzed for residues of fluopicolide and its metabolites using LC/MS/MS Methods 00782, 00782/M001, 00782/M002, and/or 00782/M003, or a modified version of 00782/M001.

Samples of tomato commodities from the tomato and grape crop field trial and tomato processing studies were analyzed for residues of fluopicolide, BAM, and PCA using Method 00782.

For the bell pepper, chili pepper, cantaloupe, cucumber, head lettuce, leaf lettuce, and summer squash crop field trials, samples were analyzed by Pyxant Labs Inc. for residues of fluopicolide, BAM, and PCA using a modified version of Method 00782/M001. The method was modified from 00782/M001 in the following ways: (1) a smaller volume of solvent was used for extraction; (2) the MTBE liquid/liquid partition step was eliminated; and (3) the same diluted sample was used for the analysis of all three compounds by LC/MS/MS.

Samples of potato commodities from the potato crop field trial and processing studies were analyzed for residues of fluopicolide, BAM, and PCA using Method 00782/M001.

For the celery and spinach crop field trials, samples were analyzed for residues of fluopicolide, BAM, and PCA using a method identified as Pyxant method METH 1611-00.02. A complete copy of the method was included in the submissions. Although not stated in METH 1611-00.02, the method is clearly a modified version of 00782/M001, and is identical to the modified version used by Pyxant for the bell pepper, chili pepper, cantaloupe, cucumber, head lettuce, leaf lettuce, and summer squash crop field trials.

Samples of wheat straw, grain, and forage from the storage stability study were analyzed for residues of fluopicolide, 3-OH-BAM, BAM, and P1X using LC/MS/MS Methods 00782/M001, 00782/M002, and 00782/M003.

Samples of wheat forage, hay, grain, straw, and processed commodities from the extensive field rotational crop study and rotated wheat processing study were analyzed for residues of fluopicolide and its metabolites BAM, PCA, P1X, and 3-OH-BAM using a combined and modified version of LC/MS/MS Methods 00782/M002 (for determination of fluopicolide, BAM, PCA, and P1X) and 00782/M003 (for determination of 3-OH-BAM). The extraction steps of the methods were modified to minimize ion suppression, and the same final extract was used for determination of all analytes.

HED notes that for the storage stability, crop field trial, processing, and field rotational crop submissions associated with this petition, residues of each analyte were reported in terms of the analyte (i.e., residues of metabolites were not converted to parent equivalents).

***Conclusions*:** Acceptable plant data collection methods were used to generate field trial, storage stability, and processing data.

An acceptable LC/MS/MS plant enforcement method (Method RM-43C-2) is available for fluopicolide (parent) in plants. The LOQ for fluopicolide (parent) is 0.01 ppm. Method RM-43C-2 will be forwarded to FDA for inclusion in PAM II.

Livestock commodities

DER Reference: 46708516.der.doc

Valent U.S.A. Corporation has submitted an LC/MS/MS method, Method AR 303-02, for the determination of residues of fluopicolide and its metabolites AE C653711 (BAM) and AE C657188 (PCA) in/on milk, meat, fat, liver, and kidney of cattle. This method was used for data

collection in samples of beef commodities from the livestock feeding study submitted in conjunction with DP Number 327026.

The method includes instructions for determining free compounds and bound compounds; bound compounds are to be determined in liver and kidney samples only. Because the procedure for determination of bound compounds involves acid hydrolysis of the samples followed by extraction of the hydrolysate, the procedure determines free + bound compounds in liver and kidney.

For the determination of free compounds in beef tissues (meat, fat, liver, and kidney), samples are extracted twice with water, acetonitrile (ACN), and 0.1% formic acid. The extracts are combined and diluted to volume with water and 0.1% formic acid. The final extract is filtered and diluted prior to analysis by LC/MS/MS.

For the determination of free compounds in milk, samples are extracted with water, ACN and 0.3% formic acid and then extracted twice with ACN and 0.5% formic acid. The extracts are combined and diluted to volume with water and 0.1% formic acid. The final extract is filtered and diluted prior to analysis by LC/MS/MS.

For the determination of free + bound compounds in liver and kidney, samples are mixed with water and concentrated HCl and then heated at 100 °C for one hour. After cooling, the mixture is extracted twice with ACN. The combined extracts are neutralized and diluted to volume with water. The final extract is filtered and diluted prior to analysis by LC/MS/MS.

The validated limits of quantitation (LOQs) for each analyte are 0.01 ppm for milk, 0.02 ppm for meat, and 0.05 ppm for fat, liver, and kidney.

The method was adequately validated using samples of milk, meat, fat, liver, and kidney of cattle. Recoveries of fluopicolide, BAM, and PCA averaged 93% (standard deviation of 8.0%), 102% (standard deviation of 9.2%), and 99% (standard deviation of 10.4%), respectively, from samples of milk, meat, fat, liver, and kidney fortified at the LOQ and 10x LOQ and analyzed using the procedures for free compounds. Recoveries of fluopicolide, BAM, and PCA averaged 92% (standard deviation of 7.2%), 101% (standard deviation of 12.3%), and 83% (standard deviation of 6.6%), respectively, from samples of beef liver and kidney fortified at the LOQ and 10x LOQ and analyzed using the procedures for free + bound compounds. Based on the method validation data, LC/MS/MS (Method AR 303-02) is adequate for data collection.

ACB/BEAD has reviewed Method AR 303-02 to determine if it would be suitable for enforcement purposes (email from C. Stafford to A. Acierto dated 11/15/07) for cattle commodities. ACB concluded the method is not suitable for enforcement purposes since the method quantitates parent and BAM by monitoring only one MRM ion transition for each analyte. The method does not meet the Agency criteria as a confirmatory method since it doesn't monitor two or more transition for each analyte. Further, there are some large, close-eluting peaks in the liver and kidney controls, leading to the potential for false positives supporting the need for a confirmatory step. ACB/BEAD recommends that the petitioner revise the method to include an alternate LC column as they did for the plant method.
No method to determine residues of fluopicolid in poultry commodities has been proposed.

***Conclusions*:** Adequate method validation data have been submitted for LC/MS/MS (Method AR 303-02); the data are sufficiently representative of the expected residue levels for the beef commodities included in the petition associated with DP Number 327026. No radiovalidation data were submitted for the method; however, HED has concluded that radiovalidation data are not required because the extraction solvents used in the method are similar to those used in the cattle metabolism study.

Based on the method validation data, the LC/MS/MS method AR 303-02 for livestock is adequate for data collection purposes. The validated limits of quantitation (LOQs) for each analyte are 0.01 ppm for milk, 0.02 ppm for meat, and 0.05 ppm for fat, liver, and kidney.

Method 303-02 has been reviewed and is not acceptable as an enforcement method. A confirmatory procedure is required for the LC/MS/MS Method 303-02 to be considered an adequate enforcement method for ruminant commodities.

860.1360 Multiresidue Methods

Residue Chemistry Memo DP Number 321209, 1/23/2007, A. Acierto (PP#5E6903; MRID 46708525)

Adequate multiresidue method testing data for fluopicolide and its metabolites BAM, PCA, P1X, and BAM-OH were submitted in conjunction with the previous petition (PP#5E6903). Based on the results of the testing, the multiresidue methods are not appropriate for determining residues of fluopicolide or its metabolites (BAM, PCA, P1X, and BAM-OH). The data have been forwarded to FDA for further evaluation.

860.1380 Storage Stability

Plant commodities

DER Reference: 46708418.der.doc (Wheat commodities)
46708526.der.doc (Extrapolation of storage stability to 48 months)
46708527.der.doc (Potato, sugar beet, tomato, and wheat processed commodities)
Residue Chemistry Memo DP Number 321209, 1/23/2007, A. Acierto (PP#5E6903)

Storage stability studies

The available storage stability data are summarized below and presented in Table 4.

A storage stability study with fluopicolide and its metabolites BAM and PCA in cabbage leaves, grape, potato tuber, and wheat grain was submitted in conjunction with the previous petition (PP#5E6903). The study indicated that residues of fluopicolide and its metabolites BAM and PCA are stable at ≤-18 °C for up to 30 months in cabbage leaves, grape, potato tuber, and wheat grain.

Valent U.S.A. submitted the interim results of a storage stability study with fluopicolide and its metabolites 3-OH-BAM, BAM and P1X in wheat straw, grain, and forage. Untreated samples of these commodities were fortified with a mixture of fluopicolide and BAM, and separately with

3-OH-BAM and P1X at a nominal fortification level of 0.1 ppm for each analyte. Wheat straw samples were fortified with all four analytes, and wheat grain and forage samples were fortified with 3-OH-BAM and P1X. Samples were placed in frozen storage at ≤-18 ºC and analyzed at storage intervals of approximately 0, 30, 90, 180 and 360 days.

Samples of wheat straw, grain, and forages were analyzed for residues of fluopicolide, 3-OH-BAM, BAM, and P1X using LC/MS/MS Methods 00782/M001, M002, and M003. The reported LOQ was 0.01 ppm for each analyte in each matrix. The methods were adequate for data collection based on acceptable concurrent method recoveries.

The storage stability data indicate that residues of fluopicolide and its metabolites 3-OH-BAM, BAM, and P1X are stable at ≤-18 °C for up to 12 months in wheat straw, and residues of 3-OH-BAM and P1X are stable at ≤-18 °C for up to ~12 months in wheat grain and forage. The petitioner has stated that additional storage intervals of 18 months and 24 months will be investigated, and the final storage stability study will be submitted upon completion.

Valent U.S.A. also submitted the results of a storage stability study with fluopicolide and its metabolites BAM and PCA in sugar beet, tomato, wheat, and potato processed commodities. Untreated samples of sugar beet dried pulp, molasses, and refined sugar, tomato paste and puree, wheat bran, flour, and shorts, and potato chips, dried flakes, and wet peel were fortified with a mixed standard of [phenyl-UL-^{14}C]fluopicolide, [phenyl-UL-^{14}C]BAM, and [pyridine-2,6-^{14}C]PCA, at fortification levels of 0.30-0.31, 0.17-0.18, and 0.26-0.35 ppm, respectively. Samples were placed in frozen storage at ≤-10 ºC and analyzed at storage intervals of 0-7, 29-36, and 911-925 days.

Samples of sugar beet, tomato, wheat, and potato processed commodities were extracted using 0.1 M sulfuric acid or acetone/0.1 M sulfuric acid. Following solid-phase extraction cleanup, the extracts were radioassayed by LSC and then analyzed by HPLC. The recovered residue for each sample was determined by multiplying the total radioactivity, determined by radioassay, by the relative percentage of each analyte in each extract, determined by HPLC. An LOQ was not reported for this method. The method was adequate for data collection based on acceptable concurrent method recoveries.

The storage stability data indicate that residues of fluopicolide and its metabolites BAM and PCA are stable at ≤-10 °C for up to 30 months in sugar beet, tomato, wheat, and potato processed commodities.

Valent U.S.A. Corporation also submitted a study in which the results of a previously submitted storage stability study were extrapolated to a longer storage interval. The data from the previously submitted 30-month storage stability study (46474036.Der.doc, 11/29/06, A. Acierto) with fluopicolide and its metabolites BAM and PCA in cabbage leaves, grape, potato tuber, and wheat grain were used to extrapolate to a 48-month storage interval for each analyte in each crop.

The 48-month storage stability recoveries were calculated using a simple linear fit of the 0-, 3-, 6-, 12-, 18-, 24- and 30-month corrected recoveries for each analyte. Based on the estimated corrected recoveries and the observed slopes of the linear regression fits, there appears to be a potential for slight decline of fluopicolide and PCA residues in cabbage leaves and potato tuber,

fluopicolide residues in grape, and BAM residues in wheat grain after 48 months of frozen storage (≤-18 °C); the linear regression analyses yielded lines with negative slopes for these commodities. The data also indicated that fluopicolide residues are likely to be stable in wheat grain, residues of BAM are likely to be stable in cabbage leaves, grapes, and potato tubers, and residues of PCA are likely to be stable in grapes and wheat grain during 48 months of frozen storage; the linear regression analyses for these commodities yielded lines with positive slopes.

The study reviewer conducted linear regression analyses of the data, in cases where the slope was found to be negative, to calculate the correlation coefficients. The correlation coefficients were determined to be ≤0.48. Because the proposed extrapolation represents a much longer interval (1.6x) than is supported by actual storage stability data and in consideration of the low correlation coefficients, HED does not believe it would be appropriate to use the extrapolated data to make conclusions regarding the stability of residues of fluopicolide and PCA in cabbage and potato tuber, residues of fluopicolide in grape, or residues of BAM in wheat grain following 48 months of storage.

Sample storage intervals and conditions

All samples from the crop field trial and field rotational crop studies associated with this petition were stored frozen prior to analysis. Samples from the potato, tomato, and wheat processing studies were stored frozen. The maximum storage intervals of samples from the crop field trial, processing, and field rotational crop studies associated with this petition are presented below. Unless otherwise noted, samples were stored at the analytical lab at ≤ -20°C.

Tuberous and corm vegetable subgroup: The maximum storage interval from harvest to analysis was 896 days (~30 months). For the potato processing study, the maximum storage interval of the samples from processing to extraction was 589 days (20 months).

Leafy vegetables, except Brassica, group: The maximum storage intervals from harvest to extraction were 1,149 days (38 months) for celery, 878 days (29 months) for head lettuce, 877 days (29 months) for leaf lettuce, and 1,169 days (38 months) for spinach.

Fruiting vegetable group: The maximum storage intervals from harvest to analysis were 554 days (19 months) for bell pepper, 508 days (17 months) for chili pepper, and 646 days (21 months) for tomato. For the tomato processing study, the maximum storage interval from harvest to extraction for analysis of tomatoes and the processed commodities was 378 days (12 months). Tomatoes (MRID 46708536) were stored at < -15°C.

Cucurbit vegetable group: The maximum storage interval from harvest to extraction was 560 days (19 months) for cantaloupe, 597 days (20 months) for cucumber, and 624 days (21 months) for summer squash.

Grape: The maximum storage interval from harvest to extraction was 219 days (7 months). Grapes were stored at ≤ -15°C.

Rotational wheat commodities: Maximum storage intervals from harvest to analysis were 24.0 months for wheat forage, 24.5 months for wheat hay, 20.7 months for wheat grain, and 24.4 months for wheat straw. For the wheat processing study, maximum storage intervals from harvest (RAC) or processing to analysis were ~20 months for wheat grain and 17 months for wheat processed commodities.

TABLE 4.	**Summary of Stability of Residues of Fluopicolide, BAM, and PCA in Cabbage Leaves, Grape, Potato Tuber, Sugar Beet, Tomato, and Wheat, and Processed Commodities.**				
RAC	Spike Level (ppm)	Storage Interval (months)	Processed Commodity	Spike Level (ppm)	Storage Interval (months)
Fluopicolide					
Cabbage leaves	0.1	30			
Grape	0.1	30			
Potato tuber	0.1	30			
Wheat grain	0.1	30	Wheat straw	0.1	12
Refined sugar	0.3	30	Sugar beet molasses	0.3	30
Tomato paste	0.3	30	Beet dried pulp	0.3	30
Tomato puree	0.3	30	Wheat flour	0.3	30
Wheat bran	0.3	30	Wheat shorts	0.3	30
Potato flakes	0.3	30	Potato chips	0.3	30
			Potato wet peel	0.3	30
BAM					
Cabbage leaves	0.1	30			
Grape	0.1	30			
Potato tuber	0.1	30			
Wheat grain	0.1	30	Wheat straw	0.1	12
Refined sugar	0.18	30	Sugar beet molasses	0.18	30
Tomato paste	0.18	30	Beet dried pulp	0.18	30
Tomato puree	0.18	30	Wheat flour	0.18	30
Wheat bran	0.18	30	Wheat shorts	0.18	30
Potato flakes	0.18	30	Potato chips	0.18	30
			Potato wet peel	0.18	30
PCA					
Cabbage leaves	0.1	30			
Grape	0.1	30			
Potato tuber	0.1	30			
Wheat grain	0.1	30			
Refined sugar	0.35	30	Sugar beet molasses	0.35	30
Tomato paste	0.35	30	Beet dried pulp	0.35	30
Tomato puree	0.35	30	Wheat flour	0.35	30
Wheat bran	0.35	30	Wheat shorts	0.35	30
Potato flakes	0.35	30	Potato chips	0.35	30
			Potato wet peel	0.35	30
P1X					
Wheat grain	0.10	12			
Wheat straw	0.10	12			

TABLE 4.	**Summary of Stability of Residues of Fluopicolide, BAM, and PCA in Cabbage Leaves, Grape, Potato Tuber, Sugar Beet, Tomato, and Wheat, and Processed Commodities.**				
RAC	Spike Level (ppm)	Storage Interval (months)	Processed Commodity	Spike Level (ppm)	Storage Interval (months)
Wheat forage	0.10	12			
3-OH-BAM					
Wheat grain	0.10	12			
Wheat straw	0.10	12			
Wheat forage	0.10	12			

***Conclusions*:** The submitted storage stability studies are adequate to demonstrate that residues of fluopicolide and its metabolites 3-OH-BAM, BAM, and P1X are stable at ≤-18 °C for up to 12 months in wheat straw; that residues of 3-OH-BAM and P1X are stable at ≤-18 °C for up to ~12 months in wheat grain and forage. Further, the submitted storage stability results adequately demonstrate that residues of fluopicolide and its metabolites BAM and PCA are stable at ≤-10 °C for up to 30 months in sugar beet, tomato, wheat, and potato processed commodities

Storage stability data submitted previously (PP#5E6903) indicate that residues of fluopicolide and its metabolites BAM and PCA are stable at ≤-18 °C for up to 30 months in cabbage leaves, grape, potato tuber, and wheat grain. The petitioner presented data extrapolating the results of the 30-month storage stability study to a 48-month storage interval for each analyte in each crop. HED does not believe that a general conclusion regarding the stability of fluopicolide, BAM, and PCA in cabbage, grape, potato, and wheat grain following 48 months of frozen storage can be made using these data. The available storage stability data should be considered interim data. Storage stability data to support the full duration of the study period should be submitted.

The available storage stability data for fluopicolide, BAM, and PCA in/on cabbage, grape, and potato tuber, which indicate stability for 30 months, are adequate to support the submitted grape, cucurbit vegetable, leafy vegetable (except celery and spinach), and potato field trials. The available storage stability data on tomato paste and puree can be used in lieu of storage stability data on the tomato RAC, and can be used along with the data on cabbage and grapes to support the submitted fruiting vegetable field trials. All field trial samples from these crops (except celery and spinach) were stored ≤30 months prior to analysis.

Additional storage stability data are needed for celery and spinach. Samples of celery and spinach were stored up to 38 months prior to analysis; HED concludes that the available 30-month storage stability data may not be extrapolated to 38 months to support these crop field trials; storage stability data for any representative leafy vegetable should be submitted to support the full duration of the study period for celery and spinach.

Adequate storage stability data are available for residues of fluopicolide, BAM and PCA in/on wheat grain and bran, flour and shorts. Interim data are available for residues of 3-OH-BAM and P1X in/on wheat grain, forage, and straw (for up to 12 months). However, to support the wheat field rotational crop study, storage stability data are needed reflecting the stability of P1X in wheat grain for 21 months and for fluopicolide and BAM in wheat forage and straw for 24 months. While storage stability data for 21 months are not available for 3-OH-BAM in wheat

grain, and P1X and PCA in wheat forage and straw, these are not regulated metabolites; therefore additional storage stability data are not required for these metabolites. The requested additional storage stability data for residues of P1X in wheat grain is also needed to support the wheat processing study. The available and requested storage stability data for wheat straw will be translated to wheat hay. Storage stability data on wheat grain can be translated to the wheat processed commodities.

Livestock commodities

DER Reference: 46708528.de2.doc

Valent U.S.A. has submitted the results of a storage stability study with fluopicolide and its metabolites in cattle commodities.

Samples of homogenized milk, muscle, fat, liver, and kidney from undosed cattle were separately fortified with fluopicolide and a mixed standard of BAM and PCA at 0.1 ppm each for milk and muscle and 0.5 ppm each for fat, liver, and kidney. Samples were stored frozen (~-18 °C) and analyzed at intervals of 13, 51, and 83 days for milk, 4 months for muscle and fat, or 9 months for kidney and liver.
The results indicate that under these conditions, residues of fluopicolide and its metabolites BAM and PCA are stable for up to 83 days in milk, for up to 4 months in muscle and fat, and for up to 9 months in liver and kidney.

Samples of cattle matrices were analyzed for residues of fluopicolide and its metabolites (BAM and PCA) using LC/MS/MS Method No. AR 303-02. This method is adequate for data collection based on acceptable method recoveries. The validated LOQs were 0.010 ppm for each analyte in milk, 0.020 ppm for each analyte in muscle, and 0.050 ppm for each analyte in fat, liver, and kidney.

In the cattle feeding study, milk and tissue samples were stored frozen prior to analysis; maximum storage intervals were 30 days for milk, 20 days for cream, 13 days for skim milk, 66 days for muscle, 95 days for fat, and 277-280 days for liver and kidney.

***Conclusions*:** The submitted storage stability data are adequate to support the storage intervals and conditions of samples from the cattle feeding study.

860.1400 Water, Fish, and Irrigated Crops

There are no proposed uses that are relevant to this guideline topic.

860.1460 Food Handling

There are no proposed uses that are relevant to this guideline topic.

860.1480 Meat, Milk, Poultry, and Eggs

DER Reference: 46708528.de1.doc
46708529.der.doc

There are livestock feedstuffs associated with the proposed new uses on potato and rotated wheat. The dietary burdens of fluopicolide *per se* to livestock, based on reasonably balanced diets, are presented in Table 5. The dietary burdens are 0.21 ppm for beef cattle, 0.29 ppm for dairy cattle, and 0.035 ppm for swine and poultry (e-mail, J. Stokes, 4/30/07).

Table 5. Calculation of Dietary Burdens of Fluopicolide Residues to Livestock.

Feedstuff	Type[1]	% Dry Matter[2]	% Diet[2]	Recommended Tolerance (ppm)	Dietary Contribution (ppm)[3]
Beef Cattle R: 15%; CC: 75 %; PC: 10%					
Wheat, hay	R	88	15	0.50	0.08
Potato, processed waste	CC	15	30	0.05	0.10
Wheat, milled byproducts	CC	88	40	0.07	0.032
CC (untreated)	CC	N/A	5	N/A	--
PC (untreated)	PC	N/A	10	N/A	--
TOTAL BURDEN	--	--	100	--	**0.21**
Dairy Cattle R: 45%; CC: 45 %; PC: 10%					
Wheat, hay	R	88	40	0.50	0.23
R (untreated)	R	N/A	5	N/A	--
Potato, processed waste	CC	15	10	0.05	0.033
Wheat, milled byproducts	CC	88	35	0.07	0.028
PC (untreated)	PC	N/A	10	N/A	--
TOTAL BURDEN	--	--	100	--	**0.29**
Poultry CC: 75 %; PC: 25%					
Wheat, milled byproducts	CC	88	50	0.07	0.035
CC (untreated)	CC	N/A	25	N/A	--
PC (untreated)	PC	N/A	25	N/A	--
TOTAL BURDEN	--	--	100	--	**0.035**
Swine CC: 85 %; PC: 15%					
Wheat, milled byproducts	CC	88	50	0.07	0.035
CC (untreated)	CC	N/A	35	N/A	--
PC (untreated)	PC	N/A	15	N/A	--
TOTAL BURDEN	--	--	100	--	**0.035**

[1] R: Roughage; CC: Carbohydrate concentrate; PC: Protein concentrate.
[2] OPPTS 860.1000 Table 1 Feedstuffs (October 2006).
[3] Contribution = ([tolerance /% DM] X % diet) for beef and dairy cattle; contribution = ([tolerance] X % diet) for poultry and swine.
[4] N/A: Not applicable. Tolerances/uses of fluopicolide have not been registered or proposed for this feedstuff.

In addition, since there are likely to be measurable residues of the fluopicolide metabolite, BAM in livestock feedstuffs, and HED has determined that the residues of concern in animal commodities includes BAM, HED has also calculated a BAM dietary burden in connection with the Human Health risk assessment for BAM (*2,6-Dichlorobenzamide (BAM) as a Metabolite/Degradate of Fluopicolide and Dichlobenil. Human Health Risk Assessment for Proposed Uses of Fluopicolide on Tuberous and Corm Vegetables, Leafy Vegetables (except*

Brassica), Fruiting Vegetables, Cucurbit Vegetables, Grapes, Turf, and Ornamentals, and for Indirect or Inadvertent Residues on the Rotational Crop Wheat, DP #345918, N. Dodd, 11/21/07).

Wet apple pomace is the only livestock feed associated with crops with established/pending dichlobenil tolerances. Wet apple pomace is fed to beef and dairy cattle. There are no poultry or swine feedstuffs associated with the established/pending uses of dichlobenil.

Feed items from potatoes (potato culls and processed potato waste) and wheat (grain, forage, hay, straw, aspirated grain fractions, milled byproducts) are the only livestock feeds from fluopicolide uses on tuberous and corm vegetables, leafy vegetables, fruiting vegetables, cucurbit vegetables, grapes, and the rotational crop wheat.

The dietary burdens of BAM residues in livestock from dichlobenil and fluopicolide uses, based on reasonably balanced diets, are presented in the table below. The dietary burdens of BAM are 0.13 ppm for beef cattle, 0.12 ppm for dairy cattle, and 0.009 ppm for swine and poultry.

Table 6. Calculation of Dietary Burdens of BAM Residues in Livestock from Fluopicolide and Dichlobenil Uses.*

Feedstuff	Type[1]	% Dry Matter[2]	% Diet[2]	BAM Maximum Residues (ppm)	Dietary Contribution (ppm)[3]
Beef Cattle R: 15%; CC: 75 %; PC: 10%					
Wheat, hay	R	88	15	0.102	0.017
Potato, processed waste	CC	15	30	0.05[4]	0.10
Wheat, milled byproducts	CC	88	40	0.018[5]	0.0082
CC (untreated)	CC	N/A	5	N/A[6]	--
PC (untreated)	PC	N/A	10	N/A	--
TOTAL BURDEN	--	--	100		**0.13**
Dairy Cattle R: 45%; CC: 45 %; PC: 10%					
Wheat, hay	R	88	40	0.102	0.046
R (untreated)	R	N/A	5	N/A	--
Wet apple pomace	CC	40	10	0.271	0.068
Wheat, milled byproducts	CC	88	35	0.018[5]	0.0072
PC (untreated)	PC	N/A	10	N/A	--
TOTAL BURDEN	--	--	100		**0.12**
Poultry CC: 75 %; PC: 25%					
Wheat, milled byproducts	CC	88	50	0.018[5]	0.009
CC (untreated)	CC	N/A	25	N/A	--
PC (untreated)	PC	N/A	25	N/A	--
TOTAL BURDEN	--	--	100		**0.009**
Swine CC: 85 %; PC: 15%					
Wheat, milled byproducts	CC	88	50	0.018[5]	0.009
CC (untreated)	CC	N/A	35	N/A	--
PC (untreated)	PC	N/A	15	N/A	--
TOTAL BURDEN	--	--	100		**0.009**

[1] R: Roughage; CC: Carbohydrate concentrate; PC: Protein concentrate.

[2] OPPTS 860.1000 Table 1 Feedstuffs (October 2006).
[3] Contribution = ([tolerance /% DM] X % diet) for beef and dairy cattle; contribution = ([tolerance] X % diet) for poultry and swine.
[4]The value of 0.05 ppm for processed potato waste is based on a concentration factor for wet peel of 4.9x and the LOQ (0.01 ppm) as the BAM residue in the RAC samples.
[5] Residues of BAM in wheat grain (field accumulation in rotational wheat study: MRID 46708547) were below the calculated LOD of 0.0029-0.0077 ppm; the LOQ is 0.01 ppm. BAM concentration factors are 1.7x for wheat bran, 0.7x for flour, 1.1x for middlings, 1.2x for shorts, and 1.8x for germ. The value of 0.018 ppm for wheat milled byproducts and aspirated grain fractions is based on the highest concentration factor of 1.8x for BAM and a grain (RAC) residue of 0.01 ppm (LOQ) for BAM.
[6] N/A: Not applicable.

Fluopicolid

Cattle: Valent U.S.A. Corporation has submitted a cattle feeding study with fluopicolide. Three treatment groups of three dairy cows each were dosed orally with fluopicolide in the feed at dose rates corresponding to 0.5, 1.7, and 5.7 ppm (dry feed weight) for 28 consecutive days. (These dosing levels as compared to the dietary burden are 1.7x, 5.9x, and 20x , respectively, for dairy cattle and 2.4x, 8.1x, and 27x, respectively, for beef cattle. Cows were milked twice daily, and samples were composited daily for each cow. Cows were sacrificed within 17 hours of the final dose. Samples of liver, kidneys, fat (composite of mesenterial, perirenal, and subcutaneous), and muscle (composite of round and loin) were collected from each cow. Samples of milk collected on study days 1, 4, 7, 10, 13, 16, 19, 22, 25, and 28 from all dose levels were reserved for analysis. Samples of cream and skim milk were generated from milk samples collected on study day 22 (high dose group only).

Samples of cattle matrices were analyzed for residues of fluopicolide, BAM, and PCA using LC/MS/MS Method No. AR 303-02. This method is adequate for data collection based on acceptable method recoveries. The validated limits of quantitation (LOQs) were 0.010 ppm for each analyte in milk, 0.020 ppm for each analyte in muscle, and 0.050 ppm for each analyte in fat, liver, and kidney.

Milk and tissue samples were stored frozen prior to analysis; maximum storage intervals were 30 days for milk, 20 days for cream, 13 days for skim milk, 66 days for muscle, 95 days for fat, and 277-280 days for liver and kidney. To support the sample storage intervals, the petitioner conducted a storage stability study with milk, muscle, fat, liver, and kidney; the results of this study are reported in the 860.1380 DER for this MRID (46708528.de2.doc). The storage stability results indicate that fortified residues of fluopicolide, BAM, and PCA are stable during frozen storage for up to 83 days in milk, 4 months in fat and muscle, and 9 months in liver and kidney. These data are adequate to support the storage intervals and conditions of samples from this feeding study.

Residues of fluopicolide were below the LOQ (<0.010 ppm) in all samples of milk and skim milk from the 5.7 ppm dose group, except for one sample of milk from study day 4 (0.013 ppm) and one sample from study day 28 (0.024 ppm). Residues of fluopicolide were below the LOQ in all samples of milk tested from the 0.5 ppm dose group (study days 1 and 4) and the 1.7 ppm dose group (study days 1, 4, 7, and 10). Residues of fluopicolide were 0.012-0.018 ppm in cream samples (study day 22) from the 5.7 ppm dose group. Fluopicolide residues were below the LOQ (<0.020 ppm) in all samples of muscle from all three dose groups, and residues were below the LOQ (<0.050 ppm) in all samples of fat, liver, and kidney from the 5.7 ppm dose group. Samples of fat, liver, and kidney from the 0.5 and 1.7 ppm dose groups were not analyzed.

Residues of BAM and PCA were below the LOQ (<0.010 ppm each) in all samples of milk, cream, and skim milk from the 5.7 ppm dose group, and in all samples of milk tested from the 0.5 ppm dose group (study days 1 and 4) and the 1.7 ppm dose group (study days 1, 4, 7, and 10). Residues of BAM and PCA were below the LOQ (<0.020 ppm each) in all samples of muscle from all three dose groups, and residues were below the LOQ (<0.050 ppm each) in all samples of fat, liver, and kidney from the 5.7 ppm dose group. Samples of fat, liver, and kidney from the 0.5 and 1.7 ppm dose groups were not analyzed.

BAM
A BAM ruminant feeding study was not submitted with this petition. Given the likelihood of measurable residues of BAM in livestock feed items as a result of treating RACs with fluopicolid, a 28-day BAM feeding study must be submitted or referenced. HED has determined that tolerances, at the limit of quantitation of the analytical method, are needed for ruminant commodities.

***Conclusions*:** The submitted fluopicolide dairy cattle feeding study data are acceptable. At the 5.7 ppm dose level, residues of fluopicolide (parent) were 0.024 ppm in milk and 0.018 ppm cream. Residues of fluopicolide were below the LOQ in all tissue samples (<0.020 ppm in muscle and <0.050 ppm in fat, liver, and kidney) from the highest dosing level, and residues of BAM and PCA were below the LOQ in all milk samples (<0.010 ppm) and tissue samples (<0.020 ppm in muscle and <0.050 ppm in fat, liver, and kidney) from the highest dosing level.

A BAM ruminant feeding study must be submitted or referenced. Pending review of the 28-day BAM ruminant feeding study, HED tentatively concludes that finite residues of BAM may be present in ruminant commodities as a result of feeding fluopicolide treated feed items. The petitioner should propose tolerances for milk, meat by products, fat and muscle of cattle, goat, horse, and sheep at the analytical method limit of quantitation (LOQ) for each commodity. The validated limits of quantitation (LOQs) for the LC/MS/MS method 303-02 for BAM are 0.01 ppm for milk, 0.02 ppm for meat, and 0.05 ppm for fat, liver, and kidney.

Poultry: Valent U.S.A. submitted a request to waive the requirements for a poultry feeding study (MRID 46708529).

EPA calculated a poultry dietary burden of 0.035 (see Table 5). The poultry feeding levels of 1 and 10 ppm in the poultry metabolism study using [2,6-^{14}C-pyridinyl]fluopicolide correspond to 29x and 286x , respectively, of the dietary burden. The poultry feeding levels of 1.2 and 10.7 ppm in the poultry metabolism study using [U-^{14}C-phenyl]fluopicolide correspond to 34x and 306x , respectively, of the dietary burden. TRR following dosing at 1 ppm using [2,6-^{14}C-pyridinyl]fluopicolide were 0.001-0.004 ppm in egg white, 0.001-0.018 ppm in egg yolk, 0.002-0.004 ppm in fat, 0.031-0.052 ppm in liver, 0.002-0.003 ppm in skin (with fat), and 0.001-0.002 ppm in muscle. TRR following dosing at 10 ppm using [2,6-^{14}C-pyridinyl]fluopicolide were 0.004-0.023 ppm in egg white, 0.004-0.104 ppm in egg yolk, 0.014-0.044 ppm in fat, 0.237-0.357 ppm in liver, 0.013-0.039 ppm in skin, and 0.007-0.015 ppm in muscle. Total radioactive residues (TRR) following dosing with [U-^{14}C-phenyl]fluopicolide at 1.2 ppm were 0.002-0.018 ppm in egg white, 0.001-0.024 ppm in egg yolk, 0.004-0.007 ppm in fat, 0.086-0.224 ppm in liver, 0.004-0.011 ppm in skin (including subcutaneous fat), and 0.003-0.006 ppm in muscle. TRR following dosing with [U-^{14}C-phenyl]fluopicolide at 10.7 ppm were 0.005-0.072 ppm in egg white, 0.003-0.224 ppm in egg yolk, 0.042-0.099 ppm in fat, 0.602-1.69 ppm in liver, 0.060-0.087 ppm in skin, and 0.031-0.047 ppm in muscle. The maximum fluopicolide (parent) residues found were in egg: 17 ppb in egg yolk, equivalent to 5.8 ppb in whole egg (31.0% yolk x 17 ppb +58.0% egg white x 1 ppb = 5.8 ppb in whole egg; North, M.O, and Bell, D. D., *Commercial Chicken Production Manual, 4th ed., 1990*). The maximum residues of BAM were 361 ppb parent equivalents (178 ppb BAM equivalents) in liver following dosing with [U-^{14}C-phenyl]fluopicolide at 10.7 ppm (306x the dietary burden).

No poultry metabolism data for the fluopicolide metabolite, BAM was submitted or referenced. However, given the very low calculated dietary BAM dietary burden, HED concludes that it is unlikely that there will be measurable residues of BAM in poultry commodities as a result of the proposed uses on fluopicolide.

Conclusions: No poultry feeding studies are required for either fluopicolide or BAM based on the available metabolism studies and the calculated dietary burdens. There is no reasonable expectation of finite residues of fluopicolide (parent) in poultry commodities [40 CFR §180.6(a)(3)].

860.1500 Crop Field Trials

Tuberous and corm vegetable, subgroup 1C
DER Reference: 46708537.der.doc

HED notes that the petitioner has requested tolerances for only potato and sweet potato, however, the submitted data support the establishment of a tolerance for the tuberous and corm vegetable crop subgroup 1C.

Valent U.S.A. Corporation has submitted field trial data for fluopicolide on potatoes. Nineteen field trials (seventeen harvest and two decline) were conducted during the 2001 growing season in the United States encompassing Zones 1 (1 trial in Pennsylvania and 1 trial in New York), 2 (1 trial in New Jersey), 3 (1 trial in Florida), 5 (1 trial in Minnesota, 1 trial in Ohio, 1 trial in Illinois, 2 trials in Wisconsin, and 1 trial in Michigan), 9 (1 trial in Colorado), 10 (1 trial in California) and 11 (2 trials in Oregon, 1 trial in Washington and 4 trials in Idaho). At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar applications of fluopicolide, formulated as a 40% suspension concentrate. Each application was made at a nominal rate of 0.119 lb ai/A for a total seasonal application rate of 0.357 lb ai/A/season (~1x the proposed rate) and the retreatment interval was 5 ± 2 days. An adjuvant was added to the spray mixture for all applications. At each trial location, one untreated control and two treated mature raw agricultural commodity (RAC) samples were collected 7 ± 1 days following the last test substance application. In addition, at two of the test sites, one control and duplicate treated RAC samples were also harvested at 2, 5, 10, and 14 days after the last application (DALA) to determine residue decline.

Potato samples were analyzed for residues of fluopicolide (parent) and its metabolites BAM and PCA using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) Method 00782/M001. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

RAC samples were stored frozen ($\leq$-20^{o}C) prior to analysis. The maximum storage interval from harvest to analysis was 896 days (30 months). A storage stability study demonstrated that residues of fluopicolide, BAM, and PCA are stable in/on potatoes stored for up to 30 months at $\leq$-18^{o}C; therefore, adequate storage stability data are available to support the storage conditions and intervals of samples from the potato field trials.

The maximum residues of fluopicolide (parent) were 0.013 in/on potatoes harvested 7-days after the last of three foliar applications of the 40% SC formulation at a total rate of 0.350 to 0.372 lb ai/A. The maximum residues of PCA were 0.045 ppm. (There are nineteen potato field trials and 38 samples. PCA was found in two samples in one field study in Pennsylvania at 0.0429 and 0.0447 ppm. The other field trials have <0.01 ppm PCA.) Residues of BAM were less than the LOQ (<0.01 ppm) in all samples. Fluopicolide-derived residues were not detected above the LOQ (0.01 ppm) in either of the two residue decline studies; therefore, residue decline could not be assessed.

The results from these field trials are discussed below and summarized in Table 6.1.

TABLE 6.1. Summary of Residue Data from Crop Field Trials with Fluopicolide.

Matrix	Total Applic. Rate (lb a.i./A)	PHI (days)	Residue Levels* (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Fluopicolide									
Potatoes	0.350 to 0.372	6 to 8	38	<0.01	0.0126	<0.01	<0.01	<0.01	0.0012
BAM (AE C653711)									
Potatoes	0.350 to 0.372	6 to 8	38	<0.01	<0.01	NA	NA	NA	NA
PCA (AE C657188)									
Potatoes	0.350 to 0.372	6 to 8	38	<0.01	0.0447	0.0438	<0.01	< 0.010	0.009

HAFT = Highest Average Field Trial.
Statistical calculations were performed using a value of ½ LOQ when residues were reported as <LOQ or <LOD.
LOQ = 0.01 ppm for fluopicolide, BAM and PCA.
LOD = 0.003 ppm for fluopicolide, 0.004 ppm for BAM and 0.002 ppm for PCA.
Note: BAM and PCA are not expressed as parent equivalents.
PCA was found in two samples in one field study in Pennsylvania at 0.0429 and 0.0447 ppm. The other field trials have <0.01 ppm PCA.

Conclusions: The maximum residues of fluopicolide (parent) were 0.013 in/on potatoes harvested 7-days after the last of three foliar applications of the 40% SC formulation at a total rate of 0.350 to 0.372 lb ai/A. The maximum residues of PCA were 0.045 ppm. (There are nineteen potato field trials and 38 samples. PCA was found in two samples in one field study in Pennsylvania at 0.0429 and 0.0447 ppm. The other field trials have <0.01 ppm PCA.) Residues of BAM were less than the LOQ (<0.01 ppm) in all samples. Fluopicolide-derived residues were not detected above the LOQ (0.01 ppm) in either of the two residue decline studies; therefore, residue decline could not be assessed.

The submitted field trial data reflect the use of three foliar applications of the 40% SC formulation of fluopicolide (EXP 11067B) at total rates of ~0.357 lb ai/A on potatoes grown in the United States with a 7 ± 1-day PHI. An acceptable method was used for quantitation of residues in/on potatoes. The submitted storage stability data (refer to the DER for MRIDs 46474036-46474037) indicate that residues of fluopicolide, BAM, and PCA are stable in/on potatoes stored frozen for up to ~30 months at ≤-18 °C. The available storage stability data support the storage intervals of samples from the potato field trials.

The number and locations of the potato field trials are in accordance with OPPTS Guideline 860.1500 to support a tolerance for the tuberous and corm crop subgroup 1C. The use pattern of the field trials adequately reflects the use pattern proposed for tuberous and corm vegetables.

The residues values of fluopicolide were below the LOQ in/on all potato tuber samples, except for one sample in which the residue was detected at 0.013, ppm. Therefore, the tolerance setting as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP was not used since dataset with LOQ >60% would be unreliable. However, the available field trial data will support a tolerance of 0.02 ppm for residues of fluopicolide *per se* in/on tuberous and corm vegetables, subgroup 1C, based on the highest residue value observed in the field trial data.

Leafy vegetable, except *Brassica*, group 4

DER Reference: 46708533.der.doc (Head lettuce)
46708534.der.doc (Leaf lettuce)
46708539.der.doc (Celery)
46708540.der.doc (Spinach)

Valent has submitted magnitude of the residue studies for celery, head lettuce, leaf lettuce, and spinach, the representative crops of group 4. The results from these field trials are discussed below and summarized in Table 6.2. HED notes that the field trial data were conducted prior to a determination of the metabolites to be regulated in leafy vegetables. Subsequently, the Fluopicolide Risk Assessment Team concluded that PCA was not a regulated metabolite in leafy vegetables; however, the data on PCA residues are included here since they were provided by the petitioner.

Table 6.2. Summary of Residue Data from Group 4 Crop Field Trials with Fluopicolide.									
Commodity	Total Applic. Rate (lb ai/A) [kg ai/ha]	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
CELERY (proposed use = 0.375 lb ai/A total application rate, 10-day minimum RTI, 2-day PHI)									
Fluopicolide									
Celery	0.354-0.365 [0.397-0.410]	2	12	0.325	13.6	9.9	3.13	4.05	3.93
BAM									
Celery	0.354-0.365 [0.397-0.410]	2	12	<0.01	0.041	0.039	NA	NA	NA
PCA									
Celery	0.354-0.365 [0.397-0.410]	2	12	<0.01	0.024	0.020	NA	NA	NA
HEAD LETTUCE (proposed use = 0.375 lb ai/A total application rate, 10-day minimum RTI, 2-day PHI)									
Fluopicolide									
Head lettuce	0.350-0.368 (0.392-0.414)	2	14	0.455	7.15	6.34	2.39	2.68	2.06
BAM									
Head lettuce	0.350-0.368 (0.392-0.414)	2	14	<0.01	0.0132	0.012	<0.01	<0.01	NA
PCA									
Head lettuce	0.350-0.368 (0.392-0.414)	2	14	<0.01	<0.01	NA	NA	NA	NA
LEAF LETTUCE (proposed use = 0.375 lb ai/A total application rate, 10-day minimum RTI, 2-day PHI)									
Fluopicolide									
Leaf lettuce	0.349-0.364 [0.391-0.408]	2	14	0.444	11.7	9.78	6.43	6.37	2.96
BAM									
Leaf lettuce	0.349-0.364 [0.391-0.408]	2	14	<0.01	0.038	0.031	<0.01	0.012	0.010
PCA									
Leaf lettuce	0.349-0.364 [0.391-0.408]	2	14	<0.01	<0.01	<0.01	NA	NA	NA
SPINACH (proposed use = 0.375 lb ai/A total application rate, 10-day minimum RTI, 2-day PHI)									
Fluopicolide									
Spinach	0.357-0.365 [0.400-0.410]	2	14	5.43	16.8	16.2	8.53	9.71	3.87
BAM									
Spinach	0.357-0.365 [0.400-0.410]	2	14	0.022	0.188	0.170	0.065	0.072	0.047
PCA									
Spinach	0.357-0.365 [0.400-0.410]	2	14	<0.01	0.119	0.076	0.013	0.022	0.025

[1] HAFT = Highest average field trial result.

Celery: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on celery.

Seven field trials (six harvest and one decline) were conducted in the United States during the 2002 growing season in Zones 3 (1 trial in Florida), 5 (1 trial in Michigan) and 10 (5 trials in California). At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar applications of fluopicolide formulated as a 40% suspension concentrate of fluopicolide (active ingredient), with a 5 ± 2 day retreatment interval. Each application was made at a nominal rate of 0.119 lb ai/A for a total seasonal application rate of 0.357 lb ai/A/season (~1x the proposed rate). An adjuvant was added to the spray mixture for all applications. At each trial location, one untreated control and two treated mature celery raw agricultural commodity (RAC) samples were collected 2 days following the last test substance application [2-day pre-harvest interval (PHI)]. In addition, at one of the California test sites, one control and one treated RAC sample were also harvested at 1, 3, 5, and 7 days after the last application (DALA) to determine residue decline.

Celery samples were analyzed for residues of fluopicolide (parent) and its metabolites BAM and PCA using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS), method METH1611-00.02. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries. The LOQ was 0.01 ppm for each analyte in celery).

Samples were stored frozen ($\leq$ - 20^{o}C) prior to analysis; the maximum storage interval from harvest to extraction was 1,149 days (38 months). No storage stability data specific for celery are available. Residues of fluopicolide, BAM, and PCA are stable in/on cabbage leaves [*Brassica* (Cole) Leafy Vegetable Crop Group] and grapes stored frozen at ≤-18 °C for up to 30 months. The storage interval in the cabbage leaf/grape storage stability study was approximately 8 months less than the maximum storage interval in the celery crop field trial study.

The maximum average residues of fluopicolide (parent), BAM, and PCA were 9.85 ppm, 0.039 ppm and 0.020 ppm in/on celery harvested 2 days after the last of three foliar applications of the 40% SC formulation (EXP 11067B) at a total rate of 0.354 to 0.365 lb ai/A.

Residues of fluopicolide increased as PHI increased in the decline study samples. The petitioner did not provide an explanation for this observation.

Head lettuce: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on head lettuce. Seven field trials (six harvest and one decline) were conducted during the 2002 growing season in the United States: 1 trial in New York (Zones 1), 1 trial in Florida (Zone 3), and 5 trials in California (Zone 10). Each test location contained control and treated plots. EXP 11067B is formulated as a 4 lb ai/gal suspension concentrate (SC). Three foliar spray applications were made with fluopicolide 5 ± 2 days apart to each treated plot at a target rate of 0.119 lb ai/A/application. The achieved total seasonal rates ranged from 0.350 to 0.368 lb ai/A (~1x the proposed rate). An adjuvant was added to the spray mixture for all applications.

At each trial location, two control and four treated mature head lettuce raw agricultural commodity (RAC) samples were collected 2 days following the last test substance application [2-day preharvest interval (PHI)]. One control and two treated samples were harvested with wrapper leaves intact, and one control and two treated samples were harvested and all wrapper leaves were removed. In addition, at the Florida test site, head lettuce RAC samples were harvested with and without wrapper leaves at 1, 3, 5, and 7 days after the last application to

determine residue decline.

Head lettuce samples were analyzed to quantify residues of fluopicolide (parent) and its metabolites AE C653711 (BAM) and AE C657188 (PCA) with high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) Method 00782/M001. Method verification was performed prior to sample analysis and concurrent recoveries were performed during sample analysis to demonstrate acceptable method performance. The limit of quantitation (LOQ) was 0.01 ppm for each analyte for head lettuce.

Head lettuce samples were stored frozen prior to analysis; the maximum storage interval from harvest to analysis was 878 days (29 months). The Analytical Report stated that the samples were stored frozen at $\leq$-20 ^{o}C. No storage stability data are available for head lettuce; however, residues of fluopicolide, BAM, and PCA are stable in/on cabbage leaves [*Brassica* (Cole) leafy crop vegetable Crop Group] and grapes stored frozen at $\leq$ -18 ^{o}C for up to 30 months. Adequate storage stability data are available on cabbage and grapes to support the storage conditions and intervals of samples from the head lettuce field trials.

In head lettuce samples collected with wrapper leaves, the highest average field trial fluopicolide-derived residue was 6.34 ppm with a maximum residue of 7.15 ppm at the proposed PHI of 2 ± 1 days. Residues of BAM were less than the LOQ in all but two samples. The maximum BAM residue of these two samples was 0.0132 ppm. Residues of PCA were less than the LOQ in all samples. In head lettuce samples collected without wrapper leaves, the highest average field trial fluopicolide-derived residue was 0.31 ppm with a maximum residue of 0.324 ppm. Residues of BAM and PCA were less than the LOQ in all samples. Residue decline data showed no general tendency to increase or decline with increasing pre-harvest intervals. However, it should be noted that for both the head lettuce samples collected with wrappers and those collected without wrappers, residues spiked at 2-3 days after the last application (DALA) and then decreased to 1 DALA levels.

The results of the head lettuce field trials are presented in Table 6.2. In/on samples of head lettuce with wrapper leaves harvested 2 days after the last of three foliar applications of the 4 lb/gal FlC formulation at a total rate of 0.350-0.368 lb ai/A (~1x), the maximum residues of fluopicolide were 7.15 ppm. The maximum residues of BAM were 0.013 ppm and residues of PCA were <LOQ in/on all samples. In/on samples of head lettuce without wrapper leaves, the maximum fluopicolide residues were 0.324 ppm; residues of BAM and PCA were <LOQ in/on all samples.

In the residue decline samples, the maximum observed fluopicolide residues occurred at the 3-day PHI in/on samples with wrapper leaves and at the 2-day PHI in/on samples without wrapper leaves. Residues of BAM and PCA were below the LOQ in/on all residue decline samples.

Leaf lettuce: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on leaf lettuce. Seven field trials (six harvest and one decline) were conducted in the United States encompassing Zones 1 (1 trial in New York), 3 (1 trial in Florida) and 10 (5 trials in California) during the 2002 growing season. At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar spray applications of fluopicolid, formulated as a 40% suspension concentrate (SC) of fluopicolide (active ingredient), at 5 ± 2 day retreatment intervals. Each application was performed at a nominal application rate of 0.119

ai/A, in spray volumes ranging from 19.2 to 23.9 gal/A. The achieved total seasonal application rates ranged from 0.349 to 0.364 lb a.i./A/season (~1x the proposed rate). An adjuvant was added to the spray mixture for all applications.

At each trial location, one untreated control and two treated mature leaf lettuce raw agricultural commodity (RAC) samples were collected 2 days following the last test substance application [2-day preharvest interval (PHI)]. In addition, at one of the California test sites, one control and duplicate treated mature leaf lettuce samples were also harvested at 1, 3, 5 and 7 days after the last application to determine residue decline.

Leaf lettuce samples were analyzed for residues of fluopicolide (parent) and its metabolites BAM (AE C653711) and PCA (AE C657188) using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) Method 00782/M001. Method validation was performed prior to sample analysis using head lettuce samples and concurrent recoveries were performed during sample analysis. The limit of quantitation (LOQ) was 0.01 ppm for each analyte for leaf lettuce. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Leaf lettuce samples were stored frozen ($\leq$ -20^{o}C) prior to analysis; the maximum storage interval from harvest to extraction was 877 days (29 months). No storage stability data are available for leaf lettuce; however, residues of fluopicolide, BAM and PCA are stable in/on cabbage leaves [*Bassica* (Cole) Leafy Vegetable Crop Group] and grapes stored frozen at <-18°C for 30 months. Adequate stability data are available on cabbage and grapes to support the storage conditions and intervals of samples from the leaf lettuce field trials.

The maximum residue of fluopicolide was 11.7 ppm in/on leaf lettuce harvested 2 days after the last of three foliar applications of the 40% SC formulation (EXP 11067B) at a total rate of 0.349 to 0.364 lb a.i./A. The maximum residue of BAM was 0.038 ppm. Residues of PCA were less than the limit of quantitation (0.01 ppm) in/on all leaf lettuce samples. Residue decline data show that fluopicolide (parent) residues generally decrease with increasing preharvest intervals.

Spinach: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on spinach. Seven field trials (six harvest and one decline) were conducted in the United States encompassing Zones 1 (1 trial in New Jersey), 2 (1 trial in Virginia), 6 (2 trials in Texas), 9 (1 trial in Colorado), and 10 (1 trial in Arizona and 1 trial in California) during the 2002 growing season. At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar applications of fluopicolid, formulated as a 4 lb ai/gal suspension concentrate, at 5 ± 1 day retreatment intervals. Each application was performed at a nominal application rate of 0.119 lb ai/A, for a total seasonal application rate of 0.357 to 0.365 lb ai/A/season (~1x the proposed rate). A spreader/sticker was added to the spray mixture for all applications. At each trial location, one untreated control and two treated spinach raw agricultural commodity (RAC) samples were collected 2 days following the last test substance application [2-day preharvest interval (PHI)]. In addition, at the Virginia test site, one control and duplicate treated spinach samples were also harvested at 1, 3, 5, and 7 days after the last application to determine residue decline.

Spinach samples were analyzed for residues of fluopicolide (parent) and its metabolites BAM (AE C653711) and PCA (AE C657188) via high pressure liquid chromatography/triple stage

quadropole mass spectrometry (HPLC/MS/MS) detection, method METH1611-00.02. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries. The LOQ was 0.01 ppm for each analyte in spinach.

Samples were stored frozen (≤- 20°C) prior to analysis for a maximum of 1169 days (38 months) from harvest to analysis. Storage stability on spinach are not available. Residues of fluopicolide, BAM, and PCA are stable in/on cabbage leaves [*Brassica* (Cole) Leafy Vegetable Crop Group] and grapes stored frozen at ≤-18 °C for 30 months. The storage interval in the cabbage/grape storage stability study was approximately 8 months less than the maximum storage interval in the spinach crop field trial study.

The maximum residue of fluopicolide was 16.8 ppm in/on spinach harvested 2 days after the last of three foliar applications of the 40% SC formulation (EXP 11067B) at a total rate of 0.357 to 0.365 lb a.i./A. The maximum residues of BAM and PCA were 0.188 ppm and 0.119 ppm (after 3 days), respectively. Residue decline data showed that parent fluopicolide residues generally decrease with increasing preharvest intervals, BAM residues remain relatively constant with increasing preharvest intervals, and PCA residues generally increase with increasing preharvest intervals.

***Conclusions*:** Adequate storage stability data are available on cabbage and grapes to support the storage conditions and intervals of samples from the head lettuce and leaf lettuce field trials. Pending submission of storage stability data for a representative leafy vegetable to support the 38-month frozen storage interval of celery and spinach, the submitted leafy vegetable field trial data are adequate.

Residues of fluopicolide (parent) in/on untrimmed celery harvested at a 2-day PHI, ranged from 0.325 ppm to 13.6 ppm. Residues of BAM ranged from <0.01 ppm to 0.041 ppm (residues were only detected above the LOQ in samples from two sites) and residues of PCA ranged from <0.01 ppm to 0.024 ppm (residues were only detected above the LOQ in samples from one site). Residues of fluopicolide, BAM and PCA were nonquantifiable (<0.01 ppm) in/on all untreated celery samples. Residues of fluopicolide increased as PHI increased in the decline study samples. The petitioner did not provide an explanation for this observation. Storage stability data were not provided for celery. Although storage stability data were provided for cabbage leaves and grapes, the storage interval in the storage stability studies (30 months) does not reflect the maximum storage duration in the celery crop field trial study (38 months).

Residue data in/on head lettuce with wrappers ranged from 0.455 to 7.15 ppm for fluopicolide (parent). Residues of the metabolite PCA were less than LOD in all samples. Residues of the metabolite BAM were slightly above the LOQ in two samples (0.0116 and 0.0132 ppm) and were less than the LOQ in all remaining samples. In three samples, BAM residues were between LOD and LOQ (range of 0.0058 to 0.0094). In head lettuce samples without wrappers, residues of fluopicolide (parent) ranged from < 0.01 to 0.324 ppm. Residues of both the metabolites PCA and BAM were nonquantifiable (<0.01 ppm) for all without-wrapper samples. For the residue decline study, average fluopicolide residues show no general tendency to increase or decline with increasing pre-harvest intervals. No storage stability data are available for head lettuce; however, adequate stability data are available on cabbage and grapes to support the storage conditions and intervals of samples from the head lettuce field trials.

The residues of fluopicolide (parent) in/on leaf lettuce were greater than the LOQ in all samples, with residues ranging from 0.444 to 11.7 ppm. Residues of the metabolite BAM were greater than the LOQ in half of the samples, with a maximum residue of 0.038 ppm. BAM residues in the remaining samples were <LOQ, with residues in six of the samples between the LOD and LOQ (0.00639 ppm to 0.00995 ppm). Residues of the metabolite PCA were less than the LOQ in/on all samples, with residues between the LOD and LOQ in four of the samples (0.00173 ppm and 0.00789 ppm). In the residue decline study, fluopicolide residues showed a general decline with increasing preharvest intervals, decreasing from 5.50 ppm one day after the last application to 2.33 ppm seven days after the last application. No storage stability data are available for leaf lettuce; however, adequate stability data are available on cabbage and grapes to support the storage conditions and intervals of samples from the leaf lettuce field trials. Residues of fluopicolide, BAM and PCA are stable in/on cabbage leaves [*Brassica* (Cole) Leafy Vegetable Crop Group] and grapes stored frozen at <-18°C for 30 months.

Residues of fluopicolide (parent) and BAM in/on spinach at the 2-day PHI were greater than the LOQ in all samples, ranging from 5.43 to 16.80 ppm for fluopicolide and ranging from 0.022 to 0.188 ppm for BAM. Residues of PCA were less than the LOD in 3 samples and between the LOD and LOQ in 3 samples (range of 0.00822 ppm to 0.00915 ppm). PCA residues in the remaining samples collected at a 2-day PHI ranged from 0.0131 ppm to 0.0899 ppm. Residues of fluopicolide, BAM and PCA were nonquantifiable (<0.01 ppm) in/on all untreated spinach samples. Residue decline data showed that parent fluopicolide residues generally decrease with increasing preharvest intervals, BAM residues remain relatively constant with increasing preharvest intervals, and PCA residues generally increase with increasing preharvest intervals. Storage stability data were not provided for spinach. Although storage stability data were provided for cabbage leaves and grapes, the storage interval in the storage stability studies (30 months) does not reflect the maximum storage duration in the spinach crop field trial study (38 months). The submitted spinach field trial data are adequate pending submission of storage stability data for spinach or any representative leafy vegetable stored frozen for 38 months,.

The number and locations of the leafy vegetable field trials are in accordance with OPPTS Guideline 860.1500 for leafy vegetable, except *Brassica*, group 4. The use pattern of the field trials adequately reflects the use pattern proposed for leafy vegetables. The *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, along with the tolerance spreadsheet, was used to calculate the recommended tolerance for the leafy vegetables, except brassica group. The available field trial data will support a tolerance for residues of fluopicolide *per se* in/on leafy vegetable, except *Brassica*, group 4 at 25 ppm. The tolerance calculation for leafy vegetables is presented in Appendix II.

Fruiting vegetable, group 8

DER Reference: 46708530.der.doc (Bell pepper)
46708535.der.doc (Chili pepper)
46708536.der.doc (Tomato)

Valent has submitted magnitude of the residue studies for bell pepper, non-bell (chili) pepper, and tomato, the representative crops of group 8. The results from these field trials are discussed below and summarized in Table 6.3. While PCA is not a regulated metabolite, residues for PCA are included here as they were provided by the registrant for completeness.

Table 6.3. Summary of Residue Data from Group 8 Crop Field Trials with Fluopicolide.

Commodity	Total Applic. Rate (lb ai/A) [kg ai/ha]	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
BELL PEPPER (proposed use = 0.375 lb ai/A total application rate, 7-day minimum RTI, 2-day PHI)									
Fluopicolide									
Bell pepper	0.349-0.358 [0.391-0.401]	2	14	0.0411	0.557	0.523	0.099	0.156	0.163
BAM									
Bell pepper	0.349-0.358 [0.391-0.401]	2	14	<0.01	<0.01	NA	NA	NA	NA
PCA									
Bell pepper	0.349-0.358 [0.391-0.401]	2	14	<0.01	<0.01	NA	NA	NA	NA
CHILI PEPPER (proposed use = 0.375 lb ai/A total application rate, 7-day minimum RTI, 2-day PHI)									
Fluopicolide									
Chili pepper	0.355-0.363 [0.398-0.407]	2	6	0.0837	0.576	0.516	0.300	0.302	0.198
BAM									
Chili pepper	0.355-0.363 [0.398-0.407]	2	6	<0.01	<0.01	NA	NA	NA	NA
PCA									
Chili pepper	0.355-0.363 [0.398-0.407]	2	6	<0.01	<0.01	NA	NA	NA	NA
TOMATO (proposed use = 0.375 lb ai/A total application rate, 7-day minimum RTI, 2-day PHI)									
Fluopicolide									
Tomato	0.356-0.368 [398.9-412.8]	2	24	0.015	0.420	0.375	0.145	0.150	0.094
BAM									
Tomato	0.356-0.368 [398.9-412.8]	2	24	<0.01	<0.01	NA	NA	NA	NA
PCA									
Tomato	0.356-0.368 [398.9-412.8]	2	24	<0.01	0.013	0.012	NA	NA	NA

[1] HAFT = Highest average field trial result.

Bell pepper: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on bell

peppers. Seven field trials (six harvest and one decline) were conducted in the United States encompassing Zones 2 (1 trial in Georgia), 3 (1 trial in Florida), 5 (1 trial in Ohio), 6 (1 trial in Texas), and 10 (3 trials in California) during the 2002 growing season. At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar applications of EXP 11067B, formulated as a 4 lb ai/gal suspension concentrate (SC), at 5 ± 1 day retreatment intervals. Each application was performed at a nominal application rate of 0.119 lb ai/A, for a total seasonal application rate of 0.357 lb ai/A/season. An adjuvant was added to the spray mixture for all applications. At each trial location, one untreated control and two treated mature bell pepper raw agricultural commodity (RAC) samples were collected 2 days following the last test substance application [2-day preharvest interval (PHI)]. In addition, at one of the California test sites, one control and duplicate treated mature bell pepper samples were also harvested at 1, 3, 5, and 7 days after the last application to determine residue decline.

Bell pepper samples were analyzed for residues of fluopicolide (parent) and its metabolites BAM (AE C653711) and PCA (AE C657188) using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) Method 00782/M001. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Samples were stored frozen (≤ -20 °C) prior to analysis; the maximum storage interval from harvest to analysis was 554 days (19 months). No storage stability data are available for bell peppers.

The maximum residue of fluopicolide was 0.557 ppm in/on bell peppers harvested 2 days after the last of three foliar applications of the 40% SC formulation (EXP 11067B) at a total rate of 0.349 to 0.358 lb ai/A. Residues of BAM and PCA were each less than the limit of quantitation (0.01 ppm) in all samples. Residue decline data show that fluopicolide residues generally decrease with increasing preharvest intervals.

Chili pepper: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on chili peppers. Three field trials were conducted in the United States encompassing Zones 8 (1 trial in Texas), 9 (1 trial in Arizona) and 10 (1 trial in California) during the 2002 growing season. At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar applications of EXP 11067B, formulated as a 40% suspension concentrate (SC) of fluopicolide (active ingredient) at 5 day retreatment intervals. Each application was performed at a nominal application rate of 0.119 lb a.i./A in spray volumes ranging from 30.1 to 41.7 gal/A. The achieved total seasonal rates ranged from 0.355 to 0.363 lb a.i./A. An adjuvant was added to the spray mixture for all applications.

At each trial location, one untreated and two treated mature chili pepper raw agricultural commodity (RAC) samples were collected two days following the last test substance application [2-day preharvest interval (PHI)].

Chili pepper samples were analyzed for residues of fluopicolide (AE C653206) and its metabolites BAM (AE C653711) and PCA (AE C657188) using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) Method 00782/M001. Method verification was performed prior to sample analysis and concurrent recoveries were performed during sample analysis to demonstrate acceptable method performance. The limit of quantitation (LOQ) was 0.01 ppm for each analyte for chili peppers.

The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Chili pepper samples were stored frozen prior to analysis; the maximum storage interval from harvest to analysis was 508 days (17 months) prior to extraction. The samples were stored frozen at $\leq$-20°C. No storage stability data are available on chili peppers.

Fluopicolide residues were determined in/on chili peppers harvested at the proposed PHI of 2 days after the last of three foliar applications of the SC formulation (EXP 11067B) at a total rate of 0.355 to 0.363 lb a.i./A. The highest average field trial residue of fluopicolide was 0.516 ppm and the maximum residue of fluopicolide was 0.576 ppm. Residues of BAM and PCA were each less than the limit of quantitation (0.01 ppm) in all samples.

Tomato: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on tomatoes. Twelve field trials (ten harvest and two decline) were conducted in the United States encompassing Zones 1 (1 trial in Pennsylvania), 2 (1 trial in South Carolina), 3 (2 trials in Florida), 5 (1 trial in Michigan), and 10 (7 trials in California) during the 2001 growing season. At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar applications of EXP 11067B, formulated as a 40% suspension concentrate (SC) of fluopicolide (active ingredient), at 5 ± 1 day retreatment intervals. Each application was performed at a nominal application rate of 0.119 lb a.i./A, in spray volumes ranging from 19.9 to 45.3 gal/A. The achieved total seasonal rates ranged from 0.356 to 0.368 lb a.i./A. An adjuvant was added to the spray mixture for all applications.

At each trial location, one untreated and two treated mature tomato raw agricultural commodity (RAC) samples were collected two days following the last test substance application [2-day preharvest interval (PHI)]. In addition, at two California test sites (Trials 27776-08 and 27776-09), tomato RAC samples were harvested at 1, 3, 5, and 7 days after the last application to determine residue decline.

Tomato samples were analyzed for residues of fluopicolide (AE C653206) and its metabolites BAM (AE C653711) and PCA (AE C657188) using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) Method 00782/M001. The limit of quantitation (LOQ) was 0.01 ppm for each analyte for tomatoes. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Tomato samples were stored frozen prior to analysis; the maximum storage interval from harvest to extraction was 646 days (21 months). Samples were stored frozen at the field sites for 2 days to 4 months at temperatures ranging from -34°F to 26.5°F, prior to storage at the laboratory at <-15°C. No storage data are available for tomatoes (RAC).

The highest average field trial residue of fluopicolide was 0.375 ppm and the maximum residue of fluopicolide was 0.420 ppm in/on tomatoes harvested 2 days after the last of three foliar applications of the SC formulation (EXP 11067B) at a total rate of 0.356 to 0.368 lb a.i./A. Residues of BAM were less than the limit of quantitation (0.01 ppm) in all samples. Residues of PCA were less than the limit of quantitation (0.01 ppm) in all but one sample. PCA was found in one tomato sample from Trial 27776-1008 at a concentration of 0.013 ppm. Residue decline data shows a general tendency of fluopicolide residues to decrease with increasing preharvest

intervals.

***Conclusions*:** The submitted fruiting vegetable field trial data are adequate.

Residues of fluopicolide (parent) were greater than the LOQ in all the bell pepper field samples, ranging from 0.0411 to 0.557 ppm. Residues of the metabolite BAM were less than LOD in all samples and residues of the metabolite PCA were less than the LOQ in all samples. In 5 samples, PCA residues were between the LOD and LOQ (range of 0.00328 ppm to 0.00569 ppm). Residues of fluopicolide, BAM and PCA were nonquantifiable (<0.01 ppm) in/on all untreated bell pepper samples. For the residue decline study, average fluopicolide residues showed a general decline with increasing preharvest intervals, decreasing from an average of 0.571 ppm one day after the last application to 0.380 ppm seven days after the last application. Storage stability data were not provided for bell peppers; however, storage stability data on cabbage leaves, grapes, and tomato paste and puree, which indicated stability of fluopicolide, BAM, and PCA at <-18°C for 30 months, will be used to support bell peppers.

Residues of fluopicolide (parent) were greater than the LOQ in all samples, ranging from 0.0837 to 0.576 ppm. Residues of the metabolite BAM and PCA were each less than the LOD in all samples. Residues of fluopicolide, BAM and PCA were nonquantifiable (<0.01 ppm) in/on all untreated chili pepper samples. Storage stability data were not provided for chili peppers; however, storage stability data on cabbage leaves, grapes, and tomato paste and puree, which indicated stability of fluopicolide, BAM, and PCA at <-18°C for 30 months, will be used to support chili peppers.

At the 2-day PHI, residues of fluopicolide (parent) were greater than the LOQ in all samples, ranging from 0.015 to 0.420 ppm. Residues of the metabolite BAM were less than the LOQ in all samples. Residues of the metabolite PCA were less than the LOQ in all samples except one at 0.013 ppm. Residues of fluopicolide, BAM and PCA were non-quantifiable (<0.01 ppm) in/on all untreated tomato samples. Residue decline data shows a general tendency of AE C638206 residues to decrease with increasing pre-harvest intervals. Storage stability data were not provided for the raw agricultural commodity (RAC) tomato but storage stability data on tomato paste and puree, which indicated stability of fluopicolide, BAM, and PCA <-18°C for 30 months, will be used to support the RAC.

The number and representative geographical locations of the field trials are in accordance with OPPTS Guideline 860.1500 in/on the fruiting vegetable group. The use pattern of the field trials adequately reflects the use pattern proposed for fruiting vegetables. The available field trial data will support a tolerance for residues of fluopicolide in/on fruiting vegetable group 8 at 1.6 ppm; the tolerance calculation for fruiting vegetables is presented in Appendix II.

Cucurbit vegetable, group 9

DER Reference: 46708531.der.doc (Cantaloupe)
46708532.der.doc (Cucumber)
46708538.der.doc (Squash)

Valent has submitted magnitude of the residue studies for cantaloupe, cucumber, and summer squash, the representative crops of group 9. The results from these field trials are discussed below and summarized in Table 6.4.

Table 6.4. Summary of Residue Data from Group 9 Crop Field Trials with Fluopicolide.

Commodity	Total Applic. Rate (lb ai/A) [kg ai/ha]	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
CANTALOUPE (proposed use = 0.375 lb ai/A total application rate, 10-day minimum RTI, 2-day PHI)									
Fluopicolide									
Cantaloupe	0.352-0.362 [0.395-0.406]	2	18	<0.01	0.258	0.181	0.055	0.068	0.061
BAM									
Cantaloupe	0.352-0.362 [0.395-0.406]	2	18	<0.01	<0.01	NA	NA	NA	NA
PCA									
Cantaloupe	0.352-0.362 [0.395-0.406]	2	18	<0.01	<0.01	NA	NA	NA	NA
CUCUMBER (proposed use = 0.375 lb ai/A total application rate, 10-day minimum RTI, 2-day PHI)									
Fluopicolide									
Cucumber	0.349-0.361 (0.391-0.405)	2	12	<0.01	0.057	0.050	0.020	0.024	0.0147
BAM									
Cucumber	0.349-0.361 (0.391-0.405)	2	12	<0.01	<0.01	NA	NA	NA	NA
PCA									
Cucumber	0.349-0.361 (0.391-0.405)	2	12	<0.01	<0.01	NA	NA	NA	NA
SUMMER SQUASH (proposed use = 0.375 lb ai/A total application rate, 10-day minimum RTI, 2-day PHI)									
Fluopicolide									
Summer squash	0.354-0.367 [0.399-0.411]	2	12	0.0135	0.0506	0.0448	0.0322	0.0301	0.0120
BAM									
Summer squash	0.354-0.367 [0.399-0.411]	2	12	<0.01	<0.01	NA	NA	NA	NA
PCA									
Summer squash	0.354-0.367 [0.399-0.411]	2	12	<0.01	0.0207	0.0173	<0.01	<0.01	0.0060

[1] HAFT = Highest average field trial result.

Cantaloupe: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on cantaloupe. Nine field trials (eight harvest and one decline) were conducted in the United States

encompassing Zones 2 (1 trial in North Carolina), 5 (1 trial in Illinois), 6 (2 trials in Texas), and 10 (1 trial in Arizona and 4 trials in California) during the 2002 growing season. At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar applications of EXP 11067B, formulated as a 40% suspension concentrate (SC) of fluopicolide (active ingredient), at 5 ± 1 day retreatment intervals. Each application was made at a nominal rate of 0.119 lb ai/A for a total seasonal application rate of 0.357 lb ai/A/season. An adjuvant was added to the spray mixture for all applications. At each trial location, one untreated control and two treated mature cantaloupe raw agricultural commodity (RAC) samples were collected 2 days following the last test substance application [2-day preharvest interval (PHI)]. In addition, at one of the California test sites, one control and duplicate treated mature cantaloupe samples were also harvested at 1, 3, 5, and 7 days after the last application (DALA) to determine residue decline.

Cantaloupe samples were analyzed for residues of fluopicolide (parent) and its metabolites BAM (AE C653711) and PCA (AE C657188) using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) Method 00782/M001. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Samples were stored frozen (≤ -20°C) prior to analysis; the maximum storage interval from harvest to extraction was 560 days (19 months). No storage stability data are available for cantaloupe.

The maximum average residue of fluopicolide (parent) was 0.258 ppm in/on cantaloupes harvested 2 days after the last of three foliar applications of the 40% SC formulation (EXP 11067B) at a total rate of 0.355 to 0.362 lb ai/A. Residues of BAM and PCA were each less than the limit of quantitation (0.01 ppm) in all samples.

In the residue decline study, the fluopicolide residues increased and decreased throughout the 7-day residue decline period. At the end of the decline period (7 DALA), average residues were only slightly less than average residues on 1 DALA.

Cucumber: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on cucumbers. Six field trials (five harvest and one residue decline) were conducted in the United States during the 2002 growing season. Two trials were conducted in North Carolina and Georgia (Zone 2), 1 trial in Florida (Zone 3), 1 trial each in Illinois and Michigan (Zone 5) and 1 trial in Texas (Zone 6). Each test location contained one control and one treated plot. The treated plots received three broadcast foliar applications of EXP 11067B, formulated as a 40% suspension concentrate (SC), at 5 ± 2 day retreatment intervals. Each application was made at a nominal rate of 0.119 lb ai/A for a total seasonal application rate of 0.357 lb ai/A/season. An adjuvant was added to the spray mixture for all applications.

At each trial location, one untreated control and two treated mature raw agricultural commodity (RAC) samples were collected 2 days following the last test substance application [2-day pre-harvest interval (PHI)]. In addition, at the Georgia test site, one control and duplicate treated RAC samples were also harvested at 1, 3, 5, and 7 days after the last application to determine residue decline.

Cucumber samples were analyzed to quantify residues of fluopicolide (parent) and its

metabolites AE C653711 (BAM) and AE C657188 (PCA) with high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) using Method 00782/M001. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

RAC samples were stored frozen (≤-20°C) prior to analysis. The maximum storage interval from harvest to analysis was 597 days (20 months). No storage stability data are available for cucumber.

The maximum residue of fluopicolide was 0.057 ppm in/on cucumber harvested 2 days after the last of three foliar applications of the 40% SC formulation (EXP 11067B) at a total rate of 0.349 to 0.361 lb ai/A. Residues of BAM and PCA were each less than the limit of quantitation (0.01 ppm) in all samples. Residue decline data show that fluopicolide residues generally decrease with increasing preharvest intervals.

Summer squash: Valent U.S.A. Corporation has submitted field trial data for fluopicolide on summer squash. A total of six field trials (five harvest and one decline) were conducted during the 2002 growing season in the United States: 1 trial in Pennsylvania (Zones 1), 1 trial in North Carolina (Zone 2), 1 trial in Georgia (Zone 2), 1 trial in Florida (Zone 3), 1 trial in Wyoming (Zone 5), and 1 trial in California (Zone 10). At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar applications of EXP 11067B, formulated as a 40% suspension concentrate (SC), at 5 ± 2 day retreatment intervals. Each application was made at a nominal rate of 0.119 lb ai/A for a total seasonal application rate of 0.357 lb ai/A/season. An adjuvant was added to the spray mixture for all applications. At each trial location, one untreated control and two treated mature raw agricultural commodity (RAC) samples were collected 2 days following the last test substance application [2-day pre-harvest interval (PHI)]. In addition, at one test site, one control and duplicate treated RAC samples were also harvested at 1, 3, 5, and 7 days after the last application to determine residue decline.

Squash samples were analyzed for residues of fluopicolide (parent) and its metabolites BAM (AE C653711) and PCA (AE C657188) using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) Method 00782/M001. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

RAC samples were stored frozen prior to analysis. The maximum storage interval from harvest to extraction was 624 days (21 months). The Analytical Report stated that the samples were stored frozen at ≤ -20 °C. No storage stability data are available for squash.
The maximum residues of fluopicolide (parent) and PCA were 0.0506 ppm and 0.0207 ppm in summer squash plants harvested 2 days after the last of three foliar applications of the 40% SC formulation (EXP 11067B) at a total rate of 0.354 to 0.367 lb ai/A. Maximum residues at a 3-day PHI were 0.0572 ppm parent and 0.0397 PCA. Residues of BAM were less than the limit of quantitation of 0.01 ppm in all samples. For the residue decline study performed at the Enigma, GA test site, fluopicolide-derived residues increased up to 3 days after the last application (DALA), then decreased rapidly with increasing pre-harvest interval.

***Conclusions*:** The submitted cucurbit vegetable field trial data are adequate.

The submitted cantaloupe field trial data reflect the use of three foliar applications of the 40% SC formulation of fluopicolide (EXP 11067B) at total rates of ~0.357 lb ai/A on cantaloupes grown in the United States with a 2-day PHI. An acceptable method was used for quantitation of residues in/on cantaloupes. Residues of fluopicolide (parent) in/on cucumber samples from the 2-day PHI ranged from <LOQ (one sample) to 0.057 ppm. Residues of BAM and PCA were each <LOQ in/on all cucumber samples. Residues of BAM were present in one sample at 0.00325 ppm and residues of PCA were detected in 7 samples at concentrations ranging from 0.00209 to 0.00649 ppm. For the residue decline study, average fluopicolide residues declined with increasing preharvest intervals; residues decreasing from an average of 0.019 ppm one day after the last application to <LOQ seven days after the last application. Storage stability data were not provided for cucumber; however, storage stability data on cabbage leaves and grapes, which indicated stability of fluopicolide, BAM, and PCA at <-18°C for 30 months, will be used to support the stability of cucumber

The submitted cucumber field trial data reflect the use of three foliar applications of the 40% SC formulation of fluopicolide (EXP 11067B) at total rates of 0.349 to 0.361 lb ai/A on cucumbers grown in the United States with a 2-day PHI. An acceptable method was used for quantitation of residues in/on cucumber plants. Residues of fluopicolide (parent) in/on cucumber samples from the 2-day PHI ranged from <LOQ (one sample) to 0.057 ppm. Residues of BAM and PCA were each <LOQ in/on all cucumber samples. Apparent residues of BAM were present in one sample at 0.00325 ppm and apparent residues of PCA were detected in 7 samples at concentrations ranging from 0.00209 to 0.00649 ppm. Residues of fluopicolide, BAM and PCA were nonquantifiable (<0.01 ppm) in/on all untreated cucumber samples. For the residue decline study, average fluopicolide residues showed a general decline with increasing preharvest intervals, with residues decreasing from an average of 0.019 ppm one day after the last application to <LOQ seven days after the last application. Storage stability data were not provided for cucumber; however, storage stability data on cabbage leaves and grapes, which indicated stability of fluopicolide, BAM, and PCA at <-18°C for 30 months, will be used to support cucumber. There were no unusual weather conditions that appear to have adversely impacted the results of the study. It does not appear that the agricultural practices used adversely impacted the results of the study.

The submitted summer squash field trial data reflect the use of three foliar applications of the 40% SC formulation of fluopicolide (EXP 11067B) at total rates of ~0.357 lb ai/A on summer squash plants grown in the United States with a 2-day PHI. Concurrent recoveries on squash were acceptable. Maximum residues for fluopicolide (parent) and its metabolite PCA were 0.0506 ppm and 0.0207 ppm, respectively. Residues of BAM were not detected above the LOQ in any of the summer squash samples. There were no residues above the LOD in the squash samples from any of the 6 trials. Storage stability data were not provided for squash; however, storage stability data on cabbage leaves and grapes, which indicated stability of fluopicolide, BAM, and PCA at <-18°C for 30 months, will be used to support squash. A residue decline study indicated that residues at a 3-day PHI are slightly higher. For the residue decline study performed at the Enigma, GA test site, fluopicolide-derived residues increased up to 3 DALA, then decreased rapidly with increasing pre-harvest interval.

The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for cucurbit vegetable, group 9. The use pattern of the field trials adequately reflects the use pattern proposed for cucurbit vegetables. The available field trial data will support a tolerance

for residues of fluopicolide in/on cucurbit vegetable, group 9 at 0.50 ppm; the tolerance calculation for cucurbit vegetables is presented in Appendix II.

Grape

DER Reference: 46708541.der.doc

Valent has submitted a magnitude of the residue study for grape; the results from these field trials are discussed below and summarized in Table 6.5.

Table 6.5. Summary of Residue Data from Grape Field Trials with Fluopicolide.

Commodity	Total Applic. Rate (lb ai/A) [kg ai/ha]	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
GRAPE (proposed use = 0.375 lb ai/A total application rate, 12-day minimum RTI, 21-day PHI)									
Fluopicolide									
Grape	0.346-0.401 [0.387-0.449]	20-21	32	0.065	1.10	0.985	0.210	0.312	0.289
BAM									
Grape	0.346-0.401 [0.387-0.449]	20-21	32	<0.01	<0.01	NA	NA	NA	NA
PCA									
Grape	0.346-0.401 [0.387-0.449]	20-21	32	<0.01	0.013	0.012	<0.01	< 0.01	NA

[1] HAFT = Highest average field trial result.

Valent U.S.A. Corporation has submitted field trial data for fluopicolide on grapes. Sixteen field trials were conducted in Canada and the United States during the 2002 growing season in Zones 1 (2 trials in New York), 5 (4 trials in Ontario), 10 (8 trials in California), and 11 (1 trial in Washington and 1 trial in British Columbia). At each test location, there was one untreated and one treated plot. The treated plots received three broadcast foliar applications of EXP 11067B, formulated as a 4 lb ai/gal suspension concentrate (SC), at 5 ± 1 day retreatment intervals. Each application was made at a nominal rate of 0.119 lb ai/A for a total seasonal application rate of 0.346 lb ai/A to 0.401 lb ai/A (~ 1x). The use of an adjuvant was not mentioned in the study. At each trial location, one bulk untreated control and two bulk treated mature raw agricultural commodity (RAC) samples were collected 21 ± 1 days following the last test substance application [21-day preharvest interval (PHI)].

Grape samples were analyzed for residues of fluopicolide (parent) and its metabolites BAM (AE C653711) and PCA (AE C657188) using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) (refer to the DER for MRID 46474027). The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Samples were stored frozen (≤-15 °C) prior to extraction; the maximum storage interval from harvest to extraction was 219 days (7 months). According to the petitioner, the field sample

residues were not corrected for in-storage dissipation because of the reported stability of fluopicolide in frozen storage. Residues of fluopicolide, BAM, and PCA are stable in/on grapes stored frozen (≤-18 °C) for 30 months (refer to the DER for MRIDs 46474036-46474037).

The maximum residues of fluopicolide (parent) and PCA were 1.10 ppm and 0.013 ppm in/on grapes harvested 20- to 21-days after the last of three foliar applications of the 40% SC formulation (EXP 11067B) at a total rate of 0.346 to 0.401 lb ai/A. Residues of BAM were below the limit of quantitation (0.010 ppm) in all samples.

***Conclusions*:** The submitted grape field trial data reflect the use of three foliar applications of the 40% SC formulation of fluopicolide (EXP 11067B) at total rates ranging from 0.346 lb ai/A to 0.401 lb ai/A on grapes grown in Canada and the United States with a 21 ± 1-day PHI. Maximum residues for fluopicolide (parent) and its metabolite, PCA, were 1.10 ppm and 0.013 ppm, respectively. Residues of BAM were not detected in any of the grape samples. Acceptable storage stability data were provided for grapes.

The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for grapes. The use pattern of the field trials adequately reflects the use pattern proposed for grapes. The available field trial data will support a tolerance for residues of fluopicolide in/on grapes at 2.0 ppm.

860.1520 Processed Food and Feed

DER Reference: 46708542.der.doc (Grape)
46708543.der.doc (Tomato)
46708544.der.doc (Rotated wheat)
46708545.der.doc (Potato)
Residue Chemistry Memo DP Number 321209, 1/23/2007, A. Acierto (PP#5E6903)

Grape

Valent U.S.A. Corporation has submitted a processing study with white grapes harvested from the crop field trials conducted in 2000 in Europe (Maine-et Loire, France and Hesse, Germany). A SE10 Suspo-Emulsion (similar to a 95 g/L EC formulation) formulation of fluopicolide was applied four times to white grapes at a ~130 g ai/ha/application rate (~0.116 lb ai/A/application) for a total application rate of ~520 g ai/ha (~0.46 lb ai/A), and harvested 21 days after final treatment. The grapes were processed into pomace and pasteurized and non-pasteurized must, yeast, young wine, and mature wine following typical commercial practices. The data submitted were reviewed in conjunction with the petition to establish tolerances for fluopicolide on grapes and raisins (see PP#5E6903; DP Number 321209, 1/23/07, A. Acierto).

Residues of fluopicolide and its metabolites BAM and PCA in white grapes and processed fractions were quantitated using liquid chromatography and tandem mass spectrometry according to Method AGREDOC C024784 (IF-101/05424-00), which was developed and validated by Institut Fresenius. The stated limit of quantitation (LOD) was 0.01 mg/kg and the limit of detection (LOD) was not explicitly determined, however the petitioner assumed it to be less than 0.001 mg/kg. This method was deemed adequate for data collection based on acceptable concurrent method recovery data.

The maximum storage interval from the harvest to extraction for analysis was 25 months for grapes and 26 months for processed commodities. A storage stability study on grapes was previously conducted in which residues of fluopicolide, BAM, and PCA were found to be stable in/on grapes stored frozen (≤-18 °C) for up to 30 months. However, no storage stability data are available for the processed fractions.

Residues of fluopicolide, BAM, and PCA in/on raw agricultural commodity (RAC) grapes were 0.51-0.62, 0.01-0.02, and 0.01-0.02 mg/kg, respectively. The available processing data (refer to the DER for MRIDs 46474104, 46474105, 46708542, PP#5E6903) indicate that residues of fluopicolide concentrate in pomace (average processing factor of 1.9x) and yeast (average processing factor of 4.5x for pasteurized and 7.4x for non-pasteurized); residues did not concentrate in must or wine (≤0.5x average processing factors). Residues of BAM and PCA did not concentrate significantly in any commodity, with the following exceptions: residues of PCA may concentrate in pomace (average processing factor of 2x) and non-pasteurized yeast (average processing factor of 3x). The processed commodities for grapes are raisin and juice (OPPTS 860.1000). The theoretical concentration factor for raisins is 4.7x. (based on the loss of water on processing grapes into raisins; OPPTS 860.1520, Table 2). The theoretical concentration factor for juice is 1.2x (based into separation into components; OPPTS 860.1520, Table 3).

Potato

Valent U.S.A. Corporation has submitted a study examining the transfer of fluopicolide into processed potato commodities. The raw agricultural commodity (RAC) was harvested 7 days following the last of three broadcast foliar applications of EXP 11067B, formulated as a 4 lb ai/gal suspension concentrate (SC), made at an exaggerated target application rate of 0.59 lb ai/A/application (661 g ai/ha). The total achieved application rate was 1.75 lb ai/A/season (1,962 g ai/ha), approximately 5x the proposed maximum seasonal application. The applications were made at re-treatment intervals of 5 days. Following harvesting, the potatoes were processed into flakes, chips, and wet peels.

Residues of fluopicolide in/on potato samples were quantitated using high pressure liquid chromatography/triple stage quadropole mass spectrometry (HPLC/MS/MS) Method 00782/M001. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

The maximum storage interval of the samples (stored frozen at ≤-20°C) from processing to extraction was 589 days (20 months). Residues of fluopicolide, BAM, and PCA are stable in/on potato tubers stored frozen at ≤-18°C for up to 30 months (refer to the DER for MRIDs 46474036-46474037). An adequate storage stability study on potato processed commodities has been conducted (MRID 46708527). The study indicates that residues of fluopicolide, BAM, and PCA are stable in/on potato flakes, chips and wet peels stored frozen at ≤-10 °C for up to 30 months.

Residues of fluopicolide (parent) and its metabolites were non-quantifiable (<0.01 ppm) in the RAC samples. The processed fractions were analyzed and fluopicolide (parent) was detected above the LOQ in the potato wet peels at an average residue concentration of 0.049 ppm (n=2). Fluopicolide (parent) and its metabolites (BAM and PCA) were not detected above the LOQ in

any of the other processed fractions. A concentration factor of 4.9 was calculated for fluopicolide in the wet peels using the LOQ (0.01 ppm) as the average fluopicolide residue in the RAC samples. A concentration factor for the remaining processed commodities could not be determined because fluopicolide and its metabolites were not detected above the LOQ in the RAC and processed commodity samples. The concentration factor in wet peel confirms the theoretical concentration factor of 5x for potatoes.

Tomato

Valent U.S.A. Corporation has submitted a processing study with tomatoes. The tomatoes received three applications of a nominal 480 g/L suspendable concentrate (SC) formulation of fluopicolide at an exaggerated application rate of 667 g ai/ha/application (0.594 lb ai/A/application), which was five times the proposed label rate [three applications of the fungicide each at a rate of 133 g ai/ha (0.119 lb ai/A)]. The total seasonal application rate was ~ 1.78 lb ai/A. Applications were made at 5 ± 1day intervals such that the last application was 2 days before harvest [2-day preharvest interval (PHI)]. The tomatoes were processed into tomato puree and tomato paste.

Residues of fluopicolide and its metabolites BAM and PCA in tomatoes and processed fractions were quantitated using liquid chromatography and tandem mass spectrometry according to Method AGREDOC C024784 (IF-101/05424-00), which was developed and validated by Institut Fresenius. The stated limit of quantitation (LOQ) was 0.01 ppm for all analytes and the limit of detection (LOD) was 0.0018 ppm for fluopicolide (parent), 0.0018 ppm for BAM and 0.0029 ppm for PCA. This method was deemed adequate for data collection based on acceptable concurrent method recovery data.

The maximum storage interval from the harvest to extraction for analysis of tomatoes and the processed commodities was just over 12 months. The samples were stored frozen but the storage temperature of the samples was not provided. No storage stability data are available for tomato (RAC) but storage stability data for tomato paste and puree can be used for the RAC.. Storage stability data are available which indicate that residues of fluopicolide and its metabolites BAM and PCA are stable at $\leq$ -10 ^{o}C for up to 30 months in tomato paste and puree (MRID 46708527). Untreated tomato paste and puree were spiked for the storage stability study.

Residues of fluopicolide (parent) ranged from 0.23 to 0.34 ppm in tomato raw agricultural commodity (RAC) samples harvested 2 days following treatment at ~ 1.78 lb ai/A/season, from 0.48 to 0.49 ppm in tomato puree samples, and from 0.59 to 0.79 ppm in tomato paste samples. No residues of BAM were detected in either tomatoes or their processed commodities. Residues of PCA were only found at a level above the LOQ (0.01 ppm) in one tomato paste sample at 0.011 ppm. The processing data indicate that residues of the parent compound fluopicolide may concentrate in tomato puree (1.7x) and tomato paste (2.4x). Processing factors could not be determined for BAM and PCA as the RAC samples at the exaggerated rate did not have quantifiable residues of these metabolites. These concentration factors are generally in agreement with the theoretical concentration factor of 1.4x for tomato puree and 5.5x for tomato paste (based on the loss of water on processing tomatoes into puree and paste; OPPTS 860.1520, Table 2).

Wheat

Valent U.S.A. Corporation has submitted a processing study with rotated wheat grain. In a trial conducted in IL, a single spray application of a 4 lb ai/gal suspension concentrate formulation [equivalent to a flowable concentrate (FlC) formulation] of fluopicolide was applied to bare soil at an exaggerated rate of 1.77 lb ai/A. The rotational crop, winter wheat, was planted into the treated soil 36 days after application. Bulk wheat grain samples were collected at normal commercial harvest and processed into bran, flour, middlings, shorts and germ using simulated commercial practices.

Samples of wheat grain and its processed commodities were analyzed for residues of fluopicolide and its metabolites BAM (AE C653711), PCA (AE C657188), P1X (AE 1344122), and 3-OH-BAM (AE C657378) using a combined and modified version of LC/MS/MS Methods 00782/M002 (for determination of fluopicolide, BAM, PCA, and P1X) and 00782/M003 (for determination of 3-OH-BAM). The extraction steps of the methods were modified to minimize ion suppression, and the same final extract was used for determination of all analytes. The method was adequate for data collection based on acceptable concurrent method recovery data. The validated limit of quantitation (LOQ) was 0.01 ppm for each analyte in each wheat matrix.

Samples of wheat grain and its processed commodities were reportedly stored frozen prior to analysis at <2 ºC. Samples were shipped frozen on the day of harvest to the processing facility, where they were stored frozen until processing. Processing was initiated 82 days following harvest, after which samples were stored frozen, then shipped to Bayer CropScience, where they were stored frozen until shipment to the analytical facility. Storage temperatures at the analytical facility were reported (≤-20 ºC). Maximum storage intervals from harvest (RAC) or processing to analysis were ~20 months for grain and 17 months for processed commodities. Adequate storage stability data are available indicating that residues of fluopicolide, BAM and PCA are stable in/on wheat grain stored at ≤-18 °C for up to 30 months (DP Number 321209, 1/23/07, A. Acierto) and in wheat bran, flour and shorts stored at ≤-10 °C for up to 30 months (refer to 46708527.der.doc). In addition, adequate storage stability data are available indicating that residues of 3-OH-BAM and P1X are stable at ≤-18 °C for up to ~12 months in/on wheat grain (refer to 46708418.der.doc); the petitioner has indicated that this study is ongoing (up to 24 months). No storage stability data are available for residues of 3-OH-BAM or P1X in wheat processed commodities but the storage stability data on wheat grain can be used to support the data on processed commodities.

In wheat grain harvested at maturity following planting 36 days after soil treatment at 1.77 lb ai/A, average residues of fluopicolide were 0.017 ppm, residues of BAM were below the LOQ (0.007 ppm), residues of PCA were 0.230 ppm, residues of 3-OH-BAM were 0.025 ppm, and residues of P1X were 0.130 ppm.

The processing data indicate that residues of fluopicolide may concentrate in bran, middlings, shorts, and germ, with average processing factors of 3.0x, 1.5x, 2.0x, and 4.7x, respectively. Residues of PCA may concentrate in bran, middlings, and shorts, with average processing factors of 1.9x, 1.3x, and 1.8x, respectively. Residues of 3-OH-BAM may concentrate in bran, shorts, and germ with average processing factors of 3.0x, 1.5x, and 1.5x, respectively, and residues of P1X appear to concentrate only in bran and shorts, with average processing factors of 2.2x and 1.4x, respectively. It appears that residues of BAM may also concentrate slightly in bran, middlings, shorts, and germ (average estimated processing factors of 1.7x, 1.1x, 1.2x, and

1.8x, respectively); however, because residues were below the LOQ in grain, as well as middlings and shorts, these results are inconclusive.

No concentration of residues was observed in flour; average processing factors were estimated at 0.4x for fluopicolide, 0.7x for BAM, 1x for PCA, 0.3x for 3-OH-BAM and 0.6x for P1X. In addition, residues of 3-OH-BAM and P1X do not appear to concentrate in middlings, with average processing factors of 1x, and residues of PCA and P1X do not appear to concentrate in germ (0.9x and 0.7x respective average processing factors).

The observed processing factors do not exceed the theoretical concentration factors of 7.7x for bran, 1.4x for flour, and 8.3x for shorts (based on separation into components; Table 3 of OPPTS 860.1520) for fluopicolide and its metabolites BAM, PCA, 3-OH-BAM and P1X in wheat flour, bran, middlings, shorts, and germ.

Table 7. Summary of Processing Factors for Fluopicolide.

RAC	Processed Commodity	Average Processing Factor [1]			
		Fluopicolide	BAM	PCA	P1X
Potato	Chips	NC	NC	NC	NA
	Flakes	NC	NC	NC	NA
	Wet peels	4.0x[2]	NC	NC	NA
Tomato	Paste	2.4x	NC	NC	NA
	Puree	1.4x[3]	NC	≥1x	NA
Wheat	Bran	3.0x	~1.7x	1.9x	2.2x
	Flour	~0.4x	~0.7x	1x	0.6x
	Middlings	1.5x	~1.1x	1.3x	1x
	Shorts	2.0x	~1.2x	1.8x	1.4x
	Germ	4.7x	~1.8x	0.9x	0.7x

[1] NC = Not calculated; a processing factor could not be calculated for this matrix as residues were below the LOQ in both the RAC and the processed commodity. NA = Not applicable. Estimated (~) processing factors were calculated when residues were reported below the LOQ in the RAC and/or the processed matrix.
[2] The observed processing factor (>4.9x) exceeded the theoretical value of 4.0x; therefore, the theoretical value of 4.0x will be used.
[3] The observed processing factors for puree (1.7-1.8x) exceeded the theoretical value of 1.4x; therefore, the theoretical value of 1.4x will be used.

***Conclusions*:** The submitted grape, potato, and tomato processing data are adequate to satisfy data requirements. The wheat processing study is adequate pending submission of storage stability data for residues of P1X on wheat grain stored frozen for 20 months to support the storage conditions and intervals of samples of wheat grain and its processed commodities from the rotated wheat processing study.

The grape processing data indicate that fluopicolide residues do not concentrate in must; therefore, it is unlikely that residues would concentrate in grape juice. Adequate storage stability data are available to support the grape processing studies. A tolerance for fluopicolide residues in juice is not required. The grape processing data indicate that fluopicolide residues concentrate in raisins. Based on the HAFT residue for grapes (0.985 ppm) and the average processing factor for raisins (3.4x), the expected residues in raisins would be 3.3 ppm. Therefore, the

recommended 6.0 ppm tolerance for raisins (PP#5E6903) would be an appropriate tolerance for residues of fluopicolide.

The processing data for potato indicate that fluopicolide residues do not concentrate in chips and flakes but do concentrate in wet peels. Adequate storage stability data are available to support the potato processing study. In the potato crop field trials, residues of fluopicolide were quantifiable in only one sample, at 0.0126 ppm; however, detectable residues (residues between the limit of detection and the LOQ) were observed in 19 samples. The observed processing factor (>4.9x) exceeded the theoretical value of 4.0x for potato waste, therefore, the theoretical value of 4.0x was used [OPPTS 8601520 (f) (2)(ii)]. Based on the HAFT residues for fluopicolide in potato tubers (0.011 ppm) and the average theoretical processing factor for wet peels (4.0x), the expected residues in wet peel would be 0.05 ppm. Because this value is greater than the proposed 0.02 ppm tolerance for tuberous and corm vegetables, a tolerance for processed potato waste is needed. A tolerance of 0.05 ppm would be appropriate.

The processing data for tomato indicate that fluopicolide residues concentrate in tomato paste and puree. Adequate storage stability data are available to support the tomato processing study. Based on the HAFT residues for tomatoes (0.375 ppm) and the average processing factors for puree (1.4x) and paste (2.4x), expected residues would be 0.65 ppm for puree and 0.9 ppm for paste. Because both these values are below the recommended tolerance of 1.6 ppm for the fruiting vegetable crop group, no tolerances for tomato puree or paste are needed.

The processing data for wheat indicate that fluopicolide residues do not concentrate in flour but do concentrate in bran (3.0x), middlings (1.5x), shorts (2.0x), and germ (4.7x); PCA may concentrate in bran (1.9x), middlings (1.3x), and shorts (1.8x); and P1X may concentrate in bran (2.2x) and shorts (1.4x). Storage stability data are available which indicate stability of fluopicolide, BAM, and PCA in wheat grain at ≤-18°C for 30 months and stability of 3-OH-BAM and P1X in wheat grain at ≤-18°C for 12 months. Additional storage stability data are needed for P1X in wheat grain for 20 months to support the storage conditions and intervals of samples of wheat grain and its processed commodities in the wheat processing study. Storage stability data on wheat grain can be translated to the processed commodities.

860.1650 Submittal of Analytical Reference Standards

An analytical standard for fluopicolide, with an expiration date of 8/16/08, is currently available in the National Pesticide Standards Repository (personal communication with Dallas Wright, ACB, 2/15/07).

An analytical reference standard for the metabolite 2,6-dichlorobenzamide (BAM) must be sent to USEPA, National Pesticide Standards Repository/Analytical Chemistry Branch/OPP, 710 Mapes Road, Fort George G. Meade, MD 20755-5350.

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860.1850 Confined Accumulation in Rotational Crops

DER Reference: 46708546.der.doc

Valent U.S.A. Corporation has submitted a confined rotational crop study with [U-^{14}C-phenyl]fluopicolide (PH label) and [2,6-^{14}C-pyridinyl]fluopicolide (PY label). Each radiolabeled test substance was combined with nonlabeled fluopicolide, formulated as a suspension concentrate, mixed with adjuvant, and applied to bare sandy loam soil at a rate equivalent to 0.36 lb ai/A (400 g ai/ha); the specific activity of the applied test substances ranged from 39.6-41.5 µCi/mg. Rotational crops (lettuce, radish, and wheat) were planted 29, 133, and 365 days after soil treatment. The in-life and analytical phases of the study were conducted by Bayer CropScience (Pikeville, NC and Frankfurt, Germany).

Total radioactive residues (TRR) accumulated at ≥0.01 ppm in all rotated crop matrices planted at the 29-, 133-, or 365-day plantback intervals (PBIs). TRR were highest in 29-day PBI matrices, ranging from 0.083 ppm in radish root to 13.56 ppm in wheat straw. TRR decreased at the 133-day PBI, ranging from 0.02 ppm in radish root and wheat grain to 0.84 ppm in wheat straw. Residues increased slightly at the 365-day PBI, ranging from 0.02 ppm in radish root to 2.37 ppm in wheat straw. The petitioner attributed the increased residues in 365-day PBI matrices to seasonal variations; 133-day PBI crops were planted in October and developed over the winter, and 365-day PBI crops were planted in March and developed over the summer.

The majority of the radioactivity (87-97% TRR in lettuce; 86-99% in radish top; 89-97% in radish root; 77-95% in wheat forage; 58-94% in wheat grain; and 58-90% TRR in wheat straw) was extracted from rotational crop matrices using acetonitrile (ACN) and ACN/water; Soxhlet extraction with ACN/water released an additional 1-12% TRR from 29-day PBI lettuce and radish commodities, 18-19% TRR from 29-day PBI wheat forage, and 2-8% TRR from 133- and 365-day PBI wheat forage and 29-, 133-, and 365-day PBI wheat grain and straw. The nonextractable residues of wheat forage and straw were also subjected to mild acid or base hydrolysis procedures which released 2-16% TRR (acid hydrolysis) or 9-23% TRR (base hydrolysis). Nonextractable residues following extraction and hydrolysis procedures accounted for <0.05 ppm in all rotational lettuce and radish matrices, and in all rotational wheat commodities from the 133- and 365-day PBIs; nonextractable residues in wheat commodities from the 29-day PBI accounted for <7% TRR or <0.03 ppm. Extraction values were normalized; reported accountabilities before normalization were ≥97% for all commodities with the following exceptions: 365-day PBI lettuce (89%; PH label); 133-day radish top (92%; PH label); 365-day PBI radish root (95%; PH label); 365-day PBI wheat grain (94%; PH label); and 133-day PBI wheat straw (93%; PY label).

Residues were identified and quantitated primarily by HPLC, with confirmation and structure elucidation using LC/MS, LC/MS/MS, and NMR analyses. Fluopicolide and seven discrete metabolites were identified in rotational crops by HPLC analysis. Because of the two-ring structure of fluopicolide, metabolites resulting from cleavage of fluopicolide at the bond between the carbon attached to the pyridine ring and the amide nitrogen of the parent compound were identified in either PH samples [metabolites AE C653711 (BAM) and AE 657378 (3-OH-BAM)] or PY samples [AE C657188 (PCA), AE 653598, AE 1344122, and AE B102859]. Fluopicolide and the double-ring metabolite AE C643890 were identified in both phenyl and pyridinyl labeled samples.

In lettuce and radish top, total identified residues ranged from 63-92% TRR. Fluopicolide was identified in all lettuce and radish top samples, at 2.1-26.6% TRR (0.013-1.644 ppm) in PH samples and 25.2-79.9% TRR (0.024-1.072 ppm) in PY samples. The major metabolite in PH

label samples was AE C653711, at 60.9-87.5% TRR (0.070-4.381 ppm). In PY samples, AE 1344122 and AE C657188 were identified in 29- and 365-day PBI samples, at 3.3-13.0% TRR for AE 1344122 and 10.4-27.1% TRR for AE C657188. The metabolites AE C653598 (365-day PBI lettuce only) and AE B102859 were also identified in PY samples, at ≤9% TRR each.

In radish root, total identified residues ranged from 81-91% TRR. Fluopicolide was identified in all radish root samples, at 24.2-55.8% TRR (0.006-0.069 ppm); fluopicolide was found at >0.01 ppm in all samples with the exception of PH label 133- and 365-day PBI samples. The major metabolite in PH label samples was AE C653711, at 43.2-60.9% TRR (0.013-0.062 ppm). In PY samples, AE 1344122 and AE C657188 were identified at all PBIs, at 2.9-9.6% TRR for AE 1344122 and 9.6-33.5% TRR for AE C657188. The metabolite AE C653598 was identified in 365-day PBI root at 9.5% TRR, and metabolite AE B102859 was identified in 133-day root, at 19.1% TRR.

In wheat forage, total identified residues ranged from 57-97% TRR. Fluopicolide was identified in all forage samples, at 4.8-36.6% TRR (0.042-1.812 ppm) in PH samples and 26.2-33.7% TRR (0.041-1.445 ppm) in PY samples. The major metabolite in PH label samples was AE C657378, at 32.7% TRR (1.619 ppm) and 28.9% TRR (0.065 ppm) in 29- and 133-day PBI samples, respectively, and 59.3% TRR (0.513 ppm) in 365-day PBI forage. AE C653711 was the only other metabolite identified in 133- and 365-day PBI PH samples, at 5.1% and 14.8% TRR, respectively; this metabolite was found in 29-day PBI PH forage at 6.3% TRR. In PY samples, AE C657188 was a major metabolite in 29-day PBI forage, at 43.0% TRR (1.844 ppm); it was found in 133- and 365-day PBI forage at 5.4% and 8.2% TRR, respectively. AE 1344122 was a major metabolite in 133- and 365-day PBI PY forage, at 41.0% TRR and 18.3% TRR, respectively; it was found in 29-day PBI forage at 3.8% TRR. AE B102859 was found in 133- and 365-day PBI forage, at 9.9-10.5% TRR; metabolite AE C653598 was found in 365-day PBI forage, at 6.3% TRR; and metabolite AE C643890 was found in 29-day PBI forage (both labels), at <2% TRR. An additional eight metabolites were identified by LC/MS analyses in 29-day PBI wheat forage, each present at ≤6.2% TRR (≤0.307 ppm). These metabolites, P2ab, P2c, P4a, P4b, P4c, P5, P10, and P11, were proposed to be hydroxylated or sulfhydrylated versions of fluopicolide or its metabolites, with or without conjugation to glucose, malonic acid, glyceric acid or amino acid.

In wheat grain, total identified residues ranged 44-50% TRR in PH samples and 81-85% TRR in PY samples. Fluopicolide was identified in all wheat grain samples, at 1.8-27.3% TRR (0.001-0.046 ppm); fluopicolide was found at >0.01 ppm only in 29-day PBI samples. At the 29-day PBI, the major metabolites were AE C643890 (13.1% TRR, 0.021 ppm; PH label) and AE C657188 (69.6% TRR, 1.809 ppm; PY label); AE C657188 was found at lower levels in 133- and 365-day PBI samples (10.9-14.2% TRR, 0.010-0.025 ppm). In 133- and 365-day PBI samples, the major metabolites were AE 1344122 (64.9-66.6% TRR, 0.064-0.116 ppm; PY label), AE C657378 (23.3-24.5% TRR, 0.005-0.013 ppm; PH label), and AE C653711 (17.9-19.0% TRR, 0.004-0.010 ppm; PH label). AE 1344122 and AE C653711 were identified in 29-day PBI samples, at 13.1% TRR (0.341 ppm; PY label) and 3.6% TRR (0.006 ppm; PH label), respectively.

In wheat straw, total identified residues ranged 40-91% TRR. Fluopicolide was identified in all straw samples, at 7.2-23.1% TRR (0.131-3.132 ppm) in PH samples and 25.7-34.9% TRR (0.089-2.462 ppm) in PY samples. The major metabolite in PH label samples was AE C657378,

at 13.6% TRR (1.844 ppm) and 14.6% TRR (0.123 ppm) in 29- and 133-day PBI samples, respectively, and 28.0% TRR (0.663 ppm) in 365-day PBI PH forage. AE C653711 was the only other metabolite identified in 133- and 365-day PBI PH samples, at 25.5% and 5.1% TRR, respectively (0.215 and 0.121 ppm, respectively); this metabolite was found in 29-day PBI PH straw at 3.4% TRR. In PY samples, AE B120859 was a major metabolite in 133-day PBI straw, at 21.5% TRR (0.075 ppm); this metabolite was not found in 29- or 365-day PBI samples. AE 1344122 was a major metabolite in 365-day PBI straw, at 14.2% TRR (0.143 ppm); it was found at <8% TRR in 29- and 133-day PBI straw. AE C653598 and AE C657188 were found in 133- and 365-day straw at ≤9.4% TRR (≤0.048 ppm) each; AE C657188 was also found in 29-day PBI straw at 7.0% TRR. An additional eight metabolites were identified by LC/MS analyses in 29-day PBI wheat straw. These metabolites, P4a, P4b, P4c, P5, P8a, P8b, P10, and P11, were proposed to be hydroxylated or sulfhydrylated versions of fluopicolide or its metabolites, with or without conjugation to glucose, malonic acid, glyceric acid or amino acid. Metabolites P4a, P4b, and P4c together accounted for 8.6-15.6% TRR (1.100-1.166 ppm) in wheat straw, and metabolites P8a and P8b together accounted for 7.1-9.9% TRR; the remaining metabolites were present at ≤6.0% TRR.

HED notes that, in general, the levels of fluopicolide were found to decrease significantly with increasing PBI in the PH label samples. The same trend was not observed in PY samples; fluopicolide levels in PY samples were generally the same at all three PBIs.

All samples were initially extracted within 114 days of harvest, with the exception of 365-day PBI wheat grain and straw, which were extracted 180-194 days after collection. Samples of 133- and 365-day PBI commodities were analyzed within 19.5 months of collection, and samples of 29-day PBI commodities were analyzed within 39.0 months of collection. Adequate storage stability data were provided to support the storage intervals and conditions of all samples from this study.

Based on the submitted confined rotational crop study, the petitioner proposed a metabolic pathway for fluopicolide in rotational crops; see Figure C.3.1. The metabolism of fluopicolide in rotational crops appears to be more extensive than that observed in primary crops (grapes, lettuce, and potato; refer to the DERs for MRIDs 46474026, 46708520, and 46708521). The major metabolites identified were AE C653711 (BAM), AE C657188 (PCA), AE 1344122 (P1X) and AE C657378 (3-OH-BAM). P1X, 3-OH-BAM, and two other rotational crop metabolites (AE C653598, 3-chloro-5-(trifluoromethyl)-2-pyridine carboxamide, and AE B102859, 3-chloro-5-(trifluoromethyl)-2-pyridinol) were not observed in the primary crop metabolism studies. The petitioner did not provide any information on whether any of the observed metabolites were known soil degradates.

Based on the submitted confined rotational crop study, the petitioner proposed a metabolic pathway for fluopicolide in rotational crops; the proposed pathway is presented in Appendix III.

***Conclusions*:** The submitted confined rotational crop data are adequate to satisfy data requirements. The metabolism of fluopicolide in rotational crops appears to be more extensive than that observed in primary crops (grapes, lettuce, and potato); four rotational crop metabolites, 3-OH-BAM, P1X, AE C653598, and AE B102859, were not observed in the primary crop metabolism studies.

Adequate storage stability data were provided to support the storage intervals and conditions of all samples from this study.

The submitted confined rotational crop studies indicate the potential for quantifiable fluopicolide and metabolite residues in rotated crop commodities. In HED's RARC1 meeting held on 7/19/07, HED determined that the residue of concern for the tolerance expression for rotational crops is fluopicolide (parent). The residues of concern for the risk assessment for cereal grains as rotational crops are fluopicolide (parent), BAM, PCA, and P1X in grain for human food, and fluopicolide (parent) and BAM in forage/hay/straw and grain for livestock feed. The residues of concern for the risk assessment for all rotational crops except cereal grains are fluopicolide (parent) and BAM.

860.1900 Field Accumulation in Rotational Crops

DER Reference: 46708547.der.doc

Valent U.S.A. Corporation has submitted the results of an extensive field rotational crop study on wheat. Twenty-one field trials were conducted in Zones 2 (NJ; 1 trial), 4 (AR; 1 trial), 5 (IL, MI, NE, WI, and OH; 6 trials), 6 (TX; 1 trial), 7 (ND, NE, SD; 5 trials), 8 (CO, KS, NM, and TX; 6 trials) and 11 (WA; 1 trial) during the 2001-2002 growing season.

The results from the rotational crop field trials show that maximum residues of fluopicolide, BAM, PCA, and P1X were, respectively, 0.213, 0.123, , 0.043, and 0.064 ppm in/on wheat forage; 0.501, 0.102, 0.064, and 0.073 ppm in/on hay; 0.014, <0.01, 0.062 and 0.075 ppm in/on grain; and 0.350, 0.050, 0.043, and 0.055 ppm in/on straw planted 29 to 37 days following the last application of fluopicolide to a primary crop of potatoes at 0.346-0.372 lb ai/A.

Table 8. Summary of Residue Data in Rotational Wheat Commodities Following Treatment of a Primary Crop with Fluopicolide.

Commodity	Applic. Rate (lb ai/A) [g ai/ha]	PBI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Wheat, forage	0.346-0.372 [388-417]	29-37	Fluopicolide	42	<0.01	0.213	0.160	0.027	0.044	0.047
			BAM	42	<0.01	0.123	0.106	0.019	0.028	0.027
			PCA	42	<0.01	0.043	0.027	0.010	0.013	0.007
			P1X	42	<0.01	0.064	0.057	0.012	0.018	0.013
Wheat, hay	0.346-0.372 [388-417]	29-37	Fluopicolide	42	0.014	0.501	0.364	0.051	0.100	0.119
			BAM	42	<0.01	0.102	0.095	0.010	0.022	0.024
			PCA	42	<0.01	0.064	0.055	0.010	0.018	0.013
			P1X	42	<0.01	0.073	0.070	0.025	0.028	0.017
Wheat, grain	0.346-0.372 [388-417]	29-37	Fluopicolide	42	<0.01	0.014	0.014	0.010	0.010	0.001
			BAM	42	<0.01	<0.01	<0.01	0.010	0.010	0.000
			PCA	42	<0.01	0.062	0.060	0.011	0.016	0.011
			P1X	42	<0.01	0.075	0.075	0.019	0.025	0.020

Table 8. Summary of Residue Data in Rotational Wheat Commodities Following Treatment of a Primary Crop with Fluopicolide.										
Commodity	Applic. Rate (lb ai/A) [g ai/ha]	PBI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Wheat, straw	0.346-0.372 [388-417]	29-37	Fluopicolide	42	<0.01	0.350	0.338	0.034	0.055	0.075
			BAM	42	<0.01	0.050	0.050	0.010	0.015	0.011
			PCA	42	<0.01	0.043	0.040	0.010	0.012	0.007
			P1X	42	<0.01	0.055	0.049	0.020	0.021	0.011

[1] HAFT = Highest average field trial result.

***Conclusions*:** Under the conditions and parameters used in the study, the data depicting residues in the rotational crop wheat are tentatively classified as scientifically acceptable, pending submission of additional storage stability data reflecting the stability of P1X in wheat grain for 21 months and for fluopicolide and BAM in wheat forage and straw for 24 months. The available storage stability data for wheat straw will be translated to wheat hay.

The tolerance calculation for wheat is presented in Appendix II.

In the confined rotational crop study, residues of fluopicolide >0.01 ppm were observed in/on all rotational crop commodities at all PBIs, with the exception of wheat grain at the 133- and 365-day PBIs. Based on these results and the proposed rotational crop restrictions, limited field rotational crop studies must be conducted at a 12-month PBI with representative leafy vegetable, root vegetable, and cereal grain crops. Although the petitioner is proposing a 30-day PBI for wheat and has submitted supporting field rotational crop data, limited field rotational crop data for another cereal grain, preferably a small grain, are needed to represent all grain crops other than wheat that may be rotated at a 12-month PBI. If the results of the limited field rotational crop studies indicate the potential for quantifiable fluopicolide residues of concern in/on rotational crops at a 12-month PBI, then extensive field rotational crop studies will be required for all crops the petitioner wishes to allow for rotation at a 12-month PBI.

860.1550 Proposed Tolerances

HED is recommending a revision of the proposed tolerance expression for fluopicolide in/on plants to address issues of quantifiable residues 2,6-dichlorobenzamide (BAM) in/on RACs resulting from fluopicolide application. HED has determined that the terminal residue of concern in cucurbit vegetable, fruiting vegetable, grape, leafy vegetable, and tuberous and corm vegetable commodities for the tolerance expression is fluopicolide [2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]benzamide] as an indicator of combined residues of fluopicolide and its metabolite, 2,6-dichlorobenzamide.

No Codex, Canadian, or Mexican MRLs have been established for fluopicolide.

Pending submission of the requested storage stability data/information, adequate field trial data are available for tuberous and corm vegetables (subgroup 1C), leafy vegetables (except *Brassica*, group 4), fruiting vegetables (group 8), cucurbit vegetables (group 9), and grapes. The available field trial data will support tolerances for residues of fluopicolide in/on grape at 2.0 ppm, the cucurbit vegetable group 9 at 0.50 ppm, the fruiting vegetable group 8 at 1.6 ppm, the leafy

vegetable, except *brassica*, group 4 at 25 ppm, and the tuberous and corm vegetable (subgroup 1D except potato) at 0.02 ppm. Because the majority of residues in potatoes were below the LOQ, the tolerance spreadsheet in the Agency's *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* was not utilized for determining an appropriate tolerance level for the tuberous and corm vegetable subgroup. The tolerance calculations for cucurbit vegetables, fruiting vegetables, leafy vegetables, and grapes are presented in Appendix II. The data indicate that the proposed tolerances of 0.8 ppm and 20 ppm for the fruiting vegetable and leafy vegetable crop groups are too low; increased tolerances of 1.6 ppm and 25 ppm are needed.

Pending submission of the requested storage stability information, adequate extensive field rotational crop data are available for wheat forage, hay, grain, and straw. The available field trial data will support tolerances for indirect or inadvertent residues of fluopicolide in/on wheat forage at 0.20 ppm, wheat hay at 0.50 ppm, wheat grain at 0.02 ppm, and wheat straw at 0.50 ppm; the tolerance calculation for rotated wheat forage, hay, and straw are presented in Appendix II. For wheat grain, the majority of residues were below the LOQ; therefore, the tolerance spreadsheet was not used for wheat grain.

Adequate processing data for grapes, potatoes, tomatoes, and wheat are available pending submission of the requested storage stability data/information. The available processing data indicate that residues of fluopicolide are not likely to concentrate in grape juice, in potato chips and flakes, or in wheat flour. Residues of fluopicolide were found to concentrate in raisins, processed potato waste (wet peels), tomato paste and puree, and wheat milled byproducts (bran, germ, middlings, and shorts). The processing data indicate that the proposed tolerance of 6 ppm for raisins is appropriate. In addition, tolerances for processed potato waste and wheat milled byproducts must be proposed, at 0.05 ppm and 0.07 ppm, respectively. Separate tolerances for tomato processed commodities are not needed as residues in these commodities are not expected to exceed the recommended tolerance of 1.6 ppm for the fruiting vegetable group.

The available cattle feeding study data indicate that tolerances for ruminant and swine commodities are not needed to support the requested fluopicolide uses. The need for tolerances for poultry commodities will be determined after the required poultry metabolism data have been submitted.

The proposed tolerances should be revised to reflect the recommended tolerance levels and correct commodity definitions as specified in Table 9; individual tolerances for the members of each of the requested crop groups are not needed. Tolerances to be established when rotational crop and livestock issues are resolved are specified in Table 10.

Table 9. Tolerance Summary for Fluopicolide.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Tolerances to be established under "(a) *General*" (1):			
Tuberous and corm vegetables subgroup 1C			
Arracacha	0.02	0.02	*Vegetable, tuberous and corm, except potato, subgroup 1D*
Arrowroot	0.02		
Artichoke, Chinese	0.02		
Artichoke, Jerusalem	0.02		
Canna, edible	0.02		

Cassava, bitter and sweet	0.02		
Chayote (root)	0.02		
Chufa	0.02		
Dasheen	0.02		
Ginger	0.02		
Leren	0.02		
Sweet potato	0.02		
Tanier	0.02		
Turmeric	0.02		
Yam bean	0.02		
Yam, true	2		
Vegetable, leafy, except *brassica*, group 4			
Head Lettuce	20	25	*Vegetable, leafy, except brassica, group 4*
Leaf Lettuce	20		
Spinach	20		
Arugula	20		
Chervil	20		
Chinese spinach	20		
Corn salad	20		
Dandelion	20		
Dock (sorrel)	20		
Edible chrysanthemum	20		
Endive	20		
Garden cress	20		
Garden purslane	20		
Garland Chrysanthemum	20		
New Zealand spinach	20		
Orach	20		
Parsley	20		
Red chicory	20		
Upland cress	20		
Vine spinach	20		
Winter purslane	20		
Cardoon	20		
Celery	20		
Celtuce	20		
Chinese celery	20		
Fennel	20		
Rhubarb	20		
Swiss chard	20		
Vegetable, fruiting, group 8			
Tomato/Cherry tomato	0.8	1.6	*Vegetable, fruiting, group 8*
Sweetpepper	0.8		
Bell pepper	0.8		
Chili pepper	0.8		
Cooking pepper	0.8		
Pimiento	0.8		
Eggplant	0.8		
Groundcherry	0.8		
Pepino	0.8		
Tomatillo	0.8		
Vegetable, cucurbit, group 9			
Cantaloupe	0.4	0.50	*Vegetable, cucurbit, group 9*
Citron melon	0.4		
Muskmelon	0.4		

Watermelon	0.4		
Chayote (fruit)	0.4		
Chinese waxgourd	0.4		
Cucumber	0.4		
Gherkin	0.4		
Gourd, edible	0.4		
Momordica spp	0.4		
Pumpkin	0.4		
Squash, summer	0.4		
Squash, winter	0.4		
Other			
Grape	2	2.0	
Raisins	6	6.0	*Grape, raisin*

Tolerances to be established when rotational crop and livestock issues are resolved are specified in Table 10.

Table 10. Tolerance Summary for Fluopicolide (To be Established When Deficiencies are Resolved).			
Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Tolerances to be established under "(a) *General*" (1):			
Tuberous and corm vegetables subgroup 1C			
Potato	0.02	0.02	*Vegetable, tuberous and corm, subgroup 1C*
Other			
Potato, processed potato waste	None proposed	0.05	
Tolerances to be established under "(a) *General*" (2):			
Cattle fat	None proposed	0.05	*Cattle, fat*
Cattle meat	None proposed	0.02	*Cattle, meat*
Cattle meat byproducts	None proposed	0.05	*Cattle, meat byproducts*
Goat fat	None proposed	0.05	*Goat, fat*
Goat meat	None proposed	0.02	*Goat, meat*
Goat meat byproducts	None proposed	0.05	*Goat, meat byproducts*
Horse fat	None proposed	0.05	*Horse, fat*
Horse meat	None proposed	0.02	*Horse, meat*
Horse meat byproducts	None proposed	0.05	*Horse, meat byproducts*
Milk	None proposed	0.01	*Milk*
Sheep fat	None proposed	0.05	*Sheep, fat*
Sheep meat	None proposed	0.02	*Sheep, meat*
Sheep meat byproducts	None proposed	0.05	*Sheep, meat byproducts*
Tolerances to be established under "(d) *Indirect or inadvertent residues*":			
Wheat forage	0.2	0.20	*Wheat, forage*
Wheat grain	0.02	0.02	*Wheat, grain*
Wheat hay	0.5	0.50	*Wheat, hay*
Wheat straw	0.5	0.50	*Wheat, straw*
Wheat, milled byproducts	None proposed	0.07	
Wheat, aspirated grain fractions	None proposed	0.07	

References

DP #:	329686
Subject:	Fluopicolide (AE C638206) in/on imported grapes, domestic use in/on food crops and ornamental turf. Request for Petition Method Validation.
From:	A. Acierto
To:	F. Siegelman
Date:	6/8/07
MRIDs:	46474027-46474031, 46708522-46708525 and 46708516

DP #:	321209
Subject:	Fluopicolide. PP#5E6903; Petition for Tolerances on Imported Grapes and Raisins. Summary of Analytical Chemistry and Residue Data.
From:	Amelia M. Acierto
To:	Janet Whitehurst /Tony Kish
Date:	1/23/07
MRIDs:	46474025, 46474026, 46474027, 46474028, 46474029, 46474030, 46474031, 46474032, 46474033, 46474034, 46474035, 46474036, 46474037, 46474038, 46474039, 46474040, 46474041, 46474042, 46474043, 46474044, 46474045; 46474101, 46474102, 46474103, 46474104, 46474105, 46474106; 46708525, 46708542.

DP Number:	339155
Subject:	PP# 5E6903 & 5F7016. Review of Revised Proposed Tolerance Enforcement Method for Fluopicolide. PC Code:027412. DBarcode: D329578 & D329670. ACB Project #:B06-22.
From:	Charles Stafford
To:	A. Acierto
Date:	3/14/07
MRIDs:	None. Valent Report Number C20070031

DP #:	339157
Subject:	PP#5E6903. Fluopicolide. Amendment to Address the Requirements to Establish Tolerances on Imported Grapes and Raisins.
From:	Amelia M. Acierto
To:	Janet Whitehurst /Tony Kish
Date:	6/01/07

DP Number:	318332
Subject:	FEE. Secondary Product Chemistry Review on Fluopicolide technical (Import Tolerance)
From:	S. Mathur
To:	J. Whitehurst/T. Kish
Date:	10/17/06
MRIDs:	46474001-46474023, 46478409, and 46478410

Attachments:
International Residue Limit Status sheet
Appendix I - Chemical Name and Structure Table
Appendix II - Tolerance Assessment Calculations
Appendix III - Proposed Metabolic Pathway for Fluopicolide in Rotational Crops

INTERNATIONAL RESIDUE LIMIT STATUS

Chemical Name: 2,6-dichloro-N-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]-benzamide	Common Name: Fluopicolide	X Proposed tolerance □ Reevaluated tolerance □ Other	Date: 2/13/2007

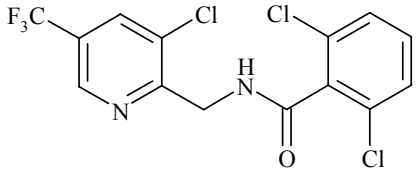
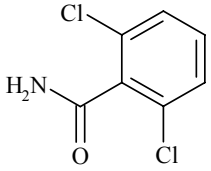
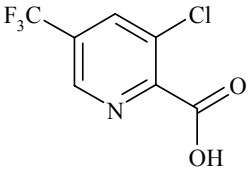
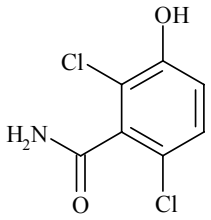
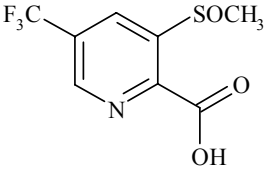
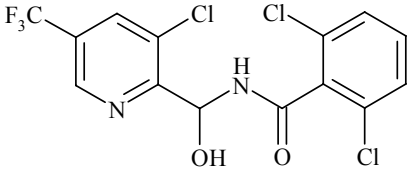
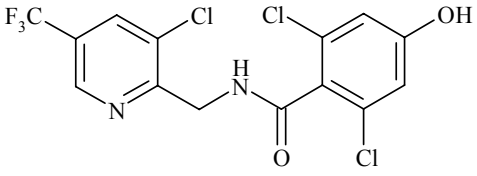
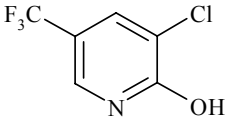
Codex Status (Maximum Residue Limits)	U. S. Tolerances
√ No Codex proposal step 6 or above □No Codex proposal step 6 or above for the crops requested	Petition Number: PP#5F7016 DP Number: 327026 Other Identifier:
Residue definition (step 8/CXL): N/A	Reviewer/Branch: A. Acierto/RAB3
	Residue definition: Fluopicolide *per se*

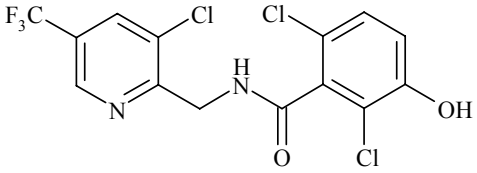
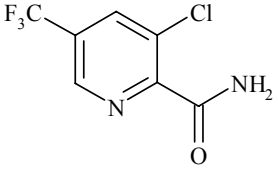
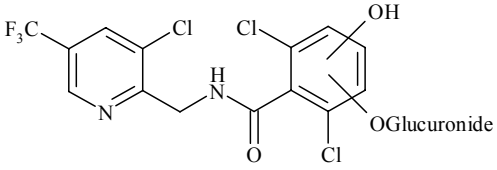
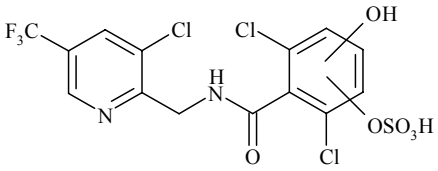
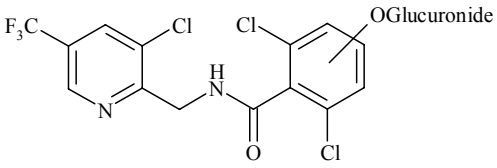
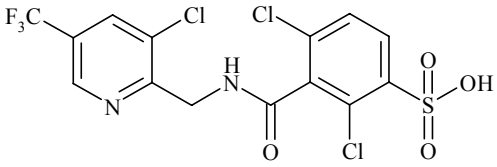
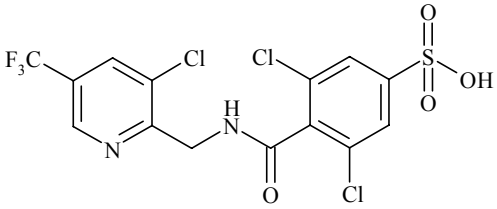
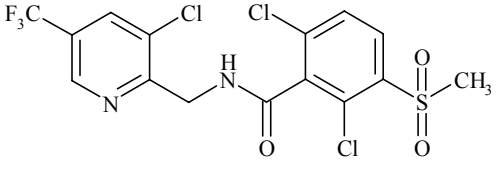
Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		Tuberous and corm vegetables subgroup 1C	0.02
		Vegetable, leafy, except *brassica*, group 4	20
		Vegetable, fruiting, group 8	0.8
		Vegetable, cucurbit, group 9	0.4
		Grape	2
		Raisins	6
		Wheat forage	0.2
		Wheat grain	0.02
		Wheat hay	0.5
		Wheat straw	0.5

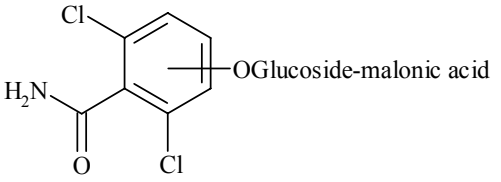
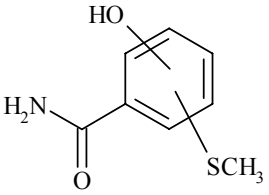
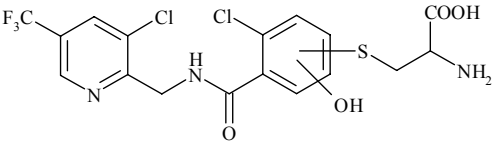
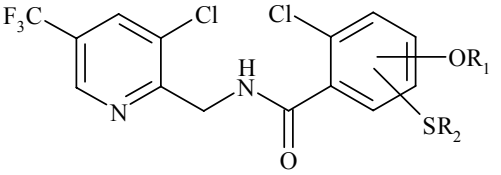
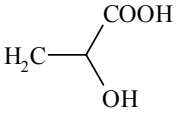
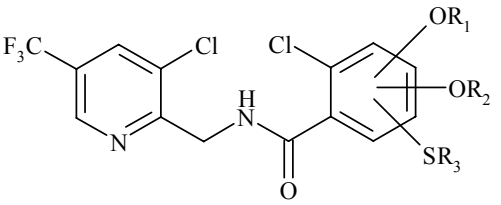
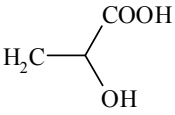
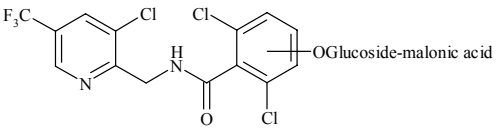
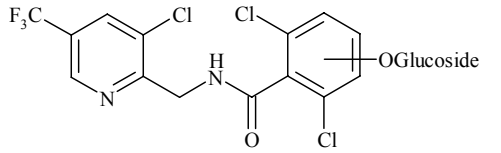
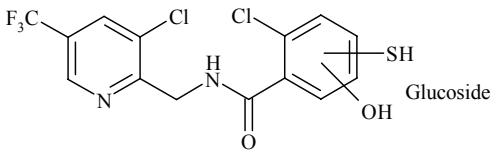
Limits for Canada	Limits for Mexico
√ No Limits □No Limits for the crops requested	√ No Limits □No Limits for the crops requested
Residue definition: N/A	Residue definition: N/A

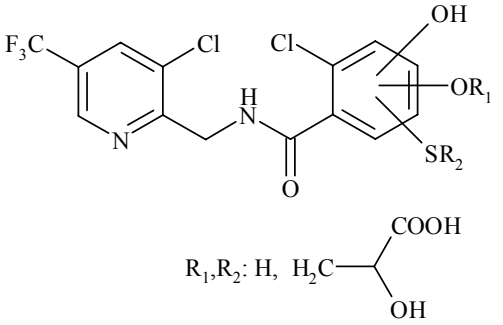
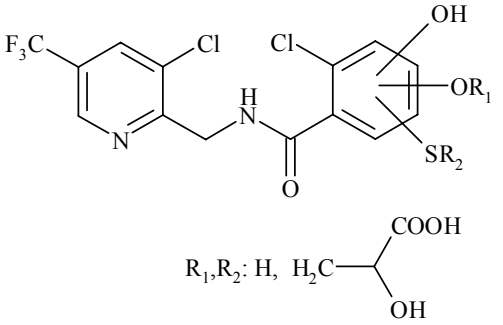
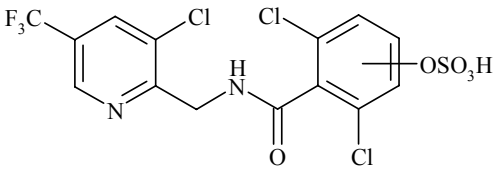
Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)

Notes/Special Instructions:
S. Funk, 02/20/2007.

Appendix I. Chemical Names and Structures of Fluopicolide and its Transformation Products.		
Common name/code	Chemical name	Chemical structure
Fluopicolide AE C638206	2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl-2-pyridinyl]methyl]benzamide	
AE C653711 BAM	2,6-dichlorobenzamide	
AE C657188 PCA	3-chloro-5-trifluoromethylpyridine-2-carboxylic acid	
AE C657378 3-OH-BAM or BAM-OH	2,6-dichloro-3-hydroxybenzamide	
AE 1344122 P1X	3-methylsulfinyl-5-trifluoromethylpyridine-2-carboxylic acid	
AE 0608000	*N*-[(3-chloro-5-trifluoromethylpyridin-2-yl)(hydroxy)methyl]-2,6-dichlorobenzamide	
AE 0712556	2,6-dichloro-*N*-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-4-hydroxybenzamide	
AE B102859 (Pyridinol)	3-chloro-5-(trifluoromethyl)-2-pyridinol	

Appendix I. Chemical Names and Structures of Fluopicolide and its Transformation Products.		
Common name/code	Chemical name	Chemical structure
AE C643890	2,6-dichloro-*N*-[(3-chloro-5-(trifluoromethyl)-2-pyridinyl)methyl]-3-hydroxybenzamide	
AE C653598	3-chloro-5-(trifluoromethyl)-2-pyridine carboxamide	
Dihydroxy glucuronide of fluopicolide		
Dihydroxy sulfate of fluopicolide		
Hydroxy glucuronide of fluopicolide		
Hydroxy sulfate of fluopicolide		 
Metabolite 1	2,6-dichloro-*N*-{[3-chloro-5-(trifluoromethyl)pyridin-2-yl]methyl}-3-(methylsulfonyl)benzamide	

Appendix I. Chemical Names and Structures of Fluopicolide and its Transformation Products.		
Common name/code	Chemical name	Chemical structure
P2ab P2a and P2b proposed to be isomers with differences in chromatographic behavior		
P2c		
P4a		
P4b		 R_1,R_2: Glucoside, 
P4c		 R_1,R_2,R_3: H, Glucoside, 
P5		
P8a Two components characterized as glucoside conjugates		 

Appendix I. Chemical Names and Structures of Fluopicolide and its Transformation Products.		
Common name/code	Chemical name	Chemical structure
P8b Position of hydroxylation and OR_1 and SR_2 unknown		
P10 isomer to P8b; position of hydroxylation and OR1 and SR2 unknown		
P11		

Appendix II. Tolerance Assessment Calculations.

For each of the crops listed below, the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, along with the tolerance spreadsheet, was used for calculating recommended tolerances. As specified in the SOP, the minimum of the 95% upper confidence limit (UCL) on the 95th percentile and the point estimate of the 99th percentile was selected as the tolerance value in cases when the dataset was large (greater than 15 samples) and reasonably lognormal. For datasets that were small (≤15 samples) and reasonably lognormal, the upper bound estimate of the 95th percentile based on the median residue value was compared to the minimum of the 95% UCL on the 95th percentile and the point estimate of the 99th percentile, and the minimum value was selected as the tolerance value. For datasets that were not lognormal, the upper bound on the 89th percentile was selected as the tolerance value (distribution-free method). The rounding procedures specified in the SOP were also used.

Tuberous and corm vegetables, Crop group 1, Subgroup 1C

The dataset used to establish a tolerance for fluopicolide on the tuberous and corm vegetables consisted of field trial data for potato, representing application rates of 0.36 lb ai/A (3 applications at 0.119 lb ai/A/application) with a 7-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates and PHIs are within 25% of the maximum label application rate and minimum label PHI, respectively. The fluopicolide residue values were less than the LOQ (<0.01 ppm). Values below the LOQ are generally referred to as censored data. The use of maximum likelihood estimation (MLE) techniques to estimate the mean and standard deviation of dataset is normally recommended if more than 10-15% of the dataset is censored but not for datasets with large degree of censoring (i.e., >60%) since the technique becomes unreliable. Since the residues of fluoicolide were below the LOQ in/on all potato tuber samples, except one in which the residue was detected at 0.013, ppm, no calculation was necessary.

Leafy vegetable, except *Brassica*, group 4

The dataset used to establish a tolerance for fluopicolide on the leafy vegetable crop group consisted of field trial data for celery, head lettuce, leaf lettuce, and spinach, representing application rates of 0.36 lb ai/A (3 applications at 0.119 lb ai/A/application) with a 2-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates and PHIs are within 25% of the maximum label application rate and minimum label PHI, respectively. The residue values used to calculate the tolerance are provided in Table II-1.

All field trial sample results were above the LOQ and each dataset was small (less than 15 samples). Since there were no values reported below the LOQ, maximum likelihood estimation (MLE) procedures were not needed to impute censored values.

The dataset for each crop was entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plots for celery, head lettuce, and spinach (Figures II-1, II-3, and II-7) provided in the spreadsheet indicate that with the exception of leaf lettuce, the datasets are each reasonably lognormal. The results from the approximate Shapiro-Francia test statistic (Figures II-2, II-4, and II-8) confirmed that the assumption of lognormality should not be rejected for

celery, head lettuce, or spinach. For leaf lettuce, the result from the approximate Shapiro-Francia test statistic (Figure II-6) indicated that the assumption of lognormality should be rejected, and visual inspection of the lognormal probability plot (Figure II-5) confirmed that the dataset is not lognormal.

Using the tolerance spreadsheet, the recommended tolerances were 25 ppm for celery, 17 ppm for head lettuce, 16 ppm for leaf lettuce, and 25 ppm for spinach. Because the minimum and maximum recommended tolerances differ by less than 5x, a crop group tolerance is appropriate for leafy vegetable. The recommended value is 25 ppm, the maximum of the recommended individual tolerances.

Table II-1. Residue data used to calculate tolerance for fluopicolide on the leafy vegetable (except *Brassica*) crop group.

Regulator:	EPA	EPA	EPA	EPA
Chemical:	Fluopicolide	Fluopicolide	Fluopicolide	Fluopicolide
Crop:	Celery (untrimmed)	Head lettuce	Leaf lettuce	Spinach
PHI:	2 days	2 days	2 days	2 days
App. Rate:	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.	Valent U.S.A.	Valent U.S.A.	Valent U.S.A.
MRID Citation:	46708539	46708533	46708534	46708540
	Residues of Fluopicolide (ppm)			
	4.900	2.080	7.860	6.860
	5.200	2.450	11.700	6.130
	1.110	0.455	7.610	11.800
	1.350	0.500	6.290	15.500
	6.680	1.180	4.330	5.430
	6.530	2.330	3.330	6.840
	0.983	0.475	4.990	15.500
	1.030	0.616	0.444	16.800
	0.762	4.160	6.560	8.550
	0.325	3.450	7.550	8.510
	6.100	4.320	5.300	11.500
	13.600	2.880	3.860	9.210
		5.520	9.020	6.480
		7.150	10.300	6.780

Figure II- 1. Lognormal probability plot of fluopicolide field trial data for untrimmed celery.

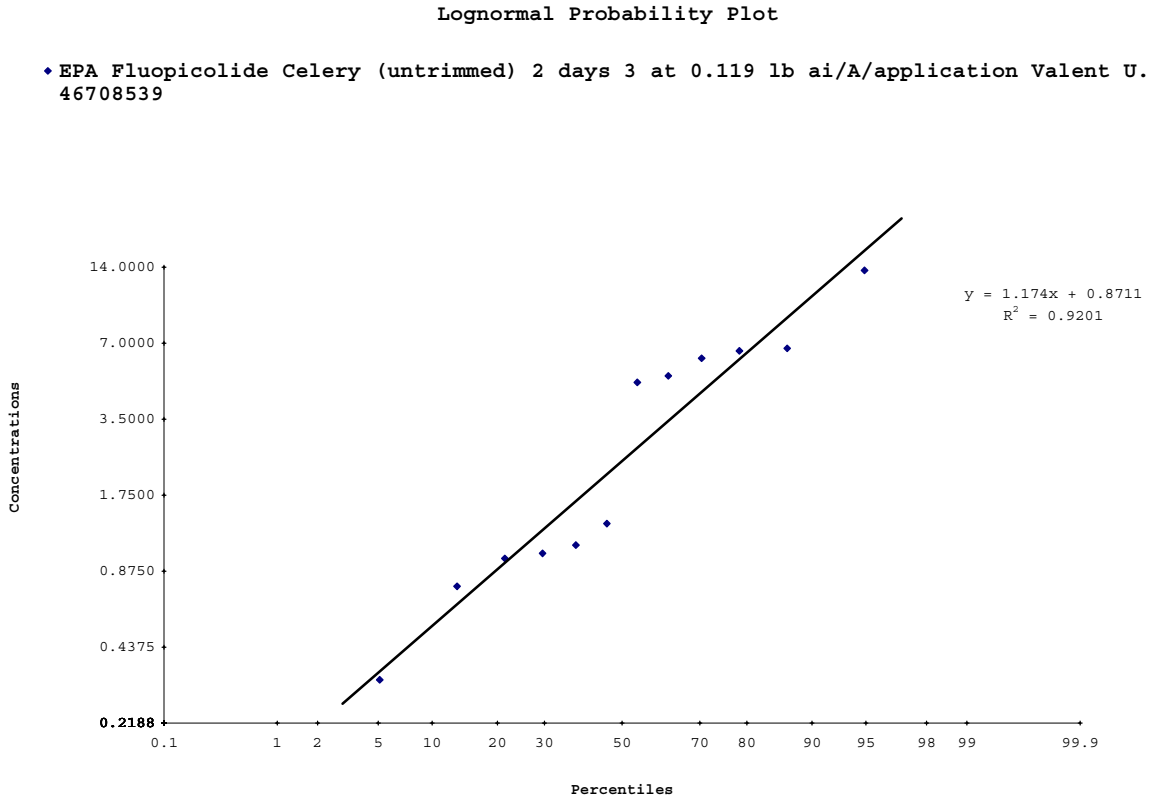


Figure II- 2. Tolerance spreadsheet summary of fluopicolide field trial data for untrimmed celery.

Regulator:	EPA
Chemical:	Fluopicolide
Crop:	Celery (untrimmed)
PHI:	2 days
App. Rate:	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.
MRID Citation:	46708539
n:	12
min:	0.33
max:	13.60
median;	3.13
average:	4.05

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	11 (15)	14 (19)	17 (--)
EU Method I Log Normal	17 **(60)**	**40** (190)	90 (--)
EU Method II Distribution-Free		13	
California Method μ + 3σ		**16**	
UPLMedian95th		25	
Approximate Shapiro-Francia Normality Test		0.9201 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 3. Lognormal probability plot of fluopicolide field trial data for head lettuce.

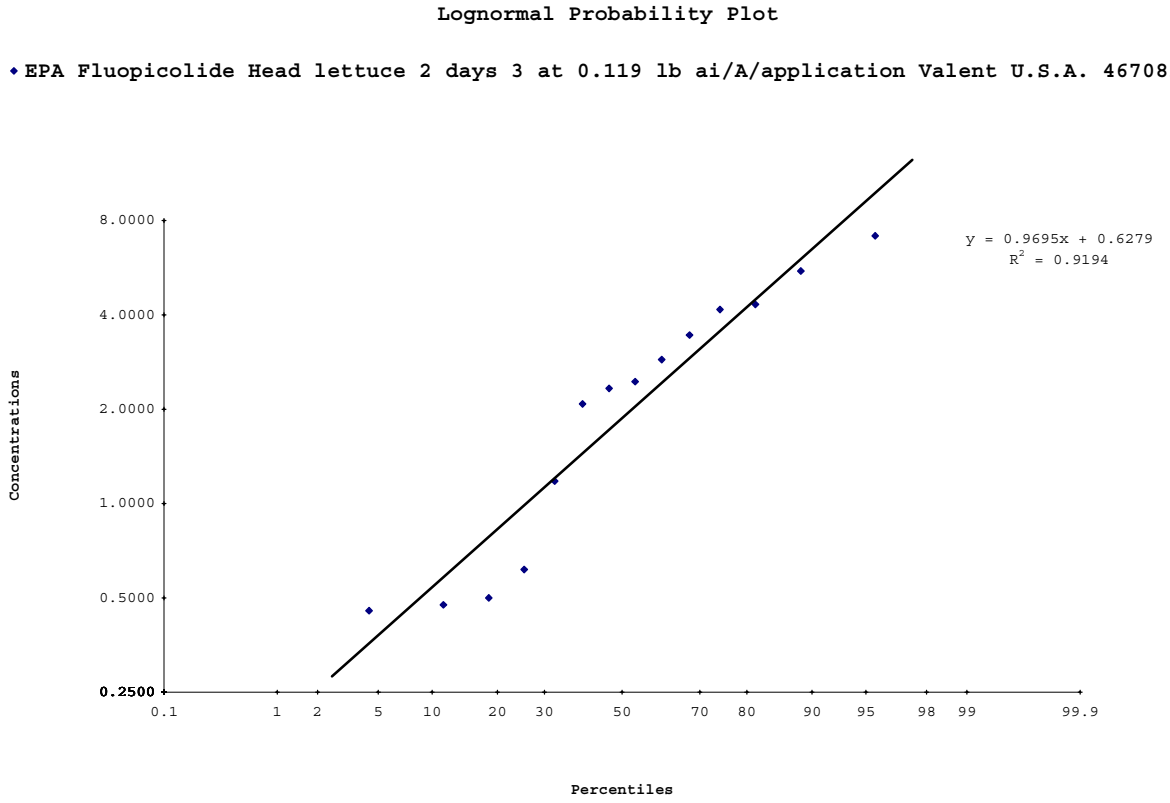


Figure II- 4. Tolerance spreadsheet summary of fluopicolide field trial data for head lettuce.

Regulator:	EPA
Chemical:	Fluopicolide
Crop:	Head lettuce
PHI:	2 days
App. Rate:	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.
MRID Citation:	46708533
n:	14
min:	0.46
max:	7.15
median;	2.39
average:	2.68

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	7.0 (9.0)	8.0 (11)	10 (--)
EU Method I Log Normal	10 **(25)**	**18** (60)	40 (--)
EU Method II Distribution-Free		9.0	
California Method μ + 3σ		**9.0**	
UPLMedian95th		17	
Approximate Shapiro-Francia Normality Test		0.9194 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 5. Lognormal probability plot of fluopicolide field trial data for leaf lettuce.

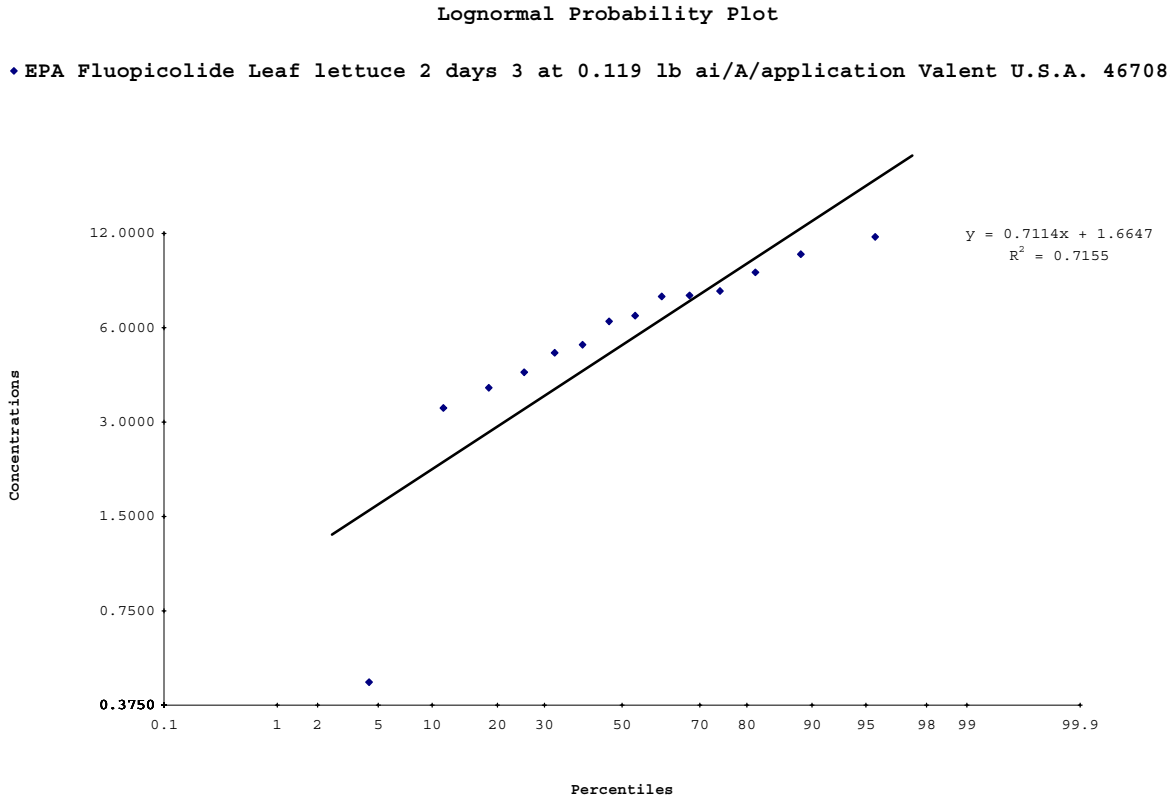


Figure II- 6. Tolerance spreadsheet summary of fluopicolide field trial data for leaf lettuce.

Regulator: EPA
Chemical: Fluopicolide
Crop: Leaf lettuce
PHI: 2 days
App. Rate: 3 at 0.119 lb ai/A/application
Submitter: Valent U.S.A.
MRID Citation: 46708534

n: 14
min: 0.44
max: 11.70
median; 6.43
average: 6.37

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	12 (15)	14 (17)	16 (--)
EU Method I Log Normal	20 **(45)**	**35** (95)	65 (--)
EU Method II Distribution-Free		17	
California Method μ + 3σ		16	
UPLMedian95th		**45**	
Approximate Shapiro-Francia Normality Test		0.7155 p-value <= 0.01: Reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 7. Lognormal probability plot of fluopicolide field trial data for spinach.

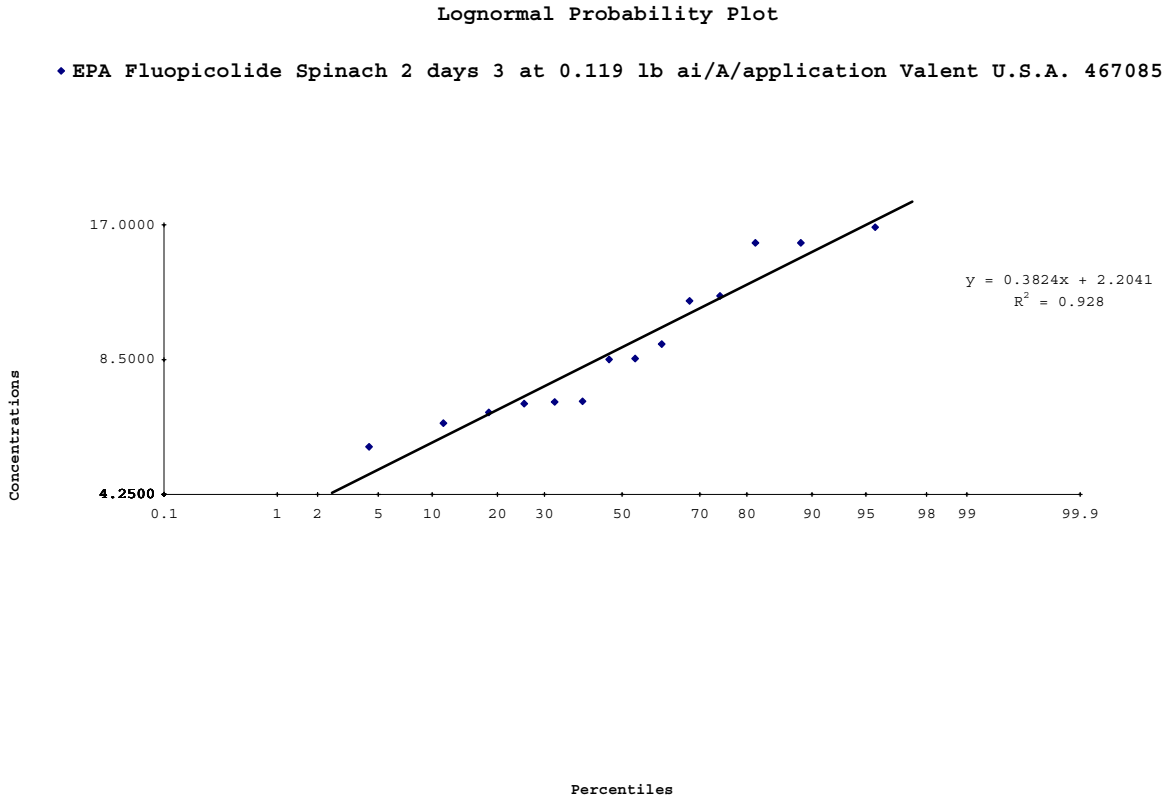


Figure II- 8. Tolerance spreadsheet summary of fluopicolide field trial data for spinach.

Regulator:	EPA
Chemical:	Fluopicolide
Crop:	Spinach
PHI:	2 days
App. Rate:	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.
MRID Citation:	46708540
n:	14
min:	5.43
max:	16.80
median;	8.53
average:	9.71

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	17 (20)	19 (25)	25 (--)
EU Method I Log Normal	17 **(25)**	**25** (40)	30 (--)
EU Method II Distribution-Free	30		
California Method μ + 3σ	**25**		
UPLMedian95th	**60**		
Approximate Shapiro-Francia Normality Test	0.9280 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Fruiting vegetable, group 8

The dataset used to establish a tolerance for fluopicolide on the fruiting vegetable crop group consisted of field trial data for bell pepper, chili pepper, and tomato, representing application rates of 0.36 lb ai/A (3 applications at 0.119 lb ai/A/application) with a 2-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates and PHIs are within 25% of the maximum label application rate and minimum label PHI, respectively. The residue values used to calculate the tolerance are provided in Table II-2.

All field trial sample results were above the LOQ. Since there were no values reported below the LOQ, MLE procedures were not needed to impute censored values. The datasets for bell and chili pepper were each <15 samples, and the combined dataset was >15 samples; these datasets were entered into the tolerance spreadsheet separately and together. The dataset for tomato was >15 samples.

The dataset for each crop was entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plots (Figures II-9, II-11, II-13, and II-15) provided in the spreadsheet indicate that the datasets are each reasonably lognormal. The results from the approximate Shapiro-Francia test statistic (Figures II-10, II-12, II-14, and II-16) confirmed that the assumption of lognormality should not be rejected. Because the combined bell pepper and nonbell pepper dataset was found to be reasonably lognormal, the combined data were used for tolerance setting purposes.

Using the tolerance spreadsheet, the recommended tolerances were 1.1 ppm for bell and nonbell pepper and 0.70 ppm for tomato. Because the minimum and maximum recommended tolerances differ by less than 5x, a crop group tolerance is appropriate for fruiting vegetable. The recommended value is 1.1 ppm, the maximum of the recommended individual tolerances.

Table II-2. Residue data used to calculate tolerance for fluopicolide on the fruiting vegetable crop group.

Regulator:	EPA	EPA	EPA
Chemical:	Fluopicolide	Fluopicolide	Fluopicolide
Crop:	Bell pepper	Chili pepper	Tomato
PHI:	2 days	2 days	2 days
App. Rate:	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.	Valent U.S.A.	Valent U.S.A.
MRID Citation:	46708530	46708535	46708536
	Residues of Fluopicolide (ppm)		
	0.047	0.096	0.200
	0.041	0.084	0.280
	0.092	0.358	0.190
	0.060	0.241	0.190
	0.167	0.456	0.053
	0.095	0.576	0.041
	0.148		0.170
	0.103		0.170
	0.194		0.150

Table II-2. Residue data used to calculate tolerance for fluopicolide on the fruiting vegetable crop group.			
Regulator:	EPA	EPA	EPA
Chemical:	Fluopicolide	Fluopicolide	Fluopicolide
Crop:	Bell pepper	Chili pepper	Tomato
PHI:	2 days	2 days	2 days
App. Rate:	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.	Valent U.S.A.	Valent U.S.A.
MRID Citation:	46708530	46708535	46708536
	Residues of Fluopicolide (ppm)		
	0.104		0.130
	0.044		0.081
	0.041		0.058
	0.489		0.083
	0.557		0.100
			0.190
			0.130
			0.015
			0.062
			0.170
			0.140
			0.330
			0.420
			0.100
			0.150

Figure II- 9. Lognormal probability plot of fluopicolide field trial data for bell pepper.

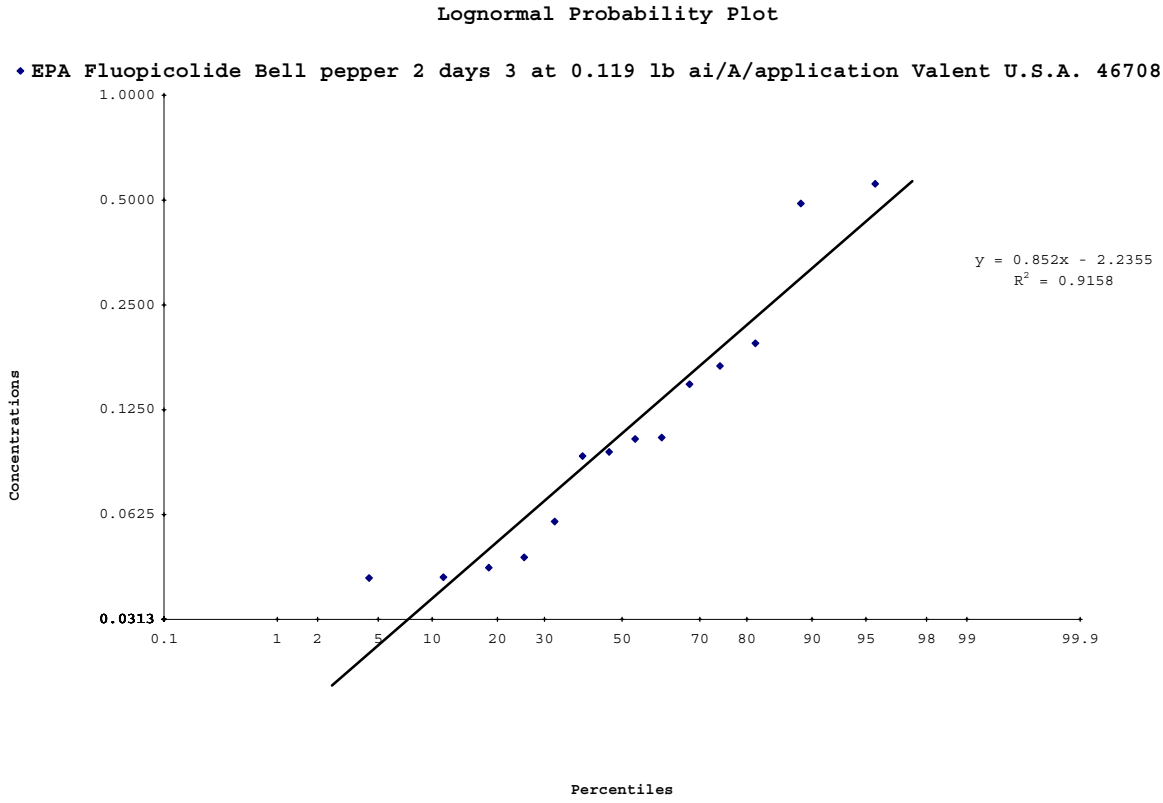


Figure II- 10. Tolerance spreadsheet summary of fluopicolide field trial data for bell pepper.

Regulator:	EPA
Chemical:	Fluopicolide
Crop:	Bell pepper
PHI:	2 days
App. Rate:	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.
MRID Citation:	46708530
n:	14
min:	0.04
max:	0.56
median;	0.10
average:	0.16

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.45 (0.60)	0.60 (0.80)	0.70 (--)
EU Method I Log Normal	0.45 **(1.0)**	**0.80** (2.5)	1.5 (--)
EU Method II Distribution-Free		0.35	
California Method μ + 3σ		**0.70**	
UPLMedian95th		0.70	
Approximate Shapiro-Francia Normality Test		0.9158 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 11. Lognormal probability plot of fluopicolide field trial data for chili pepper.

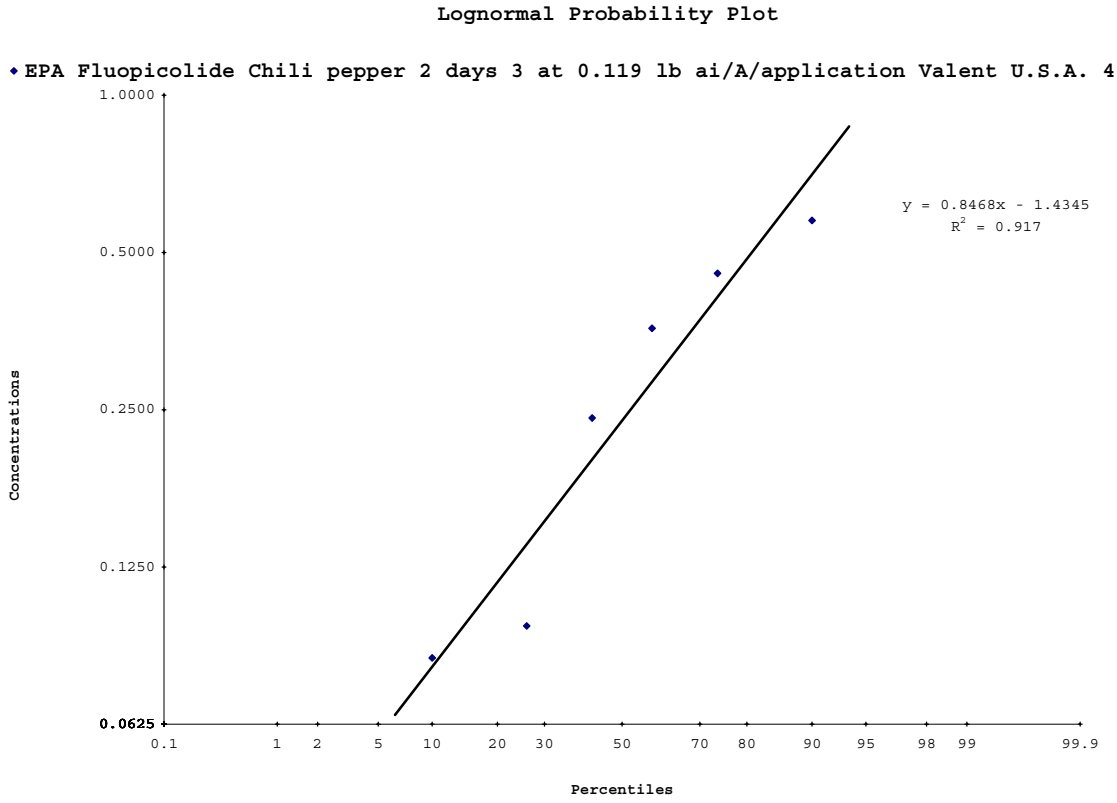


Figure II- 12. Tolerance spreadsheet summary of fluopicolide field trial data for chili pepper.

Regulator:	EPA
Chemical:	Fluopicolide
Crop:	Chili pepper
PHI:	2 days
App. Rate:	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.
MRID Citation:	46708535
n:	6
min:	0.08
max:	0.58
median;	0.30
average:	0.30

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.70 (1.1)	0.80 (1.4)	1.0 (--)
EU Method I Log Normal	1.0 **(5.0)**	1.6 (15)	3.0 (--)
EU Method II Distribution-Free	1.0		
California Method μ + 3σ	**0.90**		
UPLMedian95th	**3.5**		
Approximate Shapiro-Francia Normality Test	0.9170 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Figure II- 13. Lognormal probability plot of fluopicolide field trial data for bell and nonbell pepper.

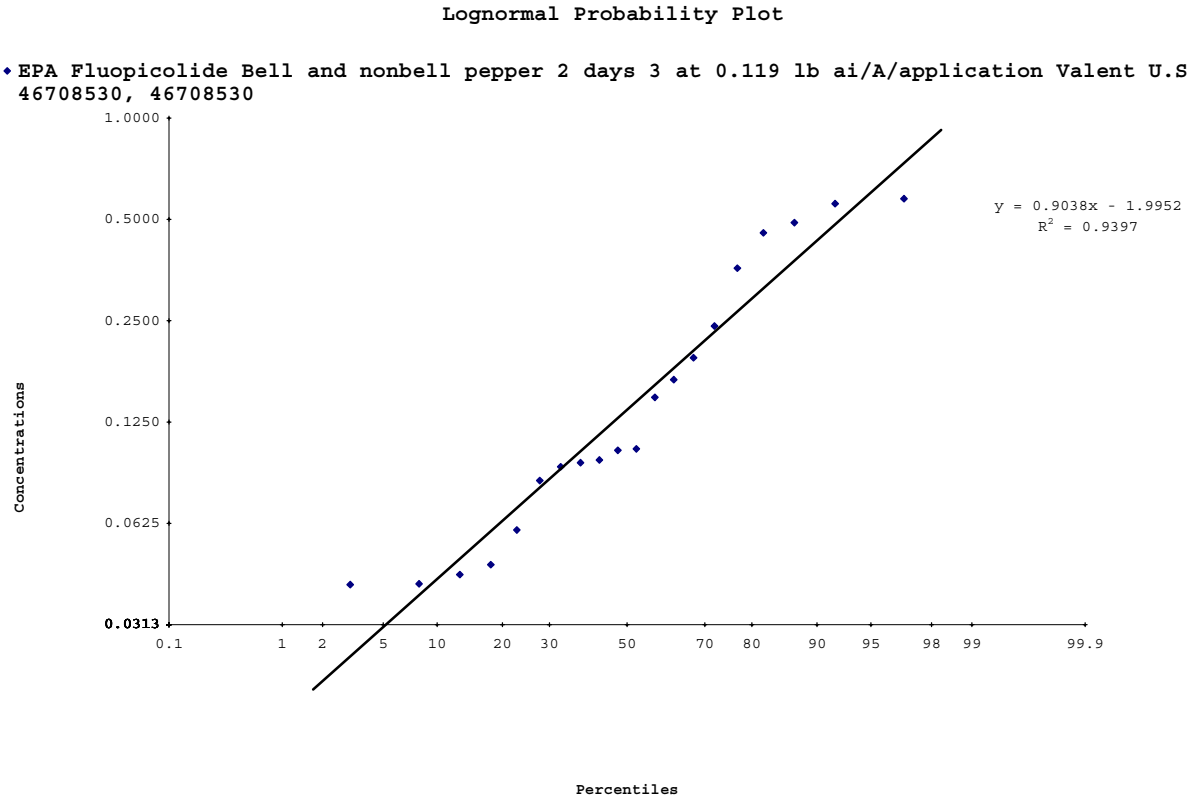


Figure II- 14. Tolerance spreadsheet summary of fluopicolide field trial data for bell and nonbell pepper.

	Regulator: EPA **Chemical:** Fluopicolide **Crop:** Bell and nonbell pepper **PHI:** 2 days **App. Rate:** 3 at 0.119 lb ai/A/application **Submitter:** Valent U.S.A. **MRID Citation:** 46708530, 46708530 **n:** 20 **min:** 0.04 **max:** 0.58 **median;** 0.10 **average:** 0.20		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.50 (0.70)	0.70 (0.90)	0.80 (--)
EU Method I Log Normal	0.60 **(1.2)**	1.1 (3.0)	2.5 (--)
EU Method II Distribution-Free	0.70		
California Method μ + 3σ	**0.80**		
UPLMedian95th	**0.70**		
Approximate Shapiro-Francia Normality Test	0.9397 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Figure II- 15. Lognormal probability plot of fluopicolide field trial data for tomato.

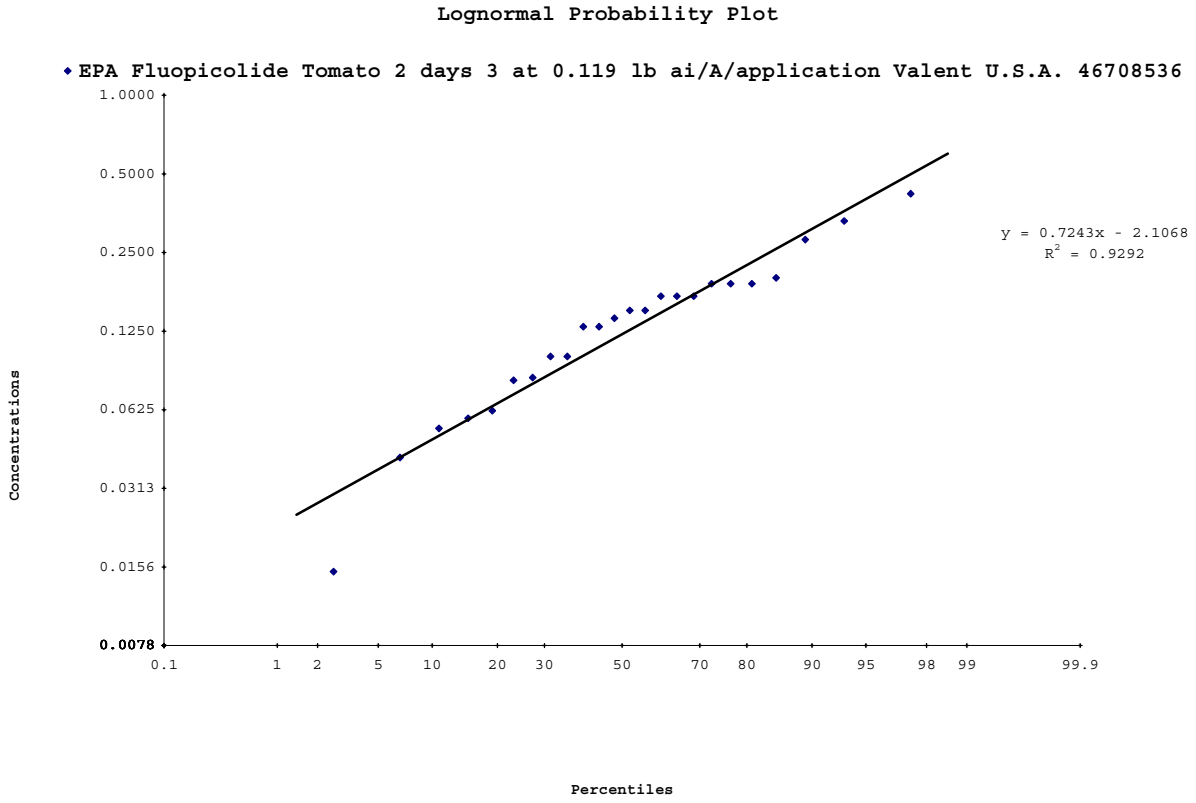


Figure II- 16. Tolerance spreadsheet summary of fluopicolide field trial data for tomato.

Regulator: EPA
Chemical: Fluopicolide
Crop: Tomato
PHI: 2 days
App. Rate: 3 at 0.119 lb ai/A/application
Submitter: Valent U.S.A.
MRID Citation: 46708536

n: 24
min: 0.02
max: 0.42
median; 0.15
average: 0.15

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.35 (0.40)	0.40 (0.45)	0.45 (--)
EU Method I Log Normal	0.45 **(0.70)**	**0.70** (1.3)	1.2 (--)
EU Method II Distribution-Free		0.40	
California Method μ + 3σ		**0.45**	
UPLMedian95th		**0.90**	
Approximate Shapiro-Francia Normality Test		0.9292 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Cucurbit vegetable, group 9

The dataset used to establish a tolerance for fluopicolide on the cucurbit vegetable crop group consisted of field trial data for cantaloupe, cucumber, and summer squash, representing application rates of 0.36 lb ai/A (3 applications at 0.119 lb ai/A/application) with a 2-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates and PHIs are within 25% of the maximum label application rate and minimum label PHI, respectively. The residue values used to calculate the tolerance are provided in Table II-3.

All field trial sample results for summer squash were above the LOQ and 11 of 12 sample results for cucumber were above the LOQ; each dataset consisted of 12 samples. For cantaloupe, 3 of the 16 sample results were below the LOQ. Since less than 10% of the sample results for cucumber and summer squash were below the LOQ, MLE procedures were not needed to impute censored values. However, because 15% of the cantaloupe results were below the LOQ, the MLE procedure was used to impute censored values.

The datasets for cantaloupe, cucumber and summer squash were entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plots (Figures II-17a, II-18a and II-19) provided in the spreadsheet indicate that the datasets are each reasonably lognormal. The results from the approximate Shapiro-Francia test statistic (Figures II-17b, II-18b and II-20) confirmed that the assumption of lognormality should not be rejected.

Using the tolerance spreadsheet, the recommended tolerances were 0.08 ppm each for cucumber and summer squash. The maximum observed residue value for cantaloupe was 0.258 ppm. Because these values differ by less than 5x, a crop group tolerance is appropriate for cucurbit vegetable. The petitioner has proposed a tolerance of 0.4 ppm; the available data indicate that 0.50 ppm is an appropriate value for the tolerance.

Table II-3. Residue data used to calculate tolerance for fluopicolide on the cucurbit vegetable crop group.

Regulator:	EPA	EPA	EPA
Chemical:	Fluopicolide	Fluopicolide	Fluopicolide
Crop:	Cantaloupe	Cucumber	Summer squash
PHI:	2 days	2 days	2 days
App. Rate:	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.	Valent U.S.A.	Valent U.S.A.
MRID Citation:	46708531	46708532	46708538
	Residues of Fluopicolide (ppm)		
	0.043	0.016	0.039
	0.069	0.031	0.051
	0.053	0.013	0.014
	0.048	<0.01	0.014
	0.066	0.016	0.017
	0.040	0.011	0.027
	0.030	0.024	0.034
	0.060	0.029	0.042
	<0.01	0.028	0.040

Table II-3. Residue data used to calculate tolerance for fluopicolide on the cucurbit vegetable crop group.			
Regulator:	EPA	EPA	EPA
Chemical:	Fluopicolide	Fluopicolide	Fluopicolide
Crop:	Cantaloupe	Cucumber	Summer squash
PHI:	2 days	2 days	2 days
App. Rate:	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.	Valent U.S.A.	Valent U.S.A.
MRID Citation:	46708531	46708532	46708538
	Residues of Fluopicolide (ppm)		
	<0.01	0.015	0.035
	0.040	0.057	0.019
	0.057	0.043	0.030
	0.080		
	0.098		
	0.104		
	0.258		
	<0.01		
	0.163		

Figure II- 17a. Lognormal probability plot of fluopicolide field trial data for cantaloupe.

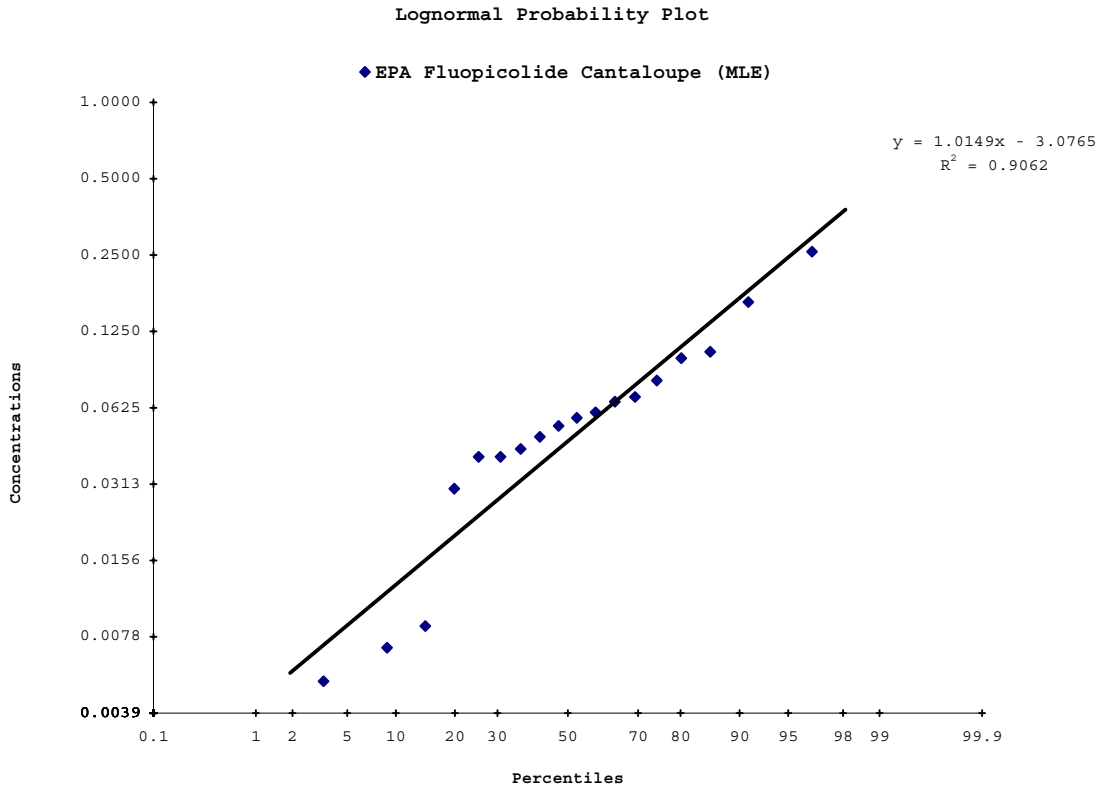


Figure II- 17b. Tolerance spreadsheet summary of fluopicolide field trial data for cantaloupe.

	Regulator: EPA		
	Chemical: Fluopicolide		
	Crop: Cantaloupe (MLE)		
	PHI: 2 days		
	App. Rate: 0.119 lb ai/A/application		
	Submitter: Valent USA		
	n: 18		
	min: 0.01		
	max: 0.26		
	median; 0.06		
	average: 0.07		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.20 (0.25)	0.25 (0.30)	0.30 (--)
EU Method I Log Normal	0.25 **(0.60)**	**0.50** (1.5)	1.1 (--)
EU Method II Distribution-Free		0.20	
California Method μ + 3σ		**0.30**	
UPLMedian95th		**0.40**	
Approximate Shapiro-Francia Normality Test	0.9062 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values round Y

Figure II- 18a. Lognormal probability plot of fluopicolide field trial data for cucumber.

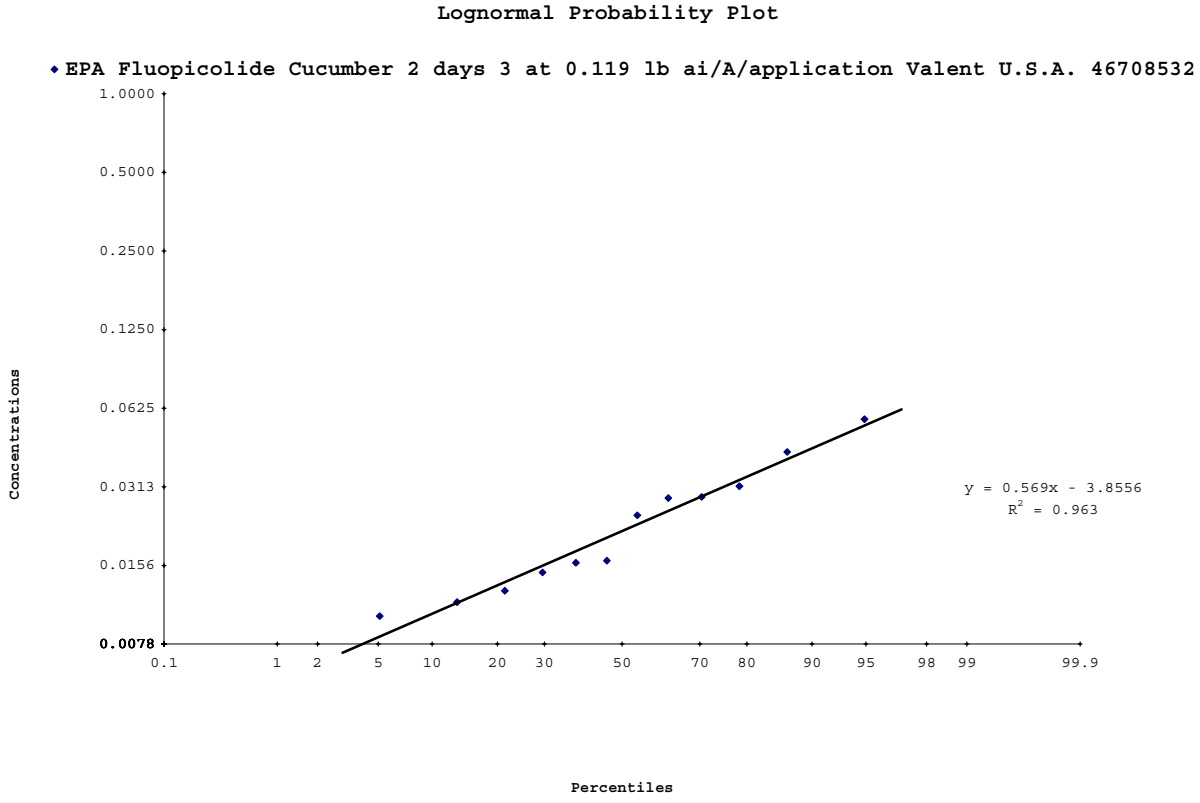


Figure II- 18b. Tolerance spreadsheet summary of fluopicolide field trial data for cucumber.

	Regulator: EPA		
	Chemical: Fluopicolide		
	Crop: Cucumber		
	PHI: 2 days		
	App. Rate: 3 at 0.119 lb ai/A/application		
	Submitter: Valent U.S.A.		
	MRID Citation: 46708532		
	n: 12		
	min: 0.01		
	max: 0.06		
	median; 0.02		
	average: 0.02		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.05 (0.07)	0.06 (0.08)	0.07 (--)
EU Method I Log Normal	0.06 **(0.10)**	**0.08** (0.20)	0.15 (--)
EU Method II Distribution-Free	0.07		
California Method μ + 3σ	**0.07**		
UPLMedian95th	**0.15**		
Approximate Shapiro-Francia Normality Test	0.9630 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Figure II- 19. Lognormal probability plot of fluopicolide field trial data for summer squash.

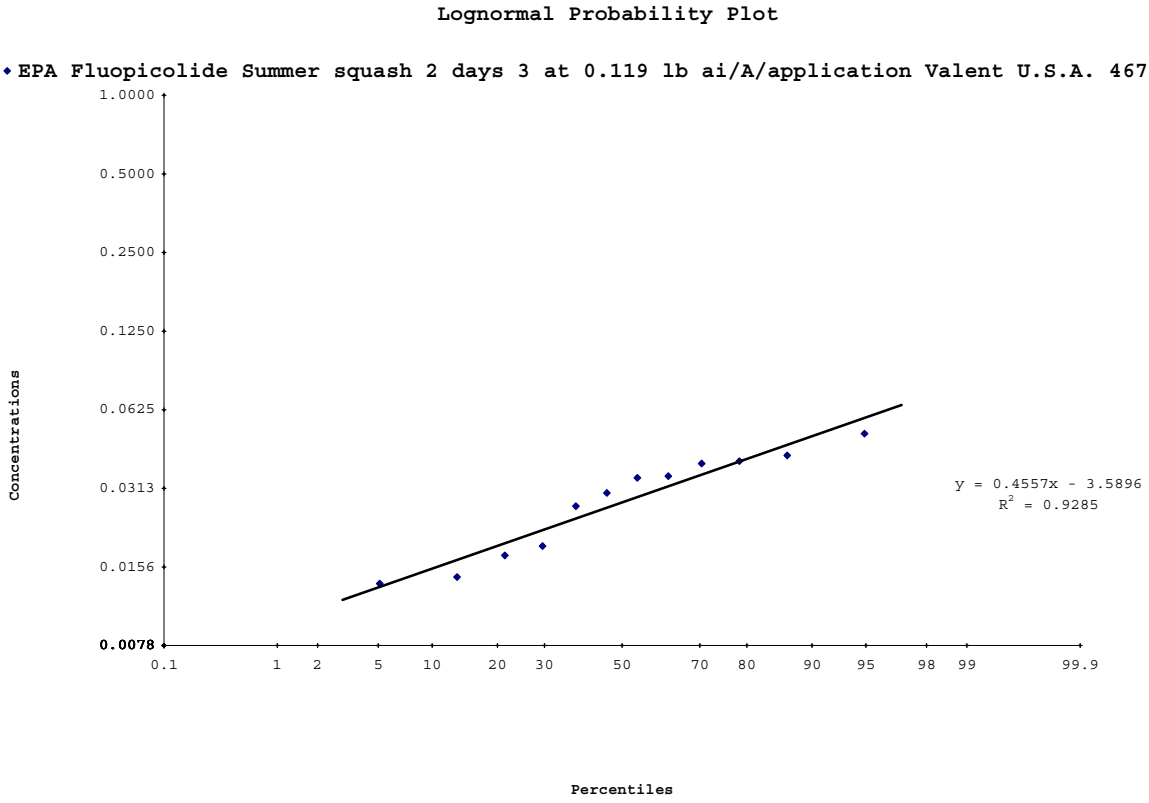


Figure II- 20. Tolerance spreadsheet summary of fluopicolide field trial data for summer squash.

Regulator:	EPA
Chemical:	Fluopicolide
Crop:	Summer squash
PHI:	2 days
App. Rate:	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.
MRID Citation:	46708538
n:	12
min:	0.01
max:	0.05
median;	0.03
average:	0.03

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.05 (0.07)	0.06 (0.08)	0.07 (--)
EU Method I Log Normal	0.06 **(0.10)**	**0.08** (0.15)	0.15 (--)
EU Method II Distribution-Free	0.08		
California Method μ + 3σ	**0.07**		
UPLMedian95th	**0.25**		
Approximate Shapiro-Francia Normality Test	0.9285 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Grape

The dataset used to establish a tolerance for fluopicolide on grape consisted of field trial data representing application rates of 0.36 lb ai/A (3 applications at 0.119 lb ai/A/application) with a 20- to 21-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates and PHIs are within 25% of the maximum label application rate and minimum label PHI, respectively. The residue values used to calculate the tolerance are provided in Table II-4.

All field trial sample results were above the LOQ and the dataset was large (32 samples).

The dataset was entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plot (Figure II-21) provided in the spreadsheet indicate that the dataset was reasonably lognormal. The results from the approximate Shapiro-Francia test statistic (Figure II-22) confirmed that the assumption of lognormality should not be rejected.

Using the tolerance spreadsheet, the recommended tolerance for grape was 1.4 ppm. HED has recently recommended for a tolerance for fluopicolide residues in grape at 2.0 ppm, in support of use on imported grapes. The available domestic crop field trial data for grape indicate that the recommended tolerance of 2.0 ppm is appropriate.

Table II-4. Residue data used to calculate tolerance for fluopicolide on grape.

Regulator:	EPA	
Chemical:	Fluopicolide	
Crop:	Grape (domestic)	
PHI:	20-21 days	
App. Rate:	3 at 0.119 lb ai/A/application	
Submitter:	Valent U.S.A.	
MRID Citation:	46708541	
	Residues of Fluopicolide (ppm)	
	0.440	0.100
	0.320	0.077
	0.070	0.120
	0.065	0.130
	0.260	0.093
	0.210	0.098
	0.220	0.980
	0.320	0.990
	0.250	0.850
	0.220	1.100
	0.560	0.190
	0.320	0.150
	0.100	0.140
	0.130	0.130
	0.180	0.430
	0.210	0.530

Figure II-21. Lognormal probability plot of fluopicolide field trial data for grape.

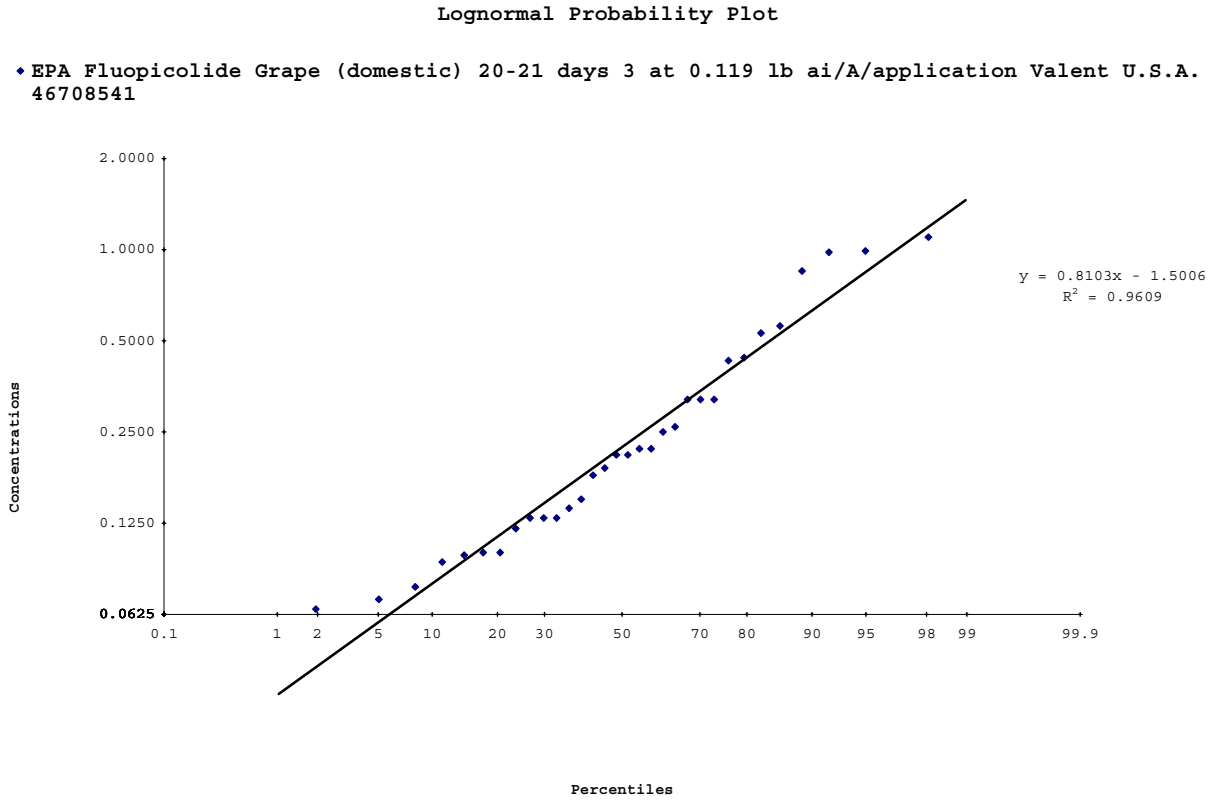


Figure II- 22. Tolerance spreadsheet summary of fluopicolide field trial data for grape.

Regulator:	EPA
Chemical:	Fluopicolide
Crop:	Grape (domestic)
PHI:	20-21 days
App. Rate:	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.
MRID Citation:	46708541
n:	32
min:	0.07
max:	1.10
median;	0.21
average:	0.31

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.80 (1.0)	1.0 (1.2)	1.3 (--)
EU Method I Log Normal	0.90 **(1.4)**	**1.5** (3.0)	3.0 (--)
EU Method II Distribution-Free	0.90		
California Method μ + 3σ	**1.2**		
UPLMedian95th	**1.2**		
Approximate Shapiro-Francia Normality Test	0.9609 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Rotated wheat commodities

The dataset used to establish a tolerance for fluopicolide on rotated wheat forage, hay, and straw consisted of extensive field rotational crop data for wheat; fluopicolide was applied to a primary crop at ~0.36 lb ai/A (3 applications at ~0.119 lb ai/A/application) and wheat was planted 29-37 days after last application. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates and plantback intervals (PBIs) are within 25% of the maximum label application rate and proposed label PBI, respectively. The residue values used to calculate the tolerance are provided in Table II-5.

All field trial sample results, with the exception of one wheat forage result and four wheat straw results, were above the LOQ, and each dataset was large (42 samples).

The dataset for each crop was entered into the tolerance spreadsheet. The results from the approximate Shapiro-Francia test statistic (Figures II-24, II-26, and II-28) indicate that the assumption of lognormality should be rejected for each crop, and visual inspection of the lognormal probability plots (Figures II-23, II-25, and II-27) confirmed that the datasets are not lognormal.

Using the tolerance spreadsheet, the recommended tolerances were 0.20 ppm for wheat forage, 0.50 ppm for wheat hay, and 0.30 ppm for wheat straw. The recommended tolerances for wheat forage and hay are appropriate. However, method validation data for residues of fluopicolide in/on wheat straw indicated marginally adequate performance, with recoveries ranging 61.5-75.5%. These low recoveries, in combination with the 0.30-ppm tolerance calculated by the tolerance spreadsheet, indicate that the proposed tolerance of 0.50 ppm for wheat straw is appropriate.

Table II-5. Residue data used to calculate tolerances for fluopicolide on rotated wheat forage, hay, and straw.

Regulator:	EPA	EPA	EPA
Chemical:	Fluopicolide	Fluopicolide	Fluopicolide
Crop:	Rotated wheat forage	Rotated wheat hay	Rotated wheat straw
PBI:	29-37 days	29-37 days	29-37 days
App. Rate:	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.	Valent U.S.A.	Valent U.S.A.
MRID Citation:	46708547	46708547	46708547
	Residues of Fluopicolide (ppm)		
	0.027	0.046	0.030
	0.023	0.039	0.036
	0.017	0.057	0.046
	0.012	0.039	0.055
	0.013	0.041	0.023
	0.015	0.032	0.023
	0.018	0.059	0.018
	0.019	0.063	0.016
	0.015	0.029	0.010
	0.013	0.030	0.011

Table II-5. Residue data used to calculate tolerances for fluopicolide on rotated wheat forage, hay, and straw.			
Regulator:	EPA	EPA	EPA
Chemical:	Fluopicolide	Fluopicolide	Fluopicolide
Crop:	Rotated wheat forage	Rotated wheat hay	Rotated wheat straw
PBI:	29-37 days	29-37 days	29-37 days
App. Rate:	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.	Valent U.S.A.	Valent U.S.A.
MRID Citation:	46708547	46708547	46708547
	Residues of Fluopicolide (ppm)		
	0.039	0.056	0.038
	0.038	0.060	0.029
	0.028	0.037	0.030
	0.022	0.040	0.034
	0.026	0.071	0.036
	0.021	0.071	0.050
	0.049	0.045	0.037
	0.013	0.033	0.059
	0.033	0.057	0.017
	0.031	0.037	0.025
	0.050	0.030	0.024
	0.047	0.021	0.021
	0.022	0.020	<0.01
	0.022	0.023	<0.01
	0.014	0.014	<0.01
	0.015	0.021	<0.01
	0.025	0.056	0.014
	0.022	0.034	0.013
	0.047	0.030	0.044
	0.042	0.077	0.034
	0.189	0.501	0.326
	0.121	0.043	0.350
	0.028	0.397	0.054
	0.015	0.331	0.046
	0.039	0.344	0.188
	0.051	0.290	0.181
	0.060	0.089	0.040
	<0.01	0.077	0.042
	0.141	0.184	0.020
	0.115	0.307	0.036
	0.106	0.147	0.117
	0.213	0.224	0.102

Figure II- 23. Lognormal probability plot of fluopicolide rotational crop trial data for wheat forage.

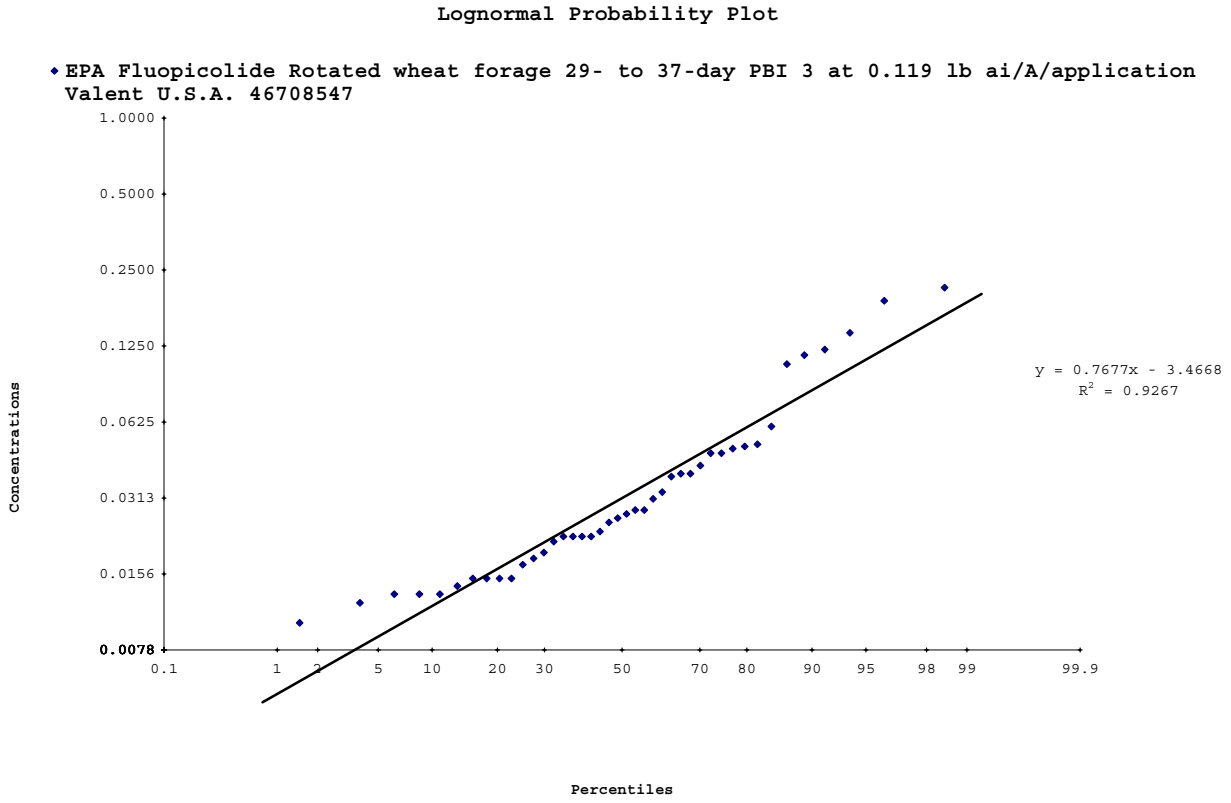


Figure II- 24. Tolerance spreadsheet summary of fluopicolide rotational crop trial data for wheat forage.

Regulator: EPA
Chemical: Fluopicolide
Crop: Rotated wheat forage
PHI: 29- to 37-day PBI
App. Rate: 3 at 0.119 lb ai/A/application
Submitter: Valent U.S.A.
MRID Citation: 46708547

n: 42
min: 0.01
max: 0.21
median; 0.03
average: 0.04

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.15 (0.15)	0.20 (0.20)	0.20 (--)
EU Method I Log Normal	0.15 **(0.20)**	**0.20** (0.35)	0.35 (--)
EU Method II Distribution-Free		0.10	
California Method μ + 3σ		0.20	
UPLMedian95th		**0.15**	
Approximate Shapiro-Francia Normality Test		0.9267 0.05 >= p-value > 0.01 : Reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 25. Lognormal probability plot of fluopicolide rotational crop trial data for wheat hay.

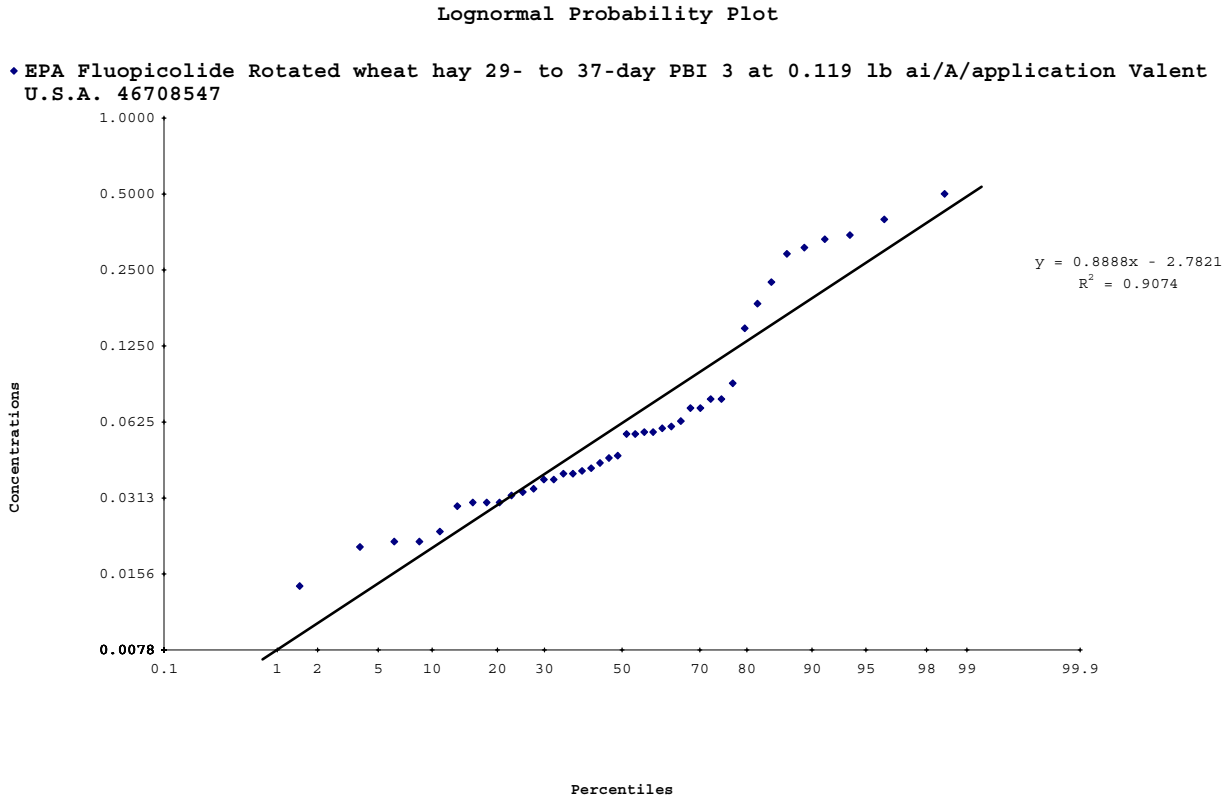


Figure II- 26. Tolerance spreadsheet summary of fluopicolide rotational crop trial data for wheat hay.

Regulator: EPA
Chemical: Fluopicolide
Crop: Rotated wheat hay
PHI: 29- to 37-day PBI
App. Rate: 3 at 0.119 lb ai/A/application
Submitter: Valent U.S.A.
MRID Citation: 46708547

n: 42
min: 0.01
max: 0.50
median; 0.05
average: 0.10

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.30 (0.40)	0.40 (0.45)	0.50 (--)
EU Method I Log Normal	0.30 **(0.45)**	**0.60** (0.90)	1.1 (--)
EU Method II Distribution-Free		0.20	
California Method μ + 3σ		**0.50**	
UPLMedian95th		**0.30**	
Approximate Shapiro-Francia Normality Test		0.9074 p-value <= 0.01: Reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 27. Lognormal probability plot of fluopicolide rotational crop trial data for wheat straw.

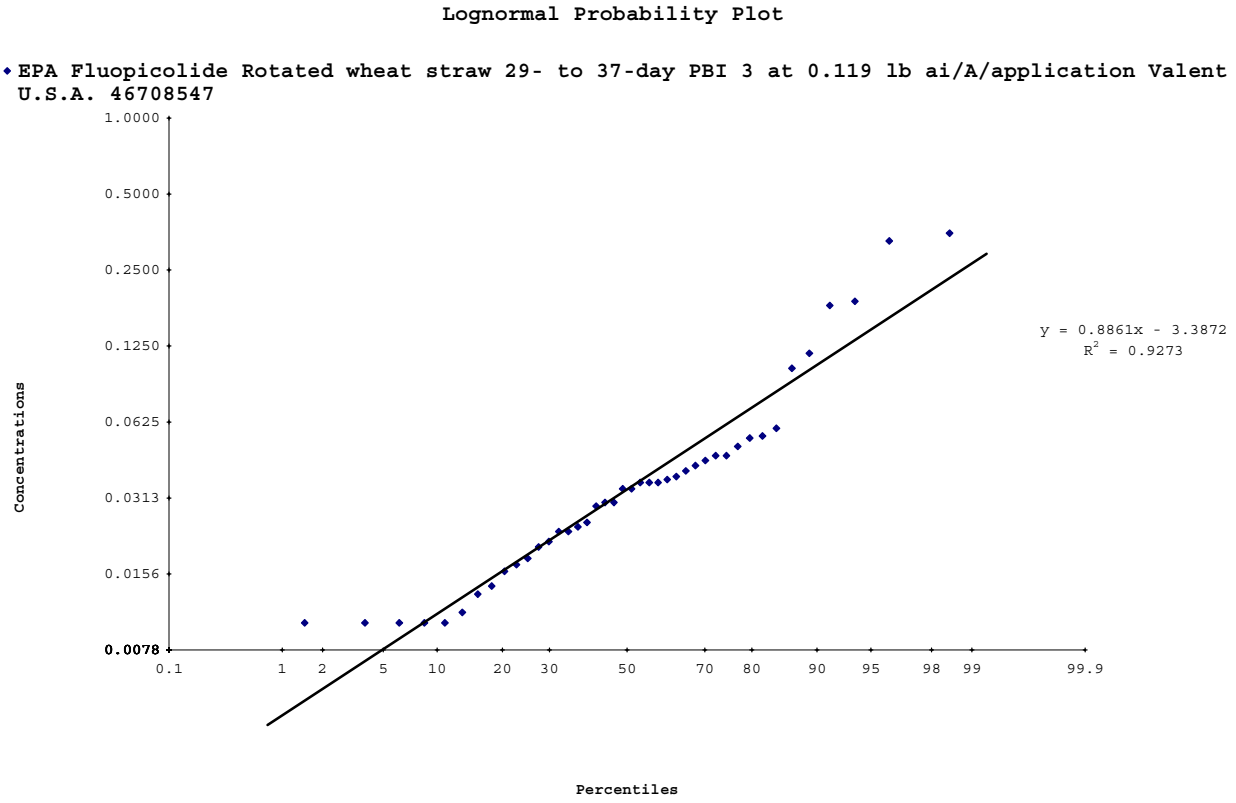


Figure II- 28. Tolerance spreadsheet summary of fluopicolide rotational crop trial data for wheat straw.

Regulator:	EPA
Chemical:	Fluopicolide
Crop:	Rotated wheat straw
PHI:	29- to 37-day PBI
App. Rate:	3 at 0.119 lb ai/A/application
Submitter:	Valent U.S.A.
MRID Citation:	46708547
n:	42
min:	0.01
max:	0.35
median;	0.03
average:	0.06

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.20 (0.25)	0.25 (0.30)	0.30 (--)
EU Method I Log Normal	0.15 **(0.25)**	**0.30** (0.50)	0.60 (--)
EU Method II Distribution-Free		0.10	
California Method μ + 3σ		0.30	
UPLMedian95th		**0.20**	
Approximate Shapiro-Francia Normality Test		0.9273 0.05 >= p-value > 0.01 : Reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Appendix III. Proposed Metabolic Pathway for Fluopicolide in Rotational Crops.