CYAZOFAMID (281)

The first draft was prepared by Dr Michael Doherty, United States Environmental Protection Agency, Washington, DC, USA

EXPLANATION

Cyazofamid (ISO common name, published) is a fungicide belonging to both the cyano-imidazole and sulphonamide classes of compounds. The biochemical mode of action is inhibition of all stages of fungal development. It is registered for control of and protection against Oomycete fungi. Cyazofamid was considered for the first time for toxicology and residues by the 2015 JMPR.

Note that throughout this document, values are listed to the precision provided in the submitted reports, except for method recoveries (whole number) and values calculated by the JMPR (two significant figures for processing factors and for combined residues of cyazofamid and CCIM). All rounding was in accordance with ISO standards.

IDENTITY

ISO common name	Cyazofamid (published)
Chemical Name	
IUPAC	4-chloro-2-cyano-N,N-dimethyl-5-*p*-tolylimidazole-1-sulfonamide
CAS	4-chloro-2-cyano-N,N-dimethyl-5-(4-methylphenyl)-1H-imidazole-1-sulfonamide
CIPAC No.	653
CAS No.	120116-88-3
Structural Formula	
Molecular formula	$C_{13}H_{13}ClN_4O_2S$
Molecular mass	324.8

Physical and chemical properties

Table 1 Physical and chemical properties of cyazofamid

Property	Guideline and method	Test material specification and purity	Findings	Reference/ Remarks
Technical Grade Active Ingredient				
Physical state and colour	EC Annex II Section 2.4 and 40 CFR 158.190 Pesticide Assessment Guidelines Subdivision D: Product Chemistry Guidelines	Cyazofamid TGAI Lot 9506 96.4%	Munsell colour (24.5°C) = 5Y 9/1 "ivory" Physical state (25.3°C) = "solid powder"	RA-1006

Property	Guideline and method	Test material specification and purity	Findings	Reference/ Remarks
	63-2, 3, 4			
Solubility in organic solvents	40 CFR 158.190 Pesticide Assessment Guidelines, Subdivision D: Product Chemistry Guidelines 63-8 and EC Annex II Section 2.7	Cyazofamid TGAI Lot 9506, 95.5%	Solubility (g/L;21.2 ± 1 °C) Acetone 45.64 Ethyl Acetate 16.49 Dichloromethane 102.12 Acetonitrile 30.59 Methanol 1.74 Toluene 6.00 Hexane 0.03 n-Octanol 0.04 2-Propanol 0.43	RA-1033 Test material unstable in methanol, toluene, and n-octanol. Equilibrium achieved and maintained; did not impact study results.
Flammability	OPPTS 830.7000 and EC Annex II Section 2.11.1	Cyazofamid TGAI Lot 9506 95.5%	Test substance was “non-flammable”	RA-1029
Auto-flammability	OPPTS 830.7000 and EC Annex II Section 2.11.2	Cyazofamid TGAI Lot 9506 95.5%	No auto flammable behaviour was observed	RA-1029
Explosive Properties	EEC Directive 92/69/EEC, Part A.14	Cyazofamid TGAI Lot 9506 95.5%	The substance was not considered to be explosive: 1) not thermally sensitive 2) not shock sensitive 3) not sensitive to friction	RA-1049
Pure Active Ingredient				
Melting, freezing or solidification point	EC Annex II Section 2.1.1 and 40 CFR 158.190 Pesticide Assessment Guidelines, Subdivision D: Product Chemistry Guidelines 63-2, 3, 4	Cyazofamid PAI Lot 9505 99.1%	Mean melting point 152.7 °C	RA-1005
Boiling point			Not relevant. Material is a solid and does not have a low melting point	RA-1005
Relative density of purified active substance	EC Annex II Section 2.2 and 40 CFR 158.190 Pesticide Assessment Guidelines, Subdivision D: Product Chemistry Guidelines 63-2, 3, 4	Cyazofamid PAI Lot 9505 99.1%	$D_{20/4}$ = 1.446 ± 0.0009	RA-1005
Vapour pressure of purified active substance	OPPTS 830.7950 and EEC Method A.4 Vapour Pressure	Cyazofamid PAI Lot 9704-1 99.1%	<1 x 10-7 torr (1.33 x 10-5 Pascal)	RA-1030
Physical state and colour	EC Annex II Section 2.4 and 40 CFR 158.190 Pesticide Assessment Guidelines Subdivision D: Product Chemistry Guidelines 63-2, 3, 4	Cyazofamid PAI Lot 9505 99.1%	Munsell color at 24.3 °C = N 9.5/90.0%R “white” Physical state at 25.4 °C = “solid powder”	RA-1005

Property	Guideline and method	Test material specification and purity	Findings	Reference/ Remarks
Dissociation Constant	EU Guideline 2.9.4 and OECD Guideline for Testing of Chemicals 112	Cyazofamid PAI Lot 9505 99%	Because no quantifiable spectral differences were observed from 200-750 nm, it was concluded that no pKa was evident in the pH range of 2-12 (20 ± 1 °C) using this method	RA-1007
Solubility in organic solvents	Pesticide Assessment Guidelines, Subdivision D: Product Chemistry Guidelines 63-8 and Japan MAFF 9 Nousan, Notification No. 5089 Product Chemistry Guidelines	Cyazofamid PAI Lot 9704-1 99.1%	Solubility (g/L; 20 ± 1 °C) Acetone 41.92 Ethyl Acetate 15.63 Dichloromethane 101.84 Acetonitrile 29.42 Methanol 1.54 Toluene 5.28 Hexane 0.03 n-Octanol 0.25 2-Propanol 0.39	RA-1044
Solubility in water	OPPTS 830.7840 and EC Annex II Section 2.6	Cyazofamid PAI, Lot 9505 99.0%	Mean solubility at 20 ± 1 °C pH 5 – 121 ppb pH 7 – 107 ppb pH 9 – 109 ppb	RA-1010 Test material was unstable in water; however, equilibrium was achieved and study results were not impacted.
n-octanol/ water partition coefficient	OPPTS 830.7570 and EC Annex II Section 2.8	Cyazofamid PAI Lot 9505, 99.0%	At 24-25 °C, the octanol/water partition coefficient was 1585 (Log Kow = 3.2)	RA-1037
Direct phototrans-formation of purified active substance in water	United States EPA Guideline 161-2 EC Directive, Annex II, Sections 2.9.2 and 7.2.1.2	[^{14}C-Bz]Cyazofamid, Lot CP-1863-2, purity ≥99.5%; [^{14}C-Im]Cyazofamid, Lot CP-1864, purity ≥99.5%; Cyazofamid PAI Lot 9505, 99.0%	[14C]Cyazofamid and product half-lives **Cyazofamid(Bz)** 28 minutes **Cyazofamid(Im)** 34 minutes **Cyazofamid(Bz)** CCIM 20.7 days CCTS 2.3 days HTID 46.1 days **Cyazofamid(Im)** CCIM 25.6 days CCTS 2.1 days HTID 41.6 days	RA-4013
Hydrolysis at pH 4, 7, and 9	United States EPA Guideline 161-1 EC Directive, Annex II, Sections 2.9.1 and 7.2.1.1	[^{14}C-Bz]Cyazofamid, Lot CP-1863-2, purity ≥99.5%; [^{14}C-Im]Cyazofamid, Lot CP-1864, purity ≥99.5%;	At pH 4, 5, 7 and 9 at 25ºC, the main product of hydrolysis was CCIM. After 30 days, CCIM represented 82-83% of the radioactivity in the pH 4, 5 and 7 samples and 74-77% of the radioactivity in the pH 9 samples. At pH 9, further	RA-4003

<table>
<tr><th>Property</th><th>Guideline and method</th><th>Test material specification and purity</th><th>Findings</th><th>Reference/ Remarks</th></tr>
<tr><td></td><td></td><td>Cyazofamid PAI Lot
9505, 99.0%</td><td>reaction formed CCIM-AM. At the end of the study, CCIM-AM represented 9-10% of the radioactivity in the pH 9 samples. The course of the hydrolysis was the same at 50 ºC.
Half-lives in days
(20 °C is an estimate)
<table>
<tr><td></td><td>25 ºC</td><td></td><td>20 ºC</td></tr>
<tr><td>pH</td><td>Bz</td><td>Im</td><td>Bz</td></tr>
<tr><td>4</td><td>12.4</td><td>12.3</td><td>24.6</td></tr>
<tr><td>5</td><td>13.3</td><td>12.6</td><td>27.2</td></tr>
<tr><td>7</td><td>12.1</td><td>12.3</td><td>24.8</td></tr>
<tr><td>9</td><td>11.8</td><td>10.6</td><td>24.8</td></tr>
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Cyazofamid is registered as a suspension concentrate (SC) formulation containing 400 g ai/L.

METABOLISM AND ENVIRONMENTAL FATE

Metabolism and environmental fate studies were conducted with cyazofamid labelled in either the imidazole (Im) or benzene (Bz) rings (Figure 1 and Figure 2, respective).

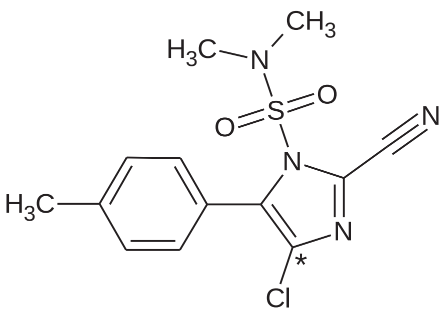


Figure 1. [imidazole-14C]cyazofamid

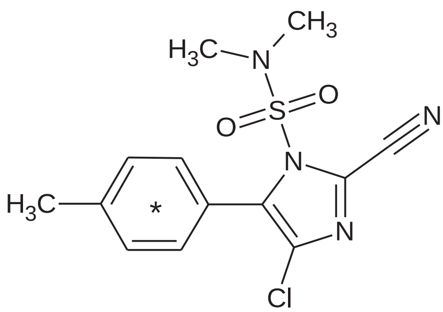
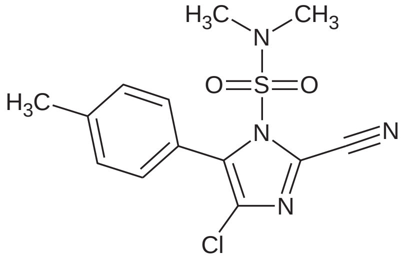
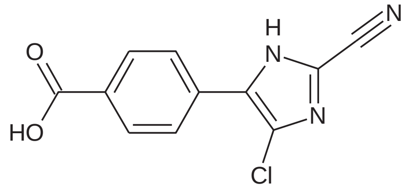
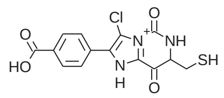
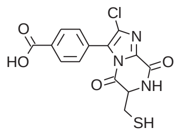
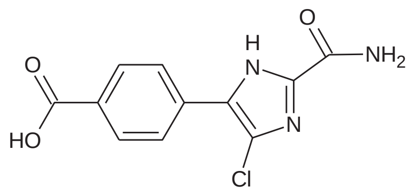
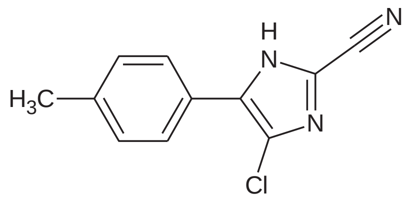
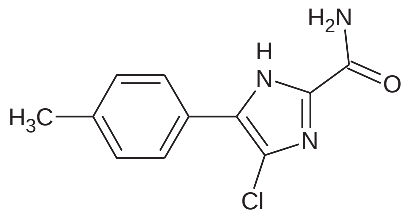
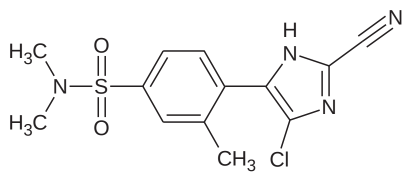
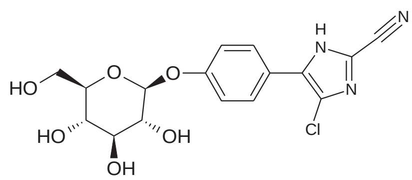


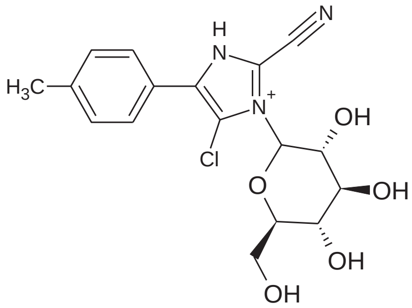
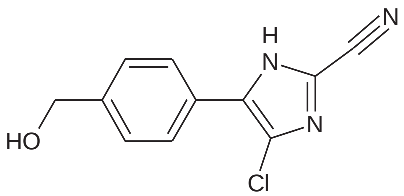
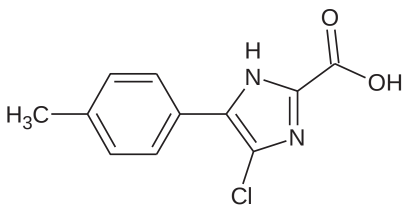
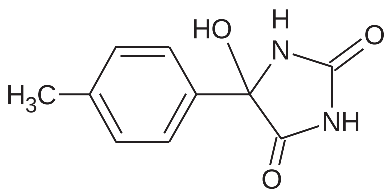
Figure 2. [benzene-14C]cyazofamid

Chemical names, structures, and code names of metabolites and degradation products of cyazofamid are shown below (Table 2). All of the compounds in Table 2 were identified in at least one matrix in studies with radiolabelled cyazofamid.

Table 2 Known metabolites and degradation products of cyazofamid

Code Names	Chemical name, molecular formula, molar mass	Structure	Where found ≥ 10% TRR
Cyazofamid	4-chloro-2-cyano-N,N-dimethyl-5-*p*-tolylimidazole-1-sulfonamide		Tomato Lettuce Potato (rinsate only) Confined rotational lettuce tops

Code Names	Chemical name, molecular formula, molar mass	Structure	Where found ≥ 10% TRR
CCBA	4-(4-chloro-2-cyanoimidazol-5-yl)benzoic acid		Hen kidney Hen liver
CCBA (cysteine conjugates)		 	Goat kidney Goat fat Goat muscle Milk
CCBA-AM	4-(4-chloro-2-amidoimidazol-5-yl)benzoic acid		Milk
CCIM	4-chloro-5-p-tolylimidazole-2-carbonitrile		Goat fat Goat muscle Hydrolysis Photolysis Aerobic soil metabolism Confined rotational lettuce tops
CCIM-AM	4-chloro-5-p-tolylimidazole-2-carboxamide		Goat liver Goat fat Hydrolysis Aerobic soil metabolism Confined rotational lettuce tops
CCTS	6-(4-chloro-2-cyanoimidazol-5-yl)-N,N-dimethyl-m-toluenesulfonamide		Photolysis
CGCN	4-chloro-5-(4-{[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl]oxy}phenyl)-1H-imidazole-2-carbonitrile		Rotational crops

Code Names	Chemical name, molecular formula, molar mass	Structure	Where found ≥ 10% TRR
5CGTC	4-chloro-2-cyano-5-(4-methylphenyl)-3-[(3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl]-1H-imidazol-3-ium		Rotational crops
CHCN	4-chloro-5-(4-hydroxymethylphenyl)imidazole-2-carbonitrile		Hen kidney (conjugated) Hen liver (conjugated)
CTCA	4-chloro-5-p-tolylimidazole-2-carboxylic acid		Aerobic soil metabolism
HTID	5-hydroxy-5-(4-methylphenyl)imidazolidine-2,4-dione		Rotational crops

Plant metabolism

The Meeting received studies depicting the metabolism of cyazofamid in grape, tomato, lettuce, and potato. All of the studies were conducted with cyazofamid which was radiolabelled, separately in the imidazole (Im) and the benzene (Bz) ring (see Figs. 1 and 2).

Grape

The nature of the residues of cyazaofamid in Pinot Noir grapes were investigated by Mamouni (1997, Report RA-3002). For each radiolabel position, five applications of cyazofamid, formulated as a suspension concentrate, were made to grapevines growing in the field. All five applications were at a rate of ca. 100 g ai/ha and were made at intervals of 21–25 days. Grapes were harvested 44 days after the last treatment (DAT). Harvested grapes were crushed and assayed for total radioactivity. The harvested grapes were also processed into wine, yielding vin de goutte, vin de presse, and marc, and into juice, yielding juice and pulp. Both types of wine were clarified using bentonite and/or centrifugation. Radioactivity was determined by combustion/LSC (grapes and solid material after preparation of wine and juice) or direct LSC [wine (raw and clarified) and juice]. Neither characterization nor identification of residues was reported in the study.

Mean (n=5) TRR in grapes was 0.31 mg eq./kg (0.62 % of applied) for the Im label and 0.53 mg eq./kg (0.89% of applied) for the Bz label. When the grapes were processed into wine, TRR (both labels) distributed as approximately 15% into vin de goutte (0.21 mg eq./L), 10% into vin de presse (0.32 mg eq./L), and 70% into marc (3.7 mg eq./kg). A small amount (<6% TRR) of radioactivity was associated with the nylon bag used to press the grapes. Following clarification, 74 to 90% of the initial radioactivity remained in the vin de goutte and 50 to 60% remained in the vin de presse. When the grapes were processed into juice, TRR (both labels) distributed as 33% (0.30 mg eq./L) into juice and 54% (1.4 mg eq./kg) into marc. More radioactivity was retained by the nylon bag (12% TRR) used for juicing than the bag used for wine making.

Tomato

The metabolism of cyazofamid in tomato was investigated by Neal and Gupta (1999, Report RA-3009). For each radiolabel position, four applications of cyazofamid, formulated as a suspension concentrate (10% ai) and at rates of approximately 60, 95, 95, and 95 g ai/ha, were made at 7-day intervals to foliage of tomato plants grown in the field. At additional test plots, applications were made at exaggerated rates (nominally 4×). Samples from the exaggerate-rate trials were not analysed.

Mature tomato fruits and foliage were harvested 1 DAT. The harvested fruits were rinsed with ACN, homogenized, and centrifuged to separate juice from pulp. Radioactivity was determined by LSC for the rinsate and juice, and by combustion/LSC for the pulp. Residues in pulp were extracted with hexane, ethyl acetate, and H_2O, separately. Tomato rinsate, juice, and pulp extracts were subjected to various levels of clean-up and HPLC analysis. For juice, the TM-1 fractions from the HPLC analysis underwent ion exchange chromatography, hydrolysis of oligosaccharides, oxidation and reduction of sugars, dimedone adduction, esterification, and acetylation treatments to characterize the residues. Pulp samples were subjected to chemical treatments in order to fractionate the material into its cell wall components for determination of radioactivity in natural plant constituents.

The TRR in fruits, measured as a sum of residues in surface rinses, juice, and pulp were 0.080 mg eq./kg for the Im label and 0.290 mg eq./kg for the Bz label. Of the total residue, the majority was contained in the surface rinse (54% and 83% for the Im and Bz labels, respectively). Of the radioactivity remaining in the fruits, approximately 71-87% was in the pulp fraction. HPLC analysis indicated the presence of 18 metabolites. Across all sample components, cyazofamid was the only major residue, accounting for ca. 78% TRR (0.064 and 0.22 mg/kg). Other residues were < 6% TRR and < 0.02 mg eq./kg (Table 3).

Table 3 Characterization and identification of radioactive residues in tomato

	[Bz-^{14}C]		[Im-^{14}C]	
Metabolite	mg eq./kg	% TRR	mg eq./kg	% TRR
Total	0.2896		0.0801	
Cyazofamid	0.2212	76.4	0.064	79.9
CCBA	0.0015	0.5	0.0004	0.5
CCBA-AM	0.0001	0.03	n.d.	n.d.
Ester of CCBA	0.0008	0.3	0.0003	0.4
CCBG [a]	0.0009	0.3	0.0004	0.5
CCIM	0.0128	4.4	0.004	5.0
CCIM-AM	0.0028	1.0	0.0003	0.4
CCTS	0.0049	1.7	0.0012	1.5
CDTS	0.0028	1.0	0.0005	0.6
CHCN	0.0011	0.4	0.0001	0.1
CHCN conjugate	0.0007	0.2	0.0001	0.1
HTID	0.0011	0.4	0.0001	0.1
TM-1	0.0157	5.4	0.002	2.5
TM-1a	0.0013	0.4	0.0001	0.1
TM-3	0.0008	0.3	0.0002	0.2
TM-4	0.0007	0.2	0.0001	0.1
TM-5	0.0006	0.2	0.0001	0.1
TM-12	0.0005	0.2	n.d.	n.d.
Unextracted	0.0091	3.1	0.0021	2.6

[a] TRR and % TRR values are reported for fraction TM-6, which was found to contain, in part, CCBG.

Analysis of the TM-1 fraction showed incorporation of radioactivity into sugars (sucrose, glucose, and fructose) and citric acid (specific amounts not reported. Analysis of the post-extraction solids (PES) from the tomato pulp demonstrated incorporation of radioactivity in structural components (Table 4).

Table 4 Distribution of radioactivity into structural components of tomato pulp PES

	[Im-^{14}C]		[Bz-^{14}C]	
Matrix/Substance	mg eq./kg	%TRR of PES	mg eq./kg	%TRR of PES
PES pulp	0.0021	100	0.0091	100
Cellulose	0.0001	4.1	0.0008	8.4
Hemicellulose	0.0001	6.5	0.0009	10.0
Lignin	0.0002	8.6	0.0020	21.7
Pectin	0.0002	10.0	0.0010	10.7
Protein	0.0002	9.7	0.0009	9.8
Starch	0.0002	9.4	0.0007	8.2
Water-soluble polysaccharides	0.0003	14.6	0.0011	12.1
Solid residue	0.0001	2.4	0.0003	2.8
Total	0.0014	65.5	0.0076	83.7

Results from foliage were similar to those from fruits and are not further evaluated herein.

Lettuce

The metabolism of cyazofamid in glasshouse-grown lettuce was investigated by Gupta and Song (2002, Report RA-3092). Three applications of cyazofamid, formulated as a suspension concentrate (10% ai) containing both the Bz and Im radiolabel in a 1:1 ratio, were made to lettuce at a nominal rate of 100 g ai/ha. Applications were made on a 14-day interval and the final application was two weeks prior to harvest of mature leaves.

Harvested lettuce samples were homogenized and the TRRs in each sample were determined by combustion analysis and LSC. Samples were extracted three times with ACN:H_2O (60:40, 0.1% acetic acid; v/v). Radioactivity in the extracts was determined by LSC and the extracted residues were analysed by HPLC. Metabolites were isolated from the extract by HPLC fraction collection. Fractions were subjected to acid and base hydrolysis, and ion-exchange chromatography. Radioactivity of PES was determined by combustion/LSC, followed by chemical treatments to isolate radioactivity in cell wall components.

Total radioactive residues were 0.85 mg eq./kg, of which 97% was extracted (Table 5). Analysis of the extracts showed parent to be the predominant residue. Four metabolites were identified, of which CCIM was the most abundant (0.31 mg/kg, 3.7% TRR). Other identified metabolites were < 0.01 mg/kg (<1% TRR). Analysis of the extract and the PES showed incorporation of radioactivity into natural products (0.028 mg eq./kg, 3.3% TRR and 0.022 mg eq./kg, 2.6% TRR, respectively).

Table 5 Characterization and identification of residues in lettuce following application of cyazofamid

	Combined [Im-^{14}C] and [Bz-^{14}C]	
Matrix/fraction/metabolite	mg eq./kg	%TRR
Mature lettuce	0.85	100
Extracted residue	0.83	97.4
Cyazofamid	0.76	89.3
CCIM	0.031	3.7
CCTS	0.0041	0.5
CDTS	0.0052	0.6
Natural products	0.028	3.3
PES	0.022	2.6
Water-soluble polysaccharides	0.0051	0.60
Starch	0.0063	0.74

	Combined [Im-^{14}C] and [Bz-^{14}C]	
Matrix/fraction/metabolite	mg eq./kg	%TRR
Protein	0.0043	0.50
Cellulose, hemicellulose, pectin	0.0029	0.34
Lignin	0.0022	0.26

Potato

The metabolism of cyazofamid in both field-grown and greenhouse-grown potato was investigated by Gupta (1999, Report RA-3008). For each radiolabel position, cyazofamid was formulated as a soluble concentrate (10% ai) and applications were made to the foliage of growing plants on a one-week interval, with the final application being 7 days before harvest. For the field study, three applications were made at rates of either 100 (1 plant) or 400 (3 plants) g ai/ha. For the greenhouse study, five applications were made at a rate of 400 (3 plants) g ai/ha.

Samples of potato tuber were harvested, washed gently with water to remove soil, and then air dried. Tubers were rinsed with ACN:H_2O (80:20, v/v) prior to homogenization and the radioactivity in the rinsate was determined by LSC. One subsample from the field study and two samples from the greenhouse study were peeled prior to homogenization to determine residue levels in peel. Tuber samples and one separated peel/pulp sample were extracted sequentially with ACN, ACN:H_2O (80:20, v/v), and ACN:H_2O (50:50, v/v). Radioactivity in each extract was assayed. Extractable residues were analysed by HPLC. PES were analysed for incorporation of radioactivity into natural products. Potato foliage samples were also harvested and analysed. Residue in foliage was ca. 97% parent compound; therefore, detailed evaluation is not presented herein.

The majority of the radioactivity remained with the tuber after the ACN:H_2O rinse (Table 6). Based on the samples from the greenhouse study, approximately 20% of the residue in the rinsed potato was associated with the peel. The result from the field study indicates 50%, but that figure may be less robust due to the low residue levels and the results reflecting only one plant.

Table 6 Average (n=3) total radioactive residues (mg eq./kg) in and on potato tubers following treatment with cyazofamid

	[Im-^{14}C]		[Bz-^{14}C]	
Treatment	Rinsate	Tuber	Rinsate	Tuber
Field, 3×100 g ai/ha	0.00027	0.0019	0.00005[a]	0.0008[a]
Peel (% of TRR in tuber)	--	--	--	50
Pulp (% of TRR in tuber)	--	--	--	50
Field, 3×400 g ai/ha	0.00040	0.0051	0.00030	0.0053
Greenhouse, 5×400 g ai/ha	0.0014	0.022	0.0023	0.016
Peel (% of TRR in tuber)	--	21	--	22
Pulp (% of TRR in tuber)	--	79	--	78

[a] Results from one plant

The majority of the residue in the rinsate from the greenhouse 5×400 g ai/ha treatment consisted of cyazofamid (0.0009-0.0018 mg/kg, 67–80% TRR), with lesser amounts of CCIM (0.0003 mg/kg, 14–20% TRR; Table 7). For the tubers, three metabolite fractions were found in the extracts of peel and pulp. The majority of the radioactivity (0.005 mg/kg, ca. 30% TRR) was associated with a fraction that was shown to consist primarily of starch. The remaining two fraction were determined to be cyazofamid (0.001 mg/kg, 4.8% TRR) and CCIM (0.0002 mg/kg, 1% TRR). The balance of the radioactivity was not extracted.

Table 7 Identification of radioactive residues in rinsate and tuber extracts following treatment with cyazofamid

	[Im-^{14}C]		[Bz-^{14}C]	
Treatment/Matrix	mg/kg	% TRR	mg/kg	% TRR
Field, 3×100 g ai/ha				
Rinsate	0.00027 (eq)	--	0.00005 (eq)	--
Cyazofamid	--	--	--	--
CCIM	--	--	--	--
Starch	--	--	--	--
Tuber	0.0019 (eq)	--	0.0008 (eq)	--
Cyazofamid	0.00006	1.5	0.0	0.0
CCIM	0.00011	2.8	0.0	0.0
Starch	0.0012	30	0.0004	52.8
Greenhouse, 5×400 g ai/ha				
Rinsate	0.0014 (eq)	--	0.0023 (eq)	--
Cyazofamid	0.0009	67	0.0018	80
CCIM	0.0003	20	0.0003	14
Starch	0.0001	6.2	0.0001	2.6
Tuber	0.022 (eq)	--	0.016 (eq)	--
Cyazofamid	0.00083	4.7	0.0011	4.8
CCIM	0.0002	1.5	0.00017	0.6
Starch	0.0050	30	0.0049	23

Overall, the metabolism of cyazofamid in grape, tomato, lettuce, and potato is similar. The metabolic pathway proposed for grapes in the industry submission is provided as an illustrative example in Figure 3.

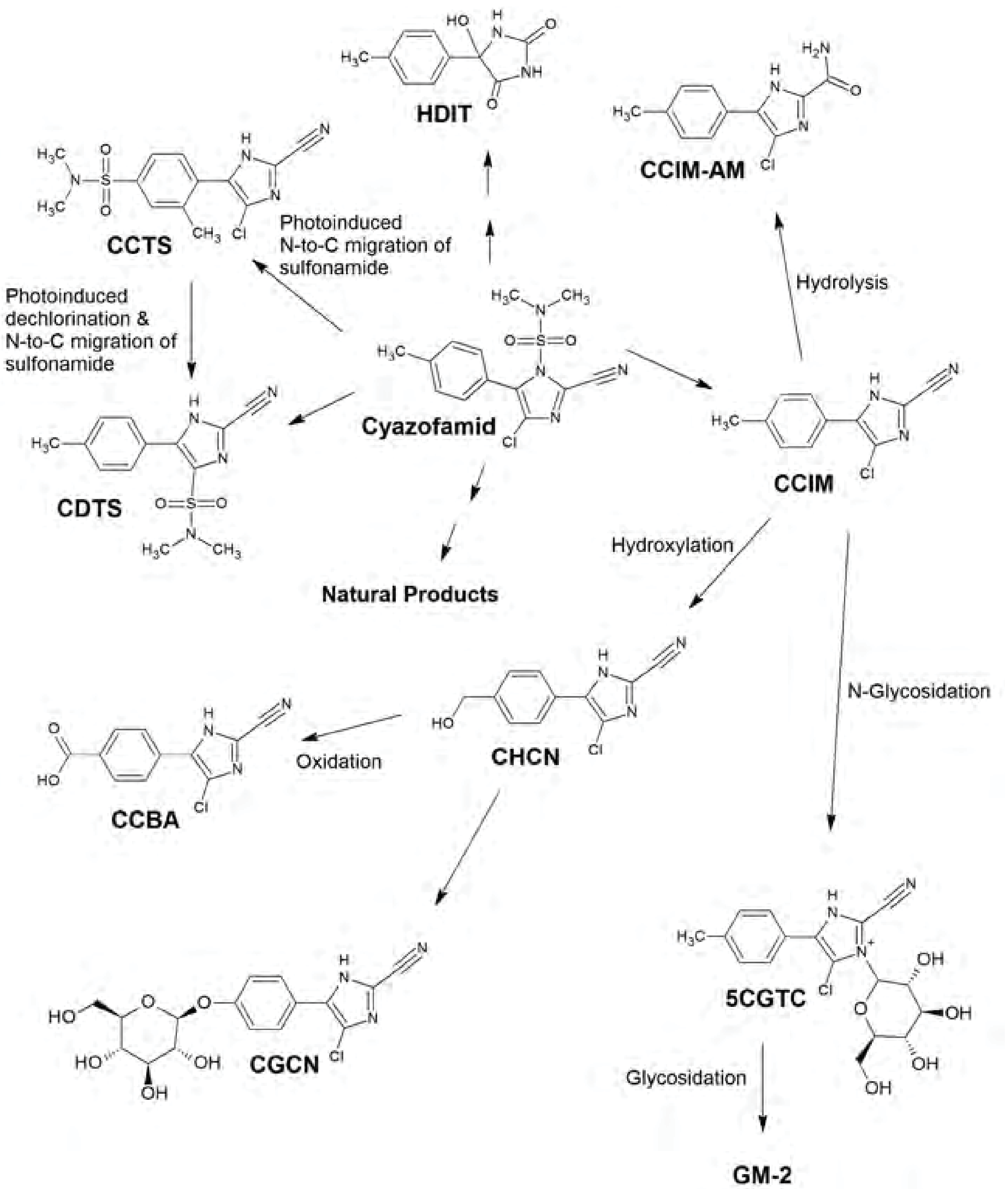


Figure 3 Proposed metabolic pathway of cyazofamid in target and rotational crops.

Animal Metabolism

The Meeting received metabolism studies on laboratory animals, lactating goats, and laying hens. All of the studies with laboratory animals, lactating goats, and laying hens were conducted with cyazofamid which was radiolabelled, separately, in the benzene ring [(u)Benzene-^{14}C; Bz] or the number 4 carbon of the imidazole ring [Imidazole-4-^{14}C; Im].

Laboratory animals

Examination of radioactivity following gavage dosing of Bz- and Im-radiolabelled cyazofamid to rats indicated that cyazofamid is well absorbed, with the majority of excretion occurring via urine. In a biotransformation study where blood, liver, and stomach (with contents) were analysed 0.5 hours after a dosing of [^{14}C-Bz] cyazofamid, most (97.2%) of the radiolabel in the stomach contents was the parent compound and a small fraction was CCIM. Analysis of the liver from this group showed only 6.1% of the radiolabel was cyazofamid, while 24.2% was CCIM and 41.9% was CCBA. In the plasma, there was no cyazofamid and the majority of radiolabel was CCIM. These data demonstrate that a dose of cyazofamid is rapidly metabolized, and that CCIM is a major metabolite in the initial metabolism of cyazofamid. At 0.5 hours after a dose of [^{14}C-Bz]-CCIM, all of the radiolabel in the stomach contents was CCIM, and most of the radiolabel in liver (76.5%) and plasma (67.9%) was CCIM. CCBA, the main metabolite seen in these tissues 0.5 hours after dosing with CCIM, was also found in the blood and liver from the animals dosed with cyazofamid. Concentrations in blood and liver were greater in the CCIM-dosed animals than that in cyazofamid treated animals, suggesting that CCIM was much more rapidly absorbed than cyazofamid.

Lactating goats

The metabolism of cyazofamid in lactating goats was investigated by Hatzenbeler and Savides (1998, Study RA-3001). For each radiolabel position, two goats were dosed for five days at 32.5 mg/day (Im) or 25.4 mg/day (Bz; both equivalent to ca. 10 ppm in the diet). Milk was collected twice daily, and excreta and stanchion washes were collected once daily throughout the study. Goats were terminated ca. 8 hours after the final dosing, at which point tissues and blood were collected for analysis.

Total radioactive residues (TRR) in urine stanchion wash, and milk were determined by direct liquid scintillation counting (LSC). The TRR in faeces, blood, and tissues was determined by combustion followed by LSC. Samples were processed differently, depending on the matrix. Milk from the Day 5 sampling was extracted twice with acetonitrile (ACN). The extract was then concentrated and the residues partitioned against hexane; the aqueous partition was concentrated prior to analysis by HPLC. Kidney, liver, and faeces were extracted once with ACN followed by two extractions with ACN:H_2O (50:50, v/v). The ACN and ACN:H_2O were concentrated, separately, and analysed by HPLC. The post-extraction solids (PES) were dried, combusted, and analysed by LSC to determine unextracted radioactivity. Liver PES were further processed by acid (1.0 M HCl) and base (1.0 M NaOH) hydrolysis and enzyme (protease) digestion, followed by LSC analysis and, in the case of the enzyme digest samples, HPLC. Muscle and fat samples were extracted two times with ACN:H_2O (75:25, v/v). The extracts were combined, concentrated, and analysed by HPLC. The PES were dried, combusted or solubilized, and analysed by LSC to determine unextracted radioactivity. The limit of detection for the LSC analysis was defined to be twice the disintegrations per minute of control samples, which translated to 0.001 to 0.005 mg eq./kg.

Four HPLC systems were used to analyse samples. All were reverse-phase systems using UV and radioactive flow detectors. The systems differed in the mobile phase gradients that were used, the specific column (though all were C-18), and the mobile phase modifiers (acetic acid or tetrabutylammonium bromide).

The total recovery of radioactivity was 58 and 60% of the administered dose (AD) for the Im and Bz labels, respectively (Table 8). The totals do not include the GI tract or its contents. Nearly 100% of the radioactivity was recovered in the excreta (99+%), with the principal residues being unchanged parent compound in faeces (ca. 85% TRR, ca. 7 mg eq./kg) and CCBA in urine (86-92% TRR, 1.6–2.2 mg eq./kg). Radioactivity in milk was low, ranging from 0.002 mg eq./kg to 0.010 mg eq./kg. The levels of TRR appeared to plateau for the Bz label by Day 2; however, the Im label showed a consistent increase over the five-day treatment period. Major metabolites (>10% TRR) identified in milk were CCBA (42% TRR, 0.004 mg eq./kg maximum on Day 5) and CCBA-AM (29% TRR, 0.002 mg eq./kg maximum on Day 5); all other identified residues in milk were <5% TRR (< 0.001 mg eq./kg). Radioactivity in liver was ca.

0.12 mg eq./kg, with CCIM-AM being the only major residue (12% TRR, 0.014 mg eq./kg). In kidney, the major residue was the cysteine conjugate of CCBA (70% TRR, 0.073 mg eq./kg). In muscle and fat, the major residues were CCBA and CCIM. In muscle, the two residues occurred at similar TTR levels (ca. 25%) and were low (≤ 0.002 mg eq./kg). In fat, CCBA occurred at higher levels than CCIM in terms of both relative (38–58% TRR vs. 26–33% TRR) and absolute (0.003–0.006 mg eq./kg vs. 0.002-0.003 mg eq./kg) amounts.

Table 8 Total radioactive residues (TRRs) of [^{14}C]cyazofamid in tissues, body fluids and excreta of lactating goats following exposure equivalent to 10 ppm in the diet

	[Im-^{14}C]Cyazofamid		[Bz-^{14}C]Cyazofamid	
Matrix	mg eq./kg	% of admin. dose	mg eq./kg	% of admin. dose
Tissues and milk				
Fat (omental)	0.010	0.01	0.006	< 0.01
Fat (perirenal)	0.010	< 0.01	0.010	< 0.01
Liver	0.12	0.13	0.11	0.10
Kidney	0.11	0.02	0.070	0.01
Milk (Day 5)	0.01	0.01	0.006	< 0.01
Muscle (loin)	0.006	0.03	0.004	0.03
Muscle (rear leg)	≤0.01	≤0.01	≤0.01	≤0.01
Blood and Excreta (average)				
Blood	0.059	0.13	0.053	0.15
Feces	6.7	8.7	6.5	9.2
Urine	2.3	2.9	1.8	2.7
Stanchion Wash	0.058	0.050	0.050	0.058
Total Recovery	--	58.2	--	60.0

Table 9 Time course of total radioactive residues (TRRs) of [Im-^{14}C]cyazofamid in milk and excreta

	Milk [a]				Urine				FAeces				Wash			
	mg eq./kg		% of AD		mg eq./kg		% of AD		mg eq./kg		% of AD		mg eq./kg		% of AD	
Samp. Day	Im	Bz	Im	Bz	Im	Bz	Im	Bz	Im	Bz	Im	Bz	Im	Bz	Im	Bz
1	0.005	0.005	0.01	0.00	2.2	1.9	2.6	3.0	3.6	3.5	5.2	5.3	0.11	0.069	0.04	0.05
2	0.006	0.005	0.01	0.00	2.2	1.7	3.4	3.2	6.7	7.2	9.9	11	0.027	0.031	0.03	0.04
3	0.007	0.005	0.01	0.01	2.2	1.9	3.3	3.2	7.4	7.7	12	13	0.035	0.037	0.04	0.05
4	0.008	0.005	0.01	0.00	2.4	1.7	3.5	2.7	8.5	7.5	13	12	0.029	0.037	0.03	0.05
5	0.010	0.006	0.01	0.00	2.5	2.0	1.6	1.5	7.4	6.8	3.5	4.5	0.095	0.074	0.11	0.10

[a] Weighted average of the morning and evening collections.

Table 10 Summary of extraction of radioactive residues from the cyazofamid goat metabolism study

			% TRR					
	TRR (mg eq./kg)		ACN		ACN:H_2O [a]		PES	
Matrix	[Im-^{14}C]	[Bz-^{14}C]	[Im-^{14}C]	[Bz-^{14}C]	[Im-^{14}C]	[Bz-^{14}C]	[Im-^{14}C]	[Bz-^{14}C]
Fat (omental)	0.010	0.006	--	--	100	100	0	0
Fat (perirenal)	0.010	0.010	--	--	100	100	0	0
Kidney	0.106	0.070	43	41	56	60	7	8
Liver	0.125	0.111	19	17	22	24	51	53
1.0 M HCl	--	--	--	--	--	--	12	--
1.0 M NaOH	--	--	--	--	--	--	18	--
Protease	--	--	--	--	--	--	15	--
Milk [b]	0.010	0.006	89	91	--	--	6	8
Muscle	0.006	0.004	--	--	73	74	27	26

[a] For kidney and liver, ACN:H_2O was 50:50 (v/v) and was subsequent to ACN extraction. For fat and muscle, ACN:H_2O was 75:25 (v/v) and was the only extraction solvent.

[b] Milk from Day 5.

Table 11 Characterization of radioactive residues in kidney

	Kidney			
	[Im-^{14}C]		[Bz-^{14}C]	
Fraction	mg eq./kg	%TRR	mg eq./kg	%TRR
TRR	0.106	100.0	0.070	100.0
Solvent Extracted	0.104	99.0	0.072	101.2
Cyazofamid	< 0.001	0.1	< 0.001	0.2
CCBA	0.010	8.4	0.003	4.2
CCBA-AM	0.007	7.0	0.005	6.2
CCBA (Cysteine conjugate)	0.073	69.7	0.050	70.0
CCIM	0.001	0.3	< 0.001	0.3
CCIM-AM	0.005	5.0	0.006	7.6
CSBA	0.004	3.6	0.003	4.5
Bound	0.008	7.2	0.006	7.6
Recovered	0.012	106.2	0.077	108.8

Table 12 Characterization of radioactive residues in liver

	Liver			
	[Im-^{14}C]		[Bz-^{14}C]	
Fraction	mg eq./kg	%TRR	mg eq./kg	%TRR
TRR	0.125	100.0	0.111	100.0
Solvent Extracted	0.052	41.1	0.046	40.9
Cyazofamid	< 0.001	0.3	< 0.001	0.2
CCBA (incl. Cysteine conjugate)	0.006	4.7	0.006	5.1
CCBA-AM	0.014	9.9	0.010	8.5
CCIM	0.002	1.4	0.002	1.6
CCIM-AM	0.014	11.1	0.014	12.2
Polar Region	0.007	5.0	0.004	3.4
Bound	0.064	51.4	0.057	52.9
Exhaustive extraction	--	--	0.058	46.4
1.0 M HCl				
Released	--	--	0.030	23.8
Organic soluble	--	--	0.008	6.2
Aqueous soluble	--	--	0.020	15.7
Bound	--	--	0.028	22.6
1.0 M NaOH				
Released	--	--	0.045	36.2
Organic soluble	--	--	0.010	8.2
Aqueous soluble	--	--	0.012	9.8
Emulsion layer	--	--	0.018	14.2
Bound	--	--	0.013	10.2
Protease				
Released	--	--	0.036	29.1
Organic soluble	--	--	--	--
Aqueous soluble	--	--	--	--
Bound	--	--	0.022	17.3
Recovered	0.116	92.5	0.104	93.8

Table 13 Characterization of radioactive residues in omental fat

	Omental Fat			
	[Im-^{14}C]		[Bz-^{14}C]	
Fraction	mg eq./kg	%TRR	mg eq./kg	%TRR
TRR	0.010	100.0	0.006	100.0
Solvent Extracted	0.010	100.0	0.006	100.0
Cyazofamid	< 0.001	3.7	< 0.001	1.9
CCBA (incl. Cysteine conjugate)	0.004	38.3	0.003	43.8
CCBA-AM	< 0.001	1.8	< 0.001	5.0
CCIM	0.003	30.5	0.002	33.4
CCIM-AM	< 0.001	4.1	< 0.001	5.4

Fraction	Omental Fat			
	[Im-^{14}C]		[Bz-^{14}C]	
	mg eq./kg	%TRR	mg eq./kg	%TRR
Polar Region	0.001	9.3	< 0.001	2.3
Bound	< 0.002	-	< 0.002	-
Recovered	0.010	100.0	0.006	100.0

Table 14 Characterization of radioactive residues in perirenal fat

Fraction	Perirenal Fat			
	[Im-^{14}C]		[Bz-^{14}C]	
	mg eq./kg	%TRR	mg eq./kg	%TRR
TRR	0.010	100.0	0.010	100.0
Solvent Extracted	0.010	100.0	0.010	100.0
Cyazofamid	< 0.001	1.2	< 0.001	0.6
CCBA (incl. Cysteine conjugate)	0.005	48.8	0.006	57.6
CCBA-AM	< 0.001	0.6	< 0.001	0.7
CCIM	0.003	28.6	0.003	26.1
CCIM-AM	0.001	5.2	0.001	10.7
Polar Region	0.001	5.5	< 0.001	1.5
Bound	< 0.002	-	< 0.002	-
Recovered	0.010	100.0	0.010	100.0

Table 14 Characterization of radioactive residues in milk

Fraction	Milk (Day 5)			
	[Im-^{14}C]		[Bz-^{14}C]	
	mg eq./kg	%TRR	mg eq./kg	%TRR
TRR	0.010	100.0	0.006	100.0
Solvent Extracted	0.009	89.0	0.005	91.4
Cyazofamid	< 0.001	1.0	< 0.001	1.2
CCBA (incl. Cysteine conjugate)	0.004	41.3	0.003	42.3
CCBA-AM	< 0.001	3.3	0.002	28.6
CCIM	< 0.001	0.4	< 0.001	0.7
CCIM-AM	< 0.001	1.9	< 0.001	2.6
Polar Region	0.003	30.6	< 0.001	1.6
Bound	0.001	6.4	< 0.001	7.5
Recovered	0.009	95.4	0.006	98.9

Table 16 Characterization of radioactive residues in muscle

Fraction	Muscle (loin)			
	[Im-^{14}C]		[Bz-^{14}C]	
	mg eq./kg	%TRR	mg eq./kg	%TRR
TRR	0.006	100.0	0.004	100.0
Solvent Extracted	0.004	73.2	0.003	73.6
Cyazofamid	< 0.001	1.0	< 0.001	0.7
CCBA (incl. Cysteine conjugate)	0.001	22.4	0.001	24.0
CCBA-AM	< 0.001	2.0	< 0.001	3.8
CCIM	0.002	22.6	0.001	26.8
CCIM-AM	< 0.001	3.6	< 0.001	6.9
Polar Region	0.001	11.9	< 0.001	2.6
Bound	0.002	26.8	0.001	26.4
Recovered	0.006	100.0	0.004	100.0

In summary, cyazofamid was not a significant residue in goat tissues or milk. The principal residues in were CCBA (free or cysteine-conjugated), CCIM, and their amide analogues. Although these metabolites are considered major residues based on percent of TRR, the absolute levels in mg eq./kg were generally low. The HPLC system used for most matrices did not separate CCBA from its cysteine conjugate; however, the results from the analysis of kidney samples indicates that the cysteine conjugate likely makes up the majority of the CCBA-related residues. Extraction with ACN and/or ACN:H_2O extracted 73-101% of the radioactive residues from all matrices except liver (ca. 41%). Treatment of liver PES with acid, base, or enzymatic extraction released an additional 24-36% of the residue, of which a greater proportion partitioned into the aqueous or aqueous+emulsion fractions. Further identification was not possible due to low levels of radioactivity and matrix interferences. Analysis of the enzymatic extraction showed a number of radiolabelled components, none greater than 0.005 mg eq./kg. The proposed metabolic pathway in goats is summarized in Figure 4.

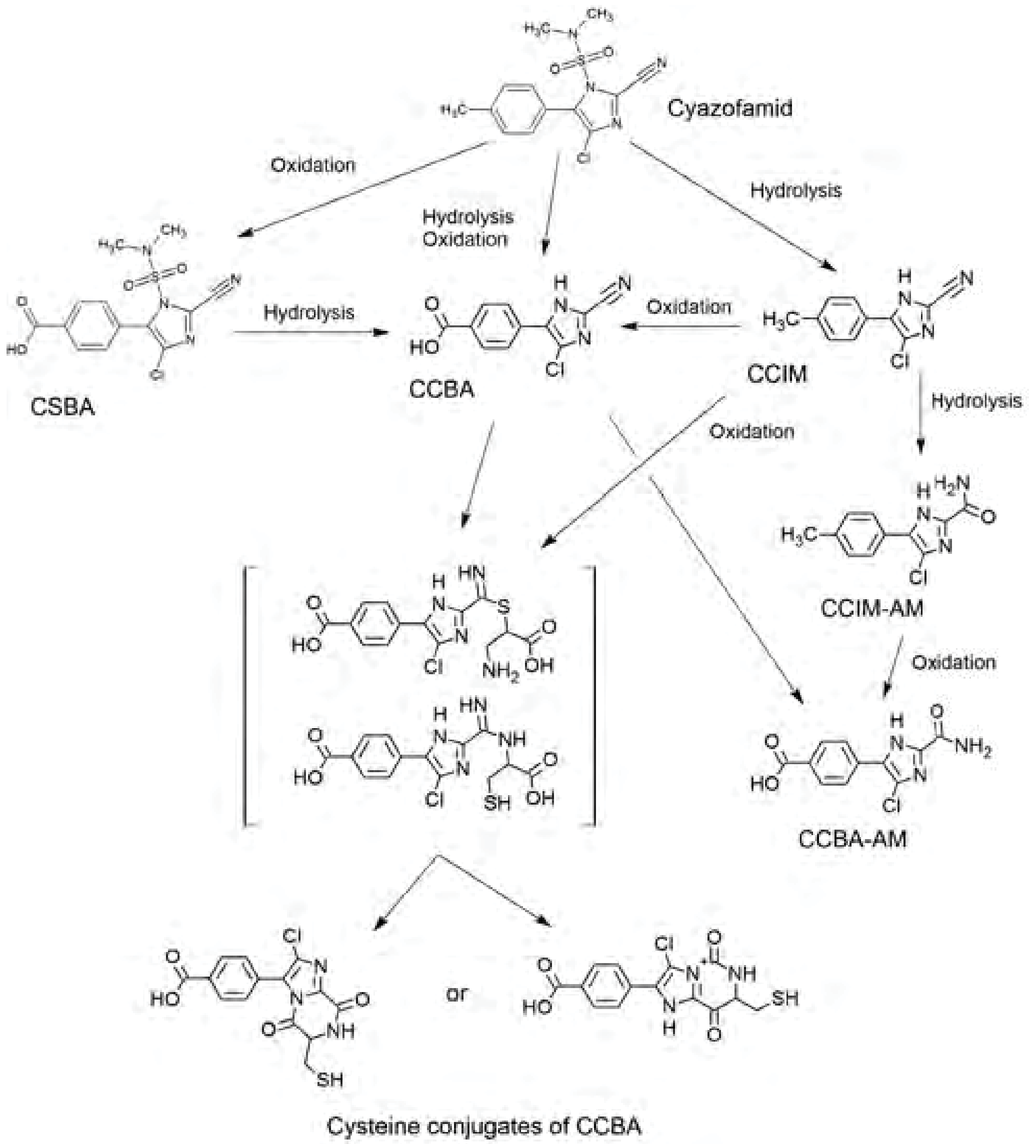


Figure 4 Proposed metabolic pathway of cyazofamid in lactating goat

Laying hens

The metabolism of cyazofamid in laying hens was investigated by Gupta and Bassett (1999, Study RA-3011). Cyazofamid was radiolabelled in the imidazole (Im) or benzene (bz) rings. For each radiolabel position, a group of ten hens was dosed for five consecutive days at ca. 1.1 mg/bird/day (equivalent to ca. 10 ppm in the diet). Eggs were collected twice daily, pooled based on test group from the evening and morning collections, and separated into yolks and whites. Excreta were collected once daily throughout the study. Hens were sacrificed 9 hours after the final dosing, at which point tissues and blood were collected for analysis.

All samples were mixed or homogenized prior to subsampling for analysis. Tissues were homogenized in the presence of dry ice. Total radioactive residues were determined by combustion and LSC for all tissues and for egg white. The TRR of egg yolk was determined by direct LSC of solubilized sample. Excreta were extracted with ACN, and the TRR was determined by LSC of the extract and combustion/LSC of the PES. Samples of kidney and liver were each extracted with ACN (2×) followed by ACN:H_2O (50:50, v/v + 0.2-1% acetic acid; 2×). The PES from kidney, liver, and excreta were treated with 1.0 M HCl, protease, amylase, collagenase, 6.0 M HCl, and 1.0 M NaOH, in that order. The metabolic profiles of solvent-extracted liver, kidney, and excreta residues and 1.0 M HCl-extracted excreta residues were determined by HPLC. Samples of egg, breast muscle, thigh muscle, blood, fat, skin, and cage wash were not assayed for metabolite profiles due to the low level of radioactivity in those matrices. The limit of detection for the LSC analysis was defined to be twice the disintegrations per minute of control samples, which translated to 0.006 mg eq./kg. Approximately 30% of the TRR in liver and approximately 50% of the TRR in kidney was extracted. Further treatments of the PES quantitatively released the unextracted residues remaining from the solvent extraction.

Five HPLC systems were used to analyse samples. All were reverse-phase systems using UV and radioactive flow detectors. The systems differed in the mobile phase gradients that were used and the specific column (four C-18, one phenyl).

Approximately 90% of the administered dose was excreted and < 0.1% was accounted for in tissues (liver and kidney; Table 17). Residues identified in excreta were cyazofamid, CCBA, CCIM, CCTS, CHCN, and unidentified conjugates of CHCN. Total radioactive residues were < 0.006 mg eq./kg in all samples of eggs, muscle, blood, fat, and skin; as such, residue plateau in eggs could not be assessed. In kidney (

Table 18), the only major residues for both label positions were CHCN conjugates (15% TRR, 0.0044-0.0086 mg eq./kg), CCBA (12% TRR, 0.0035-0.0064 mg eq./kg), and unextracted residues (56% TRR, 0.017–0.031 mg eq./kg). In liver (Table 19), the only major residues were unextracted residues (75% TRR, 0.033–0.066 mg eq./kg). Further workup of the post-extraction solids in kidney and liver released the entire unextracted residue (104 and 109%, respectively) from the Bz label and nearly all from the Im label (95 and 87%, respectively). The majority of the residue was extracted with the 1 M HCl, protease, and amylase treatments (Table 20). In the 1 M HCl hydrolysate of kidney and liver PES, the major identified residues (Table 21) were CHCN conjugate (30-67%TRR) and CCBA (14% TRR; liver from Im label only). Residues of all fractions in the hydrolysate were ≤ 0.01 mg eq./kg and most were < 0.001 mg eq./kg.

Table 17 Total radioactive residues (TRRs) in tissues and excreta of hens following exposure equivalent to 10 ppm in the diet

Matrix	[Im-^{14}C]		[Bz-^{14}C]	
	mg eq./kg	% of dose	mg eq./kg	% of dose
Eggs and Tissues				
Egg	< 0.006	--	< 0.006	--
Fat	< 0.006	--	< 0.006	--
Kidney	0.058	0.01	0.029	0.01
Liver	0.088	0.05	0.044	0.03
Muscle (breast)	< 0.006	--	< 0.006	--
Muscle (thigh)	< 0.006	--	< 0.006	--
Skin	< 0.006	--	< 0.006	--
Blood and Excreta				
Blood	< 0.006	--	< 0.006	--
Cage wash	2.37	1.92	1.09	1.31
Excreta	51.2	90.3	41.1	84.9

Table 18 Characterization of radioactive residues in kidney

Fraction	Kidney			
	[Im-^{14}C]		[Bz-^{14}C]	
	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR	0.0288	100	0.0578	100
Cyazofamid	0.0001	0.4	0.0002	0.3
CCBA	0.0035	12.3	0.0064	11.1
CCIM	0.0002	0.8	0.0005	0.8
CCTS	0.0002	0.6	0.0003	0.6
CHCN	0.0004	1.2	0.0009	1.6
CHCN Conjugates [a]	0.0049	17.2	0.0096	16.8
CM-2	0.0002	0.6	0.0003	0.4
CM-3	0.0002	0.6	0.0003	0.6
CM-6	0.0003	1.0	0.0005	0.8
CM-7	0.0007	2.3	0.0005	0.9
CM-10	0.0007	2.4	0.0012	2.1
CM-11	0.0004	1.3	0.0006	1.0
CM-12	0.0002	0.6	0.0003	0.6
Solvent Extractable	0.0120	41.3	0.0216	37.6
PES	0.0171	59.4	0.0312	54.0

[a] Combination of fractions CM-1, CM-4, and CM-5

Table 19 Characterization of radioactive residues in liver

Fraction	Liver			
	[Im-^{14}C]		[Bz-^{14}C]	
	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR	0.088	100	0.044	100
Cyazofamid	< 0.006	--	0.0004	0.4
CCBA	0.0002	0.5	0.0015	1.7
CCIM	0.0002	0.4	0.0013	1.5
CCTS	0.0002	0.4	0.0007	0.8
CHCN	0.0001	0.3	0.0013	1.5
CHCN Conjugates [a]	0.0018	4.1	0.0111	12.5
CM-2	0.0002	0.5	0.0002	0.3
CM-3	0.0001	0.2	0.0002	0.3
CM-6	0.0001	0.3	0.0006	0.7
CM-7	0.0001	0.2	0.0004	0.4
CM-10	0.0008	1.8	0.0007	0.8
CM-11	0.0010	2.2	0.0009	1.1
CM-12	0.0005	1.1	0.0003	0.3
Solvent Extractable	0.0053	12.0	0.0192	21.9
PES	0.0327	74.5	0.0660	75.2

[a] Combination of fractions CM-1, CM-4, and CM-5.

Table 20 Exhaustive extraction of kidney and liver post-extraction solids

Fraction	[Im-^{14}C]			[Bz-^{14}C]		
	mg eq./kg	%TRR	% unextracted residue	mg eq./kg	%TRR	% unextracted residue
Kidney						
PES	0.0312	54.0	--	0.0171	59.5	--
Acid (1 M HCl)	0.0150	26.7	49.4	0.0086	30.0	50.5
Protease	0.0060	9.8	18.2	0.0032	11.0	18.6
Amylase	0.0060	9.5	17.6	0.0043	14.8	24.9
Collagenase	0.0010	1.7	3.2	0.0004	1.5	2.5
Acid (6 M HCl)	0.0010	1.0	1.9	0.0003	0.9	1.6
Base (1 M NaOH)	0.0020	2.8	5.1	0.0011	3.8	6.3

Fraction	[Im-^{14}C]			[Bz-^{14}C]		
	mg eq./kg	%TRR	% unextracted residue	mg eq./kg	%TRR	% unextracted residue
Total	0.0310	51.5	95.4	0.079	62.0	104.4
Liver						
PES	0.0660	75.2	--	0.0327	74.6	--
Acid (1 M HCl)	0.0156	17.7	23.6	0.0078	17.8	23.8
Protease	0.0017	1.9	2.5	0.0108	24.7	33.1
Amylase	0.0116	13.2	17.6	0.0130	29.6	39.7
Collagenase	0.0072	8.2	10.9	0.0012	2.8	3.7
Acid (6 M HCl)	0.0026	2.9	3.9	0.0004	0.9	1.2
Base (1 M NaOH)	0.0185	21.1	28.1	00.026	5.8	7.8
Total	0.0572	65.0	86.6	0.0592	81.6	109.3

Table 21 Distribution of radiolabelled residues in the acid hydrolysate from hen liver/kidney post-extraction solids

Fraction	mg eq./kg			% TRR		
	Liver [Im-^{14}C]	Kidney [Bz-^{14}C]	Kidney [Im-^{14}C]	Liver [Im-^{14}C]	Kidney [Bz-^{14}C]	Kidney [Im-^{14}C]
TRR	0.0156	0.0086	0.015	100.0	100.0	100.0
Cyazofamid	0.0001	0.0001	0.0001	0.6	1.2	0.7
CHCN Conjugate	0.0073	0.0026	0.0101	46.8	30.2	67.3
CHCN	0.0001	0.0001	0.0001	0.6	1.2	0.7
CCBA	0.0022	0.0002	0.0003	14.1	2.3	2.0
CCTS	0.0002	0	0.0001	1.3	0.0	0.7
CCIM	0.0006	0	0.0001	3.8	0.0	0.7
CM-2	0.002	0.001	0.0001	12.8	11.6	0.7
CM-3	0.002	0.0016	0.0012	12.8	18.6	8.0
CM-6	0.0001	0.0003	0.0002	0.6	3.5	1.3
CM-7	0.0001	0.0001	0.0001	0.6	1.2	0.7
CM-10	0.0004	0.0004	0.0008	2.6	4.7	5.3
CM-11	0.0003	0.0002	0.0004	1.9	2.3	2.7
CM-12	0.0001	0	0.0001	0.6	0.0	0.7

In summary, the poultry metabolism study shows essentially no transfer of cyazofamid residues into poultry eggs, meat, fat, and skin, and only very little transfer of residues into poultry offal. CCBA and conjugates of CHCN were the only identified residues occurring at greater than 10% TRR in any matrix; even so, the absolute levels of these metabolites were low. The proposed metabolic pathway of cyazofamid in laying hens is portrayed in Figure 5.

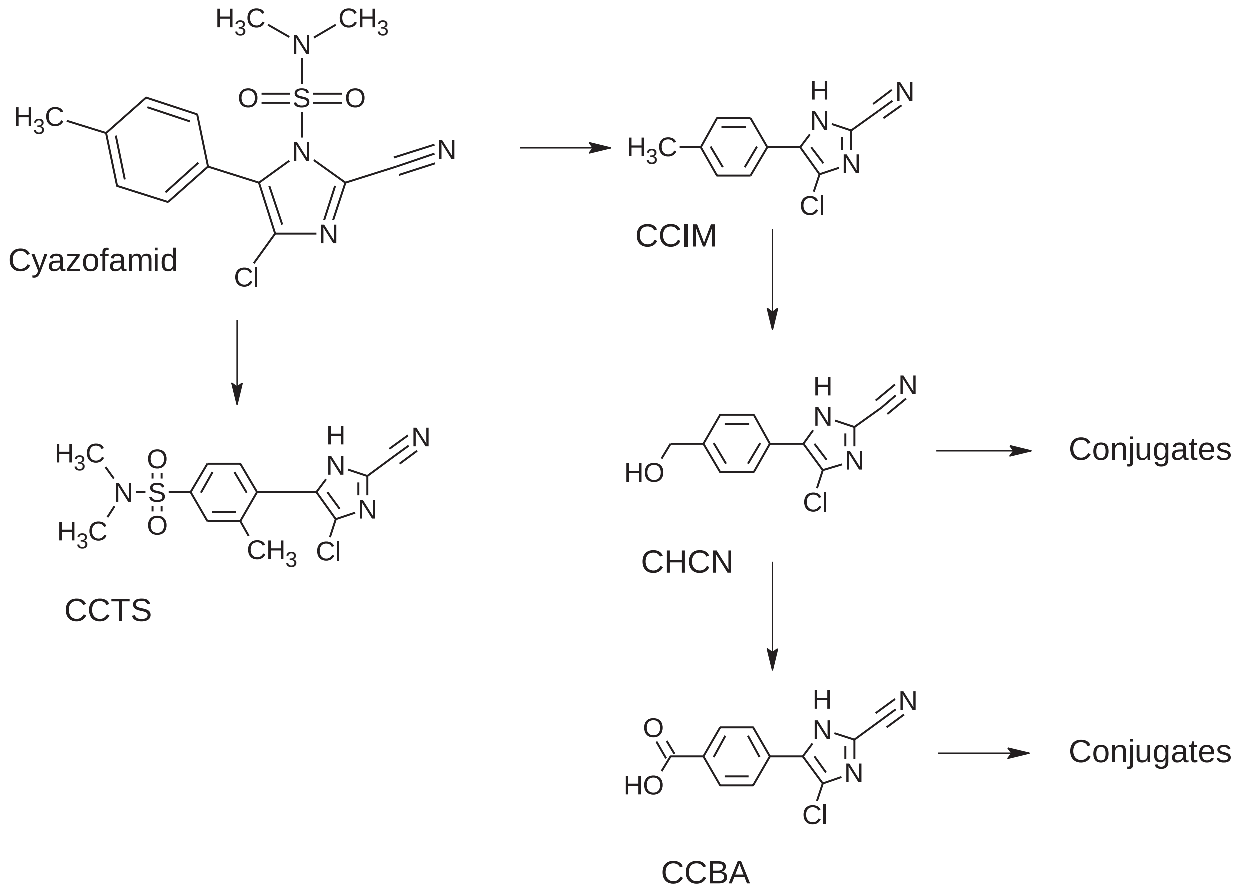


Figure 5 Proposed metabolic pathway of cyazofamid in laying hens

Environmental fate

The Meeting received studies for cyazofamid depicting the aqueous hydrolysis, aqueous and soil photolysis, aerobic soil metabolism, and a confined rotational crop study with carrot, lettuce, and wheat.

Hydrolysis

Hydrolysis of cyazofamid was investigated by I. S. Hendrix and T.R. Neal (1997, RA-4003; see Table 1).

The test material was hydrolysed, with half-lives ranging from 10.6 days to 13.3 days at 25 °C and from 0.39 to 0.55 days at 50 °C.

Hydrolysis of the cyazofamid metabolites CCIM, CCIM-AM, and CTCA was investigated in a separate study by T. Repko (1999, RA-4205). Each of the three compounds, radiolabelled in the benzene ring, was dissolved in sterile buffered solutions (pH 4, 7, and 9) with acetonitrile (< 1%) as a co-solvent. The solutions were maintained in darkness at 50±0.1 °C and sampled after 0 and 5 days. Hydrolysis of each test substance was minimal, as summarized in Table 22.

Table 22 Hydrolysis of cyazofamid metabolites at 50 °C

	Concentration of test material (mg/L)					
	CCIM		CCIM-AM		CTCA	
pH	Day 0	Day 5	Day 0	Day 5	Day 0	Day 5
4	0.062	0.062	0.067	0.067	0.062	0.057
7	0.062	0.061	0.067	0.066	0.062	0.060

pH	Concentration of test material (mg/L)					
	CCIM		CCIM-AM		CTCA	
	Day 0	Day 5	Day 0	Day 5	Day 0	Day 5
9	0.092	0.060	0.067	0.064	0.062	0.060

Photolysis

Photolysis of cyazofamid in **aqueous buffer** was investigated by Hendrix (1999, Report RA-4013; see Table 1). Cyazofamid degraded very rapidly, with a half-life of approximately 30 minutes. Cyazofamid also dissipated in the dark-control samples, with recovery falling to 21% by Day 26.

Photolysis of cyazofamid on the surface of a loamy sand **soil** was investigated by Shelby (1999, Report RA-4018). Cyazofamid, radiolabelled in either the benzene (Bz) ring or the imidazole (Im) ring, was applied to soil and exposed to simulated sunlight for 30 days (12-hr light/dark cycle). At intervals throughout the study, samples were extracted with ACN and water and analysed by radio-HPLC. Reference standards included in the study design were cyazofamid, CCIM, CCIM-AM, CHCN, CHCA, CCBA, CTCA, CTI, and CCIS

Mass balance recovery in the study was acceptable, ranging from 75 to 102% (Table 23). The proportion of unextracted residues increased during the 30-day exposure period. In the study, CCIM was formed from parent cyazofamid. The CCIM was then reduced to CCIM-AM and then oxidized to CCBA. CCBA underwent further degradation to unidentified products. As with the aqueous photolysis study, residues of cyazofamid in dark-control samples declined during the exposure period. Calculated first-order $DT_{50}$and DT_{90} times for cyazofamid were similar between the light-irradiated samples and their dark-control counterparts. Although the initial degradation of cyazofamid is not significantly impacted by photolytic processes, time-course data indicate that photolysis does impact the amount of CCBA metabolite present in the samples (

Table 24). Formation of CO_2 was minimal (12% Im, 3% Bz).

Table 23 Percent of applied radioactivity from the soil photolysis study with cyazofamid

Time, days	Extracted		Unextracted		Total	
	Dark	Light	Dark	Light	Dark	Light
[Im-^{14}C]						
0	94	94	2	2	96	96
3	97	87	5	5	102	92
7	89	82	9	10	98	92
14	81	70	14	23	95	93
21	58	72	17	30	75	102
30	81	54	20	29	101	82
[Bz-^{14}C]						
0	94	94	2	2	96	96
3	87	93	4	8	91	101
7	84	83	11	14	95	97
14	77	84	20	13	97	97
21	70	93	15	27	85	90
30	76	59	22	37	98	96

Table 24 Percent TRR of residues in soil from the soil photolysis study

Time, days	Cyazofamid		CCIM		CCIM-AM		CCBA	
	Dark	Light	Dark	Light	Dark	Light	Dark	Light
[Im-^{14}C]								
0	91	91	3	3	0	0	0	0
3	67	53	25	24	2	3	0	0
7	42	33	40	33	3	5	1	1
14	19	19	12	34	3	4	45	2
21	8	12	18	16	3	2	19	28
30	8	5	12	19	2	3	54	13
[Bz-^{14}C]								

Time, days	Cyazofamid		CCIM		CCIM-AM		CCBA	
	Dark	Light	Dark	Light	Dark	Light	Dark	Light
0	90	90	3	3	0	0	0	0
3	61	57	22	25	2	2	0	1
7	39	27	36	34	1	4	0	3
14	16	29	11	39	2	4	45	3
21	17	17	17	24	3	4	31	9
30	9	5	15	19	2	3	44	17

Aerobic soil metabolism

Two studies depicting the metabolism and degradation kinetics of cyazofamid in aerobic soils were submitted. In the first, Hartman (1997, Report RA-4004) treated a loamy sand soil with benzene- (Bz) or imidazole- (Im) radiolabelled cyazofamid to a level of 0.1 mg/kg. After thorough mixing, the soils samples were placed into a metabolism apparatus (dark conditions, 20 °C) and analysed 0, 1, 3, 5, 10, 15, 20, 26, 30, 44, and 59 days after treatment. In the second study (Hartman, Korsch, and Lentz, 1999, Report RA-4012), a sandy loam soil (20 °C), a sandy soil (20 °C and 10 °C), and a loamy sand soil (20 °C) were treated in the same manner as the first study and incubated under aerobic conditions for 30 or 45 days (20 °C) or 110 days (10 °C), with samples taken intermittently for analysis.

In both studies, soil samples were extracted twice with ACN/H_2O (80/20, v/v), and the extracts were analysed for total radioactivity by LSC. At later sampling times (first study ≥ Day 20, second study ≥ Day 7), additional extractions were done with ACN/H_2O (50/50, v/v) followed by 0.1N NaCl. All extracts were analysed by HPLC. Radioactivity in the PES was determined by combustion/LSC. In addition, PES from the 10- and 59-Day samples in the first study were fractionated into their various organic matter constituentsand the radioactivity in those fractions was assayed combustion/LSC or direct LSC.

Mass balance from both studies was acceptable. Average recovery of radioactivity across extracted, unextracted, and CO2 fractions and across all soils, temperatures, and sampling times ranged from 96% to 100% of applied. Over the time course of the studies, unextracted residues increased from < 5% of applied material at Hour 0 to 35–64% at termination. Similarly, 14CO2 increased from 0% of applied radioactivity at the onset of the incubation period to 14% at study termination. Results from the first and second studies from incubations at 20 °C gave similar DT50 estimates of approximately 5 days. Estimated DT90 values were more diverse, ranging in the first study from 16 to 25 days and in the second study from 35 to 39 days. Dissipation times were longer at the 10 °C incubation temperature, averaging 16 days for DT50 and > 110 days for DT90. Degradates identified in the two studies were CCIM, CCIM-AM, and CTCA. All occurred at ≥ 10% of the applied radioactivity at some point in the study; as such, they would be ≥ 10% TRR and are considered to be major degradates. In terms of relative kinetics, parent compound appears to first degrade to CCIM, which peaks early in the temporal profile, followed by CCIM-AM. Degradate CTCA forms last; data are inconclusive of whether CTCA has peaked by study termination. Characterization of the PES from the first study showed association of radioactivity predominantly with fulvic acid and to a lesser extent humin and humic acid.

Confined rotational crop studies

The fate of cyazofamid as it relates to rotational crops was investigated by McFadden (1999, Report OR-4019). In that study, carrot, lettuce, and wheat were planted into a loamy sand soil that had been treated with cyazofamid, radiolabelled in either the benzene (Bz) or imidazole (Im) ring, at a rate of ca. 500 g/ha (100 g/ha×5 applications at 7-day interval). The crops were planted into the soil at 31, 120, and 360 days after treatment. At each plant-back interval (PBI), samples of immature and mature crop were collected.

Harvested samples were homogenized in the presence of dry ice and stored frozen (≤ 7 days) prior to analysis. Total radioactive residues in each sample were determined by combustion. Further analysis of the samples was determined by their TRR levels: <

0.01 mg eq./kg, no further analyses were attempted; between 0.01 and 0.05 mg eq./kg, samples underwent limited solvent extraction; and > 0.05 mg eq./kg, samples underwent a more exhaustive extraction. Limited extraction consisted of three extractions with ACN/0.1% formic acid (9/1, v/v) followed by partitioning against methylene chloride. Extracts and PES were analysed for radioactivity by LSC (combustion/LSC for PES). The aqueous fraction was neutralized with 0.2 M potassium carbonate, concentrated, and filtered prior to carbohydrate analysis by HPLC. The more exhaustive extraction was performed on the organic fraction by diluting it with 0.1 N formic acid to make a 1:4 solvent:formic acid solution, and then partitioning it twice with ethyl acetate and cleaned up by solid-phase extraction. All eluents from solid-phase extraction were assayed by LSC and ACN/H_2O eluates were analysed by HPLC. Residues in PES from wheat tissues were characterized by acid hydrolysis in addition to combustion analysis.

Total radioactive residues in the rotational crops are shown in Table 25. In all samples, residues resulting from the Im treatment were greater than those from the Bz treatment. Decreases in TRR were generally modest between the 31- and 120-day PBIs and then more pronounced between the 120- and 360-day intervals. Characterization of residues is based on residues in the 31- and 120-day PBI samples due to the low levels of radioactivity in the 36-day PBI samples.

Mass balance of radioactivity was generally adequate, with recovery of radioactivity from the aqueous fraction, the organic fraction, and PES, combined, ranging from 61 to 123% of the TRR. Low recoveries were associated with highly pigmented extracts and may be due to quenching during LSC rather than actual low recovery.

Table 25 Summary of TRRs in rotational crops at each plant-back interval following application of cyazofamid

Crop	Harvest (DAT)			TRR (mg eq./kg)					
				[Im-^{14}C]			[Bz-^{14}C]		
PBI (DAT)	31	120	360	31	120	360	31	120	360
Carrot (immature)	94	202	460	0.059	0.025	0.011	0.017	0.020	0.005
Carrot (foliage)	150	228	511	0.074	0.045	0.018	0.019	0.019	0.005
Carrot (root)	150	228	511	0.018	0.010	0.003	0.009	0.006	0.002
Lettuce (immature)	86	145	448	0.037	0.022	0.004	0.016	0.009	0.002
Lettuce (mature)	108	179	479	0.015	0.008	0.006	0.005	0.004	0.007
Wheat (forage)	66	157	405	0.510	0.097	0.015	0.108	0.029	0.006
Wheat (chaff)	251	291	571	0.269	0.289	0.017	0.046	0.027	0.012
Wheat (straw)	251	291	571	0.498	0.209	0.031	0.126	0.085	0.015
Wheat (grain)	251	291	571	0.090	0.062	0.002	0.024	0.014	0.001

DAT = Days after last treatment.

Total radioactivity in extracts from lettuce (all PBIs), carrot (120- and 360-day PBIs), and wheat grain (all PBIs) was low, and samples were not further analysed to determine the nature of the residues. HPLC analysis of carrot tops (Im label only) from the 31-day PBI showed residues of CCBA (2.2% TRR), CCIM (10.4% TRR), CCIM-AM (39.5% TRR, 0.001 mg/kg), and cyazofamid (20.1% TRR, 0.003 mg/kg). Radioactivity in wheat forage and chaff was associated primarily with carbohydrates (0.01-0.195 mg eq./kg); levels of cyazofamid and metabolites were ≤ 0.003 mg eq./kg. Similar results occurred for wheat straw. The proposed metabolic pathway for cyazofamid in rotational crops was included previously in Figure 3.

RESIDUE ANALYSIS

Summary of analytical methods

Methods for the analysis of cyazofamid and CCIM used in the residue trials are generally the same, consisting of solvent extraction (usually acetonitrile) followed by partitioning and solid-phase extraction clean-up steps. Analysis of the residue was most frequently accomplished using LC-

MS/MS, although some studies used HPLC-UV or GC-NPD. The methods are summarized in Table 26. The LC-MS/MS and HPLC-UV methods underwent independent laboratory validation and appear to be suitable for enforcement purposes.

Table 26 Overview of the analytical methods submitted for cyazofamid and CCIM

Report ID	Matrix	Extraction	Clean-up	Separation/ Analysis/LOQ	Concurrent Recovery (%) (n) Mean ± Std. Dev.	
					Cyazofamid	CCIM
RA-3058, RA-3091	Grapes & processed commodities	Acetonitrile (2X)	Partitioning (hexane followed by aqueous sodium sulfate/methylene chloride) Florisil® solid-phase extraction	HPLC-UV, C-18 column LOQ[a] = 0.01 mg/kg	(13) 92±20	(13) 105±25
RA-3067, RA-3090	Cucumber, squash, melon				(16)91±14 (16)86±12 (8)83±15	(16)94±21 (16)90±14 (8)102±19
RA-3065, RA-3077, RA-3089	Tomato				(14)98±15	(15)94±22
RA-3066, RA-3075, RA-3093	Potato & processed commodities				(22)79±15 (16)90±17	(25)92±19 (18)90±8
RA-3202A, RA-3203A, RA-3204A	Potato	Acetone	Partitioning (methylene chloride) Gel-permeation chromatography	GC-NPD LOQ[a] = 0.05 mg/kg	(16)96±4	--
RA-3082, RA-3083, RA-3084, RA-3085, RA-3086, RA-3095	Grapes	Acetonitrile/ acetone (8/2, v/v) (2X)	Partitioning (hexane followed by aqueous sodium sulfate/methylene chloride) Florisil® solid-phase extraction	HPLC-UV, C-18 column LOQ[a] = 0.01 mg/kg	(77)86±10	(75)90±9
RA-3123	Broccoli	Acetonitrile (2X)	Partitioning (hexane) Polymeric solid-phase extraction	LC-MS/MS, propyl column LOQ[a] = 0.01 mg/kg	(10)104±19	(10)98±23
RA-3124	Cabbage				(9)97±18	(9)91±19
RA-3096, RA-3199	Lettuce				(13)90±7	(13)88±9
RA-3125	Mustard greens				(10)95±21	(10)98±31
RA-3126	Spinach				(9)93±24	(9)91±27
RA-3195, RA-3198	Beans				(12)87±7	(12)88±5
RA-3107	Carrot				(26)83±8	(26)69±7
RA-3197	Basil				(17)88±8	(17)90±6
RA-3127	Hops	Acetonitrile	Partitioning (hexane) Extract split Cyazofamid: NH_2 SPE CCIM: Polymeric SPE	LC-MS/MS, propyl column LOQ[a] = 0.05 mg/kg	(20)82±17	(20)86±18
RA-3169, RA-3188, RA-3190 RA-1166	Hops	Acetonitrile/ acetone (8/2, v/v)	C-18 SPE	LC-MS/MS, C-18 column LOQ[a] = 0.01 mg/kg	(10)89±4	(10)92±3
RA-1166	Onion				(3)99±3	(3)99±4
RA-3101	Pepper	Acetonitrile/H_2O with 2% acetic acid (1/1, v/v)	Partitioning (methylene chloride) Florisil® solid-phase extraction	LC-MS/MS, C-18 column LOQ[a] = 0.01 mg/kg	(12)92±6	(12)95±4

[a] Defined as the lowest limit of method validation.

Plant materials

Methods used for the analysis of residues of cyazofamid and CCIM in plant materials in residue trials are all very similar (see Table 26). Extraction of homogenized sample is by a relatively polar solvent followed, in most cases, by partitioning of the residue into a non-polar solvent. Further clean-up is by solid-phase extraction using various sorbents. Most of the methods use either LC-MS/MS or HPLC-UV for separation and detection of the analytes. Method validation recoveries across all matrices and fortification levels (0.01–100 mg/kg) ranged from 63 to 128%, with a weighted average and relative standard deviation of 90±8% (Table 27).

Three methods underwent independent laboratory validation and were determined to be suitable for compliance purposes. In the first method, validated using bulb onion, lettuce, and green hops (Study RA-1177), cyazofamid and CCA are extracted by homogenizing the sample in 120 mL of acetonitrile/acetone (8/2, v/v), isolating the extract by vacuum filtration, and reducing the volume of the extract to 5 mL by rotary evaporation. Clean-up of the extract is by C-18 solid-phase extraction, and analysis of the residues is by LC-MS/MS on a C-18 column with an isocratic mobile phase consisting of acetonitrile (80%) and 0.2% acetic acid in water (20%). Mass transitions [M+H$^+$] of 325.1 m/z→108.0 m/z for cyazofamid and 218.3 m/z→183.2 m/z for CCIM are used for quantification. Confirmation of cyazofamid is made using the same ion transitions but with a cyano column on a gradient mobile phase. Confirmation of CCIM is based on a mass transition of 218.3 m/z→139.2 m/z. A confirmatory transition for cyazofamid is available (325.1 m/z→261.2 m/z).

In the second method, validated using barley grain and olive (Study RA-1177), cyazofamid and CCIM are extracted by shaking samples in 10 mL water followed by 10 mL acetonitrile (barley), or 10 mL acetonitrile only (olive). The extracts are then cleaned up using dispersive solid-phase extraction (onto magnesium sulfate, sodium chloride, sodium citrate dibasic sesquihydrate, and sodium citrate tribasic dihydrate). Analysis of the residues is the same as described in the first method.

In the third method, validated using tomato (Study RA-3062), cyazofamid and CCIM are extracted with acetonitrile. Co-extracted materials are then partitioned into hexane, which is discarded. Residues in the acetonitrile portion are then concentrated by rotary evaporation. A second partitioning is then done using sodium sulfate (2%) and methylene chloride. The methylene chloride phase is retained and evaporated to dryness. Residues of cyazofamid and CCIM are dissolved in ethyl ether and cleaned up by passing over a Florisil® column. After elution from the column, the ethyl ether is evaporated and the residues dissolved in acetonitrile/0.5% ascorbic acid in water (1/1, v/v) for analysis by HPLC-UV. Separation is achieved on a C18 column using a mobile phase of acetonitrile/0.5% ascorbic acid in water (1/1, v/v); detection is a 280 nm.

Table 27 Summary of analyte recoveries from method validations of methods for cyazofamid and CCIM

Report	Method Summary	Matrix	Analyte	Fortification, mg/kg	n	Recovery, % Mean ± Std. Dev.
RA-1177	Solvent: ACN:Acetone Cleanup: C18 (onion, lettuce, hops) Dispersive SPE (olive, barley) Analysis: LC-MS/MS	Onion	Cyazofamid	0.01-0.1	10	85 ± 15
			CCIM	0.01-0.1	10	86 ± 10
		Lettuce	Cyazofamid	0.01-0.1	10	70 ± 9
			CCIM	0.01-0.1	10	86 ± 10
		Olive	Cyazofamid	0.01-0.1	10	98 ± 8
			CCIM	0.01-0.1	10	94 ± 9
		Barley grain	Cyazofamid	0.01-0.1	10	94 ± 12
			CCIM	0.01-0.1	10	86 ± 20
		Hops (fresh)	Cyazofamid	0.01-0.1	10	104 ± 10
			CCIM	0.01-0.1	10	109 ± 14

Report	Method Summary	Matrix	Analyte	Fortification, mg/kg	n	Recovery, % Mean ± Std. Dev.
RA-3062	Solvent: ACN Cleanup: Hexane, $MeCl_2$, Florisil Analysis:HPLC-UV	Tomato	Cyazofamid	0.01-1.0	4	90.6 ± 8.2
			CCIM	0.01-1.0	4	87.9 ± 3.1
RA-1172	Solvent: ACN:Acetone Cleanup: C18 Analysis: LC-MS/MS	Onions	Cyazofamid	0.01-0.1	10	86 ± 2
			CCIM	0.01-0.1	10	91 ± 3
		Hops (fresh)	Cyazofamid	0.01-0.1	10	85 ± 3
			CCIM	0.01-0.1	10	88 ± 3
		Hops (dried cones)	Cyazofamid	0.01-0.1	10	99 ± 3
			CCIM	0.01-0.1	10	100 ± 7
RA-1101	Solvent: ACN Cleanup: Hexane, $MeCl_2$, Florisil Analysis:HPLC-UV	Grapes	Cyazofamid	0.01-0.6	14	83 ± 12
			CCIM	0.01-0.6	14	83 ± 12
		Potatoes	Cyazofamid	0.01-0.1	18	86 ± 8
			CCIM	0.01-0.1	18	82 ± 7
		Tomatoes	Cyazofamid	0.01-1.0	31	94 ± 14
			CCIM	0.01-1.0	31	103 ± 18
		Cucumber	Cyazofamid	0.01-0.1	23	92 ± 15
			CCIM	0.01-0.1	23	93 ± 18
		Cantaloupe	Cyazofamid	0.01-0.1	20	90 ± 15
			CCIM	0.01-0.1	20	92 ± 14
		Summer squash	Cyazofamid	0.01-0.1	15	85 ± 14
			CCIM	0.01-0.1	15	103 ± 15
		Potato (wet peel)	Cyazofamid	0.01-0.5	6	92 ± 7
			CCIM	0.01-0.5	6	106 ± 11
		Potato (flakes)	Cyazofamid	0.01-0.5	6	87 ± 10
			CCIM	0.01-0.5	6	89 ± 3
		Potato (chips)	Cyazofamid	0.01-0.5	6	92 ± 7
			CCIM	0.01-0.5	6	68 ± 4
		Tomato (paste)	Cyazofamid	0.01-0.5	7	86 ± 9
			CCIM	0.01-0.5	7	88 ± 6
		Tomato (puree)	Cyazofamid	0.01-0.2	6	89 ± 12
			CCIM	0.01-0.2	6	88 ± 4
		Raisins	Cyazofamid	0.01-0.5	6	67 ± 10
			CCIM	0.01-0.5	6	83 ± 11
		Grape (juice)	Cyazofamid	0.2	8	77 ± 5
			CCIM	0.2	8	80 ± 4
RA-3003	Solvent: ACN Cleanup: Hexane, $MeCl_2$, Florisil Analysis:HPLC-UV	Potato	Cyazofamid	0.01-1.0	6	97 ± 12
			CCIM	0.01-1.0	9	80 ± 13
		Tomato	Cyazofamid	0.01-1.0	6	84 ± 13
			CCIM	0.01-1.0	6	86 ± 5
		Grape	Cyazofamid	0.01-1.0	10	71 ± 9
			CCIM	0.01-1.0	6	74 ± 7
		Must	Cyazofamid	0.01-1.0	6	97 ± 18
			CCIM	0.01-1.0	6	90 ± 3
		Wine	Cyazofamid	0.01-1.0	9	78 ± 9
			CCIM	0.01-1.0	4	81 ± 1

Stability of residues in stored samples

The stability of cyazofamid and CCIM in frozen storage has been investigated in bean, grape (homogenized and unhomogenized; cyazofamid only), oilseed rape, potato, and tomato. For all matrices except grape, samples were spiked, separately, with cyazofamid and CCIM. Samples were placed into frozen storage and analysed after varying durations in frozen storage to determine the amounts of analyte remaining in the sample. For grape, a large sample of was collected from a field trial location and split into two subsamples. One subsample was homogenized and the other was maintained as whole, unhomogenized grapes. Both subsamples were placed into stored frozen.

Incurred residues of cyazofamid were analysed at various storage durations to determine the amount of compound remaining.

Residues of both analytes were stable (≥ 70% remaining) for at least 400 days in beans and oilseed rape, and for up to 181 days in potato. In tomato, cyazofamid was stable for up to 365 days and CCIM was stable for at least 1093 days. In grape, residues of cyazofamid appeared to be more stable in unhomogenized matrix, generally showing > 70% remaining for the 365-day duration of the study versus homogenized matrix, in which the percent remaining was generally <70% at sampling times greater than 8 days. Interpretation of the cyazofamid stability data in grape is complicated by the experimental design and the variability in residue levels, especially for the unhomogenized grape subsample.

In addition to the specific storage stability studies summarized above, a storage stability component was included in the experimental designs of studies conducted by IR-4. The storage stability data from these studies do not include analysis of residues at 0 days. If fortifications were made correctly, the data indicate that under frozen storage conditions, cyazofamid and CCIM are stable for at least 860 days in cabbage; for at least 634 days in lettuce; for at least 977 days in mustard greens; for at least 949 days in spinach; at least 887 days in bean pods with seeds, at least 889 days in bean plants with pods, and at least 140 days in ben seeds without pods; and at least 509 days in hops cones. Cyazofamid was stable for at least 284 days in fresh basil and 297 days in dried basil; however, CCIM was not stable in either commodity (47% remaining in fresh basil and 59% remaining in dried basil). Neither cyazofamid nor CCIM were shown to be stable in carrot, with 58% cyazofamid and 38% CCIM remaining after 374 days in storage.

Table 28 Storage Stability of cyazofamid and CCIM in dry beans (Report RA-3171)

Analyte	Fortification, mg/kg	Storage Time, days	n	Avg. Conc., mg/kg	Avg. % Remaining	Std. Dev.	Concurrent Recovery
Cyazofamid	0.1	1	3	0.10	100	0	100
		29	2	0.090	90	0	92
		95	2	0.090	90	0	94
		209	2	0.075	75	7	84
		400	2	0.095	95	7	88
CCIM	0.1	1	3	0.090	90	0	92
		29	2	0.090	90	0	91
		95	2	0.090	90	0	94
		209	2	0.085	85	7	87
		400	2	0.10	100	0	90

Table 29 Storage Stability of cyazofamid in grape berries (Report RA-3088)

Matrix State	Fortification, mg/kg [a]	Storage Time, days	n	Avg. Conc., mg/kg	Avg. % Remaining	Std. Dev.	Concurrent Recovery
Homogenized	0.74	0	3	0.74	100	5	93
		8	3	0.73	99	14	100
		15	3	0.47	63	4	87
		28	3	0.39	53	6	89
		64	3	0.56	76	9	85
		125	3	0.51	69	8	97
		244	3	0.47	63	6	80
		365	3	0.49	66	9	82
Unhomogenized	0.70	0	3	0.70	100	54	90
		8	3	0.59	84	25	97
		15	3	0.50	71	6	93
		28	3	0.58	83	24	86
		64	3	0.68	97	19	84
		125	3	0.63	90	7	94
		244	3	0.81	120	17	83
		365	3	0.76	110	29	94

[a] Samples were not fortified. The value specified is the average concentration from the samples at the 0-Day sampling.

Table 30 Storage Stability of cyazofamid and CCIM in oilseed rape seed (Report RA-3171)

Analyte	Fortification, mg/kg	Storage Time, days	n	Avg. Conc., mg/kg	Avg. % Remaining	Std. Dev.	Concurrent Recovery
Cyazofamid	0.1	1	3	0.097	97	6	100
		29	2	0.090	90	0	92
		95	2	0.090	90	0	91
		209	2	0.090	90	0	92
		400	2	0.085	85	7	96
CCIM	0.1	1	3	0.090	90	0	96
		29	2	0.085	85	7	88
		95	2	0.090	90	0	92
		209	2	0.090	90	0	94
		400	2	0.090	90	0	93

Table 31 Storage Stability of cyazofamid and CCIM in potato tuber (Report RA-3064)

Analyte	Fortification, mg/kg	Storage Time, days	n	Avg. Conc., mg/kg	Avg. % Remaining	Std. Dev.	Concurrent Recovery
Cyazofamid	0.5	0	4	0.54	110	10	110
		1	4	0.49	98	4	100
		3	4	0.46	92	4	92
		7	4	0.56	110	18	120
		14	4	0.44	88	9	88
		29	4	0.43	86	4	92
		91	4	0.44	88	2	98
		181	4	0.37	74	4	84
		367	4	0.32	64	9	100
		793	4	0.29	58	3	90
		1099	4	0.30	60	13	94
CCIM	0.5	0	4	0.49	98	5	88
		1	4	0.41	82	4	96
		14	4	0.44	88	2	100
		29	4	0.38	76	7	92
		104	4	0.33	66	4	80
		181	4	0.46	92	5	92
		469	4	0.31	62	12	82
		784	4	0.26	52	6	74
		1091	4	0.31	62	9	110

Table 32 Storage Stability of cyazofamid and CCIM in tomato fruit (Report RA-3063)

Analyte	Fortification, mg/kg	Storage Time, days	n	Avg. Conc., mg/kg	Avg. % Remaining	Std. Dev.	Concurrent Recovery
Cyazofamid	0.5	0	4	0.49	98	15	96
		1	4	0.46	92	10	90
		7	4	0.42	84	7	90
		14	4	0.45	90	7	88
		29	4	0.45	90	2	100
		91	4	0.45	90	3	86
		179	4	0.38	76	15	98
		365	4	0.45	90	5	110
		798	4	0.33	66	8	84
		1099	4	0.31	62	7	76
CCIM	0.5	0	4	0.51	100	9	100
		1	4	0.48	96	10	100
		29	4	0.39	78	4	78

Analyte	Fortification, mg/kg	Storage Time, days	n	Avg. Conc., mg/kg	Avg. % Remaining	Std. Dev.	Concurrent Recovery
		90	4	0.42	84	5	78
		180	4	0.50	100	6	88
		467	4	0.43	86	5	96
		788	4	0.38	76	1	88
		1093	4	0.38	76	5	110

Table 33 Storage Stability of cyazofamid and CCIM in IR-4 studies

Crop	Analyte	Storage Time, days	n	Avg. % of Nominal Remaining	Std. Dev.	Concurrent Recovery	Reference
Cabbage	Cyazofamid	860	3	112	4	115	RA-3124
	CCIM	860	3	100	1	100	
Lettuce	Cyazofamid	634	3	72	13	83	RA-3196
	CCIM	634	3	78	12	80	
Mustard greens	Cyazofamid	977	3	112	0	115	RA-3125
	CCIM	977	3	108	6	117	
Spinach	Cyazofamid	949	3	102	2	120	RA-3126
	CCIM	949	3	118	5	117	
Beans (plants with pods)	Cyazofamid	889	3	80	5	94	RA-3198
	CCIM	889	3	76	5	88	
Beans (pods with seeds)	Cyazofamid	887	3	78	15	86	
	CCIM	887	3	88	12	88	
Beans (seeds without pods)	Cyazofamid	140	3	80	4	85	
	CCIM	140	3	76	2	93	
Carrot	Cyazofamid	374	3	58	5	75	RA-3107
	CCIM	374	3	38	2	91	
Basil (fresh)	Cyazofamid	284	3	80	5	83	RA-3197
	CCIM	284	3	47	1	88	
Basil (dried)	Cyazofamid	297	3	78	1	88	
	CCIM	297	3	59	1	82	
Hops (dry cones)	Cyazofamid	509	3	86	7	79	RA-3127
	CCIM	509	3	78	2	87	

USE PATTERN

Table 34 Good agricultural practices (GAPs) authorized for cyazofamid

Crop	Country	Application method(s)	Growth stage	Rate, kg (max), ai/ha	No.	Retreatment interval (min), days	PHI, days
Grape	Germany	Broadcast spray (incl. chemigation)	BBCH 15-61	0.025	8	12-14	21
			BBCH 61-71	0.05			
			BBCH 71-75	0.075			
			BBCH 75-85	0.1			
	USA[a]	Broadcast spray (incl. chemigation)	n.s.	0.08	6	10-14	30
Brassica (cole) leafy vegetables [Crop Group 5] [h]	USA[c]	Transplant soil drench	n.s.	0.753	6	7-10	0
		soil incorporation		0.58			
		broadcast spray (incl. chemigation)		0.08			
Cucurbit vegetables [Crop Group 9] [i]	USA[a]	Broadcast spray (incl. chemigation)	n.s.	0.08	6	7-10	0
Fruiting vegetables [Crop Group 8-10] [j]	USA[a]	Broadcast spray (incl. chemigation)	n.s.	0.08	6	7-10	0

Crop	Country	Application method(s)	Growth stage	Rate, kg (max), ai/ha	No.	Retreatment interval (min), days	PHI, days
Tomato (glasshouse)	USA	Transplant soil drench	At planting and up to 1 week before transplanting	0.01 kg ai/hL	1	--	--
Leafy greens [Crop Subgroup 4A] [k]	USA[a]	Broadcast spray (incl. chemigation)	n.s.	0.08	6	7-10	0
Lettuce	Canada	Broadcast spray (incl. chemigation)	n.s.	0.08	6	7-14	0
Mustard greens	USA[c]	Transplant soil drench	n.s.	0.753	6	7-10	0
		soil incorporation		0.58			
		broadcast spray (incl. chemigation)		0.08			
Beans (succulent podded and succulent shelled)	USA[d]	Broadcast spray (incl. chemigation)	n.s.	0.08	6	7-14	0
Carrot	USA[e]	Broadcast spray (incl. chemigation)	n.s.	0.175	5	14-21	14
Potato	Brazil	Broadcast spray (incl. chemigation)	n.s.	0.10	6	7-10	7
	Canada[f]	Broadcast spray (incl. chemigation)	n.s.	0.08	6	7	7
Tuberous and corm vegetables [Crop Subgroup 1C] [l]	USA[g]	In-furrow	In-furrow application at planting	0.178	10	7-10	7
		broadcast spray (incl. chemigation)	Lay-by/hilling	0.08			
Basil	USA[b]	Broadcast spray (incl. chemigation)	n.s.	0.088	9	7-10	0
Hops	USA[a]	Broadcast spray (incl. chemigation)	n.s.	0.08	6	7-10	3

[a] Do not apply more than 480 g ai/ha/season

[b] Do not apply more than 790 g ai/ha/season. Can be applied to basil grown in a glasshouse

[c] Make a single soil application followed by 5 foliar applications. Do not apply more than 1.15 kg ai/ha/season

[d] Do not apply more than 480 g ai/ha/season. Do not apply to cowpeas used for livestock feed

[e] Do not apply more than 877 g ai/ha/season

[f] Last 2 applications to be made at maximum rate, plant-back interval 30 days

[g] Do not apply more than 800 g ai/ha/season; Last 2-3 applications to be made at maximum rate

[h] Crop Group 5 = Broccoli; broccoli, Chinese (gai lon); broccoli raab (rapini); Brussels sprouts; cabbage; cabbage, Chinese (bok choy); cabbage, Chinese (napa); cabbage, Chinese mustard (gai choy); cauliflower; cavalo broccolo; collards; kale; kohlrabi; mizuna; mustard greens; mustard spinach; and rape greens

[I] Crop Group 9 = Chayote (fruit) ; Chinese waxgourd (Chinese preserving melon) ; citron melon ; cucumber ; gherkin ; gourd, edible (includes hyotan, cucuzza, hechima, Chinese okra); Momordica spp. (includes balsam apple, balsam pear, bitter melon, Chinese cucumber); muskmelon (hybrids and/or cultivars of Cucumis melo; includes true cantaloupe, cantaloupe, casaba, crenshaw melon, golden pershaw melon, honeydew melon, honey balls, mango melon, Persian melon, pineapple melon, Santa Claus melon, and snake melon); pumpkin ; squash, summer (includes crookneck squash, scallop squash, straightneck squash, vegetable marrow, zucchini); squash, winter (includes butternut squash, calabaza, hubbard squash, acorn squash, spaghetti squash); and watermelon

[j] Crop Group 8-10 = African eggplant; bush tomato; cocona; currant tomato; eggplant; garden huckleberry; goji berry; groundcherry; martynia; naranjilla; okra; pea eggplant; pepino; pepper, bell; pepper, nonbell; roselle; scarlet eggplant; sunberry; tomatillo; tomato; tree tomato

[k] Crop Subgroup 4A = Amaranth; arugula; chervil; chrysanthemum, edible-leaved; chrysanthemum, garland; corn salad; cress, garden; cress, upland; dandelion; dock; endive; lettuce; orach; parsley; purslane, garden; purslane, winter; radicchio (red chicory); spinach; spinach, New Zealand; spinach, vine

[l] Crop Subgroup 1C = Arracacha; arrowroot; artichoke, Chinese; artichoke, Jerusalem; canna, edible; cassava, bitter and sweet; chayote (root); chufa; dasheen; ginger; leren; potato; sweet potato; tanier; turmeric; yam bean; yam, true

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The Meeting received data from supervised residue trials conducted on grape, basil, hops, broccoli, cabbage, cucumber, summer squash, muskmelon, peppers, tomato, head and leaf lettuce, mustard greens, spinach, snap bean, lima bean, carrot, and potato. In all trials, a soluble concentrate (SC) formulation was applied as a tank mixture prepared uniquely for that trial site. Trials were conducted in the USA for all crops. In addition, trials on grapes were conducted in Argentina, Mexico, Northern Europe, and Southern Europe; trials on lettuces were conducted in Canada; trials on potato were conducted in Canada and Brazil; and trials on hops were conducted in Germany and the USA. Trials on basil included field-grown and glasshouse-grown crops.

The field trial reports included method validation data, as recoveries from spiked samples at levels reflecting those observed in the field trial samples; dates from critical events during the study, including application, harvest, storage, and analysis; as well as detailed information on the field site and treatment parameters. Analytical reports were sufficiently detailed and included example chromatograms and example calculations. Samples were analysed by the methods described above. The results are supported by concurrent recoveries ranging, across all commodities, 77–95% ± 4–21% (mean ± RSD) for cyazofamid and 86–101% ± 5–19% for CCIM. The maximum durations for samples in frozen storage were:

- Grape = 295 days,
- Broccoli = 773 days,
- Cabbage = 860 days,
- Cucumber = 552 days,
- Summer squash = 535 days,
- Muskmelon = 278 days,
- Peppers = 272 days (bell) and 268 days (non-bell),
- Tomato = 455 days,
- Lettuce = 634 days (head) and 624 days (leaf),
- Mustard greens = 965 days,
- Spinach = 927 days,
- Snap bean = 945 days,
- Lima bean = 147 days,
- Carrot = 443 days,
- Potato = 535 days,
- Basil = 284 days (fresh) and 297 days (dried), and
- Hops = 552 days.

Except for carrot (cyazofamid and CCIM) and basil (CCIM only), the storage durations are less than or equal to those for which residues have been demonstrated to be stable. Unless otherwise noted in the tables below, harvested commodities were maintained whole in the field and not cut or homogenized until they reached the analytical laboratory.

The field trial study designs included control plots. All measured residues from control plots were < 0.01 mg/kg (i.e., < LOQ) and are not included in the summary tables in this evaluation. In the summary tables, values used for making maximum residue level recommendations are underlined, values used for dietary intake estimates are italicized, and highest individual values for estimating dietary intake are bolded. Trial locations that appear to be dependent are grouped by a heavy cell border in the tables (e.g., Table 36).

Supervised trials for cyazofamid:

Category	Crop	Table
Berries and other small fruits	Grape (FB 0269)	35
Brassica (cole or cabbage) vegetables, head cabbage, flowerhead Brassicas	Broccoli (VB 0400)	36
	Cabbage (VB 4175)	37
Fruiting vegetables, cucurbits	Cucumber (VC 0424)	38
	Summer squash (VC 0431)	39
	Muskmelon (VC 4239)	40
Fruiting vegetables, other than cucurbits	Peppers (VO 0051)	41
	Tomato (VO 0448)	42
Leafy vegetables (including Brassica leafy vegetables)	Lettuce, head/leaf (VL 0482/VL0483)	43
	Mustard greens (VL 0485)	44
	Spinach (VL 0502)	45
Legume vegetables	Lima bean, young pods and/or immature beans(VP 0534)	46
	Snap bean, young pods (VP 4453)	47
Root and tuber vegetables	Carrot (VR 0577)	48
	Potato (VR 0589)	49
Herbs	Basil (HH 0722)	50
Dried herbs	Hops, dry (DH 1100)	51

Table 35 Residues of cyazofamid and CCIM in **grape** following foliar application.

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
GAP: Germany	8×(100)	12-14	21	--	--	--	--
GAP: USA	6×(80)	10-14	30	--	--	--	--
Kerman, CA (1999) USA *Thompson Seedless* 010222-C	8×(~100)	11-14	0	0.29, 0.31 (0.30)	0.010, 0.020 (0.015)	0.30, 0.34 (0.32)	RA-3058
			7	0.44, 0.42 (0.43)	0.030, 0.020 (0.025)	0.48, 0.45 (0.47)	
			14	0.36, 0.34 (0.35)	0.020, 0.020 (0.020)	0.39, 0.37 (0.38)	
			21	0.32, 0.16 (0.24)	0.020, 0.010 (0.015)	0.35, 0.17 (0.26)	
			28	0.16, 0.30 (0.23)	0.010, 0.020 (0.015)	0.17, 0.33 (0.25)	
Fresno, CA (1999) USA *Thompson Seedless* 010222-D	8×(~100)	10-14	21	0.080, 0.070 (0.075)	0.010, 0.010 (0.010)	0.095, 0.085 (0.090)	
Madera, CA (1999) USA *Thompson Seedless* 010222-E	8×(~100)	10-14	21	0.19, 0.16 (0.18)	0.010, 0.010 (0.010)	0.20, 0.17 (0.19)	
St. Gilles, Languedoc (1999) France *Carignan* PRE 99081 A06	8×(100)	11-13	0	0.12, 0.12 (0.12)	< 0.01, < 0.01 (< 0.010)	< 0.13, < 0.13 (< 0.13)	RA-3082
			7	0.10, 0.12 (0.11)	< 0.01, < 0.01 (< 0.010)	< 0.11, < 0.13 (< 0.12)	

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
			14	0.020, 0.030 (0.025)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.045 (< 0.040)	
			21	0.040, 0.040 (<u>0.040</u>)	< 0.01, < 0.01 (< 0.010)	< 0.055, < 0.055 (< *0.055*)	
			28	0.010, 0.010 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Rudesheim (1999) Germany *Riesling* 99/025-0	8×(100)	11-14	0	0.14, 0.13 (0.14)	< 0.01, < 0.01 (< 0.010)	< 0.15, < 0.14 (< 0.15)	RA-3083
			7	0.070, 0.080 (0.075)	< 0.01, < 0.01 (< 0.010)	< 0.085, < 0.095 (< 0.090)	
			14	0.040, 0.050 (0.045)	< 0.01, < 0.01 (< 0.010)	< 0.055, < 0.065 (< 0.060)	
			21	0.030, 0.040 (<u>0.035</u>)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.055 (< *0.050*)	
			28	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	
Rudesheim (1999) Germany *Riesling* 99/026-0	8×(100)	11-14	21	0.030, 0.040 (0.035)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.055 (< 0.050)	
Nogent L'Abbesse, Champagne-Ardenne (1999) France *Chardonnay* EA990162FR01	9×(100)	11-13	0	0.22, 0.27 (0.25)	< 0.01, < 0.01 (< 0.010)	< 0.23, < 0.28 (< 0.26)	RA-3086
			7	0.11, 0.13 (0.12)	< 0.01, < 0.01 (< 0.010)	< 0.12, < 0.14 (< 0.13)	
			14	0.090, 0.11 (0.10)	< 0.01, < 0.01 (< 0.010)	< 0.10, < 0.12 (< 0.11)	
			21	0.090, 0.090 (<u>0.090</u>)	< 0.01, < 0.01 (< 0.010)	< 0.10, < 0.10 (< *0.10*)	
			28	0.060, 0.050 (0.055)	< 0.01, < 0.01 (< 0.010)	< 0.075, < 0.065 (< 0.070)	
Fumane, Verona (1999) Italy *Rondinella* EA990162IT01	8×(100)	11-13	0	0.69, 0.78 (0.74)	0.010, 0.010 (0.010)	0.70, 0.79 (0.75)	
			7	0.71, 0.93 (0.82)	< 0.01, < 0.01 (< 0.010)	< 0.72, < 0.94 (< 0.83)	
			14	0.41, 0.41 (0.41)	0.010, 0.010 (0.010)	0.42, 0.42 (0.42)	
			22	0.69, 0.62 (<u>0.66</u>)	0.010, 0.010 (0.010)	**0.70**, 0.63 (*0.67*)	
			28	0.43, 0.51 (0.47)	< 0.01, < 0.01 (< 0.010)	< 0.44, < 0.52 (< 0.48)	
San Maria della Versa (1999) Italy *Barbera* EA990162IT02	9×(100)	11-14	21	0.02, 0.03, 0.03, 0.03 (<u>0.03</u>)	< 0.01, < 0.01, < 0.01, < 0.01 (< 0.01)	< 0.035, < 0.045, < 0.045, < 0.045 (< *0.042*)	
Los Ruices, Valencia (1999) Spain *Bobal* 99069-F/G	8×(87.5)	11-13	21	0.010, 0.010 (<u>0.010</u>)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	RA-3084
Sobreiros-Alenquer, Estremadura (1999) Portugal *Santarem* P99004R	8×(75)	11-12	21	0.050, 0.050, 0.070, 0.070 (<u>0.060</u>)	< 0.01, < 0.01, < 0.01, < 0.01 (< 0.010)	< 0.065, < 0.065, < 0.085, < 0.085 (< *0.075*)	RA-3085

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
Lujan de Cuyo, Mendoza (2001) Argentina *Emperor* MDG-011-01	8×(~100)	10-16	21	0.33, 0.35 (0.34)	0.020, 0.020 (0.020)	0.36, 0.38 (0.37)	RA-3091
Los Mochis, Sinaloa (2001) Mexico *Superior* MDG-011-02	8×(~100)	11-13	21	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 36 Residues of cyazofamid and CCIM in broccoli following foliar application in the USA (Study RA-3123)

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
GAP: USA [Brassica (cole) leafy vegetables]	1 soil at plant (753) + 5 foliar (80)	7-10	0	--	--	--
Salinas, CA (2006) *Everest* 09717.06-CA*38 [b c]	132 soil + 5×(~82) foliar	55, 6-7	0	0.91, 0.76 (0.84)	< 0.01, < 0.01 (< 0.010)	< 0.**92**, < 0.77 (< *0.85*)
Salinas, CA (2006) *Marathon* 09717.06-CA*39 [b c]	132 soil + 5×(~80) foliar	48, 7-8	0	0.41, 0.33 (0.37)	< 0.01, < 0.01 (< 0.010)	< 0.42, < 0.34 (< *0.38*)
Holtville, CA (2006) *Heritage* 09717.06-CA40 [d]	130 soil + 6×(~81) foliar	58, 6-8	0	0.26, 0.19 (0.23)	< 0.01, < 0.01 (< 0.010)	< 0.27, < 0.20 (< *0.24*)
Holtville, CA (2006) *Triathalon* 09717.06-CA41 [d]	128 soil + 5×(~83) foliar	65, 7-8	0	0.28, 0.39 (0.34)	< 0.01, < 0.01 (< 0.010)	< 0.29, < 0.40 (< *0.35*)
Aurora, OR (2006) *General* 09717.06-OR27 [b]	132 soil + 6×(~81) foliar	19, 6-8	0	0.47, 0.45 (0.46)	< 0.01, < 0.01 (< 0.010)	< 0.48, < 0.46 (< *0.47*)
Weslaco, TX (2006) *Gypsy* 09717.06-TX*13 [b]	132 soil + 5×(~83) foliar	64, 6-8	0	0.18, 0.27 (0.23)	< 0.01, < 0.01 (< 0.010)	< 0.19, < 0.28 (< *0.24*)

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

[b] Samples were cut in the field.

[c] Final application and harvest differed between these trials by 53 days.

[d] Final application and harvest differed between these trials by 0 days.

Table 37 Residues of cyazofamid and CCIM in **cabbage** (with wrapper leaves) following foliar application in the USA (Study RA-3124)

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
GAP: USA [Brassica (cole) leafy vegetables]	1 soil at plant (753) + 5 foliar (80)	7-10	0	--	--	--
Salinas, CA (2006) *Charmant* 09082.06-CA*42 [b]	132 soil + 5×(~82) foliar	62, 6-8	0	0.25, 0.25 (0.25)	< 0.01, < 0.01 (< 0.010)	< 0.26, < 0.26 (< *0.26*)
Brighton, CO (2006) *Rocket*	132 soil + 5×(~82) foliar	36, 6-7	0	0.30, 0.29 (0.30)	< 0.01, < 0.01 (< 0.010)	< 0.31, < 0.30 (< *0.31*)

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
09082.06-CO05 [b]						
Citra, FL (2006) *Bravo* 09082.06-FL17 [b]	132 soil + 5×(~85) foliar	42, 7	0	0.61, 0.50 (<u>0.56</u>)	0.016, 0.012 (0.014)	0.63, 0.52 (*0.58*)
Salisbury, MD (2006) *Prima* 09082.06-MD21 [b]	132 soil + 5×(~81) foliar	31, 6-8	0	0.87, 0.63 (<u>0.75</u>)	0.025, 0.020 (0.023)	**0.91**, 0.66 (*0.78*)
Bridgeton, NJ (2006) *Wisconsin Golden Acre* 09082.06-NJ08 [b]	132 soil + 5×(~78) foliar	31, 6-8	0	0.40, 0.16 (<u>0.28</u>)	0.013, < 0.01 (0.012)	0.42, < 0.17 (< *0.30*)
Freeville, NY (2006) *Bobcat* 09082.06-NY07 [b]	132 soil + 6×(~77) foliar	77, 6-7	0	0.22, 0.17 (<u>0.20</u>)	< 0.01, < 0.01 (< 0.010)	< 0.23, < 0.18 (< *0.21*)
Charleston, SC (2006) *Copenhagen* 09082.06-SC*05 [b]	133 soil + 5×(~80) foliar	63, 7-8	0	0.16, 0.14 (<u>0.15</u>)	< 0.01, < 0.01 (< 0.010)	< 0.17, < 0.15 (< *0.16*)
Weslaco, TX (2006) *Blue Vantage* 09082.06-TX*14 [b]	132 soil + 5×(~82) foliar	78, 6-7	0	0.33, 0.31 (<u>0.32</u>)	< 0.01, < 0.01 (< 0.010)	< 0.34, < 0.32 (< *0.33*)
Arlington, WI (2006) *Blue Vantage* 09082.06-WI10 [b]	135 soil + 5×(~79) foliar	60, 6-8	0	0.12, 0.13 (<u>0.13</u>)	< 0.01, < 0.01 (< 0.010)	< 0.13, < 0.14 (< *0.14*)

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

[b] Samples were cut in the field.

Table 38 Residues of cyazofamid and CCIM in **cucumber** following foliar application in the USA

Location (Year) *Variety* Site ID [Study ID]	Application s # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
GAP: USA [Cucurbit vegetables]	6×(80)	7-10	0	--	--	--	--
Cary, NC (1999) *Poinsett* B	6×(~81)	2-12	0	0.020, 0.010 (0.015)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.025 (< 0.030)	RA-3067
			1	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			3	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Pelham, GA (1999) *Thunder* E	6×(~81)	7	7	0.030, 0.040 (0.035)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.055 (< 0.050)	
Jupiter, FL (1999) *Meteor* G	6×(~80)	7	7	0.020, < 0.01 (0.015)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.025 (< 0.030)	
Macon, MO (1999) *Long Green* H	6×(~82)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Arkansaw, WI (1999) *Lucky Strike* *Hybrid* J	6×(~80)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Eakly, OK	6×(~81)	7	7	< 0.01, < 0.01	< 0.01, < 0.01	< 0.025, < 0.025	

Location (Year) *Variety* Site ID [Study ID]	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
(1999) *Straight Eight* L				(< 0.010)	(< 0.010)	(< 0.025)	
Cotton, GA (2000) *Cross Country (Pickling)* 3	6×(~45)	6-8	0	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	RA-3090
Hobe Sound, FL (2000) *Speedway* 5	6×(~82)	7	0	0.020, 0.020 (0.020)	0.010, 0.010 (0.010)	0.035, 0.035 (*0.035*)	
Arkansaw, WI (2001) *Hybrid Eureka* 7	6×(~80)	6-8	0	0.010, < 0.01 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Clarence, MO (2001) *Bush Champion* 9	6×(~79)	6-8	0	0.030, 0.020 (0.025)	< 0.01, < 0.01 (< 0.010)	**< 0.045**, < 0.035 (< *0.040*)	
Eakly, OK (2001) *Boston Pickling* 10	6×(~78)	6-7	0	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< *0.035*)	

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 39 Residues of cyazofamid and CCIM in **summer squash** following foliar application in the USA

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
GAP: USA [Cucurbit vegetables]	6×(80)	7-10	0	--	--	--	--
North Rose, NY (1999) *Zucchini Select* A	6×(~80)	7	0	0.020, 0.030 (0.025)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.045 (< *0.040*)	RA-3067
			1	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	
			3	0.010, 0.010 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Cary, NC (1999) *Early Prolific Straightneck* D	6×(~80)	7	7	0.010, < 0.01 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Chipley, FL (1999) *Prelude II Hybrid* F	6×(~78)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Theilman, MN (1999) *Monet, Yellow Straightneck* I	6×(~79)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Porterville, CA	6×(~79)	7	7	< 0.01, 0.010 (0.010)	< 0.01, < 0.01	< 0.025,	

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
(1999) *Peter Pan* P					(< 0.010)	< 0.025 (< 0.025)	
Rose Hill, NC (2001) *Early Prolific Straightneck* 1	6×(~79)	6-8	0	0.030, 0.020 (<u>0.025</u>)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.035 (< *0.040*)	RA-3090
Quincy, FL (2000) *Yellow Crook Neck* 4	78 + 5×(~45)	6-7	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Arkansaw, WI (2001) *Hybrid Monet* 6	6×(~80)	6-8	0	0.040, 0.040 (<u>0.040</u>)	< 0.01, < 0.01 (< 0.010)	< 0.055, < 0.055 (< *0.055*)	
Porterville, CA (2001) *Peter Pan* 13	6×(~81)	6-8	0	0.050, 0.030 (<u>0.040</u>)	< 0.01, < 0.01 (< 0.010)	**< 0.065**, < 0.045 (< *0.055*)	

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 40 Residues of cyazofamid and CCIM in **muskmelon** following foliar application in the USA

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
GAP: USA [Cucurbit vegetables]	6×(80)	7-10	0	--	--	--	--
Cary, NC (1999) *Hales Best Jumbo* C [b]	6×(~81)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	RA-3067
Arkansaw, WI (1999) *Cantaloupe Hybrid Pulsar* K [b]	6×(~80)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Eakly, OK (1999) *Tesoro* M [b]	6×(~79)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
San Luis Obispo, CA (1999) *Gold Master* N	6×(~81)	7-8	7	0.010, 0.020 (0.015)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.035 (< 0.030)	
Kerman, CA (1999) *Hales Best Jumbo* O	6×(~80)	7	7	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	
Visalia, CA (1999) *Hales Best Jumbo* Q	6×(~78)	7	0	0.030, 0.030 (<u>0.030</u>)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.045 (< *0.045*)	
			1	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	
			3	0.010, < 0.01 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Rose Hill, NC (2001) *Hales Best Jumbo*	6×(~81)	7	0	0.060, 0.070 (<u>0.065</u>)	< 0.01, 0.010 (0.010)	< 0.075, **0.085** (< *0.080*)	RA-3090

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
2							
Arkansaw, WI (2001) *Hybrid Primo* 8 [b]	6×(~81)	7	0	0.030, 0.030 (0.030)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.045 (< *0.045*)	
Eakly, OK (2001) *Tesoro* 11 [b]	6×(~79)	6-7	0	0.030, 0.010 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.025 (< *0.035*)	
Fresno, CA (2001) *Top Mark Cantaloupe* 12	6×(~80)	7	0	0.010, 0.020 (0.015)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.035 (< *0.030*)	
Holtville, CA (2000) *IMPAC Cantaloupe* 14	6×(~81)	5-8	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

[b] Samples were cut in the field.

Table 41 Residues of cyazofamid and CCIM in **peppers** following foliar application in the USA (Study RA-3101)

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
GAP: USA [Fruiting vegetables]	6×(80)	7-10	0	--	--	--
Sweet Peppers						
Goldsboro, NC (2006) *Heritage* 01	6×(~79)	7	0	0.037, 0.038 (0.038)	< 0.01, < 0.01 (< 0.010)	< 0.052, < 0.053 (< *0.052*)
Jennings, FL (2006) *Aristotle* 02	6×(~79)	7	0	0.055, 0.060 (0.058)	< 0.01, < 0.01 (< 0.010)	< 0.070, < 0.075 (< *0.072*)
Northwood, ND (2006) *Lady Bell* 03	6×(~78)	6-8	0	0.079, 0.065 (0.072)	< 0.01, < 0.01 (< 0.010)	< 0.094, < 0.080 (< *0.087*)
			1	0.073, 0.030 (0.052)	< 0.01, < 0.01 (< 0.010)	< 0.088, < 0.045 (< 0.066)
			3	0.033, 0.027 (0.030)	< 0.01, < 0.01 (< 0.010)	< 0.048, < 0.042 (< 0.045)
			7	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)
Hinton, OK (2006) *California Wonder* 05	6×(~79)	7-8	0	0.071, 0.12 (0.098)	< 0.01, < 0.01 (< 0.010)	< 0.086, < 0.13 (< *0.11*)
Fresno, CA (2006) *Taurus* 07	6×(~80)	7	0	0.048, 0.062 (0.055)	< 0.01, < 0.01 (< 0.010)	< 0.063, < 0.077 (< *0.070*)
Madera, CA (2006) *Macabbi* 09	6×(~80)	6-8	0	0.16, 0.28 (0.22)	< 0.01, 0.014 (0.012)	< 0.17, **0.30** (< *0.24*)
Chili Peppers						
Northwood, ND (2006) *Long Red Cayenne* 04	6×(~78)	6-8	0	0.28, 0.21 (0.24)	0.017, < 0.01 (0.014)	0.31, < 0.22 (< *0.27*)
Dill City, OK (2006) *Anaheim* 06	6×(~78)	6-8	0	0.32, 0.30 (0.31)	0.014, 0.014 (0.014)	**0.34**, 0.32 (*0.33*)
Fresno, CA (2006) *Anaheim (Sonora)* 08	6×(~80)	7	0	0.25, 0.25 (0.25)	0.013, < 0.01 (0.012)	0.27, < 0.26 (< *0.27*)

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 42 Residues of cyazofamid and CCIM in **tomato** following foliar application in the USA

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
GAP: USA [Fruiting vegetables]	6×(80)	7-10	0	--	--	--	--
North Rose, NY (1999) *Mountain Pride* A	6×(~79)	7	7	0.020, 0.030 (0.025)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.045 (< 0.040)	RA-3065
Cary, NC (1999) *Better Boy* B	6×(~80)	2-12	0	0.050, 0.060 (0.055)	< 0.01, < 0.01 (< 0.010)	< 0.065, < 0.075 (< 0.070)	
			1	0.040, 0.030 (0.035)	< 0.01, < 0.01 (< 0.010)	< 0.055, < 0.045 (< 0.050)	
			3	0.030, 0.020 (0.025)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.035 (< 0.040)	
			7	0.020, < 0.01 (0.015)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.025 (< 0.030)	
Chipley, FL (1999) *Florida-47* C	6×(~81)	7	7	< 0.01, 0.010 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Jupiter, FL (1999) *Sanibel* D	6×(~82)	7	7	< 0.01, 0.010 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Orlando, FL (1999) *Florida-47* E	6×(~79)	7	7	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	
Proctor, AR (1999) *Better Boy* F	6×(~81)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Visalia, CA (1999) *Rio Grande* G	6×(~79)	7	0	0.020, 0.030 (0.025)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.045 (< *0.040*)	
			1	0.060, 0.060 (0.060)	< 0.01, < 0.01 (< 0.010)	< 0.075, < 0.075 (< 0.075)	
			3	0.060, 0.070 (0.065)	< 0.01, < 0.01 (< 0.010)	< 0.075, < 0.085 (< 0.080)	
			7	0.020, 0.010 (0.015)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.025 (< 0.030)	
Fresno, CA (1999) *Celebrity* H	6×(~80)	7	7	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	
Suisun, CA (1999) *Heinz 9281* I	6×(~79)	7	7	0.030, 0.020 (0.025)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.035 (< 0.040)	
Manteca, CA (1999) *HP-108* J	6×(~79)	7	7	0.020, 0.030 (0.025)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.045 (< 0.040)	
Woodland, CA (1999) *Rio Grande* K	6×(~76)	7	7	0.040, 0.060 (0.050)	< 0.01, < 0.01 (< 0.010)	< 0.055, < 0.075 (< 0.065)	
San Luis Obispo, CA (1999) *Shady Lady* L	6×(~79)	6-8	7	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	
King City, CA (1999) *Mountain Fresh* M	6×(~80)	7-8	7	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	
Huron, CA (1999) *Roma* N	6×(~80)	7	7	0.030, 0.030 (0.030)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.045 (< 0.045)	
Kerman, CA (1999) *Roma*	6×(~80)	7	7	0.020, 0.020 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.035, < 0.035 (< 0.035)	

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
O-1							
Porterville, CA (1999) *ACC* 55 *VF* P	6×(~79)	7	7	0.030, 0.030 (0.030)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.045 (< 0.045)	
Fresno, CA (1999) *Heinz 9382* Q	6×(~81)	6-8	7	0.040, 0.030 (0.035)	< 0.01, < 0.01 (< 0.010)	< 0.055, < 0.045 (< 0.050)	
Hughson, CA (1999) *Cannery Row* R	6×(~80)	7	7	0.060, 0.060 (0.060)	< 0.01, < 0.01 (< 0.010)	< 0.075, < 0.075 (< 0.075)	
San Luis Obispo, CA (2000) *Shady Lady* Plot 2	6×(~79)	6-8	0	0.050, 0.020 (0.035)	< 0.01, < 0.01 (< 0.010)	< 0.065, < 0.035 (< 0.050)	RA-3077
			7	0.030, 0.020 (0.025)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.035 (< 0.040)	
Plot 3	6×(~80)	6-7	0	0.050, 0.030 (0.040)	< 0.01, < 0.01 (< 0.010)	< 0.065, < 0.045 (< 0.055)	
			7	0.040, 0.060 (0.050)	< 0.01, < 0.01 (< 0.010)	< 0.055, < 0.075 (< *0.065*)	
North Rose, NY (2001) *Floradade* 1	6×(~80)	7	0	0.060, 0.040 (0.050)	0.010, 0.010 (0.010)	0.075, 0.055 (*0.065*)	RA-3089
Quincy, FL (2001) *Solo Set* 2	80 + 5×(~45)	6-7	0	0.010, 0.010 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Hobe Sound, FL (2001) *Sanibel* 3	6×(~82)	6-8	0	0.060, 0.090 (0.075)	< 0.01, < 0.01 (< 0.010)	< 0.075, < 0.10 (< *0.090*)	
Winter Garden, FL (2001) *Better Boy* 4	6×(~80)	6-7	0	0.070, 0.060 (0.065)	< 0.01, < 0.01 (< 0.010)	< 0.085, < 0.075 (< *0.080*)	
Proctor, AR (2001) *Better Bush* 5	6×(~80)	7	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Madera, CA (2001) *Celebrity* 6	6×(~81)	7	0	0.030, 0.030 (0.030)	< 0.01, < 0.01 (< 0.010)	< 0.045, < 0.045 (< *0.045*)	
Fresno, CA (2001) *Super Roma* 7	6×(~81)	7	0	0.050, 0.050 (0.050)	< 0.01, < 0.01 (< 0.010)	< 0.065, < 0.065 (< *0.065*)	
Hickman, CA (2001) *9775* 8	6×(~80)	7	0	0.16, 0.13 (0.15)	< 0.01, < 0.01 (< 0.010)	**< 0.17**, < 0.14 (< *0.16*)	
Dixon, CA (2001) *Brigade* 9	6×(~80)	6-8	0	0.050, 0.030 (0.040)	< 0.01, < 0.01 (< 0.010)	< 0.065, < 0.045 (< *0.055*)	
Fresno, CA (2001) *Shady Lady* 10	6×(~80)	7	0	0.13, 0.080 (0.11)	0.020, 0.010 (0.015)	0.16, 0.095 (*0.13*)	
Watsonville, CA (2001) *Sunbolt* 11	6×(~77)	6-8	0	0.050, 0.050 (0.050)	< 0.01, < 0.01 (< 0.010)	< 0.065, < 0.065 (< *0.065*)	
San Luis Obispo, CA (2001) *Shady Lady* 12	6×(~82)	7	0	0.030, 0.040 (0.035)	0.010, < 0.01 (0.010)	0.045, < 0.055 (< *0.050*)	
Porterville, CA (2001) *Ace 55* 13	6×(~80)	7	0	0.020, 0.040 (0.030)	< 0.01, 0.010 (0.010)	< 0.035, 0.055 (< *0.045*)	

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 43 Residues of cyazofamid and CCIM in **lettuce** following foliar application. In non-independent trial sets, final application and harvest occurred on the same day within a set

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
GAP: USA [Leafy greens]	6×(80)	7-10	0	--	--	--	
GAP: Canada [Lettuce]	6×(80)	7-14	0	--	--	--	
Head Lettuce (without wrapper leaves)							
Delhi, ON (2009) Canada *Great Lakes 659* AAFC08-053RA-690 [b]	7×(~80)	21, 15, 6-8	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	RA-3199
St. Jean-sir-Richelieu, QC (2009) Canada *Ithica* AAFC08-053RA-691 [b]	6×(~79)	19, 7-8	0	0.050, 0.070 (0.060)	< 0.01, < 0.01 (< 0.010)	< 0.065, < 0.085 (< 0.075)	
Agassiz, BC (2009) Canada *Mighty Joe MI* AAFC08-053RA-692	6×(~81)	18, 6-8	0	0.57, 0.54 (0.56)	0.013, 0.012 (0.013)	0.59, 0.56 (0.57)	
Head Lettuce (with wrapper leaves)							
Delhi, ON (2009) Canada *Great Lakes 659* AAFC08-053RA-690 [b]	7×(~80)	21, 15, 6-8	0	0.050,0.090 (0.070)	< 0.01, < 0.01 (< 0.010)	< 0.065, < 0.10 (< *0.085*)	RA-3199
St. Jean-sir-Richelieu, QC (2009) Canada *Ithica* AAFC08-053RA-691 [b]	6×(~79)	19, 7-8	0	0.41, 0.50 (0.46)	0.010, 0.010 (0.010)	0.42, 0.51 (*0.47*)	
Agassiz, BC (2009) Canada *Mighty Joe MI* AAFC08-053RA-692	6×(~81)	18, 6-8	0	1.3, 1.1 (1.2)	0.022, 0.021 (0.022)	1.3, 1.1 (*1.2*)	
Freeville, NY (2008) USA *Ponderosa* 10037.08-NY31	6×(~80)	6-7	0	0.78, 0.67 (0.73)	0.013, 0.012 (0.013)	0.80, 0.69 (*0.74*)	RA-3196
Citra, FL (2008) USA *Optima* 10037.08-FL49 [b]	6×(~81)	7	0	1.7, 1.3 (1.5)	0.029, 0.022 (0.026)	1.7, 1.3 (*1.5*)	
Salinas, CA (2008) USA *Samurai* 10037.08-CA*05 [b]	7×(~81)	42, 6-8	0	1.3, 1.4 (1.4)	0.015, 0.014 (0.015)	1.3, 1.4 (*1.4*)	
Salinas, CA (2008) USA *Gabilan* 10037.08-CA*04 [b]	7×(~81)	42, 6-8	0	1.7, 1.6 (1.7)	0.018, 0.015 (0.017)	1.7, 1.6 (*1.7*)	
Parlier, CA (2008) USA *Great Lakes 659* 10037.08-CA02 [b]	6×(~82)	72, 5-8	0	2.0, 1.6 (1.8)	0.011, < 0.01 (0.011)	**2.0**, <1.6 (<*1.8*)	
Las Cruces, NM (2008) USA *Salinas* 10037.08-NM11	7×(~80)	70, 6-8	0	0.24, 0.28 (0.26)	< 0.01, < 0.01 (< 0.010)	< 0.25, < 0.29 (< *0.27*)	
Holtville, CA (2008) USA *Deuce* 10037.08-CA03 [b]	6×(~80)	78, 6-8	0	0.60, 0.65 (0.63)	< 0.01, < 0.01 (< 0.010)	< 0.61, < 0.66 (< *0.64*)	
Holtville, CA (2008)	6×(~79)	78,	0	0.29, 0.43	< 0.01,	< 0.30, < 0.44	

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
USA *Quest* 10037.08-CA19 [b]		6-8		(0.36)	< 0.01 (< 0.010)	(< *0.37*)	
Ste-Clotilde, QC (2008) Canada *Estival* 10037.08-QC08 [b]	6×(~82)	14, 6-8	0	0.63, 0.62 (0.63)	0.017, 0.016 (0.017)	0.66, 0.64 (*0.65*)	
Harrow, ON (2008) Canada *Mighty Joe* 10037.08-ON19 [b]	6×(~80)	28, 6-7	0	0.19, 0.20 (0.20)	< 0.01, < 0.01 (< 0.010)	< 0.20, < 0.21 (< *0.21*)	
Leaf Lettuce							
Delhi, ON (2009) Canada *Simpson Elite* AAFC08-053RA-693	6×(~80)	6-8	0	3.0, 2.6 (2.8)	0.050, 0.037 (0.044)	3.1, 2.7 (*2.9*)	RA-3199
St. Jean-sir-Richelieu, QC (2009) Canada *Panther* (*Romaine*) AAFC08-053RA-694	6×(~81)	19, 7-8	0	0.48, 0.58 (0.53)	< 0.01, 0.011 (0.011)	< 0.49, 0.60 (< *0.55*)	
Salisbury, MD (2008) USA *Tropicana* 10037.08-MD23 [b]	6×(~80)	15, 7-8	0	0.83, 0.69 (0.76)	0.031, 0.022 (0.027)	0.88, 0.72 (*0.80*)	RA-3196
Citra, FL (2008) USA *Two Star* 10037.08-FL50 [b]	6×(~80)	7	0	1.9, 1.6 (1.8)	0.021, 0.021 (0.021)	1.9, 1.6 (*1.8*)	
Las Cruces, NM (2008) USA *Oakleaf* 10037.08-NM14	7×(~82)	36, 7-8	0	2.9, 3.3 (3.1)	0.036, 0.043 (0.040)	3.0, 3.4 (*3.2*)	
Las Cruces, NM (2008) USA *Salad Bowl* 10037.08-NM12	6×(~82)	51, 7-8	0	4.5, 3.5 (4.0)	0.045, 0.037 (0.041)	4.6, 3.6 (*4.1*)	
Holtville, CA (2008) USA *Greenleaf* 10037.08-CA07 [b]	6×(~80)	73, 7	0	1.2, 1.5 (1.4)	0.010, 0.013 (0.012)	1.2, 1.5 (*1.4*)	
Salinas, CA (2008) USA *Kremlin* 10037.08-CA*22	6×(~80)	26, 6-8	0	2.6, 2.5 (2.6)	0.039, 0.034 (0.037)	2.7, 2.6 (*2.6*)	
			4	1.5, 1.3 (1.4)	0.021, 0.019 (0.020)	1.5, 1.3 (1.4)	
			7	1.1, 1.2 (1.2)	0.015, 0.018 (0.017)	1.1, 1.2 (1.2)	
			15	0.42, 0.35 (0.39)	< 0.01, < 0.01 (< 0.010)	< 0.43, < 0.36 (< 0.40)	
			21	0.069, 0.15 (0.11)	< 0.01, < 0.01 (< 0.010)	< 0.084, < 0.16 (< 0.12)	
Salinas, CA (2008) USA *Pacifica* 10037.08-CA*21	6×(~82)	33, 6-8	0	2.9, 3.1 (3.0)	0.032, 0.034 (0.033)	2.9, 3.2 (*3.0*)	
Parlier, CA (2008) USA *Waldmann's Green* 10037.08-CA06	6×(~82)	27, 7	0	2.6, 2.8 (2.7)	0.040, 0.041 (0.041)	2.7, 2.9 (*2.8*)	

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
Jordan Station, ON (2008) Canada *Green Tower* 10037.08-ON20 [b]	6×(~83)	20, 6-7	0	1.0, 0.73 (0.87)	0.018, 0.013 (0.016)	1.0, 0.75 (*0.89*)	
Ste-Clotilde, QC (2008) Canada *Green Tower* 10037.08-QC07 [b]	6×(~84)	14, 6-8	0	0.91, 0.87 (0.89)	0.024, 0.025 (0.025)	0.95, 0.91 (*0.93*)	
Agassiz, BC (2008) Canada *Lasting Green 1* 10037.08-BC06 [b]	6×(~84)	28, 6-7	0	4.4, 4.5 (4.4)	0.041, 0.043 (0.042)	4.5, **4.6** (*4.5*)	

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

[b] Samples were cut in the field.

Table 44 Residues of cyazofamid and CCIM in **mustard greens** following soil + foliar application in the USA (Study RA-3125)

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
GAP: USA [Brassica (cole) leafy vegetables]	1 soil at plant (753) + 5 foliar (80)	7-10	0	--	--	--
Salinas, CA (2006) *Green Wave Mustard* 09083.06-CA*43	132 soil + 5×(~81) foliar	8, 6-7	0	2.9, 3.9 (3.4)	0.030, 0.040 (0.035)	2.9, 4.0 (*3.5*)
Riverside, CA (2006) *Florida Broadleaf* 09083.06-CA44	133 soil + 5×(~82) foliar	21, 6-8	0	3.0, 3.6 (3.3)	0.032, 0.032 (0.032)	3.0, 3.6 (*3.3*)
Citra, FL (2006) *Florida Broadleaf* 09083.06-FL18	131 soil + 5×(~87) foliar	7	0	6.0, 5.9 (6.0)	0.094, 0.090 (0.092)	6.1, 6.0 (*6.1*)
Tifton, GA (2006) *Green Wave* 09083.06-GA*06	132 soil + 5×(~84) foliar	15, 6-7	0	6.8, 5.8 (6.3)	0.056, 0.050 (0.053)	**6.9**, 5.9 (*6.4*)
Salisbury, MD (2006) *Green Wave* 09083.06-MD06	132 soil + 5×(~81) foliar	16, 6-8	0	5.5, 5.5 (5.5)	0.050, 0.050 (0.050)	5.6, 5.6 (*5.6*)
Bridgeton, NJ (2006) *Southern Curled* 09083.06-NJ09	132 soil + 5×(~79) foliar	7-9	0	3.0, 4.0 (3.5)	0.13, 0.17 (0.15)	3.2, 4.3 (*3.7*)
Jackson, TN (2006) *Florida Broadleaf* 09083.06-TN06	132 soil + 5×(~84) foliar	7-8	0	1.5, 1.3 (1.4)	0.11, 0.10 (0.11)	1.7, 1.4 (*1.6*)
Weslaco, TX (2006) *Florida Broadleaf* 09083.06-TX*15	132 soil + 5×(~81) foliar	20, 7	0	2.1, 1.7 (1.9)	0.038, 0.032 (0.035)	2.2, 1.7 (*2.0*)
			1	1.2, 1.4 (1.3)	0.019, 0.019 (0.019)	1.2, 1.4 (1.3)
			3	0.33, 0.38 (0.36)	< 0.01, 0.012 (0.011)	< 0.34, 0.40 (< 0.37)
			6	0.061, 0.066 (0.064)	< 0.01, < 0.01 (< 0.010)	< 0.076, < 0.081 (< 0.078)
			7	0.022, 0.024 (0.023)	< 0.01, < 0.01 (< 0.010)	< 0.037, < 0.039 (< 0.038)
Arlington, WI (2006) *Florida Broadleaf* 09083.06-WI11	137 soil + 5×(~80) foliar	6-8	0	3.8, 3.6 (3.7)	0.19, 0.17 (0.18)	4.1, 3.9 (*4.0*)

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 45 Residues of cyazofamid and CCIM in **spinach** following foliar application in the USA (Study RA-3126)

Location (Year) *Variety* Site ID [Study ID]	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
GAP: USA [Leafy greens]	6×(80)	7-10	0	--	--	--
Salinas, CA (2006) *Whale* F1 *06*/*Smooth leaf* 09265.06-CA*36 [b]	5×(~80)	6-7	0	3.9, 3.3 (<u>3.6</u>)	0.044, 0.045 (0.045)	4.0, 3.4 (*3.7*)
Salinas, CA (2006) *Space F1*/*Smooth leaf* 09265.06-CA*37 [b]	5×(~78)	6-8	0	3.0, 3.6 (<u>3.3</u>)	0.036, 0.032 (0.034)	3.1, 3.6 (*3.4*)
Fort Collins, CO (2006) *Bloomsdale Savoy* 09265.06-CO04	5×(~79)	6-7	0	2.4, 1.9 (<u>2.2</u>)	0.036, 0.032 (0.049)	2.5, 1.9 (*2.2*)
			1	2.5, 1.6 (2.1)	0.031, 0.023 (0.027)	2.5, 1.6 (2.1)
			3	1.2, 1.2 (1.2)	0.015, 0.012 (0.014)	1.2, 1.2 (1.2)
			4	0.90, 1.0 (0.95)	0.013, 0.016 (0.015)	0.92, 1.0 (0.97)
			6	0.69, 0.82 (0.76)	< 0.01, 0.011 (0.011)	< 0.70, 0.84 (< 0.77)
Bridgeton, NJ (2006) *Melody* 09265.06-NJ07	5×(~80)	6-7	0	6.3, 6.5 (<u>6.4</u>)	0.12, 0.12 (0.12)	6.5, **6.7** (*6.6*)
Freeville, NY (2006) *Tyee F1* 09265.06-NY06	5×(~80)	6-8	0	2.1, 1.9 (<u>2.0</u>)	0.031, 0.027 (0.029)	2.1, 1.9 (*2.0*)
Charleston, SC (2006) *Skooku*, *Hybrid* 09265.06-SC*04	5×(~82)	7-8	0	2.6, 3.1 (<u>2.9</u>)	0.081, 0.094 (0.088)	2.7, 3.2 (*3.0*)
Crossville, TN (2006) *Bloomsdale* 09265.06-TN07	5×(~82)	6-8	0	3.6, 3.2 (<u>3.4</u>)	0.10, 0.086 (0.093)	3.7, 3.3 (*3.5*)
Jackson, TN (2006) *Bloomsdale* 09265.06-TN08	5×(~82)	7	0	1.8, 2.2 (<u>2.0</u>)	0.088, 0.011 (0.050)	1.9, 2.2 (*2.1*)
Weslaco, TX (2006) *Spargo F1* 09265.06-TX11 [c]	5×(~81)	6-7	0	1.7, 1.4 (<u>1.6</u>)	0.064, 0.054 (0.059)	1.8, 1.5 (*1.6*)
Weslaco, TX (2006) *Samish* 09265.06-TX*12 [c]	5×(~79)	6-8	0	4.1, 5.1 (<u>4.6</u>)	0.13, 0.15 (0.14)	4.3, 5.3 (*4.8*)

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

[b] Final application and harvest differed between these trials by 20 days.

[c] Final application and harvest differed between these trials by 43 days.

Table 46 Residues of cyazofamid and CCIM in **lima bean** following foliar application in the USA (Study RA-3195)

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
GAP: USA [Beans (succulent podded and succulent shelled)	6×(80)	7-14	0	--	--	--
Irvine, CA (2009) *Fordhook 242* 09532.09-CA134	7×(~80)	6-7	0	< 0.01, < 0.01 (<u>< 0.010</u>)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)
Parlier, CA (2009) *Fordhook 242*	6×(~81)	6-8	0	< 0.01, < 0.01 (<u>< 0.010</u>)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
09532.09-CA135						(< *0.025*)
Kimberly, ID (2009) *M15 Lima* 09532.09-ID20	6×(~81)	6-8	0	0.033, 0.047 (0.040)	< 0.01, < 0.01 (< 0.010)	< 0.048, **< 0.062** (< *0.055*)
Salisbury, MD (2009) *Eastland* 09532.09-MD15	6×(~80)	6-8	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)
Salisbury, MD (2009) *Burpee Improved* 09532.09-MD24	6×(~80)	6-8	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)
Clinton, NC (2009) *Ford Hook* 09532.09-NC30	7×(~80)	6-7	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)
Clinton, NC (2009) *Thorogreen* 09532.09-NC31	7×(~84)	6-7	1	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)
Arlington, WI (2009) *Cypress* 09532.09-WI20	6×(~80)	7-8	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 47 Residues of cyazofamid and CCIM in **snap bean** following foliar application in the USA (Study RA-3198)

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
GAP: USA [Beans (succulent podded and succulent shelled)	6×(80)	7-14	0	--	--	--
Irvine, CA (2007) *Jade* 09094.07-CA10	7×(~82)	7-8	0	0.21, 0.19 (0.20)	< 0.01, < 0.01 (< 0.010)	< 0.22, < 0.20 (< *0.21*)
Salinas, CA (2007) *Tongue of Fire* 09094.07-CA*09	6×(~80)	6-8	0	0.056, 0.061 (0.059)	< 0.01, < 0.01 (< 0.010)	< 0.071, < 0.076 (< *0.073*)
Tifton, GA (2007) *Bluelake Bush 274* 09094.07-GA*11	6×(~80)	6-8	0	0.22, 0.17 (0.20)	< 0.01, < 0.01 (< 0.010)	**< 0.23**, < 0.18 (< *0.21*)
			2	0.22, 0.16 (0.19)	< 0.01, < 0.01 (< 0.010)	< 0.23, < 0.17 (< 0.20)
			7	0.16, 0.15 (0.16)	< 0.01, < 0.01 (< 0.010)	< 0.17, < 0.16 (< 0.17)
			12	0.15, 0.11 (0.13)	< 0.01, < 0.01 (< 0.010)	< 0.16, < 0.12 (< 0.14)
Salisbury, MD (2007) *Prorider* 09094.07-MD01	6×(~87)	6-9	0	0.094, 0.11 (0.10)	< 0.01, < 0.01 (< 0.010)	< 0.11, < 0.12 (< *0.12*)
Holt, MI (2007) *Bush Blue Lake 156* 09094.07-MI36	6×(~80)	7-8	0	0.10, 0.13 (0.12)	< 0.01, < 0.01 (< 0.010)	< 0.11, < 0.14 (< *0.13*)
Bridgeton, NJ (2007) *Strike* 09094.07-NJ05	6×(~80)	6-9	0	0.17, 0.20 (0.19)	< 0.01, < 0.01 (< 0.010)	< 0.18, < 0.21 (< *0.20*)
Moxee, WA (2007) *Jade* 09094.07-WA*01	6×(~80)	7	0	0.038, 0.053 (0.046)	< 0.01, < 0.01 (< 0.010)	< 0.053, < 0.068 (< *0.060*)
Arlington, WI (2007) *Hystyle* 09094.07-WI06	6×(~81)	6-8	0	0.012, 0.026 (0.019)	< 0.01, < 0.01 (< 0.010)	< 0.027, < 0.041 (< *0.034*)

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 48 Residues of cyazofamid and CCIM in **carrot** following foliar application (Study RA-3107)

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Storage time (days)
GAP: USA	5×(175)	14-21	14	--	--		--
Laingsburg, MI (2004) USA *Paramount S7540* 08522.04-MI09	5×(~175)	14-22	15	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	244
Laingsburg, MI (2004) USA *Paramount S7540* 08522.04-MI09 (a)	5×(~175)	14-22	15	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	244
Citra, FL (2004) USA *Indiana F1* 08522.04-FL25	5×(~175)	12-21	14	0.021, 0.023 (0.022)	< 0.01, < 0.01 (< 0.010)	< 0.036, < 0.038 (< 0.037)	352
Weslaco, TX (2004) USA *Six Pence F1* 08522.04-TX24	5×(~178)	13-35	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	373
			7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	366
			15	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	358
			20	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	353
			29	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	344
Tifton, GA (2004) USA *Nelson F1* 08522.04-GA*09	5×(~175)	16-92	14	0.027, 0.026 (0.027)	< 0.01, < 0.01 (< 0.010)	< 0.042, < 0.041 (< 0.041)	443
Moxee, WA (2004) USA *Enterprise F1* 08522.04-WA*04	5×(~178)	15-33	16	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	272
Moxee, WA (2004) USA *Enterprise F1* 08522.04-WA*04 (a)	5×(~175)	15-33	16	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	272
Salinas, CA (2004) USA *Mokum* 08522.04-CA*55	5×(~177)	7-21	14	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	270
Holtville, CA (2004) USA *Choctaw* 08522.04-CA52	5×(~175)	14-64	13	0.040, 0.027 (0.034)	< 0.01, < 0.01 (< 0.010)	< 0.055, < 0.042 (< 0.048)	91
Holtville, CA (2004) USA *Choctaw* 08522.04-CA52 (a)	5×(~175)	14-64	13	0.023, 0.035 (0.029)	< 0.01, < 0.01 (< 0.010)	< 0.038, < 0.050 (< 0.044)	91
Parlier, CA (2004) USA *Danvers Half Long 126* 08522.04-CA53	5×(~179)	12-34	0	0.028, 0.012 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.043, < 0.027 (< 0.035)	300
			8	0.044, 0.014	< 0.01, < 0.01	< 0.059, < 0.029	292

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Storage time (days)
				(0.029)	(< 0.010)	(< 0.044)	
			14	0.026, 0.018 (0.022)	< 0.01, < 0.01 (< 0.010)	< 0.041, < 0.033 (< 0.037)	286
			21	0.018, 0.021 (0.020)	< 0.01, < 0.01 (< 0.010)	< 0.033, < 0.036 (< 0.034)	279
			28	0.023, 0.020 (0.022)	< 0.01, < 0.01 (< 0.010)	< 0.038, < 0.035 (< 0.036)	272
Riverside, CA (2004) USA *SXC 3293* 08522.04-CA54	5×(~175)	13-73	14	0.033, **0.045** (0.039)	< 0.01, < 0.01 (< 0.010)	< 0.048, < 0.060 (< 0.054)	105
Riverside, CA (2004) USA *SXC 3293* 08522.04-CA54 (a)	5×(~177)	13-73	14	0.033, 0.032 (0.033)	< 0.01, < 0.01 (< 0.010)	< 0.048, < 0.047 (< 0.047)	105
Elm Creek, MB (2004) Canada *Kamanan* 08522.04-MB01	5×(~175)	14-50	14	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	241
Elm Creek, MB (2004) Canada *Cheyenne* 08522.04-MB02	5×(~175)	14-50	14	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	241
Hunter River, PE (2004) Canada *Sweetness* II 08522.04-PE01	5×(~175)	12-35	13	0.027, 0.030 (0.029)	< 0.01, < 0.01 (< 0.010)	< 0.042, < 0.045 (< 0.043)	237
Napierville, QC (2004) Canada *Sun 255* 08522.04-QC04	5×(~175)	13-55	15	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	239
Napierville, QC (2004) Canada *Sunrise* 08522.04-QC05	5×(~175)	13-55	15	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	239

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 49 Residues of cyazofamid and CCIM in potato following soil+foliar and/or foliar application

Location (Year) Country *Variety* Site ID [Study ID]	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
GAP: Brazil	6×(100)	7-10	7	--	--	--	--
GAP: Canada	6×(80)	7	7	--	--	--	--
GAP: USA [Tuberous and corm vegetables]	1 in-furrow at-planting (178) + 9×(80)	7-10	7	--	--	--	--
Eaton Township, PQ (2001) Canada *Shepody* 01	10×(~80)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	RA-3093
New Glasgow, PE (2001) Canada *Russett Burbank EII* 02	10×(~80)	6-8	8	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	

Location (Year) Country *Variety* Site ID [Study ID]	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
New Glasgow, PE (2001) Canada *Yukon Gold E4* 04	8×(~80) + 154	6	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			1	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			3	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Nictaux, NS (2001) Canada *Superior* 03	6×(~80) + 2×(~160)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Sheffild Mills, NS (2001) Canada *Atlantic* 05	10×(~80)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
St-Paul d'Abbotsford, PQ (2001) Canada *Chiefton* 06	10×(~80)	6-7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Medicine Hat, AB (2001) Canada *Russett Burbank* 07	10×(~81)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Abbotsford, BC (2001) Canada *Russett Burbank* 08	10×(~82)	6-9	7	< 0.01, 0.010 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Leduc, AB (2001) Canada *Yukon Gold* 09	10×(~80)	6-7	8	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Northwood, ND (2000) USA *Atlantic* Plot 2	10×(~82)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	RA-3075
Northwood, ND (2000) USA *Atlantic* Plot 3	10×(~82)	6-8	7	< 0.01, 0.010 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Ibipora, Parana (2000) Brazil *Bintje* Plot 1	9×(100)	7	0	< 0.05	n.r.	Not applicable	RA-3202A
			3	< 0.05	n.r.	Not applicable	
			7	< 0.05	n.r.	Not applicable	
			14	< 0.05	n.r.	Not applicable	
Ibipora, Parana (2000) Brazil *Bintje* Plot 2	9×(200)	7	0	< 0.05	n.r.	Not applicable	
			3	< 0.05	n.r.	Not	

Location (Year) Country *Variety* Site ID [Study ID]	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
						applicable	
			7	< 0.05	n.r.	Not applicable	
			14	< 0.05	n.r.	Not applicable	
Botucatu, Sao Paulo (2001) Brazil *Bintje* Plot 2	6×(100)	7	3	< 0.05	n.r.	Not applicable	
Botucatu, Sao Paulo (2001) Brazil *Bintje* Plot 3	6×(200)	7	3	< 0.05	n.r.	Not applicable	
Engenheiro Coelho, Sao Paulo (2000) Brazil *Bintje* Plot 2	6×(100)	5-8	3	< 0.05	n.r.	Not applicable	
Engenheiro Coelho, Sao Paulo (2000) Brazil Bintje Plot 3	6×(200)	5-8	3	< 0.05	n.r.	Not applicable	
North Rose, NY (1999) USA *Green Mountain* A	10×(~80)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	RA-3066
Orno, ME (1999) USA *FL-1533* B	10×(~80)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Cary, NC (1999) USA *Kennebec* C	10×(~80)	7-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Live Oak, FL (1999) USA *Red Pontiac* D	10×(~81)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Northwood, ND (1999) USA *Atlantic* E	10×(~80)	6-8	0	0.010, < 0.01 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			1	0.010, 0.010 (0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			3	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Fisher, MN (1999) USA *Red Norland* F	8×(~80) + 159	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
Arkansaw, WI (1999) USA *Russett Burbank* G	10×(~80)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Macon, MO (1999)	4×(~83) + 3×(~167)	4-10	7	< 0.01,	< 0.01,	< 0.025,	

Location (Year) Country *Variety* Site ID [Study ID]	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
USA *Irish Cobbler* H				< 0.01 (< 0.010)	< 0.01 (< 0.010)	< 0.025 (< 0.025)	
New Holland, OH (1999) USA *Landsglad* I	10×(~80)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Center, CO (1999) USA *Norkotah* J	10×(~80)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Kerman, CA (1999) USA *White Rose* K	10×(~80)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Rupert, ID (1999) USA *Russett Burbank* L	10×(~80)	6-8	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Minidoka, ID (1999) USA *Russett Burbank* M	10×(~80)	6-7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
American Falls, ID (1999) USA *Russett Burbank* N	10×(~79)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Payette, ID (1999) USA *Russett Burbank* O	10×(~80)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Hillsboro, OR (1999) USA *Russett Burbank* P	10×(~80)	7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Yakima, WA (1999) USA *Norkotah* Q	10×(~80)	5-8	0	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			1	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			3	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< 0.025)	
			7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Ephrata, WA (1999) USA *Russett Burbank* R2	10×(~80)	5-7	7	< 0.01, < 0.01 (< 0.010)	< 0.01, < 0.01 (< 0.010)	< 0.025, < 0.025 (< *0.025*)	
Ephrata, WA (1999) USA *Russett Burbank* R3	9×(~80) + 1×(~800)	5-7	3	< 0.01, 0.020 (0.011)	< 0.01, < 0.01 (0.010)	< 0.025, < 0.035 (< 0.030)	

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

n.r. = Not Reported

Table 50 Residues of cyazofamid and CCIM in **sweet basil** following foliar application in the USA (Study RA-3197)

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Fresh/ Dried	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
GAP: USA	9×(88)	7-10	0	--	--	--	--
Salisbury, MD (2009) *Genovese Compact Improved* 10118.09-MD04 Field Grown	9×(~90)	6-8	0	Fresh	2.3, 2.7 (2.5)	0.041, 0.046 (0.044)	2.4, 2.8 (*2.6*)
			4		1.1, 0.82 (0.96)	0.013, 0.013 (0.013)	1.1, 0.84 (0.98)
			7		0.32, 0.69 (0.51)	< 0.01, 0.012 (0.011)	< 0.33, 0.71 (< 0.52)
			10		0.52, 0.89 (0.71)	< 0.01, < 0.01 (< 0.010)	< 0.53, < 0.90 (< 0.72)
			14		0.13, 0.51 (0.32)	< 0.01, 0.014 (0.012)	< 0.14, 0.53 (< 0.34)
Clinton, NC (2009) *Genovese* 10118.09-NC16 Field Grown	9×(~87)	6-7	0	Fresh	10, 8.7 (9.4)	0.19, 0.18 (0.18)	**10**, 9.0 (*9.6*)
Salinas, CA (2009) *Italian Large Leaf* 10118.09-CA*82 Field Grown	9×(~90)	6-8	0	Fresh	3.2, 2.6 (2.9)	0.029, 0.025 (0.027)	3.2, 2.6 (*2.9*)
Maricopa, AZ (2009) *Lemon* 10118.09-AZ*01 Field Grown	9×(~87)	6-8	0	Fresh	6.9, 7.6 (7.2)	0.062, 0.071 (0.066)	7.0, 7.7 (*7.3*)

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Table 51 Residues of cyazofamid and CCIM in fresh and dried **hops** cones following foliar application

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
GAP: USA	6×(80)	7-10	3	--	--	--	--
Fresh Cones							
Wolnzach-Gebrontshausen, Pfaffenhofen (2011) Germany *Hallertauer Tradition* FHO11-RE01-DE01	6×(93-193)	8-14	0	0.47	< 0.01	< 0.48	RA-3190
			6	0.42	< 0.01	< 0.43	
			13	0.42	< 0.01	< 0.43	
Wolnzach-Gebrontshausen, Pfaffenhofen (2011) Germany *Perle* FHO11-RE01-DE02	6×(95-197)	9-14	0	0.49	< 0.01	< 0.50	
			7	0.11	< 0.01	< 0.12	
			14	0.050	< 0.01	< 0.065	
Wolnzach-Gebrontshausen, Pfaffenhofen (2011)	6×(88-204)	10-16	0	0.49	< 0.01	< 0.50	

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
Germany *Spalter Select* FHO11-RE01-DE03							
			7	0.23	< 0.01	< 0.24	
			14	0.21	< 0.01	< 0.22	
Wolnzach-Gebrontshausen, Pfaffenhofen (2011) Germany *Hallertauer Magnum* FHO11-RE01-DE04	6×(95-188)	11-15	0	0.23	< 0.01	< 0.24	
			7	0.040	< 0.01	< 0.055	
			14	0.050	< 0.01	< 0.065	
Wolnzach-Gebrontshausen, Pfaffenhofen (2012) Germany *Hallertauer Tradition* FHO12-RE01-DE01	6×(89-198)	12-16	21	1.02	< 0.01	<1.0	RA-3169
Wolnzach-Gebrontshausen, Pfaffenhofen (2012) Germany *Perle* FHO12-RE01-DE02	6×(83-195)	11-16	21	0.48	< 0.01	< 0.49	
Wolnzach-Gebrontshausen, Pfaffenhofen (2012) Germany *Spalter Select* FHO12-RE01-DE03	6×(97-193)	11-16	21	0.47	< 0.01	< 0.48	
Wolnzach-Gebrontshausen, Pfaffenhofen (2012) Germany *Hallertauer Magnum* FHO12-RE01-DE04	6×(86-192)	11-16	21	0.20	< 0.01	< 0.21	
Sondershausen, Kyffhauser (2013) Germany *Northern Brewer* FHO13-RE01-DE01	6×(96-201)	14	21	0.67	< 0.01	< 0.68	RA-3188
Golzern, Leipzig (2013) Germany *Nugget* FHO13-RE01-DE02	6×(96-184)	11-17	21	0.32	< 0.01	< 0.33	
Dried Cones							
Parma, ID (2007) USA *Nugget* ID01	6×(~79)	7-8	4	5.7, 6.9 (6.3)	0.13, 0.13 (0.13)	5.9, 7.1 (*6.5*)	RA-3127
Hubbard, OR (2007) USA *Nugget* OR04	6×(~82)	6-8	2	2.8, 3.6 (3.2)	0.21, 0.28 (0.24)	3.1, 4.0 (*3.6*)	
Benton County, WA (2007) USA *Nugget* WA02	6×(~83)	6-8	3	2.5, 2.5 (2.5)	0.42, 0.45 (0.44)	3.1, 3.2 (*3.1*)	
Norfolk, ON (2013) Canada *Nugget* A9823.13-ON12	6×(~82)	6-7	0	14	0.30	14	A9823
			4	7.6, 5.8, 7.7, **7.9** (7.2)	0.17, 0.22, 0.18, 0.12 (0.17)	7.9, 6.1, 8.0, **8.1** (7.5)	
			7	7.4	0.10	7.5	
			14	4.9	0.073	5.0	
Prosser, WA (2013) USA	6×(~82)	6-8	3	3.5, 3.4, 1.9, 2.9	0.19, 0.20, 0.16, 0.17	3.8, 3.7, 2.1, 3.2 (*3.2*)	

Location (Year) Country *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)	Reference
Tomahawk A9823.13-WA03				(2.9)	(0.18)		
Wolnzach-Gebrontshausen, Pfaffenhofen (2011) Germany *Hallertauer Tradition* FHO11-RE01-DE01	6×(93-193)	8-14	20	0.32	0.09	0.45	RA-3190
			27	0.26	0.12	0.44	
Wolnzach-Gebrontshausen, Pfaffenhofen (2011) Germany *Perle* FHO11-RE01-DE02	6×(95-197)	9-14	21	0.20	0.17	0.45	
			28	0.5	0.28	0.92	
Wolnzach-Gebrontshausen, Pfaffenhofen (2011) Germany *Spalter Select* FHO11-RE01-DE03	6×(88-204)	10-16	21	4.6	1.3	6.5	
			28	3.1	0.75	4.2	
Wolnzach-Gebrontshausen, Pfaffenhofen (2011) Germany *Hallertauer Magnum* FHO11-RE01-DE04	6×(95-188)	11-15	21	1.0	0.40	1.6	
			28	1.1	0.37	1.7	
Wolnzach-Gebrontshausen, Pfaffenhofen (2012) Germany *Hallertauer Tradition* FHO12-RE01-DE01	6×(89-198)	12-16	21	4.7	0.40	5.3	RA-3169
Wolnzach-Gebrontshausen, Pfaffenhofen (2012) Germany *Perle* FHO12-RE01-DE02	6×(83-195)	11-16	21	4.5	0.36	5.0	
Wolnzach-Gebrontshausen, Pfaffenhofen (2012) Germany *Spalter Select* FHO12-RE01-DE03	6×(97-193)	11-16	21	3.6	0.22	3.9	
Wolnzach-Gebrontshausen, Pfaffenhofen (2012) Germany *Hallertauer Magnum* FHO12-RE01-DE04	6×(86-192)	11-16	21	2.1	0.33	2.6	
Sondershausen, Kyffhauser (2013) Germany *Northern Brewer* FHO13-RE01-DE01	6×(96-201)	14	21	9.3	0.95	11	RA-3188
Golzern, Leipzig (2013) Germany *Nugget* FHO13-RE01-DE02	6×(96-184)	11-17	21	4.8	1.0	6.3	

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

FATE OF RESIDUES IN STORAGE AND PROCESSING

Nature of the residue during processing

High-temperature hydrolysis

High-temperature hydrolysis of cyazofamid was investigated by J. Bernal (2014, RA-3186). In the study, [^{14}C]cyazofamid (radiolabel position not specified) was spiked into buffered solutions, in triplicate, at a target concentration of 1 mg/L. The spiked solutions were put into conditions, in the dark, simulating pasteurisation (90 °C, pH 4, 20 min.); baking, brewing, boiling (100°C, pH 5, 60 min); and sterilisation (120 °C, pH 6, 20 min.). Prior to and after processing, an aliquot from each sample was collected and analysed by LSC for total radioactivity and by radio-HPLC for determination of hydrolysis products. Mass balance of radioactivity after processing was 102, 107, and 116% for 90 °C/pH4, 100 °C/pH5, and 120 °C/pH6, respectively. The correlation between temperature and mass balance was surmised in the study report to be due to better solubilisation after heating.

Radio-HPLC analysis showed a single peak prior to processing and two peaks after processing. The second peak was shown to be the cyazofamid metabolite CCIM. Under pasteurisation conditions, most of the cyazofamid was converted to CCIM; under the other two conditions tested, 100% of the test material converted to CCIM (Table 52).

Table 52 High-temperature hydrolysis radio-HPLC results for cyazofamid

	% of Radiolabel			
	Start		End	
Conditions	Cyazofamid	CCIM	Cyazofamid	CCIM
90°C, 20 minutes, pH 4	100	0	21	79
	100	0	18	82
	100	0	16	84
100°C, 60 minutes, pH 5	100	0	0	100
	100	0	0	100
	100	0	0	100
120°C, 20 minutes, pH 6	100	0	0	100
	100	0	0	100
	100	0	0	100

Residues after processing

The Meeting received data depicting residues of cyazofamid and CCIM in raw and processed commodities of basil, hops, grape, tomato, and potato.

For basil, fresh leaves and stem from field trial samples (see Table 50[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

) were dried according to "local commercial practices," with a recommended procedure of placing the sample in a drier, at 43–49 °C, for 24 hours. Stability of CCIM has not been demonstrated for the storage durations used in the study.

Table 53 Residues of cyazofamid and CCIM in **dried basil** following foliar applications in the USA (Study RA-3197)

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Fresh/ Dried	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
GAP: USA	9×(88)	7-10	0	--	--	--	--
Salisbury, MD (2009) *Genovese Compact Improved* 10118.09-MD04 Field Grown	9×(~90)	6-8	0	Dried	9.3, 10 (9.7)	1.0, 1.1 (1.1)	11, 12 (*11*)
Clinton, NC (2009) *Genovese*	9×(~87)	6-7	0	Dried	14, 12 (13)	11, 11 (11)	30, 28

Location (Year) *Variety* Site ID	Applications # × (rate) (g ai/ha)	RTIs (days)	DAT	Fresh/ Dried	Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg eq./kg)
10118.09-NC16 Field Grown							(*29*)
Salinas, CA (2009) *Italian Large Leaf* 10118.09-CA*82 Field Grown	9×(~90)	6-8	0	Dried	15, 14 (14)	10, 10 (10)	30, 29 (*29*)
Maricopa, AZ (2009) *Lemon* 10118.09-AZ*01 Field Grown	9×(~87)	6-8	0	Dried	36, 43 (40)	2.0, 2.2 (2.1)	39, **46** (*43*)
Citra, FL (2010) *Genova* 10118.09-FL29 Glasshouse Grown	9×(89)	7-8	0	Dried	14, 15 (14)	0.062, 0.069 (0.066)	14, 15 (*15*)
Parlier, CA (2009) *Aroma 2 OG* 10118.09-CA81 Glasshouse Grown	9×(~87)	7	0	Dried	15, 12 (14)	0.10, 0.072 (0.086)	15, 12 (*14*)

[a] Molecular weight ratio cyazofamid:CCIM = 1.49. Combined = Cyazofamid residue + (CCIM residue × 1.49)

Hop cones from plots treated six times at 96–201 g ai/ha were harvested, dried, and processed into beer. Dried cones were stored, frozen, for ca. 90 days prior to processing into beer. Residues of both cyazofamid and CCIM were reduced upon processing (Table 54).

In one of the grape studies conducted in the USA (RA-3058), grapes harvested from trials approximating the USA GAP were processed into raisins by sun drying for 37 days. Residues of cyazofamid and CCIM decreased during processing of grapes into raisins. Grapes/raisins from this study were stored frozen for a total of 249 days from sampling to analysis. For both cyazofamid and CCIM, the processing factor is <1, indicating that residues are reduced upon processing.

In grape trials conducted in France (RA-3082), Germany (RA-3083), and Italy (RA-3086), samples of treated grapes were processed into must and wine using simulated commercial practices suitable for each grape type and region. In the case of France, wine was divided into young wine and mature wine, and both must and wine were assayed before and after pasteurisation. In the trial from Germany, wine was divided into young and mature wine; processed products were not pasteurised. Frozen storage time for must and wine samples ranged from 237 to 412 days. For must, the processing factors for cyazofamid were rather variable, ranging from 0.21 to 2.3. There is a trend for cyazofamid to concentrate in must from red varieties but not in must from white varieties. NOTE: Method issue for raisins

Tomatoes for processing were obtained from a field trial which received five applications at the target rate and a final application at a 3X exaggerated rate (RA-3065). Samples were processed into paste and puree (RA-3065) using simulated commercial practices. Residues of cyazofamid did not show concentration in either paste or puree; however, residues of CCIM may concentrate in those commodities.

For potato, samples of tubers taken from a field-trial plot receiving nine applications at the target GAP rate and a tenth application at a 10× exaggerated rate were processed into wet peels, potato flakes, and potato chips (RA-3066). The processing followed simulated commercial practices. Samples were stored frozen from 95 to 422 days. Residues were <LOQ in all samples; therefore, meaningful processing factors could not be calculated.

Table 54 Residues of cyazofamid, CCIM, and combined (cyazofamid + CCIM as cyazofamid equivalents) in raw and processed commodities for estimation of long-term dietary exposure

	Residues (mg/kg)							
	Raw Commodity			Processed Commodity				
Processed Commodity	Cyaz.	CCIM	Combined	Cyaz.	CCIM	Combined	Proc. factor	Reference
Grape								
Dried (raisin)	0.44, 0.42	0.03, 0.02	0.48, 0.45 (0.47)	0.08, 0.07	0.02, 0.02	0.11, 0.10 (0.10)	0.22	RA-3058
Must	0.04, 0.05	< 0.01, < 0.01	0.06, 0.07 (0.06)	0.09, 0.09	< 0.01, < 0.01	0.10, 0.10 (0.10)	1.8	RA-3082
	0.03, 0.03	< 0.01, < 0.01	0.05, 0.05 (0.05)	0.07, 0.07	< 0.01, < 0.01	0.09, 0.09 (0.09)	1.9	
	0.11, 0.13	< 0.01, < 0.01	0.12, 0.14 (0.13)	0.04, 0.01	< 0.01, < 0.01	0.06, 0.03 (0.04)	0.30	
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	0.01, 0.01	< 0.01, < 0.01	0.03, 0.03 (0.03)	0.50	RA-3083
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	0.01, 0.01	0.01, 0.01	0.03, 0.03 (0.03)	0.50	RA-3083
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	0.05, 0.05	< 0.01, < 0.01	0.07, 0.07 (0.07)	1.3	RA-3086
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	0.02, 0.02	0.006, 0.007	0.03, 0.03 (0.03)	0.59	
Wine	0.04, 0.05	< 0.01, < 0.01	0.06, 0.07 (0.06)	< 0.01, < 0.01	0.02, 0.02	0.04, 0.04 (0.04)	0.66	RA-3082
	0.11, 0.13	< 0.01, < 0.01	0.12, 0.14 (0.13)	< 0.01, < 0.01	0.01, < 0.01	0.03, 0.03 (0.03)	0.18	
	0.03, 0.03	< 0.01, < 0.01	0.05, 0.05 (0.05)	< 0.01, < 0.01	0.01, 0.01	0.03, 0.03 (0.03)	0.55	
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	< 0.01, < 0.01	0.01, 0.01	0.03, 0.03 (0.03)	0.50	RA-3086
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	< 0.01, < 0.01	< 0.01, < 0.01	0.03, 0.03 (0.03)	0.50	RA-3083
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	< 0.01, < 0.01	0.01, 0.01	0.03, 0.03 (0.03)	0.50	
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	< 0.01, < 0.01	< 0.01, < 0.01	0.03, 0.03 (0.03)	0.50	
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	< 0.01, < 0.01	< 0.01, < 0.01	0.03, 0.03 (0.03)	0.50	
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	< 0.01, < 0.01	< 0.01, < 0.01	0.03, 0.03 (0.03)	0.50	
	0.03, 0.04	< 0.01, < 0.01	0.05, 0.06 (0.05)	< 0.01, < 0.01	< 0.01, < 0.01	0.03, 0.03 (0.03)	0.50	
Hops								
Beer	9.43, 7.35	1.7, 1.3	12, 9.3 (11)	< 0.01, < 0.01	< 0.01, < 0.01	0.03, 0.03 (0.03)	0.0023	RA-3188
Tomato								
Paste	0.04, 0.04	< 0.01, < 0.01	0.06, 0.06 (0.06)	< 0.01, < 0.01	0.02, 0.02	0.04, 0.04 (0.04)	0.72	RA-3065
Puree	0.04, 0.04	< 0.01, < 0.01	0.06, 0.06 (0.06)	< 0.01, < 0.01	0.01, 0.01	0.03, 0.03 (0.03)	0.45	

Table 55 Residues of cyazofamid, CCIM, and combined (cyazofamid as CCIM equivalents + CCIM) in raw and processed commodities for estimation of short-term dietary exposure

	Residues (mg/kg)					
	Raw Commodity			Processed Commodity		
Processed Commodity	Cyaz.	CCIM	Combined	CCIM	Processing factor	Reference
Grape						
Dried (raisin)	0.44, 0.42	0.03, 0.02	0.33, 0.30 (0.31)	0.02, 0.02 (0.02)	0.064	RA-3058
Must	0.04, 0.05	< 0.01, < 0.01	0.04, 0.04 (0.040)	< 0.01, < 0.01 (0.01)	0.25	RA-3082
	0.03, 0.03	< 0.01, < 0.01	0.03, 0.03 (0.030)	< 0.01, < 0.01 (0.01)	0.33	
	0.11, 0.13	< 0.01, < 0.01	0.08, 0.10 (0.091)	< 0.01, < 0.01 (0.01)	0.11	

	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	< 0.01, < 0.01 (0.01)	0.30	RA-3083
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	0.01, 0.01 (0.01)	0.30	RA-3083
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	< 0.01, < 0.01 (0.01)	0.30	RA-3086
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	0.006, 0.007 (0.01)	0.19	
Wine	0.04, 0.05	< 0.01, < 0.01	0.04, 0.04 (0.040)	0.02, 0.02 (0.02)	0.50	RA-3082
	0.11, 0.13	< 0.01, < 0.01	0.08, 0.10 (0.091)	0.01, < 0.01 (0.01)	0.11	
	0.03, 0.03	< 0.01, < 0.01	0.03, 0.03 (0.030)	0.01, 0.01 (0.01)	0.33	
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	0.01, 0.01 (0.01)	0.30	RA-3086
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	< 0.01, < 0.01 (0.01)	0.30	RA-3083
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	0.01, 0.01 (0.01)	0.30	
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	< 0.01, < 0.01 (0.01)	0.30	
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	< 0.01, < 0.01 (0.01)	0.30	
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	< 0.01, < 0.01 (0.01)	0.30	
	0.03, 0.04	< 0.01, < 0.01	0.03, 0.04 (0.033)	< 0.01, < 0.01 (0.01)	0.30	
Hops						
Beer	9.43, 7.35	1.7, 1.3	8.0, 6.2 (7.1)	< 0.01, < 0.01 (0.01)	0.0014	RA-3188
Tomato						
Paste	0.04, 0.04	< 0.01, < 0.01	0.04, 0.04 (0.037)	0.02, 0.02 (0.02)	0.54	RA-3065
Puree	0.04, 0.04	< 0.01, < 0.01	0.04, 0.04 (0.037)	0.01, 0.01 (0.01)	0.27	

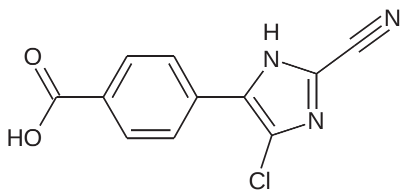
APPRAISAL

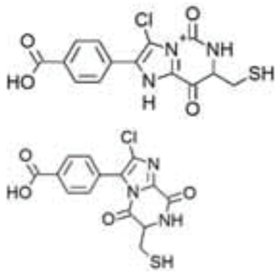
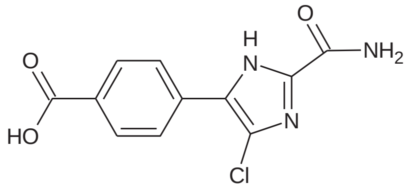
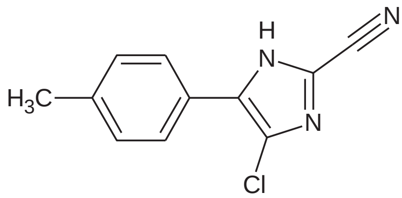
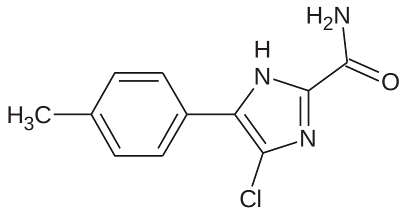
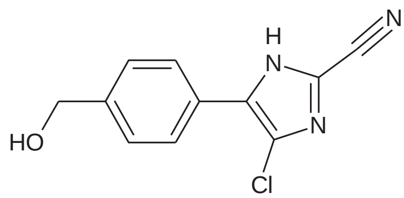
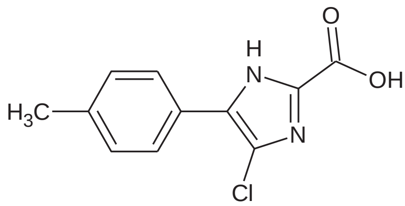
Cyazofamid (ISO common name, published) is a fungicide belonging to both the cyano-imidazole and sulphonamide classes of compounds. The biochemical mode of action is inhibition of all stages of fungal development. It was considered for the first time by the 2015 JMPR for toxicology and for residues.

The IUPAC name for cyazofamid is 4-chloro-2-cyano-*N*,*N*-dimethyl-5-*p*-tolylimidazole-1-sulfonamide and the CA name is 4-chloro-2-cyano-N,N-dimethyl-5-(4-methylphenyl)-1H-imidazole-1-sulfonamide, with registry number 120116-88-3.

Cyazofamid with ^{14}C radiolabelling in the benzene ring or in the imidazole ring was used in the metabolism and environmental fate studies. In this appraisal, these positions are referred to as the Bz and Im labels, respectively.

The following abbreviations, along with IUPAC names and structures, are used for the metabolites discussed in this appraisal:

CCBA	4-(4-chloro-2-cyanoimidazol-5-yl)benzoic acid	

CCBA (cysteine conjugates)		
CCBA-AM	4-(4-chloro-2-amidoimidazol-5-yl)benzoic acid	
CCIM	4-chloro-5-p-tolylimidazole-2-carbonitrile	
CCIM-AM	4-chloro-5-p-tolylimidazole-2-carboxamide	
CHCN	4-chloro-5-(4-hydroxymethylphenyl) imidazole-2-carbonitrile	
CTCA	4-chloro-5-p-tolylimidazole-2-carboxylic acid	

Plant metabolism

The Meeting received studies depicting the metabolism of cyazofamid in grapes, tomatoes, lettuce, and potatoes. All of the studies were conducted with cyazofamid which was radiolabelled, separately, in the benzene and imidazole rings.

Cyazofamid was applied five times, at ca. 100 g ai/ha at 21–25-day intervals, to grapevines growing in the field. Grapes were harvested 44 days after the last application (DALA). TRR in grapes was greater following treatment with Bz-labelled material (0.53 mg eq/kg, 0.89% of applied) than with Im-labelled material (0.31 mg eq/kg, 0.62% of applied). When processed into wine, radioactivity distributed primarily into the marc (wet pomace; 70% TRR, 3.7 mg eq/kg), with significantly lesser amounts in the vin de goutte (juice prior to pressing; 15% TRR, 0.21 mg eq/L) and vin de presse (juice after pressing; 10% TRR, 0.32 mg eq/L), indicating radioactivity may have been associated with surface residues. For grapes processed into juice, a similar trend was observed: 54% TRR (1.4mg eq/kg) in the marc and 33% TRR (0.3 mg eq/L) in the juice. Neither characterization nor identification of residues was reported in the study.

Metabolism of cyazofamid on tomatoes was investigated following treatment of field-grown plants with four foliar applications of cyazofamid at approximately 60, 95, 95, and 95 g ai/ha at 7-day intervals. In fruits harvested 1 DALA, TRR (surface rinses + juice + pulp) was 0.08 mg eq/kg from the Im treatment and 0.29 mg eq/kg from the Bz treatment. Of the total residue, the majority was contained in the surface rinse (54% and 83% for the Im and Bz labels, respectively). Of the radioactivity remaining in the fruits after rinsing, 71–81% TRR (ca. 0.033 mg eq/kg) was associated with the pulp and 13–29% TRR (ca. 5.5 mg eq/kg) was associated with the juice. Extraction of the pulp with, sequentially, hexane, ethyl acetate, and water released 75% of the radioactivity from the Bz-labelled sample and 90% from the Im-labelled sample. The principal residue from both labels was parent cyazofamid (ca. 78% TRR; 0.064 mg eq/kg Im, 0.22 mg/kg Bz), which is not unexpected given the short interval between application and harvest. The next-highest identified residue was CCIM (ca. 4–5% TRR, 0.004–0.13 mg/kg). A chromatographic fraction which was shown to consist primarily of radiolabelled sugars and citric acid accounted for 2.5–5.4% TRR (0.002–0.16 mg eq/kg), indicating breakdown of cyazofamid and incorporation into natural plant constituents.

Metabolism in lettuce was investigated following foliar treatment of glasshouse-grown plants. Three applications were made at a nominal rate of 100 g ai/ha on 14-day intervals. The test material was a mixture of cyazofamid labelled, separately, in the Im and Bz positions (in a 1:1 ratio). Lettuce leaves were harvested 14 DALA. Total radioactive residues were 0.85 mg eq/kg in the harvested leaves and 97% of the residues were extracted with ACN:H_2O (60:40, v/v with 0.1% acetic acid). Cyazofamid made up 89% of the TRR (0.76 mg/kg). No other compounds occurred at > 10% TRR. CCIM occurred at 3.7% TRR (0.031 mg/kg). Radioactivity in natural plant constituents occurred at 3.3% TRR (0.028 mg eq/kg). Based on analysis of the post-extraction solids (PES), those plant constituents consisted of starch and other water-soluble polysaccharides, protein, cellulose, and lignin.

Metabolism of cyazofamid was investigated in both field-grown and glasshouse-grown potatoes. In the field study, three foliar applications were made at rates of 100 or 400 g ai/ha. In the glasshouse study, five foliar applications were made at a rate of 400 g ai/ha. In both cases, applications were made on a 7-day interval and harvesting was done 7 DALA. In foliage, nearly all of the residue was cyazofamid. In tubers, the majority of the radioactivity was associated with the pulp. Sequential extractions of the pulp with ACN, ACN:H_2O (80:20, v/v), and ACN:H_2O (50:50, v/v) released 43 to 70% of the radioactivity, with the Bz-labelled samples generally being at the higher end of that range. In rinses of the tubers, the majority of the residue was cyazofamid (67–80% TRR, 0.0009–0.0018 mg/kg) and CCIM (14–20% TRR, 0.003 mg/kg); whereas in the tuber itself, the majority of the radioactivity was associated with starch (23–30% TRR, 0.005 mg/kg). Cyazofamid and CCIM were both < 5% TRR in tubers.

In plant metabolism studies with identification of residues, cyazofamid was the major residue in aerial portions of the plants and there was consistent demonstration of incorporation of radioactivity into natural plant components. The available data indicate that cyazofamid is translocated. The metabolite CCIM was consistently identified in these studies but never occurred at greater than 10% TRR.

Animal metabolism

The Meeting received studies elucidating the metabolism of cyazofamid in laboratory animals, lactating goats, and laying hens.

In rats, cyazofamid is well absorbed at doses relevant to dietary exposure, and rapidly metabolised, with the majority of excretion occurring via urine. In the plasma, there was no cyazofamid and the majority of radiolabel was CCIM. At 0.5 hours after a dose of [^{14}C-Bz]-

CCIM, all of the radiolabel in the stomach contents was CCIM, and most of the radiolabel in liver (76.5%) and plasma (67.9%) was CCIM. CCBA, the main metabolite seen in these tissues 0.5 hours after dosing with CCIM, was also found in the blood and liver from the animals dosed with cyazofamid. Concentrations in blood and liver were greater in the CCIM-dosed animals than that in cyazofamid treated animals, suggesting that CCIM was much more rapidly absorbed than cyazofamid.

In goats dosed for five consecutive days at approximately 32 mg/animal/day (Im) or 25 mg/animal/day (Bz; both equivalent to 10 ppm in the diet), overall recovery of radioactivity was ca. 60% of the administered dose (AD). Most of the recovered radioactivity was in urine and faeces, with only 0.22% (Im) or 0.18% (Bz) of the AD accounted for in tissues. Despite the low retention of radioactivity, sufficient residues were present to characterize and identify specific compounds in all tissues. Total radioactive residues (TRR) in urine and faeces appeared to plateau by Day 3 of dosing. In milk from Bz-treated goats, TRR remained near the limit of quantification (LOQ, 0.005 mg eq/kg) for the duration of the dosing period. TRR did not plateau during the dosing period for the Im label, rising steadily from 0.005 mg eq/kg to 0.10 mg eq/kg. Aside from this difference in milk, there was little difference in the behaviour of cyazofamid based on the position of the radiolabel. Solvent (ACN or ACN:H_2O) extracted 74% TRR, 90% TRR, and 100% TRR in muscle, milk, and fat, respectively, and sequential extraction with ACN and ACN:H_2O extracted 92% TRR from kidney. For liver, the same sequential solvents used for kidney extracted only ca. 50% TRR. An additional 45% TRR was released from liver, in total, using HCl, NaOH, and protease treatments of the post-extraction solids (PES). Liver and kidney contained the highest levels of radioactivity (ca. 0.1 mg eq/kg). In other tissues and in milk, radioactivity was approximately an order of magnitude lower than in liver/kidney. Cyazofamid residues were < 0.001 mg/kg (0.1–0.3% TRR) in all tissues. The principal residues in tissues and milk were CCBA (free or cysteine-conjugated), CCIM, and their amide analogs. Total CCBA-related residues ranged from 12% TRR (< 0.002 mg/kg; muscle) to 85% TRR (0.090 mg/kg; kidney), and total CCIM-related residues ranged from 5.3% TRR (0.006 mg/kg; kidney) to 39% TRR (< 0.003 mg/kg; fat); the highest concentrations of CCIM-related residues was in liver, at 0.016 mg/kg (14% TRR). The chromatographic system used in the goat metabolism studies was generally not able to separate CCBA and its cysteine conjugate, and those residues were typically the main residues in all tissues.

In hens dosed for five consecutive days at 1.1 mg/bird/day (10 ppm in the diet), total radioactive residues (TRR) in excreta accounted for approximately 85–90% of the dosed material, and < 0.1% of the AD was retained in tissues/eggs. Total radioactive residues were < 0.006 mg eq/kg in all samples of eggs, muscle, blood, fat, and skin. Residue plateau in eggs could not be assessed. Acetonitrile + ACN:H_2O extraction was not efficient at solubilizing residues in kidney (ca. 50% TRR) and liver (ca. 30% TRR); however, chemical and enzymatic treatment of the resulting PES was able to release the unextracted residues, resulting in 100% recovery of TRR. In kidney, the only identified compounds occurring at > 10% TRR were CCBA (solvent-extracted; 12% TRR, 0.0035–0.0064 mg/kg), and CHCN conjugates (not further identified; solvent-extracted; 17% TRR, 0.005–0.010 mg/kg and PES acid hydrolysate; 30–67% TRR, 0.003–0.010 mg/kg). Two unidentified fractions from the acid-hydrolysate treatment, CM-2 and CM-3, accounted for ca. 15% TRR (0.001 mg eq/kg) each. Residue profiles in liver were similar to those in kidney, consisting of CCBA (acid hydrolysate only, 14% TRR, 0.002 mg/kg), CHCN conjugates (solvent extract, 12% TRR, 0.011 mg eq/kg; acid hydrolysate, 47% TRR, 0.0073 mg eq/kg), and CM-2/CM-3 (acid hydrolysate, 13% TRR, 0.002 mg eq/kg).

Overall, the animal metabolism studies show that the majority (99+%) of the dosed radioactivity is excreted. In goat, the principal terminal residues are CCBA, CCIM, and their related conjugates and amides. In hens, the principal terminal residues are CCBA, CHCN, and their conjugates. Although CCBA is common to both species, the formation of that compound appears to occur through different pathways.

Environmental fate

Cyazofamid is prone to hydrolysis (25 °C, pH 4, 7, 9). The main product of hydrolysis at 25 °C at all pH levels was CCIM, which represented ca. 82% of the radioactivity at pHs of 4, 5, and 7, and 77% at pH 9. At pH 9, CCIM-AM was found at level of ca. 10% of the radioactivity. CCIM itself is stable to hydrolysis. Cyazofamid is also prone to photolysis in aqueous systems [DT_{50} of 30 minutes], forming CCIM and CCTS; both of which undergo further photolysis. In soil, photolysis does not appear to be a significant pathway for degradation since dissipation was similar in both irradiated and dark samples.

In an aerobic soil metabolism study, cyazofamid had DT_{50} estimates of ca. five days and DT_{90} estimates ranging from 16 to 25 days. The major residues following treatment with cyazofamid were CCIM (peak on Day 3, ca. 20% AD, ca 0.025 mg eq/kg), CCIM-AM (peak on Day 7, 13% AD, 0.016 mg eq/kg), and CTCA (peak ca. Day 20 at ca. 20% of the applied dose, 0.025 mg eq/kg). The aerobic soil metabolism study also showed an increase in unextracted residues over time (up to 64% at study termination) as well as production of $^{14}CO_2$ (14% of applied material by study termination). In unextracted residues, radioactivity was associated predominantly with fulvic acid as well as humin and humic acid.

In a study with confined rotational crops, bare soil was treated with 5× 100 g/ha (for both radiolabel positions on a 7-day interval). Crops of lettuce, carrot, and wheat were put into the treated soil at plant-back intervals (PBIs) of 31, 120, and 360 days. For all PBIs, residues in lettuce, carrot root, carrot tops (Days 120 and 360), and wheat grain were too low to allow residue identification/characterization. In carrot tops (Day 31 only), residues of CCBA (2.2% TRR), CCIM (10.4% TRR), CCIM-AM (39.5% TRR, 0.001 mg/kg), and cyazofamid (20.1% TRR, 0.003 mg/kg) were identified. In wheat chaff, forage and straw, residues were associated primarily with carbohydrates (0.01–0.20 mg eq/kg). Residues of cyazofamid and metabolites were ≤ 0.003 mg eq/kg in those matrices. No field rotational crop or field dissipation studies were provided. The Meeting concluded that the confined rotational crop study adequately reflects critical gap conditions and that residues are not expected in rotational crops following treatments according to the GAPs under consideration.

Overall, there are no indications that cyazofamid or any of its degradation products are expected to accumulate in soils. Significant dissipation pathways in an agricultural system appear to be hydrolysis and potentially photolysis. The DT_{90} estimates for cyazofamid in the aerobic soil metabolism study indicate that applications made more than ca. 1 month prior to harvest will not contribute significantly to the residue levels in harvested crops.

Methods of residue analysis

The Meeting received analytical methods for the analysis of cyazofamid and CCIM in plant matrices. Method validation recoveries were reported for grapes, cucurbit vegetables, root crops, Brassica vegetables, leafy vegetables, beans, peppers, and hops. Three methods for plant matrices underwent independent laboratory validation. No methods were submitted for analysis of animal materials or soil (aside from the techniques used in the studies with radiolabelled material).

In summary, extraction of residues in field trial samples was accomplished with ACN, ACN:H_2O (80:20, v/v), ACN:H_2O w/ 2% acetic acid (50:50, v/v), ACN:acetone (80:20, v/v) or acetone. Extracted residues were then generally cleaned up by partitioning into a non-polar organic solvent, with additional clean-up by solid-phase extraction (or in one case gel-permeation chromatography). Analysis of residues was by LC-MS/MS, HPLC-UV, or GC-NPD. Three methods underwent independent laboratory validation. For those methods, extraction of cyazofamid and CCIM is by ACN:acetone, H_2O followed by acetonitrile, or acetonitrile only. Clean-up varies across the three methods, consisting of traditional solid-phase extraction (C_{18}), dispersive solid-phase extraction (magnesium sulphate, sodium chloride, sodium citrate dibasic sesquihydrate, and sodium citrate tribasic dehydrate), or liquid/liquid partitioning (hexane and methylene chloride, sequentially) with Florisil® solid-phase extraction. For the validated methods, residue separation and quantitation is by LC-MS/MS in positive ionisation mode or by HPLC-UV (280 nm). For LC-MS/MS, evaluated ion transitions [M+H+] for quantification were

325.1 m/z→108.0 m/z for cyazofamid and 218.3 m/z→183.2 m/z for CCIM. Confirmation of cyazofamid is made using the same ion transitions, but with a cyano column on a gradient mobile phase. Confirmation of CCIM is based on a mass transition of 218.3 m/z→139.2 m/z. Based on results from other submitted studies, a confirmatory transition for cyazofamid is available (325.1 m/z→261.2 m/z). Method validation testing resulted in percent recoveries for cyazofamid ranging from 70 to 111% (except for raisins at 67%) and for CCIM ranging from 74 to 120% (except for potato chips at 68%). For both analytes in all matrices, relative standard deviations of recovery were less than 21%. An LOQ of 0.01 mg/kg was achieved for all matrices and analytes.

The solvent used for extraction is similar to that used in the metabolism studies with lettuce and potato (the first two extraction solvents in the tomato metabolism study were much less polar). On that basis, the methods are expected to have adequate extraction efficiency of incurred residues.

Testing of cyazofamid and CCIM through the FDA PAM multi-residue method protocols demonstrated that for most protocols, the test compounds showed poor sensitivity, poor recovery, and/or poor chromatography. An open-literature study[1] demonstrated good recovery of both cyazofamid (80% to 105%) and CCIM (75% to 99%) from fortified crop samples using the QuEChERS method, with relative standard deviations of ≤ 16%.

Analytical methods are available for analysis of cyazofamid and CCIM in plant commodities. Analytical methods for the analysis of cyazofamid residues in animal commodities were not provided.

Stability of residues in stored analytical samples

The Meeting received data indicating that residues of cyazofamid and CCIM are stable under frozen conditions as follows:

Matrix	Cyazofamid	CCIM
Grape (homogenized)	Up to 8 days	No Data
Grape (unhomogenized)	At least 365 days	No Data
Basil (fresh)	At least 284 days	Not stable [a] (less than 284 days)
Basil (dried)	At least 297 days	Not stable [a] (less than 297 days)
Hops cones	At least 509 days	At least 509 days
Cabbage	At least 860 days	At least 860 days
Tomato	Up to 365 days	At least 1093 days
Lettuce	At least 634 days	At least 634 days
Mustard greens	At least 977 days	At least 977 days
Spinach	At least 949 days	At least 949 days
Bean plants with pods	At least 889 days	At least 889 days
Bean pods with seeds	At least 887 days	At least 887 days
Been seeds without pods	At least 140 days	At least 140 days
Dry beans	At least 400 days	At least 400 days
Carrot	Not stable [a] (less than 374 days)	Not stable [a] (less than 374 days)
Potato	Up to 181 days	Up to 181 days

[a] Residues were measured only at the indicated storage period, and the amount remaining was < 70%. Basil and carrot samples were analysed on the same day as extraction.

Cyazofamid and CCIM were demonstrated to be stable in extracts of oilseed rape and dry beans for at least four days. Stability of these analytes in extracts from other matrices was not reported.

Definition of the residue

In plants, parent cyazofamid was the only compound to occur as a major residue in metabolism studies, and suitable methods are available for analysis. CCIM was consistently identified in

[1] Lee, H. Kim, E, Lee, JH. Sung, JH, Choi, H, and Kim, JH. 2014. Bull Environ Contam Toxicol 93(5):586-90. Analysis of cyazofamid and its metabolite in the environmental and crop samples using LC-MS/MS.

metabolism studies as a minor residue and occurred at levels that were typically at least five-fold lower than cyazofamid, and typically < 0.01 mg/kg, in supervised residue trials. The Meeting considered residues of cyazofamid in rotational crops and concluded that uptake of residues from soil into rotational crops will be insignificant. Cyazofamid is expected to degrade during the production of processed products; especially those in which heating and/or hydrolysis occurs, resulting in the formation of CCIM. Nevertheless, levels of CCIM in processed commodities are generally low.

Cyazofamid exhibited low acute oral toxicity, and there was an absence of developmental toxicity and any other toxicological effects that would be likely to be elicited by a single dose. The primary plant metabolite, CCIM, however, was more acutely toxic than the parent compound and resulted in clinical signs at all doses tested in acute toxicity studies. For long-term exposures, the toxicity of CCIM is adequately addressed by parent cyazofamid.

The Meeting concluded that the residue definition for enforcement of MRLs in plant commodities is the parent compound, cyazofamid, only. Furthermore, the Meeting concluded that the residue definition for assessing long-term dietary intake from plant commodities is the combined residues of cyazofamid and CCIM, expressed as cyazofamid. An ARfD is not necessary for cyazofamid; however, the current Meeting established an ARfD for CCIM, and the residue definition for assessing short-term dietary intake from plant commodities is CCIM.

Studies depicting the nature of the residues in animals show generally low transfer of residues to tissues, milk, and eggs. Metabolism studies indicate that of the amount retained, residues are expected to be highest in offal and lower by approximately an order of magnitude in other matrices. Cyazofamid was not detected in any livestock matrix. The metabolite CCBA (free and as cysteine conjugates) was consistently found as a major residue (> 10% TRR, ranging from 0.002 mg/kg to 0.09 mg/kg) in goat and hen commodities. Data from goat kidney indicate that the cysteine conjugates form the majority of the CCBA residues (separate free/conjugated residue data were not reported for other matrices). The Meeting was uncertain about the relative amounts of free and cysteine-conjugated CCBA in tissues other than liver and about the availability of reference standards for cysteine-conjugated CCBA. The Meeting agreed not to establish residue definitions for livestock commodities.

Definition of the residue for compliance with the MRLs for plant commodities: *Cyazofamid.*

Definition of the residue for long-term dietary intake from plant commodities: *Cyazofamid and CCIM, expressed as cyazofamid.*

Noting that the current meeting established an ARfD for CCIM (in the absence of an ARfD for cyazofamid), the definition of the residue for short-term dietary intake from plant commodities is *CCIM.*

Definition of the residue for compliance with the MRLs and for dietary intake for animal commodities: *Not defined.*

Results of supervised residue trials on crops

The Meeting received supervised residue trial data for grapes, basil, hops, broccoli, cabbage, cucumber, summer squash, muskmelon, peppers, tomatoes, head and leaf lettuce, mustard greens, spinach, snap beans, lima beans, carrots, and potatoes. The trials were conducted in the USA for all crops, as well as Argentina, Europe (north and south), and Mexico for grapes; Germany for hops; Canada for lettuces; and Brazil and Canada for potatoes. For basil, residue data reflect both field and glasshouse growing conditions. All residue results are supported by adequate method and storage stability data unless otherwise noted.

For field trials with cabbage, all cabbage heads were cut in the field in order to reduce the size/weight of the sample; for lettuce and muskmelon, some samples were cut in the field. A comparison of the residue levels in field-cut and uncut samples indicates that field-cutting did not compromise the quality of the residue data obtained from field-cut samples.

For estimating dietary intake, combined residues (cyazofamid + CCIM) were calculated by multiplying the individual sample results from field trials of CCIM by the molecular weight factor of 1.49 (cyazofamid molecular weight = 324.8, CCIM molecular weight = 217.7) and adding the result to the corresponding residue of cyazofamid. For residues below the LOQ, the residue was assumed to be at the LOQ for calculation purposes; the “less than” designation was retained only if both residues were below the LOQ. Examples are shown below:

Cyazofamid	CCIM	Combined (expressed to two significant figures)
0.5 mg/kg	0.06 mg/kg	0.5 mg/kg + (0.06 mg/kg × 1.49) = 0.59 mg/kg
0.5 mg/kg	< 0.01 mg/kg	0.5 mg/kg + (0.01 mg/kg × 1.49) = 0.51 mg/kg
< 0.01 mg/kg	0.06 mg/kg	0.01 mg/kg + (0.06 mg/kg × 1.49) = 0.099 mg/kg
< 0.01 mg/kg	< 0.01 mg/kg	< 0.01 mg/kg + (< 0.01 mg/kg × 1.49) = < 0.025 mg/kg

Grapes

In grapes, the critical GAP based on highest application rate and shortest PHI is from the registration in Germany (eight foliar applications at 0.1 kg ai/ha on a 12- to 14-day interval with a 21-day PHI). Only a single field trial is available from Germany; however, additional residue trials matching the critical GAP are available from France, Italy, Spain, and Portugal. The Meeting noted that in all of these trials, grapes were stored as whole berries and, therefore, the residue levels are supported by the available storage stability data.

Mean field trial residues of cyazofamid from independent field trials matching the critical GAP (n=7) were: 0.01, 0.03, 0.04, 0.04, 0.06, 0.09, and 0.66 mg/kg.

Based on those data, the Meeting estimated a maximum residue level for grapes of 1.5 mg/kg.

From the trials cited above, residues of CCIM were (n=7): < 0.01 (7) mg/kg. For assessing short-term dietary intake from grapes, the HR, from a single sample, is 0.01 mg/kg.

From the trials cited above, the combined residues of cyazofamid and CCIM, expressed as cyazofamid, were (n=7): 0.02, 0.04, 0.05, 0.06, 0.08, 0.1, and 0.67 mg/kg. For assessing long-term dietary intake from grapes, the STMR from that data set is 0.06 mg/kg.

Brassica (Cole or Cabbage) Vegetables, Head Cabbage, Flowerhead Brassicas

The critical GAP is from the registration of cyazofamid on the Brassica (Cole) leafy vegetables crop group in the USA (one soil application at 0.753 kg ai/ha followed by five foliar applications at 0.08 kg ai/ha on a 7-10-day interval with a zero-day PHI). Supervised residue trials matching this GAP are available from the USA.

Mean field trial residues of cyazofamid in broccoli from independent field trials matching the critical GAP (n=5) were: 0.23, 0.34, 0.37, 0.46, and 0.84 mg/kg.

Mean field trial residues of cyazofamid in cabbage (with wrapper leaves) from independent field trials matching the critical GAP (n=9) were: 0.13, 0.15, 0.20, 0.25, 0.28, 0.30, 0.32, 0.56, and 0.75 mg/kg.

Noting that the residue trials address crops in the Codex commodity designation Brassica (Cole or cabbage) vegetables, head cabbage, flowerhead Brassicas and that the median residues from each crop are within a 5-fold range, the Meeting determined that a group MRL is appropriate. The cyazofamid residue data across the test crops are not significantly different by the Kruskal-Wallis test; therefore, the Meeting grouped the data together and is estimating a group maximum residue level for Brassica (Cole or cabbage) vegetables, head cabbage, flowerhead Brassicas based on the following cyazofamid residue data set (n=14): 0.13, 0.15, 0.20, 0.23, 0.25, 0.28, 0.30, 0.32, 0.34, 0.37, 0.46, 0.56, 0.75, and 0.84 mg/kg.

Based on those data, the Meeting estimated a maximum residue level for Brassica (Cole or cabbage) vegetables, head cabbage, and flowerhead Brassicas of 1.5 mg/kg.

From the trials cited above, residues of CCIM were (n=14): < 0.01 (11), 0.012, 0.014, and 0.023 mg/kg. For assessing short-term dietary intake from Brassica (Cole or cabbage) vegetables, head cabbage, flowerhead Brassicas, the HR, from a single sample, is 0.025 mg/kg.

From the trials cited above, the combined residues of cyazofamid and CCIM, expressed as cyazofamid, were (n=14): 0.14, 0.16, 0.21, 0.24, 0.26, 0.3, 0.31, 0.33, 0.35, 0.38, 0.47, 0.58, 0.78, and 0.85 mg/kg. For assessing long-term dietary intake from Brassica (Cole or cabbage) vegetables, head cabbage, flowerhead Brassicas, the STMR from that data set is 0.31 mg/kg.

Fruiting vegetables, Cucurbits

The critical GAP is from the registration of cyazofamid on the cucurbit vegetables crop group in the USA (six foliar applications at 0.08 kg ai/ha on a 7–10-day interval with a zero-day PHI). Supervised residue trials matching this GAP are available from the USA.

Mean field trial residues of cyazofamid in cucumber from independent field trials matching the critical GAP (n=4) were: 0.01 and 0.02 (3) mg/kg.

Mean field trial residues of cyazofamid in summer squash from independent field trials matching the critical GAP (n=4) were: 0.02 (2) and 0.04 (2) mg/kg.

Mean field trial residues of cyazofamid in muskmelon from independent field trials matching the critical GAP (n=6) were: < 0.01, 0.02 (3), 0.03 (2), and 0.06 mg/kg.

Noting that the residue trials address crops in the Codex commodity designation Fruiting Vegetables, Cucurbits and that the median residues from each crop are within a 5-fold range, the Meeting determined that a group MRL is appropriate. The cyazofamid residue data across the test crops are not significantly different by the Kruskal-Wallis test; therefore, the Meeting grouped the data together and is estimating a group maximum residue level for Fruiting Vegetables, Cucurbits based on the following cyazofamid residue data set (n=14): < 0.01, 0.01, 0.02 (5), 0.03 (2), 0.04 (2), and 0.06 mg/kg..

Based on those data, the Meeting estimated a maximum residue level for Fruiting Vegetables, Cucurbits of 0.09 mg/kg.

From the trials cited above, residues of CCIM were (n=14): < 0.01 (12) and 0.01 (2) mg/kg. For assessing short-term dietary intake from Fruiting Vegetables, Cucurbits, the HR, from a single sample, is 0.01 mg/kg.

From the trials cited above, the combined residues of cyazofamid and CCIM, expressed as cyazofamid, were (n=14): 0.02 (2), 0.03, 0.04 (7), 0.04, 0.06 (2), and 0.08 mg/kg. For assessing long-term dietary intake from Fruiting Vegetables, Cucurbits, the STMR from that data set is 0.04 mg/kg.

Fruiting vegetables, other than Cucurbits (except Sweet Corn and Mushroom)

The critical GAP is from the registration of cyazofamid on the fruiting vegetables crop group in the USA (six foliar applications at 0.08 kg ai/ha on a 7–10-day interval with a zero-day PHI). Supervised residue trials matching this GAP are available from the USA.

Mean field trial residues of cyazofamid in peppers, sweet (including pimento or pimiento) from independent field trials matching the critical GAP (n=6) were: 0.038, 0.055, 0.058, 0.072, 0.098, and 0.22 mg/kg.

Mean field trial residues of cyazofamid in peppers, chili from independent field trials matching the critical GAP (n=3) were: 0.24, 0.25, and 0.31 mg/kg.

Mean field trial residues of cyazofamid in tomatoes from independent field trials matching the critical GAP (n=14) were: < 0.010, 0.025, 0.030 (2), 0.035, 0.040, 0.050 (4), 0.065, 0.075, 0.11, and 0.15 mg/kg.

Noting that the residue trials in the USA address crops in the Codex commodity designation Fruiting Vegetables, Other Than Cucurbits (except Sweet Corn and Mushrooms), the Meeting considered whether a group MRL is appropriate. Based on the five-fold difference in the median residue values, The Meeting concluded that a group recommendation is appropriate. Analysis of the data set by the Kruskal-Wallis test indicated that the residues are not from the same populations and should not be combined when estimating the maximum residue level. Of the crops in this category, field trials with chilli pepper resulted in the greatest median residue level and greatest overall single-sample residue; however, the number of trials on chilli pepper is insufficient for making a group recommendation and the Meeting decided to make recommendations for the individual crops.

The Meeting estimated a maximum residue levels for sweet peppers at 0.4 mg/kg, for chilli peppers at 0.8 mg/kg, and for tomato at 0.2 mg/kg. Furthermore, the Meeting extrapolated the tomato data to eggplant and estimated a maximum residue level for eggplant at 0.2 mg/kg.

From the trials cited above, residues of CCIM and their associated HRs (from single samples) for assessing short-term dietary intake were as follows:

Sweet pepper (n=5): < 0.01 (4) and 0.012 mg/kg [HR = 0.014 mg/kg]

Chili pepper (n=3): 0.012 and 0.014 (2) mg/kg [HR = 0.017 mg/kg]

Tomato (n=15): < 0.01 (13), 0.01, and 0.015 mg/kg [HR = 0.02 mg/kg]; and by extension,

Eggplant: [HR = 0.02 mg/kg].

From the trials cited above, the combined residues of cyazofamid and CCIM, expressed as cyazofamid, and their associated STMRs for assessing long-term dietary intake were as follows:

Sweet pepper (n=5): 0.05, 0.07, 0.07, 0.09, and 0.24 mg/kg [STMR = 0.072 mg/kg]

Chilli pepper (n=3): 0.27 (2) and 0.33 mg/kg [STMR = 0.027 mg/kg];

Tomato (n=15): 0.02 (2), 0.04 (3), 0.05, 0.06 (5), 0.08, 0.09, 0.13, and 0.16 mg/kg [STMR = 0.06 mg/kg]; and by extension, Eggplant: [STMR = 0.06 mg/kg].

Leafy Vegetables (Including Brassica Leafy Vegetables)

The critical GAPs are from the registration of cyazofamid on the leafy greens crop subgroup in the USA (six foliar applications at 0.08 kg ai/ha on a 7–10-day interval with a zero-day PHI) and *Brassica* (Cole) leafy vegetables crop group in the USA (for mustard greens; one soil application at 0.753 kg ai/ha followed by five foliar applications at 0.08 kg ai/ha on a 7–10-day interval with a zero-day PHI). Supervised residue trials matching this GAP are available from Canada (head lettuce only) and the USA.

Mean field trial residues of cyazofamid in head lettuce from independent field trials matching the critical GAP (n=11) were: 0.070, 0.20, 0.26, 0.46, 0.63 (2), 0.73, 1.2, 1.5, 1.7, and 1.8 mg/kg.

Mean field trial residues of cyazofamid in leaf lettuce from independent field trials matching the critical GAP (n=11) were: 0.53, 0.76, 0.87, 0.89, 1.4, 1.8, 2.7, 2.8, 3.0, 4.0, and 4.4 mg/kg.

Mean field trial residues of cyazofamid in mustard greens from independent field trials matching the critical GAP (n=9) were: 1.4, 1.9, 3.3, 3.4, 3.5, 3.7, 5.5, 6.0, and 6.3 mg/kg.

Mean field trial residues of cyazofamid in spinach from independent field trials matching the critical GAP (n=10) were: 1.6, 2.0 (2), 2.2, 2.9, 3.3, 3.4, 3.6, 4.6, and 6.4 mg/kg.

Noting that the residue trials address crops in the Codex commodity designation Leafy Vegetables, the Meeting considered whether a group MRL is appropriate. The differences in median residue values across all four crops is greater than five-fold, indicating that a crop group recommendation is not appropriate. As median residue values for head lettuce, leaf lettuce, and spinach are within a five-fold range, the Meeting decided to make a recommendation for leafy vegetables, except Brassica leafy vegetables and to use data from mustard greens to make a recommendation for Brassica leafy vegetables.

Analysis of the residue data for lettuces and spinach by Kruskal-Wallis indicates that the residues are not from the same population and should not be combined when estimating the maximum residue level. Of these crops, the data from spinach has the highest median and highest residue.

On the basis of the data from spinach, the Meeting estimated a maximum residue level for Leafy Vegetables, except Brassica Leafy Vegetables at 10 mg/kg.

From the trials cited above, residues of CCIM and their associated HRs (from single samples) for assessing short-term dietary intake were as follows:

Head lettuce (n=11): < 0.010 (4), 0.01, 0.011, 0.013, 0.017 (2), 0.022, and 0.026 mg/kg [HR = 0.029 mg/kg];

Leaf lettuce (n=11): 0.011, 0.012, 0.016, 0.021, 0.025, 0.027, 0.037, 0.041 (2), 0.042, and 0.044 mg/kg [HR = 0.05 mg/kg];

Spinach (n=10): 0.029, 0.034, 0.045, 0.049, 0.05, 0.059, 0.088, 0.093, 0.12, and 0.14 mg/kg [HR = 0.15 mg/kg].

From the trials cited above, the combined residues of cyazofamid and CCIM, expressed as cyazofamid, and their associated STMRs for assessing long-term dietary intake were as follows:

Head lettuce (n=11): 0.08, 0.21, 0.27, 0.47, 0.64, 0.65, 0.74, 1.2, 1.5, 1.7, and 1.8 mg/kg [STMR = 0.65 mg/kg]

Leaf lettuce (n=11): 0.55, 0.80, 0.89, 0.93, 1.4, 1.8, 2.8, 2.9, 3.0, 4.1, and 4.5 mg/kg [STMR = 1.8 mg/kg];

Spinach (n=10): 1.6, 2.0, 2.1, 2.2, 3.0, 3.4, 3.5, 3.7, 4.8, and 6.6 mg/kg [STMR = 3.2 mg/kg].

For estimating dietary intake of the combined residues of cyazofamid and CCIM from leafy vegetables, except Brassica leafy vegetables, the data from spinach provide the highest residue estimate, with an STMR of 3.2 mg/kg.

For Brassica leafy vegetables, the Meeting estimated a maximum residue level of 15 mg/kg based on the data from mustard greens.

Residues of CCIM were (n=9): 0.032, 0.035 (2), 0.05, 0.053, 0.092, 0.11, 0.15, and 0.18 mg/kg. For assessing short-term dietary intake from Brassica leafy vegetables, the HR, from a single sample, is 0.19 mg/kg.

Combined residues of cyazofamid and CCIM in Mustard Greens were (n=9): 1.6, 2.0, 3.3, 3.5, 3.7, 4.0, 5.6, 6.1, and 6.4 mg/kg. For assessing long-term dietary intake from Brassica leafy vegetables, the STMR from that data set is 3.7 mg/kg.

Beans and beans, shelled

The critical GAP is from the registration of cyazofamid on beans (succulent podded and succulent shelled) in the USA (six foliar applications at 0.08 kg ai/ha on a 7–14-day interval with a zero-day PHI). Supervised residue trials in lima beans matching this GAP are available from the USA.

Mean field trial residues of cyazofamid in lima beans from independent field trials matching the critical GAP (n=6) were: < 0.010 (5) and 0.040 mg/kg.

Mean field trial residues of cyazofamid in snap beans from independent field trials matching the critical GAP (n=8) were: 0.018, 0.046, 0.059, 0.10, 0.12, 0.19, and 0.20 (2) mg/kg.

Noting that the residue trials in the USA address crops in the Codex commodity designation Legume Vegetables, the Meeting considered whether a group MRL is appropriate. Based on the spread in the median residue values, the Meeting determined that the residues from the trials are too dissimilar and that a group MRL is not appropriate.

The Meeting used the residue data from lima beans to estimate a maximum residue level for beans, shelled of 0.07 mg/kg.

From the trials cited above, residues of CCIM were (n=6): < 0.01 (6) mg/kg. For assessing short-term dietary intake from beans, shelled, the HR, from a single sample, is 0.01 mg/kg.

From the trials cited above, the combined residues of cyazofamid and CCIM, expressed as cyazofamid, were (n=6): 0.025 (5), and 0.06 mg/kg. For assessing long-term dietary intake from beans, shelled, the STMR from that data set is 0.025 mg/kg.

The Meeting used the residue data from snap beans to estimate a maximum residue level for beans, except broad bean and soya bean of 0.4 mg/kg.

From the trials cited above, residues of CCIM were (n=8): < 0.01 (8) mg/kg. For assessing short-term dietary intake from beans, except broad bean and soya bean, the HR, from a single sample, is 0.01 mg/kg.

From the trials cited above, the combined residues of cyazofamid and CCIM, expressed as cyazofamid, were (n=8): 0.04, 0.06, 0.07, 0.12, 0.13, 0.20, and 0.21 (2) mg/kg. For assessing long-term dietary intake from beans, except broad bean and soya bean the STMR from that data set is 0.125 mg/kg.

Carrot and potato

The critical GAP for carrots is from the registration of cyazofamid on carrots in the USA (five foliar applications at 0.175 kg ai/ha on a 14–21-day interval with a 14-day PHI). Supervised residue trials matching this GAP are available from Canada and the USA.

Mean field trial residues of cyazofamid in carrots from independent field trials matching the critical GAP (n=15) were: < 0.010 (9), 0.022 (2), 0.027, 0.029, 0.034, and 0.039 mg/kg. Carrot samples were stored frozen for 91 to 443 days prior to analysis. Stability of cyazofamid in carrots during frozen storage was not demonstrated (58% remaining at 374 days, no other time points sampled). As a result, the Meeting did not estimate a maximum residue level, HR, or STMR for carrot.

The critical GAP for potatoes is from the registration of cyazofamid on potatoes in Brazil (six foliar applications at 0.1 kg ai/ha on a 7–10-day interval with a seven-day PHI). The submitted residue trials conducted in Brazil did not match the critical GAP. However, supervised residue trials matching this GAP are available from the USA.

Mean field trial residues of cyazofamid in potatoes from independent field trials matching the critical GAP (n=23) were: < 0.010 (23). A single sample from an exaggerated rate (10-fold for the final application only) had a quantifiable residue of cyazofamid (0.02 mg/kg)

Based on those data and the results from the metabolism study, the Meeting estimated a maximum residue level for potato of 0.01* mg/kg.

From the trials cited above, residues of CCIM were: < 0.01 mg/kg. For assessing short-term dietary intake from potato, the HR, from a single sample, is 0.01 mg/kg.

From the trials cited above, the combined residues of cyazofamid and CCIM, expressed as cyazofamid, were (n=23): < 0.025 (23) mg/kg. Noting the low residue at the exaggerated rate, the Meeting decided to set the STMR at 0.01 mg/kg for assessing long-term dietary intake from potato.

Basil and hops

In basil, the critical GAP is from the registration in the USA (nine foliar applications at 0.088 kg ai/ha on a 10–14-day interval with a zero-day PHI). Mean field trial residues of cyazofamid in basil (sweet) from independent field trials conducted in the USA and matching the critical GAP (n=4) were: 2.5, 2.9, 7.2, and 9.4 mg/kg.

Stability of CCIM in sweet basil was not demonstrated (47% remaining at 284 days, the only time point analysed). As the data are insufficient for evaluating dietary intake, the Meeting is not making a recommendation for residues of cyazofamid in sweet basil.

In hops, the critical GAP is from the registration in the USA (six foliar applications at 0.06–0.08 kg ai/ha on a 7–10-day interval with a 3-day PHI). Mean field trial residues of cyazofamid in dried cones from independent field trials conducted in Canada and the USA and matching the critical GAP (with DAT ranging from 2 to 4 days; n=5) were: 2.5, 2.9, 3.2, 6.3, and 7.4 mg/kg.

Based on those data, the Meeting estimated a maximum residue level for hops (dried cones) of 15 mg/kg.

From the trials cited above, residues of CCIM were (n=5): 0.13, 0.17, 0.18, 0.24, and 0.44 mg/kg. For assessing short-term dietary intake from hops (dried cones), the HR, from a single sample, is 0.45 mg/kg.

From the trials cited above, the combined residues of cyazofamid and CCIM, expressed as cyazofamid, were (n=5): 3.1, 3.2, 3.6, 6.5, and 7.5 mg/kg. For assessing long-term dietary intake from hops (dried cones), the STMR from that data set is 3.6 mg/kg.

Fate of residues during processing

High-temperature hydrolysis

The Meeting received a study investigating the high-temperature hydrolysis of cyazofamid. Samples of aqueous buffered solutions were spiked with cyazofamid at ca. 1 mg/L and put under conditions simulating pasteurisation (90 °C, pH 4, 20 min.); baking, brewing, boiling (100 °C, pH 5, 60 min); and sterilisation (120 °C, pH 6, 20 min.). Solutions were analysed by HPLC-MS/MS prior to and after processing. Cyazofamid was readily hydrolysed to CCIM (ca. 80% for pasteurisation and 100% for both baking/brewing/boiling and sterilisation).

Based on the results of the high-temperature hydrolysis study, the Meeting assumed 100% yield in the conversion of cyazofamid to CCIM in all foods other than those specified as “raw” when conducting the short-term intake assessment for CCIM.

Residues after processing

In basil, the critical GAP is from the registration in the USA (nine foliar applications at 0.088 kg ai/ha on a 10–14-day interval with a zero-day PHI). Mean field trial residues of cyazofamid in dried basil from independent field trials conducted in the USA and matching the critical GAP (n=6) were: 9.7, 13, 14 (3), and 40 mg/kg

Stability of CCIM in basil (dry) was not demonstrated (59% remaining at 297 days, the only time point analysed). As the data are insufficient for evaluating dietary intake, the Meeting is not making a recommendation for residues of cyazofamid in basil (dry).

The Meeting received data depicting the concentration/dilution of residues during processing of grapes into raisins, must and wine; tomato into paste and puree; and potatoes into wet peel, chip, and flake commodities. Processed commodities were derived using simulated commercial practices. The residue data are supported by adequate analytical methods. Storage stability data demonstrate that residues of cyazofamid and CCIM are stable in those commodities under the conditions and storage periods used in the processing studies. Residues in raw and processed commodities are supported by adequate concurrent recovery data, with the exception of cyazofamid in raisins (67±10%) and CCIM in potato chips (68±4%).

Cyazofamid did not concentrate in any processed commodity. As no concentration of residues was observed, recommendations for maximum residue levels for grapes, tomatoes, or potatoes processed commodities are not necessary. The Meeting noted that for the potato commodities, residues were < LOQ in all samples and processing factors could not be calculated; however, the tubers used in the processing study were treated at an exaggerated rate such that quantifiable residues are not expected in processed commodities even if concentration is occurring upon processing.

For estimating short-term dietary intake, the Meeting based processing factors on the combined residues of cyazofamid (as CCIM equivalents) and CCIM in raw commodities and residues of CCIM only in processed commodities. When residues were < 0.01 in a sample, they were assumed to be 0.01 for purposes of deriving a processing factor.

For grapes, the combined residues of cyazofamid (as CCIM equivalents) and CCIM from field trials at the critical GAP were: 0.017, 0.033, 0.037, 0.050, 0.070, and 0.45 mg/kg, with an STMR of 0.044 mg/kg and an HR, from a single sample, of 0.47 mg/kg.

For tomatoes, the combined residues of cyazofamid (as CCIM equivalents) and CCIM from field trials at the critical GAP were: 0.017, 0.027, 0.030 (2), 0.033, 0.037, 0.044 (4), 0.054, 0.060, 0.075, and 0.11 mg/kg, with an STMR of 0.044 mg/kg and an HR, from a single sample, of 0.12 mg/kg.

For dried hops, the combined residues of cyazofamid (as CCIM equivalents) and CCIM from field trials at the critical GAP were: 2.1 (2), 2.4, 4.4, 5.0, and 5.1 mg/kg, with an STMR of 3.4 mg/kg and an HR, from a single sample, of 5.4 mg/kg.

For estimating long-term dietary intake, the Meeting based processing factors on the combined residues of cyazofamid and CCIM, expressed as cyazofamid, in raw and processed commodities. For all raw and processed commodities except potato, residues of parent or CCIM were quantifiable and processing factors could be derived. When residues were < 0.01 in a sample, they were assumed to be 0.01 for purposes of deriving a processing factor.

Crop	Processed commodity	Long-term processing factor [a]	Short-term yield factor [b]	Long-term processing factor [a]	Short-term yield factor [b]	STMR-P (Cyazofamid + CCIM), mg/kg	STMR-P (CCIM), mg/kg	HR-P (CCIM), mg/kg
Grape	Fruit (RAC)	–	–	–	–	STMR [c] = 0.06	STMR [d] = 0.044	HR [d] = 0.47
	Dried	0.22	0.064	0.22	0.064	0.013	0.0028	0.030
	Must	0.3, 0.5 (2), 0.59, 1.3, 1.8, 1.9	0.11, 0.25, 0.3 (3), 0.33	0.59	0.3	0.035	0.013	0.14
	Wine	0.18, 0.5 (7), 0.55, 0.66	0.11, 0.3 (7), 0.33, 0.5	0.5	0.3	0.03	0.013	0.14
Tomato	Fruit (RAC)	–	–	–	–	STMR = 0.06	STMR [d] =	HR [d] = 0.12

Crop	Processed commodity	Long-term processing factor [a]	Short-term yield factor [b]	Long-term processing factor [a]	Short-term yield factor [b]	STMR-P (Cyazofamid + CCIM), mg/kg	STMR-P (CCIM), mg/kg	HR-P (CCIM), mg/kg
							0.044	
	Paste	0.72	0.54	0.72	0.54	0.043	0.024	0.069
	Puree	0.45	0.27	0.45	0.27	0.027	0.012	0.034
Potato	Tuber (RAC)	–	–	–	–	STMR [c] = 0.01	STMR [d] = 0.01	HR [d] = 0.01
	Chips	Not calculated		Not calculated		0.01	0.01	0.01
	Flakes	Not calculated		Not calculated		0.01	0.01	0.01
	Wet peel	Not calculated		Not calculated		0.01	0.01	0.01
Hops	Dried cones (RAC)	–	–	–	–	STMR [c] = 3.6	STMR [d] = 3.4	HR [d] = 5.4
	Beer	0.002	0.0014	0.002	0.0014	0.0072	0.0048	0.0076

[a] [Cyazofamid + CCIM (cyazofamid equivalents) in the processed commodity] ÷ [cyazofamid + CCIM (cyazofamid equivalents) in the raw commodity].

[b] CCIM in the processed commodity ÷ [cyazofamid (CCIM equivalents) + CCIM in the raw commodity].

[c] Cyazofamid + CCIM (cyazofamid equivalents)

[d] Cyazofamid (CCIM equivalents) + CCIM

Residues in animal commodities

The Meeting has not made a determination as to the residue definitions for compliance and dietary intake for animal commodities. Furthermore, the Meeting did not receive animal feeding studies or residue data for livestock feedstuffs from some crops considered in this appraisal (grape: grape pomace, beans: vines). The Meeting did not make a recommendation for animal commodities.

RECOMMENDATIONS

Definition of the residue for compliance with the MRLs for plant commodities: *Cyazofamid*.

Definition of the residue for estimating long-term dietary intake from plant commodities: *Cyazofamid plus CCIM, expressed as cyazofamid*.

Definition of the residue for estimating short-term dietary intake from plant commodities (to be compared to the ARfD for CCIM; an ARfD was determined to be unnecessary for cyazofamid): *CCIM*.

Definition of the residue for compliance with the MRLs and for dietary intake for animal commodities: *Not defined.*

CCN	**Commodity**	**Recommended Maximum residue level (mg/kg)**		**STMR or STMR-P mg/kg**	**HR or HR-P mg/kg**
		New	**Previous**		
VP 0061	Beans, except broad bean and soya bean	0.4	--	0.125 [Cyaz]	--
				0.01 [CC-R]	0.01 [CC-R]
				0.017 [CC-C]	0.042 [CC-C]
VP 0062	Beans, shelled	0.07	--	0.025 [Cyaz]	--
				0.01 [CC-R]	0.01 [CC-R]
				0.084 [CC-C]	0.16 [CC-C]
VB 0040	Brassica (cole or cabbage) vegetables, Head cabbages, Flowerhead brassicas	1.5	--	0.31 [Cyaz]	--
				0.01 [CC-R]	0.025 [CC-R]
				0.22 [CC-C]	0.64 [CC-C]

CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P mg/kg	HR or HR-P mg/kg
		New	Previous		
VL 0054	Brassica leafy vegetables	15	--	3.7 [Cyaz]	--
				0.053 [CC-R]	0.19 [CC-R]
				2.4 [CC-C]	4.8 [CC-C]
VO 0440	Egg plant	0.2		0.06 [Cyaz]	--
				0.01 [CC-R]	0.02 [CC-R]
				0.044 [CC-C]	0.13 [CC-C]
VC 0045	Fruiting vegetables, Cucurbits	0.09	--	0.04 [Cyaz]	--
				0.01 [CC-R]	0.01 [CC-R]
				0.027 [CC-C]	0.057 [CC-C]
FB 0269	Grapes	1.5	--	0.06 [Cyaz]	--
				0.01 [CC-R]	0.01 [CC-R]
				0.044 [CC-C]	0.47 [CC-C]
DH 1100	Hops, dry	15	--	3.6 [Cyaz]	--
				3.4 [CC-C]	5.4 [CC-C]
VL 0053	Leafy vegetables (except Brassica leafy vegetables)	10	--	3.2 [Cyaz]	--
				0.054 [CC-R]	0.15 [CC-R]
				2.2 [CC-C]	4.5 [CC-C]
VO 0445	Peppers, sweet (including Pimento or pimiento)	0.4	--	0.072 [Cyaz]	--
				0.01 [CC-R]	0.014 [CC-R]
				0.054 [CC-C]	0.2 [CC-C]
VO 0444	Peppers, chili	0.8	--	0.27 [Cyaz]	--
				0.014 [CC-R]	0.017 [CC-R]
				0.18 [CC-C]	0.23 [CC-C]
VR 0589	Potato	0.01*	--	0.01	--
				0.017 [CC-R, CC-C]	0.017 [CC-R, CC-C]
VO 0448	Tomato	0.2	--	0.06 [Cyaz]	--
				0.01 [CC-R]	0.02 [CC-R]
				0.044 [CC-C]	0.13 [CC-C]
	Cyazofamid + CCIM (long-term only)				
DF 0269	Dried grapes (=currants, raisins and sultanas)			0.013	
	Grapes – Must			0.035	
	Grapes – Wine			0.03	
	Cabbage - raw			--	
	Cabbage – not raw			--	
VW 0448	Tomato – Paste			0.043	
MW 0448	Tomato – Purée			0.027	
	Head lettuce – raw			--	
	Head lettuce – not raw			--	
	Leaf lettuce – raw			--	
	Leaf lettuce – not raw			--	
	Potato – all forms			0.025	
DH 1100	Hops, Dry			3.6	
	Hops – Beer			0.0072	
	CCIM (short-term only)				
DF 0269	Dried grapes (=currants, raisins and sultanas)			0.0028	0.03
	Grapes – Must			0.013	0.14
	Grapes – Wine			0.013	0.14
	Cabbage - raw			0.01	0.025
	Cabbage – not raw			0.22	0.64

CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P mg/kg	HR or HR-P mg/kg
		New	Previous		
VW 0448	Tomato – Paste			0.024	0.065
MW 0448	Tomato – Puree			0.012	0.032
	Head lettuce – raw			0.011	0.029
	Head lettuce – not raw			0.43	1.4
	Leaf lettuce – raw			0.027	0.05
	Leaf lettuce – not raw			1.2	3.1
	Potato – all forms			0.017	0.017
DH 1100	Hops, Dry			3.4	5.4
	Hops – Beer			0.0048	0.0076

FUTURE WORK

As future work, the Meeting recommends that methods be developed to assay residues of CCBA (free and conjugated) in animal commodities, and that any such methods include suitable digestion steps for liver.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDIs) of cyazofamid were calculated for the 17 GEMS/Food cluster diets using STMRs/STMR-Ps estimated by the current Meeting. The ADI for cyazofamid is 0–0.2 mg/kg bw. The calculated IEDIs for cyazofamid were 0–4% of the maximum ADI.

The Meeting concluded that the long-term intakes of residues of cyazofamid, when cyazofamid is used in ways that have been considered by the JMPR, are unlikely to present a public health concern.

Short-term intake

The International Estimated Short-Term Intakes (IESTI) of CCIM were calculated for food commodities and their processed commodities using HRs/HR-Ps or STMRs/STMR-Ps estimated by the current Meeting. The ARfD for CCIM is 0.2 mg/kg bw. The calculated maximum IESTI for CCIM was 90% of the ARfD for all commodities. The Meeting concluded that the short-term intake of residues of CCIM resulting from uses of cyazofamid, when cyazofamid is used in ways that have been considered by the JMPR, is unlikely to present a public health concern.

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