Cyazofamid (281)

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EXPLANATION

Cyazofamid, a cyanoimidazole fungicide was considered for the first time by the JMPR in 2015 when residue definitions and health-based guidance values were established and a number of maximum residue limits were recommended for grapes and a range of vegetables.

The 2015 JMPR established an ADI of 0–0.2 mg/kg bw for cyazofamid and an ARfD of 0.2 mg/kg bw for CCIM. An ARfD was determined to be unnecessary for cyazofamid:

The 2015 JMPR established residue definitions for plant commodities:-

For compliance with the MRL for plant commodities: *cyazofamid.*

For long-term dietary risk assessment: cyazofamid plus CCIM, expressed as cyazofamid

For acute dietary risk assessment: *CCIM*

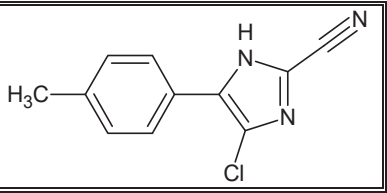
Residue definitions were not defined for animal commodities since the 2015 JMPR was uncertain about the relative amounts of free and cysteine-conjugated CCBA (consistently found as a major residue >10% TRR) in tissues other than liver and about the availability of reference standards for cysteine-conjugated CCBA.

The Forty-ninth Session of the CCPR (2017) scheduled cyazofamid for the evaluation of additional uses by the 2018 JMPR. The current Meeting received new GAP information for bulb vegetables and new supporting residue information from the manufacturer.

Cyazofamid is 4-chloro-2-cyano-N,N-dimethyl-5-*p*-tolylimidazole-1-sulfonamide (CAS 120116-88-3). It is relatively insoluble in water (0.1 mg/L), prone to hydrolysis (forming mostly CCIM), exhibits low volatility (1.33×10^{-5} Pa at 25 °C) and has a log P_{OW} of 3.2.

Cyazofamid

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

CCIM	4-chloro-5-p-tolylimidazole-2-carbonitrile	

METHODS OF RESIDUE ANALYSIS

Methods of analysis

The 2015 JMPR reviewed and summarised analytical method descriptions and validation data for cyazofamid and its CCIM metabolite, involving several extraction methods (acetonitrile, acetone, and acetonitrile/acidified water), partitioning steps (non-polar solvents), SPE clean-up procedures and LC-MS/MS analysis, concluding that these methods were suitable for estimating maximum residue levels.

The analytical methods used in the new supervised residue trials on spring onion, bulb onion and chives were modifications of these methods. For spring onions and bulb onions, cyazofamid and CCIM residues were extracted with acetonitrile:water:acetic acid (49:49:2), with centrifuged extracts being diluted with acetonitrile:water (50:50), filtered (PTFE) and further diluted with acetonitrile:water:acetic acid before LC-MS/MS analysis (without further clean-up). In the residue trials on chives, residues were extracted twice with acetonitrile, partitioned with hexane, concentrated and re-dissolved in acetonitrile:water (20:80) before SPE clean-up, dilution with acetonitrile:water (50:50) and LC-MS/MS analysis.

In both methods, quantification of the analytes was achieved by comparison with external standards of cyazofamid and CCIM and LOQs of 0.01 mg/kg were obtained.

Table 1 Method validation and concurrent recovery data for analytical methods for the determination of residues of cyazofamid and CCIM

Reference	Analyte	Matrix	Fortification	Recovery rate [%]		RSD	n
			level [mg/kg]	mean	range	[%]	
IB-2014-JAM-005-01-01	Cyazofamid	Bulb onion	0.01	82	75–87	5.2	6
			0.1	79	76–82	2.6	4
			2.0	77	76–77		2
	CCIM		0.01	85	81–89	3.4	6
			0.1	78	76–83	3.6	4
			2.0	76	74–77		2
	Cyazofamid	Spring onion	0.01		96		1
			0.1		79		1
	CCIM		0.01		88		1
			0.1		78		1
IR-4 PR No.10265	Cyazofamid	Chives, fresh	0.01	93	88–105	6.7	7
			0.5	92	88–97	4.4	4
			1.0	88	85–92	3.0	5
			20	88			1
			25	90	84–97	7.4	3
	CCIM		0.01	90	75–139	24	7
			0.5	101	91–106	6.7	4
			1.0	89	86–93	2.9	5
			20	97			1
			25	100	95–104	4.5	4
	Cyazofamid	Chives, dried	0.01	90	80–100	9.8	6
			0.5	89	88–90	1.3	3
			10	90	84–93	4.5	4
			25	90	84–99	8.8	3
	CCIM		0.01	66	61–77	9.2	6
			0.5	84	82–86	2.4	3
			10	88	83–91	2.8	4
			25	88	83–91	4.7	3

Stability of residues in stored analytical samples

The stability of residues of cyazofamid and CCIM in crops was evaluated by the JMPR in 2015. Storage stability in high water content commodities has been shown in seven different crops, between at least 284 days and at least 977 days for cyazofamid and, except for fresh basil, between at least 634 days and at least 1093 days for CCIM.

Table 2 Stability of cyazofamid and CCIM residues in high water commodities (JMPR 2015)

Matrix	Storage stability [days]	
	Cyazofamid	CCIM
Basil (fresh)	At least 284 days	Not stable [a] (less than 284 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

Matrix	Storage stability [days]	
	Cyazofamid	CCIM
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

[a] Residues were measured only at the indicated storage period, and the amount remaining was < 70%.

In the recent studies on chives, a storage stability component was included in the experimental design, with untreated fresh and dried chive samples being fortified with 5 mg/kg cyazofamid or CCIM and analysed after 472–477 days in frozen storage. The fortified samples were not analysed at the beginning of the storage intervals. If the fortifications were made correctly, the data indicate that under frozen storage conditions, cyazofamid and CCIM are stable in fresh chives for at least 472 days after storage at < -20 °C. In dried chives, residues were less stable.

Table 3 Stability of cyazofamid and CCIM residues in chives [Ref: IR-4 PR No.10265]

Matrix	Analyte	Storage period [days]	% Recovery	Mean % recovery after storage	Mean % procedural recovery
Fresh chive	cyazofamid	472	75, 73, 74	74	89
Dry chive	cyazofamid	477	65, 58, 54	59	86
Fresh chive	CCIM	472	73, 77, 74	75	89
Dry chive	CCIM	477	65, 65, 65	65	82

USE PATTERNS

Information on recently authorised GAP in the USA was provided to the Meeting for foliar applications to bulb vegetables and herbs. This GAP information is summarised in the following table.

Table 4 Recently authorised uses of cyazofamid (400 SC formulation)

Crop	Country	Application				Max/season		PHI (days)	Remarks
		method	max kg ai/ha	max kg ai/hL	water L/ha	no	kg ai/ha		
Bulb vegetables									
Bulb vegetables (US-3.07)	USA	foliar	0.087		470–700	6	0.47	0	7–10 day RTI. Include surfactant if applying <560 L/ha. Also can be applied by air or chemigation.
Herbs (US-19A)	USA	foliar	0.087		470–700	9	0.785	0	7–10 day RTI. Include surfactant if applying <560 L/ha. Also can be applied by air or chemigation and on greenhouse crops.

RTI = Re-treatment interval

USA: Bulb vegetables = **Chive, fresh leaves**; chive, Chinese fresh leaves; daylily, bulb; elegans hosta; fritillaria, bulb and leaves; garlic, bulb; garlic, great-headed, bulb; garlic, serpent, bulb; kurrat; lady's leek; leek; leek, wild; lily, bulb; onion, Beltsville bunching; onion, bulb; onion, Chinese, bulb; onion, fresh; onion, green; onion, macrostem; onion, pearl; onion, potato, bulb; onion, tree, tops; onion, Welsh, tops; shallot, bulb; shallot, fresh leaves; cultivars, varieties, and/or hybrids of these.

USA: Herbs (subgroup) = angelica; balm; basil; borage; burnet; camomile; catnip; chervil (dried); **chive**; Chinese chive; clary; coriander leaf (cilantro or Chinese parsley); costmary; culantro (leaf); curry (leaf); dillweed; horehound; hyssop; lavender; lemongrass; lovage (leaf); marigold; marjoram (includes sweet or annual marjoram, wild marjoram or oregano, and pot marjoram); nasturtium; parsley (dried); pennyroyal; rosemary; rue; sage; summer and winter savory; sweet bay; tansy; tarragon; thyme; wintergreen; woodruff; and wormwood.

RESIDUES RESULTING FROM SUPERVISED TRIALS

The Meeting received supervised field trial data on the following crops.

Crop Group	Commodity	Region	Table No.
Bulb vegetables	Spring onion	North America	5
	Chive	North America	6
	Bulb onions	North America	7

The supervised trials were well documented with laboratory and field reports. Laboratory reports included method validation including procedural recoveries with spiking at residue levels similar to those occurring in samples from the supervised trials. Dates of analyses or duration of residue sample storage were also provided. Although trials included control plots, no control data are recorded in the tables unless residues in control samples exceeded the LOQ.

When multiple applications were made to a crop, the application rate, spray concentration and spray volume were not always identical from one application to the next. If the variation was small, only the final values for application rate, concentration and spray volume are recorded. For larger variations all values were recorded.

Results from replicated field plots are presented as individual values and have not been corrected for concurrent method recoveries. When residues were not detected they are shown as below the LOQ (e.g. <0.01 mg/kg). Residues and application rates have been rounded to two significant digits. Average values have been calculated from the residue results prior to rounding and the results from trials conducted according to the maximum GAP and used for the estimation of maximum residue levels have been underlined. Where the results of duplicate analyses are available, the highest individual value has been selected as the HR for dietary intake estimation.

In addition to the description and details of the field trials and analytical methods, each report included a summary of the method validation, procedural recoveries, and concurrent recoveries in stored frozen samples.

In the trials where duplicate samples have been analysed, both the individual results and the average value have been reported (in brackets). Where results from separate plots with distinguishing characteristics such as different formulations, varieties or treatment schedules were reported, results are listed for each plot, and the highest value has been used in calculations of maximum residue levels, HRs and STMRs.

Bulb vegetables

Green onions, subgroup of

Spring onion

In supervised trials conducted in the USA on outdoor spring onions, unreplicated plots (46–124 square metres) were treated with 6 foliar sprays of an SC 400 formulation of cyazofamid, with added surfactant, using knapsack or tractor-mounted boom sprayers (3–6 nozzles) to apply 0.074–0.085 kg ai/ha in water volumes of 220–350 L/ha, with added non-ionic surfactant and with a re-treatment interval of 6–8 days.

Plants were pulled from at least 12 locations within each plot, either shaken to remove loose soil or trimmed to remove the roots. Duplicate samples of at least 2 kg were frozen within 45 minutes of sampling and stored frozen for up to 159 days before LC-MS/MS analysis for cyazofamid and CCIM. Concurrent recovery rates in samples spiked with 0.01–0.1 mg/kg cyazofamid or CCIM were 79–96% for cyazofamid and 78–88% for CCIM, with a reported LOQ of 0.01 mg/kg.

Table 5 Residues in spring onions from supervised trials in North America, involving six foliar applications of cyazofamid (400 SC formulation).

SPRING ONION Country, year Location (variety)	Application				DALA	Residues (mg/kg)			Reference & Comments
	no	kg ai/ha	water (L/ha	rate/season (kg ai/ha)		Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a)] (mg/kg)	
GAP: USA	6	0.87		0.47	0	7–10 day RTI, max 3 sprays consecutive sprays			
USA, 2014 North Rose, NY Wayne County (Green Banner)	6	0.076–0.08	317–333	0.469	0 (< 0.5 h)	0.36, 0.56 (<u>0.46</u>)	0.019, 0.0175 (0.018)	0.39, 0.59 (0.49)	IB-2014-JAM-005-01
USA, 2014 Bagley, IA Guthrie County (Evergreen)	6	0.074–0.081	221–352	0.455	0 (≤ 1 h)	0.46, 0.5 (<u>0.48</u>)	0.0115, 0.012 (0.012)	0.48, 0.51 (0.5)	IB-2014-JAM-005-02

SPRING ONION Country, year Location (variety)	Application				DALA	Residues (mg/kg)			Reference & Comments
	no	kg ai/ha	water (L/ha	rate/season (kg ai/ha)		Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a)] (mg/kg)	
USA, 2014 Northwood, ND Grand Forks County (Yellow Sweet Spanish Onion)	6	0.077–0.079	277–283	0.466	0 (3.5 h)	0.8, 0.735 (0.77)	0.014, 0.0125 (0.013)	0.82, 0.75 (0.79)	IB-2014-JAM-005-04 0.5-0.7 kg sample size
USA, 2014 Levelland, TX Hockley County (Candy)	6	0.079–0.085	282–286	0.477	0 (2 h)	0.57, 0.51 (0.54)	0.013, 0.012 (0.012)	0.59, 0.53 (0.56)	IB-2014-JAM-005-05
USA, 2014 Nipomo, CA San Luis Obispo County (Ishikura Improved Bunching)	6	0.073–0.079	285–287	0.466	0 (7 h)	1.15, 1.0 (1.085)	0.011, 0.011 (0.011)	**1.2**, 1.0 (1.1)	IB-2014-JAM-005-06 Bulbs halved in the field

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

Chives

In supervised trials conducted in the USA on outdoor and glasshouse chives, unreplicated plots were treated with 9 foliar sprays of an SC 400 formulation of cyazofamid, using knapsack plot sprayers or tractor-mounted boom sprayers (4–8 nozzles) to apply 0.085–0.092 kg ai/ha in water volumes of 200–420 L/ha, with added non-ionic surfactant and with a re-treatment interval of 6–8 days. Plot sizes in the glasshouse trials were 7–15 square metres and were 58–186 square metres in the outdoor trials.

Duplicate leaf samples (min 0.5 kg) were taken by clipping or cutting the leaves to just above ground level from at least 12 areas within each plot, frozen within 3 hours of sampling and stored frozen for up to 281 days before LC-MS/MS analysis for cyazofamid and CCIM. Concurrent recovery rates in samples spiked with 0.01–20 mg/kg cyazofamid or CCIM were 81–89% for cyazofamid and 62–89% for CCIM, with a reported LOQ of 0.01 mg/kg.

In most of the outdoor trials, additional samples of fresh leaves were air-dried or dehydrated at 39–57 °C for 24–48 hours before being frozen and stored for up to 373 days before analysis. Concurrent recovery rates in samples spiked with 0.01 mg/kg or 10 mg/kg cyazofamid were 80–93%. Concurrent recovery rates for CCIM were 62–68% (0.01 mg/kg spiked samples) and 86–89% (10 mg/kg spiked samples).

Table 6 Residues in chives from supervised trials in North America, involving nine foliar applications of cyazofamid (400 SC formulation)

CHIVES Country, year Location (variety)	Application				DALA	Residues (mg/kg)			Reference & Comments
	no	kg ai/ha	water (L/ha	rate/season (kg ai/ha)		Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a)] (mg/kg)	
GAP: USA	9	0.87		0.785	0	7–10 day RTI, max 3 sprays consecutive sprays			
USA, 2010 Davis, CA (Common herb)	9	0.085–0.091	290–309	0.782	Fresh 0 3 7 10 14 Dried 0	 1.2, 1.2 (1.2) 0.40, 0.44 (0.42) 0.24, 0.27 (0.26) 0.12, 0.14 (0.13) 0.059, 0.053 (0.056) 2.9	 0.039, 0.049 (0.044) 0.014, 0.013 (0.014) <0.01, <0.01 (<0.01) <0.01, <0.01 (<0.01) <0.01, <0.01 (<0.01) 0.25	 1.3, 1.3 (1.3) 0.42, 0.46 (0.44) <0.25, 0.28 (0.27) 0.13, 0.15 (0.14) 0.073, 0.068 (0.071) 3.3	IR4 PR 10265 10-CA24
USA, 2010 Salinas, CA (Purly)	9	0.086–0.091	243–421	0.793	Fresh 0 Dried 0	 1.6, 1.7 (1.7) 8.4	 0.025, 0.024 (0.025) 2.1	 1.6, 1.7 (1.7) 11.5	IR4 PR 10265 10-CA*26
USA, 2011 Citra, FL (Staro)	9	0.087–0.091	375–384	0.798	Fresh 0 Dried 0	 3.6, 3.0 (3.3) 13	 0.029, 0.028 (0.029) 0.4	 3.6, 3.0 (3.3) 14	IR4 PR 10265 10-FL06 68% DW
USA, 2010 Salisbury, MD 21801-8437 (Fancy)	9	0.087–0.089	290–300	0.79	Fresh 0	 0.75, 0.91 (0.83)	 0.059, 0.062 (0.061)	 0.84, 1.0 (0.92)	IR4 PR 10265 10-MD03
USA, 2010 Salisbury, MD 21801-8437 (Fancy)	9	0.086–0.089	281–290	0.791	Fresh 0 Dried 0	 3.0, 2.6 (2.8) 11	 0.15, 0.16 (0.16) 3.8	 3.2, 2.8 (3.0) 17	IR4 PR 10265 10-MD04 84% DW
USA, 2010 Charleston, SC (Common)	9	0.087–0.089	346–375	0.793	Fresh 0 Dried 0	 1.0, 1.1 (1.1) 3.3	 0.19, 0.2 (0.2) 0.93	 1.3, 1.4 (1.3) 4.7	IR4 PR 10265 10-SC*02
USA, 2010 Greenhouse Fayetteville, AR (Chinese)	9	0.086–0.09	281–290	0.795	Fresh 0	 0.86, 0.49 (0.68)	 <0.01, <0.01 (<0.01)	 0.87, 0.51 (0.69)	IR4 PR 10265 10 -AR20
USA, 2010 Greenhouse Parlier, CA (Staro OG)	9	0.086–0.091	234–328	0.8	Fresh 0	 3.2, 3.5 (3.4)	 0.049, 0.04 (0.045)	 3.3, **3.6** (3.4)	IR4 PR 10265 10-CA25
USA, 2010 Greenhouse Raleigh, NC (Staro)	9	0.083–0.092	206–234	0.77	Fresh 0	 0.85, 1.0 (0.93)	 0.04, 0.043 (0.042)	 0.91, 1.1 (0.99)	IR4 PR 10265 10-NC04

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

Onion, bulb

In supervised trials conducted in the USA on bulb onions, unreplicated plots (20–124 square metres) were treated with 6 foliar sprays of an SC 400 formulation of cyazofamid, with added surfactant, using knapsack or tractor-mounted boom sprayers (3–8

nozzles) to apply 0.073–0.083 kg ai/ha in water volumes of 230–330 L/ha, with added non-ionic surfactant and with a re-treatment interval of 6–8 days.

Plants were pulled from at least 12 locations within each plot, the tops and roots were removed, the bulbs brushed to remove loose dirt and duplicate samples of at least 2.3 kg were frozen within one hour of sampling and stored frozen for up to 168 days before LC-MS/MS analysis for cyazofamid and CCIM. Concurrent recovery rates in samples spiked with 0.01–2.0 mg/kg cyazofamid or CCIM were 75–82% for cyazofamid and 74–81% for CCIM, with a reported LOQ of 0.01 mg/kg.

Table 7 Residues in bulb onions from supervised trials in North America, involving six foliar applications of cyazofamid (400 SC formulation)

ONION, BULB Country, year Location (variety)	Application				DALA	Residues (mg/kg)			Reference & Comments
	no	kg ai/ha	water (L/ha	rate/season (kg ai/ha)		Cyazofamid (mg/kg)	CCIM (mg/kg)	Combined [a] (mg/kg)	
GAP: USA	6	0.87		0.47	0	7–10 day RTI, max 3 sprays consecutive sprays			
USA, 2014 North Rose, NY Wayne County (Madras)	6	0.078–0.079	327–330	0.471	0 (≤ 5 h)	0.083, 0.097 (0.09)	<0.01, <0.01 (<0.01)	0.098, 0.11 (0.1)	IB-2014-JAM-005-07
USA, 2014 Bagley, IA Guthrie County (Hybrid Candy)	6	0.075–0.08	272–309	0.465	0 (5.75 h)	0.042, 0.033 (0.038)	<0.01, <0.01 (<0.01)	0.057, 0.048 (0.053)	IB-2014-JAM-005-08
USA, 2014 Leonard, MO Shelby County (Candy)	6	0.079–0.083	256–297	0.485	0 (≤ 3 h)	0.04, 0.037 (0.039)	<0.01, <0.01 (<0.01)	0.055, 0.052 (0.054)	IB-2014-JAM-005-09
USA, 2014 Northwood, ND Grand Forks County (Yellow Sweet Spanish Onion)	6	0.077–0.079	276–283	0.466	0 (≤ 9.5 h)	0.04, 0.042 (0.041)	<0.01, <0.01 (<0.01)	0.055, 0.057 (0.056)	IB-2014-JAM-005-12
USA, 2014 Hinton, OK Caddo County (Candy)	6	0.076–0.08	230–258	0.466	0 (≤ 7 h)	0.035, 0.043 (0.039)	<0.01, <0.01 (<0.01)	0.05, 0.058 (0.054)	IB-2014-JAM-005-13
USA, 2014 Levelland, TX Hockley County (Candy)	6	0.078–0.079	281–287	0.472	0 (1.25 h)	0.065, 0.053 (0.059)	<0.01, <0.01 (<0.01)	0.08, 0.068 (0.074)	IB-2014-JAM-005-14
USA, 2014 Madera, CA Madera County (Fresno White)	6	0.08–0.081	282–286	0.481	0 (≤ 1 h) 1 3 7	0.85, 0.87 (0.86) 0.71, 0.51 (0.61) 0.38, 0.36 (0.37) 0.18, 0.18 (0.18)	0.024, 0.023 (0.023) 0.03, 0.0225 (0.026) 0.023, 0.019 (0.021) 0.013, 0.014 (0.014)	0.89, **0.9** (0.895) 0.75, 0.55 (0.65) 0.42, 0.39 (0.4) 0.2, 0.2 (0.2)	IB-2014-JAM-005-15
USA, 2014 Nipomo, CA San Luis Obispo County (Renegade)	6	0.073–0.079	285–287	0.466	0 (5.25 h)	0.088 0.11 (0.097)	<0.01, <0.01 (<0.01)	0.1, 0.12 (0.11)	IB-2014-JAM-005-16 Bulbs halved in the field
USA, 2014 Payette, ID Payette County (Vaquero)	6	0.079–0.081	282–288	0.482	0 (≤ 8 h)	0.035, 0.029 (0.032)	<0.01, <0.01 (<0.01)	0.05, 0.044 (0.047)	IB-2014-JAM-005-17
Canada, 2014 Scotland, Ontario Brant County (Redwing)	6	0.075–0.081	288–311	0.473	0 (≤ 1.5 h)	0.041, 0.068 (0.055)	<0.01, <0.01 (<0.01)	0.056, 0.083 (0.067)	IB-2014-JAM-005-10

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

APPRAISAL

Cyazofamid, a cyanoimidazole fungicide was considered for the first time by the JMPR in 2015 when residue definitions and health-based guidance values were established and a number of maximum residue limits were recommended for grapes and a range of vegetables.

The 2015 JMPR established an ADI of 0–0.2 mg/kg bw for cyazofamid. An ARfD of 0.2 mg/kg bw was established for 4-chloro-5-p-tolylimidazole-2-carbonitrile (CCIM) and an ARfD was determined to be unnecessary for cyazofamid.

The 2015 JMPR established the following residue definitions:

The residue definition for compliance with the MRL for plant commodities: *cyazofamid.*

The residue definition for long-term dietary risk assessment: *cyazofamid plus CCIM, expressed as cyazofamid*

The residue definition for acute dietary risk assessment: *CCIM*

The Forty-ninth Session of the CCPR (2017) scheduled cyazofamid for the evaluation of additional uses by the 2018 JMPR. The current Meeting received new GAP information for bulb vegetables, new supporting residue trial and storage stability studies.

Stability of pesticide residues in stored analytical samples

The stability of residues of cyazofamid and CCIM in crops was evaluated by the JMPR in 2015. In the listed commodities with a high water content (in the fresh legume, brassica vegetable, leafy vegetable and fruiting vegetable groups), cyazofamid residues in stored frozen samples were shown to be stable for at least 284 days and except for basil (fresh), CCIM residues were stable for at least 634 days.

In the recent studies on chives, a storage stability component was included in the experimental design, and while the fortified samples were not analysed at the beginning of the storage intervals, the data indicate that cyazofamid and CCIM are stable in stored frozen samples of fresh chives for at least 472 days, but that residues were not shown to be stable in dried chives in frozen storage.

Results of supervised residue trials on crops

The Meeting received new GAP information and/or new supporting residue information from the manufacturer for spring onions, chives and bulb onions.

For estimating dietary exposure, 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 mol. weight = 324.8, CCIM mol. weight = 217.7) and adding the result to the corresponding residue of cyazofamid. For calculation purposes, when residues below the LOQ, the residue was assumed to be at the LOQ. 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

Bulb vegetables

Bulb onions, subgroup of

The GAP for cyazofamid on bulb vegetables (including dry bulb onions) in the USA is 6 × 0.087 kg ai/ha, with a minimum re-treatment interval of 7 days, a PHI of 0 days and a maximum seasonal rate of 0.47 kg ai/ha.

In 10 trials conducted in North America and matching the USA bulb vegetables GAP, residues found in onion bulbs were:

Cyazofamid: 0.032, 0.038, 0.039, 0.039, 0.041, 0.055, 0.059, 0.09, 0.097 and 0.86 mg/kg.

CCIM: < 0.01 (9) and 0.026 mg/kg with the highest individual sample residue being 0.03 mg/kg

Combined residues(cyazofamid+CCIM): 0.047, 0.053, 0.054, 0.054, 0.056, 0.067, 0.074, 0.1, 0.11 and 0.895 mg/kg (n = 10).

Noting that bulb onion is a representative commodity for the Bulb Onions subgroup, and that the GAP in the USA covered all commodities in this subgroup, the Meeting estimated a maximum residue level of 1.5 mg/kg for cyazofamid, a STMR of 0.0615 mg/kg for the combined residues of cyazofamid and CCIM and a HR of 0.03 mg/kg and STMR of 0.01 mg/kg for CCIM on the subgroup of Bulb onions.

Green onions, subgroup of

The GAP for bulb vegetables (including spring onions and chive leaves) in the USA for cyazofamid is 6 × 0.087 kg ai/ha, a minimum re-treatment interval of 7 days, a PHI of 0 days and a maximum seasonal rate of 0.47 kg ai/ha.

Five trials on spring onions matching the GAP in the USA for bulb vegetables were available and a further five trials on chives, involving the same application rate (0.087 kg ai/ha), re-treatment intervals and PHI but with 9 applications of 0.087 kg ai/ha.

Residues in spring onions were:

Cyazofamid: 0.46, 0.48, 0.54, 0.77 and 1.1 mg/kg.

CCIM: 0.011, 0.012, 0.012, 0.013 and 0.018 mg/kg (highest single residue of 0.019 mg/kg)

Combined residues (cyazofamid+CCIM): 0.49, 0.50, 0.56, 0.79 and 1.1 mg/kg (n = 5).

The Meeting noted that in chives, residues declined rapidly (half-life of about 2 days), such that the contribution of residues from applications made more than 35 days prior to harvest would be negligible. The Meeting agreed to consider combining the data on spring onions and chives to estimate a maximum residue level for the subgroup of Green onions.

The residues in chives were:

Cyazofamid: 1.1, 1.2, 1.7, 2.8 and 3.3 mg/kg.

CCIM: 0.025, 0.029, 0.044, 0.16 and 0.2 mg/kg (highest single residue of 0.2 mg/kg)

Combined residues (cyazofamid+CCIM): 1.3, 1.3, 1.7, 3.0, and 3.3 mg/kg (n = 5).

As the median residues are within the 5-times range, and a Mann-Whitney test showed the residue populations were not from the same distribution, the Meeting agreed to estimate a maximum residue level for the green onion subgroup, based on the data set for chives.

The Meeting estimated a maximum residue level of 6 mg/kg for cyazofamid and a STMR of 1.5 mg/kg for the combined residues of cyazofamid and CCIM on the subgroup of Green onions. The Meeting estimated a HR of 0.2 mg/kg and a STMR of 0.044 mg/kg for CCIM on the subgroup of green onions.

Fate of residues during processing

In five of the outdoor trials conducted in the USA on chives, samples of fresh leaves were air-dried or dehydrated for 1–2 days before being frozen and stored for 413 days before being analysed for cyazofamid and CCIM.

The Meeting noted that residues of CCIM were not stable in dried chives and agreed the data were not sufficient to estimate maximum residue levels in dried chives.

RECOMMENDATIONS

On the basis of the data from supervised trials the Meeting concluded that the residue levels listed below are suitable for establishing maximum residue limits and for IEDI and IESTI assessment.

Definition of the residue for compliance with the MRL for plant commodities: *cyazofamid*

Definition of the residue for estimating long-term dietary risk assessment for plant commodities: *cyazofamid plus CCIM, expressed as cyazofamid*

Definition of the residue for acute dietary risk assessment for plant commodities: *CCIM*

Definition of the residue for compliance with the MRL and for estimating dietary risk assessment for animal commodities: *not defined*

	Commodity Name	Recommended maximum residue level (mg/kg)		STMR or STMR-P (mg/kg)	HR or HR-P (mg/kg)
CCN		New	Prev		
VA 0035	Bulb onions, Subgroup of (includes all commodities in this subgroup)	1.5	-	0.0615 0.01 (CCIM)	0.03 (CCIM)
VA 2032	Green onions, Subgroup of (includes all commodities in this subgroup)	6	-	1.5 0.044 (CCIM)	0.2 (CCIM)

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The ADI for cyazofamid is 0–0.2 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for cyazofamid were estimated for the 17 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by the JMPR. The results are shown in Annex 3 of the 2018 JMPR Report. The IEDIs ranged from 0–5% of the maximum ADI.

The Meeting concluded that long-term dietary exposure to residues of cyazofamid from uses considered by the JMPR is unlikely to present a public health concern

Acute dietary exposure

The ARfD for CCIM is 0.2 mg/kg bw. The International Estimate of Short Term Intakes (IESTIs) for CCIM were calculated for the food commodities and their processed commodities for which HRs/HR-Ps or STMRs/STMR-Ps were estimated by the present Meeting and for which consumption data were available. The results are shown in Annex 4 of the 2018 JMPR Report. The IESTIs varied from 0–3% of the ARfD for children and 0–1% for the general population.

The Meeting concluded that acute dietary exposure to residues of cyazofamid from uses considered by the present Meeting is unlikely to present a public health concern.

REFERENCES

Reference	Author(s)	Year	Title
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IR-4 PR No.10265	Corley, J.	2012	Cyazofamid: Magnitude of the Residues on Chives. IR-4 Project Headquarters, USA; report no. IR-4 PR No.10265. GLP, unpublished