Chlorfenapyr (254)

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EXPLANATION

Chlorfenapyr is a pro-insecticide-miticide. Its biological activity depends upon its activation to tralopyril (CL303268). Oxidative removal of the N-ethoxymethyl group of chlorfenapyr by mixed function oxidases forms CL303268. This compound uncouples oxidative phosphorylation at the mitochondria, resulting in the disruption of ATP production, cellular death, and ultimately organism mortality. It was first considered for toxicology and residues by the 2012 JMPR, where an ADI of 0–0.03 mg/kg bw and an ARfD of 0.03 mg/kg bw were established.

The 2012 JMPR recommended the following residue definition for chlorfenapyr:

Definition of the residue for compliance with the MRL for plant and animal commodities: chlorfenapyr

The residue is fat-soluble.

However, the 2012 Meeting did not reach a conclusion on the definition of the residue for dietary risk assessment for plant and animal commodities, since no appropriate health-guidance values for the metabolite CL303268 could be derived.

Chlorfenapyr was scheduled at the Forty-ninth Session of the CCPR for the evaluation of both toxicology and residues by the 2018 JMPR. The Meeting received new information on plant metabolism, analytical methods, storage stability, supervised field trials, fate during processing and the magnitude of residues during processing.

METABOLISM AND ENVIRONMENTAL FATE

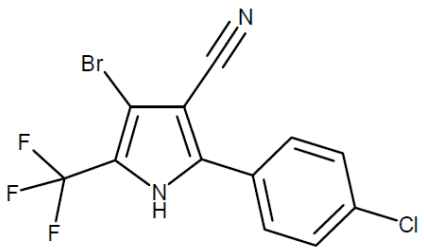
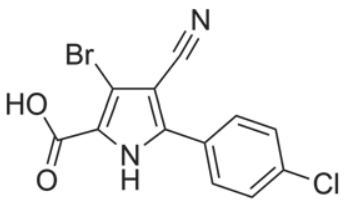
Metabolism studies were conducted using [phenyl-^{14}C]-chlorfenapyr (phenyl-label) and [pyrrole-^{14}C]-chlorfenapyr (pyrrole-label). The position of the label for both substances is presented in the following figures:

Figure 1 [phenyl U-^{14}C]-chlorfenapyr

Figure 2 [pyrrole-2-^{14}C]-chlorfenapyr

Chemical names, structures and code names of metabolites and degradation products of chlorfenapyr in relation to the current document are shown below. A full list of known metabolites is presented in the 2012 Monograph for chlorfenapyr.

Table 1 Known metabolites of chlorfenapyr

Code Names	Chemical name	Structure	Where found
Chlorfenapyr BAS 306 I M-9 CL303630 MW: 407.6 g/mol	4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-pyrrole-3-carbonitrile		Rat, plants, animals, rotational crops, soil
Tralopyril CL303268 MW: 349.5 g/mol	4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)-pyrrole-3-carbonitrile		Plants, processed products
CL322250 MW: 325.5 g/mol	4-bromo-2-(p-chlorophenyl)-5-(carboxylic)- pyrrole-3-carbonitrile		Processed products

Plant metabolism

The fate of chlorfenapyr in plants was investigated by the 2012 Meeting following foliar spray application of ^{14}C-radiolabelled active substance to oranges, tomatoes, head lettuce, potatoes and cotton.

For the current Meeting, an additional plant metabolism study on tomatoes was submitted, where nearly exclusively unchanged chlorfenapyr was recovered from fruits and leaves. Only the pyrrole label gave small residues of tralopyril (CL303268, up to 1% TRR).

Tomatoes

The metabolism of chlorfenapyr in tomatoes grown under field conditions was investigated by Schaffert D. (2017, CHLORFEN_001). Active substance radiolabelled either as [phenyl-U-^{14}C]-chlorfenapyr (phenyl label) or as [pyrrole-2-^{14}C]-chlorfenapyr (pyrrole label) was applied to tomato plants with three foliar sprays of 0.48 kg ai/ha (29 days before harvest), 0.48 kg ai/ha (15 days before harvest) and 0.24 kg ai/ha (1 day before harvest). Samples of unripe fruits (not further analysed), leaves and mature fruits were collected one day after the last application.

The samples were extracted three times with methanol and twice with water. The residual radioactive residue after solvent extraction was not further solubilized. Extracts and solid residues were analysed with liquid scintillation counting (LSC) to determine total radioactive residues (TRR). For the identification of metabolites, solvent extracts were analysed by HPLC-radioactivity and LC-MS methods. Maximum storage periods between harvest and analysis were up to 133 days.

In the following table the TRR levels found in tomato fruits and leaves for both radiolabels are summarised.

Table 2 Total radioactive residues in tomato matrices following foliar spray application of ^{14}C-chlorfenapyr

Matrix	TRR measured by combustion [mg eq/kg]	TRR calculated for the sum of extracts [mg eq/kg]
Phenyl-label		
Tomato fruits (1 DALA)	1.268	1.276
Tomato leaves (1 DALA)	38.174	34.362
Pyrrole label		
Tomato fruits (1 DALA)	1.743	1.865
Tomato leaves (1 DALA)	45.611	44.385

DALA: days after last treatment

From all samples 99.3–99.6% of the TRR was extracted, primarily with methnol (90–99.4% TRR). In Table 3 a summary of the extracted amounts is presented.

Table 3 Extracted radioactivity from tomato matrices following foliar spray application of ^{14}C-chlorfenapyr

Matrix	TRR calculated for the sum of extracts in mg eq/kg	Methanol extract in mg eq/kg (% TRR)	Water extract in mg eq/kg (% TRR)	Total extracted in mg eq/kg (% TRR)	Unextracted in mg eq/kg (% TRR)
Phenyl-label					
Tomato fruits (1 DALA)	1.3	1.3 (99)	0.002 (0.2)	1.27 (99.6)	0.005 (0.4)
Tomato leaves (1 DALA)	34.4	34.0 (99)	0.05 (0.1)	34.1 (99.2)	0.28 (0.8)
Pyrrole label					
Tomato fruits (1 DALA)	1.9	1.85 (99)	0.003 (0.2)	1.86 (99.6)	0.008 (0.4)
Tomato leaves (1 DALA)	44.4	44.0 (99)	0.078 (0.2)	44.1 (99.3)	0.30 (0.7)

DALA: days after last treatment

Identification of the extracted radioactivity showed that almost all was unchanged parent chlorfenapyr. For the pyrrole label minor amounts of tralopyril (CL303268, up to 1% TRR) were found in addition to that already present in the application solution as an impurity or degradate.

Table 4 Identification of the extracted radioactivity from tomato matrices following foliar spray application of ^{14}C-chlorfenapyr

Compound	Phenyl-label				Pyrrole-label			
	Tomato fruits		Tomato leaves		Tomato fruits		Tomato leaves	
	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
Chlorfenapyr	1.2	92.0	32.9	95.9	1.81	97.2	43.6	98.2
Tralopyril (CL303268)	-	-	-	-	0.018	1.0	0.35	0.8
Total identified	1.2	92.0	32.9	95.9	1.83	98.2	44.0	99.0
Characterized by HPLC	-	-	0.04	0.1 [a]	-	-	0.053	0.1
Characterized by aqueous extraction	0.002	0.1	-	-	0.002	0.1	-	-
Total identified and/or characterized	1.2	92.1	33.0	96.0	1.83	98.3	44.0	99.1
Unextracted	0.005	0.4	0.28	0.8	0.008	0.4	0.30	0.7
Total	1.2	92.5	33.3	96.8	1.84	98.7	44.3	99.8

[a] 8 peaks characterized (each max. 0.011 mg/kg or <0.1% TRR)

In summary, chlorfenapyr was the major component of the ^{14}C residue in oranges (55–77%), tomatoes (38–50%), lettuce (75–77%) and cottonseed (59–68%), and often the only compound present in plants at levels above 0.01 mg/kg. CL303268 was sometimes present but at low levels, <5% TRR.

RESIDUE ANALYSIS

Analytical methods

For the analysis of chlorfenapyr, tralopyril (CL303268) and the metabolite CL322250 in citrus fruits, tomatoes, dry beans, soya beans and wheat grain additional analytical methods were submitted. In the following table an overview of these methods is presented. In addition, method validation data from supervised field trials are available.

Table 5 Overview of analytical methods for chlorfenapyr, tralopyril (CL303268) and the metabolite CL322250

Method	Matrix	Extraction	Clean-Up	Detection, LOQ
G0001/01	High water High protein High acid	methanol/water (85:15, v/v)	Partition ethyl acetate	LC-MS/MS Chlorfenapyr: m/z: 465→347 & 467→349, LOQ: 0.01 mg/kg Tralopyril: m/z: 347→131 & 349→131, LOQ: 0.01 mg/kg
G0002/01	High oil High protein	methanol/water (95:5, v/v)	Partition ethyl acetate	LC-MS/MS CL322250: m/z: 325→281 & 323→279, LOQ: 0.01 mg/kg

Plant materials

Extraction efficiency

The extraction efficiency of two extraction protocols for tomato fruits and leaves obtained from the plant metabolism study by Schaffert D. (2017, CHLORFEN_001) was investigated by Schaffert D. (2017, CHLORFEN_007).

Extraction Method 1 (based on QuEChERS): An aliquot of the homogenized material was extracted with acetonitrile (tomato fruits) or water/acetonitrile (50/50, v/v) using a homogenizer. After centrifugation, the supernatant was filtered, then adjusted to a defined volume and subsequently measured by LSC.

Extraction Method 2 (based on methods M2427.02, CAV PA.0302 and G0001/01): An aliquot of the homogenized material was extracted methanol/water (85:15, v/v) using a homogenizer. After centrifugation, the volume of the supernatant was measured and the supernatant subjected to LSC.

In the following table the performance of each of the extraction protocols is summarized.

Table 6 Extraction efficiency for chlorfenapyr in tomato fruits and leaves

Extraction method	TRR			Chlorfenapyr		
	mg eq/kg	% TRR	% extracted	mg/kg	% TRR	% extracted
Tomato fruits						
Metabolism study	1.835	98.4	100	1.833	98.3	100
Method 1 QuEChERS)	1.915	103.9	105.6	1.897	102.9	104.7
Method 2 (M2427.02, CAV PA.0302 and G0001/01)	1.804	97.9	99.5	1.783	96.8	98.5
Tomato leaves						
Metabolism study	44.011	99.2	100	43.953	99.0	100
Method 1 QuEChERS)	39.179	88.4	89.1	38.832	87.6	88.5
Method 2 (M2427.02, CAV PA.0302 and G0001/01)	46.686	105.4	106.3	46.291	104.5	105.6

Method G0001/01 (Jose W.F.P. de, 2017, CHLORFEN_002 and CHLORFEN_003)

Residues are extracted with a mixture of methanol and water (85:15, v/v). An aliquot of the extract is diluted with saturated sodium chloride solution, acidified with hydrochloric acid and subsequently partitioned with water-saturated ethyl acetate. An aliquot of the organic phase is evaporated to dryness and dissolved in a mixture of methanol and water. Samples are analyzed using LC-MS/MS.

Table 7 Recovery data for method G0001/01 measuring chlorfenapyr and tralopyril in plant matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)		RSD (%)	
Chlorfenapyr			m/z: 465→347	m/z: 467→349	m/z: 465→347	m/z: 467→349
Citrus, fruit	0.01	6	83	81	2.4	5.0
	1.0	6	92	92	7.5	4.6
Beans, dry seeds	0.01	6	84	85	6.7	4.2
	1.0	6	100	99	5.0	5.4
Soya bean	0.01	6	82	83	7.5	4.0
	1.0	6	86	88	6.1	5.9
Tomato, fruit	0.01	6	75	76	6.8	2.8
	1.0	6	89	89	8.2	5.3
Wheat, grain	0.01	6	97	94	5.3	4.5
	1.0	6	90	91	3.6	6.0
Tralopyril (CL303268)			m/z: 347→131	m/z: 349→131	m/z: 347→131	m/z: 349→131
Citrus, fruit	0.01	6	97	102	2.1	1.9
	1.0	6	94	98	5.8	3.5
Beans, dry seeds	0.01	6	103	105	5.9	6.2
	1.0	6	105	104	6.2	3.4
Soya bean, seeds	0.01	6	88	88	4.3	4.0
	1.0	6	93	95	2.1	2.9
Tomato, fruit	0.01	6	93	92	4.5	1.6
	1.0	6	97	99	2.0	2.7
Wheat, grain	0.01	6	92	93	5.1	4.9
	1.0	6	95	96	3.9	1.2

An extension of the validation for Method G0001/01 with soya bean matrices at fortification levels up to 100 mg/kg was conducted by Teixeira T. (2017, CHLORFEN_004):

Table 8 Extended recovery data for method G0001/01 measuring chlorfenapyr and tralopyril in soya bean matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)		RSD (%)	
Chlorfenapyr			m/z: 465→347	m/z: 467→349	m/z: 465→347	m/z: 467→349
Soya bean, seeds	10	5	91	91	6.5	3.5
	100	6	109	104	8.7	11
Soya bean, plant	50	6	97	96	11	12
Soya bean, AGF	0.5	4	92	-	13	-
	100	3	92	-	2.6	-
Tralopyril (CL303268)			m/z: 347→131	m/z: 349→131	m/z: 347→131	m/z: 349→131
Soya bean, seeds	10	5	90	88	8.7	4.8
Soya bean, plant	50	6	96	95	3.7	1.9
Soya bean, AGF	0.01	2	99	-	-	-
	1.0	1	89	-	-	-
	10	3	93	-	2.0	-

Method G0002/01 (Jose W.F.P. de, 2017, CHLORFEN_005)

Residues of the metabolite CL322250 are extracted with a mixture of methanol and water. An aliquot of the extract is diluted with saturated sodium chloride solution, acidified with hydrochloric acid and subsequently partitioned with water-saturated ethyl acetate. An aliquot of the organic phase is evaporated to dryness and dissolved in a mixture of methanol and water. Samples were analyzed using LC-MS/MS.

Table 9 Recovery data for method G0002/01 measuring CL322250 in soya bean matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)		RSD (%)	
CL322250			m/z: 325→281	m/z: 323→279	m/z: 325→281	m/z: 323→279
Soya bean, seeds	0.01	6	102	99	13	15

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)		RSD (%)	
	1.0	6	99	94	5.6	7.4
Soya bean, oil	0.01	6	94	90	11	7.9
	1.0	6	87	85	5.2	7.0

An extension of the validation for Method G0002/01 with soya bean plants was conducted by Castro M. (2017, CHLORFEN_006):

Table 10 Extended recovery data for method G0002/01 measuring CL322250 in soya bean plants

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)		RSD (%)	
CL322250			m/z: 325→281	m/z: 323→279	m/z: 325→281	m/z: 323→279
Soya bean, plant	0.01	6	82	84	10	12
	1.0	6	90	92	2.5	2.3

Method Mitsubishi Kasei Institute of Toxicological and Environmental Science (modified) (Yabusaki T., 2003, CHLORFEN_012, already reported in 2013)

Residues of chlorfenapyr in tea are extracted with a mixture of acetone and water. Purification is performed with coagulation treatment, liquid-liquid separation and Florsil column chromatography. Samples were analyzed using GC-ECD.

Table 11 Recovery data for method Mitsubishi Kasei Institute of Toxicological and Environmental Science (modified) measuring chlorfenapyr in tea matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)
Crude tea	0.8	2	79	-
	20	2	70	-
Infusion	0.8	2	84	-

Extract storage stability (Jose W.F.P. de, 2017, CHLORFEN_005)

In the validation study for method G0002/01 also the stability of CL322250 in extract solvents stored under refrigerator conditions for a period of up to 7 days was investigated.

Table 1 Extract stability for method G0002/01 measuring CL322250 in soya bean matrices

Matrix		0 days recovery range (%)	7 days recovery range (%)
Soya bean oil	Calibration standard (MeOH/Water, 85:15, v/v)	85-104	81-106
	Final volume (MeOH/Water, 95:5, v/v)	85-107	86-106
Soya bean seeds	Calibration standard (MeOH/Water, 85:15, v/v)	94-114	93-112
	Final volume (MeOH/Water, 95:5, v/v)	94-114	97-120

Stability of pesticides in stored analytical samples

Plant matrices

Jose W.F.P. de (2017, CHLORFEN_008)

The storage stability of chlorfenapyr and tralopyril (CL303268) in different frozen (approximately -20 °C) raw agricultural commodities was determined for a period of 15 months. Homogenised samples were fortified with one of both analytes at rates of 0.1 mg/kg. These fortified commodities were stored deep frozen and analyzed after 0, 1, 3, 6, 9, 12, 14 and 15 months. At each fortification level triplicate samples were measured. In parallel, freshly fortified samples were analysed as procedural recoveries.

All samples were analysed using method G0001/01 with a LOQ of 0.01 mg/kg.

Table 13 Storage stability of chlorfenapyr and tralopyril (CL303268) in various plant matrices

Matrix	Storage in months (days)	Recovered residues in mg/kg	% remaining	Mean % remaining	Procedural recovery in % (mean)
Chlorfenapyr					
Soya bean (seeds)	0	0.075, 0.073, 0.076	75, 73, 76	75	71, 74 (73)
	1 (29)	0.104, 0.096, 0.107	104, 96, 107	102	99, 90 (94)
	3 (90)	0.111, 0.113, 0.118	112, 113, 118	114	133, 135 (134)
	6 (182)	0.09, 0.092, 0.075	90, 92, 75	85	93, 114 (104)
	12 (365)	0.072, 0.074, -	72, 74, -	73	95, 87 (91)
	15 (470)	0.093, 0.1, 0.099	93, 100, 99	97	99, 89 (94)
Dry beans (seeds)	0	0.074, 0.087, 0.085	74, 87, 85	82	88, 77 (82)
	1 (30)	0.071, 0.08, 0.071	71, 80, 71	74	79, 88 (84)
	3 (91)	0.076, 0.076, 0.079	76, 76, 79	77	87, 89 (88)
	6 (182)	0.091, 0.089, 0.088	91, 89, 88	89	84, 91 (87)
	12 (365)	0.077, 0.073, 0.072	77, 73, 72	74	79, 84 (82)
	15 (470)	0.094, 0.086, 0.072	94, 86, 72	84	115, 108 (112)
Rice, grain	0	0.067, 0.074, 0.073	67, 74, 73	71	82, 78 (80)
	1 (30)	0.088, 0.084, 0.073	88, 84, 73	81	89, 77 (83)
	3 (92)	0.108, 0.116, 0.11	108, 116, 110	111	111, 117 (114)
	6 (185)	0.119, 0.12, 0.113	119, 120, 113	117	116, 117 (117)
	9 (282)	0.091, 0.083, 0.083	91, 83, 83	86	115, 108 (112)
	12 (387)	0.088, 0.079, 0.086	88, 79, 86	85	88, 103 (95)
Apple, fruit	0	0.083, 0.075, 0.082	83, 75, 82	80	82, 72 (77)
	1 (33)	0.082, 0.084, 0.088	82, 84, 88	84	80, 86 (83)
	3 (88)	0.079, 0.074, 0.076	79, 74, 76	76	84, 87 (86)
	6 (179)	0.087, 0.083, 0.088	87, 83, 88	86	77, 79 (78)
	12 (363)	0.082, 0.074, 0.072	82, 74, 72	76	79, 90 (85)
	14 (431)	0.089, 0.092, 0.095	89, 92, 95	92	98, 88 (93)
Grapes, fruit	0	0.081, 0.082, 0.083	81, 82, 83	82	88, 91 (90)
	1 (30)	0.072, 0.080, 0.085	72, 80, 85	79	79, 88 (94)
	3 (86)	0.09, 0.091, 0.094	90, 91, 94	92	95, 93 (94)
	6 (182)	0.069, 0.066, 0.062	69, 66, 62	66	72, 78 (75)
	12 (385)	0.071, 0.075, 0.080	71, 75, 80	75	86, 97 (91)
Tralopyril	(CL303268)				
Soya bean (seeds)	0	0.097, 0.093, 0.098	97, 93, 98	96	98, 101 (99)
	1 (29)	0.089, 0.085, 0.087	89, 85, 87	87	100, 95 (98)
	3 (90)	0.088, 0.088, 0.097	88, 88, 97	91	95, 102 (99)
	6 (182)	0.072, 0.071, 0.072	72, 71, 72	72	84, 79 (81)
	12 (365)	0.082, 0.087, 0.084	82, 87, 84	84	99, 91 (95)
	15 (470)	0.082, 0.101, 0.099	82, 101, 98	94	101, 98 (100)
Dry beans (seeds)	0	0.097, 0.096, 0.1	97, 96, 100	97	101, 105 (103)
	1 (30)	0.088, 0.093, 0.099	88, 93, 99	93	92, 90 (91)
	3 (91)	0.079, 0.080, 0.092	79, 80, 92	84	90, 93 (91)
	6 (189)	0.095, 0.095, 0.095	95, 95, 95	95	102, 100 (100)
	12 (367)	0.076, 0.073, 0.08	76, 74, 80	76	76, 77 (76)
	14 (436)	0.127, 0.098, 0.113	127, 98, 113	113	100, 105 (102)
Rice, grain	0	0.092, 0.091, 0.09	92, 91, 90	91	93, 93 (93)
	1 (30)	0.098, 0.1, 0.092	98, 100, 92	97	101, 109 (105)
	3 (92)	0.078, 0.077, 0.084	78, 77, 84	80	95, 103 (99)
	6 (185)	0.084, 0.072, 0.081	84, 72, 81	79	102, 103 (102)
	10 (296)	0.086, 0.084, 0.085	86, 84, 85	85	106, 104 (105)
	12 (387)	0.078, 0.074, 0.089	78, 74, 89	81	100, 93 (96)
Apple, fruit	0	0.091, 0.092, 0.090	91, 92, 90	91	94, 92 (93)
	1 (33)	0.092, 0.098, 0.100	92, 98, 100	97	95, 100 (98)
	3 (88)	0.082, 0.081, 0.081	82, 81, 81	81	92, 95 (93)
	6 (179)	0.092, 0.094, 0.091	92, 94, 91	92	101, 106 (104)
	12 (363)	0.085, 0.088, 0.088	85, 88, 88	87	86, 87 (86)
	14 (431)	0.091, 0.08, 0.078	91, 80, 78	83	103, 97 (100)
Grapes, fruit	0	0.080, 0.095, 0.088	80, 95, 88	87	97, 96 (96)
	1 (30)	0.096, 0.1, 0.096	96, 100, 96	97	98, 103 (100)
	3 (86)	0.090, 0.091, 0.088	90, 91, 88	90	103, 105 (104)
	6 (182)	0.087, 0.087, 0.089	87, 87, 89	88	92, 86 (89)
	12 (372)	0.072, 0.083, 0.07	72, 83, 70	75	76, 81 (79)

Jose W.F.P. de (2017, CHLORFEN_005)

The storage stability of CL322250 in frozen (approximately -20 °C) soya bean seeds was determined for a period of 12 months. Homogenised samples were fortified at a rate of 0.1 mg/kg. These fortified commodities were stored deep frozen and analyzed after 0, 1, 3, 5, 6, 9 and 12 months. At each fortification level triplicate samples were measured. In parallel, freshly fortified samples were analysed as procedural recoveries.

All samples were analysed using method G0002/01 with a LOQ of 0.01 mg/kg.

Table 14 Storage stability of CL322250 in soya bean seeds

Matrix	Storage in months (days)	Recovered residues in mg/kg	% remaining	Mean % remaining	Procedural recovery in %
Chlorfenapyr					
Soya bean (seeds)	0	0.098, 0.104, 0.108	98, 104, 108	103	99
	1 (37)	0.09, 0.083, 0.094	90, 83, 94	89	110
	3 (98)	0.082, 0.10, 0.093	82, 100, 93	92	79
	5 (142)	0.067, 0.067, 0.064	67, 67, 64	66	76
	6 (191)	0.070, 0.082, 0.080	70, 82, 80	77	78
	9 (273)	0.075, 0.082, 0.073	75, 82, 73	77	82
	12 (365)	0.075, 0.074, 0.070	75, 74, 70	73	89

Castro M. (2017, CHLORFEN_006)

The storage stability of CL322250 in frozen (approximately -20 °C) soya bean seeds and whole plants was determined for a period of 7 months. Homogenised samples were fortified at a rate of 0.1 mg/kg. These fortified commodities were stored deep frozen and analyzed after 7 months. At each fortification level triplicate samples were measured. In parallel, freshly fortified samples were analysed as procedural recoveries.

All samples were analysed using method G0002/01 with a LOQ of 0.01 mg/kg.

Table 15 Storage stability of CL322250 in soya bean seeds

Matrix	Storage in months (days)	Recovered residues in mg/kg	% remaining	Mean % remaining	Procedural recovery in %
Chlorfenapyr					
Soya bean (seeds)	0	0.084, 0.081	84, 81	82	84, 81 (82)
	7 (205)	0.088, 0.088, 0.083	88, 88, 83	86	101, 103 (102)
Soya bean (whole plants)	0	0.084, 0.068	84, 68	76	84, 68 (76)
	7 (205)	0.078, 0.084, 0.077	78, 84, 77	79	99, 96 (98)

USE PATTERN

Chlorfenapyr is registered in many countries for the control of insects/mites in the field. In the following table GAP information on all crops supported with residue data are summarized.

Table 16 List of uses of chlorfenapyr

Country	Crops or crop groups	Application detail	Growth stage at last treatment	No.	Pre harvest interval (PHI) in days
		kg ai/ha			
Pulses					
Argentina	Soya beans, dry	0.19	In infestation	2	n.s.
Bolivia	Soya beans, dry	0.24	-	1	-
Brazil	Soya beans, dry	0.29	In infestation, 5 day interval	3	30

n.s. not stated

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

Residue levels were reported as measured. Application rates were always reported as chlorfenapyr equivalents. When residues were not detected they are shown as below the LOQ, e.g. <0.01 mg/kg. Application rates, spray concentrations and mean residue

results have generally been rounded to the even with two significant figures. HR and STMR values from the trials conducted according to maximum GAP have been used for the estimation of maximum residue levels. These results are underlined.

Laboratory reports included method validation including batch 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. Field reports provided data on the sprayers used and their calibration, plot size, residue sample size and sampling date. Although trials included control plots, no control data are recorded in the tables except where residues in control samples exceeded the LOQ. Residue data are recorded unadjusted for % recovery.

Chlorfenapyr - supervised residue trials

Commodity	Indoor/Outdoor	Treatment	Countries	Table
Soya beans	Outdoor	Foliar	Brazil	17

Soya bean seeds, dry

During the growing seasons 2015/2016 and 2016/2017, 10 field trials were conducted in Brazil to determine the residue levels of chlorfenapyr and the metabolite tralopyril in soya bean specimens (Teixeira T.M.I., 2017, CHLORFEN_004). In addition to the residues of these two analytes (presented in the following table), residues of the metabolite CL322250 were also analysed in parallel by Castro (2017, CHLORFEN_006). This compound was not found in any of the seed or plant samples investigated at or above the LOQ of 0.01 mg/kg. The maximum storage interval between sampling and analysis was 348 days.

Further supervised field trials involving the application of chlorfenapyr to soya beans in Brazil were reported by Porta F. (2013, CHLORFEN_009 and 2014, CHLORFEN_010) and Silva M. (2016, CHLORFEN_011). All samples collected in these trials were analysed using method SOP-PA.0302, measuring parent chlorfenapyr with a LOQ of 0.01 mg/kg. No metabolites were measured. The maximum storage period was 44 days.

Table 2 Residues of chlorfenapyr following foliar applications on soya beans

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, method, storage period
	Form.	kg ai/ha	Inter-val	kg ai/hL	Growth stage	Sample	DALT	Parent	CL303268	
Brazil, Ponta Grossa 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH78 BBCH80	Seeds	0 15 30 45	0.24 0.11 <0.01 0.013	<0.01 <0.01 <0.01 <0.01	G150192, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Aropoti 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH76 BBCH78	Seeds	0 15 30 45	1.9 0.21 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	G150193, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Itaberá 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH79 BBCH79 BBCH85	Seeds	0 15 30 45	1.9 0.033 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	G150194, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Tibagi 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH77 BBCH79	Seeds	0 15 30 45	0.41 0.013 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	G150195, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Coronel Macedo 2016 (NA 7000 IPRO)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH77 BBCH78 BBCH79	Seeds	30	0.019	<0.01	G150196, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil,	SC	0.3	-	0.38	BBCH72	Seeds	30	<0.01	<0.01	G150197,

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, method, storage period
	Form.	kg ai/ha	Inter-val	kg ai/hL	Growth stage	Sample	DALT	Parent	CL303268	
Carambei 2016 (NA 5909 RG)		0.3 0.3	5 d 5 d	0.38 0.38	BBCH73 BBCH74					CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Castro 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH77 BBCH79	Seeds	30	<0.01	<0.01	G150198, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Palmeira 2015 (NA 7000 IPRO)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH78 BBCH79	Seeds	30	<0.01	<0.01	G150199, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Ponta Grossa 2017 (M5917 IPRO)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH79 BBCH83 BBCH85	Seeds	0 15 30 45	0.21 0.026 0.024 0.046	<0.01 <0.01 <0.01 <0.01	G150200, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Itaberá 2017 (M5917 IPRO)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH73 BBCH75 BBCH77	Seeds	30	0.024	<0.01	G150201, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Senador Canedo 2013 (BRSGO 7950)	SC	0.24 0.24 0.24	5–10 d	0.3 0.3 0.3	BBCH89	Seeds	0	0.07	N/A	G130004, CHLORFEN_009, CHLORFEN_010 & CHLORFEN_011 Method: SOP-PA.0302 Storage: 2 months Reverse decline trial
					BBCH86	Seeds	15	0.01	N/A	
					BBCH79	Seeds	30	<0.01	N/A	
					BBCH74	Seeds	45	<0.01	N/A	
	SC	0.3 0.3 0.3	5–10 d	0.38 0.38 0.38	BBCH89	Seeds	0	0.12	N/A	
					BBCH86	Seeds	15	0.01	N/A	
					BBCH79	Seeds	30	<0.01	N/A	
					BBCH74	Seeds	45	<0.01	N/A	
	SC	0.36 0.36 0.36	5–10 d	0.45 0.45 0.45	BBCH89	Seeds	0	0.18	N/A	
					BBCH86	Seeds	15	0.02	N/A	
					BBCH79	Seeds	30	<0.01	N/A	
					BBCH74	Seeds	45	<0.01	N/A	
Brazil, Ponta Grossa 2013 (ARS 5909 - Apolo)	SC	0.24 0.24 0.24	5–10 d	0.3 0.3 0.3	BBCH97	Seeds	0	0.14	N/A	G130005, CHLORFEN_009, CHLORFEN_010 & CHLORFEN_011 Method: SOP-PA.0302 Storage: 2 months Reverse decline trial
					BBCH81	Seeds	15	0.01	N/A	
					BBCH79	Seeds	30	<0.01	N/A	
					BBCH79	Seeds	45	0.01	N/A	
	SC	0.3 0.3 0.3	5–10 d	0.38 0.38 0.38	BBCH97	Seeds	0	0.19	N/A	
					BBCH81	Seeds	15	0.05	N/A	
					BBCH79	Seeds	30	<0.01	N/A	
					BBCH79	Seeds	45	0.01	N/A	
	SC	0.36	5–10	0.45	BBCH97	Seeds	0	0.3	N/A	

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, method, storage period
	Form.	kg ai/ha	Inter-val	kg ai/hL	Growth stage	Sample	DALT	Parent	CL303268	
		0.36 0.36	d	0.45 0.45	BBCH81	Seeds	15	0.07	N/A	
					BBCH79	Seeds	30	<0.01	N/A	
					BBCH79	Seeds	45	0.02	N/A	
Brazil, Santo António de Possee 2013 (Poténcia)	SC	0.24 0.24 0.24	5–10 d	0.3 0.3 0.3	BBCH97	Seeds	0	0.15	N/A	G130006, CHLORFEN_009, CHLORFEN_010 & CHLORFEN_011 Method: SOP-PA.0302 Storage: 2 months Reverse decline trial
					BBCH81	Seeds	15	0.06	N/A	
					BBCH79	Seeds	30	0.03	N/A	
					BBCH79	Seeds	42	0.02	N/A	
	SC	0.3 0.3 0.3	5–10 d	0.38 0.38 0.38	BBCH97	Seeds	0	0.21	N/A	
					BBCH81	Seeds	15	0.08	N/A	
					BBCH79	Seeds	30	0.05	N/A	
					BBCH79	Seeds	42	0.02	N/A	
	SC	0.36 0.36 0.36	5–10 d	0.45 0.45 0.45	BBCH97	Seeds	0	0.31	N/A	
					BBCH81	Seeds	15	0.06	N/A	
					BBCH79	Seeds	30	0.07	N/A	
					BBCH79	Seeds	42	0.02	N/A	
Brazil, Uberlándia 2013 (M7809RR)	SC	0.24 0.24 0.24	5–10 d	0.3 0.3 0.3	BBCH77	Seeds	30	<0.01	N/A	G130007, CHLORFEN_009, CHLORFEN_010 & CHLORFEN_011 Method: SOP-PA.0302 Storage: 2 months
	SC	0.3 0.3 0.3	5–10 d	0.38 0.38 0.38	BBCH77	Seeds	30	<0.01	N/A	
	SC	0.36 0.36 0.36	5–10 d	0.45 0.45 0.45	BBCH77	Seeds	30	<0.01	N/A	
Brazil, Castro 2013 (BRS Poténcia)	SC	0.45 0.45 0.45	5–10 d	0.3 0.3 0.3	BBCH77	Seeds	30	0.04	N/A	G130008, CHLORFEN_009, CHLORFEN_010 & CHLORFEN_011 Method: SOP-PA.0302 Storage: 2 months
	SC	0.48 0.48 0.48	5–10 d	0.38 0.38 0.38	BBCH77	Seeds	30	0.06	N/A	
	SC	0.46 0.46 0.46	5–10 d	0.45 0.45 0.45	BBCH77	Seeds	30	0.08	N/A	

AGF: Aspirated grain fractions

N/A: not analysed

BBCH 71–79: 10–100% of pods have reached final length

BBCH 81–89: 10–100% of pods are ripe; beans final colour, dry and hard

Soya bean forage

See soya bean seeds, dry.

Table 18 Residues of chlorfenapyr following foliar applications on soya beans

Location,	Application					Residues, mg/kg				Report/Trial No., Reference,
Year (variety)	Form.	kg ai/ha	Inter-val	kg ai/hL	Growth stage	Sample	DALT	Parent	CL303268	method, storage period
Brazil, Ponta Grossa 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH78 BBCH80	Whole plant	0 15 30 45	22 1.2 1.7 0.8	0.018 0.011 0.021 0.011	G150192, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Aropoti 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH76 BBCH78	Whole plant	0 15 30 45	15 1.4 1.9 1.1	0.017 <0.01 0.021 0.013	G150193, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Itaberá 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH79 BBCH79 BBCH85	Whole plant	0 15 30 45	6.3 5.3 2.2 2.4	<0.01 0.026 0.023 0.033	G150194, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Tibagi 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH77 BBCH79	Whole plant	0 15 30 45	6.6 1.1 2.2 1.4	0.011 <0.01 0.019 0.016	G150195, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Coronel Macedo 2016 (NA 7000 IPRO)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH77 BBCH78 BBCH79	Whole plant	30	0.99	0.01	G150196, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Carambei 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH72 BBCH73 BBCH74	Whole plant	30	3.9	0.071	G150197, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Castro 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH77 BBCH79	Whole plant	30	1.5	0.016	G150198, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Palmeira 2015 (NA 7000 IPRO)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH78 BBCH79	Whole plant	30	1.4	0.014	G150199, CHLORFEN_004 Method: G0001/01 Storage: 9 months

AGF: Aspirated grain fractions

N/A: not analysed

BBCH 71–79: 10–100% of pods have reached final length

BBCH 81–89: 10–100% of pods are ripe; beans final colour, dry and hard

Soya bean asprirated grain fractions (AGF)

See soya bean seeds, dry.

Table 19 Residues of chlorfenapyr following foliar applications on soya beans

Location,	Application					Residues, mg/kg				Report/Trial No., Reference,
Year (variety)	Form.	kg ai/ha	Inter-val	kg ai/hL	Growth stage	Sample	DALT	Parent	CL303268	method, storage period
Brazil, Coronel Macedo 2016 (NA 7000 IPRO)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH77 BBCH78 BBCH79	AGF	30	6.5	0.05	G150196, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Carambei 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH72 BBCH73 BBCH74	AGF	30	91	1.3	G150197, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Castro 2016 (NA 5909 RG)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH77 BBCH79	AGF	30	12	0.11	G150198, CHLORFEN_004 Method: G0001/01 Storage: 9 months
Brazil, Palmeira 2015 (NA 7000 IPRO)	SC	0.3 0.3 0.3	- 5 d 5 d	0.38 0.38 0.38	BBCH75 BBCH78 BBCH79	AGF	30	12	0.072	G150199, CHLORFEN_004 Method: G0001/01 Storage: 9 months

AGF: Aspirated grain fractions

N/A: not analysed

BBCH 71–79: 10–100% of pods have reached final length

BBCH 81–89: 10–100% of pods are ripe; beans final colour, dry and hard

FATE OF RESIDUES IN STORAGE AND PROCESSING

Nature of residue during processing

The hydrolysis of chlorfenapyr (Sacchi R., 2016, CHLORFEN_015) and its metabolite tralopyril (CL303268) (Sacchi R., 2017, CHLORFEN_016) was investigated under processing conditions using ^{14}C-radiolabelled compounds. Chlorfenapyr and tralopyril (1.45 mg/kg) were separately incubated in aqueous buffer solutions at a nominal concentration of 0.41 mg/L or 1.45 mg/L, respectively, under three sets of conditions, each designed to simulate an appropriate process: 90 °C (pH 4, 20 minutes) to simulate pasteurisation, 100 °C (pH 5, 60 minutes), to simulate boiling, baking and brewing, and 120 °C (pH 6, 20 minutes) to simulate sterilisation.

Total recovered radioactivity was measured for each test solution by LCS. Radioactive components were characterised by fractionation and co-chromatography with authenticated reference compounds using HPLC or LC-MS/MS.

Table 20 Hydrolysis of ^{14}C-chlorfenapyr under simulated processing conditions

Process represented	Compound	% applied radioactivity recovered
PH 4 90 oC 20 mins (pasteurization)	Chlorfenapyr Unidentified	99.1–100.1 0.7–1.7
PH 5 100 oC 60 mins (baking/brewing/cooking)	Chlorfenapyr CL322250 Unidentified	98.7–99.1 3.4–3.5 0.8–0.9
PH 6 120 oC 20 mins (sterilization)	Chlorfenapyr CL322250	68.9–71.5 32.1–33.7

Table 21 Hydrolysis of ^{14}C-tralopyril (CL303268) under simulated processing conditions

Process represented	Compound	% applied radioactivity recovered
PH 4 90 oC 20 mins (pasteurization)	Tralopyril (CL303268) CL322250	85.4–86.2 11.8–12.7
PH 5 100 oC 60 mins (baking/brewing/cooking)	Tralopyril (CL303268) CL322250	n.d. 102.7–109.7
PH 6 120 oC 20 mins (sterilization)	Tralopyril (CL303268) CL322250	n.d. 97.8–97.9

n.d. not detected

Residues after processing

The fate of chlorfenapyr and its metabolites Tralopyril (CL303268) and CL322250 during processing of raw agricultural commodity (RAC) was investigated in soya bean using important processing procedures. As a measure of the transfer of residues into processed products, a processing factor was used, which is defined as:

Processing factor=Residue in processed product (mg/kg) ÷ Residue in raw agricultural commodity (mg/kg)

If residues in the RAC were below the LOQ, no processing factor could be derived. In case of residues below the LOQ, but above the LOD in the processed product, the numeric value of the LOQ was used for the calculation. If residues in the processed product were below the LOD, the numeric value of the LOQ was used for the calculation but the PF was expressed as “less than” (e.g. <0.5).

Soya beans

The transfer of residues of chlorfenapyr and its metabolites tralopyril (CL303268) and CL322250 were investigated in soya beans by Teixeira T. (2017, CHLORFEN_017) in three supervised field trials conducted in Brazil. The trials were performed at increased rates compared to reported GAPs using three applications of 1.5 kg ai/ha. Samples were collected 30 DALT and processed into hulls, seeds without shell, laminated beans, defatted meal, roasted defatted meal and oil.

All samples were analysed using method G0001/01 for chlorfenapyr and tralopyril (CL303268) and using method G0002/01 for CL322250. Procedural recoveries were within acceptable limits for all matrices: for soya bean seeds (n = 4, recovery: 78–119%, RSD: 8–20%), soya bean hulls (n = 6–10, recovery: 86–119%, RSD: 7–11%), soya beans without shell (n = 4–6, recovery: 84–119%, RSD: 3–8%), soya bean laminated (n = 6, recovery: 69–116%, RSD: 9–14%), soya bean defatted meal (n = 5–8, recovery: 78–116%, RSD: 7–11%), soya bean roasted defatted meal (n = 6–8, recovery: 69–120%, RSD: 4–12%) and soya bean oil (n = 12–13, recovery: 70–120%, RSD: 5–19%). The maximum storage period for all samples was up to 190 days.

Table 22 Summary of chlorfenapyr and its metabolites tralopyril (CL303268) and CL322250 in soya beans and processed commodities from three trials conducted in Brazil (3×1.5 kg ai/ha, 30 DALT)

Trial	Commodity	Chlorfenapyr		Tralopyril		CL322250	
		mg/kg	PF	mg/kg	PF	mg/kg	PF
G150202	Seeds (RAC)	0.55	-	<0.01	-	<0.01	-
	Hulls	5.05	9.2	0.022	n/a	<0.01	n/a
	Beans w/o shells	0.096	0.17	<0.01	n/a	<0.01	n/a
	Laminated beans	0.42	0.76	<0.01	n/a	<0.01	n/a
	Defatted meal	0.056	0.10	<0.01	n/a	<0.01	n/a
	Roasted defatted meal	0.14	0.25	<0.01	n/a	<0.01	n/a
	Oil, crude	1.8	3.3	<0.01	n/a	<0.01	n/a
G150203	Seeds (RAC)	0.067	-	<0.01	-	<0.01	-
	Hulls	0.66	9.9	<0.01	n/a	<0.01	n/a
	Beans w/o shells	0.037	0.55	<0.01	n/a	<0.01	n/a
	Laminated beans	0.094	1.4	<0.01	n/a	<0.01	n/a
	Defatted meal	0.014	0.21	<0.01	n/a	<0.01	n/a
	Roasted defatted meal	0.032	0.48	<0.01	n/a	<0.01	n/a
	Oil, crude	0.35	5.2	<0.01	n/a	<0.01	n/a
G150204	Seeds (RAC)	0.051	-	<0.01	-	<0.01	-
	Hulls	0.51	10	<0.01	n/a	<0.01	n/a
	Beans w/o shells	0.027	0.53	<0.01	n/a	<0.01	n/a
	Laminated beans	0.062	1.2	<0.01	n/a	<0.01	n/a
	Defatted meal	0.014	0.27	<0.01	n/a	<0.01	n/a

Trial	Commodity	Chlorfenapyr		Tralopyril		CL322250	
		mg/kg	PF	mg/kg	PF	mg/kg	PF
	Roasted defatted meal	0.012	0.24	<0.01	n/a	<0.01	n/a
	Oil, crude	0.23	4.5	<0.01	n/a	<0.01	n/a

DALT: days after last treatment

RAC: raw agricultural commodity

n/a: not applicable, RAC residues <LOQ

Table 23 Summary of chlorfenapyr residues in processed commodities

Commodity	Processing factor	Median or best estimate processing factor
Soya bean, hulls	9.2, 9.9, 10	9.9
Soya beans w/o shells	0.17, 0.53, 0.55	0.53
Laminated soya beans	0.76, 1.2, 1.4	1.2
Soya beans, defatted meal	0.1, 0.21, 0.27	0.21
Soya beans, roasted defatted meal	0.24, 0.25, 0.48	0.25
Soya beans, oil crude	3.3, 4.5, 5.2	4.5

RAC: raw agricultural commodity

Residues of the metabolites tralopyril (CL303268) and CL322250 in soya bean RAC were below the LOQ precluding the calculation of robust processing factors.

APPRAISAL

Chlorfenapyr is a pro-insecticide-miticide. Its biological activity depends upon its activation to tralopyril (CL303268). Oxidative removal of the N-ethoxymethyl group of chlorfenapyr by mixed function oxidases forms CL303268. This compound uncouples oxidative phosphorylation at the mitochondria, resulting in the disruption of ATP production, cellular death, and ultimately organism mortality. It was first considered for toxicology and residues by the 2012 JMPR, when an ADI of 0–0.03 mg/kg bw and an ARfD of 0.03 mg/kg bw were established.

The 2012 JMPR recommended the following residue definition for chlorfenapyr:

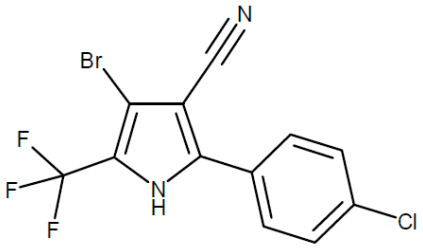
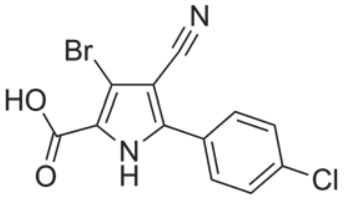
Definition of the residue for compliance with the MRL for plant and animal commodities: *chlorfenapyr*.

The residue is fat-soluble.

However, the 2012 Meeting did not reach a conclusion on the definition of the residue for dietary risk assessment for plant and animal commodities, since no appropriate health-guidance values for the metabolite CL303268 could be derived.

Chlorfenapyr was scheduled at the Forty-ninth Session of the CCPR for the evaluation of both toxicology and residues by the 2018 JMPR. The Meeting received new information on plant metabolism, analytical methods, storage stability, supervised field trials, fate during processing and the magnitude of residues during processing.

The following abbreviations are used for the metabolites discussed below:

Code Names	Chemical name	Structure	Where found
Chlorfenapyr BAS 306 I	4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-pyrrole-3-carbonitrile		Rat, plants, animals, rotational crops, soil
Tralopyril CL303268	4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)-pyrrole-3-carbonitrile		Plants, processed products
CL322250	4-bromo-2-(p-chlorophenyl)-5-(carboxylic)- pyrrole-3-carbonitrile		Processed products
CL325195	2-(4-chlorophenyl)-5-hydroxyl-4-oxo-5-(trifluoromethyl)-3-pyrrole-3-carbonitrile		Animals
CL152837	4-hydroxy-2-(p-chlorophenyl)-5-(carboxylic)- pyrrole-3-carbonitrile a hydroxylated CL303268 metabolite		Animals
CL152832	destrifluoromethyl CL303268		Animals

Code Names	Chemical name	Structure	Where found
CL152835	desbromo-N-carboxymethylmethoxy chlorfenapyr		Animals
CL325157	{[3-bromo-5-(p-chlorophenyl)-4-cyano-2-(trifluoromethyl) pyrrol-1-yl]methyl}-acetic acid		Animals

Plant metabolism

The fate of chlorfenapyr in plants was investigated by the 2012 JMPR following foliar spray application of ^{14}C-radiolabelled substance to oranges, tomatoes, head lettuce, potatoes and cotton. A detail assessment of these studies is presented in the 2012 JMPR Report. For the current Meeting, an additional plant metabolism study on tomatoes was submitted

The metabolism of chlorfenapyr in field grown tomatoes was investigated by application of phenyl- or pyrrole-^{14}C-radiolabelled substance with three foliar sprayings of 0.48 kg ai/ha (29 days before harvest), 0.48 kg ai/ha (15 days before harvest) and 0.24 kg ai/ha (1 day before harvest). Leaves and fruit collected one day after the last application were analysed for the composition of residues.

Both in leaves and fruits, the extraction of radioactivity with methanol, followed by water, was nearly complete (99.2–99.6% TRR). TRR levels in fruits ranged from 1.3 to 1.8 mg eq/kg and in leaves from 34 to 44 mg eq/kg.

The identification of the radioactive residues revealed mostly unchanged chlorfenapyr, representing 92–97% of the TRR in the fruits and 96–98% TRR in the leaves. The only metabolite identified was tralopyril (CL303268) in fruits (1.0% TRR, 0.018 mg eq/kg) and leaves (0.8% TRR, 0.35 mg eq/kg) treated with the pyrrole-label. However, small amounts of this compound were also found in the spraying solution, suggesting its formation before application.

Methods of analysis

The current Meeting received two additional analytical methods for plant matrices.

Method G0001/01 involves extraction with methanol/water (85:15, v/v) and partitioning with ethyl acetate. Analysis of chlorfenapyr and tralopyril (CL303268) is performed by LC-MS/MS. The method is suitable for measuring both analytes in matrices of high water, high protein and high acid content with a LOQ of 0.01 mg/kg.

Method G0002/01 is comparable to G0001/01, but targets the metabolite CL322250. The method is suitable for measuring the analyte in matrices of high protein and high oil content with a LOQ of 0.01 mg/kg.

Using radiovalidation, the extraction efficiency of the QuEChERS multimethod (submitted in 2012) and of the newly submitted method G0001/01 (methanol/water, 85:15 v/v) was tested on tomato leaves and fruits obtained from the plant metabolism study summarised above. Both methods were capable of extracting 97–104% of the TRR from the fruits and 88–105% of the TRR from the leaves.

A specialised method for the analysis of chlorfenapyr in tea (dried tea and infusion) was submitted in 2012. Dried tea was extracted with acetone/water. The dried tea extract or the tea infusion are cleaned by Florisil column chromotagraphy and analysed with GC-ECD detection. The current Meeting noted that the method was tested with a lowest fortification level of 0.8 mg/kg for both matrices and, in contrast to its previous evaluation in 2012, did not reach a sufficiently low LOQ to quantify residues found in infusions with acceptable reliability.

Stability of residues in stored analytical samples

The current Meeting received additional information on the storage stability of chlorfenapyr, tralopyril (CL303268) and CL322250 in plant matrices stored at -18 °C.

The parent compound and its metabolite tralopyril (CL303268) were stable for at least 12 months in grapes and rice grain, for at least 14 months in apples and dry beans and for at least 15 months in dry soya beans.

CL322250 was stable in dry soya beans for at least 12 months.

Definition of the residue

The current Meeting received new data on the toxicity of the metabolite tralopyril (CL303268) to allow consideration of residue definitions for dietary exposure to plant and animal commodities.

The Meeting also received an additional plant metabolism study on tomatoes, which exclusively showed unchanged chlorfenapyr in the samples investigated. No additional data on animal commodities was submitted.

The Meeting therefore confirms its previous recommendation of chlorfenapyr for compliance with the MRL for plant and animal commodities.

For dietary exposure purposes, the 2012 Meeting could not reach a conclusion on the residue definition due to absence of appropriate health-based guidance values for tralopyril (CL303268). The current Meeting received new toxicological information and established a potency factor of 10 for a comparison of exposure of tralopyril (CL303268) with both the ADI and the ARfD for parent chlorfenapyr. The Meeting concluded that tralopyril (CL303268), although present in low proportions up to 3.3% TRR, has the potential to contribute significantly to the overall toxicological burden due to its potency factor of 10 and – besides chlorfenapyr - should be considered for the estimation of the dietary exposure in plant commodities.

New information on the nature of residues during processing was submitted to the current Meeting (see Fate of residues during processing). Under simulated sterilization (pH6, 120°C, 20min), chlorfenapyr was significantly degraded (*ca.* 70% AR remaining) into CL322250 (32-34% AR). Formation of tralopyril (CL303268) was not observed. In an additional study conducted with tralopyril (CL303268), it was completely degraded into CL322250 under simulated baking/brewing/cooking and sterilization.

For dietary exposure assessment of CL322250, the Meeting noted that as no specific toxicity data were available for the metabolite the TTC approach could be followed[1]. The toxicological threshold for a Cramer Class 3 compound was applied (1.5 µg/kg bw). The estimated exposure based on plant commodities that may potentially be subject to sterilization (tomatoes, peppers, soya beans) and on animal commodities from the goat and laying hen metabolism studies, adjusted to the estimated livestock animals dietary burden, resulted in a maximum long-term exposure of 0.003 µg/kg bw, below the applicable threshold of toxicological concern. The Meeting concluded that CL322250 was unlikely to present a dietary exposure concern from the uses evaluated by the current Meeting.

The Meeting decided to define the residue for dietary risk assessment for plant commodities to be the sum of chlorfenapyr and 10 times its metabolite tralopyril.

For dietary risk assessment for animal commodities, chlorfenapyr was the predominant residue in most goat and poultry matrices with tralopyril (CL303268) often being present as a major metabolite (4.5–31% TRR). The Meeting concluded that both compounds should be considered for the estimation of dietary exposure in animal commodities, especially taking into account the higher relative toxicity of tralopyril compared to parent.

In ruminants, CL325195 together with its conjugates (goat liver and kidney) and CL152837 together with its conjugates (goat liver and kidney) were found in major proportions (12–48% TRR and 7–24% TRR, respectively), mainly released by hydrolysis.

In poultry tissues, the primarily conjugated metabolites CL152832 (chicken muscle and kidney, 2–23% TRR), CL152835 and CL325157 (chicken liver and kidney, 23–51% TRR) were found in major proportions, in total exceeding the residues of chlorfenapyr by up to a factor of 10.

For dietary risk assessment, the Meeting noted that for metabolites CL325195, CL152837, CL152832, CL152835 and CL325157 no information is available on their toxicity. The Meeting decided to apply the TTC approach to these metabolites. The estimated exposure based on animal commodities from the goat and laying hen metabolism studies, adjusted to the estimated livestock animals dietary burden, resulted in the following maximum long-term exposures:

CL3251950.018 µg/kg bw

CL1528370.015 µg/kg bw

CL152832< 0.001 µg/kg bw

CL1528350.003 µg/kg bw

CL3251570.003 µg/kg bw

[1] See Toxicology section of 2018 JMPR Report for further details

The Meeting noted that all estimated exposures are below the applicable threshold of toxicological concern for Cramer Class 3 compounds. The Meeting concluded that CL325195, CL152837, CL152832, CL152835 and CL325157 were unlikely to present a dietary exposure concern from the uses evaluated by the current Meeting.

In summary, the Meeting decided to define the residue for dietary risk assessment for animal commodities as the sum of chlorfenapyr and 10 times its metabolite tralopyril.

The Meeting confirmed the following residue definition for chlorfenapyr:

Definition of the residue for compliance with the MRL for animal and plant commodities: *chlorfenapyr*.

The residue is fat soluble.

The Meeting recommended the following residue definition for chlorfenapyr:

Definition of the residue for dietary risk assessment for plant and animal commodities: sum of chlorfenapyr plus 10 × 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)-pyrrole-3-carbonitrile (tralopyril)

The Meeting concluded that if future uses of chlorfenapyr result in an increase in the exposure to the metabolites CL322250, CL325195, CL152837, CL152832, CL152835 and CL325157, a reconsideration of the residue definition for dietary risk assessment may become necessary.

Results of supervised residue trials on crops

The current Meeting received supervised trial data for applications of chlorfenapyr on soya beans and tea conducted in Brazil and Japan, respectively.

In 2012, the Meeting evaluated uses of chlorfenapyr on citrus fruit, papaya, garlic, bulb onions, melons (except watermelons), peppers, egg plants, tomatoes, potatoes and green tea. However, none of the supervised field trials submitted in 2012 analysed the metabolite tralopyril (CL303268), which was considered relevant for estimating dietary exposure by the current Meeting. Based on the plant metabolism data available, the Meeting estimated the following conversion factors to account for the contribution of tralopyril:

$$Conversion\ \ Factor = 1 + \frac{10 \times \%\ \ TRR_{Tralopyril}}{\%\ \ TRR_{Chlorfenapyr}}$$

Crop group	Chlorfenapyr	% TRR tralopyril (CL303268)	Conversion factor
Citrus fruits	75.0% TRR[(a)]	3.3% TRR [a]	1.44 (1 + (10*3.3% TRR) ÷ 75.0% TRR)
Papaya	No data	No data	1.44 (extrapolation from citrus fruit, based on comparable GAP and metabolism crop group)
Garlic, bulb onions	<LOQ[(b)]	<LOQ[(b)]	1
Melons (except watermelons)	38-50% TRR[(c)]	Not detected	1
Peppers, eggplant, tomato	92-97% TRR[(d)]	Up to 1% TRR[(d)] (probable contamination)	1
Potato	<LOQ[(b)]	<LOQ[(b)]	1
Tea	75.1% TRR[(e)]	1.3% TRR[(e)]	1.17 (1+(10*1.3% TRR) ÷ 75.1% TRR)

[a] Highest chlorfenapyr/tralopyril ratio obtained from the orange metabolism study evaluated in 2012, DALA 14 following application of [2-pyrrole-^{14}C]-chlorfenapyr, corresponding to 14 day PHI from the maximum GAP used in 2012

[b] Based on the 2012 potato metabolism study as representative for root and tuberous crops, Mallipudi 1995 CK-640-008

[c] Based on the 2012 tomato metabolism study DALA 14 by Kao 1995 CK-640-007, corresponding to 14 day PHI from the maximum GAP used in 2012

[d] Based on tomato metabolism study evaluated in 2018, DALA 1 corresponding to 0 day PHI from the maximum GAP used in 2012

[e] Highest chlorfenapyr/tralopyril ratio obtained from lettuce metabolism study evaluated in 2012, DALA 3 following application of [2-pyrrole-^{14}C]-chlorfenapyr, approximating the 7 day PHI from the maximum GAPs used in 2012 and 2018

For the purpose of estimating the livestock animal's dietary burden, the Meeting noted that chlorfenapyr is the predominant residue in plants. Tralopyril (CL303286) only makes a small contribution to the residue concentration in feed commodities. Since most of tralopyril (CL303268) found in animal commodities is formed by animal metabolism after exposure to

the parent, the Meeting decided that chlorfenapyr sufficiently addresses residues in feed commodities for the estimation the livestock animals dietary burden.

The current Meeting received supervised field trial data for applications of chlorfenapyr on soya beans and tea conducted in Brazil and Japan, respectively. In soya bean trials, parent chlorfenapyr and tralopyril (CL303268) were analysed but found at levels near the LOQ (parent) or below the LOQ (tralopyril). In the metabolism study on cotton evaluated in 2012, which represents pulse and oilseed crops, no tralopyril was found in the seeds. Taking into account the overall low proportion of tralopyril in the total residue (up to 3.3% TRR) in all crops investigated, the Meeting concluded that the LOQ in combination with a toxicological potency factor of 10 results in a strong overestimation of the true residue. Therefore, the metabolite is only added to the parent residue, when both analytes were found at levels above the LOQ. An example of the calculation is presented in the table below:

Chlorfenapyr	Tralopyril (CL303268)	Total residue (sum of chlorfenapyr and 10 × tralopyril, expressed as chlorfenapyr)
< 0.01 mg/kg	< 0.01 mg/kg	< 0.01 mg/kg
0.03 mg/kg	< 0.01 mg/kg	0.03 mg/kg
0.03 mg/kg	0.01 mg/kg	0.13 mg/kg (0.03 mg/kg + 10×0.01 mg/kg)

Citrus fruit (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr on citrus in Brazil (three foliar spray applications at 15 g ai/hL with a PHI of 14 days) and identified the following residue populations based on the supervised field trials submitted:

In oranges, chlorfenapyr residues in whole fruit from trials in Brazil, matching the GAP in Brazil were (n = 7): 0.14, 0.18, 0.39, 0.44, 0.53, 0.54 and 0.87 mg/kg.

In limes, chlorfenapyr residues in whole fruit from trials in Brazil, matching the GAP in Brazil were (n = 8): 0.05, 0.08, 0.13, 0.15, 0.17, 0.28, 0.31 and 0.49 mg/kg.

The 2012 Meeting estimated a maximum residue level of 1.5 mg/kg for citrus fruits, based on the dataset for orange fruits. However, the current Meeting noted that the previous proposal on citrus fruits was not in line with the current procedure for estimating crop group maximum residue levels and the Codex Food Classification System. As a result the Meeting decided to limit its recommendations to the specific citrus crop subgroups.

The Meeting estimated a maximum residue level of 0.8 mg/kg for the subgroup of Lemons and Limes.

The Meeting estimated a maximum residue level of 1.5 mg/kg for the subgroup of Oranges, Sweet, Sour.

The current Meeting noted that in the metabolism study on oranges evaluated in 2012 the pulp (7 DAT) contained a maximum of 1.7% of the TRR.

The current Meeting applied a conversion factor of 1.44 and a whole fruit to pulp factor of 0.017 (based on the highest relative amount of TRR found in the pulp) to the median and highest residues in limes and estimated a STMR value of 0.004 mg/kg (0.16 mg/kg × 1.44 × 0.017) and a HR value of 0.012 mg/kg (0.49 mg/kg × 1.44 × 0.017) for total chlorfenapyr in the pulp of limes and lemons. For kumquats, which are consumed with peel, the Meeting estimated a STMR value of 0.23 mg/kg (0.16 mg/kg × 1.44) and a HR value of 0.71 mg/kg (0.49 mg/kg × 1.44).

The current Meeting applied a conversion factor of 1.44 and a whole fruit to pulp factor of 0.017 (based on the highest relative amount of TRR found in the pulp) to the median and highest residues in oranges and estimated a STMR value of 0.011 mg/kg (0.44 mg/kg × 1.44 × 0.017) and a HR value of 0.021 mg/kg (0.87 mg/kg × 1.44 × 0.017) for total chlorfenapyr in orange pulp.

For the purpose of estimating residues in processed and animal commodities, the current Meeting also estimated a median residue of 0.44 mg/kg for chlorfenapyr in citrus fruits, based on oranges.

Papaya (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr on papaya in Brazil (three foliar spray applications at 12 g ai/hL with a PHI of 14 days) and identified the following residue population based on the supervised field trials submitted:

In papaya, chlorfenapyr residues in whole fruit from trials in Brazil, matching the GAP in Brazil were (n = 5): < 0.01, 0.03, 0.05, 0.11 and 0.12 mg/kg.

The 2012 Meeting estimated a maximum residue level of 0.3 mg/kg for papaya.

The current Meeting applied a conversion factor of 1.44 to the median and highest residue in papaya and estimated a STMR value of 0.072 mg/kg (0.05 mg/kg × 1.44) and a HR value of 0.17 mg/kg (0.12 mg/kg × 1.44).

Garlic (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr to garlic in Brazil (three foliar spray applications at 24 g ai/hL with a PHI of 14 days) and identified the following residue population based on the supervised field trials submitted:

In garlic, chlorfenapyr residues from trials in Brazil, matching the GAP in Brazil were: (n = 5): < 0.01(5) mg/kg.

The 2012 Meeting estimated a maximum residue level of 0.01(*) mg/kg for garlic.

The current Meeting applied a conversion factor of 1 to the median and highest residue in garlic and estimated STMR and HR values of 0.01 mg/kg (0.01 mg/kg × 1), respectively.

Onion, bulb (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr on bulb onions in Brazil (three foliar spray applications at 180 g ai/ha with a PHI of 14 days) and identified the following residue population based on the supervised field trials submitted:

In bulb onions, chlorfenapyr residues from trials in Brazil, matching the GAP in Brazil were: (n = 9): < 0.01(9) mg/kg.

The 2012 Meeting estimated a maximum residue level of 0.01(*) mg/kg for onions, bulb.

The current Meeting applied a conversion factor of 1 to the median and highest residue in bulb onions and estimated STMR and HR values of 0.01 mg/kg (0.01 mg/kg × 1), respectively.

Melons, except watermelons (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr on melons in Brazil (three foliar spray applications at 24 g ai/hL with a PHI of 14 days) and identified the following residue population based on the supervised field trials submitted:

In whole fruits, chlorfenapyr residues from trials in Brazil, matching the GAP in Brazil were (n = 9): < 0.01(2), 0.01, 0.02(2), 0.06(2) and 0.17(2) mg/kg.

In melon pulp, chlorfenapyr residues from trials in Brazil, matching the GAP in Brazil were (n = 5): < 0.01(4) and 0.01 mg/kg.

The 2012 Meeting estimated a maximum residue level of 0.4 mg/kg for melons, except watermelons.

The current Meeting applied a conversion factor of 1 to the median and highest residue in melon pulp and estimated a STMR value of 0.01 mg/kg (< 0.01 mg/kg × 1) and a HR value of 0.01 mg/kg (0.01 mg/kg × 1).

Peppers (including pepper, chili and pepper sweet) (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr on peppers in Brazil (three foliar spray applications at 7.2 g ai/hL with a PHI of 14 days) and identified the following residue population based on the supervised field trials submitted:

In peppers, chlorfenapyr residues from trials in Brazil, matching the GAP in Brazil were (n = 7): < 0.01, 0.01, 0.04, 0.05, 0.06, 0.13 and 0.15 mg/kg.

The 2012 Meeting estimated a maximum residue level of 0.3 mg/kg for peppers.

The current Meeting applied a conversion factor of 1 to the median and highest residue in peppers and estimated a STMR value of 0.05 mg/kg (0.05 mg/kg × 1) and a HR value of 0.15 mg/kg (0.15 mg/kg × 1).

Based on the estimated maximum residue level for peppers and a default dehydration factor of 10, the 2012 Meeting recommended a maximum residue level of 3 mg/kg for chili peppers (dry).

The current Meeting estimated a STMR value of 0.5 mg/kg (0.05 mg/kg × default factor 10) and a HR value of 1.5 mg/kg (0.15 mg/kg × default factor 10) for chili pepper (dry).

Egg plant (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr on eggplant in Mexico (up to 96 g ai/ha with a PHI of 0 days) and identified the following residue population based on the supervised field trials submitted:

In eggplant, chlorfenapyr residues from trials matching the GAP were (n = 4): 0.08, 0.09, 0.1 and 0.2 mg/kg.

The 2012 Meeting estimated a maximum residue level of 0.3 mg/kg for eggplant. However, the current Meeting noted that eggplant is a major commodity in consumption. Based on current practice, regarding the minimum number of supervised field

trials required for estimating maximum residue levels, the Meeting considered four trials as insufficient to estimate a maximum residue level for eggplant.

Tomatoes (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr to tomatoes in Brazil (three foliar spray applications at 12g ai/hL with a PHI 7 days) and identified the following residue population based on the supervised field trials submitted:

In tomatoes, proportionally adjusted chlorfenapyr residues from trials in Brazil and Argentina were (n = 8): 0.02, 0.05, 0.05, 0.06, 0.07, 0.11, 0.19 and 0.19 mg/kg.

The 2012 Meeting estimated a maximum residue level of 0.4 mg/kg for tomatoes.

The current Meeting applied a conversion factor of 1 to the median and highest residue in tomatoes and estimated a STMR value of 0.065 mg/kg (0.065 mg/kg × 1) and a HR value of 0.19 mg/kg (0.19 mg/kg × 1). The current Meeting also estimated a median residue of 0.065 mg/kg for the estimation of maximum residue levels in processed commodities.

Potato (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr on potatoes in Brazil (180 g ai/ha with a PHI of 7 days) and identified the following residue population based on the supervised field trials submitted:

In potatoes, chlorfenapyr residues from trials matching the GAP were (n = 9): < 0.01(9) mg/kg.

The 2012 Meeting estimated a maximum residue level of 0.01(*) mg/kg for potatoes.

The current Meeting applied a conversion factor of 1 to the median and highest residue in potatoes and estimated STMR and HR values of 0.01 mg/kg (< 0.01 mg/kg × 1), respectively.

Soya beans (dry)

Chlorfenapyr is registered in Brazil for soya beans at maximum rates of 3 × 0.29 kg ai/ha (5 days interval) with a PHI of 30 days. Supervised field trials from Brazil matching this GAP were submitted.

The Meeting noted that in the metabolism study on cotton seed, which is representative for pulse and oilseed crops, no formation of tralopyril was observed. Therefore supervised field trial data on soya beans without analysis of tralopyril are acceptable both for the estimation of maximum residue levels and of the dietary risk assessment.

In soya bean seeds (dry) residues of chlorfenapyr following GAP treatment (±25%) were (n = 14): < 0.01(8), 0.01, 0.013, 0.019, 0.024, 0.046 and 0.05 mg/kg.

The Meeting estimated a maximum residue level of 0.08 mg/kg and a STMR of 0.01 mg/kg for soya beans (dry).

Tea, Green, Black (black, fermented and dried) (2012)

The 2012 Meeting evaluated the data supporting the use of chlorfenapyr to tea, green, black (black, fermented and dried) in Japan (5 g ai/hL, 7 day interval with a PHI of 7 days) and identified the following residue population based on the supervised field trials submitted:

In green tea, chlorfenapyr residues from trials matching the GAP were (n = 4): 4.2, 4.5, 16 and 28 mg/kg.

The 2012 Meeting estimated a maximum residue level of 60 mg/kg for tea, green, black (black, fermented and dried).

The current Meeting applied a conversion factor of 1.17 to the median residue and estimated a STMR value of 12 mg/kg (10.25 mg/kg × 1.17), in tea, green, black (black, fermented and dried).

Soya bean fodder (hay)

Chlorfenapyr is registered in Brazil for soya beans at maximum rates of 3 × 0.29 kg ai/ha with a PHI of 30 days. Supervised field trials from Brazil according to this GAP were submitted.

In soya bean fodder (as received) residues of chlorfenapyr following GAP treatment (±25%) were (n = 8): 0.99, 1.4, 1.5, 1.7, 1.9, 2.2, 2.4 and 3.9 mg/kg.

The current Meeting estimated a maximum residue level of 7 mg/kg (DM, 85% DM content assumed) for soya bean fodder.

For the purpose of estimating residues in animal commodities, the Meeting estimated a median residue of 1.6 mg/kg and a highest residue of 3.9 mg/kg for chlorfenapyr in soya bean fodder (as received).

Soya bean aspirated grain fractions (AGF)

Chlorfenapyr is registered in Brazil for soya beans at maximum rates of 3 × 0.29 kg ai/ha (5 days interval) with a PHI of 30 days. Supervised field trials from Brazil according to this GAP were submitted.

In soya bean AGF residues of chlorfenapyr following GAP treatment (±25%) were (n = 4): 6.5, 12, 12, 91 mg/kg.

For the purpose of estimating residues in animal commodities, the Meeting estimated a median residue of 12 mg/kg for chlorfenapyr in soya bean, aspirated grain fraction.

Residues in rotational crops

The 2012 Meeting concluded that residues of chlorfenapyr in rotational crop at the minimum plant back interval of 31 days could occur, but that residues would be at or near the limit of quantification of the analytical method (0.01 mg/kg) and do not require further consideration.

Fate of residues during processing

The Meeting received information on the hydrolysis of ^{14}C-phenyl-chlorfenapyr and -tralopyril (CL303268) as well as processing studies using unlabelled material on soya beans.

In a hydrolysis study using ^{14}C-phenyl-chlorfenapyr or ^{14}C-phenyl-tralopyril (CL303268) typical processing conditions were simulated (pasteurisation, pH 4, 90 °C, 20 minutes; baking/brewing/cooking, pH 5, 100 °C, 60 minutes; and sterilisation, pH 6, 120 °C for 20 minutes).

Chlorfenapyr remained stable (98.7–100% AR remaining) for simulated pasteurization and baking/brewing/cooking. However, significant degradation into CL322250 (chlorfenapyr: 69–72% AR, CL322250: 32–34% AR) was observed during simulated sterilization.

Tralopyril (CL303268) only remained stable during simulated pasteurisation (85–86% AR remaining). For baking/brewing/cooking and sterilization it was completely degraded into CL322250.

The fate of chlorfenapyr residues has been examined in commercial processing studies on soya beans (evaluated by the current Meeting) and on citrus fruits and tomatoes (evaluated by the 2012 JMPR).

In soya beans, residues of chlorfenapyr, tralopyril (CL303268) and CL322250 were analysed. However, only parent chlorfenapyr was found above the LOQ of 0.01 mg/kg in raw commodities and in processed products. Processing factors for soya bean seeds are therefore based on parent chlorfenapyr only.

In citrus fruits and tomatoes only parent chlorfenapyr was analysed. Tralopyril (CL 303268) is included in the residue definition for dietary risk assessment purposes for plant commodities and it is more toxic than parent chlorfenapyr. The Meeting decided that the processing factors derived in 2012 do not reflect the transfer or formation potential of tralopyril residues in processed products intended for human consumption and cannot be used for the estimation of STMR-P values. However, the Meeting noted that residues in processed feed commodities based on parent can be used for estimating the livestock animals dietary burden and are not affected by the potency factor of 10 for tralopyril. The Meeting decided to use the processing factors estimated by the 2012 JMPR for this purpose.

Estimated processing factors for the commodities considered at this Meeting are summarised below.

Raw commodity	Processed commodity	Chlorfenapyr		
		Individual processing factors	Mean or best estimate processing factor	Median or STMR-P in mg/kg
Citrus (see 2012 Report) Median: 0.44 mg/kg[(a)]	Citrus pulp, wet	0.99, 1.08	1.0	Median: 0.44
	Citrus pulp, dry	0.55, 0.87, 2.3, 2.4	1.6	Median: 0.704
	Orange oil	3.1, 17, 23, 70	70 (best estimate)	-
Soya bean seeds, dry Median and STMR: 0.01 mg/kg	Meal	0.1, 0.21, 0.27	0.21	Median: 0.0021
	Oil, crude	3.3, 4.5, 5.2	4.5	STMR-P: 0.045
Tomato (see 2012 Report)	Tomato pomace, wet	63	63 (best estimate)	Median: 4.095
Median: 0.065 mg/kg	Tomato pomace, dry	157	157 (best estimate)	Median: 10.2

[a] For oranges

Based on the maximum residue level for citrus fruits of 1.5 mg/kg and the PF of 70 for orange oil, the Meeting estimated a maximum residue level of 100 mg/kg for orange oil. As no information was available on the behaviour of the metabolites tralopyril (CL303268) and CL322250 during citrus processing, no corresponding STMR-P value could be estimated.

Based on the maximum residue level for soya bean seeds, dry of 0.08 mg/kg and the PF of 4.5 for crude oil, the Meeting estimated a maximum residue level of 0.4 mg/kg for soya bean oil, crude.

Residues in animal commodities

Farm animal feeding studies

No additional information on farm animal feeding was submitted to the current Meeting. Please refer to the 2012 JMPR Report.

Estimation of livestock dietary burdens

Dietary burdens were calculated for beef cattle, dairy cattle, broilers and laying poultry based on feed items evaluated by the JMPR. The dietary burdens, estimated using the OECD diets listed in Appendix IX of the 2016 edition of the FAO manual, are presented in Annex 6 and summarised below

The Meeting was informed by an official communication of the government of Australia that no fodder crops are imported. Therefore soya bean hay, which would represent the predominant feed item for the Australian dietary burden, has been excluded for that region. Potential feed items include: citrus pulp, tomato pomace, potato culls, soya beans, soya bean meal, soya bean hay and soya bean aspirated grain fractions.

	Livestock dietary burdens for the estimation of maximum residue levels, STMRs and HRs (chlorfenapyr, ppm of dry matter diet)							
	US-Canada		EU		Australia		Japan	
	max.	mean	max.	Mean	max.	mean	max.	mean
Beef cattle	0.89	0.89	0.0.1	0.1	2.4	2.4	0.0.003	0.003
Dairy cattle	1.1	0.56	0.37	0.37	2.4 [a]	2.4 /A	0.003	0.0025
Poultry - broiler	0.003	0.003	0.008	0.008	0.002	0.002	< 0.001	< 0.001
Poultry - layer	0.003	0.003	0.47 [b]	0.20 [c]	0.002	0.002	< 0.001	< 0.001

[a] Highest maximum and mean beef or dairy cattle burden suitable for maximum residue level, STMR and HR (except milk) estimates for mammalian meat and milk

[b] Highest maximum broiler or laying hen burden suitable for maximum residue level and HR estimates for poultry tissues and eggs

[c] Highest mean broiler or laying hen burden suitable for STMR estimates for poultry tissues and eggs

Animal commodities maximum residue levels

For maximum residue level estimation, the highest residues of chlorfenapyr were estimated for the maximum dietary burden (2.4 ppm) by interpolating between the 2.2 ppm and the 6.8 ppm feeding level in the dairy cow feeding study. The highest tissue concentrations of chlorfenapyr from individual animals within those feeding groups were selected and for milk the mean residues were used.

Chlorfenapyr feeding study	Feed level	Chlorfenapyr				
	(ppm)	(mg/kg) in milk	(mg/kg) in muscle	(mg/kg) in kidney	(mg/kg) in liver	(mg/kg) in fat
Maximum residue level: dairy cattle						
Feeding study (HR for each dose group, except for milk)	2.2 6.8	0.017 0.019	0.017 0.022	< 0.05 < 0.05	< 0.05 0.054	0.429 0.597
Dietary burden and residue estimate	2.4	0.017	0.017	< 0.05	0.05	0.436

The Meeting estimated maximum residue levels of 0.6 (fat) mg/kg for chlorfenapyr in meat (from mammals other than marine mammals) and mammalian fat, 0.05 mg/kg for edible offal, mammalian and 0.03 mg/kg for milks.

For dietary exposure purposes, the available dairy cattle feeding study did not include analysis of tralopyril (CL303268). The Meeting decided to derive conversion factors based on the goat metabolism study to estimate the contribution of tralopyril (CL303268).

$$Conversion\ \ Factor = 1 + \frac{10 \times \%\ \ TRR_{Tralopyril}}{\%\ \ TRR_{Chlorfenapyr}}$$

Matrix	**% TRR found per label**		
	Chlorfenapyr	**Tralopyril**	**Total conversion factor (based on mean % TRR)**
Milk	Phenyl: 24.7% Pyrrole: 68.4% Mean: 46.6%	Phenyl: 8.4% Pyrrole: 5.5% Mean: 6.95%	**2.5** [1 + 10×6.95% ÷ 46.6%]
Muscle	Phenyl: 52% Pyrrole: 28.7% Mean: 40.4%	Phenyl: 1.9% Pyrrole: 2.5% Mean: 2.2%	**1.5** [1 + 10×2.2% ÷ 40.4%]
Kidney	Phenyl: 2.0% Pyrrole: 3.8% Mean: 2.9%	Phenyl: 1.2% Pyrrole: 3.8% Mean: 2.5%	**9.6** [1 + 10×2.5% ÷ 2.9%]
Liver	Phenyl: 3.5% Pyrrole: 6.9% Mean: 5.2%	Phenyl: 5.6% Pyrrole: 4.1% Mean: 4.85%	**10** [1 + 10×4.85% ÷ 5.2%]
Fat	Phenyl: 60.9% Pyrrole: 60.8% Mean: 60.8%	Phenyl: 4.5% Pyrrole: 12.3% Mean: 8.4%	**2.4** [1 + 10×8.4% ÷ 60.8%]

Taking into account the conversion factors derived above, the Meeting estimated both STMR and HR values of 0.043 mg/kg (0.017 mg/kg × 2.5) in milk (STMR only), 0.026 mg/kg in muscle (0.017 mg/kg × 1.5), 0.48 mg/kg in kidney (0.05 mg/kg × 9.6), 0.54 mg/kg in liver (0.054 mg/kg × 10) and 1.0 mg/kg in fat (0.436 mg/kg × 2.4), based on the total residue.

No feeding study on poultry was available to be compared with the maximum and mean dietary burden for laying hens of 0.47 ppm and 0.2 ppm, respectively. The Meeting decided to estimate maximum residues levels, STMR and HR values in poultry matrices and eggs based on the metabolism study.

Since most of the residue for dietary exposure purposes includes conjugates, only the highest dose rates involving hydrolysis were considered. Also, for the estimation of maximum residue levels and the HR, the highest single residue from each of the radiolabels is taken into account. For the estimation of STMR values, the mean of both radiolabels is considered, since no cleavage of the parent molecule was observed.

Chlorfenapyr metabolism study	Feed level	Chlorfenapyr				
	(ppm)	(mg/kg) in eggs	(mg/kg) in muscle	(mg/kg) in kidney	(mg/kg) in liver	(mg/kg) in fat
Maximum residue level: laying hens						
Metabolism study (HR for each dose group)	15 (ph) 16 (ph) 14 (py) 17 (py)	**0.168** **0.16**	**0.005** **0.0062**	 **0.095** **0.103**	 **0.107** **0.154**	**0.39** 0.29
Dietary burden and residue estimate (selected radiolabel)	0.47	0.005 (both labels)	< 0.001 (both labels)	0.003 (both labels)	0.004 (both labels)	0.012

Values in bold represent the radio-label selected for the estimation

ph: phenyl-radiolabel

py: pyrrole-radiolabel

The Meeting estimated maximum residue levels of 0.02 mg/kg for poultry meat (fat), 0.02 mg/kg for poultry fat and 0.01 mg/kg for poultry, edible offal and eggs.

Chlorfenapyr metabolism study	Feed level	Total residue				
	(ppm)	(mg/kg) in eggs	(mg/kg) in muscle	(mg/kg) in kidney	(mg/kg) in liver	(mg/kg) in fat
Dietary exposure: laying hens						
Metabolism study (HR for each dose group)	15 (ph) 16 (ph) 14 (py) 17 (py)	**1.5** 0.84	0.015 **0.02**	 0.56 **0.79**	 1.4 **2.1**	**0.58** 0.48
Dietary burden and residue estimate (selected radiolabel)	0.47 (max)	0.047	0.0007	0.022	0.058	0.018
	0.2 (mean)	0.02	0.0003	0.009	0.025	0.008

Values in bold represent the radio-label selected for the estimation

ph: phenyl-radiolabel

py: pyrrole-radiolabel

The Meeting estimated HR and STMR values of 0.047 and 0.02 mg/kg for eggs, 0.007 and 0.003 mg/kg for poultry muscle, 0.018 and 0.008 mg/kg for poultry fat, 0.022 and 0.009 mg/kg for poultry kidney and 0.058 and 0.025 mg/kg for poultry liver, respectively.

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.

The Meeting confirmed the following residue definitions for chlorfenapyr:

Definition of the residue for compliance with the MRL for plant and animal commodities: *chlorfenapyr*.

Definition of the residue for dietary risk assessment for plant and animal commodities: sum of chlorfenapyr plus 10 × 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)-pyrrole-3-carbonitrile (tralopyril)

The residue is fat soluble.

The Meeting concluded that if future uses of chlorfenapyr result in an increase in exposure to the metabolites CL322250, CL325195, CL152837, CL152832, CL152835 and CL325157, a reconsideration of the residue definition for dietary risk assessment may become necessary.

Commodity		Recommended maximum residue level, mg/kg		STMR or STMR-P, mg/kg	HR, HR-P or highest residue, mg/kg
CCN	Name	New	Previous		
HS 0444	Chili pepper, dry	3		0.5	1.5
MO 0105	Edible offal (Mammalian)	0.05		Liver: 0.54 Kidney: 0.48	Liver: 0.54 Kidney: 0.48
PE 0112	Eggs	0.01		0.02	0.047
VA 0381	Garlic	0.01*		0.01	0.01
FC 0002	Lemons and Limes, subgroup of (includes all commodities in this subgroup)	0.8		Whole fruit: 0.23 Pulp: 0.004	Whole fruit: 0.71 Pulp: 0.012
MF 0100	Mammalian fats	0.6		1.0	1.0
MM 0095	Meat (from mammals other than marine mammals)	0.6 (fat)		0.026 (muscle)	0.026 (muscle)
VC 0046	Melons, except Watermelon	0.4		0.01	0.01
ML 0106	Milks	0.03		0.043	-
VA 0385	Onion, bulb	0.01*		0.01	0.01
FC 0004	Oranges, Sweet, Sour, subgroup of (includes all commodities in this subgroup)	1.5		0.011	0.021
FI 0350	Papaya	0.3		0.072	0.17
VO 0051	Peppers	0.3		0.05	0.15
PO 0111	Poultry, edible offal of	0.01		Liver: 0.025 Kidney: 0.009	Liver: 0.058 Kidney: 0.022
PF 0111	Poultry, fats	0.02		0.008	0.018
PM 0110	Poultry, meat	0.02 (fat)		0.003 (muscle)	0.007 (muscle)
VR 0589	Potato	0.01*		0.01	0.01
VD 0541	Soya bean (dry)	0.08		0.01	-
AL 0541	Soya bean fodder	7 (DM)		Median: 1.6 (as)	Highest: 3.9 (as)
OC 0541	Soya bean, crude oil	0.4		0.045	-
VO 0448	Tomatoes	0.4		0.065	0.19
DT 1114	Tea, Green, Black (black, fermented and dried)	60		12	-

Dietary exposure and feed burden only

Commodity		Median, mg/kg	Highest residue, mg/kg
CCN	Name		
AB 0001	Citrus pulp, dry	Chlorfenapyr: 1.6	-
	Soya bean, aspirated grain fractions	Chlorfenapyr: 12 Total: 13	-
	Tomato pomace, wet	Chlorfenapyr: 4.095	-

FURTHER WORK OR INFORMATION

- Supervised field trial data involving analysis of tralopyril
- Ruminant feeding study involving analysis according to the residue definition for dietary risk assessment
- Laying hen feeding study
- Processing studies involving analysis of tralopyril and CL322250

DIETARY RISK ASSESSMENT

Long-term exposure

The ADI for chlorfenapyr is 0–0.03 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for chlorfenapyr were estimated for the 17 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by the present JMPR. The results are shown in Annex 3 of the 2018 JMPR Report. The IEDIs ranged 1–6% of the maximum ADI.

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

Acute exposure

The ARfD for chlorfenapyr is 0.03 mg/kg bw. The International Estimate of Short Term Intakes (IESTIs) for chlorfenapyr 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 0–60% of the ARfD for children and 0–60% for the general population.

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

REFERENCES

Code	Author	Year	Title, Institute, Report reference
CHLORFEN_001	Schaffert D., Jung T.	2017	Metabolism of ^{14}C-BAS 306 I in tomato, BASF SE, Limburgerhof, Germany Fed.Rep., 2016/1063265, GLP: yes, Unpublished
CHLORFEN_002	Jose W.F.P. de	2017	Validation of BASF Method Number G0001/01 for the determination of BAS 306 I and its metabolite Tralopyril in citrus (whole fruit), dry beans (seed), soybeans (seed), tomato (whole fruit) and wheat (grain) using LC-MS/MS, BASF SA, Guaratingueta, Brazil, 2016/3003983 GLP: Yes, Unpublished
CHLORFEN_003	Jose W.F.P. de	2017	Amendment 01 - Validation BASF Method Number G0001/01 for the determination of BAS 306 I and its metabolite Tralopyril in citrus (whole fruit), dry beans (seed),soybeans (seed), tomato (whole fruit) and wheat (grain) using LC-MS/MS, BASF SA, Guaratingueta, Brazil 2017/3002881, GLP: yes, Unpublished
CHLORFEN_004	Teixeira T.M.I.	2017	Residues study of Chlorfenapyr in soybean (whole plant, seeds and aspirated grain fraction _ AGF) after treatment with BAS 306 18 I, under field conditions in Brazil, BASF SA, Guaratingueta, Brazil, 2017/3002785, GLP: yes, Unpublished
CHLORFEN_005	Jose W.F.P. de	2017	Validation of CL322250 (Reg.No. 4110555) in soybeans (seed and oil) using LC-MS/MS and freezer storage stability in soybeans (seed) at approximately -20 ºC, BASF SA, Guaratingueta, Brazil, 2017/3002744, GLP: yes, Unpublished
CHLORFEN_006	Castro M.	2017	Interim report - Residue analysis of CL322250 (Reg. No.: 4110555) in soybean (whole plant, seeds) after treatment with BAS 306 18 I under field conditions in Brazil and freezer storage stability in soybeans (whole plant) at ca. -20º C, BASF SA, Guaratingueta, Brazil, 2017/3002743, GLP: yes, Unpublished
CHLORFEN_007	Schaffert D., Jung T.	2017	Investigation of the extractability of BAS 306 I in samples from a plant metabolism study, BASF SE, Limburgerhof, Germany Fed.Rep., 2016/1203115, GLP: yes, Unpublished
CHLORFEN_008	Jose W.F.P. de	2017	Interim report – Freezer storage stability of BAS 306 I (Reg. NO. 4084563) and its metabolite Tralopyril (Reg. No. 4110925) in grape (whole fruit), dry beans (seed), soybeans (seed), apple (whole fruit) and rice grain at approximately -20 °C, BASF SA, Guaratingueta, Brazil, 2017/3001087, GLP: yes, Unpublished
CHLORFEN_009	Porto F.	2013	Residue study of Chlorfenapyr in soybeans (grains) after treatment with Pirate® under field conditions in Brazil, BASF SA, Guaratingueta, Brazil, 2016/3002162, GLP: yes, Unpublished
CHLORFEN_010	Porto F.	2014	Addendum 01: Residue study of Chlorfenapyr in soybeans (grains) after treatment with Pirate® under field conditions in Brazil, BASF SA, Guaratingueta, Brazil, 2016/3002161, GLP: yes, Unpublished
CHLORFEN_011	Silva M.A.D.	2016	Addendum No. 02 - Residue study of Chlorfenapyr in soybean (grain) after treatment of PIRATE, under field conditions in Brazil, BASF SA, Guaratingueta, Brazil, 2016/3003040, GLP: yes, Unpublished
CHLORFEN_015	Sacchi R.R.	2016	BAS 306 I: Hydrolysis of ^{14}C-BAS 306 I at 90 °C, 100 °C and 120 °C, BASF SA, Guaratingueta, Brazil, 2016/3002065, GLP: yes, unpublished
CHLORFEN_016	Sacchi R.R.	2017	Hydrolysis of ^{14}C-Tralopyril (metabolite of BAS 306 I) at 90 °C, 100 °C and 120 °C, BASF SA, Guaratingueta, Brazil, 2017/3000613, GLP: yes, unpublished
CHLORFEN_017	Teixeira T.M.I.	2017	Residue study of Chlorfenapyr in soybean (seeds and processed fractions) after treatment with BAS 306 18 I under field conditions in Brazil, BASF SA, Guaratingueta, Brazil, 2017/30002786, GLP: yes, unpublished