CHLORANTRANILIPROLE (230)

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EXPLANATION

Chlorantraniliprole is a novel insecticide belonging to the class of selective ryanodine receptor agonists and was evaluated for the first time by JMPR in 2008 (T, R). The ADI of chlorantraniliprole was 0–2 mg/kg bw and the ARfD was unnecessary. The compound was listed by the 47th Session of CCPR for the JMPR to consider additional MRLs. The residue definition for compliance with MRL and for estimation of dietary intake (for animal and plant commodities) is chlorantraniliprole.

For the current evaluation the Meeting received new analytical methods for poultry commodities, residue trials on spring onions, peanuts and cereals (barley, sorghum, wheat) previously submitted to the 2014 JMPR as well as a laying hen feeding study (residue transfer study).

ANALYTICAL METHODS

Analytical method DuPont-31085 was developed and validated for the detection, quantitative analysis, and confirmation of chlorantraniliprole and metabolites in poultry tissues and eggs.

Egg samples are diluted with water and extracted twice using CH_3CN and hexane. The CH_3CN extracts are combined and the hexane layer was discarded. Concentrated formic acid is added to an aliquot of the extract to stabilize the analytes and the extracts were evaporated to dryness. The extracts were reconstituted in CH_3CN and methanol and diluted with water.

Tissue samples are soaked in water and extracted twice using CH_3CN and hexane. The CH_3CN extracts are diluted to volume using CH_3CN. An aliquot is taken and diluted with water before concentration and clean-up on a Wasters Oasis HLB SPE cartridge. Elution is with CH_3CN and ethyl acetate. An aliquot of the purified extract is evaporated to dryness. The extracts were reconstituted in CH_3CN and methanol and diluted with water. Chlorantraniliprole, IN-H2H20, IN-F9N04, IN-K7H29, IN-GAZ70, and IN-EQW78 were separated from co-extracts by reversed phase liquid chromatography (LC) and detected by mass spectrometry/mass spectrometry (MS/MS) using electrospray ionization (ESI). Quantitation was by LC/MS/MS.

Chlorantraniliprole: 484 → 453 and 484 → 286 (total ion count), IN-K9T00: 469 → 415, IN-HXH44:

482 → 386, IN-GAZ70: 451 → 414, IN-EQW78: 466 → 188 and 466 → 76 (total ion count).

Recovery data for method DuPont-31085 are summarized in Table 1 and 2.

Table 1 Recovery data for analytical methods for the determination of chlorantraniliprole and potential metabolites IN-H2H20, IN-F9N04, IN-K7H29, IN-GAZ70, and IN-EQW78 in food of animal origin

Matrix	Number of tests	Fortification level (mg/kg)	Average recovery (%)	% RSD
Chlorantraniliprole				
Whole Eggs	5 5	0.010 0.10	99 97	6.2 6.5
Egg Whites	5 5	0.010 0.10	96 95	14 3.2
Egg Yolks	5 5	0.010 0.10	109 98	11 2.5
Muscle	5 5	0.010 0.10	110 107	4.9 1.6
Liver	5 5	0.010 0.10	100 98	2.7 4.5
Fat	5 5	0.010 0.10	132 128	3.4 3.3

Matrix	Number of tests	Fortification level (mg/kg)	Average recovery (%)	% RSD
IN-H2H20				
Whole Eggs	5 5	0.010 0.10	89 91	9.2 5.3
Egg Whites	5 5	0.010 0.10	91 87	8.1 2.2
Egg Yolks	5 5	0.010 0.10	102 101	7.7 2.2
Muscle	5 5	0.010 0.10	110 107	8.1 5.2
Liver	5 5	0.010 0.10	101 97	9.6 9.0
Fat	5 5	0.010 0.10	101 116	7.7 3.1
IN-F9N04				
Whole Eggs	5 5	0.010 0.10	96 101	15 9.4
Egg Whites	5 5	0.010 0.10	95 100	17 4.3
Egg Yolks	5 5	0.010 0.10	98 98	9.6 2.2
Muscle	5 5	0.010 0.10	106 106	9.8 7.1
Liver	5 5	0.010 0.10	101 99	3.0 3.9
Fat	5 5	0.010 0.10	104 115	6.1 1.6
IN-K7H29				
Whole Eggs	5 5	0.010 0.10	102 99	5.3 8.5
Egg Whites	5 5	0.010 0.10	101 95	4.1 5.3
Egg Yolks	5 5	0.010 0.10	100 96	4.3 1.9
Muscle	5 5	0.010 0.10	102 101	8.5 3.5
Liver	5 5	0.010 0.10	97 94	5.0 4.5
Fat	5 5	0.010 0.10	105 105	6.9 2.8
IN-GAZ70				
Whole Eggs	5 5	0.010 0.10	115 108	8.3 12
Egg Whites	5 5	0.010 0.10	105 103	11 2.3
Egg Yolks	5 5	0.010 0.10	105 94	7.0 4.8
Muscle	5 5	0.010 0.10	99 102	9.1 4.0
Liver	5 5	0.010 0.10	96 94	4.1 5.9
Fat	5 5	0.010 0.10	94 94	1.2 1.9
IN-EQW78				
Whole Eggs	5 5	0.010 0.10	94 92	5.3 4.3
Egg Whites	5 5	0.010 0.10	91 90	7.6 3.5
Egg Yolks	5 5	0.010 0.10	105 94	6.1 2.7
Muscle	5 5	0.010 0.10	95 99	11 9.0
Liver	5 5	0.010 0.10	102 101	14 2.6

Matrix	Number of tests	Fortification level (mg/kg)	Average recovery (%)	% RSD
Fat	5 5	0.010 0.10	94 97	9.2 1.7

Table 2 Recovery data for analytical methods for the determination of chlorantraniliprole and metabolites IN-H2H20, IN-F9N04, IN-K7H29, IN-GAZ70, and IN-EQW78 in food of animal origin, different laboratory

Matrix	Number of tests	Fortification level (mg/kg)	Average recovery (%)	%RSD
Chlorantraniliprole				
Whole Eggs	5 5	0.010 0.10	81.8 88.8	7.6 1.3
Muscle	5 5	0.010 0.10	105.0 102.0	3.8 1.6
Liver	5 5	0.010 0.10	87.4 90.7	9.1 2.4
Skin/Fat	5 5	0.010 0.10	82.7 96.8	5.7 1.4
IN-H2H20				
Whole Eggs	5 5	0.010 0.10	90.2 82.9	10.8 3.0
Muscle	5 5	0.010 0.10	108.0 104.0	10.2 5.4
Liver	5 5	0.010 0.10	97.3 90.0	2.7 3.2
Skin/Fat	5 5	0.010 0.10	98.8 94.9	4.6 6.2
IN-F9N04				
Whole Eggs	5 5	0.010 0.10	82.8 91.8	8.4 1.5
Muscle	5 5	0.010 0.10	82.0 105.0	6.8 1.8
Liver	5 5	0.010 0.10	91.3 91.3	10.0 2.2
Skin/ Fat	5 5	0.010 0.10	76.6 97.2	9.1 3.0
IN-K7H29				
Whole Eggs	5 5	0.010 0.10	89.8 88.4	9.9 4.3
Muscle	5 5	0.010 0.10	95.7 90.6	4.0 4.3
Liver	5 5	0.010 0.10	83.2 79.1	7.0 5.8
Skin/ Fat	5 5	0.010 0.10	83.5 83.0	7.5 3.9
IN-GAZ70				
Whole Eggs	5 5	0.010 0.10	83.4 87.7	7.4 3.2
Muscle	5 5	0.010 0.10	76.9 84.5	5.1 2.1
Liver	5 5	0.010 0.10	81.1 75.2	11.7 5.1
Skin/ Fat	5 5	0.010 0.10	81.8 79.2	8.9 3.7
IN-EQW78				
Whole Eggs	5 5	0.010 0.10	86.4 82.3	12.7 3.6
Muscle	5 5	0.010 0.10	88.0 89.0	6.8 3.5

Matrix	Number of tests	Fortification level (mg/kg)	Average recovery (%)	%RSD
Liver	5 5	0.010 0.10	67.4 77.9	24.2 4.7
Skin/ Fat	5 5	0.010 0.10	80.8 81.8	8.9 5.0

Good linearity was observed during the validation of method DuPont-31085 in the range of 0.10 to 15.0 ng/mL and also during validation of DuPont-31256, Revision No. 1 in the range of 0.20 to 30.0 ng/mL for chlorantraniliprole and the metabolites. All standards were prepared in neat solvent solutions. The LOQ of the method proposed for monitoring chlorantraniliprole, IN-H2H20, IN-F9N04, IN-K7H29 and IN-EQW78 residues is 0.01 mg/kg for eggs, muscle, liver and fat/skin. Analysis of control samples resulted in no detectable apparent residues of chlorantraniliprole, IN-H2H20, IN-F9N04, IN-K7H29 and IN-EQW78. The response in the areas of the chlorantraniliprole, IN-H2H20, IN-F9N04, IN-K7H29 and IN-EQW78 peaks always corresponded to less than 20% of the LOD. It can therefore be concluded that few, if any, apparent residues or false positive values would arise.

Repeatability of this method was demonstrated by the standard deviation of the recovery values given in Table 1 and Table 2. The %RSD of recovery data obtained is within the guideline of < 20%.

During method validation two ion transitions were monitored for chlorantraniliprole, IN-H2H20, IN-F9N04, IN K7H29 and IN-EQW78. One transition was considered the quantitative transition and the second transition was considered as the confirmatory transition. The recovery data for the confirmatory transition is summarized in Table 4 below.

Table 4 Recovery data for analytical methods for the determination of chlorantraniliprole and potential metabolites IN H2H20, IN F9N04, IN K7H29, IN GAZ70, and IN EQW78 in food of animal origin

Matrix	Number of tests	Fortification level (mg/kg)	Average recovery (%)	% RSD
Chlorantraniliprole				
Whole Eggs	5 5	0.010 0.10	82.6 85.4	4.6 1.3
Muscle	5 5	0.010 0.10	103.0 101.0	2.4 2.5
Liver	5 5	0.010 0.10	89.6 88.4	3.1 3.3
Skin/ Fat	5 5	0.010 0.10	77.8 91.3	5.1 0.4
IN-H2H20				
Whole Eggs	5 5	0.010 0.10	84.2 82.9	18.5 7.9
Muscle	5 5	0.010 0.10	115.0 108.0	8.7 4.0
Liver	5 5	0.010 0.10	109.0 92.5	6.8 4.0
Skin/ Fat	5 5	0.010 0.10	111.0 102.0	20.3 3.8
IN-F9N04				
Whole Eggs	5 5	0.010 0.10	78.6 90.2	9.5 3.2
Muscle	5 5	0.010 0.10	97.5 101.0	4.5 2.4
Liver	5 5	0.010 0.10	92.0 88.8	6.3 3.3
Skin/ Fat	5 5	0.010 0.10	87.6 92.5	5.4 2.6
IN-K7H29				
Whole Eggs	5 5	0.010 0.10	62.4 83.6	16.5 1.9

Matrix	Number of tests	Fortification level (mg/kg)	Average recovery (%)	% RSD
Muscle	5 5	0.010 0.10	83.4 92.1	17.5 2.5
Liver	5 5	0.010 0.10	72.8 79.3	15.9 6.6
Skin/ Fat	5 5	0.010 0.10	77.9 88.2	17.8 3.7
IN-GAZ70				
Whole Eggs	5 5	0.010 0.10	92.7 94.5	22.9 4.6
Muscle	5 5	0.010 0.10	87.4 83.3	7.4 4.2
Liver	5 5	0.010 0.10	86.2 80.7	6.2 10.4
Skin/ Fat	5 5	0.010 0.10	89.2 80.6	13.1 3.9
IN-EQW78				
Whole Eggs	5 5	0.010 0.10	85.3 84.9	12.3 3.4
Muscle	5 5	0.010 0.10	98.5 93.6	13.2 5.7
Liver	5 5	0.010 0.10	91.8 75.7	10.4 8.1
Skin/ Fat	5 5	0.010 0.10	89.7 82.5	20.3 2.3

USE PATTERN

Information on registered uses made available to this meeting is shown in Table 4.

Table 4 Selected registered uses of chlorantraniliprole

Crop	Country	Method	GS (BBCH)	Rate (g ai/ha)	Water (L/ha)	N	Int	PHI (days)
Crop Group 3-07: Bulb Vegetables	USA	F	11-89	50-110, max 225/season	93-2337 (ground), 47-140 (aerial)	1-4	7	1
Crop Subgroup 3-07B: Bulb Vegetables, Green onion subgroup	Canada	F	11-89	50-75, max 225/season	>100	1-4	5	1
Peanuts	USA	F	11-89	50-110, max 225/season	93-2337 (ground), 47-140 (aerial)	1-4	5	1
Peanuts	Canada	F	11-89	50-75, max 225/season	>100	1-4	7	1
Cereals, except Corn and Rice	USA	F	11-89	50-110, max 225/season	467-2337 (ground), 93-140 (aerial)	1-4	7	1
Cereals, except Corn and Rice	Canada	F	11-89	50-75, max 225/season	>100 (ground) >50 (aerial)	1-3	7	1

F=foliar

US Bulb vegetable group (3-07):

Crop subgroup 3-07A. Onion, bulb, subgroup.

Onion, bulb. Daylily, bulb; fritillaria, bulb; garlic, bulb; garlic, great-headed, bulb; garlic, serpent, bulb; lily, bulb; onion, bulb; onion, Chinese, bulb; onion, pearl; onion, potato, bulb; shallot, bulb; cultivars, varieties, and/or hybrids of these.

Crop subgroup 3-07B. Onion, green, subgroup.

Onion, green. Chive, fresh leaves; chive, Chinese, fresh leaves; elegans hosta; fritillaria, leaves; kurrat; lady's leek; leek; leek, wild; Onion, Beltsville bunching; onion, fresh; onion, green; onion, macrostem; onion, tree, tops; onion, Welsh, tops; shallot, fresh leaves; cultivars, varieties, and/or hybrids of these.

US Cereal grains crop group (except corn and rice)

Barley, Buckwheat, Millet, pearl, Millet, proso (Panicum milliaceum), Oats, Rye, Sorghum (milo), Teosinte, Triticale, Wheat, Wild rice

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

Onions

Table 5 Residues from the foliar application of chlorantraniliprole to onions in the USA and Canada (previously reported by the 2014 JMPR) (replicate samples)

Country Year (Variety)	N (int)	Rate (g ai/ha)	Spray volume (L/ha)	Growth Stage	Matrix	DALA	Individual	Mean
Salinas, California (2009) White spear	2 (3)	113 113	412 421	Mature mature	Whole plant, fresh Whole plant dried	1	0.70 0.61 6.0 6.6	0.65 6.3
Holtville, California (2010) Tri-5503	2 (3)	111 112	215 224	Bulbing mature	Whole plant, fresh Whole plant dried	1	0.37 0.44 1.1 0.90	0.41 1.0
Salisbury, Maryland (2009) Evergreen hardy white	2 (3)	113 113	281 281	Mature Mature	Whole plant, fresh Whole plant dried	1	0.84 0.73 2.7 2.7	0.79 2.7
Harrow, Ontario (2009) Emerald Isle	2 (3)	118 110	318 290	Mature Mature	Whole plant, fresh Whole plant dried	1	1.5 1.5 11 11	1.5 11
St Sur Richelieu, Quebec (2009) Parade	2 (3)	112 113	393 402	5 true leaves Mature	Whole plant, fresh Whole plant dried	1	0.70 0.74 1.5 1.5	0.72 1.5

Cereals

Table 6 Residues from the foliar application of chlorantraniliprole to cereals in the USA (previously reported by the 2014 JMPR) (replicate samples)

Country Year (Variety)	N (int)	Rate (g ai/ha)	Spray volume (L/ha)	Growth Stage	Matrix	DALA	Individual	Mean
Barley								
Velva, North Dakota (2009) Tradition	2 (7)	117 115	116 115	Kernel hard Harvest ripe	Grain	1	1.8 2.2	2.0
Aurora, South Dakota (2009) Lacey	2 (7)	114 114	208 210	Mature grain Still hard	Grain	1	1.7 2.2	1.9
Kimberley, Idaho (2009) Camas Spring	2 (7)	112 112	187 187	Drying drying down	Grain	1	1.9 1.9	1.9
Sorghum								
Fargo, North Dakota (2009) LM 5001	2 (30)	112 112	139 139	Senesced via frost Ripe	Grain	1	1.2 1.1	1.2
Las Cruces, New Mexico (2009) DK 28E [last spray 18 Aug]	2 (7)	112 114	172 194	Seeding Mature grain	Grain	1	1.5 1.5	1.5
Las Cruces, New Mexico (2009) M3838 [last spray 1 Sept]	2 (7)	113 111	250 255	Hard dough to mature Mature grain	Grain	1	0.83 0.74	0.79
Wheat								
Fargo, North	2 (7)	114	124	Hard dough	Grain	1	0.22 0.23	0.23

Country Year (Variety)	N (int)	Rate (g ai/ha)	Spray volume (L/ha)	Growth Stage	Matrix	DALA	Individual	Mean
Dakota (2009) Alsen [last spray 9 Sept]		112	122	Ripe wheat				
Fargo, North Dakota (2009) Glenn [last spray 20 July]	2 (7)	113 112	140 139	Hard dough Ripe wheat	Grain	1	0.20 0.18	0.19
Velva, North Dakota (2009) Faller	2 (7)	118 115	117 115	Kernel hard Ripe for cutting	Grain	1	0.19 0.18	0.18
Aurora, South Dakota (2009) Briggs Hard Red	2 (7)	120 106	211 193	Mature Mature	Grain	1	0.26 0.25	0.25
Las Cruces, New Mexico (2010) El Dorado	2 (7)	117 118	232 252	Hard dough, mature Mature grain	Grain	1	0.43 0.39	0.41

Peanuts

Table 7 Residues from the foliar application of chlorantraniliprole to peanuts in the USA (previously reported by the 2014 JMPR) (replicate samples)

Country Year (Variety)	N (int)	Rate (g ai/ha)	Spray volume (L/ha)	Growth Stage	Matrix	DALA	Individual	Mean
Monticello, Florida (2011) Florida 7	2 (5)	112 113	127 131	89 89	Nutmeat	1	<0.01 <0.01	<0.01
Charlotte, Texas (2011) Georgia 09	2 (5)	111 113	234 234	87 88	Nutmeat	1	0.015 0.010	0.012
Quitman, Georgia (2011) Spanish McCloud	2 (5)	113 114	127 132	89 89	Nutmeat	1	<0.01 <0.01	<0.01
Sycamore, Georgia (2011) GA 06	2 (5)	112 112	121 117	Mature Mature	Nutmeat	1	<0.01 <0.01	<0.01
Levelland, Texas (2011) Tamnut OL06	2 (6)	115 113	187 187	Mature Mature	Nutmeat	1	0.022 0.046	0.034

LIVESTOCK FEEDS

Table 8a Residues in forage from the foliar application of chlorantraniliprole to cereal in the USA (previously reported by the 2014 JMPR) (replicate samples)

Country Year (Variety)	N (int)	Rate (g ai/ha)	Spray volume (L/ha)	Growth Stage	Matrix	DALA	Individual	Mean
Sorghum								
Fargo, North Dakota (2009) LM 5001	2 (7)	112 112	139 139	Early dough Soft dough	Forage	1	3.0 2.4	2.7
Las Cruces, New Mexico (2009) DK 28E	2 (7)	11 114	140 170	Milk, soft dough Soft dough	Forage	1	4.7 3.4	4.1
Las Cruces, New Mexico (2009) M3838	2 (7)	122 111	242 235	Early milk Soft to hard dough	Forage	1	3.2 3.5	3.4
Wheat								

Country Year (Variety)	N (int)	Rate (g ai/ha)	Spray volume (L/ha)	Growth Stage	Matrix	DALA	Individual	Mean
Fargo, North Dakota (2009) Glenn	2 (7)	113 113	140 140	Beginning anthesis Late anthesis	Forage	1	4.2 4.3	4.3
Velva, North Dakota (2009) Faller	2 (8)	115 114	115 114	Flag leaf Heading	Forage	1	4.0 4.8	4.4
Aurora, South Dakota (2009) Briggs Hard Red	2 (7)	113 115	203 204	Boot to flowering Flowering	Forage	1	5.0 3.7	4.3
Las Cruces, New Mexico (2010) El Dorado	2 (6)	115 114	191 209	Early boot Late boot	Forage	1	4.6 4.6	4.6

Table 8b Residues in hay from the foliar application of chlorantraniliprole to cereals in the USA (previously reported by the 2014 JMPR) (replicate samples)

Country Year (Variety)	N (int)	Rate (g ai/ha)	Spray volume (L/ha)	Growth Stage	Matrix	DALA	Individual	Mean
Barley								
Velva, North Dakota (2009) Tradition	2 (8)	115 113	115 113	Flag leaf Head emergence complete	Hay	1	9.2 9.2	9.2
Aurora, South Dakota (2009) Lacey	2 (7)	113 121	205 217	Milk Soft dough	Hay	1	5.5 5.5	5.5
Kimberley, Idaho (2009) Camas Spring	2 (7)	110 111	184 186	Milk Milk to soft dough	Hay	1	9.5 12	11
Wheat								
Fargo, North Dakota (2009) Glenn	2 (7)	113 113	140 140	Beginning anthesis Late anthesis	Hay	1	8.6 10	9.5
Velva, North Dakota (2009) Faller	2 (8)	115 114	115 114	Flag leaf Heading	Hay	1	9.2 8.0	8.6
Aurora, South Dakota (2009) Briggs Hard Red	2 (7)	113 115	203 204	Boot to flowering Flowering	Hay	1	11 12	11
Las Cruces, New Mexico (2010) El Dorado	2 (6)	115 114	191 209	Early boot Late boot	Hay	1	11 10	11

Table 9 Residues in stover, straw from the foliar application of chlorantraniliprole to cereals in the USA (previously reported by the 2014 JMPR) (replicate samples)

Country Year (Variety)	N (int)	Rate (g ai/ha)	Spray volume (L/ha)	Growth Stage	Matrix	DALA	Individual	Mean
Barley								
Velva, North Dakota (2009) Tradition	2 (7)	117 115	116 115	Kernel hard Harvest ripe	Straw	1	13 15	14
Aurora, South Dakota (2009) Lacey	2 (7)	114 114	208 210	Mature grain Still hard	Straw	1	3.3 3.8	3.6
Kimberley, Idaho (2009) Camas Spring	2 (7)	112 112	187 187	Drying drying down	Straw	1	12 12	12
Sorghum								

Country Year (Variety)	N (int)	Rate (g ai/ha)	Spray volume (L/ha)	Growth Stage	Matrix	DALA	Individual	Mean
Fargo, North Dakota (2009) LM 5001	2 (30)	112 112	139 139	Senesced via frost Ripe	Stover	1	3.3 3.6	3.4
Las Cruces, New Mexico (2009) DK 28E	2 (7)	112 114	172 194	Seeding Mature grain	Stover	1	6.9 4.9	5.9
Las Cruces, New Mexico (2009) M3838	2 (7)	113 111	250 255	Hard dough to mature Mature grain	Stover	1	4.8 3.4	4.1
Wheat								
Fargo, North Dakota (2009) Glenn	2 (7)	113 112	140 139	Hard dough Ripe wheat	Straw	1	0.20 0.18	0.19
Velva, North Dakota (2009) Faller	2 (7)	118 115	117 115	Kernel hard Ripe for cutting	Straw	1	15 15	15
Aurora, South Dakota (2009) Briggs Hard Red	2 (7)	120 106	211 193	Mature Mature	Straw	1	6.5 6.3	6.4
Las Cruces, New Mexico (2010) El Dorado	2 (7)	117 118	232 252	Hard dough, mature Mature grain	Straw	1	4.2 4.8	4.5

Table 10 Processing factors for chlorantraniliprole from the processing of raw agricultural commodities (RACs) (previously reported by the 2014 JMPR)

RAC	Processed Commodity	Best Estimate Processing Factor	RAC MRL	RAC STMR	Processed Commodity STMR-P/median residue
Wheat	Aspirated Grain Fractions	33	0.02	0.01	0.34
	Bran	1.04			0.011
	Flour	0.38			0.004
	Middlings	0.28			0.003
	Shorts	0.7			0.007
	Germ	1.13			0.011

Livestock feeding study in laying hens

Vance et al. (2012 31665) dosed ISA Warren laying hens (1.64–2.22 kg bw) with chlorantraniliprole once daily for 28 consecutive days administered orally in gelatine capsules. Three groups of birds received chlorantraniliprole at target treatment levels equivalent to 3, 9, and 30 ppm in the diet. An additional group of birds were also dosed at a target of 30 ppm for 28 consecutive days, to obtain depuration data. Based on the average daily dietary intake, the actual mean weekly dose levels were equivalent to 3.9–4.5, 14.5-17.4 and 40.2-50.7 ppm. Eggs from each bird were collected and retained twice daily from day -3 until necropsy. The egg lay efficiency was 71% during the dose period and 57% during the depuration phase. Egg samples collected on days -3, 1, 4, 7, 10, 14, 17, 21, and 27. Egg white and egg yolk samples were prepared from eggs collected on days 14 and 21 only. Whole eggs collected from the depuration group on days 27, 28, and on days 1-7 post last dose. All birds were euthanized and necropsied ca. 4–5 hours post last dose with exception of the depuration group birds which were euthanized and necropsied 2, 5, and 8 days post last dose, respectively. At necropsy, whole liver (gall bladder removed), muscle (equal portions of breast muscle and leg muscle), and abdominal fat pad (with adhering skin) were removed and retained for each bird. All samples were stored frozen at -80 °C until analysis, with exception of liver samples which were extracted on the day of collection. One liver sample did require repeat analysis for the determination of residues of IN K7H29, IN-GAZ70 and IN EQW78 only (depuration group) and was stored for 3 days at ca -80 °C prior to analysis. All samples (egg and tissues) were analysed within 30 days of collection. The

maximum frozen storage intervals (ca -80 °C) were 26 days for whole eggs, 24 days for egg yolks, 23 days for egg whites, 3 days for liver, 24 days for muscle and 23 days for skin with fat.

Table 11 Description of dosing regime per treatment group for laying hens

Target dose (ppm)	Administered dose (mg/bird/day)	Feed consumption (kg/bird/day)	Equivalent level in feed (ppm)
0	0	0.088	0
3	0.390	0.092	4.8
9	1.171	0.074	18.8
30	3.904	0.088	51.9
30 depuration	3.904	0.081	56.8

The method of analysis for chlorantraniliprole, IN-H2H20, IN-F9N04, IN-K7H29, IN-GAZ70, and IN-EQW78 in eggs (including egg yolk and egg white) was modified DuPont 31085. The method involved liquid-liquid partitioning with saturated CH_3CN, saturated hexane and water. The method of analysis for chlorantraniliprole, IN-H2H20, IN-F9N04, IN-K7H29, IN-GAZ70, and IN-EQW78 in tissues was modified DuPont-31085. The method involved liquid-liquid partitioning with saturated acetonitrile, saturated hexane and water followed by solid phase extraction. The final extracts for all matrices were analysed by LC with tandem MS employing electrospray ionisation in positive mode. For each sample, all analytes were determined in a single injection. The LOQ for parent and each metabolite was 0.01 mg/kg in eggs and tissues.

Table 12 Recovery data for determination of chlorantraniliprole and metabolites in chicken tissues and eggs.

Matrix	Fortification level (mg/kg)	N	Chlorantrani-liprole	IN-EQW78	IN-F9N04	IN-GAZ70	IN-H2H20	IN-K7H29
Whole egg	0.01	51	89.3±10.7	87.4±14.3	91.6±9.7	93.7±12.1	87.1±13.1	91.4±11.3
	0.10	50	92.0±7.6	87.8±8.1	93.4±7.2	94.2±7.7	88.9±9.8	92.3±7.3
	0.4	3	94.6±0.5	92.4±0.9	98.7±0.9	99.4±1.0	95.7±2.9	94.6±1.7
	0.8	3	95.2±7.8	91.4±4.9	97.8±7.0	97.0±4.0	93.2±7.9	96.1±5.2
	Overall	107	90.9±9.2	87.8±11.3	92.8±8.5	94.2±9.9	88.4±11.4	92.0±9.3
Egg yolk	0.01	9	86.1±11.9	84.1±10.3	86.3±10.0	92.9±10.5	90.7±13.0	86.7±10.6
	0.1	9	89.2±7.8	89.6±13.0	88.9±8.4	87.5±7.2	95.0±7.0	88.3±6.5
	0.4	3	80.3±3.6	79.2±2.3	80.9±3.0	82.9±2.5	88.0±4.1	82.1±4.2
	Overall	21	86.6±9.6	85.7±11.2	86.6±8.7	89.2±8.9	92.1±9.8	86.8±8.2
Egg White	0.01	9	95.6±10.9	95.5±16.3	95.3±6.9	102±8.5	87.0±9.8	92.2±8.3
	0.10	8	92.4±6.0	85.7±9.0	97.6±5.9	96.8±6.7	85.3±4.0	93.3±7.1
	0.4	3	92.0±3.4	87.7±3.9	96.9±4.3	108±9.1	75.1±4.4	94.6±3.8
	0.8	3	90.4±2.2	89.3±1.3	94.1±2.2	103±2.2	81.0±1.7	91.9±1.4
	Overall	23	93.4±7.7	90.3±12.0	96.0±5.7	101±7.9	83.8±7.6	92.8±6.6
Liver	0.01	12	92.4±8.9	96.9±18.3	92.1±6.5	85.8±6.6	87.2±12.3	84.2±8.8
	0.1	12	96.6±6.2	84.5±6.3	93.8±6.6	83.4±5.9	89.0±9.5	86.3±5.2
	0.4	3	91.8±2.0	78.3±1.4	93.9±1.6	77.7±1.5	93.2±1.6	87.7±2.2
	Overall	27	94.2±7.4	89.1±14.4	93.0±6.1	83.7±6.2	88.7±10.3	85.6±6.7
Muscle	0.01	3	97.4±4.0	80.7±12.0	101±6.1	83.1±7.3	108±6.0	83.4±6.5
	0.1	3	95.5±4.1	75.9±4.3	96.4±2.2	79.8±1.0	96.8±4.5	88.2±3.6
	0.4	3	92.7±5.8	75.7±3.6	89.8±5.0	79.3±3.1	92.2±1.6	85.7±4.5
	Overall	9	95.2±4.6	77.4±7.1	95.7±6.4	80.7±4.4	99.1±8.2	85.7±4.8
Skin/fat	0.01	3	79.6±5.3	78.4±3.3	97.2±5.2	88.7±4.4	106±11.9	92.8±6.4
	0.1	3	85.5±5.3	78.7±6.5	105±4.6	78.1±3.4	102±2.7	88.6±4.8
	0.4	3	92.9±8.0	79.3±5.4	109±6.4	80.5±5.2	106±7.0	91.8±7.3
	Overall	9	86.0±8.0	78.8±4.6	103±6.9	82.4±6.2	105±7.3	91.1±5.8

Residues of chlorantraniliprole, IN-H2H20, IN-F9N04, IN-K7H29, IN-GAZ70, and IN-EQW78 in whole eggs generally increased over the first 10 days of dosing. Residue levels on days 10, 14, 17, 21 and 27 were comparable indicating that a plateau had been reached. Based on mean residues over the sampling period (day -3 to 27), residues of chlorantraniliprole were highest in whole eggs followed by IN H2H20, IN-GAZ70, IN-F9N04, IN-EQW78, and IN-K7H29 in decreasing order.

The maximum average residues in whole egg are summarized in Table 13. Residues in whole eggs were dose dependent, increasing with higher doses.

Table 13 Maximum average residues in whole egg and calculated residue ratios between dose levels

Analyte	4.8 ppm	18.8 ppm	51.9 ppm	18.8 ppm (ratio[A])	51.9 ppm (ratio[A])
Chlorantraniliprole	0.132	0.296	0.447	2.2	1.5
IN-H2H20	0.0703	0.149	0.295	2.1	2.0
IN-F9N04	0.0576	0.139	0.248	2.4	1.8
IN-K7H29	0.0113	0.0278	0.0627	2.5	2.3
IN-GAZ70	0.0580	0.139	0.270	2.4	1.9
IN-EQW78	0.0196	0.0448	0.0701	2.3	1.6

[A] The ratio given is for the residue at that dose divided by the residue for the next lowest group. Therefore, there is no ratio for the 3 mg/kg dietary dose group. Mean residues were calculated from actual residue values. Note 18.8/4.8 = 3.9, 51.9/18.8 = 2.8

In tissue samples obtained within ca 4-5 hours of dose completion, residue levels were highest in liver followed by skin with fat and muscle. The average residues detected in tissues are presented in Table 14. In liver, the major residue was IN-F9N04 followed by IN-H2H20, chlorantraniliprole/IN-K7H29 and IN GAZ70 in decreasing order. No residues of IN-EQW78 were detected in liver. In skin with fat, the major residue was IN-F9N04 followed by chlorantraniliprole, IN-H2H20 and IN-GAZ70 in decreasing order. No residues of IN-K7H29 or IN EQW78 above the LOQ (0.01 mg/kg) were detected in skin with fat. In muscle, the major residue was IN-F9N04 followed by IN H2H20 and chlorantraniliprole in decreasing order. Residues of IN-K7H29 and IN-GAZ70 were below the LOQ (0.01 mg/kg) in muscle. No residues of IN EQW78 were detected in muscle.

Table 14 Residue data for liver and muscle from hens dosed with chlorantraniliprole

Matrix	Collection Day	Dose Level (ppm)	Average Residues[A] (mg/kg) Chlorantraniliprole	IN-H2H20	IN-F9N04	IN-K7H29	IN-GAZ70	IN-EQW78
Liver	28	0	ND	ND	<0.001[B]	ND	ND	ND
	28	4.8	0.038	0.042	0.062	0.021	0.007[B]	ND
	28	18.8	0.092	0.113	0.153	0.060	0.018	ND
	28	51.9	0.147	0.199	0.286	0.159	0.031	ND
	30 (2 days depuration)	56.8	0.036	0.036	0.040	0.036	0.010[B]	ND
	33 (5 days depuration)	56.8	0.001[B]	ND	0.001[B]	0.003 [B]	ND	ND
	36 (8 days depuration)	56.8	ND	ND	<0.001[B]	0.001 [B]	ND	ND
Muscle	28	0	ND	ND	ND	ND	ND	ND
	28	4.8	0.011	0.010	0.013	<0.001[B]	ND	ND
	28	18.8	0.027	0.028	0.031	0.002[B]	<0.001[B]	ND
	28	51.9	0.049	0.052	0.064	0.004[B]	0.002[B]	ND
	30 (2 days depuration)	56.8	0.009[B]	0.008[B]	0.008[B]	ND	ND	ND
	33 (5 days depuration)	56.8	0.002[B]	ND	ND	ND	ND	ND
	36 (8 days depuration)	56.8	ND	ND	ND	ND	ND	ND
Skin/ fat	28	0	ND	ND	ND	ND	ND	ND
	28	4.8	0.042	0.019	0.046	0.001[B]	0.002[B]	ND
	28	18.8	0.096	0.068	0.103	0.004[B]	0.008[B]	0.002[B]
	28	51.9	0.168	0.092	0.204	0.008[B]	0.016	0.004[B]
	30 (2 days depuration)	56.8	0.031	0.014	0.026	0.002[B]	0.006[B]	ND
	33 (5 days depuration)	56.8	0.002[B]	0.001[B]	<0.001[B]	ND	ND	ND
	36 (8 days depuration)	56.8	0.003[B]	ND	0.001 [B]	ND	ND	ND

ND = not detected

[A] Residues are means from 3 independent samples from 3 subgroups in each dose group.

[B] greater than LOD but less than LOQ (0.01 mg/kg), reported as values for information only

A summary of residue depuration in eggs and tissues from birds dosed at 56.8 ppm is presented in Table 15-18. Following cessation of dosing, residues in eggs and tissues rapidly declined. Residues of chlorantraniliprole, IN-H2H20, IN-F9N04, IN-K7H29, IN-GAZ70 and IN-EQW78 in eggs from the depuration group averaged 0.331, 0.239, 0.220, 0.0581, 0.216, and 0.0511 mg/kg, respectively, on day 28. At one day post last dose (day 29), the average residues in eggs from the depuration group had declined to 0.118, 0.0797, 0.101, 0.0333, 0.0831, and 0.0187 for chlorantraniliprole, IN-H2H20, IN F9N04, IN K7H29, IN-GAZ70, and IN-EQW78, respectively. By 7 days post last dose (day 35) all residues in eggs were below LOQ (0.01 mg/kg).

In liver, residue levels of chlorantraniliprole, IN-H2H20, IN-F9N04, IN-K7H29, and IN-GAZ70 from the depuration group were 0.147, 0.199, 0.286, 0.159, and 0.0311 mg/kg, respectively on day 28. No residues were detected for IN-EQW78. By 5 days post last dose (day 33) all residues in liver were below LOQ (0.01 mg/kg) or not detected.

In skin with fat, residue levels of chlorantraniliprole, IN-H2H20, IN-F9N04, and IN-GAZ70 from the depuration group were 0.168, 0.0918, 0.204, and 0.0163 mg/kg, respectively on day 28. Residues for IN K7H29 and IN-EQW78 were below LOQ on day 28. By 5 days post last dose (day 33) all residues in skin with fat were below LOQ (0.01 mg/kg) or not detected.

In muscle, residue levels of chlorantraniliprole, IN-H2H20, and IN-F9N04 from the depuration group were 0.0491, 0.0522, and 0.0638 mg/kg, respectively on day 28. Residues for IN-K7H29 and IN-GAZ70 were below LOQ and no residues were detected for IN-EQW78 on day 28. By 2 days post last dose (day 30) all residues in muscle were below LOQ (0.01 mg/kg) or not detected. Similarly by 8 days post last dose (day 36) no residues were detectable in muscle.

Table 15 Summary table of residue depuration in eggs and tissues from hens dosed with chlorantraniliprole at 56.8 ppm

Matrix	Collection Day (Depuration Day)	Average Residues (mg/kg)[A]					
		Chlorantra-niliprole	IN-H2H20	IN-F9N04	IN-K7H29	IN-GAZ70	IN-EQW78
Whole Eggs	28	0.331	0.239	0.220	0.058	0.216	0.051
	30 (2)	0.078	0.058	0.074	0.022	0.058	0.012
	33 (5)	0.017	0.018	0.021	0.006[B]	0.020	0.003[B]
	35 (7)	0.004[B]	0.003[B]	0.005[B]	0.001[B]	0.007[B]	ND
Liver	28	0.147	0.199	0.286	0.159	0.031	ND
	30 (2)	0.036	0.036	0.040	0.036	0.010[B]	ND
	33 (5)	0.001[B]	ND	0.001[B]	0.003[B]	ND	ND
	36 (8)	ND	ND	0.001[B]	0.001[B]	ND	ND
Muscle	28	0.049	0.052	0.064	0.004[B]	0.002[B]	ND
	30 (2)	0.009[B]	0.008[B]	0.009[B]	ND	ND	ND
	33 (5)	0.002[B]	ND	ND	ND	ND	ND
	36 (8)	ND	ND	ND	ND	ND	ND
Skin with Fat	28	0.168	0.092	0.204	0.008[B]	0.016	0.003[B]
	30 (2)	0.031	0.014	0.026	0.002[B]	0.006[B]	ND
	33 (5)	0.002[B]	0.001[B]	<0.001[B]	ND	ND	ND
	36 (8)	0.003[B]	ND	0.001[B]	ND	ND	ND

ND = not detected

[A] Residues are means from 3 independent samples from 3 subgroups in each dose group. The LOQ for each analyte in all matrices was 0.01 mg/kg.

[B] Reliability of the measurement has only been established for the LOQ (0.01 mg/kg) and above.

Table 16 Residue data [A] from the feeding study on whole eggs

Dose level (ppm)	Study day	Chlorantraniliprole	IN-H2H20	IN-F9N04	IN-K7H29	IN-GAZ70	IN-EQW78
4.8	-3	ND ND ND	ND ND ND	ND ND ND	ND ND ND	ND ND ND	ND ND ND
	1	0.038 0.092 ND	0.016 0.039 ND	0.010 0.029 ND	0.002 0.004 ND	0.007 0.024 ND	0.006 0.012 ND
	4	0.050 0.130 0.079	0.019 0.062 0.043	0.014 0.064 0.058	0.005 0.010 0.012	0.012 0.053 0.050	0.008 0.019 0.011
	7	0.147 0.067 0.125	0.071 0.046 0.069	0.044 0.047 0.063	0.006 0.009 0.010	0.037 0.046 0.068	0.019 0.009 0.018
	10	0.132 0.063 0.162	0.062 0.042 0.077	0.046 0.053 0.058	0.007 0.010 0.009	0.042 0.047 0.051	0.019 0.012 0.028
	14	0.099 0.101 0.142	0.052 0.062 0.071	0.037 0.071 0.060	0.008 0.015 0.012	0.038 0.069 0.058	0.013 0.014 0.019
	17	0.089 0.092 0.104	0.043 0.048 0.048	0.039 0.044 0.048	0.007 0.007 0.009	0.035 0.041 0.048	0.013 0.014 0.016
	21	0.123 0.100 0.077	0.063 0.039 0.037	0.063 0.061 0.047	0.010 0.012 0.010	0.063 0.060 0.051	0.018 0.014 0.011
	27	0.146 0.121 0.130	0.072 0.076 0.064	0.055 0.067 0.051	0.009 0.012 0.010	0.049 0.062 0.047	0.020 0.017 0.017
18.8	-3	ND ND ND	ND ND ND	ND ND ND	ND ND ND	ND ND ND	ND ND ND
	1	ND ND 0.066	ND ND 0.033	ND ND 0.024	ND ND 0.003	ND ND 0.017	ND ND 0.008
	4	0.316 0.152 0.120	0.177 0.081 0.079	0.175 0.070 0.072	0.029 0.017 0.015	0.173 0.069 0.061	0.044 0.022 0.019
	7	0.121 0.114 0.163	0.066 0.077 0.123	0.050 0.077 0.118	0.013 0.025 0.027	0.037 0.080 0.126	0.017 0.018 0.026
	10	0.211 0.227 0.113	0.147 0.134 0.091	0.138 0.113 0.116	0.033 0.026 0.024	0.138 0.110 0.110	0.032 0.033 0.018
	14	0.512 0.180 0.197	0.220 0.108 0.118	0.193 0.085 0.139	0.030 0.022 0.022	0.183 0.098 0.135	0.073 0.030 0.031
	17	0.238 0.105 0.095	0.115 0.060 0.060	0.098 0.060 0.093	0.022 0.015 0.020	0.097 0.058 0.087	0.038 0.019 0.017
	21	0.136 0.176 0.270	0.092 0.100 0.116	0.105 0.087 0.104	0.028 0.027 0.020	0.105 0.087 0.089	0.023 0.026 0.041
	27	0.045 0.113 0.156	0.038 0.062 0.126	0.033 0.052 0.154	0.012 0.017 0.031	0.032 0.044 0.136	0.011 0.016 0.022
51.9	-3	ND ND ND	ND ND ND	ND ND ND	ND ND ND	ND ND ND	ND ND ND
	1	ND ND 0.093	ND ND 0.040	ND ND 0.023	ND ND 0.004	ND ND 0.020	ND ND 0.012
	4	0.267 0.235 0.434	0.179 0.122 0.233	0.193 0.115 0.233	0.040 0.023 0.044	0.168 0.082 0.213	0.038 0.029 0.064
	7	0.222 0.195 0.362	0.180 0.144 0.218	0.166 0.112 0.186	0.045 0.033 0.037	0.156 0.106 0.198	0.036 0.030 0.063
	10	0.208 0.442 0.667	0.145 0.300 0.411	0.139 0.173 0.222	0.045 0.035 0.049	0.128 0.221 0.222	0.035 0.072 0.100
	14	0.493 0.431 0.327	0.451 0.255 0.178	0.365 0.193 0.157	0.077 0.042 0.045	0.375 0.213 0.198	0.076 0.066 0.058
	17	0.256 0.680 0.320	0.165 0.490 0.165	0.177 0.343 0.149	0.045 0.054 0.041	0.154 0.305 0.167	0.039 0.087 0.061
	21	0.312 0.515 0.513	0.198 0.282 0.296	0.214 0.256 0.273	0.060 0.057 0.070	0.222 0.276 0.311	0.051 0.077 0.082
	27	0.123 0.504 0.274	0.0944 0.302 0.221	0.097 0.190 0.247	0.038 0.048 0.062	0.079 0.207 0.263	0.017 0.082 0.044
	27	0.212 0.506 0.297	0.132 0.224 0.185	0.116 0.213 0.242	0.029 0.040 0.046	0.103 0.254 0.206	0.032 0.086 0.038
56.8	28 (0)	0.260 0.401	0.211 0.267	0.208 0.231	0.058 0.058	0.213 0.219	0.045 0.057
	29 (1)	0.118 0.117	0.082 0.078	0.100 0.102	0.031 0.036	0.085 0.081	0.017 0.020
	30 (2)	0.053 0.103	0.038 0.078	0.069 0.080	0.019 0.025	0.052 0.064	0.008 0.016
	31 (3)	0.027 0.041	0.018 0.033	0.036 0.044	0.007 0.009	0.027 0.033	0.005 0.009
	32 (4)	0.050 0.020	0.006 0.019	0.011 0.022	0.002 0.005	0.007 0.019	ND 0.005
	33 (5)	0.017	0.019	0.021	0.006	0.020	0.003
	34 (6)	0.010	0.008	0.012	0.003	0.013	0.004

Dose level (ppm)	Study day	Chlorantraniliprole	IN-H2H20	IN-F9N04	IN-K7H29	IN-GAZ70	IN-EQW78
	35 (7)	0.004	0.003	0.005	0.001	0.007	ND

[A] 3 independent samples from 3 subgroups in each dose group

Table 17 Residue data [A] from the feeding study on egg yolks and whites

Dose level (ppm)	Study day	Residue (mg/kg) Chlorantraniliprole	IN-H2H20	IN-F9N04	IN-K7H29	IN-GAZ70	IN-EQW78
		white					
4.8	14	0.123 0.112 0.179	0.060 0.073 0.085	0.051 0.078 0.070	0.010 0.020 0.012	0.040 0.020 0.059	0.016 0.016 0.024
18.8	14	0.704 0.234 0.284	0.301 0.112 0.166	0.270 0.114 0.183	0.037 0.028 0.035	0.217 0.092 0.167	0.087 0.039 0.036
51.9	14	0.744 0.632 0.410	0.637 0.441 0.099	0.538 0.298 0.198	0.122 0.063 0.057	0.589 0.298 0.091	0.108 0.085 0.073
4.8	21	0.199 0.137 0.102	0.105 0.078 0.050	0.093 0.074 0.057	0.014 0.015 0.014	0.091 0.069 0.069	0.032 0.017 0.018
18.8	21	0.139 0.225 0.374	0.086 0.127 0.154	0.097 0.093 0.115	0.028 0.031 0.025	0.115 0.109 0.110	0.024 0.037 0.051
51.9	21	0.428 0.713 0.733	0.246 0.386 0.405	0.256 0.313 0.360	0.074 0.076 0.096	0.252 0.325 0.430	0.062 0.098 0.118
		Yolk					
4.8	14	0.0203 0.024 0.0302	0.016 0.024 0.024	0.016 0.028 0.031	0.003 0.006 0.005	0.017 0.025 0.025	0.001 0.002 0.006
18.8	14	0.138 0.053 0.055	0.090 0.048 0.059	0.101 0.050 0.079	0.011 0.011 0.012	0.115 0.056 0.058	0.038 0.013 0.011
51.9	14	0.183 0.126 0.147	0.185 0.126 0.129	0.211 0.133 0.137	0.044 0.025 0.023	0.179 0.119 0.119	0.036 0.032 0.033
4.8	21	0.035 0.025 0.024	0.028 0.021 0.020	0.026 0.028 0.033	0.005 0.006 0.006	0.020 0.022 0.024	0.006 0.001 0.005
18.8	21	0.074 0.044 0.064	0.070 0.050 0.062	0.076 0.047 0.076	0.015 0.013 0.012	0.057 0.044 0.051	0.014 0.008 0.013
51.9	21	0.145 0.100 0.131	0.140 0.111 0.113	0.158 0.134 0.138	0.035 0.028 0.028	0.124 0.096 0.124	0.030 0.021 0.035

[A] 3 independent samples from 3 subgroups in each dose group

Table 18 Residue data [A] from the feeding study on chicken tissues

Dose level (ppm)	Study day	Residue (mg/kg) Chlorantraniliprole	IN-H2H20	IN-F9N04	IN-K7H29	IN-GAZ70	IN-EQW78
		Liver					
4.8	28	0.032 0.028 0.054	0.033 0.034 0.060	0.039 0.065 0.082	0.014 0.022 0.026	0.005 0.007 0.009	ND ND ND
18.8	28	0.122 0.063 0.090	0.132 0.093 0.115	0.140 0.125 0.194	0.053 0.063 0.065	0.018 0.016 0.019	ND ND ND
51.9	28	0.152 0.110 0.178	0.208 0.168 0.222	0.372 0.239 0.247	0.200 0.158 0.120	0.035 0.033 0.026	ND ND ND
56.8	30 (2)	0.036	0.036	0.040	0.036	0.010	ND
56.8	33 (5)	0.001	ND	0.001	0.003	ND	ND
56.8	36 (8)	ND	ND	0.001	0.001	ND	ND
		Muscle					
4.8	28	0.008 0.009 0.016	0.008 0.008 0.014	0.008 0.014 0.018	ND 0.001 ND	ND ND ND	ND ND ND
18.8	28	0.036 0.020 0.025	0.033 0.027 0.023	0.029 0.032 0.032	0.001 0.002 0.002	ND 0.002 ND	ND ND ND
51.9	28	0.054 0.045 0.048	0.048 0.048 0.061	0.075 0.060 0.057	0.004 0.004 0.003	0.003 0.002 0.002	ND ND ND
56.8	30 (2)	0.009	0.008	0.009	ND	ND	ND

Dose level (ppm)	Study day	Residue (mg/kg) Chlorantraniliprole	IN-H2H20	IN-F9N04	IN-K7H29	IN-GAZ70	IN-EQW78
56.8	33 (5)	0.002	ND	ND	ND	ND	ND
56.8	36 (8)	ND	ND	ND	ND	ND	ND
		Skin/fat					
4.8	28	0.032 0.030 0.066	0.011 0.014 0.032	0.025 0.039 0.072	ND ND 0.002	ND ND ND	ND ND ND
18.8	28	0.141 0.066 0.078	0.089 0.053 0.061	0.098 0.094 0.116	0.004 0.003 0.004	0.007 0.008 0.008	0.005 ND ND
51.9	28	0.141 0.150 0.212	0.085 0.089 0.101	0.236 0.200 0.177	0.008 0.008 0.007	0.017 0.014 0.018	ND 0.006 0.005
56.8	30 (2)	0.031	0.014	0.026	0.002	0.006	ND
56.8	33 (5)	0.002	0.001	ND	ND	ND	ND
56.8	36 (8)	0.003	ND	0.001	ND	ND	ND

[A] 3 independent samples from 3 subgroups in each dose group

APPRAISAL

Chlorantraniliprole was first evaluated for residues and toxicological aspects by the 2008 JMPR. The 2008 JMPR established an ADI for chlorantraniliprole of 0–2 mg/kg bw and concluded that an ARfD was unnecessary. The residue definition for compliance with MRL and for dietary intake for plant and animal commodities is chlorantraniliprole. The residue is considered fat soluble. It was last evaluated in 2014 for additional maximum residue levels. At the 47th Session of the CCPR (2015), chlorantraniliprole was listed for consideration of further additional maximum residue levels by the 2016 JMPR.

The Meeting received information on registered use patterns, supervised residue trials on spring onions, cereals (barley, sorghum, wheat) and peanuts that were previously submitted to the 2014 JMPR as well as a residue transfer study in laying hens. Product labels were available from Canada and the United States of America.

Methods of analysis

Residue trial samples in crops were analysed using LC-MS/MS methods based on those previously evaluated by the JMPR in 2008.

An analytical method was provided reported for the analysis of chlorantraniliprole and selected metabolites (IN-K9T00, IN-HXH44, IN-GAZ70, IN-EQW78) in poultry tissues and eggs. The basic approach employs homogenisation and extraction with acetonitrile:hexane. Clean-up of tissue extracts is by SPE (hydrophilic lipophilic balanced polymer and strong anion exchange in sequence). Residues are determined by LC-MS/MS. The analytical method for chlorantraniliprole and selected metabolites was validated with LOQs of 0.01 mg/kg for each analyte.

Stability of pesticide residues in stored analytical samples

As reported by the 2014 JMPR, samples were stored frozen for periods less than the period of stability demonstrated in studies provided to the 2008 Meeting and were satisfactory.

Results of supervised residue trials on crops

Supervised residue trial data for were available for chlorantraniliprole on spring onions, cereals (barley, sorghum, wheat) and peanuts. The trials were evaluated by the 2014 JMPR.

Bulb vegetables-green onion

The critical GAP for bulb vegetables (Crop group 3-07) in the USA is for applications at a maximum rate of 110 g ai/ha, with a maximum of 225 g ai/ha/season, at intervals of 7 days and a PHI of 1 day. None of the trials from Canada and the USA approximated critical GAP in the USA as the spray interval employed was too short at 3 days.

The critical GAP for bulb vegetables, green onions (US crop subgroup 3-07B) in Canada is for applications at a maximum rate of 75 g ai/ha, with a maximum of 225 g ai/ha/season, at intervals of 5 days and a PHI of 1 day. None of the trials from Canada and the USA approximated critical GAP in Canada. The data were not suitable for application of proportionality as the number of sprays, spray intervals and application rates deviated from critical GAP.

Cereals

Chlorantraniliprole is approved for use on cereals in Canada and the USA. Critical GAP in the USA for cereals (except corn and rice) is applications at up to 110 g ai/ha, maximum seasonal application 225 g ai/ha, at intervals of 7 days with a PHI of 1 day. In trials approximating critical GAP in the USA residues in cereal grain were:

Barley (n = 3): 1.9, 1.9 and 2.0 mg/kg

Sorghum (n = 3): 0.79, 1.2 and 1.5 mg/kg

Wheat (n = 5): 0.18, 0.19, 0.23, 0.25 and 0.41 mg/kg.

The Meeting considered the number of trials in the individual cereal crops insufficient to estimate maximum residue level for barley, sorghum and wheat and decided to consider whether it would be possible to estimate a group maximum residue level for cereal grains (except corn and rice). In considering whether a group maximum residue level is possible the Meeting noted the median residues differed by more than a factor of 5; as a result it would not be appropriate to combine the trials on the individual crops to make a larger dataset, the number of trials remained insufficient to estimate a maximum residue level.

Peanuts

The critical GAP in the USA is applications at 110 g ai/ha, a maximum of 224 g ai/ha/year, with a 5 day retreatment interval and a PHI of 1 day. In five trials conducted in peanuts in the USA in which two applications of chlorantraniliprole were made at 111–115 g ai/ha (total application rate of 224–228 g ai/ha) with a 5– 6 day retreatment interval and a PHI of 1 day residues were: < 0.01, < 0.01, < 0.01, 0.012, 0.034 mg/kg.

The Meeting estimated a maximum residue level of 0.06 mg/kg and STMR of 0.01 mg/kg for chlorantraniliprole in peanuts.

Animal feeds

Cereals

Chlorantraniliprole is approved for use on cereals in Canada and the USA. Critical GAP in the USA for cereals (except corn and rice) is application at a maximum of 110 g ai/ha, maximum seasonal application 225 g ai/ha, at intervals of 7 days with a PHI of 1 day (no PHI for forage or hay). In trials approximating critical GAP in the USA residues in cereal forage were:

Sorghum forage (n = 3): 2.7, 3.4, 4.1 mg/kg.

Wheat forage (n = 4): 4.3, 4.3, 4.4, 4.6 mg/kg.

The Meeting noted that residues in sorghum and wheat forage are similar and agreed to use them in mutual support to estimate a median and highest residue for cereal forage (except maize and rice) of 4.3 and 4.6 mg/kg (as received basis) respectively.

In trials approximating critical GAP in the USA residues in cereal fodder were:

Barley hay (n = 3): 5.5, 9.2, 11 mg/kg;

Wheat hay (n = 4): 8.6, 9.5, 11, 11 mg/kg; for hay, and

Barley straw (n = 3): 3.6, 12, 14 mg/kg;

Sorghum stover (n = 3): 3.4, 4.1, 5.9 mg/kg;

Wheat straw (n = 4): 0.19, 4.5, 6.4, 15 mg/kg; for straw and stover.

The Meeting agreed to utilize the data for straw and stover to estimate a maximum residue level for fodder of cereals (except maize and rice) and decided to combine the data for straw and stover. The combined dataset is:

0.19, 3.4, 3.6, 4.1, 4.5, 5.9, 6.4, 12, 14, 15 mg/kg.

The Meeting estimated a maximum residue level of 30 mg/kg (dry weight basis), median residue of 5.2 mg/kg (as received) and highest residue of 15 mg/kg (as received) for chlorantraniliprole in fodder of cereals (except corn and rice).

Residues in animal commodities

Farm animal feeding studies

The Meeting received information on the residue levels in tissues and eggs of laying hens dosed with chlorantraniliprole at the equivalent of 4.8, 18.8 and 51.9 ppm in the feed for 28 consecutive days.

Mean and highest residues of chlorantraniliprole (parent compound) in eggs were 0.132 and 0.147 mg/kg for the 4.8 ppm group, 0.296 and 0.512 mg/kg for the 18.8 ppm group, 0.447 and 0.680 mg/kg for the 51.9 ppm group.

Mean and highest residues of chlorantraniliprole (parent compound) in liver were 0.038 and 0.054 mg/kg for the 4.8 ppm group, 0.092 and 0.122 mg/kg for the 18.8 ppm group, 0.147 and 0.178 for the 51.9 ppm group.

Mean and highest residues of chlorantraniliprole (parent compound) in muscle were 0.011 and 0.016 mg/kg for the 4.8 ppm group, 0.027 and 0.036 mg/kg for the 18.8 ppm group, 0.049 and 0.054 for the 51.9 ppm group.

Mean and highest residues of chlorantraniliprole (parent compound) in skin and fat were 0.042 and 0.066 mg/kg for the 4.8 ppm group, 0.096 and 0.141 for the 18.8 ppm group, 0.168 and 0.212 for the 51.9 ppm group.

Estimation of livestock dietary burdens

The Meeting recalculated the livestock dietary burden based on the uses considered by the current Meeting and by the 2008, 2010, 2013 and 2014 Meetings on the basis of diets listed in the 2016 edition of the FAO Manual Appendix IX (OECD Feedstuff Table). The maximum dietary burdens are 36 ppm for beef cattle and 30 ppm for dairy cattle, while the mean dietary burdens are 18 ppm for beef cattle and 17 ppm for dairy cattle. These values have changed only marginally from those calculated by the 2013 Meeting (beef cattle maximum/mean of 31.7/15.7 ppm, and dairy cattle maximum/mean of 26.8/13.1 ppm). The Meeting confirmed its previous recommendations for maximum residue levels and STMR values for meat from mammals other than marine mammals, milks and edible offal (mammalian).

The maximum and mean dietary burdens for poultry were unchanged from those previously calculated. The current Meeting noted previous maximum residue level estimates for poultry commodities were based on a laying hen metabolism study and decided to estimate residues in poultry commodities using the newly available laying hen residue transfer study.

Summary of poultry dietary burden (ppm dry matter diet)

	US-Canada		EU		Australia		Japan	
	max	mean	Max	mean	max	Mean	max	Mean
Broilers	0.064	0.064	0.073	0.051	0.118	0.118	1.454	0.869
Layers	0.064	0.064	4.8[A]	3.6[B]	0.118	0.118	0.053	0.053

[A] Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs

[B] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs

Animal commodity maximum residue levels

The calculation used to estimate highest total residues for use in estimating maximum residue levels, STMR and HR values is shown below.

	Feed level (ppm) for egg residues	Residues (mg/kg) in eggs	Feed level (ppm) for tissue residues	Residues (mg/kg)		
				Muscle	Liver	Skin and Fat
MRL						
Feeding study [A]	4.8	0.162	4.8	0.016	0.054	0.066
Dietary burden and high residue estimates	4.8	0.162	4.8	0.016	0.054	0.066
STMR						
Feeding study [B]	4.8	0.132	4.8	0.011	0.038	0.042
Dietary burden and median residue estimates	3.6	0.099	3.6	0.008	0.028	0.031

[A] highest residues for tissues and eggs

[B] mean residues for tissues and eggs

The Meeting confirmed its previous recommendations for maximum residue level of 0.2 mg/kg and recommended an STMR of 0.099 mg/kg for eggs.

The meeting estimated maximum residue levels of 0.02 mg/kg for poultry meat, 0.07 mg/kg for poultry edible offal and 0.08 mg/kg for poultry fats to replace its previous recommendations of 0.01*and 0.01* and 0.01* mg/kg respectively. The Meeting also estimated the following STMR values: poultry muscle 0.008 mg/kg; poultry fat 0.031 mg/kg; poultry edible offal 0.028 mg/kg and eggs 0.099 mg/kg.

RECOMMENDATIONS

On the basis of the data obtained from supervised residue 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 MRL and for dietary risk assessment) for plant and animal commodities: *chlorantraniliprole.*

The residue is fat soluble.

Commodity		Recommended MRL (mg/kg)		STMR or STMR-P (mg/kg)	HR, HR-P, highest residue (mg/kg)
CCN	Name	New	Previous		
PE 0112	Eggs	0.2	0.2	0.099	
SO 0697	Peanut	0.06		0.01	
PF 0111	Poultry fats	0.08	0.01*	0.031	
PM 0110	Poultry meat	0.02	0.01*	0.008	
PO 0111	Poultry, Edible offal of	0.07	0.01*	0.028	
AS 0161	Straw, fodder (dry) and hay of cereal grains and other grass-like plants (except corn and rice).	30 (dw)	-	5.2	15

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The 2008 JMPR established an Acceptable Daily Intake (ADI) of 0–2 mg/kg bw for chlorantraniliprole.

The evaluation of chlorantraniliprole resulted in recommendations for MRLs and STMR values for raw and processed commodities. Where data on consumption were available for the listed food commodities, dietary intakes were calculated for the 17 GEMS/Food Consumption Cluster Diets. The results are shown in Annex 3.

The IEDIs in the seventeen Cluster Diets, based on the estimated STMRs were 0–1% of the maximum ADI (2 mg/kg bw). The Meeting concluded that the long-term dietary exposure to residues of chlorantraniliprole from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term dietary exposure

The 2008 JMPR decided that an ARfD for chlorantraniliprole was unnecessary. The Meeting therefore concluded that the short-term dietary exposure to residues of chlorantraniliprole resulting from uses that have been considered by the JMPR is unlikely to present a public health concern.

REFERENCES

Code	Author	Year	Title, Institute, Report reference
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31256	Harris, J.A.	2011	Validation of an analytical method for the determination of chlorantraniliprole (DPX-E2Y45) and metabolites (IN-H2H20, IN-F9N04, IN-K7H29, IN-GAZ70 and IN-EQW78) in poultry eggs and tissues by LC-MS/MS and validation of an analytical method for determination of chlorantraniliprole in dose capsules by HPLC. Charles River Laboratories (UK). DuPont Report No. DuPont-31256, Revision No. 1. Unpublished.
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