5.8 CYANTRANILIPROLE (263)

TOXICOLOGY

Cyantraniliprole is the ISO-approved common name for 3-bromo-1-(3-chloro-2-pyridyl)-4′-cyano-2′-methyl-6′-(methylcarbamoyl)pyrazole-5-carboxanilide (IUPAC), with CAS No. 736994-63-1. It is a new second-generation ryanodine receptor insecticide whose pesticidal mode of action is through unregulated activation of insect ryanodine receptor channels, which leads to internal calcium store depletion and impaired regulation of muscle contraction, causing paralysis and eventual death of the insect. Cyantraniliprole is used to control insect pests in fruit crops, tree nuts, oil seed crops, cotton, grapes, rice, vegetables, ornamentals and turf around the world.

Cyantraniliprole has not been evaluated previously by JMPR and is being evaluated by the present Meeting at the request of CCPR.

All critical studies were certified as complying with GLP.

Biochemical aspects

Cyantraniliprole is readily absorbed in rats, and the absorption is similar at 10 and 150 mg/kg bw. The majority of the absorption occurs during the first 24 hours (85% of the absorbed radioactivity), and the peak plasma concentration (C_{max}) is reached approximately 2 hours after dosing, regardless of the sex or dose level. The C_{max} and area under the plasma concentration–time curve (AUC) values demonstrate a 2- to 3-fold greater exposure in female rats than in male rats. Following oral dosing, the majority of the dose is extensively distributed throughout the body. The half-life is shorter in male rats than in female rats (42–53 hours in males and 117–129 hours in females). The absorbed cyantraniliprole is readily and extensively metabolized, mainly by hydroxylation of methylphenyl and *N*-methyl carbon. Further metabolism of the hydroxylated metabolites includes *N*-methylation, nitrogen-to-carbon cyclization with loss of a water molecule, oxidation of alcohols to carboxylic acids, amide bridge cleavage, amine hydrolysis and *O*-glucuronidation. The bile is found to be very rich in metabolites, and most of the metabolites are found in both urine and faeces. IN-MLA84 (2-[3-bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazol-5-yl]-1,4-dihydro-8-methyl-4-oxo-6-quinazolinecarbonitrile) is the most abundant analyte in the blood of rats and mice of both sexes, whereas the highest concentrations in dogs are of the parent compound, cyantraniliprole.

Toxicological data

In rats, the oral LD_{50} was greater than 5000 mg/kg bw, the dermal LD_{50} was greater than 2000 mg/kg bw and the inhalation LC_{50} was greater than 5.2 mg/L. Cyantraniliprole was not a skin irritant in rabbits, an eye irritant in rabbits or a skin sensitizer.

Liver was the interspecies target of cyantraniliprole in short- and long-term studies, although dogs appeared to be more sensitive than rats. In rodents, the thyroid was also a target organ, with adverse effects on thyroid hormone metabolism.

Short-term toxicity of cyantraniliprole was examined in mice, rats and dogs. The NOAEL in a 28-day oral toxicity study in mice was 7000 ppm (equal to 1261 mg/kg bw per day), the highest dose tested. The NOAEL in a 90-day oral toxicity study in which mice were administered cyantraniliprole in the diet at a concentration of 0, 50, 300, 1000 or 7000 ppm (equal to 0, 7.2, 47.1, 150 and 1091 mg/kg bw per day for males and 0, 9.7, 58.1, 204 and 1344 mg/kg bw per day for females, respectively) was 1000 ppm (equal to 204 mg/kg bw per day), based on minimal necrosis in the liver at 7000 ppm (equal to 1344 mg/kg bw per day) in females.

In a 28-day oral toxicity study in which rats were administered cyantraniliprole in the diet at a concentration of 0, 600, 2000, 6000 or 20 000 ppm (equal to 0, 53, 175, 528 and 1776 mg/kg bw per day for males and 0, 62, 188, 595 and 1953 mg/kg bw per day for females, respectively), the NOAEL

was 600 ppm (equal to 53 mg/kg bw per day), based on liver hypertrophy and thyroid follicular cell hypertrophy observed in both sexes at 2000 ppm (equal to 175 mg/kg bw per day). In a 90-day oral toxicity study in which rats were administered a dietary concentration of 0, 100, 400, 3000 or 20 000 ppm (equal to 0, 5.7, 22, 168 and 1147 mg/kg bw per day for males and 0, 6.9, 27, 202 and 1346 mg/kg bw per day for females, respectively), the NOAEL was 100 ppm (equal to 5.7 mg/kg bw per day), based on liver hypertrophy, decreases in thyroid hormones in both sexes and histopathological changes in the thyroid in females at 400 ppm (equal to 22 mg/kg bw per day).

Three feeding studies (28 days, 90 days and 1 year) were conducted with cyantraniliprole in dogs. A NOAEL for the 28-day oral toxicity study in dogs was not determined, based on changes in body weight, nutritional parameters and clinical chemistry indicating hepatotoxicity in both sexes at 1000 ppm (equal to 35 mg/kg bw per day), the lowest dose tested. The NOAEL for the 90-day oral toxicity study in which dogs were administered cyantraniliprole at 0, 30, 10, 1000 or 10 000 ppm (equal to 0, 0.98, 3.08, 31.9 and 281 mg/kg bw per day for males and 0, 0.97, 3.48, 34.40 and 294 mg/kg bw per day for females, respectively) was 100 ppm (equal to 3.08 mg/kg bw per day), based on increased total protein, albumin and AP levels in males at 1000 ppm (equal to 31.9 mg/kg bw per day). In a 1-year dog study utilizing concentrations of 0, 40, 200, 1000 and 5000 ppm (equal to 0, 0.96, 5.67, 27.0 and 144 mg/kg bw per day for males and 0, 1.12, 6.00, 27.1 and 133 mg/kg bw per day for females, respectively), the increased levels of AP at 40 ppm were not considered adverse in view of the absence of histopathological or functional changes at this and the next higher dose (200 ppm). Therefore, the NOAEL for the 1-year oral toxicity study in dogs was 40 ppm (equal to 0.96 mg/kg bw per day), based on marginal increases in AP levels without histopathological change in the liver in both sexes, increased liver weights in males and decreased cholesterol in females at 200 ppm (equal to 5.67 mg/kg bw per day). The Meeting concluded that the overall NOAEL for oral toxicity in dogs was 100 ppm (equal to 3.08 mg/kg bw per day), and the overall LOAEL was 200 ppm (equal to 5.67 mg/kg bw per day).

Long-term toxicity studies were conducted in mice and rats. In an 18-month carcinogenicity study in which mice were administered a dietary concentration of 0, 20, 150, 1000 or 7000 ppm (equal to 0, 2.0, 15.5, 104 and 769 mg/kg bw per day for males and 0, 2.4, 18.6, 131 and 904 mg/kg bw per day for females, respectively), the NOAEL for toxicity was 1000 ppm (equal to 104 mg/kg bw per day), based on a decrease in body weight gain and increased thyroid weight in males at 7000 ppm (equal to 769 mg/kg bw per day). No increase in neoplastic incidence was observed. The NOAEL for carcinogenicity in mice was 7000 ppm (equal to 769 mg/kg bw per day), the highest dose tested.

In a 2-year toxicity and carcinogenicity feeding study in which rats were administered cyantraniliprole in the diet at 0, 20, 200, 2000 or 20 000 ppm (equal to 0, 0.8, 8.3, 84.8 and 907 mg/kg bw per day for males and 0, 1.1, 10.5, 107 and 1161 mg/kg bw per day for females, respectively), the NOAEL for toxicity was 200 ppm (equal to 8.3 mg/kg bw per day), based on increased incidences of foci of cellular alteration in the liver in males and hepatocellular vacuolation in both sexes and slight depression of body weights in females at 2000 ppm (equal to 84.8 mg/kg per day). No increase in neoplastic incidence was observed, and the NOAEL for carcinogenicity in rats was 20 000 ppm (equal to 907 mg/kg bw per day), the highest dose tested.

The Meeting concluded that cyantraniliprole is not carcinogenic in mice or rats.

Cyantraniliprole was tested for genotoxicity in vitro and in vivo in an adequate range of assays. In these assays, there was no evidence of genotoxic potential.

The Meeting concluded that cyantraniliprole is unlikely to be genotoxic.

On the basis of the lack of genotoxicity and the absence of carcinogenicity in mice and rats, the Meeting concluded that cyantraniliprole is unlikely to pose a carcinogenic risk to humans.

In a multigeneration reproductive toxicity study in which rats were given cyantraniliprole at a concentration of 0, 20, 200, 2000 or 20 000 ppm (in P generation: equal, respectively, to 0, 1.1, 11.0, 110 and 1125 mg/kg bw per day for males, 0, 1.4, 13.9, 136 and 1344 mg/kg bw per day for premating females, 0, 1.4, 13.3, 135 and 1353 mg/kg bw per day for females during gestation, and 0,

2.7, 27.0, 283 and 2782 mg/kg bw per day for females during lactation; in F generation: equal, respectively, to 0, 1.4, 14.6, 150.8 and 1583 mg/kg bw per day for males, 0, 1.9, 20.1, 203 and 2125 mg/kg bw per day for premating females, 0, 1.4, 14.7, 149 and 1518 mg/kg bw per day for females during gestation and 0, 2.7, 27.4, 277 and 2769 mg/kg bw per day for females during lactation), the NOAEL for parental toxicity was 200 ppm (equal to 11.0 mg/kg bw per day), based on increased hepatocellular hypertrophy and thyroid follicular cell hypertrophy in both sexes at 2000 ppm (equal to 110 mg/kg bw per day) in the P generation. The NOAEL for reproductive toxicity was 20 000 ppm (equal to 1344 mg/kg bw per day), the highest dose tested. The NOAEL for offspring toxicity was 2000 ppm (equal to 280 mg/kg bw per day, mean value for P and F_1 parental females during lactation), based on lower body weights of F_1 and F_2 generation pups at 20 000 ppm (equal to 2780 mg/kg bw per day, mean value for P and F_1 parental females during lactation).

In a developmental toxicity study in rats administered a dose of 0, 20, 100, 300 or 1000 mg/kg bw per day, the NOAELs for both maternal and embryo/fetal toxicity in rats were 1000 mg/kg bw per day, the highest dose tested.

In a developmental toxicity study in rabbits administered a dose of 0, 25, 100, 250 or 500 mg/kg bw per day, the NOAEL for maternal toxicity was 25 mg/kg bw per day, based on mortality, increased clinical signs of toxicity, including diarrhoea, and lower body weights and feed consumption at 100 mg/kg bw per day. The NOAEL for embryo/fetal toxicity was 100 mg/kg bw per day, based on reductions in fetal weight at 250 mg/kg bw per day.

The Meeting concluded that cyantraniliprole is not teratogenic in rats or rabbits.

In an acute neurotoxicity study in rats, the NOAEL was 2000 mg/kg bw, the highest dose tested.

In a 90-day study of neurotoxicity in which rats were administered a dose of 0, 200, 2000 or 20 000 ppm (equal to 0, 11.4, 115 and 1195 mg/kg bw per day for males and 0, 14.0, 137 and 1404 mg/kg bw per day for females, respectively), the NOAEL was 20 000 ppm (equal to 1195 mg/kg bw per day), the highest dose tested.

The Meeting concluded that cyantraniliprole is not neurotoxic.

Immunotoxicity studies were conducted in mice and rats. In a 28-day immunotoxicity study in mice, the NOAEL was 7000 ppm (equal to 1065 mg/kg bw per day), the highest dose tested. In a 28-day immunotoxicity study in rats, the NOAEL was 20 000 ppm (equal to 1699 mg/kg bw per day), the highest dose tested.

Toxicological data on metabolites and/or degradates

Acute toxicity and genotoxicity studies of metabolites were conducted. 4-[[[3-Bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]carbonyl]amino]-3-methyl-5-[(methylamino)carbonyl]benzoic acid (IN-JSE76), 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-1,4-dihydro-8-methyl-4-oxo-6-quinazolinecarboxylic acid (IN-PLT97), 6-chloro-4-methyl-11-oxo-11H-pyrido[2,1-*b*]quinazoline-2-carbonitrile (IN-N5M09) and 3-bromo-*N*-methyl-1H-pyrazole-5-carboxamide (IN-F6L99) were degradates in soil. All metabolites exhibited low acute toxicities and no genotoxicity. The NOAEL in a 28-day toxicity study of IN-JSE76 in rats was 20 000 ppm (equal to 1445 mg/kg bw per day), the highest dose tested.

Human data

No information on medical surveillance or poisoning incidents was available.

The Meeting concluded that the existing database on cyantraniliprole was adequate to characterize the potential hazards to fetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0–0.03 mg/kg bw on the basis of the overall NOAEL of 3.08 mg/kg bw per day in dog studies, based on liver effects at 5.67 mg/kg bw per day. A safety factor of 100 was applied.

The metabolites IN-N7B69, IN-MLA84, IN-MYX98 and IN-J9Z38 have been included in the residue definition. As the estimated exposure to IN-N7B69 is below the threshold of toxicological concern for Cramer class III compounds, there is no concern for this metabolite. For the other three metabolites, these have been tested in rodents through their formation from the parent compound and are therefore covered by the ADI for cyantraniliprole.

The Meeting concluded that it was not necessary to establish an ARfD for cyantraniliprole in view of its low acute toxicity and the absence of developmental toxicity and any other toxicological effects that would be likely to be elicited by a single dose.

A toxicological monograph was prepared.

Levels relevant to risk assessment of cyantraniliprole

Species	Study	Effect	NOAEL	LOAEL
Mouse	Eighteen-month study of toxicity and carcinogenicity[a]	Toxicity	1000 ppm, equal to 104 mg/kg bw per day	7000 ppm, equal to 769 mg/kg bw per day
		Carcinogenicity	7000 ppm, equal to 769 mg/kg bw per day[b]	—
Rat	Ninety-day study of toxicity[a]	Toxicity	100 ppm, equal to 5.7 mg/kg bw per day	400 ppm, equal to 22 mg/kg bw per day
	Two-year studies of toxicity and carcinogenicity[a]	Toxicity	200 ppm, equal to 8.3 mg/kg bw per day	2000 ppm, equal to 84.8 mg/kg bw per day
		Carcinogenicity	20 000 ppm, equal to 907 mg/kg bw per day[b]	—
	Multigeneration reproductive toxicity study[a,d]	Parental toxicity	200 ppm, equal to 11.0 mg/kg bw per day	2000 ppm, equal to 110 mg/kg bw per day
		Reproductive toxicity	20 000 ppm, equal to 1344 mg/kg bw per day[b]	—
		Offspring toxicity	2000 ppm, equal to 280 mg/kg bw per day	20 000 ppm, equal to 2780 mg/kg bw per day
	Developmental toxicity study[c]	Maternal toxicity	1000 mg/kg bw per day[b]	—
		Embryo and fetal toxicity	1000 mg/kg bw per day[b]	—
	Acute neurotoxicity	Toxicity	2000 mg/kg bw per day[b]	—
	Ninety-day study of neurotoxicity[a]	Neurotoxicity	20 000 ppm, equal to 1195 mg/kg bw per day[b]	—
Rabbit	Developmental	Maternal toxicity	25 mg/kg bw per day	100 mg/kg bw per day

Species	Study	Effect	NOAEL	LOAEL
	toxicity study[c]	Embryo and fetal toxicity	100 mg/kg bw per day[b]	250 mg/kg bw per day
Dog	Ninety-day and 1-year studies of toxicity[a,d]	Toxicity	100 ppm, equal to 3.08 mg/kg bw per day	200 ppm, equal to 5.67 mg/kg bw per day

[a] Dietary administration.

[b] Gavage administration.

[c] Highest dose tested.

[d] Two or more studies combined.

Estimate of acceptable daily intake

0–0.03 mg/kg bw

Estimate of acute reference dose

Unnecessary

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposure

Critical end-points for setting guidance values for exposure to cyantraniliprole

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid (in 2 h) and extensive (> 85%)
Dermal absorption	No data
Distribution	Extensive; all tissues
Potential for accumulation	Low
Rate and extent of excretion	Rapid (mainly in 48 h samples) and extensive; faeces > urine
Metabolism in animals	IN-MLA84 is abundant in mice and rats, less in dogs
Toxicologically significant compounds in animals, plants and the environment	Cyantraniliprole, IN-MLA84, IN-MYX98 and IN-J9Z38
Acute toxicity	
Rat, LD_{50}, oral	> 5000 mg/kg bw
Rat, LD_{50}, dermal	> 5000 mg/kg bw
Rat, LC_{50}, inhalation	> 5.2 mg/L
Mouse, LD_{50}, oral	> 5000 mg/kg bw
Rat, dermal irritation	Non-irritating
Rabbit, ocular irritation	Non-irritating
Sensitization	Non-sensitizing (LLNA in mice; maximization test in guinea-pigs)
Short-term toxicity	

Target/critical effect	Liver and thyroid / increases in AP and liver weights (dogs)
Lowest relevant oral NOAEL	3.08 mg/kg bw per day (dog)
Lowest relevant dermal NOAEL	1000 mg/kg bw per day (rat)
Lowest relevant inhalation NOAEC	No data
Long-term toxicity and carcinogenicity	
Target/critical effect	Liver and thyroid / increased incidence of altered foci of hepatocytes in the liver, decreased body weight gain in females
Lowest relevant NOAEL	8.3 mg/kg bw per day (rat)
Carcinogenicity	Not carcinogenic
Genotoxicity	
	Not genotoxic
Reproductive toxicity	
Reproduction target/critical effect	No reproductive toxicity
Lowest relevant parental NOAEL	11.0 mg/kg bw per day
Lowest relevant offspring NOAEL	280 mg/kg bw per day
Lowest relevant reproductive NOAEL	1344 mg/kg bw per day, the highest dose tested
Developmental toxicity	
Target/critical effect	Mortality, increased clinical signs, decreased body weight gain and lower feed consumption of dams
Lowest relevant maternal NOAEL	25 mg/kg bw per day (rabbit)
Lowest relevant developmental NOAEL	100 mg/kg bw per day (rabbit)
Neurotoxicity	
Acute and subchronic neurotoxicity	Not neurotoxic
Immunotoxicity	
Lowest relevant immunotoxicity NOAEL	1065 mg/kg bw per day, the highest dose tested (mouse)
Medical data	
	No information available

Summary

	Value	Study	Safety factor
ADI	0–0.03 mg/kg bw	Ninety-day and 1-year toxicity studies (dog)	100
ARfD	Unnecessary	—	—

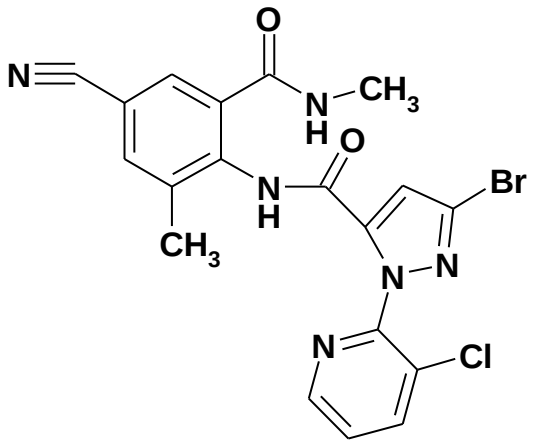
RESIDUE AND ANALYTICAL ASPECTS

Cyantraniliprole is a diamide insecticide with a mode of action (ryanodine receptor activation) similar to that of chlorantraniliprole and flubendiamide with root systemic and translaminar activity against the larval stages of lepidopteran insects; and also on thrips, aphids, and some other chewing and sucking insects.

It was scheduled by the Forty-fourth Session of the CCPR (REP12/PR) as a new compound for consideration by the 2013 JMPR. The manufacturer submitted studies on metabolism, analytical methods, supervised field trials, processing, freezer storage stability, environmental fate in soil and rotational crop residues.

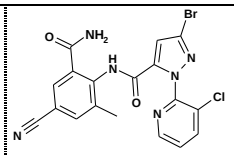
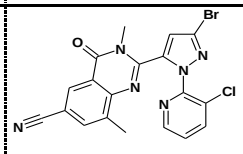
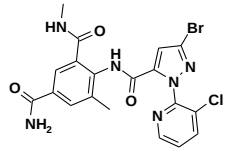
Authorisations exist for the use of cyantraniliprole in Canada, Columbia, Malaysia, New Zealand, Vietnam and in a regional grouping of countries in West Africa (CLISS).

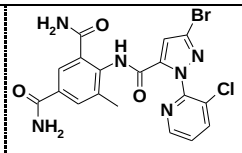
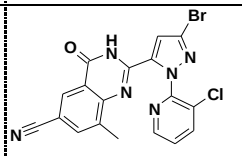
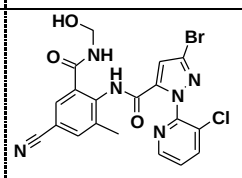
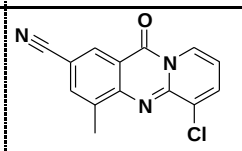
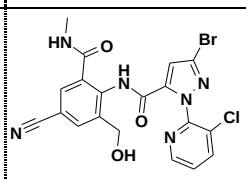
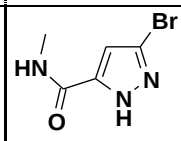
Cyantraniliprole is 3-bromo-1-(3-chloro-2-pyridyl)-4′-cyano-2′-methyl-6′-(methylcarbamoyl) pyrazole -5-carboxanilide. It is relatively insoluble in water (12 mg/L at pH 7, 6 mg/L at pH 9) and hydrolyses under alkaline conditions and at higher temperatures (above 25 °C), the major hydrolysis product being IN-J9Z38. It is not volatile (1.2×10^{-15} Pa at 20 °C), has a log P_{OW} of 1.9, its solubility in organic sovents ranges from < 1 g/L (octanol, xylene) to 5–7 g/L (methanol, dichloromethane, acetone) and is rapidly degraded by photolysis.



Cyantraniliprole (DPX-HGW86)
(MW 473.7)

The following abbreviations are used for the metabolites discussed below:

IN-HGW87		N-[2-(Aminocarbonyl)-4-cyano-6-methylphenyl]-3-bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide	
IN-J9Z38		2-[3-Bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazol-5-yl]-3,4-dihydro-3,8-dimethyl-4-oxo-6-quinazolinecarbonitrile	MW 455.7
IN-JCZ38		4-[[[3-Bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazol-5-yl]carbonyl]amino]-N′3′,5-dimethyl-1,3-benzenedicarboxamide	MW 491.7

IN-K7H19		4-[[[3-Bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazol-5-yl]carbonyl]amino]-5-methyl-1,3-benzenedicarboxamide	MW 477.7
IN-MLA84		2-[3-Bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazol-5-yl]-1,4-dihydro-8-methyl-4-oxo-6-quinazolinecarbonitrile	MW 441.7
IN-MYX98		3-Bromo-1-(3-chloro-2-pyridinyl)-N-[4-cyano-2[[(hydroxymethyl)amino]carbonyl]-6-methylphenyl]-1*H*-pyrazole-5-carboxamide	MW 489.7
IN-N5M09		6-Chloro-4-methyl-11-oxo-11*H*-pyrido[2,1-*b*]quinazoline-2-carbonitrile	MW 441.6
IN-N7B69		3-Bromo-1-(3-chloro-2-pyridinyl)-N-[4-cyano-2-(hydroxymethyl)-6-[(methylamino)carbonyl]phenyl]-1*H*-pyrazole-5-carboxamide	MW 489.7
IN-F6L99		3-Bromo-N-methyl-1H-pyrazole-5-carboxamide	MW 204

Animal metabolism

The Meeting received information on the metabolism of radiolabelled cyantraniliprole, separately ^{14}C-labelled at the 4-cyano (CN) and the pyrazole carbonyl (PC) groups, in rats, lactating goats and laying hens.

The WHO panel of the 2013 JMPR concluded that in rats, the majority of the dose was excreted within 24 to 48 hours, with about 1–5.5% TRR being recovered in tissues and that tissue elimination half-lives ranged from 2.6 days (fat) to about 6 days in whole blood.

The metabolic pathway was primarily through hydroxylation (to form IN-N7B69 and IN-MYX98), with IN-N7B69 being further metabolized to a glucuronide conjugate. Cyantraniliprole undergoes ring closure to generate IN-J9Z38 which is then in turn hydroxylated to form IN-NBC94, its carboxylic acid, and its glucuronide conjugate. IN-MYX98 is also metabolized to the closed-ring metabolite IN-MLA84, which, like IN-NBC94, is further oxidized to a hydroxylated metabolite, a carboxylic acid, and the glucuronide of the hydroxyl metabolite. Further, the hydroxylated metabolite IN-MYX98 can be N-dealkylated to form IN-HGW87 as well as being hydroxylated a second time to

form bis-hydroxy-cyantraniliprole. Cyantraniliprole can also be hydroxylated on the pyridine ring, followed by a ring closure analogous to the conversion of cyantraniliprole to IN-J9Z38.

Lactating goats were orally dosed with [CN-^{14}C]- or [PC-^{14}C]-cyantraniliprole at doses equivalent to approximately 13 ppm in the feed for 7 consecutive days and sacrificed 23 hours after the last dose.

The majority of the administered dose was recovered in excreta (84–88% in faeces, 7% in urine). About 1–2% (0.08–0.15 mg/kg) of the applied radioactivity was retained in milk, with 0.5 mg/kg (0.3% AR) found in liver and < 0.01% AR in other tissues. Solvent extraction was able to retrieve 99% TRR from milk, 90–98% TRR from fat, 61–81% TRR from muscle and 63–79% TRR from kidney. Solvent extractable TRR in the liver were lower (54–60% TRR) but an additional 21–27% TRR were recovered following digestion of the post extracted solids (PES) with protease.

In milk, TRR reached a plateau of 0.09 and 0.18 mg/kg after 2–3 days in the CN and PC label studies respectively. Cyantraniliprole was the major residue component, making up 40–50% (0.03–0.07 mg/kg) of the radiochemical label. Metabolite IN-MYX98 was also present at 15–18% TRR (0.01–0.03 mg/kg). Other metabolites (except IN-N7B69 at 11% TRR in the CN-label study) were found each < 0.01 mg/kg and less than 10% TRR.

In liver, TRR were 0.43–0.5 mg/kg. Cyantraniliprole (0.07–0.14 mg/kg) made up about 17–23% of the TRR and in kidney (TRR 0.14–0.21 mg/kg) with the major residue was also cyantraniliprole, accounting for 13–19% TRR (0.02–0.04 mg/kg).

In muscle, TRR were 0.03–0.04 mg/kg with the significant residue being cyantraniliprole, found at about 30% TRR and 0.01 mg/kg in the CN-label study and 15% TRR, 0.006 mg/kg in the PC-label study. The IN-MYX98 metabolite also accounted for 33% TRR (0.01 mg/kg) in the PC-label study.

TRR in fat were 0.05 and 0.12 mg/kg in the CN-label and PC-label studies respectively, with consistent results in omental, subcutaneous and renal fat. Cyantraniliprole was the major residue, averaging 31–42% TRR (0.01–0.025 mg/kg) with the IN-J9Z38 metabolite also accounted for 24–27% TRR (0.01–0.03 mg/kg).

Laying hens were orally dosed with [CN-^{14}C]- or [PC-^{14}C]-cyantraniliprole at doses equivalent to approximately 11 ppm in the feed for 14 consecutive days and sacrificed 23 hours after the last dose.

The majority of the administered dose was excreted, with 0.4–0.5% (0.20–0.26 mg/kg) remaining in egg whites, 0.07% (0.09 mg/kg) in yolks. Radioactivity in liver (0.14–0.2 mg/kg) accounted for 0.3–0.4% of the applied dose with muscle, abdominal fat and skin with fat each containing ≤ 0.1% AR (< 0.01 mg/kg).

In eggs, %TRR reached a plateau of about 0.1 mg/kg in yolks after 5–7 days. The %TRRs in egg white increased to 0.26–0.56 mg/kg over the first 2 days and decreased to a steady state of about 0.2–0.24 mg/kg after 7 days.

Solvent extraction was able to retrieve 79–99% TRR from eggs, 63–120% TRR from fat, 100% TRR from muscle and 53–72% TRR from skin with fat. Solvent extractable TRR in the liver were lower (17–23% TRR) but an additional 38% TRR were recovered following digestion of the post extracted solids (PES) with protease.

In eggs, cyantraniliprole was the major residue component, making up 33–42% TRR (0.09 mg/kg) in egg whites and 9–10% TRR (< 0.01 mg/kg) in yolks. Metabolite IN-J9Z38 made up about 17–29% TRR (0.03–0.08 mg/kg) in egg whites and 7–13% TRR (0.006–0.011 mg/kg in yolks. IN-MLA84 was also present in egg whites at about 18–19% TRR (0.04–0.05 mg/kg) and in yolks at about 12–17% TRR (0.01–0.015 mg/kg

In liver, TRR were 0.14–0.17 mg/kg. Cyantraniliprole was not found in any samples and while metabolites IN-JCZ38, IN-K5A78, IN-K5A79, IN-K7H19, IN-MLA84, IN-MYX98 and IN-N7B69 were identified, these were each present at <4% TRR (< 0.01 mg/kg).

In muscle, abdominal fat and skin with fat, no further analysis was conducted because of the low TRR (< 0.004 mg/kg) present.

In summary, the metabolism of cyantraniliprole in lactating goats (ruminant) and laying hen was consistent with that in the rat. Cyantraniliprole residues were rapidly eliminated in the excreta (94–100% of the dose) in goats and laying hens, with less than 1% of the total administered dose remaining in tissues and eggs and 1–2% found in milk). Cyantraniliprole was the predominant residue, with IN-N7B69 (milk), IN-MYX98 (muscle and milk), IN-J9Z38 (fat and eggs) and IN-MLA84 (eggs) being the principal metabolites present at more than 10% TRR or > 0.01 mg/kg.

Plant metabolism

The Meeting received plant metabolism studies on cotton, lettuce, tomato and rice seedlings following foliar and soil treatments with [^{14}C]-cyantraniliprole. A 1:1 (μCi/μCi ratio) mixture of [CN-^{14}C]-cyantraniliprole and [PC-^{14}C]-cyantraniliprole was used in the foliar treatments and separate treatments of the two radiolabels were applied as soil treatments.

Cotton

In cotton plants, treated 3 times with the equivalent of 0.15 kg ai/ha per application as foliar sprays, 7 days apart from 3 weeks after emergence, TRR in leaves immediately after the first treatment were 2.7 and 7.9 mg/kg immediately after the last application and after 13 days had decreased to 0.43 mg/kg. At harvest (124 days after the last application), TRRs in cotton gin by-products, lint and undelinted seed were 0.13, 0.01, and < 0.01 mg/kg, respectively.

Surface washing removed 56–70% TRR from immature leaves with a further 27–33% extracted into acidified aqueous acetone.

Cyantraniliprole was the major residue in leaves, decreasing from 70% TRR immediately after the first application to 20% TRR seven days later and accounted for 37% TRR (0.19 mg/kg) and 27% TRR (0.12 mg/kg), respectively, 7 and 13 days after the final application.

IN-NXX70, a photodegradate of IN-J9Z38, found predominately in the surface wash, accounted for 22% TRR seven days after the first application but decreased to 1% TRR in leaves sampled 7 days after the third application.

Surface washing of cotton gin by-products removed about 19% TRR (0.03 mg/kg) with a further 65% TRR (0.07 mg/kg) being extracted into acetone or with more aggressive extraction methods. Cyantraniliprole was the predominant residue, accounting for 34% TRR (0.04 mg/kg).

In plants from soil treatments where three applications of 0.15 kg ai/ha cyantraniliprole (SC formulation) were made to wetted soil at 7 day intervals from 7 weeks after emergence, TRRs in leaves from immature plants sampled up to 14 days after the last application were all ≤ 0.005 mg/kg. At maturity, 125 days after the last application, residues in lint and undelinted seed were < 0.001 mg/kg and TRR values in cotton gin by-products were 0.1 mg/kg (CN-label) and 0.02 mg/kg (PC-label).

Cyantraniliprole was the only significant residue in gin by-products, making up 26–47% TRR (0.01–0.03 mg/kg).

Lettuce

In lettuce plants, treated 3 times with the equivalent of 0.15 kg ai/ha per application as foliar sprays, 7 days apart from 3 weeks after emergence, TRR in leaves immediately after the first treatment was

11 mg/kg, 10 mg/kg immediately after the second application and about 8 mg/kg just after the last application. Seven days after the last application, TRRs had decreased to about 2 mg/kg and were 0.43 mg/kg at maturity, 32 days after the last application. Surface residues decreased from about 91% TRR immediately after the first application and 32 days after the last application surface residues were 13% TRR.

Cyantraniliprole was the major residue in leaves, decreasing from about 98% TRR immediately after the first application to 50% TRR in mature leaves, 32 days after the last application. The IN-J9Z38 metabolite, present in mature leaves at about 23% TRR (0.01 mg/kg) was only metabolite accounting for more than 5% TRR.

In plants from soil treatment where three applications of 0.15 kg ai/ha cyantraniliprole (SC formulation) were made to wetted soil at 7 day intervals from 7 weeks after emergence, TRRs (CN-label) in leaves from immature plants declined from 0.14 mg/kg immediately after the first application to about 0.05 mg/kg (7 days after the 2nd and 3rd applications) and were about 0.01 mg/kg at maturity. TRRs following the PC-label soil treatment were ≤ 0.06 mg/kg in immature leaves and at crop maturity.

Cyantraniliprole was the major radioactive component present in leaves, up to 77–84% TRR in young leaves and 37% TRR (0.004 mg/kg) and 69% TRR (0.04 mg/kg) in mature leaves for the CN-label and PC-labels respectively.

Tomato

In tomato plants, treated 3 times with the equivalent of 0.15 kg ai/ha per application as foliar sprays, 7 days apart from 3 weeks after emergence, TRR in leaves immediately after the first treatment were 2.5 mg/kg, 8.5 mg/kg immediately after the second application and 7.6 mg/kg just after the last application. Seven days after the last application, TRRs had decreased to about 2.2 mg/kg and were 1.3 mg/kg 14 days after the last application. Residues in fruit and leaves at harvest (132 days after the last treatment were < 0.01 mg/kg. The majority of the TRR (66–85%) were found in the surface wash with 15–34% TRR present in the extract.

Cyantraniliprole was the major residue in leaves, decreasing from about 95% TRR immediately after the first application to 61% TRR seven days later and accounted for 64 and 43% TRR respectively, 7 and 14 days after the last application. In leaves taken at maturity, residues in the surface wash were < 0.01 mg/kg and 0.01 mg/kg in the tissue extracts.

Concentrations of the unresolved radioactivity corresponding to both IN-MLA84 and IN-NXX70, (mostly in the surface wash) reached 11.5% TRR 7 days after the first application, decreasing to 4.4% TRR thereafter.

In plants from soil treatments where three applications of 0.15 kg ai/ha cyantraniliprole (SC formulation) were made to wetted soil in pots at 7 day intervals from 7 weeks after emergence, TRRs reached a maximum of 0.03 mg/kg in immature leaves 7 days after the last application and were < 0.01 mg/kg in leaves and 0.001 mg/kg in fruit at harvest (125 days after the last application).

Cyantraniliprole was the major radioactive component in leaves 7–14 days after the last application, ranging from 22–26% TRR (< 0.01 mg/kg).

Rice

Rice seedlings were treated with three foliar applications of 0.15 kg ai/ha at the 3–4 leaf stage and 7 and 14 days later and grown under flooded conditions (pots immersed in about 3 cm water) from 2 days after the initial treatment until 2–3 days before harvest.

TRRs in foliage were 2.1 mg/kg immediately after the first application, decreasing to 0.38 mg/kg after 7 days. Seven and 14 days after the last application, TRRS in leaves were 1.6 mg/kg and 1.2 mg/kg respectively. At harvest, 140 days after the last application, TRRs in straw were

0.45 mg/kg and 0.02 mg/kg in grain. In roots, TRRs increased from 0.24 mg/kg seven days after the first application to 0.68 mg/kg seven days after the last application and were 0.45 mg/kg at harvest. In immature leaves, 7 days after the last application, the surface wash contained about 75% TRR, reducing to 47% TRR in leaves sampled 14 days after the last treatment.

Cyantraniliprole was the major residue in immature leaves, making up 76–81% TRR (about 1.0 mg/kg) in samples taken 7 and 14 days after the last application. IN-J9Z38 was the predominant metabolite found at 0.6% TRR immediately after the first application and increasing to 11% TRR 14 days after the last application.

In straw, cyantraniliprole was the major component, accounting for 24.4% TRR (0.11 mg/kg) and cyantraniliprole was also the predominant residue in grain, accounting for 21% TRR (0.005 mg/kg).

Rice seedlings were also treated with a single soil application of 0.3 kg ai/ha (as surface-applied granules) at the 3–4 leaf stage and the plants were grown under flooded conditions (pots immersed in about 3 cm water) from 2 days after the initial treatment until 2–3 days before harvest, 175 days after treatment.

TRRs in foliage increased from 0.08 mg/kg (7 days after treatment) to 0.15 mg/kg (14 days after treatment) and reached 0.4 mg/kg after 56 days. Residues in roots were about 0.3 mg/kg after 56 days and at harvest (175 days after treatment). At harvest, TRRs were 0.28–0.3 mg/kg in straw and 0.01–0.03 mg/kg in grain.

Cyantraniliprole was the major residue in leaves sampled 56 days after treatment (49–57% TRR and about 0.2 mg/kg). The IN-J9Z38 metabolite was found in these samples at 16–22% TRR (about 0.08 mg/kg).

The major residue in straw was also cyantraniliprole (42–45% TRR, 0.13 mg/kg), with IN-J9Z38 (14–18% TRR) being the only significant metabolite, found at 14–18% TRR and in grain, cyantraniliprole accounted for 46–63% TRR (0.007–0.014 mg/kg).

In summary, cyantraniliprole was the predominant residue in most crop fractions at various sampling points up to crop maturity. Metabolites identified in foliar treated samples (with the exception of the photodegradate IN-NXX70) were also found in samples from plants treated with a soil drench application, indicating that the main metabolic pathways were similar. Overall, total radioactive residues were greater following foliar treatment than following soil application. A similar profile was observed in all studies.

The metabolite IN-J9Z38 was present at levels above 10% TRR only in rice foliage and lettuce (after foliar applications) and also in rice foliage and straw after soil treatment. Where present, residues were significantly lower (10–50%) than the levels of cyantraniliprole.

The metabolism of cyantraniliprole in plants was generally consistent with those in animals, except for the minor plant photodegradation pathway leading to the formation of IN-NXX70 and IN-QKV54).

Environmental fate

The Meeting received information on the environmental fate and behaviour of cyantraniliprole, including aerobic degradation in soil, photolysis on the soil surface, field soil dissipation, hydrolytic stability, soil and water/sediment degradation and confined and field rotational crop studies. Separate treatments of [CN-^{14}C]-cyantraniliprole and [PC-^{14}C]-cyantraniliprole were used in the confined studies.

Hydrolysis

Hydrolysis of cyantraniliprole was pH and temperature dependant. The rate of hydrolysis was significantly higher at high pH and temperature. The half lives at 15 °C decreased from 362 days (pH 4) to 126 days (pH 7) and was about 3 days at pH 9. A similar pattern was observed at the higher temperature of 35 °C, with the respective half-lives being 55 days, 7.5 days and < 1 day at pH 9. Under environmental conditions (pH 7, 25 °C) the half-life for cyantraniliprole was 212 days.

At all pH's, the predominant hydrolysis product was the cyclisation product IN-J9Z38 which accounted for about 28% AR (pH 4), 89% AR (pH 7) and 98% AR in the pH 9 samples.

Photolysis

In aqueous solutions, cyantraniliprole is rapidly degraded by photolysis. Half-lives in natural water and pH 4 sterile buffer exposed to continuous artificial sunlight for 15 days at 25 °C were 4–5 hours, with the formation of IN-NXX69, IN-NXX70, IN-QKV54 and IN-QKV55 as photodegradates. DT_{90s} were less than 16 hours.

In moist (non-sterile) soil (75% field capacity), treated with [^{14}C]-cyantraniliprole at the equivalent of 1 kg ai/ha parent residues decreased to about 1% AR after 30 days in the irradiated samples and to 33% AR in the non-irradiated samples. The IN-J9Z38 metabolite was the predominant residue (up to about 50% AR) with IN-RNU71 and IN-QKV54 also found at about 13–14% AR. Estimated photolysis DT_{50} and DT_{90} values for cyantraniliprole (derived from the difference in the degradation constants (k) for the irradiated and non-irraditaed samples) were 12 and 41 days respectively. Kinetic modeling suggested that nearly 34% of the cyantraniliprole in soil is degraded by photolysis and about 64% through soil degradation pathway.

Aerobic soil metabolism

Two studies were conducted in five soils (one loam soil, two silty clay loams, one silt loam and a sandy loam) with the equivalent of 0.4 kg ai/ha [CN-^{14}C]-cyantraniliprole or [PC-^{14}C]-cyantraniliprole. In these studies, the moist soils were incubated in the dark for up to a year at 20 °C or 22 °C.

Half-lives for cyantraniliprole were 9 days in the loam soil, 21–39 days in the silty clay loams, 44 days in the silty loam and 92 days in the sandy loam.

DT_{50} values for the seven major transformation products (average DT_{50} values in brackets) were: IN-JCZ38 (8 days), IN-K5A79 (64 days), IN-K5A77 (132 days), IN-J9Z38 (139 days), IN-JSE76 (410 days), IN-K5A78 (423 days) and IN-PLT97 (1032 days).

Soil dissipation

Ten field studies were conducted to investigate the degradation and mobility of cyantraniliprole under field conditions. In all of the trials a single application of 0.3 kg ai/ha or 0.45 kg ai/ha was made to bare soil in late spring or early summer and cropped soils were also treated in three of these studies. Soil samples were collected to a maximum depth of 90 cm, immediately prior to application and at pre-determined intervals over an 18 month period.

Cyantraniliprole was rapidly degraded in field soils with half-lives ranging from 17 to 51 days. While laboratory studies suggested that pH had some effect on degradation rates, degradation rate under field conditions does not appear to be pH-dependent. Downward mobility of the parent compound as well as its metabolites was limited, with residues rarely found below 15 cm. Soil metabolites formed in the bare soil treatments at levels greater than 10% of the initial soil concentration were IN-J9Z38 (max 42%), IN-K5A78 (max 17%), IN-JSE76 (max 14%), IN-JCZ38 (max 13%) and IN-K5A77 (max 11%). Lower metabolite levels were observed in soil from the cropped soil treatments, predominantly IN-J9Z38 (max 27%) and IN-JCZ38 (max 13%).

The mean temperature-normalized field DT_{50} value from all studies was 32 days, consistent with the mean laboratory derived value.

Water/sediment dissipation

Under anaerobic conditions, cyantraniliprole degraded in the water phase and also partitioned to the sediment where it was further degraded and incorporated into the sediment organic fraction. The major degradate was IN-J9Z38, present in the total system at up to 23–40% AR (0.09–0.16 ppm) during the first 28 days after treatment and declining to 5–7% AR (0.02–0.03 ppm) at the end of the study period (Day 100).

The aerobic degradation of [^{14}C]-cyantraniliprole was studied in a water/silt-loam system and a water/sand system treated with [PC-^{14}C]-cyantraniliprole at a rate of 0.5 µg ai/g and incubated outdoors for 14 days under natural sunlight at 23±2 °C.

In the water phase, cyantraniliprole residues were 1–2% AR at the end of the 14-day study period and in the sediment phase, after reaching maximum levels of 15–22% AR after 2–3 days, residues declined to 6–9% AR on Day 14.

One significant degradate, IN-J9Z38, was found in the surface water at a maximum of about 15–27% AR after 3–5 days and declining to 4.5% AR (silt-loam system) and 12% AR (sand system) at the end of the 14-day study period. In the sediment extracts residues of IN-J9Z38 increased from about 2% AR at Day 1 to about 42% AR at Day 14.

The calculated half-lives in the water/sediment systems were 3.5–4.4 days for cyantraniliprole and 40 days for the IN-J9Z38 metabolite.

Residues in succeeding crops

In two rotational crop metabolism studies using [PC-^{14}C]-cyantraniliprole or [CN-^{14}C]-cyantraniliprole, wheat, soya bean, lettuce and red beet were planted as rotational crops 25–30 and 120 days after a single bare soil application of 0.3 kg ai/ha in one study and 0.45 kg ai/ha in the second study. In the second study, after 365 days aging, a further planting of wheat was made in the 30-day rotation plots.

In the first rotation crops, total radioactive residues in food items ranged from 0.02–0.06 mg/kg in wheat grain, 0.08–0.11 mg/kg in lettuce, 0.02–0.03 mg/kg in beet roots and 0.04 mg/kg in soya bean seeds. Higher residues were seen in animal feed items; wheat hay and straw (0.97–1.6 mg/kg), soya bean foliage (0.19 mg/kg) and beet foliage (0.11 mg/kg).

The metabolic fates of cyantraniliprole in the three rotational crops were similar. Cyantraniliprole was the predominant residue in wheat straw and hay (41–53% TRR, 0.4–0.85 mg/kg), wheat grain (10–36% TRR, < 0.01–0.02 mg/kg), soya bean foliage (36% TRR, 0.07 mg/kg), red beet roots (21–27% TRR, < 0.01 mg/kg) and lettuce (60–69% TRR, 0.05–0.08 mg/kg). No cyantraniliprole was detected in soya bean seeds and parent residues in beet foliage were 3–4% TRR.

In food commodities, IN-MYX98 was the only significant metabolite present above 10% TRR, being found in 2nd rotation (120 day) lettuce leaves at 16% TRR but < 0.01 mg/kg. In animal feed commodities, IN-J9Z38 was found in wheat hay, forage and straw at up to 13% TRR (0.18 mg/kg) and IN-K7H19 was present in wheat hay and straw at 10–11% TRR (0.04–0.06 mg/kg) in the 365 day rotation crop.

Overall, the metabolism in rotational crops was consistent with metabolism seen in primary crops and in the animal studies.

Rotational crop field studies were conducted in Europe and North America to estimate residue uptake in follow crops. In two European studies, where spinach, lettuce, spring barley, oats,

soya bean and radish were planted into bare soil treated with 0.2 kg ai/ha or 0.45 kg ai/ha at plant-back intervals of 14, 30, 120, 270 and 365 days, with the exception of soya bean (seeds and forage) and radish tops, residues of cyantraniliprole and metabolites were not found in succeeding crops. In soya bean forage, residues of cyantraniliprole were 0.02–0.03 mg/kg and in soya bean seed, residues of the IN-N7B69 metabolite were < 0.01 mg/kg.

In five North American studies, bare soil was treated with 3 applications of cyantraniliprole at about 5 day intervals to achieve a total seasonal application rate of 0.45 kg ai/ha. In three of these studies, four rotational crops (lettuce/spinach, oats, radish and soya bean) were planted 14, 30, 120, and 365 days after the last application. In the other two studies, strawberries, turnip, sugar beet, garden beet, radish, carrot, bean, pea, soya bean, alfalfa, clover, field corn, sweet corn, sorghum, rice, wheat, Bermuda grass, brome grass, clover, bluegrass and peanut were planted 30 days after the last application.

Residues of cyantraniliprole and metabolites in the first rotation crops (30 day plant-back interval were below 0.05 mg/kg in commodities for human consumption (cereal grains, root crops, legumes and pulses, leafy vegetables). Higher residues were reported in animal feed commodities, up to 0.2 mg/kg in forage crops and 0.3 mg/kg in most hays and straws. Highest residues were found in soya bean hay, up to 0.63 mg/kg in one sample.

In the first rotation crops (30 day plant-back interval (PBI)), highest residues of cyantraniliprole were above 0.01 mg/kg in radish roots (0.02 mg/kg), radish and turnip tops (0.02–0.04 mg/kg), legume forages (0.02–0.14 mg/kg), legume hays (0.05–0.63 mg/kg), leafy vegetables (0.03 mg/kg), cereal forages (0.01–0.11 mg/kg), cereal hays and straws (0.07–0.21 mg/kg), forage grasses (0.01–0.09 mg/kg) and grass hays (0.02–0.23 mg/kg).

Metabolites present at more than 0.01 mg/kg were IN-J9Z38 (up to 0.03 mg/kg in cereal and legume hays and straws), IN-JZ38 (in cereal and legumes, up to 0.06 mg/kg hays and 0.03 mg/kg in forages) and IN-MLA84 (in legumes, up to 0.02 mg/kg in forage and 0.07 mg/kg in hays).

Methods of analysis

Several analytical methods have been reported for the analysis of cyantraniliprole and up to eight metabolites in plant and animal commodities. The basic approach employs extraction with acetonitrile/water and analysis by high pressure liquid chromatography with tandem mass spectrometry.

For plant and processed plant commodities, the HPLC-MS/MS method used in most of the supervised residue field trials, was validated for the analysis of cyantraniliprole and its metabolites (IN-N7B69, IN-JCZ38, IN-K7H19, IN-MYX98, IN-MLA84 and IN-J9Z38) in a range of representative matrices. The LOQ is 0.01 mg/kg for each analyte. Adequate extraction efficiencies were demonstrated in plant matrices using radiolabelled samples from metabolism and confined rotational crop studies.

For animal commodities, the HPLC-MS/MS method was validated for the analysis of cyantraniliprole, IN-HGW87, IN-N7B69, IN-K7H19, IN-JCZ38, IN-MYX98, IN-J9Z38 and IN-MLA84 in livestock tissues, milk and eggs. After extraction with acetonitrile, extracts are partitioned against hexane before SPE clean-up and analysis. The LOQ is 0.01 mg/kg for each analyte. The method was validated by an independent laboratory using kidney, muscle, and milk. The extraction efficiency was successfully demonstrated with samples of liver, muscle, milk, egg white, and egg yolk from livestock metabolism studies.

The DFG S19 multi-residue method with LC-MS/MS analysis was validated for the analysis of cyantraniliprole residues in tomato (representing high water content), orange (high acid content), wheat grain (high starch content) and almond (high oil content), and is suitable as an enforcement method for cyantraniliprole in plant commodities. It was also validated in milk, eggs, meat and liver as being a suitable enforcement method for cyantraniliprole residues in animal commodities.

The US-FDA PAM multi-residue methods were shown to be unsuitable for the detection and enforcement of cyantraniliprole and metabolites (Protocols A through F).

Stability of pesticide residues in stored analytical samples

Freezer storage stability of cyantraniliprole and metabolites IN-F6L99, IN-J9Z38, IN-JCZ38, IN-K7H19, IN-MLA84, IN-MYX98, IN-N5M09 and IN-N7B69 was investigated in five representative commodities: apples (high-water content), grapes (high-acid content), potatoes (high-starch content), dry bean seeds (high-protein content), and peanuts (high-oil content).

Residues were shown to be stable in these representative substrates for at least 24 months in frozen storage, with residues in the stored samples being greater than 80% of the spiked levels except in peanuts (high oil content), where reduced recoveries were observed at all storage intervals for the metabolites IN-JCZ38, IN-K7H19 and IN-N7B69.

Definition of the residue

In animal commodities, the predominant residues identified in the metabolism studies were cyantraniliprole, IN-J9Z38, IN-MLA84, IN-N7B69 and IN-MYX98. Where residues were found in animal tissues in the metabolism studies or the feeding studies, cyantraniliprole was the major or a significant component. Noting that a multi-residue method was available to measure cyantraniliprole in animal commodities, the Meeting agreed that for MRL-compliance, the residue definition for animal commodities should be cyantraniliprole.

The compound cyantraniliprole has a log K_{ow} of 1.9, suggesting that it is not fat soluble, and this is supported by the residue distribution in muscle and fat reported in a cow feeding study, where the residues in fat were generally only about 2-fold higher than in muscle. The Meeting therefore concluded that cyantraniliprole is not fat soluble.

For dietary intake estimation, in addition to the parent compound, metabolites found at significant levels in the animal metabolism studies were IN-N7B69 (milk), IN-MYX98 (muscle and milk), IN-J9Z38 (fat and eggs) and IN-MLA84 (eggs). In the feeding studies, at doses that reflect the expected animal burden, these individual metabolites were also found at levels ranging from about 20% to 100% of the parent concentrations in different matrices but when combined, were generally found at levels close to those of the parent.

IN-N7B69 was found in milk at a level equivalent to parent and at about half the parent concentration in kidney. IN-J9Z38 was present in eggs at about 50% parent concentration. IN-MLA84 was found in cattle liver at about 60% of the parent concentration and in eggs at about 50% parent concentration. IN-MYX98, found in eggs at about 20% parent and in poultry liver at about 135% of parent.

These metabolites also occur in rats, are not considered more toxic than the parent compound, are adequately covered in the derived toxicological reference dose and a validated HPLC-MS/MS method is available to analyse for them.

The Meeting agreed that while not all of these metabolites would occur in all tissues; these four metabolites (IN-N7B69, IN-J9Z38, IN-MLA84 and IN-MYX98) should be included in the residue definition for dietary intake estimation for animal commodities. The Meeting considered that if animal commodities were analysed only for cyantraniliprole, a conservative correction factor of 2 could be applied for the purpose of dietary intake estimation to account for these metabolites.

In plant commodities from treated crops, the metabolism studies indicated that cyantraniliprole was the major residue in rice, lettuce, cotton and tomato. In rotational crops, where residues are present, cyantraniliprole is also the main residue in food commodities. The Meeting noted that a multi-residue method exists to measure parent residues and agreed that for MRL-compliance, the residue definition for plant commodities should be cyantraniliprole.

The only metabolite identified in the plant metabolism studies at more than 10% TRR or greater than 0.01 mg/kg in commodities at harvest was IN-J9Z38, reported in leaves from foliar-treated rice (11% TRR and 0.13 mg/kg), rice straw from rice grown in treated soil (up to 18% TRR and 0.05 mg/kg) and in foliar-treated lettuce where residues of 23% TRR (0.01 mg/kg) were measured in mature leaves from seedling plants treated up to 32 days before sampling. The Meeting noted that in the supervised field trials, residues of IN-J9Z38 were also reported in some trials, but mostly < 0.01 mg/kg and rarely found at levels more than 10% of the cyantraniliprole residue.

In rotational crops, metabolite residues in food commodities did not exceed 0.01 mg/kg, with IN-J9Z38, IN-JZ38 and IN-MLA84 only present in animal feeds (cereal and legume forage, hays and straws) at up to 0.07 mg/kg.

In processed food commodities, metabolites IN-J9Z38 and to a lesser extent IN-N5M09 and IN-F6L99 were formed under conditions of heat and/or hydrolysis. In addition to cyantraniliprole, only IN-J9Z38 was observed at significant levels, being the predominant residue in cooked spinach, cottonseed oil and present at more than 50% of the parent levels in tomato paste, apple sauce and canned olives. IN-N5M09 and IN-F6L99 were only quantifiable in a few processed food commodities (e.g., cooked spinach, apple sauce) and were much lower than the levels of the parent compound and IN-J9Z38.

The main metabolite in some processed commodities (IN-J9Z38) was also observed in the animal metabolism studies and the toxicology of IN-J9Z38 is addressed in the rat studies and covered by the derived reference dose. Sufficient toxicological information is available to confirm that the IN-J9Z38 metabolite is no more toxic than cyantraniliprole and analytical methods are available to measure this metabolite.

The Meeting concluded that for dietary intake risk assessment, the residue definition for plant commodities should be cyantraniliprole but that for processed commodities, the IN-J9Z38 should also be included.

Proposed definition of the residue (for compliance with the MRL, animal and plant commodities*): cyantraniliprole*.

Proposed definition of the residue (for estimation of dietary intake for unprocessed plant commodities): *cyantraniliprole*.

Proposed definition of the residue (for estimation of dietary intake for processed plant commodities): *sum of cyantraniliprole and IN-J9Z38, expressed as cyantraniliprole*.

Proposed definition of the residue (for estimation of dietary intake for animal commodities: *sum of cyantraniliprole, 2-[3-Bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-3,4-dihydro-3,8-dimethyl-4-oxo-6-quinazolinecarbonitrile [IN-J9Z38], 2-[3-Bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-1,4-dihydro-8-methyl-4-oxo-6-quinazolinecarbonitrile [IN-MLA84], 3-Bromo-1-(3-chloro-2-pyridinyl)-N-[4-cyano-2-(hydroxymethyl)-6-[(methylamino)carbonyl]phenyl]-1H-pyrazole-5-carboxamide [IN- N7B69] and 3-Bromo-1-(3-chloro-2-pyridinyl)-N-[4-cyano-2[[(hydroxymethyl)amino]carbonyl]-6-methylphenyl]-1H-pyrazole-5-carboxamide [IN- MYX98], expressed a cyantraniliprole*.

The residue is not fat soluble.

Results of supervised residue trials on crops

The Meeting received supervised trial data for foliar and soil applications of cyantraniliprole on a range of fruit and vegetable crops, rice, tree nuts, oilseeds and coffee and for seed treatments (potatoes, oil-seed rape). These trials were conducted mainly in Europe and/or North America.

Where residues have been reported as ND (<LOD) the values have been considered as <LOQ (< 0.01 mg/kg) for the purposes of MRL setting. If a higher residue level was observed at a longer PHI than the GAP, the higher value has been used in MRL setting.

The Meeting noted that GAP has been authorised for the use of cyantraniliprole and that product labels were available from Canada, Columbia, New Zealand Malaysia, Vietnam and from a regional group of countries in West Africa. Supervised trial data were provided for citrus, grapes, olives, pomegranate, beans and sunflower, but no GAP information was available to support maximum residue level estimations for these commodities.

Pome fruits

The critical GAP for cyantraniliprole on pome fruit is in Canada, up to 4 foliar applications of 0.05–0.15 kg ai/ha applied at least 7 days apart with a PHI of 3 days and with a total of 0.45 kg ai/ha/season.

In trials on apples in North America matching the Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.06, 0.07, 0.1, 0.12, 0.13, 0.13, 0.15, 0.15, 0.16, 0.17, 0.18, 0.21, 0.26, 0.26, 0.29 and 0.31 mg/kg (n=16).

In trials on pears in North America matching the Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.08, 0.1, 0.12, 0.14, 0.16, 0.23, 0.42, 0.44, 0.56 and 0.58 mg/kg (n=10).

The Meeting noted that the GAP in Canada was for pome fruit and that the medians of the two data sets differed by less than 5-fold and agreed to consider a group maximum residue level. As the Mann-Whitney U-test indicated that the residue populations for apples and pears were not different it was agreed to combine the results to give a data set of: 0.06, 0.07, 0.08, 0.1, 0.1, 0.12, 0.12, 0.13, 0.13, 0.14, 0.15, 0.15, 0.16, 0.16, 0.17, 0.18, 0.21, 0.23, 0.26, 0.26, 0.29, 0.31, 0.42, 0.44, 0.56 and 0.58 mg/kg (n=26) for the pome fruit crop group.

The Meeting estimated an STMR of 0.16 mg/kg and a group maximum residue level of 0.8 mg/kg for cyantraniliprole on pome fruit.

Stone fruits

The critical GAP for cyantraniliprole on stone fruit is in Canada, up to 4 foliar applications of 0.05–0.15 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 7 days apart with a PHI of 3 days.

In trials on cherries in North America matching the Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues in whole fruit were: 0.3, 0.32, 0.7, 0.8, 0.89, 0.9 and 3.4 mg/kg (n=7). In flesh residues were: 0.33, 0.36, 0.89, 0.93, 0.96, 0.98 and 3.8 mg/kg (n=7).

In trials on peaches in North America matching the Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.16, 0.18, 0.19, 0.19, 0.23, 0.24, 0.28, 0.34, 0.39, 0.45, 0.51, 0.79 and 0.81 mg/kg. In flesh, residues were: 0.19, 0.19, 0.2, 0.23, 0.25, 0.27, 0.34, 0.35, 0.42, 0.49, 0.56, 0.89 and 0.94 mg/kg (n=13).

In trials on plums in North America matching the Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.03, 0.05, 0.06, 0.06, 0.06, 0.07, 0.12, 0.19 and 0.28 mg/kg. In flesh, residues were: 0.03, 0.05, 0.06, 0.06, 0.07, 0.07, 0.13, 0.2 and 0.29 mg/kg (n=9).

The Meeting noted that the GAP in Canada was for stone fruit and that the medians of the data sets for cherries, peaches and plums differed more than 5-fold and agreed not to consider a group maximum residue level for stone fruit.

The Meeting estimated an STMR of 0.93 mg/kg (based on residues in flesh), and based on residues in the whole fruit, estimated a subgroup maximum residue level of 6 mg/kg for cyantraniliprole on cherries.

The Meeting estimated an STMR of 0.34 mg/kg (based on residues in flesh, and based on residues in the whole fruit, estimated a subgroup maximum residue level of 1.5 mg/kg for cyantraniliprole on peaches.

The Meeting estimated an STMR of 0.07 mg/kg (based on residues in flesh) and based on residues in the whole fruit, estimated a subgroup maximum residue level of 0.5 mg/kg for cyantraniliprole on plums.

Bush berries

The critical GAP for cyantraniliprole on bush berries is in Canada, up to 4 foliar applications of 0.05–0.15 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 7 days apart with a PHI of 3 days.

In trials on blueberries in North America matching the Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.42, 0.51, 0.52, 0.52, 0.75, 0.8, 1.5, 1.5 and 2.0 mg/kg (n=9).

The Meeting noted that blueberry can be used as a representative crop for bush berries and estimated an STMR of 0.75 mg/kg and a subgroup maximum residue level of 4.0 mg/kg for cyantraniliprole on bush berries.

Bulb vegetables

The critical GAP for cyantraniliprole on bulb vegetables is in Canada, up to 4 foliar applications of 0.1–0.15 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 5 days apart with a PHI of 1 day.

In trials on bulb onions in North America matching the Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: < 0.01, < 0.01, < 0.01, < 0.01, 0.01, 0.02, 0.02, 0.02, 0.02 and 0.03 mg/kg (n=10).

The Meeting noted that the GAP in Canada also includes use on garlic and shallot and agreed to extrapolate the data for bulb onions to these commodities.

The Meeting estimated an STMR of 0.02 mg/kg and a maximum residue level of 0.05 mg/kg for cyantraniliprole on onion, bulb, garlic and shallot.

In trials on spring onions (green onions) in North America matching the Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.38, 0.63, 1.3, 1.6 and 4.1 mg/kg (n=5).

The Meeting noted that the GAP in Canada also includes use Welsh onion and agreed to extrapolate the data for spring onions to onion, Welsh.

The Meeting estimated an STMR of 1.3 mg/kg and a maximum residue level of 8.0 mg/kg for cyantraniliprole on spring onion and onion, Welsh.

Brassica (cole or cabbage) vegetables

The critical GAP for cyantraniliprole on brassica vegetables is in Canada, up to 4 foliar applications of 0.025–0.15 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 5–7 days apart with a PHI of 1 day.

In trials on broccoli in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.22, 0.28, 0.51, 0.59, 0.61, 0.69, 0.82 and 1.1 mg/kg (n=8).

In trials on cauliflowers in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues in the flower heads were: 0.01 and 0.08 mg/kg (n=2).

In trials on head cabbage in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues in cabbages (with wrapper leaves) were: 0.29, 0.32, 0.32, 0.42, 0.47, 0.56, 0.57, 0.65, 0.71, 0.86 and 0.95 mg/kg (n=11).

The Meeting noted that the GAP in Canada was for brassica vegetables and that the medians of the data sets for broccoli and cabbage differed by less than 5-fold (insufficient data on cauliflower) and agreed to consider a group maximum residue level. In deciding on the data set to use for estimating a group maximum residue level, since a Mann-Whitney U-test indicated that the residue populations for broccoli and cabbage were not different, it was agreed to combine the results to give a data set of: 0.01, 0.08, 0.22, 0.28, 0.29, 0.32, 0.32, 0.42, 0.47, 0.51, 0.56, 0.57, 0.59, 0.61, 0.65, 0.69, 0.71, 0.82, 0.86, 0.95 and 1.1 mg/kg (n=21) for brassica vegetables.

The Meeting estimated an STMR of 0.56 mg/kg and a group maximum residue level of 2.0 mg/kg for cyantraniliprole on brassica (cole or cabbage) vegetables. The Meeting also estimated a highest residue of 1.1 mg/kg for calculating animal dietary burdens.

Fruiting vegetables, Cucurbits

The critical GAP for cyantraniliprole on cucurbit vegetables is in Canada, up to 4 foliar applications of 0.025–0.15 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 5–7 days apart with a PHI of 1 day.

In trials on cucumber in North America matching the GAP of Canada (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.02, 0.02, 0.02, 0.03, 0.04, 0.05, 0.05, 0.07, 0.12 and 0.16 mg/kg (n=10).

In trials on summer squash in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.01, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09 and 0.11 mg/kg (n=9).

In trials on melons in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.04, 0.05, 0.08, 0.09, 0.09, 0.1, 0.11, 0.15 and 0.17 mg/kg (n=9). In these trials, cyantraniliprole residues in the melon edible portion were all < 0.01 (n=9)

The Meeting noted that the GAP in Canada was for cucurbit vegetables and that the medians of the data sets for cucumber, summer squash and melons differed by less than 5-fold and agreed to consider a group maximum residue level. In deciding on the data set to use for estimating a group maximum residue level, since a Kruskal-Wallis H-test indicated that the residue populations for cucumber, summer squash and melons were not different, it was agreed to combine the results to give a data set of: 0.01, 0.02, 0.02, 0.02, 0.03, 0.03, 0.04, 0.04, 0.04, 0.05, 0.05, 0.05, 0.05, 0.06, 0.07, 0.07, 0.08, 0.08, 0.09, 0.09, 0.09, 0.1, 0.11, 0.11, 0.12, 0.15, 0.16 and 0.17 mg/kg (n=28) for cucurbit vegetables.

The Meeting estimated an STMR of 0.01 mg/kg for cucurbits with an inedible peel (based on the melon data on residues in flesh), an STMR of 0.065 mg/kg (based on the summer squash data) for cucurbits with an edible peel and a group maximum residue level of 0.3 mg/kg for cyantraniliprole on fruiting vegetables, Cucurbits.

Fruiting vegetables, other than Cucurbits

The critical GAP for cyantraniliprole on fruiting vegetables (except cucurbits) is in Canada, up to 4 foliar applications of 0.025–0.15 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 5–7 days apart with a PHI of 1 day.

In trials on tomatoes in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.04, 0.05, 0.06, 0.06, 0.07, 0.07, 0.07, 0.07, 0.08, 0.08, 0.08, 0.09, 0.09, 0.1, 0.12, 0.14, 0.14, 0.16, 0.17 and 0.26 mg/kg (n=20).

In trials on sweet peppers in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.03, 0.04, 0.06, 0.07, 0.07, 0.08, 0.08, 0.15, 0.21, 0.24 and 0.28 mg/kg (n=11).

In trials on chili peppers (non-bell peppers) in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.07, 0.07, 0.08, 0.09, 0.1, 0.2, 0.25, 0.31 and 0.42 mg/kg (n=9).

The Meeting noted that the GAP in Canada was for fruiting vegetables (except cucurbits) and that the medians of the data sets for sweet peppers, tomatoes and chili peppers differed by less than 5-fold and agreed to consider a group maximum residue level. In deciding on the data set to use for estimating a group maximum residue level, since a Kruskal-Wallis H-test indicated that the residue populations for sweet peppers, tomatoes and chili peppers were not different, it was agreed to combine the results to give a data set of: 0.03, 0.04, 0.04, 0.05, 0.06, 0.06, 0.06, 0.07, 0.07, 0.07, 0.07, 0.07, 0.07, 0.07, 0.07, 0.08, 0.08, 0.08, 0.08, 0.08, 0.08, 0.09, 0.09, 0.09, 0.1, 0.1, 0.12, 0.14, 0.14, 0.15, 0.16, 0.17, 0.2, 0.21, 0.24, 0.25, 0.26, 0.28, 0.31 and 0.42 mg/kg (n=40) for the non-cucurbit fruiting vegetables group.

The Meeting estimated an STMR of 0.08 mg/kg and a group maximum residue level of 0.5 mg/kg for cyantraniliprole on fruiting vegetables, other than Cucurbits (excluding sweet corn and mushrooms).

For dried chili peppers, applying the default processing factor of 7 to the data set for fresh chili peppers, the Meeting estimated an STMR-P of 0.7 mg/kg and a maximum residue level of 5 mg/kg for cyantraniliprole on dried chili peppers.

Leafy vegetables (including Brassica leafy vegetables)

The critical GAP for cyantraniliprole on leafy vegetables is in Canada, up to 4 foliar applications of 0.025–0.15 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 5–7 days apart with a PHI of 1 day.

In trials on head lettuce in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 0.02, 0.08, 0.16, 0.18, 0.64, 0.75, 0.83, 1.3, 1.6, 1.8, 2.1 and 2.7 mg/kg (n=12).

In trials on leaf lettuce in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 1.1, 1.2, 2.1, 2.4, 2.4, 2.5, 3.2, 3.3, 4.0, 5.3, 6.8 and 6.8 mg/kg (n=12).

In trials on spinach in North America matching the critical Canadian GAP (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 3.8, 4.1, 4.2, 4.6, 4.7, 4.9, 5.8, 8.2, 10 and 13 mg/kg (n=10).

In trials on mustard greens in North America matching the critical Canadian GAP for vegetable brassicas (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: 2.4, 3.4, 3.9, 5.5, 5.8, 6.0, 7.1, 7.2, 8.0, 13 and 19 mg/kg (n=11).

The Meeting noted that the GAP in Canada was for leafy vegetables and that the medians of the data sets for leaf lettuce, spinach and mustard greens (but not head lettuce) differed by less than 5-fold and agreed to consider a group maximum residue level for leafy vegetables except head lettuce. In deciding on the data set to use for estimating a group maximum residue level, since a Kruskal-Wallis H-test indicated that the residue populations for leaf lettuce, spinach and mustard greens were not different it was agreed to combine the results to give a data set of: 1.1, 1.2, 2.1, 2.4,

2.4, 2.4, 2.5, 3.2, 3.3, 3.4, 3.8, 3.9, 4.0, 4.1, 4.2, 4.6, 4.7, 4.9, 5.3, 5.5, 5.8, 5.8, 6.0, 6.8, 6.8, 7.1, 7.2, 8.0, 8.2, 10, 13, 13 and 19 mg/kg for leafy vegetables (n=33) except head lettuce and to use the head lettuce data to estimate a maximum residue level for head lettuce.

The Meeting estimated an STMR of 4.7 mg/kg and a group maximum residue level of 20 mg/kg for cyantraniliprole on leafy vegetables (except head lettuce).

The Meeting estimated an STMR of 0.79 mg/kg and a maximum residue level of 5 mg/kg for cyantraniliprole on head lettuce.

Root and tuber vegetables

The critical GAP for cyantraniliprole on root and tuber vegetables is in Canada, up to 4 foliar applications of 0.05–0.15 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 5–14 days apart with a PHI of 7 days.

In trials on potatoes in North America matching the critical Canadian GAP for foliar applications to root and tuber vegetables (with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season), cyantraniliprole residues were: < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, 0.01, 0.02, 0.02 and 0.03 mg/kg (n=20).

The Meeting also noted that residues of cyantraniliprole may also arise in potatoes planted as rotational crops, and agreed to consider maximum residue level recommendations for potatoes when discussing rotational crop residues.

Stalk and stem vegetables

The critical GAP for cyantraniliprole on celery is in Canada, up to 4 foliar applications of 0.025–0.15 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 5–7 days apart with a PHI of 1 day.

In trials on celery in North America matching the critical Canadian GAP for leafy vegetables (including celery), with 3 applications of 0.15 kg ai/ha, 0.45 kg ai/ha/season, cyantraniliprole residues were: 0.28, 0.73, 1.0, 1.1, 1.2, 2.0, 2.3, 2.5, 4.7, 5.7 and 9.1 mg/kg (n=11).

The Meeting estimated an STMR of 2.0 mg/kg and a maximum residue level of 15 mg/kg for cyantraniliprole on celery.

Rice

The critical GAP for cyantraniliprole on rice is in Vietnam, for foliar applications of 0.05–0.1 kg ai/ha with a PHI of 5 days.

Results were available from six trials on rice in China where three foliar applications of cyantraniliprole were applied up to 7 days before harvest.

The Meeting agreed that these data did not match the GAP in Vietnam in that the PHI deviated from GAP by more than 25%.

Tree nuts

The critical GAP for cyantraniliprole on tree nuts is in Canada, up to 4 foliar applications of 0.05–0.1 kg ai/ha with a total of 0.45 kg ai/ha/season, applied at least 7 days apart with a PHI of 5 days.

In six trials on almonds in USA, 3 foliar sprays of 0.15 kg ai/ha (0.45 kg ai/ha/season) were applied at 6–8 day intervals up to 5 days before harvest.

In six trials on pecans in USA, 3 foliar sprays of 0.15 kg ai/ha (0.45 kg ai/ha/season) were applied at 6–8 day intervals up to 5 days before harvest.

The Meeting noted that since both the number of applications and the treatment rates in the trials for almonds and pecans did not match the Canadian GAP, the use of the proportionality approach to estimate maximum residue levels was not appropriate.

Oilseeds

The critical GAP for cyantraniliprole on cotton is in the region of West Africa, up to 3 foliar applications of 0.05 kg ai/ha with a total of 0.15 kg ai/ha/season, applied at least 14 days apart with a PHI of 7 days.

Results were available from trials conducted in USA on cotton, where three foliar applications of 0.15 kg ai/ha cyantraniliprole were applied at 6–8 day intervals up to 7–9 days before harvest.

The Meeting noted that the application rates used in the USA trials were higher and the retreatment intervals were shorter than the GAP in West Africa and the Meeting agreed that the concept of proportionality could not be used to recommend a maximum residue level for cyantraniliprole on cotton seed.

The critical GAP for cyantraniliprole on oil seed crops (excluding cotton and peanut) is in Canada, up to 4 foliar applications of 0.025–0.1 kg ai/ha with a total of 0.11 kg ai/ha/season, applied at least 7 days apart with a PHI of 7 days.

Results were available from trials on oilseed rape and on sunflower in North America, where 3 foliar sprays of 0.15 kg ai/ha (0.45 kg ai/ha/season) were applied at 5–9 day intervals up to 7 days before harvest.

The Meeting noted that for both oilseed rape and sunflower, in addition to the application rate in the field trials differing from the Canadian GAP, the lower seasonal application rate associated with the Canadian GAP supports only a single application of the maximum recommended application rate of 0.1 kg ai/ha, compared to the three applications used in the field trials.

The Meeting concluded that these trials did not match the Canadian GAP.

Seed for beverages and sweets

The critical GAP for cyantraniliprole on coffee is in Columbia, one foliar application of 2.5–3.5 g ai/5 litres/100 trees, equivalent to 0.125–0.175 kg ai/ha with a total of 0.3 kg ai/ha/season, with a PHI of 28 days.

In two Brazilian trials matching the Columbian GAP, cyantraniliprole residues were < 0.01 and 0.02 mg/kg.

The Meeting noted that in a further six trials in Brazil involving foliar applications that matched the Columbian GAP but where two soil drenches (0.01–0.06 g ai/100 ml/plant to achieve the equivalent of 0.2 kg ai/ha/treatment) were also applied approximately 90 and approximately 120 days before harvest, cyantraniliprole residues were < 0.01 (5) and 0.01 mg/kg.

The Meeting agreed that since the early season soil drench treatments did not appear to contribute to the final residue in coffee beans, the data from these two sets of results could be combined, giving a data set of: < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, 0.01 and 0.02 mg/kg, to recommend a maximum residue level for cyantraniliprole on coffee beans.

The Meeting estimated an STMR of 0.01 mg/kg and a maximum residue level of 0.03 mg/kg for cyantraniliprole on coffee bean.

Estimation of residues in plant commodities grown as potential succeeding crops

Residues of cyantraniliprole, while not persistent, can be taken up by following crops. In Canada, the GAP includes a maximum seasonal foliar application rate of 0.45 kg ai/ha for most crops except oil seeds where the maximum seasonal rate is 0.11 kg ai/ha. In Columbia, the maximum seasonal rate for onions and Welsh onions is 0.3 kg ai/ha and in West Africa, the total seasonal rate on cotton is 0.15 kg ai/ha.

In Canada, recommended plant-back intervals (PBIs) have been established for crops likely to be grown in rotation with treated crops. In general, for annual crops for human consumption and where MRLs have been established, there is no plant-back interval specified, but for crops likely to be used as animal feed (cereals, grasses, legumes etc) the label recommends a 30-day plant-back interval.

Field rotational crop studies conducted in USA on a range of representative crops, involving treatment rates equivalent a 0.45 kg ai/ha maximum seasonal rate to bare soil, reported cyantraniliprole residues of less than 0.05 mg/kg in representative food commodities and higher residues in animal feed commodities.

The Meeting agreed that the results of the USA field rotational crop studies, in particular the cyantraniliprole residues reported from the 30 day PBI crops, could be used to estimate residues in follow crops.

Leafy vegetables (including Brassica leafy vegetables)

Highest cyantraniliprole residues in rotational leafy vegetables were < 0.01 mg/kg in spinach and beet tops, 0.02 mg/kg in lettuce and turnip tops and 0.04 mg/kg in radish tops. These levels are adequately covered by the recommendations for leafy vegetables.

Root and tuber vegetables

Cyantraniliprole residues in rotational root and tuber vegetables ranged from < 0.01 to 0.014 mg/kg (n=29, median < 0.01 mg/kg) in beet roots, turnip roots, carrot roots and radish roots.

The Meeting agreed to use the data from 20 field trials on potatoes in North America, treated according to the Canadian GAP for root and tuber vegetables (residues in tubers ranging from < 0.01 to 0.03 mg/kg, STMR 0.01 mg/kg, n=20) and the results of the rotational crop studies on root and tuber vegetables to recommend a group maximum residue level for potatoes (to accommodate residues in follow-crop potatoes that may also be treated with cyantraniliprole).

The Meeting established a maximum residue level of 0.05 mg/kg, a highest residue of 0.044 mg/kg (for estimating animal dietary burdens) and a median residue of 0.02 mg/kg for cyantraniliprole on potato.

The Meeting also agreed to use the rotational crop studies on root and tuber vegetables to recommend a group maximum residue level for the remaining root and tuber vegetables to accommodate residues in these crops grown as follow-crops.

The Meeting established a maximum residue level of 0.05 mg/kg, a highest residue of 0.014 mg/kg and a median residue of 0.01 mg/kg for cyantraniliprole on root and tuber vegetables except potato.

Miscellaneous fodder root crops

The Meeting also agreed to use the results of the rotational crop studies on root and tuber vegetables (residues ranging from < 0.01 to 0.014 mg/kg, median < 0.01 mg/kg, n=29) to recommend maximum residue levels for turnips and fodder beet to accommodate residues in these crops grown as follow-crops.

The Meeting established a maximum residue level of 0.02 mg/kg, a highest residue of 0.014 mg/kg and a median residue of 0.01 mg/kg for cyantraniliprole on fodder beet and turnip fodder.

Legume animal feeds

Cyantraniliprole residues in legume animal feeds (forage) ranged from < 0.01 to 0.14 mg/kg (n=24, median < 0.01 mg/kg) in clover forage, bean forage, pea forage, alfalfa forage and soya bean forage. For the purpose of estimating livestock dietary burdens, the Meeting agreed to combine the data on rotational crop residues in legume animal feeds to estimate residues in legume feed crops grown as follow-crops.

Meeting estimated a median residue of 0.01 mg/kg and a highest residue of 0.14 mg/kg for cyantraniliprole in legume forages (fresh weight).

Cyantraniliprole residues in legume animal feeds (fodders) ranged from < 0.01 to 0.58 mg/kg (n=24, median 0.017 mg/kg) in peanut hay, clover hay, pea hay, bean, alfalfa hay and soya bean hay. The Meeting agreed to combine the data on rotational crop residues in legume fodder crops to recommend a group maximum residue level to accommodate residues in these crops grown as follow-crops.

The Meeting established a median residue of 0.017 mg/kg and a highest residue of 0.58 mg/kg (0.67 mg/kg DM after correction for an average dry matter content of 87%) and recommended a maximum residue level of 0.8 mg/kg (dry weight) for cyantraniliprole in legume animal feeds.

Cereal and grass forages, straws and hays

Cyantraniliprole residues in cereal and grass forage ranged from < 0.01 to 0.053 mg/kg (n=23, median < 0.01 mg/kg) in corn forage, sorghum, Bermuda grass and brome grass forages, oat forage, bluegrass forage and wheat forage. For the purpose of estimating livestock dietary burdens, the Meeting agreed to combine the data on rotational crop residues in cereal and grass forages to estimate residues in cereal and grasses grown as follow-crops.

Meeting established an STMR of 0.01 mg/kg and a highest residue of 0.053 mg/kg for cyantraniliprole in cereal and grass forages (fresh weight).

Cyantraniliprole residues in cereal and grass straws and hays ranged from < 0.01 to 0.14 mg/kg (median < 0.01 mg/kg) in sorghum stover, rice straw, corn stover, brome grass hay, Bermuda grass hay, oat straw, wheat straw, oat hay, wheat hay bluegrass hay. The Meeting agreed to combine the data on rotational crop residues in cereal and grass straws and hays to recommend a group maximum residue level to accommodate residues in these crops grown as follow-crops.

The Meeting established a median residue of 0.01 mg/kg and a highest residue of 0.14 mg/kg (0.16 mg/kg DM after correction for an average dry matter content of 89%) and recommended a maximum residue level of 0.2 mg/kg (dry weight) for cyantraniliprole in straw, fodder (dry) and hay of cereal grains and other grass-like plants.

Miscellaneous fodder leaf crops

The Meeting agreed to use the results of the rotational crop studies on beet, turnip and radish tops (residues ranging from < 0.01 to 0.021 mg/kg (n=22, median < 0.01 mg/kg) to estimate residues in fodder beet tops and the miscellaneous fodder leaf crops listed in the OECD Feedstuffs Table to accommodate residues in these commodities grown as follow-crops.

The Meeting established median residue of 0.01 mg/kg and a highest residue of 0.021 mg/kg for cyantraniliprole on sugar beet tops, fodder beet tops or leaves, kale forage, rape greens and turnip tops (fresh weight).

Fate of residues during processing

The effect of processing on the nature of residues was investigated in buffer solutions under conditions simulating pasteurisation, boiling and sterilisation. Cyantraniliprole was stable under most processing conditions. Hydrolysis to IN-J9Z38 was a significant pathway under sterilisation conditions (20 minutes at 120 °C and pH 6) making up 12–14% AR. Other degradates present were IN-F6L99 and IN-N5M09 making up a further 5–8% AR.

The fate of cyantraniliprole residues has been examined in a number of studies simulating household and commercial processing of potatoes, spinach, tomatoes, oranges, apples, plums, cottonseed, olives and grapes. Estimated processing factors and STMR-Ps for the commodities considered at this Meeting are summarized below.

Summary of selected processing factors and STMR-P values for cyantraniliprole

RAC	Commodity (RAC: STMR mg/kg [b]	Cyantraniliprole+IN-J9Z38 [a]			
		Processing factors	PF best estimate	RAC STMR (mg/kg)	STMR-P (mg/kg)
Potato	RAC: tubers			0.02	
	flakes	0.1	0.1		0.002
	waste	0.1	0.1		0.002
	peeled tubers	0.1	0.1		0.002
	chips	0.1	0.1		0.002
	wet peel	2.3	2.3		0.046 hi-res 0.1 [c]
	culls	1.0	1.0		0.02
	fries	0.1	0.1		0.002
	unpeeled, boiled	0.1	0.1		0.002
	unpeeled m'waved	< 0.33	< 0.33		0.006
Spinach	RAC: leaves			4.7	
	cooked leaves	0.81, 1.0, 1.2	1.0		4.7
Tomato	RAC: fruit (0.08 mg/kg)				
	washed	0.15, 0.17, < 0.29	0.17		0.014
	peeled	< 0.08, < 0.08, 0.1	< 0.08		0.006
	sun-dried	3.0, 3.7, 3.8	3.7		0.3
	canned	< 0.02, < 0.05, < 0.08	< 0.05		0.004
	juice	< 0.15, < 0.17, 0.19	< 0.17		0.014
	wet pomace	0.75, 1.0, 2.2	1.0		0.08
	dry pomace	1.7, 3.2, 4.0	3.2		0.26
	paste	0.62, 0.86, 1.0	0.86		0.07
	puree	0.23, 0.25, 0.43	0.25		0.02
Apple	RAC: fruit			0.16	
	washed	0.46, 0.58, 0.63	0.58		0.09
	puree	0.88, 1.0, 1.3	1.0		0.16
	canned	0.04, 0.13, 0.15	0.13		0.02
	frozen	0.62, 0.96, 1.5	0.96		0.15
	juice	0.19, 0.31, 0.38	0.31		0.05
	wet pomace	0.77, 1.0, 1.2	1.0		0.16
	dry pomace	2.0, 2.7, 3.9	2.7		0.43
	sauce	2.2, 2.4, 2.7	2.2		0.35
Plum	RAC: flesh			0.34	
	dried prunes	1.3, 1.6, 2.0	1.6		0.54

[a] Each PF value represents a separate study where residues were above the LOQ in the RAC and is the ratio of the combined cyantraniliprole+IN-J9Z38 metabolite residues in the processed item divided by the combined residues of cyantraniliprole+IN-J9Z38 in the RAC.

[b] Residues in the RAC are the sum of cyantraniliprole and IN-J9Z38

[c] Based on the highest residue in the RAC (0.044 mg/kg)

The Meeting noted that in the studies available, cyantraniliprole residues did not concentrate in food commodities during processing except in apple sauce and in dehydrated commodities such as dried prunes and sun-dried tomatoes. Residues also concentrated in dry pomace (apple and tomato).

In three plum processing studies conducted in USA, cyantraniliprole residues increased (median processing factor of 1.5) when fresh prunes (flesh) were dried to a moisture content of 15–18% (from about 85% in fresh fruit).

The Meeting estimated a maximum residue level for prunes of 0.8 mg/kg based on the maximum residue level estimated for plums of 0.5 mg/kg and a median processing factor of 1.6.

Residues in animal commodities

Farm animal dietary burden

The Meeting estimated the dietary burden of cyantraniliprole in farm animals on the basis of the diets listed in Annex 6 of the 2009 JMPR Report (OECD Feedstuffs Derived from Field Crops). Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are presented in Annex 6 and are summarized below.

Estimated maximum and mean dietary burdens of farm animals

	Animal dietary burden, cyantraniliprole, ppm of dry matter diet							
	US-Canada		EU		Australia		Japan	
	max	mean	max	mean	max	mean	max	mean
Beef cattle	0.34	0.2	1.9 [a]	0.98 [c]	0.68	0.14	0.13	0.004
Dairy cattle	0.45	0.1	1.9 [b]	0.95 [d]	0.67	0.11	0.29	0.02
Poultry-broiler	0.0	0.0	0.05 [e]	0.02 [f]	0.0	0.0	0.0	0.0
Poultry-layer	0.0	0.0	0.37 [g]	0.19 [h]	0.0	0.0	0.0	0.0

[a] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian tissues

[b] Highest maximum dairy cattle dietary burden suitable for MRL estimates for mammalian milk

[c] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian tissues.

[d] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[e] Highest maximum poultry dietary burden suitable for MRL estimates for poultry tissues.

[f] Highest mean poultry dietary burden suitable for STMR estimates for poultry tissues.

[g] Highest maximum poultry dietary burden suitable for MRL estimates for poultry eggs.

[h] Highest mean poultry dietary burden suitable for STMR estimates for poultry eggs.

For beef and dairy cattle, the calculated maximum dietary burden suitable for estimating maximum residue levels in mammalian tissues and milk is 1.9 ppm dry weight of feed and the calculated mean dietary burdens, suitable for estimating STMRs in mammalian tissues and in milk are 0.98 ppm and 0.95 ppm dry weight of feed respectively.

For poultry, noting that in some countries, laying hens may also be consumed, the calculated maximum dietary burden suitable for estimating maximum residue levels in poultry tissues and eggs is 0.37 ppm dry weight of feed and the calculated mean dietary burden, suitable for estimating STMRs in poultry tissues and in eggs is 0.19 ppm dry weight of feed.

Farm animal feeding studies

The Meeting received information on the residue levels arising in animal tissues and milk when dairy cows were dosed with cyantraniliprole for 28 days at the equivalent of 3.5, 12, 35 and 112 ppm in the diet. A separate dose group (112 ppm) was used to estimate residue depuration of cyantraniliprole and its major metabolites.

In milk, residues reached a plateau after about 5 days. Average residues of cyantraniliprole were 0.03 mg/kg in the 3.5 ppm dose group and increased to 0.7 mg/kg in the highest dose group (112 ppm). In skim milk, cyantraniliprole residues were about 60% of the whole milk levels (0.016 mg/kg up to 0.47 mg/kg) and 0.066 mg/kg up to 1.8 mg/kg in cream. Residues of IN-N7B69, the predominant metabolite in milk, increased from 0.03 mg/kg to 0.28 mg/kg over the four dose groups while residues of the other metabolites (IN-MLA84, IN-J9Z38 and IN-MYX98) were present at levels at least ten-fold lower than parent.

In muscle, maximum residues of cyantraniliprole increased from 0.01 mg/kg to 0.33 mg/kg in the four dose groups, with IN-J9Z38 being the predominant metabolite, found at more than 0.01 mg/kg only in the two highest dose groups (up to 0.04 mg/kg). Other metabolites were ≤ 0.01 mg/kg at all dose levels.

In fat, maximum residues of cyantraniliprole increased from 0.015 mg/kg to 0.58 mg/kg in the four dose groups, with IN-J9Z38 being the predominant metabolite, found at 0.012 mg/kg (low dose) up to 0.45 mg/kg (highest dose). Other metabolites were found at lower levels, more than 5-fold lower that parent and only IN-N7B69 was present at more than 0.01 mg/kg, found at 0.02 mg/kg in the highest dose group.

In kidney, maximum residues of cyantraniliprole increased from 0.03 mg/kg to 0.89 mg/kg in the four dose groups, with IN-N7B69 being the predominant metabolite, found at 0.012 mg/kg (low dose) up to 0.15 mg/kg (highest dose). Other metabolites were found at levels more than 5-fold lower that parent, with residues of IN-J9Z38 and IN-MYX98 present above 0.01 mg/kg only in the two higher dose groups.

In liver, maximum residues of cyantraniliprole increased from 0.066 mg/kg to 2.1 mg/kg in the four dose groups, with IN-MLA84 being the predominant metabolite, present at 0.04 mg/kg in the lowest dose group and up to 0.57 mg/kg in the highest dose group. Metabolite IN-N7B69 residues were up to 0.01 mg/kg in the lowest dose group, increasing to 0.08 mg/kg in the highest dose group and other metabolites were all < 0.01 mg/kg except in the highest dose group where levels of < 0.03 mg/kg were found.

Residue depletion was studied in cows dosed orally for 28 days with the equivalent of 112 ppm cyantraniliprole. Parent residues depleted to < 0.01 mg/kg in muscle within 4 days after the last dose, were < 0.01 mg/kg in milk, liver and kidney within 10 days and < 0.01 mg/kg in fat within 15 days. Metabolites were all < 0.01 mg/kg in all matrices after 4 days except IN-J9Z38 (< 0.01 within 10 days in kidney and 15 days in fat), IN-MLA84 (< 0.01 mg/kg within 10 days in liver) and IN-N7B69 (< 0.01 mg/kg within 10 days in kidney).

The Meeting also received information on the residues in tissues and eggs when laying hens were dosed with cyantraniliprole for 28 days at levels equivalent to 3, 10 and 30 ppm in the diet. A separate dose group (30 ppm) was used to estimate residue depuration of cyantraniliprole and its major metabolites.

In eggs, residues reached a plateau after about 3 days. Average residues of cyantraniliprole were 0.08 mg/kg in the 3 ppm dose group and increased to 0.8 mg/kg in the highest dose group (30 ppm). In egg whites, cyantraniliprole was the predominant residue, averaging 0.08 mg/kg in the low dose group up to 0.64 mg/kg in the high dose group. Lower levels of parent were found in egg yolks, averaging 0.015 mg/kg (low dose) up to 0.1 mg/kg (high dose). Residues of IN-J9Z38, the predominant metabolite in eggs, present at levels of about 50% of parent, increased from 0.04 mg/kg to 0.4 mg/kg over the three dose groups while residues of IN-MLA84 and IN-MYX98 were present at

levels of 0.015 mg/kg in the low dose group up to 0.12 in the high dose group. In general, residues of these metabolites were about 2-fold higher in egg whites than in the yolks.

In muscle, maximum residues of cyantraniliprole increased from 0.003 mg/kg to 0.05 mg/kg in the three dose groups, with the only metabolites found at more than 0.01 mg/kg being IN-MYX98 and IN-HGW87 (up to 0.02 mg/kg in the highest dose group. Other metabolites were all ≤0.01 mg/kg at all dose levels.

In skin + fat, maximum residues of cyantraniliprole increased from 0.014 mg/kg to 0.16 mg/kg in the three dose groups, with IN-MYX98 being the predominant metabolite, found at 0.005 mg/kg (low dose) up to 0.05 mg/kg (highest dose). Other metabolites were found at lower levels, with IN-J9Z38 and IN-HGW87 present at more than 0.01 mg/kg only in the highest dose group (0.021 mg/kg and 0.023 mg/kg respectively).

In liver, maximum residues of cyantraniliprole increased from 0.03 mg/kg to 0.24 mg/kg in the three dose groups. Metabolite IN-MLA84 was present at levels similar to the parent (0.034 mg/kg in the lowest dose group and up to 0.32 mg/kg in the highest dose group). Maximum IN-MLA84, IN-HGW87 and IN-N7B69 residues were 0.01–0.02 mg/kg in the lowest dose group and 0.07–0.1 mg/kg in the highest dose group. Other metabolites were all < 0.01 mg/kg in all dose groups.

In the residue depuration dose group (30 ppm), residues depleted to < 0.01 mg/kg in all matrices within 5 days of the last dose (within 9 days in liver, when the first sample was taken).

Animal commodity maximum residue levels

The maximum dietary burden for beef and dairy cattle is 1.9 ppm. The mean dietary burdens are 0.98 ppm (beef cattle) and 0.95 ppm (dairy cattle). Residue levels of cyantraniliprole and the metabolites included in the residue definition in milk and tissues were obtained by extrapolation below the 3.5 ppm feeding level in the dairy cow feeding study.

Cyantraniliprole feeding study	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues [a] (mg/kg) in			
				Muscle	Liver	Kidney	Fat
MRL beef or dairy cattle							
Feeding study [b]	3.5	0.03	3.5	0.011	0.066	0.031	0.015
Dietary burden and high residue	1.9	0.016	1.9	0.006	0.036	0.017	0.008
STMR beef or dairy cattle							
Feeding study [c]	3.5	0.03	3.5	0.008	0.094	0.042	0.024
Dietary burden and residue estimate	0.95	0.016	0.98	0.002	0.026	0.012	0.007

[a] Residue values used in estimating STMRs are the sum of cyantraniliprole and metabolites IN-N7B69, IN-J9Z38, IN-MLA84 and IN-MYX98, expressed as cyantraniliprole

[b] highest residues for tissues and mean residues for milk

[c] mean residues for tissues and mean residues for milk

Residues of cyantraniliprole expected in cattle milk and tissues for use in estimating maximum residue levels are: 0.008 mg/kg (fat), 0.006 mg/kg (muscle), 0.036 mg/kg (liver) and 0.017 mg/kg (kidney) and the mean residue for milk is 0.016 mg/kg.

The Meeting estimated maximum residue levels of 0.01 mg/kg for cyantraniliprole in meat (from mammals other than marine mammals), 0.05 mg/kg for edible offal (mammalian), 0.01 mg/kg for mammalian fat and 0.02 mg/kg for milks. Estimated STMRs (parent plus metabolites) for dietary intake estimation are 0.002 mg/kg for meat, 0.026 mg/kg for edible offal, 0.007 mg/kg for fat and 0.016 mg/kg for milk.

For poultry, the maximum dietary burden is 0.37 ppm and the mean dietary burden is 0.19 ppm (based on the diet for laying hens). Residue levels of cyantraniliprole and the metabolites included in the residue definition in eggs and tissues were obtained by extrapolation below the 3.0 ppm feeding level in the dairy cow feeding study.

Cyantraniliprole feeding study	Feed level	Residues	Feed level	Residues [a] (mg/kg) in			
	(ppm) for egg residues	(mg/kg) in egg	(ppm) for tissue residues	Muscle	Liver	Skin	Fat
MRL broiler or laying hen							
Feeding study [b]	3.0	0.082	3.0	0.0055	0.03	0.014	
Dietary burden and high residue	0.37	0.01	0.37	0.0007	0.004	0.002	
STMR broiler or laying hen							
Feeding study [c]	3.0	0.082	3.0	0.007	0.062	0.016	
Dietary burden and residue estimate	0.19	0.01	0.19	0.0004	0.004	0.001	

[a] Residue values used in estimating STMRs are the sum of cyantraniliprole and metabolites IN-N7B69, IN-J9Z38, IN-MLA84 and IN-MYX98, expressed as cyantraniliprole

[b] highest residues for tissues and mean residues for egg

[c] mean residues for tissues and mean residues for egg

Residues of cyantraniliprole expected in eggs and poultry tissues for use in estimating maximum residue levels are: 0.002 mg/kg (skin plus fat), 0.0007 mg/kg (muscle), 0.004 mg/kg (liver) and the mean residue for eggs is 0.01 mg/kg.

The Meeting estimated maximum residue levels of 0.01 mg/kg for cyantraniliprole in poultry meat, 0.01 mg/kg for poultry offal, 0.01 mg/kg for poultry fat and 0.015 mg/kg for eggs. Estimated STMRs for dietary intake estimation are 0 mg/kg for poultry fat, 0 mg/kg for poultry meat, 0.004 mg/kg for poultry offal and 0.01 mg/kg for eggs.

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 assessment.

Definition of the residue (for compliance with the MRL, animal and plant commodities): *cyantraniliprole*.

Definition of the residue (for estimation of dietary intake for unprocessed plant commodities): *cyantraniliprole*.

Definition of the residue (for estimation of dietary intake for processed plant commodities): *sum of cyantraniliprole and 2-[3-Bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-3,4-dihydro-3,8-dimethyl-4-oxo-6-quinazolinecarbonitrile*.

Proposed definition of the residue (for estimation of dietary intake for animal commodities: sum of: *cyantraniliprole, 2-[3-Bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-3,4-dihydro-3,8-dimethyl-4-oxo-6-quinazolinecarbonitrile, 2-[3-Bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-1,4-dihydro-8-methyl-4-oxo-6-quinazolinecarbonitrile, 3-Bromo-1-(3-chloro-2-pyridinyl)-N-[4-cyano-2-(hydroxymethyl)-6-[(methylamino)carbonyl]phenyl]-1H-pyrazole-5-carboxamide and 3-Bromo-1-(3-chloro-2-pyridinyl)-N-[4-cyano-2[[(hydroxymethyl)amino]carbonyl]-6-methylphenyl]-1H-pyrazole-5-carboxamide*.

The residue is not fat soluble.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intake (IEDI) for cyantraniliprole was calculated for the food commodities for which STMRs or HRs were estimated and for which consumption data were available. The results are shown in Annex 3.

The International Estimated Daily Intakes of cyantraniliprole for the 13 GEMS/Food regional diets, based on estimated STMRs were 1–10% of the maximum ADI of 0.03 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of cyantraniliprole from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The 2013 JMPR decided that an ARfD was unnecessary. The Meeting therefore concluded that the short-term intake of cyantraniliprole residues is unlikely to present a public health concern.