5.17 OXATHIAPIPROLIN (291)

TOXICOLOGY

Oxathiapiprolin is the ISO-approved common name for 1-[4-[4-[5-(2,6-difluorophenyl)-4,5-dihydro-1,2-oxazol-3-yl]-1,3-thiazol-2-yl]piperidin-1-yl]-2-[5-methyl-3-(trifluoromethyl)pyrazol-1-yl]ethanone (IUPAC), with the CAS number 1003318-67-9. It is a novel fungicide from the piperidinyl thiazole isoxazoline class, targeting the oxysterol binding protein with a new biochemical mode of action; the fungicide prevents zoospore germination, sporangia germination and mycelial growth, as well as inhibiting zoospore release. Oxathiapiprolin protects growing plant (stem) leaves and fruit.

Oxathiapiprolin has not previously been evaluated by JMPR and was reviewed by the present Meeting at the request of CCPR.

All critical studies contained statements of compliance with GLP and were conducted in accordance with relevant national or international test guidelines, unless otherwise indicated.

Biochemical aspects

In metabolism studies conducted in rats using oxathiapiprolin labelled with ^{14}C at the 5- isoxazoline or 5-pyrazole position, oxathiapiprolin was moderately absorbed (< 50%, based on urine, bile and carcass) at the low dose (10 mg/kg bw) and showed evidence of saturation at the high dose (200 mg/kg bw), with low absorption (< 10%, based on urine, bile and carcass). There were few differences between the sexes and labels. At the low dose, the time to reach the maximum concentration in plasma (T_{max}) was between 1.75 and 3.0 hours for both labels; at the high dose, T_{max} values were 0.25 hour for the isoxazoline label and between 2.75 and 9.5 hours for the pyrazole label. In the low-dose studies, mean terminal elimination half-lives ranged from 40 to 51 hours; at the high dose, mean terminal elimination half-lives ranged from 5 to 14 hours. C_{max} and AUC values were slightly lower for the pyrazole label than for the isoxazoline label, and there was a significant comparative reduction in C_{max} and AUC values at the high dose. There was no evidence of accumulation. The main route of excretion was in the faeces within the first 48 hours of administration. Tissue distribution was extensive, but tissue concentrations were low, with slightly higher concentrations of radioactivity in the liver, kidneys, lungs and red blood cells.

The predominant component was unchanged parent and accounted for 17–87% of the administered low or high dose of either label. Metabolism of the absorbed oxathiapiprolin involved multiple reaction sites, including hydroxylation in various positions, leading to many low-level identified and tentatively identified metabolites in the faeces, bile and urine. Metabolism investigations in the repeated-dose studies showed that IN-Q7N24 ((*R*)-oxathiapiprolin), an enantiomer of oxathiapiprolin, was 3- to 4-fold more rapidly metabolized than the enantiomer IN-Q7N25 ((*S*)-oxathiapiprolin) in the liver, or there were differences in absorption.

Toxicological data

In rats, oxathiapiprolin is of low acute toxicity via the oral (LD_{50} > 5000 mg/kg bw), dermal (LD_{50} > 5000 mg/kg bw) and inhalation routes (LC_{50} > 5.1 mg/L). Oxathiapiprolin is non-irritating to the skin and slightly irritating to the eyes of rabbits. It was not a dermal sensitizer in guinea-pigs.

Overall, oxathiapiprolin showed low mammalian toxicity on repeated administration.

In short-term toxicity studies in the mouse with dietary administration over 28 and 90 days, no adverse effects were reported up to the top dose levels, which were at least 1058 mg/kg bw per day. In similar studies in the rat, no adverse effects were reported up to the top dose levels, which were 1096 mg/kg bw per day. In the dog, short-term dietary studies ranged from 28 days to 1 year, with no adverse findings up to the top dose levels, which were at least 1242 mg/kg bw per day.

In long-term toxicity and carcinogenicity studies in mice and rats, no signs of systemic toxicity or treatment-related increases in neoplastic lesions were reported up to the highest dose levels tested, which were 948 mg/kg bw per day and 735 mg/kg bw per day in mice and rats, respectively.

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

Oxathiapiprolin has been tested in an adequate range of genotoxicity studies, both in vitro and in vivo. No evidence of genotoxicity was found.

The Meeting concluded that oxathiapiprolin is unlikely to be genotoxic.

In view of the lack of genotoxicity and the absence of carcinogenicity in mice and rats, the Meeting concluded that oxathiapiprolin is unlikely to pose a carcinogenic risk to humans.

In a one-generation range-finding reproductive toxicity study in rats, which tested dietary concentrations of 0, 2000, 10 000 and 20 000 ppm (equal to 0, 129, 653 and 1321 mg/kg bw per day for males and 0, 150, 715 and 1507 mg/kg bw per day for females, respectively), there were no adverse findings in the parental generation. In the offspring, body weights were decreased in males and females and balanopreputial separation was delayed in males at 20 000 ppm (equal to 1321 mg/kg bw per day).

In a two-generation reproductive toxicity study in rats, which tested dietary concentrations of 0, 500, 1500, 6000 and 17 000 ppm (reduced to 0, 300, 900, 3500 and 10 000 ppm in the gestation and lactation periods in females to equalize compound intake; equal to 0, 29.2, 86.4, 346 and 1013 mg/kg bw per day for males and 0, 34.3, 106, 430 and 1210 mg/kg bw per day for females, respectively), the parental toxicity NOAEL was 17 000/10 000 ppm (equal to 1013 mg/kg bw per day), the highest dose tested. The offspring toxicity NOAEL was 6000/3500 ppm (equal to 430 mg/kg bw per day, maternal intake), based on delayed balanopreputial separation in offspring at 17 000/10 000 ppm (equal to 1210 mg/kg bw per day). The reproductive toxicity NOAEL was 17 000/10 000 ppm (equal to 1013 mg/kg bw per day), the highest dose tested.

In developmental toxicity studies in rats and rabbits, there were no adverse effects on either maternal or embryo/fetal parameters up to the limit dose of 1000 mg/kg bw per day.

Three assays were performed to assess the ability of oxathiapiprolin to affect endocrine function in vitro and in vivo. In an in vitro H295R steroidogenesis assay, there was no evidence of an effect on testosterone or estradiol levels up to the highest dose tested, 7.9×10^{-6} mol/L. In a uterotrophic assay in ovariectomized adult female rats and a 15-day endocrine assay in male rats, there were no effects up to the limit dose of 1000 mg/kg bw per day.

In an acute neurotoxicity study in rats, animals were tested at a dose of 0, 200, 1000 or 2000 mg/kg bw per day administered by gavage. The NOAEL was 2000 mg/kg bw, the highest dose tested.

The Meeting concluded that oxathiapiprolin is not neurotoxic.

In a 28-day immunotoxicity study in female mice, animals were tested at a dose of 0, 200, 800, 3500 or 7000 ppm (equal to 0, 38, 151, 645 and 1432 mg/kg bw per day, respectively) administered in the diet. The NOAEL was 7000 ppm (equal to 1432 mg/kg bw per day), the highest dose tested.

The Meeting concluded that oxathiapiprolin is not immunotoxic.

Toxicological data on metabolites and/or degradates

Genotoxicity studies were performed on five metabolites: IN-E8S72 (5-(trifluoromethyl)-1*H*-pyrazole-3-carboxylic acid; plant, goat and rat metabolite), IN-RAB06 (1-[2-[4-[4-[5-(2,6-difluorophenyl)-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-1-piperidinyl]-2-oxoethyl]-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylic acid; rat, goat and soil metabolite), IN-RDT31 (1-[4-[4-[5-(2,6-

difluorophenyl)-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-4-hydroxy-1-piperidinyl]-2-[5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl]ethanone; rat and soil metabolite), IN-SXS67 (1-β-D-glucopyranosyl-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylic acid; goat and plant metabolite) and IN-WR791 (5-methyl-3-(trifluoromethyl)-1*H*-pyrazole-1-acetic acid; rat and plant metabolite). Additionally, a short-term toxicity study was conducted with IN-E8S72 (5-(trifluoromethyl)-1*H*-pyrazole-3-carboxylic acid; rat and plant metabolite).

IN-E8S72 was negative in Ames, chromosomal aberration and mammalian gene mutation studies in vitro and a bone marrow micronucleus assay in vivo.

IN-SXS67 was negative in Ames and chromosomal aberration assays. IN-SXS67 is the glucose conjugate of IN-E8S72.

IN-RAB06 was negative in Ames, chromosomal aberration and mammalian gene mutation assays.

IN-RDT31 was negative in Ames, chromosomal aberration and mammalian gene mutation assays.

IN-WR791 was negative in Ames and chromosomal aberration assays.

In a 28-day dietary toxicity study in the rat with IN-E8S72, the NOAEL was 15 000 ppm (equal to 1157 mg/kg bw per day), the highest dose tested.

The Meeting concluded that these metabolites are all covered by studies in the rat, including IN-SXS67, which is a glucose conjugate of IN-E8S72.

Human data

No information was submitted.

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

Toxicological evaluation

The Meeting established an ADI of 0–4 mg/kg bw on the basis of the NOAEL of 430 mg/kg bw per day in a two-generation study in rats for delayed balanopreputial separation in offspring at 1210 mg/kg bw per day. A safety factor of 100 was applied.

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

Levels relevant to risk assessment of oxathiapiprolin

Species	Study	Effect	NOAEL	LOAEL
Mouse	Eighteen-month study of toxicity and carcinogenicity[a]	Toxicity	7 000 ppm, equal to 948 mg/kg bw per day[b]	–
		Carcinogenicity	7 000 ppm, equal to 948 mg/kg bw per day[b]	–
Rat	Two-year study of toxicity and carcinogenicity[a]	Toxicity	18 000 ppm, equal to 735 mg/kg bw per day[b]	–
		Carcinogenicity	18 000 ppm, equal to	–

Species	Study	Effect	NOAEL	LOAEL
			735 mg/kg bw per day[b]	
	Two-generation study of reproductive toxicity[a]	Reproductive toxicity	17 000/10 000 ppm, equal to 1 013 mg/kg bw per day[b]	–
		Parental toxicity	17 000/10 000 ppm, equal to 1 013 mg/kg bw per day[b]	–
		Offspring toxicity	6 000/3 500 ppm, equal to 430 mg/kg bw per day	17 000/10 000 ppm, equal to 1 210 mg/kg bw per day
	Developmental toxicity study[c]	Maternal toxicity	1 000 mg/kg bw per day[b]	–
		Embryo and fetal toxicity	1 000 mg/kg bw per day[b]	–
	Acute neurotoxicity study[a]	Neurotoxicity	2 000 mg/kg bw per day[b]	–
Rabbit	Developmental toxicity study[c]	Maternal toxicity	1 000 mg/kg bw per day[b]	–
		Embryo and fetal toxicity	1 000 mg/kg bw per day[b]	–
Dog	Thirteen-week and 1-year studies of toxicity[c,d]	Toxicity	36 000 ppm, equal to 1 415 mg/kg bw per day[b]	–

[a] Dietary administration.

[b] Highest dose tested.

[c] Gavage administration.

[d] Two or more studies combined.

Acceptable daily intake (ADI)

0–4 mg/kg bw

Acute reference dose (ARfD)

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 oxathiapiprolin

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid, < 50% at low dose and < 10% at high dose

Dermal absorption	No data
Distribution	Widely distributed, highest concentrations in liver, kidneys, lungs and red blood cells
Potential for accumulation	No evidence of accumulation
Rate and extent of excretion	Rapid and essentially complete within 7 days
Metabolism in animals	17–87% excreted unchanged at low and high doses; multiple identified or tentatively identified metabolites; hydroxylation in various positions
Toxicologically significant compounds in animals and plants	Oxathiapiprolin
Acute toxicity	
Rat, LD_{50}, oral	> 5 000 mg/kg bw
Rat, LD_{50}, dermal	> 5 000 mg/kg bw
Rat, LC_{50}, inhalation	> 5.1 mg/L
Rabbit, dermal irritation	Not irritating
Rabbit, ocular irritation	Slightly irritating
Guinea-pig, dermal sensitization	Not sensitizing (maximization test)
Short-term studies of toxicity	
Target/critical effect	None
Lowest relevant oral NOAEL	1 058 mg/kg bw per day, highest dose tested (mouse)
Lowest relevant dermal NOAEL	1 000 mg/kg bw per day, highest dose tested (rat)
Lowest relevant inhalation NOAEC	No data
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	None
Lowest relevant NOAEL	735 mg/kg bw per day, highest dose tested (rat)
Carcinogenicity	Not carcinogenic in mice or rats[a]
Genotoxicity	
	No evidence of genotoxicity[a]
Reproductive toxicity	
Target/critical effect	Delayed balanopreputial separation
Lowest relevant parental NOAEL	1 013 mg/kg bw per day, highest dose tested (rat)
Lowest relevant offspring NOAEL	430 mg/kg bw per day (rat)
Lowest relevant reproductive NOAEL	1 013 mg/kg bw per day, highest dose tested (rat)
Developmental toxicity	
Target/critical effect	None
Lowest relevant maternal NOAEL	1 000 mg/kg bw per day, highest dose tested (rat, rabbit)
Lowest relevant embryo/fetal NOAEL	1 000 mg/kg bw per day, highest dose tested (rat, rabbit)
Neurotoxicity	
Acute neurotoxicity NOAEL	2 000 mg/kg bw, highest dose tested (rat)
Subchronic neurotoxicity NOAEL	No data

Developmental neurotoxicity NOAEL	No data
Other toxicological studies	
Immunotoxicity	1 432 mg/kg bw per day, highest dose tested (mouse)
Mechanistic/mode of action studies	No effects on endocrine function in vitro or in vivo
Studies on metabolites	
IN-E8S72	No evidence of genotoxicity
	NOAEL: 1 157 mg/kg bw per day (28-day rat)
IN-RAB06	No evidence of genotoxicity
IN-RDT31	No evidence of genotoxicity
IN-SXS67	No evidence of genotoxicity
IN-WR791	No evidence of genotoxicity
Human data	
	No studies submitted

[a] Unlikely to pose a carcinogenic risk to humans via exposure from the diet.

Summary

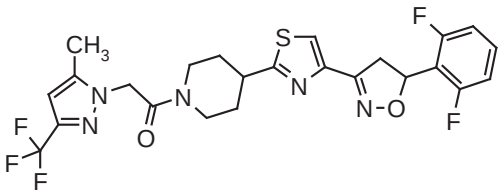
	Value	**Study**	**Safety factor**
ADI	0–4 mg/kg bw	Reproductive toxicity study (rat)	100
ARfD	Unnecessary	–	–

RESIDUE AND ANALYTICAL ASPECTS

Oxathiapiprolin is a systemic piperidinyl thiazole isoxazoline fungicide effective against oomycete pathogens, acting by inhibiting mycelial growth and zoospore release, encystment and mobility. It exhibits translaminar efficacy and gives systemic disease control following soil applications.

It was scheduled by the 47th Session of the CCPR as a new compound for consideration by the 2016 JMPR. The manufacturer submitted studies on metabolism, analytical methods, supervised field trials, processing, freezer storage stability and environmental fate in soil.

Authorisations exist for the use of oxathiapiprolin as foliar treatments or as soil treatments at planting (band/in-furrow or in transplant water) or via drip irrigation in a number of countries in Asia, the Pacific, Central and South America, and are pending in Europe and other countries. GAP information was available from Australia, China, New Zealand and North America.

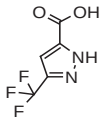
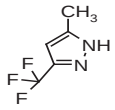
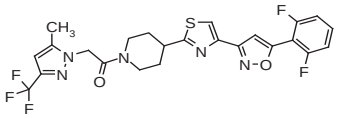
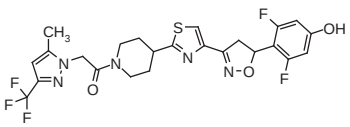
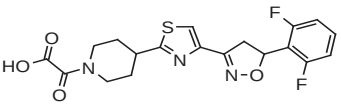
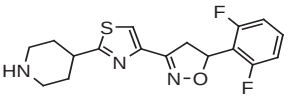


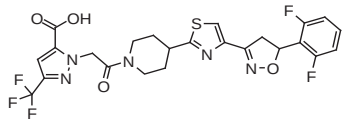
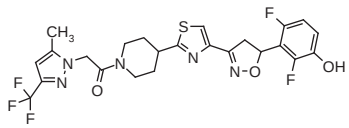
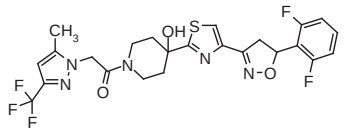
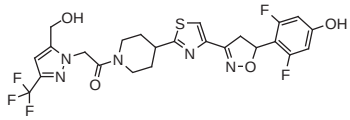
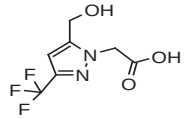
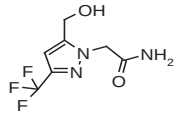
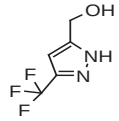
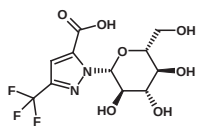
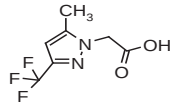
Oxathiapiprolin

(MW 539.53)

Oxathiapiprolin is a racemic mixture of (R)-oxathiapiprolin and (S)-oxathiapiprolin enantiomers with a low vapour pressure and water solubility (≈0.18 mg/L) that is not pH dependent. It is soluble in medium polarity organic solvents (e.g. dichloromethane, acetone or acetonitrile), but only slightly soluble in hexane. The octanol/water partition co-efficient (Log P_{OW} 3.6) is not pH dependent.

The following abbreviations are used for the major metabolites discussed below:

Code	Name and Matrix	Structure
IN-E8S72	5-(Trifluoromethyl)-1H-pyrazole-3-carboxylic acid Rat, plants, goat, soil	
IN-KJ552	3-Methyl-5-(trifluoromethyl)-1H-pyrazole Rat, plants	
IN-Q7D41	1-[4-[4-[5-(2,6-Difluorophenyl)-3-isoxazolyl]-2-thiazolyl]-1-piperidinyl]-2-[5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]ethanone Rat (transitory), goat, hen, soil, plants	
IN-Q7H09	1-[4-[4-[5-(2,6-Difluoro-4-hydroxyphenyl)-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-1-piperidinyl]-2-[5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]ethanone Rat, plants, hen, goat	
IN-Q9L80	4-[4-[5-(2,6-Difluorophenyl)-4,5-dihydro-3-isoxazolyl)-2-thiazolyl]-α-oxo-1-piperidineactetic acid Rat, plants	
IN-QPS10	4-[4-[5-(2,6-Difluorophenyl)-4,5-dihydro-3-isoxazolyl)-2-thiazolyl]piperidine Plants, soil	

Code	Name and Matrix	Structure
IN-RAB06	1-[2-[4-[4-[5-(2,6-Difluorophenyl)-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-1-piperidinyl]-2-oxoethyl]-3-(trifluoromethyl)-1H-pyrazole-5-carboxylic acid Rat, goat, hen, soil	
IN-RDG40	1-[4-[4-[5-(2,6-Difluoro-3-hydroxyphenyl)-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-1-piperidinyl]-2-[5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]ethanone Rat, plants, hen, goat	
IN-RDT31	1-[4-[4-[5-(2,6-Difluorophenyl)-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-4-hydroxy-1-piperidinyl]-2-[5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]ethanone Rat, soil	
IN-RLB67	1-[4-[4-[5-(2,6-Difluoro-4-hydrophenyl)-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-1-piperidinyl]-2-[5-(hydroxymethyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]ethanone Rat, goat	
IN-RZB20	5-(Hydroxymethyl)-3-(trifluoromethyl)-1H-pyrazole-1-acetic acid Rat, plants	
IN-RZB21	5-(Hydroxymethyl)-3-(trifluoromethyl)-1H-pyrazole-1-acetamide Plants	
IN-RZD74	3-(Trifluoromethyl)-1H-Pyrazole-5-methanol Plants, transient in goat, hen, rat	
IN-SXS67	1-ß-D-Glucopyranosyl-3-(-(trifluoromethyl)-1H-pyrazole-5-carboxylic acid Plants	
IN-WR791	5-Methyl-3-(trifluoromethyl)-1H-pyrazole-1-acetic acid Plants, goat, rat, soil	

Plant metabolism

The Meeting received plant metabolism studies on potato, grape and lettuce following foliar applications of [^{14}C]oxathiapiprolin and on courgette, lettuce, wheat, turnips and potato grown in [^{14}C]oxathiapiprolin-treated soil.

Grapes-foliar applications

In a study on outdoor grapes, [^{14}C]oxathiapiprolin was applied to vines as three foliar treatments of 0.07 kg ai/ha, at flowering (BBCH 63–65), at BBCH 73 (cereal grain sized berries) and at BBCH 79 (pre-bunch-closure, adjacent berries on bunch beginning to touch). Foliage samples were taken at immediately after each treatment, 14 days after Treatments 2 and 3, and at grape maturity (76 DAT 3). Berry (grape) samples were taken 14 days after the second treatment, immediately after the third treatment, 14 days later and at grape maturity.

The majority of the radioactive residue in the berries and foliage was removed by surface washing and/or initial extraction (69–99% TRR). At maturity, 76 days after the third application, total radioactive residues were 0.30–0.32 mg eq/kg in berries and 1.1–1.38 mg eq/kg in foliage. Unextracted residues were about 10–16% TRR in foliage, 6.4–7.5% TRR in immature berries and about 15% TRR in mature berries.

Oxathiapiprolin was the major component identified in immature berries (36–74% TRR, 0.17–0.41 mg/kg) and accounted for 41% TRR (0.13 mg/kg) at maturity in [thiazole-^{14}C]-treated berries but was not the major residue in the [pyrazole-^{14}C]-treated berries, making up about 10% TRR (0.03 mg/kg). Chiral HPLC analysis showed no change in the isomer ratio over the study period.

In the [pyrazole-^{14}C]-treated mature berries, the polar pyrazole-specific metabolites IN-WR791 (19% TRR, 0.06 mg eq/kg) and IN-E8S72 (14% TRR, 0.04 mg eq/kg) were the predominant residues. Numerous minor metabolites were also identified or detected in berries, none of which were present at more than 6.2% TRR (0.02 mg eq/kg).

Oxathiapiprolin was also the predominant component identified in foliage, declining to 32–60% TRR (0.44–0.67 mg/kg) at grape maturity. Eleven minor identified metabolites and numerous unidentified metabolites were detected in foliage, the highest of which was IN-Q7H09, found at up to 5% TRR (0.36 mg eq/kg).

Lettuce-foliar applications

In a confined study on lettuce, three applications of 0.07 kg ai/ha [^{14}C]oxathiapiprolin were applied at 10 day intervals from BBCH 15 (5-leaf stage) to BBCH 19 (9-leaf stage) and leaves were sampled immediately after each application, 10 days after the first and second applications and 3, 7, 14 days after the last application.

The majority of the radioactive residue in the foliage was removed by surface washing and/or initial extraction (83–99.7% TRR). Unextracted residues in samples taken 7–14 days after treatment ranged from 7–14% TRR in the [pyrazole-^{14}C]-treated plants and from 14–17% TRR in the [thiazole-^{14}C]-treated plants.

Oxathiapiprolin was the major residue in all samples, making up 65% TRR (0.34 mg/kg) in the mature leaves (14 DAT 3) from the [pyrazole-^{14}C]-treated plants and 57% TRR (0.27 mg/kg) in the leaves from the [thiazole-^{14}C]-treated plants. Chiral chromatographic analysis confirmed that the enantiomeric ratio remained unchanged over the study period.

The predominant metabolite in lettuce foliage was IN-Q7H09 (5.1% TRR–0.032 mg eq/kg). Other metabolites including multiple hydroxylated oxathiapiprolin compounds made up not more than 6% TRR (< 0.05 mg eq/kg).

Potato-foliar applications

In a confined study on potatoes, three applications of 0.07 kg ai/ha [^{14}C]oxathiapiprolin were applied just before flowering (BBCH 53), at first flowering (BBCH 59) and 14 days later (end of flowering, BBCH 69). Foliage samples (whole plants) were taken immediately after the first application, before and after the second and third (final) applications, and fourteen days after the final application. The final (maturity) harvest was taken 28 days after the final application. Potato tuber samples were taken before the third (final) treatment, 14 days after the final treatment (14 DAT 3) and at final harvest (28 DAT 3).

Radioactive residues in mature tubers were low (0.012 mg eq/kg [pyrazole-^{14}C] and 0.005 mg eq/kg [thiazole-^{14}C]) and were not investigated further. Unextracted tuber residues were < 0.01 mg eq/kg for both radiolabels. In foliage, the majority (75–96% TRR) of the radioactive residue was removed by surface washing and initial extraction (0.13–0.19 mg eq/kg extracted from mature foliage).

In foliage, oxathiapiprolin was the major residue component, accounting for 25–59% TRR, found in mature foliage samples at 0.04 mg/kg (pyrazole-label) and 0.11 mg/kg (thiazole-label). A range of minor metabolites were individually present at no greater than 8% TRR.

Potato-soil application

Seed potatoes were sown into a loam soil (3.1% organic matter, pH 5.3) immediately after a single soil application of [^{14}C]oxathiapiprolin at a rate equivalent to 0.6 kg ai/ha. Foliage and tubers were sampled 37 days after treatment (BBCH 65) and at maturity (BBCH 91), 72 days after treatment.

The total radioactive residues increased from 0.02–0.03 mg eq/kg (37DAT) to 0.05–0.11 mg eq/kg (72 DAT) in foliage and decreased from 0.01–0.02 mg eq/kg (37 DAT) to < 0.01 mg eq/kg (72 DAT) in tubers. More than 80% of the radioactive residue in tubers and foliage was extracted with acetonitrile, with unextracted residues being 0.003 mg eq/kg in tubers and up to 0.01 mg eq/kg in foliage. Extracts from tubers from the [isoxazoline ^{14}C]-oxathiapiprolin plots were low (up to 0.01 mg eq/kg) and were not investigated further.

Oxathiapiprolin was not a major residue, present at < 10% TRR and < 0.005 mg/kg in tubers and foliage. IN-WR791 was the major component identified in mature tubers (25% TRR and 0.003 mg eq/kg) with IN-E8S72 (14% TRR) and IN-RZB20 (12% TRR) also present at levels of 0.001–0.002 mg eq/kg. Unresolved IN-RZB21/IN-RZD74 and IN-RZB20 were the principal components identified in foliage (11–13% TRR, up to 0.015 mg eq/kg).

Lettuce-soil application

Lettuce seeds were sown into a loam soil (3.1% organic matter, pH 5.3) immediately after a single soil application [^{14}C]oxathiapiprolin at a rate equivalent to 0.6 kg ai/ha and leaves were sampled 44 days after treatment (BBCH 45) and at maturity, 57 days after treatment.

The total radioactive residues in lettuce samples grown in [isoxazoline-^{14}C]-oxathiapiprolin treated soil were less than the limit of quantification (0.01 mg eq/kg) and were not investigated further. TRR in lettuce samples grown in [pyrazole-^{14}C]-treated soil were < 0.02 mg eq/kg, with 88–91% TRR being removed in the initial acetonitrile extract and unextracted residues accounted for 9.5–12% TRR (0.002 mg eq/kg).

Oxathiapiprolin was not detected in any of the samples. Metabolites making up more than 10% TRR in immature and mature foliage samples were IN-WR791 (23% TRR and 30% TRR respectively), IN-E8S72 (19–21%TRR) and IN RZB21/IN-RZD74 (19–21% TRR) but all individually found at 0.004 mg eq/kg or less.

Courgette-soil application

Courgette seeds were sown into a loam soil (3.1% organic matter, pH 5.3) immediately after a single soil application of either [^{14}C]oxathiapiprolin at a rate equivalent to 0.6 kg ai/ha with leaf and fruit samples being taken 44 days after treatment (BBCH 71) and at maturity, 79 days after treatment.

In samples taken from the plants grown in [pyrazole ^{14}C]-treated soil, total radioactive residues increased over time from 0.045 mg eq/kg (44DAT) to 0.17 mg eq/kg (79 DAT) in foliage and from 0.013 to 0.023 mg eq/kg in the corresponding fruit samples.

Conversely, the TRR in the foliage from [isoxazoline-^{14}C]-treated soil decreased over time from 0.028 mg eq/kg (44 DAT) to 0.008 mg eq/kg (79 DAT) and TRRs in fruit were below the limit of detection throughout the study (< 0.006 mg eq/kg). Residues in the mature fruit and leaf samples were < 0.01 mg eq/kg and not investigated further.

The majority (77–97%) of the radioactive residue in the foliage and fruit was extracted in the initial acetonitrile extracts. Unextracted residues were up to 23% TRR (0.006 mg eq/kg) in foliage (isoxazoline-label) and less than 10% TRR in fruit and in foliage from the pyrazole-labelled plants.

In fruit from plants grown in the [pyrazole-^{14}C]-treated soil, oxathiapiprolin was found at trace levels (0.5% TRR, < 0.001 mg/kg) in immature fruit but not in mature fruit.

IN-WR791 was the major component identified in fruit, found at 0.008 mg eq/kg (57% TRR) in immature fruit and 0.016 mg eq/kg (74% TRR) in mature fruit. Six other metabolites were identified at low levels (each < 5% TRR and up to 0.001 mg eq/kg).

In foliage, oxathiapiprolin was the predominant residue (24% TRR, 0.007 mg/kg) identified in the immature foliage grown in [isoxazoline-^{14}C]-treated soil and found in mature foliage from the [pyrazole-^{14}C]-treated soil at low levels (4.6% TRR, 0.008 mg/kg).

Major metabolites in immature foliage (44 DAT) were IN-WR791 (24% TRR, 0.011 mg eq/kg) and IN-E8S72 (24% TRR, 0.011 mg eq/kg). Other metabolites making up more than 10% TRR were IN Q7H09 (18.5% TRR), IN-RZB20 (17% TRR) and IN-RZB21/IN-RZD74 (13% TRR). None of these other metabolites exceeded 0.008 mg eq/kg. Unidentified components each did not exceed 2–3% TRR.

Major metabolites in mature foliage (79 DAT) were IN-WR791 (27.5% TRR, 0.047 mg eq/kg) and IN-E8S72 (21% TRR, 0.036 mg eq/kg). IN-RZB20 and IN-RZB21/IN-RZD74 were also present, each at about 0.02 mg eq/kg (11–12% TRR). Unidentified components each did not exceed 3% TRR.

In summary, when oxathiapiprolin was applied as a foliar treatment, parent compound was the major residue in lettuce, potato foliage, grape leaves and berries, making up 10–85% TRR. Chiral chromatographic analysis indicates that the enantiomeric ratio did not change over the study periods.

In grape berries, the significant metabolites were the cleavage products IN-WR791 (19% TRR, 0.6 mg eq/kg) and IN-E8S72 (14% TRR, 0.04 mg eq/kg). In grape leaves, lettuce and potato foliage, metabolites including IN Q7H09 (up to 0.36 mg eq/kg in grape leaves) were present in most samples, all individually present at less than 10% TRR.

Following soil applications, oxathiapiprolin is a minor component of the total residue in potato tubers, courgettes and foliage (lettuce, potato, grape, and courgette). Metabolites found above 10% TRR were pyrazole cleavage products (IN-WR791, IN-E8S72, IN-RZB21/IN-RZD74 and RZB20), each present at less than 0.05 mg eq/kg.

Animal metabolism

The Meeting received animal metabolism studies on rats, lactating goats and laying hens where animals were dosed with oxathiapiprolin radiolabelled in the pyrazole ring, the thiazole ring or the

isoxazoline ring (rat) and in lactating goats dosed with pyrazole-labelled IN-E8S72, a glucoside plant metabolite of oxathiapiprolin.

In rats, the metabolism of oxathiapiprolin was reviewed in the framework of the toxicological evaluation by the current Meeting.

Lactating goats were orally dosed with [^{14}C]oxathiapiprolin at rates equivalent to 14.2–14.3 ppm in the feed for 7 consecutive days and sacrificed 12 hours after the last dose.

The total recovery was 94–99.6% of the administered radioactivity (AR), with 84–86% being recovered from the urine, faeces, and cage wash, 8–12% found in the gastrointestinal tract, 0.1–0.2% in milk and 0.7–1% in edible tissues. Radioactivity plateaued in milk within 5 days.

Total radioactive residue levels were 0.01–0.02 mg eq/kg in milk, 0.75–0.97 mg eq/kg in liver, 0.07–0.08 mg eq/kg in kidney, 0.009–0.013 mg eq/kg in muscle and 0.025–0.03 mg eq/kg in fats.

Solvent extractions released 52–100% TRR from tissues and milk and subsequent enzymatic hydrolysis released another 26–29% TRR from liver.

Oxathiapiprolin accounted for 8.7–11% TRR (0.002 mg/kg) in milk, 6.4–12% TRR (0.05–0.11 mg/kg) in liver, 13–14% TRR (0.01 mg/kg) in kidney, 27–43% TRR (0.004 mg/kg) in muscle, and 36–58% TRR (< 0.016 mg/kg) in the fat fractions. Chiral chromatographic analysis confirmed that the oxathiapiprolin enantiomeric ratio remained unchanged over the study period.

The major metabolites in goat matrices were IN-E8S72 (maximum 24% TRR, 0.02 mg eq/kg in kidney) and the mono-hydroxy metabolites (including IN-RDG40 and IN-Q7H09) in liver (up to 0.13 mg/kg, 13% TRR) and in kidney (0.013 mg eq/kg, up to 21% TRR).

In a lactating goat study examining the fate of IN-SXS67 (the glucoside conjugate of IN-E8S72, not found in animals), one animal was dosed orally with 18.95 ppm [pyrazole-^{14}C]- IN-SXS67 in the diet for 7 days and the animal was sacrificed 6 hours after administration of the last dose.

Residues were rapidly excreted in urine and faeces (95–100% AR) and the total recovery of administered radiocarbon was 97.7%.

Unchanged IN-SXS67 made up 77% TRR (0.03 mg/kg) in liver and 58% TRR in kidney (0.28 mg/kg) while its aglycone metabolite, IN-E8S72 accounted for 16% TRR (0.006 mg eq/kg) in liver and 39% TRR (0.19 mg eq/kg) in kidney.

Laying hens were orally dosed with [^{14}C]oxathiapiprolin (pyrazole-label or thiazole-label) at doses equivalent to 17.4–17.8 ppm in the feed for 14 consecutive days and sacrificed 6 hours after the last dose.

More than 95% of the total administered dose was recovered from the excreta and cage wash. About 0.02% AR was recovered in edible tissues and another 0.01–0.02% AR found in the eggs. Radioactivity plateaued in whole eggs within 6 days.

TRRs in edible tissues and eggs from both the radiolabels were low (< 0.03 mg eq/kg) except for the liver which had higher residues (0.1 mg eq/kg).

Solvent extractions released 46–54% TRR in liver, 56–79% TRR in eggs and 87–94% TRR from fat and skin + fat. Subsequent protease treatments released another 21–54% TRR from liver and eggs.

While oxathiapiprolin was found in all tissues and eggs, levels were not more than 0.01 mg/kg. Oxathiapiprolin made up 10–22% TRR (0.002–0.003 mg/kg) in eggs, 4.0–8.0% TRR (0.004–0.008 mg/kg) in liver, 28–66% TRR (0.01 mg/kg) in abdominal fat, and 22–37% TRR (0.003–0.004) mg/kg in skin with fat.

IN-RAB06 was the only identified component present at more than 0.01 mg eq/kg, detected only in liver at up to 0.014 mg eq/kg (7.7–13.5% TRR).

IN-RDG40/IN-Q7H09 accounted for 15–33% TRR (0.003–0.005 mg eq/kg) in skin and fat, IN-Q7D41 was detected in eggs and fats (5–10% TRR, 0.001–0.002 mg eq/kg) but was not observed in liver.

Environmental fate

The Meeting received information on the environmental fate and behaviour of oxathiapiprolin, including hydrolytic stability, photochemical degradation in soils and aerobic metabolism studies.

Hydrolysis

Radiolabelled oxathiapiprolin incubated in the dark in sterile aqueous buffered solutions at pH 5, 7, and 9 for 5 days at 50 °C was stable with no major transformation products being observed.

Photochemical degradation in soil

In a 15-day photochemical degradation study in a sandy loam soil, 88% AR (moist soil) and 84–97% AR (dry soil) was able to be extracted, with no quantifiable levels of evolved $^{14}CO_2$ or non-specific volatile organic components.

Oxathiapiprolin accounted for 70% AR in moist soil and 80% AR in the dry soil after 15 days of continuous irradiation. Degradates IN-RDT31, IN-E8S72, IN-RAB06 and at least 15 minor transformation products were also found, all below 6% AR at two consecutive sampling intervals or 10% AR at a single sampling interval.

Calculated photodegradation DT_{50} values for oxathiapiprolin were 28.2 days (moist soil) and 36.3 days (dry soil) and the DT_{90} values were 93.5 days and 120.7 days respectively.

Aerobic soil metabolism

Aerobic degradation of radiolabelled oxathiapiprolin (0.2 mg/kg) was investigated in five different soils (120–134 days in the dark at 20 °C). Volatile organics were not produced in significant amounts and about 12% AR was evolved as $^{14}CO_2$. Chiral HPLC analysis in one study showed no change in the isomer ratio over the study period.

DT_{50} values for oxathiapiprolin ranged from 18 to 134 days at 20 ºC (geometric mean of 76 days). The predominant degradation products were IN-RAB06 (up to 13% AR), IN-RDT31, IN-QPS10 and IN-E8S72, each making up 7–9% AR.

The proposed degradation pathways include cleavage of the pyrazole ring to form IN-QPS10 and IN-E8S72; hydroxylation of the methyl group on the pyrazole ring followed by oxidation to form IN-RAB06 and hydroxylation at the 4-position of the piperidine ring to form IN-RDT31 (with subsequent cleavage to IN-WR791 and further degradation to IN-E8S72.

In ten field dissipation studies conducted in Europe and North America and involving bare soil treatments of 0.2–0.77 kg ai/ha oxathiapiprolin, DT_{50} values ranged from 5–205 days (geometric mean of 26 days). Residues of parent and degradates were found mostly in the upper soil segment (0–15 cm) with the highest concentration in the 0–5 cm layer and rarely found below 15 cm depth.

Laboratory degradation and field dissipation studies were also conducted with the four degradates where residues exceeded 5% AR at two or more consecutive sampling points. Geometric mean half-lives were 37 days (IN-RAB06), 48 days (IN-QPS10), 141 days (IN-RDT31) and 323 days (IN-E8S72).

Rotational crops

Two confined rotational crop studies using wheat, lettuce and turnip as rotational crops planted in bare sandy loam soil treated at rates equivalent to 0.21 kg ai/ha or 0.6 kg ai/ha. Plant-back intervals ranged from 30 to 365 days.

In samples from the rotational crops from soils treated with 0.21 kg ai/ha [isoxazoline^{14}C]- and [thiazole^{14}C]-oxathiapiprolin, TRRs were low (up to 0.013 mg eq/kg), and were higher in the samples from the soils treated with [pyrazole^{14}C]-oxathiapiprolin, attributed to the higher root uptake of polar metabolites derived from the pyrazole moiety.

Highest TRRs in food crops were 0.26 mg eq/kg (wheat grain), 0.02 mg eq/kg (mature lettuce, and turnip roots). In animal feed items, highest TRRs were 0.76 mg eq/kg (wheat straw), 0.27–0.3 mg eq/kg (wheat forage and hay) and 0.09–0.12 mg eq/kg (turnip tops).

In crop samples from soils treated with 0.6 kg ai/ha [isoxazoline^{14}C]-oxathiapiprolin, TRRs in food items ranged were also low, up to 0.09 mg eq/kg (wheat straw). In the pyrazole-label samples, highest TRRs in food crops were 0.19 mg eq/kg (wheat grain) and 0.02–0.04 mg eq/kg in lettuce and turnip roots). In animal feed items, highest TRRs were 0.7 mg eq/kg (wheat straw), 0.23–0.26 mg eq/kg (wheat forage and hay) and 0.09 mg eq/kg (turnip tops).

Oxathiapiprolin residues were not detectable in most rotational crops in both studies, and where present, residues were < 0.01 mg/kg and less than 15% TRR). Metabolites present at more than 0.01 mg eq/kg and above 10% TRR were IN-WR791, IN-E8S72, IN-SXS67, IN-RZB20 and IN-RZB21/IN-RZD74.

In the study approximating the maximum seasonal application rate (0.6 kg ai/ha), metabolites present in food commodities were IN-WR791 (23–37% TRR, 0.03–0.05 mg eq/kg), IN-RZB20 (up to 13% TRR, 0.015 mg eq/kg) and IN-E8S72 (up to 14% TRR, 0.02 mg eq/kg in wheat grain and up to 35% TRR, 0.01 mg eq/kg in immature lettuce.

In animal feed commodities, metabolites present above 10% TRR and 0.1 mg eq/kg were in wheat straw, IN-SXS67 at 26–39% TRR and up to 0.27 mg eq/kg, IN-RZB20 at 17–26% TRR and up to 0.15 mg eq/kg and IN-RZB21/IN-RZD74 at 12–15% TRR and up to 0.1 mg eq/kg.

Field rotational crop studies

In a series of rotational crop field trials involving total application rates of 0.12–0.56 kg ai/ha, residues of oxathiapiprolin and metabolites were measured in a number of representative root and tuber vegetables, leafy vegetables, stem vegetables, Brassica vegetables, bulb vegetables, legumes/pulses, cereals, oilseeds, and small berries at plant-back intervals ranging from 8 days to 365 days.

When scaled to a seasonal application rate of 0.56 kg ai/ha, residues of oxathiapiprolin in rotational crops at all plant-back intervals were ≤ 0.01 mg/kg in all commodities except legume feed commodities (≤ 0.04 mg/kg).

Residues of IN-WR791 were 0.01 mg/kg or less in all rotational food crops except leafy vegetables (< 0.02 mg/kg) and cereal forage and hay (< 0.03 mg/kg) when scaled to the maximum seasonal rate.

Scaled maximum residues of the metabolite IN-E8S72 in food commodities were < 0.01 mg/kg except in strawberries, green onions and oilseeds (<0.02 mg/kg), legume vegetables and pulses (<0.05 mg/kg) and were up to 0.35 mg/kg in leafy vegetables. In animal feed commodities, maximum IN-E8S72 residues above 0.1 mg/kg occurred in legume and cereal hays (up to 0.15 mg/kg).

Scaled maximum residues of IN-SXS67 (the glucose conjugate of IN-E8S72) in food commodities were ≤ 0.01 mg/kg except in strawberries (0.02 mg/kg), cereal grains and leafy

vegetables (0.02 mg/kg), legume vegetables (0.04 mg/kg), pulses and root crops (0.07-0.08 mg/kg4 mg/kg) . In animal feed commodities, maximum residues above 0.1 mg/kg were in legume forage and hay (0.13–0.16 mg/kg) and cereal straw, forage and hay (0.26–0.9 mg/kg).

The Meeting concluded that since the application rates in the confined rotational crop studies and the field trials generally covered the range of GAP treatment rates for foliar or soil applications to annual crops, residues of parent are not expected in food commodities from rotational crops following treatments according to the GAPs under consideration. In livestock feed commodities, parent residues could occur at low levels (up to 0.04 mg/kg in legume feed commodities).

Residues of metabolite IN-WR791 can be expected at low levels (up to 0.02–0.04 mg/kg) in leafy vegetables and cereal forage and hay.

Residues of < 0.05 mg/kg of IN-E8S72 can be expected in legume vegetables and, pulses, with expected levels of 0.15 mg/kg in legume and cereal hays and up to 0.35 mg/kg in leafy vegetables. Residues of the glucose conjugate (IN-SXS67) can be expected at levels of 0.02–0.08 mg/kg in food commodities and up to 0.9 mg/kg in legume and cereal feed commodities.

Methods of analysis

Analytical methods have been reported and validated for the analysis of oxathiapiprolin and metabolites in plant and animal commodities.

Data generation methods involved extraction with either formic acid:water:acetonitrile or formic acid:methanol, dilution with acetonitrile and water and separation of oxathiapiprolin and metabolites by reverse-phase LC-MS/MS. An additional SPE clean-up step was included for some matrices. Animal matrices were extracted with hexane:acetonitrile and acetonitrile:water. Quantitation was performed using mass transitions 540→500 and 540→163 for oxathiapiprolin. The LOQ for each analyte was 0.01 mg/kg.

For MRL-compliance, several multi-residue methods are available. Method DFG S 19 (LC-MS/MS module) is suitable for the analysis of oxathiapiprolin and metabolites IN-SXS67, IN-RZB20, IN-RZD74, IN-E8S72, IN-WR791, IN-RDG40, and IN-Q7H09 in representative samples with a high water content, high acid/water content, high acid content and high starch content with LOQs of 0.01 mg/kg for each analyte. However, in rape seed (high oil content), average recoveries were less than 70% in samples spiked with 0.01 mg/kg and 0.1 mg/kg.

Method DFG S 19 (LC-MS/MS module) is also suitable for the analysis of oxathiapiprolin and IN-Q7H09, IN-RDG40, IN-RLB67, and IN RAB06 in muscle, fat, liver, milk and eggs, with LOQs of 0.01 mg/kg for each analyte. However, for IN-Q7H09 in fat, the average recovery was 67% in the 0.01 mg/kg spiked samples, resulting in a higher LOQ of 0.1 mg/kg.

The QuEChERS multi-residue method was evaluated for measuring residues of oxathiapiprolin in commodities of plant origin (lettuce, wheat grain, orange, and maize grain) with LOQs of 0.01 mg/kg. However, the method did not adequately extract incurred oxathiapiprolin residues from dry crops such as wheat straw.

The Meeting concluded that suitable data generation methods are available to measure oxathiapiprolin and metabolites in plant and animal commodities and the multi-residue method DFG S 19 is suitable for monitoring residues of oxathiapiprolin and some metabolites in plant commodities with high water content, high acid content, dry crop commodities and also in animal commodities.

Stability of pesticide residues in stored analytical samples

Residues of oxathiapiprolin and metabolites IN-Q7H09, IN RDG40, IN E8S72, IN-RZB20, IN RZD74, IN SXS67, and IN WR791were stable in analytical samples stored frozen (-18 to -20 °C) for at least the storage intervals used in the supervised residue trials, with residues in the stored samples usually more than 80% of the spiked sample levels. In general, residue stability was shown for at

least 18 months in representative commodities with high water content (wheat forage, and tomato), high starch content (potato, and wheat grain), high protein content (dry bean seed), high oil content (soya bean seed), high acid content (grape) and low moisture content (wheat straw, and dry grape pomace). The exception was for the metabolite IN-RDG40 in soya bean seed (high oil content), where residues were stable for up to 3 months.

Definition of the residue

Plant commodities

In the plant metabolism studies involving foliar applications, oxathiapiprolin was the predominant residue, accounting for 25–85% TRR in lettuce, potato and grape leaves and in most grape samples (10%, 0.03 mg/kg mature grapes from the pyrazole-label treatment).

When applied as soil treatments in the plant and rotational crop metabolism studies and in the rotational crop field trials, oxathiapiprolin, if detected, was a minor component of the total residue. However, in the supervised field trials involving soil treatments, oxathiapiprolin was the predominant residue but present at levels lower than those following foliar applications.

The Meeting considered that a suitable MRL-compliance residue definition for plant commodities would be oxathiapiprolin (parent only).

When considering a residue definition for dietary intake estimation, the Meeting noted that in food commodities, metabolites making up more than 10% TRR and > 0.01 mg eq/kg in the metabolism studies, detected in field trials or present in rotational crops above 0.01 mg/kg (after scaling to seasonal application rate of 0.56 kg ai/ha) were IN-WR791, IN-E8S72 and its glucose conjugate IN-SXS67.

IN-WR791 was detected occasionally in the supervised field trials, at concentrations of 0.01–0.02 mg/kg following foliar applications (up to 0.1 mg/kg in grape leaves). In the food commodities from the rotational crop field trials, after scaling to a seasonal application rate of 0.56 kg ai/ha, IN-WR791 residues were only found in legume vegetables (up to 0.015 mg/kg) and in leafy vegetables (0.02 mg/kg).

The toxicity of IN-WR791 is no greater than the parent, and as the residue contribution to the maximum long-term toxicological burden is minor (< 5%), the Meeting agreed that IN-WR791 need not be included in the residue definition for dietary intake risk assessment.

IN-E8S72 and its glucose conjugate (IN-SXS67) were found in crops following soil applications and in rotational crops, at levels of 0.02–0.03 mg/kg but higher(0.04–0.8 mg/kg) in legume vegetables, pulses and root crops and up to 0.35 mg/kg in leafy vegetables. To estimate the long-term toxicological burden of these metabolites, the Meeting used the data from the crop rotation field studies (after scaling to the maximum seasonal rate of 0.56 kg ai/season) to calculate mean residues (expressed as oxathiapiprolin equivalents) for the relevant crop groups where significant levels of these metabolites could be expected. These mean values are summarised below.

Crop group [A]	Mean in rotational crops after residues scaled to 560 g ai/ha (mg parent eq/kg)[B]			
	Oxathiapiprolin	IN-E8S72	IN-SXS67	Total
Leafy vegetables [C]	< 0.01	0.30	< 0.016	0.33
Legume vegetables	< 0.01	0.047	0.026	0.083
	< 0.01	0.065	0.043	0.12
Pulses	0.004 (liver)[E]	0.006 (kidney [D]	0.009 (kidney)[D]	0.015 (kidney) 0.004 (liver)
Edible offal	93.8F	22.5	11.1	

Crop group [A]	Mean in rotational crops after residues scaled to 560 g ai/ha (mg parent eq/kg)[B]			
	Oxathiapiprolin	IN-E8S72	IN-SXS67	Total
IEDI (ug/person /day)	< 0.01	0.30	< 0.016	0.33

[A] Median residues of IN-E8S72 and IN-SXS67 were < LOD in representative root and tuber vegetables, stem vegetables, head and flowerhead Brassica vegetables, bulb vegetables, cereals, oilseeds, and small berries

[B] Based on metabolite:oxathiapiprolin conversion factors of 2.99 (IN-E8S72) and 1.58 (IN-SXS67)

[C] Mature leaves, including leafy Brassicas

[D] From consumption of rotational crop feed commodities

[E] For total dietary exposure

IN-E8S72 was identified in the rat metabolism studies and its toxicity is no greater than the parent. Its IN-SXS67 conjugate is a plant metabolite and following consideration of its structural characteristics, the WHO experts' panel were of the opinion that it would be of no greater toxicity than the parent.

As the combined residue contribution of these metabolites to the long-term toxicological burden for oxathiapiprolin is significant (about 36% that of parent), the Meeting considered that IN-E8S72 and IN-SXS67 should be included in the residue definition for estimation of dietary intake for plant commodities.

Animal commodities

In the goat and hen metabolism studies, only about 1–2% of the applied doses remained in goat tissues and about 0.02% remained in hen tissues, with 0.1–0.2% of the dose being eliminated in eggs and milk respectively.

Oxathiapiprolin was found in most matrices, mostly present at more than 10% TRR and above 0.01 mg/kg in goat liver (up to 0.11 mg/kg), fats (0.01–0.016 mg/kg) and kidney (0.01 mg/kg).

Since oxathiapiprolin was the predominant residue in eggs, muscle and fat and a major component of the residue in liver and kidney, the Meeting considered that a suitable MRL-compliance residue definition for animal commodities would be oxathiapiprolin (parent only).

For dietary intake estimation, metabolites exceeding 10% TRR and more than 0.01 mg/kg in animal commodities were IN-RAB06 in poultry liver (8–14%TRR), IN-E8S72 in goat kidney (24% TRR) and the combined hydroxy metabolites including IN-RDG40 and IN-Q7H09 in goat liver (11–13% TRR) and kidney (16–20% TRR).

Noting that the toxicity of IN-RAB06, IN-RDG40 and IN-Q7H09 are each no greater than the parent and since their concentrations in animal commodities are low, the Meeting concluded that their contribution to the long-term toxicological burden would be insignificant and that they need not be included in the residue definition for dietary intake risk assessment for animal commodities.

Since the overall intake of IN-E8S72 contributes significantly to the toxicological burden, the Meeting agreed that IN-E8S72, together with its glucose conjugate (IN-SXS67) should be included in the residue definition for dietary intake risk assessment for animal commodities.

The Meeting therefore considered that a suitable residue definition for estimation of dietary intake for animal commodities would be the sum of oxathiapiprolin, IN-E8S72 and IN-SXS67, expressed as parent.

The Meeting noted that multi-residue methods exists to measure oxathiapiprolin residues in plant and animal commodities and agreed that for MRL-compliance and dietary intake estimation for plant and animal commodities the residue definitions should be oxathiapiprolin.

The Meeting noted that the octanol/water partition coefficient (Log P_{ow}) for oxathiapiprolin was 3.6, suggesting a potential for the residue to be fat soluble. Information on relative concentrations in muscle and fat were in the animal metabolism studies inconclusive on the relative distribution of residues in muscle and fat and the Meeting concluded that the residue is not fat soluble.

Proposed definition of the residue for compliance with the MRL: *oxathiapiprolin.*

Proposed definition of the residue for estimation of dietary intake for plant and animal commodities): *Sum of: oxathiapiprolin, 5-(Trifluoromethyl)-1H-pyrazole-3-carboxylic acid and 1-ß-D-Glucopyranosyl-3-(-(trifluoromethyl)-1H-pyrazole-5-carboxylic acid*, expressed as parent.

The residue is not fat soluble.

Results of supervised residue trials on crops

The Meeting received supervised trial data for oxathiapiprolin applied as foliar or soil treatments on grapes, indoor tomatoes and cucumbers and on a range of vegetable field crops. These trials were conducted in China, Europe and North America. GAP information was available from Australia, Canada, China, New Zealand and the USA.

Where residues have been reported in the studies as being not detected or not quantifiable, the values have been considered as < LOQ for the purposes of MRL setting.

Residues in rotational crops

The Meeting noted that in rotational crops, significant residues of IN-E8S72 and/or its glucose conjugate (IN-SXS67) can be expected in legumes, pulses, leafy vegetables and cereal crops.

For the purposes of dietary exposure estimation, the Meeting agreed to include the residues of IN-E8S72 and IN-SXS67 (expressed as parent equivalents) in the long-term dietary intake estimate for oxathiapiprolin, and to estimate mean residue values of 0.33 mg/kg for leafy vegetables; 0.083 mg/kg for legume vegetables; and 0.12 mg/kg for pulses to account for the presence of these metabolites in rotational food crops. Their presence in non-rotational crops was below LOQ.

Grapes

Results from supervised field trials on grapes conducted in China and Europe were provided to the Meeting. The GAP in China is for a maximum of two foliar applications of 4–5 g ai/hL, with a 14-day PHI.

In four independent trials on grapes conducted in China and matching the Chinese GAP, oxathiapiprolin residues were 0.17, 0.37, 0.38 and 0.5 mg/kg.

Residues in five trials from Europe matching the GAP in China were 0.02, 0.2, 0.2, 0.21 and 0.23 mg/kg.

Since the Mann-Whitney test indicated that the populations from the trials in China and Europe were not statistically different, the Meeting agreed to use the global data set approach to estimate a maximum residue level based on the combined data set of: 0.02, 0.17, 0.2, 0.2, 0.21, 0.23, 0.37, 0.38 and 0.5 mg/kg.

The Meeting estimated an STMR of 0.21 mg/kg and a maximum residue level of 0.9 mg/kg for oxathiapiprolin on grapes.

Bulb vegetables

Results from supervised trials on dry bulb onions and spring onions conducted in North America were provided to the Meeting.

The critical GAP for bulb vegetables in the USA is for a maximum of four foliar applications of 35 g ai/ha, with a maximum seasonal rate of 140 g ai/ha and with a PHI of 0 days.

Onion, Bulb

In ten independent trials on bulb onions conducted in North America and matching the USA GAP, oxathiapiprolin residues were < 0.01, < 0.01, < 0.01, 0.01, 0.01, 0.01, 0.01, 0.02, 0.02 and 0.03 mg/kg.

The Meeting estimated an STMR of 0.01 mg/kg and a maximum residue level of 0.04 mg/kg for oxathiapiprolin on onion, bulb.

Noting that the GAP in the USA included other crops in their onion bulb subgroup, the Meeting agreed to extrapolate these recommendations to garlic, shallots and great-headed garlic.

Spring onion

In four independent trials on spring onions conducted in North America and matching the USA GAP, oxathiapiprolin residues were 0.45, 0.57, 0.63 and 0.85 mg/kg.

The Meeting estimated an STMR of 0.6 mg/kg and a maximum residue level of 2.0 mg/kg for oxathiapiprolin on spring onion.

Noting that the GAP in the USA was for bulb vegetables, the Meeting agreed to extrapolate these recommendations to leek and Welsh onion.

Brassica (cole or cabbage) vegetables, Head cabbages, Flowerhead brassicas

Results from supervised trials on broccoli, cauliflower and head cabbages conducted in North America were provided to the Meeting.

The critical GAP for Head and Stem Brassica vegetables in the USA is for a maximum of four foliar applications of 35 g ai/ha, with a maximum seasonal rate of 140 g ai/ha and with a PHI of 0 days

Broccoli

In five independent trials on broccoli conducted in North America and matching the USA GAP, oxathiapiprolin residues were 0.08, 0.17, 0.22, 0.23 and 0.81 mg/kg.

The Meeting estimated an STMR of 0.22 mg/kg and a maximum residue level of 1.5 mg/kg for oxathiapiprolin on broccoli.

Cabbages, head

In ten independent trials on head cabbage conducted in North America and matching the USA GAP, oxathiapiprolin residues were 0.04, 0.06, 0.06, 0.12, 0.12, 0.16, 0.22, 0.29, 0.32 and 0.42 mg/kg.

The Meeting estimated an STMR of 0.14 mg/kg, a highest residue of 0.46 mg/kg (for livestock dietary burden estimation) and a maximum residue level of 0.7 mg/kg for oxathiapiprolin on cabbages, head.

Cauliflower

In five independent trials on cauliflower conducted in North America and matching the USA GAP, oxathiapiprolin residues were 0.08, 0.08, 0.08, 0.09 and 0.14 mg/kg.

The Meeting estimated an STMR of 0.08 mg/kg and a maximum residue level of 0.3 mg/kg for oxathiapiprolin on cauliflower.

Fruiting vegetables, Cucurbits

Results from supervised trials on protected and field cucumbers, summer squash (courgettes, squash) and melons (cantaloupes) conducted in Europe and North America were provided to the Meeting.

The critical GAP for cucurbit vegetables in the USA is for either a maximum of four foliar applications of 35 g ai/ha, with a maximum seasonal rate of 140 g ai/ha and with a PHI of 0 days or 2–4 soil drench or drip irrigation treatments of up to 280 g ai/ha up to 0 days before harvest and with a maximum seasonal rate of 560 g ai/ha. The label also specifies the use of either foliar or soil treatments, but not both.

Cucumber

In four independent trials on protected cucumbers conducted in North America and matching the USA GAP for foliar applications (max 4 × 35 g ai/ha, 0-day PHI), oxathiapiprolin residues were 0.02, 0.04, 0.04, and 0.04 mg/kg.

In 11 independent trials on field cucumbers conducted in North America and matching the USA GAP for foliar applications, oxathiapiprolin residues were < 0.01, < 0.01, 0.01, 0.01, 0.02, 0.03, 0.03, 0.03, 0.04, 0.07 and 0.09 mg/kg.

In 10 independent trials matching the soil treatment GAP in the USA, residues of oxathiapiprolin were < 0.01 (9) and 0.01 mg/kg.

Summer squash

In 10 independent trials on field squash conducted in North America and matching the USA GAP for foliar applications, oxathiapiprolin residues were 0.01, 0.02, 0.02, 0.03, 0.03, 0.03, 0.04, 0.04, 0.08 and 0.12 mg/kg.

In 14 independent trials matching the soil treatment GAP in the USA, residues of oxathiapiprolin were < 0.01 (10), 0.01, 0.02, 0.03 and 0.08 mg/kg following pre-harvest treatments (0-day PHI).

Melons

In 11 independent trials on field melons (conducted in North America and matching the USA GAP for foliar applications, oxathiapiprolin residues were 0.01, 0.02, 0.03, 0.03, 0.04, 0.04, 0.05, 0.06, 0.07, 0.09 and 0.12 mg/kg.

In 11 independent trials matching the soil treatment GAP in the USA, residues of oxathiapiprolin were < 0.01 (7), 0.02, 0.02, 0.02 and 0.03 mg/kg.

The Meeting noted that the median residues in cucumbers, summer squash and melons from the foliar treatment field trials were within a 5-fold range (0.03–0.045 mg/kg) and that the Kruskall-Wallis test indicated that the populations were not statistically different. The Meeting therefore agreed to combine the data sets to estimate a group MRL for cucurbits. The combined data set is < 0.01, < 0.01, 0.01 (4), 0.02 (4), 0.03 (8), 0.04 (5), 0.05, 0.06, 0.07, 0.07, 0.08, 0.09, 0.09, 0.12 and 0.12 mg/kg.

The Meeting estimated an STMR of 0.03 mg/kg and a maximum residue level of 0.2 mg/kg for oxathiapiprolin on fruiting vegetables, cucurbits.

The Meeting also noted that oxathiapiprolin residues following soil applications were lower than the associated foliar treatments, and would be accommodated by the proposed group maximum residue level.

Fruiting vegetables, other than Cucurbits

Results from supervised trials on protected and field peppers and tomatoes conducted in Europe and North America were provided to the Meeting.

The critical GAP for fruiting vegetables (other than cucurbits) in the USA is for either a maximum of four foliar applications of 35 g ai/ha, with a maximum seasonal rate of 140 g ai/ha and with a PHI of 0 days or 2–4 soil drench or drip irrigation treatments of up to 280 g ai/ha up to 0 days before harvest and with a maximum seasonal rate of 560 g ai/ha. The label also specifies the use of either foliar or soil treatments, but not both.

Peppers

In two independent trials on protected bell peppers conducted in North America and matching the USA GAP for foliar applications (max 4 × 35 g ai/ha, 0-day PHI), oxathiapiprolin residues were 0.06 and 0.12 mg/kg.

In 10 independent trials on field bell peppers conducted in North America and matching the USA GAP for foliar applications, oxathiapiprolin residues were 0.02, 0.02, 0.02, 0.03, 0.03, 0.04, 0.04, 0.05, 0.05 and 0.12 mg/kg.

In five independent trials on field non-bell peppers conducted in North America and matching the USA GAP for foliar applications, oxathiapiprolin residues were 0.03, 0.06, 0.06, 0.08 and 0.12 mg/kg.

In 11 independent trials on bell and non-bell peppers matching the soil treatment GAP in the USA, residues of oxathiapiprolin were < 0.01 (14) and 0.02 mg/kg.

For dried chilli peppers, applying the default processing factor of 10 to the STMR and the maximum residue level estimated for fruiting vegetables, other than cucurbits, the Meeting estimated an STMR of 0.4 mg/kg and a maximum residue level of 4 mg/kg for oxathiapiprolin on chilli peppers, dried.

Tomatoes

In four independent trials on protected tomatoes conducted in North America and matching the USA GAP for foliar applications (max 4 × 35 g ai/ha, 0-day PHI), oxathiapiprolin residues were < 0.01, < 0.01, 0.03 and 0.08 mg/kg in tomatoes.

In 19 independent trials on field tomatoes, conducted in North America and matching the USA GAP for foliar applications, oxathiapiprolin residues were < 0.01, 0.02 (3), 0.03 (4), 0.04 (3), 0.05, 0.05, 0.08, 0.08, 0.1, 0.12, 0.14 and 0.31 mg/kg in tomatoes.

In 21 independent trials on field tomatoes matching the soil treatment GAP in the USA, residues of oxathiapiprolin were < 0.01 (18), 0.03, 0.05 and 0.24 mg/kg.

The Meeting noted that the median residues in bell peppers, non-bell peppers and tomatoes from the foliar treatment trials were within a 5-fold range and that the Kruskall-Wallis test indicated that the populations were not statistically different. The Meeting therefore agreed to combine the data sets to estimate a group MRL for fruiting vegetables other than cucurbits. The combined data set is < 0.01, 0.02 (6), 0.03 (7), 0.04 (5), 0.05 (4), 0.06, 0.06, 0.08 (3), 0.1, 0.12 (3), 0.14 and 0.31 mg/kg.

The Meeting estimated an STMR of 0.04 mg/kg and a maximum residue level of 0.4 mg/kg for oxathiapiprolin on fruiting vegetables, other than cucurbits (except mushrooms and sweetcorn).

The Meeting also noted that oxathiapiprolin residues in peppers and tomatoes following soil applications were lower than the associated foliar treatments, and would be accommodated by the estimated group maximum residue level.

Leafy vegetables

Results from supervised trials on field lettuce and spinach conducted in Europe and North America were provided to the Meeting.

The critical GAP for leafy greens (including lettuce and spinach) in the USA is for either a maximum of four foliar applications of 35 g ai/ha, with a maximum seasonal rate of 140 g ai/ha and with a PHI of 0 days or a maximum of four soil drench or drip irrigation treatments of up to 280 g ai/ha up to 0 days before harvest and with a maximum seasonal rate of 560 g ai/ha. The label also specifies the use of either foliar or soil treatments, but not both.

Lettuce

In 10 independent trials on field head lettuce conducted in North America and matching the USA GAP for foliar applications, oxathiapiprolin residues were 0.23, 0.28, 0.3, 0.5, 0.57, 0.7, 0.82, 0.83, 1.3 and 1.4 mg/kg.

In these trials, residues of oxathiapiprolin in head lettuce from plots treated according to the soil treatment GAP in the USA, were < 0.01 (8), 0.37 and 0.43 mg/kg.

The Meeting estimated a median residue of 0.64 mg/kg and a maximum residue level of 3.0 mg/kg for oxathiapiprolin on lettuce, head.

In field studies on rotational crops, mean residues of IN-E8S72 and IN-SXS67 (expressed as parent equivalents were 0.33 mg eq/kg in leafy vegetables. The Meeting decided to add the mean residue found in the leafy vegetable rotational crop studies to the median residue from the lettuce (foliar application) field trials to estimate an overall STMR of 0.97 mg eq/kg for lettuce, head.

In 10 independent trials on field open-head lettuce conducted in North America and matching the USA GAP for foliar applications, oxathiapiprolin residues were 0.54, 0.8, 0.81, 1.2, 1.8, 1.9, 1.9, 1.9, 2.0 and 3.0 mg/kg.

In these trials, residues of oxathiapiprolin in open-head lettuce from plots treated according to the soil treatment GAP in the USA, were < 0.01 (4), 0.01, 0.02, 0.07, 0.09 and 0.37 mg/kg.

The Meeting estimated a median residue of 1.85 mg/kg and a maximum residue level of 5.0 mg/kg for oxathiapiprolin on lettuce, leaf.

In field studies on rotational crops, mean residues of IN-E8S72 and IN-SXS67 (expressed as parent equivalents were 0.33 mg eq/kg in leafy vegetables. The Meeting decided to add the mean residue found in the leafy vegetable rotational crop studies to the median residue from the lettuce (foliar application) field trials to estimate an overall STMR of 2.2 mg eq/kg for lettuce, leaf.

Spinach

In 10 independent trials on field spinach conducted in North America and matching the USA GAP for foliar applications, oxathiapiprolin residues were 1.4, 1.6, 2.2, 2.4, 3.2, 3.5, 4.0, 5.7, 6.4 and 6.5 mg/kg.

In these trials, residues of oxathiapiprolin in spinach from plots treated according to the soil treatment GAP in the USA, were < 0.01 (3), 0.01, 0.11, 0.12, 1.6, 1.8, 2.0 and 2.1 mg/kg.

The Meeting estimated a median residue of 3.35 mg/kg and a maximum residue level of 15 mg/kg for oxathiapiprolin on spinach.

In field studies on rotational crops, mean residues of IN-E8S72 and IN-SXS67 (expressed as parent equivalents were 0.33 mg eq/kg in leafy vegetables. The Meeting decided to add the mean residue found in the leafy vegetable rotational crop studies to the median residue from the spinach (foliar application) field trials to estimate an overall STMR of 3.7 mg eq/kg for spinach.

The Meeting also noted that oxathiapiprolin residues in lettuce and spinach following soil applications would be accommodated by the estimated maximum residue levels.

Legume vegetables

Results from supervised trials on peas conducted in North America were provided to the Meeting.

The critical GAP for succulent shelled and edible-podded peas in the USA is for up to four foliar applications of 35 g ai/ha, with a maximum seasonal rate of 140 g ai/ha and with a PHI of 0 days.

Peas, shelled (succulent seeds)

In five independent trials matching the GAP in the USA, residues of oxathiapiprolin in succulent peas (without pods) were < 0.01, < 0.01, 0.01, 0.03 and 0.03 mg/kg.

The Meeting estimated a median residue of 0.01 mg/kg and a maximum residue level of 0.05 mg/kg for oxathiapiprolin on peas, shelled.

In field studies on rotational crops, mean residues of IN-E8S72 and IN-SXS67 (expressed as parent equivalents were 0.083 mg eq/kg in legume vegetables. The Meeting decided to add the mean residue found in the legume vegetable rotational crop studies to the median residue from the pea (foliar application) field trials to estimate an overall STMR of 0.09 mg eq/kg for peas, shelled.

Peas (pods and succulent = immature seeds)

In five independent trials matching the GAP in the USA, residues of oxathiapiprolin in succulent peas (with pods) were 0.2, 0.3, 0.3, 0.28 and 0.55 mg/kg.

The Meeting estimated a median residue of 0.3 mg/kg and a maximum residue level of 1.0 mg/kg for oxathiapiprolin on peas (pods and succulent seeds).

In field studies on rotational crops, mean residues of IN-E8S72 and IN-SXS67 (expressed as parent equivalents were 0.083 mg eq/kg in legume vegetables. The Meeting decided to add the mean residue found in the legume vegetable rotational crop studies to the median residue from the pea (foliar application) field trials to estimate an overall STMR of 0.38 mg eq/kg for peas (pods and succulent seeds).

Root and tuber vegetables

Results from supervised trials on potatoes and ginseng conducted in North America were provided to the Meeting.

Potato

The critical GAP for tuberous and corm vegetables (including potato) in the USA is for a maximum of four foliar applications of 35 g ai/ha, with a PHI of 5 days. In addition, there is an option for two foliar sprays of 50 g ai/ha over flowering, and a maximum seasonal rate of 200 g ai/ha.

In 18 independent trials matching the close-to-harvest GAP in the USA but using a higher application rate of 50 g ai/ha, oxathiapiprolin residues in tubers were all < 0.01 mg/kg.

The Meeting estimated an STMR of 0 mg/kg and a maximum residue level of 0.01* mg/kg for oxathiapiprolin on potato and agreed to extrapolate these estimates to sweet potato.

Ginseng

The critical GAP for ginseng in the USA is for a maximum of four foliar applications per year of 35–280 g ai/ha, with a PHI of 14 days and a maximum total rate of 560 g ai/ha/year.

In four independent trials conducted in the USA and involving two close-to-harvest foliar applications of 280 g ai/ha, oxathiapiprolin residues in dried ginseng roots (10–30% moisture content) were 0.04, 0.04, 0.04 and 0.05 mg/kg.

The Meeting estimated an STMR of 0.04 mg/kg and a maximum residue level of 0.15 mg/kg for oxathiapiprolin on ginseng dried (including red ginseng).

Fate of residues during processing

Oxathiapiprolin is stable to hydrolysis in aqueous media within a pH range of 4 to 9 (< 10% degradation after 5 days at 50 ºC), and is also stable under conditions simulating pasteurisation, baking, brewing, boiling and sterilisation, with recovery rates of 95–97%.

The fate of oxathiapiprolin residues has been examined in a number of studies simulating household processing of melons (peeling), lettuce and Brassica vegetables (washing), and commercial processing of grapes, potatoes and tomatoes.

Residues of oxathiapiprolin increased in commodities such as raisins, dried tomatoes and in the grape and tomato pomaces and potato peel waste, where processing involves a reduction in moisture content, with no residue concentration in the other processed commodities.

For the commodities considered (grapes, potatoes and tomatoes) the Meeting estimated processing factors and STMR-Ps for their processed food or feed commodities are summarised below.

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

RAC (STMR)	Matrix	Oxathiapiprolin [a]		STMR-P (mg/kg)
		Calculated processing factors	PF median	
Grape (0.21 mg/kg)	Raw juice	0.26, 0.27, 0.28, 0.46	0.28	0.059
	Wet pomace	1.0, 1.4, 1.5, 1.9, 2.0, 3.1, 4.0, 5.4	2.0	0.42
	Juice	0.13, 0.14, 0.18, 0.22	0.16	0.034
	Raisins	0.93, 1.3, 1.6, 4.1	1.4	0.29
	Wine	00.08, 0.1, 0.17, 0.18	0.14	0.029
	Must	0.58, 62, 1.9	0.62	0.13
Potato (0 mg/kg)	Tubers			
	Culls	0.1, 0.13, 0.7	0.13	0
Tomato (0.04 mg/kg)	Tomatoes			
	Sun-dried	2.9, 6.9, 7.4	6.9	0.28
	Canned (peeled)	< 0.02, < 0.04, < 0.04	< 0.04	0.0016
	Juice	0.16, 0.16, 0.29	0.16	0.006
	Wet pomace	11, 13, 13	13	0.52
	Paste	0.69, 1.1, 1.1	1.1	0.044

[a] Each value represents a separate study where residues were above the LOQ in the RAC. The factor is the ratio of oxathiapiprolin residues in the processed item divided by the residue of oxathiapiprolin in the RAC.

For oxathiapiprolin in processed tomato commodities, based on a processing factor of 6.9 for sun-dried tomatoes and the estimated maximum residue level of 0.4 mg/kg for fruiting vegetables, other than cucurbits, the Meeting estimated an STMR-P of 0.28 mg/kg and a maximum residue level of 3 mg/kg for oxathiapiprolin on for tomato, dried.

For dried grapes, based on a processing factor of 1.4 and the estimated maximum residue level of 0.9 mg/kg for grapes, the Meeting estimated an STMR-P of 0.29 mg/kg and a maximum residue level of 1.3 mg/kg for oxathiapiprolin on for dried grapes.

Residues in animal commodities

Farm animal feeding studies

No lactating cow feeding studies were provided. In the lactating goat metabolism studies, goats were dosed with approximately 14 ppm oxathiapiprolin in the feed for 7 days. The highest residue of oxathiapiprolin or a metabolite in tissues or milk was 0.11 mg/kg for oxathiapiprolin in liver.

No poultry feeding studies were provided. In the poultry metabolism study, laying hens were dosed with approximately 17.6 mg oxathiapiprolin/kg feed for 14 days. Residues of oxathiapiprolin were all not more than 0.01 mg/kg in tissues and eggs.

In a supplementary lactating goat metabolism study, goats were dosed with approximately 19 ppm IN-SXS67 in the feed for 7 days. The highest residues in tissues or milk were in kidney, 0.28 mg/kg for IN-SXS67 and 0.19 mg eq/kg for IN-E8S72 and residues in liver were 0.03 mg/kg and 0.006 mg eq/kg respectively. TRRs in milk, muscle and fat were lower and not investigated further.

Farm animal dietary burden

The Meeting estimated the dietary burden of oxathiapiprolin in farm animals on the basis of the diets listed in Appendix IX of the 2009 edition of the JMPR Manual. Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are presented in Annex X. Livestock feed commodities considered by the Meeting were grape pomace, tomato pomace, potato culls and waste and cabbage heads/leaves.

Estimated maximum and mean dietary burdens of farm animals

	Animal dietary burden, oxathiapiprolin, ppm of dry matter diet							
	US-Canada		EU		Australia		Japan	
	max	mean	max	mean	max	mean	max	mean
Beef cattle	0	0	0.19	0.19	0.56 [A]	0.56 [C]	0	0
Dairy cattle	0	0	0.19	0.19	0.56 [B]	0.56 [D]	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.

The Meeting also estimated a mean dietary burden of 0.4 ppm for IN-SXS67 in farm animals exposed to residues of this metabolite in rotational crop feed and forage items.

Animal commodity maximum residue levels

In the ruminant metabolism study, lactating goats were dosed with approximately 14 mg oxathiapiprolin/kg feed for 7 days. The highest residues of oxathiapiprolin in tissues or milk were seen in liver at 0.11 mg/kg.

The 14 ppm dose rate used in the goat metabolism studies is about 25 × the highest estimated cattle dietary burden of 0.56 ppm/day and the Meeting estimated that oxathiapiprolin residues in tissues and milk from cattle exposed to the maximum dietary burden would be not more than 0.004 mg/kg (in liver).

The Meeting estimated maximum residue levels of 0.01* mg/kg for oxathiapiprolin in meat (from mammals other than marine mammals), edible offal (mammalian), mammalian fat and for milks.

Estimated STMRs for dietary intake estimation are 0 mg/kg for meat, 0 mg/kg for fat and 0 mg/kg for milk.

For edible offal, the Meeting estimated a mean residue of 0.004 mg/kg (liver) to accommodate exposure from parent residues in feed items.

Based on the mean dietary burden of 0.4 ppm for IN-SXS67 from rotational crop feed items the Meeting estimated mean residues of 0.006 mg (IN-SXS67) and 0.004 mg eq/kg (IN-E8S72) for kidney to accommodate exposure to residues of IN-E8S72 in rotational crops.

When expressed as oxathiapiprolin equivalents, the mean residues in kidney are 0.009 mg eq/kg for IN-SXS67 and 0.006 mg eq/kg for IN-E8S72 and the Meeting estimated an overall STMR of 0.015 mg/kg for edible offal (mammalian).

As no poultry feed items were identified, the Meeting estimated maximum residue levels of 0.01* mg/kg for oxathiapiprolin in poultry meat, poultry offal, poultry fat and eggs. Estimated STMRs for dietary intake estimation are 0 mg/kg for meat, 0 mg/kg for edible offal, 0 mg/kg for fat and 0 mg/kg for milk.

RECOMMENDATIONS

On the basis of the data from supervised trials the Meeting concluded that the residue levels listed in Annex 1 are suitable for establishing maximum residue limits and for IEDI assessment.

Definition of the residue for compliance with the MRL: *oxathiapiprolin.*

Definition of the residue for estimation of dietary intake: *Sum of: oxathiapiprolin, 5-(Trifluoromethyl)-1H-pyrazole-3-carboxylic acid and 1-ß-D-Glucopyranosyl-3-(-(trifluoromethyl)-1H-pyrazole-5-carboxylic acid, expressed as parent.*

The residue is not fat soluble.

DIETARY RISK ASSESSMENT

Long-term dietary exposure

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

The International Estimated Daily Intakes of oxathiapiprolin for the 17 GEMS/Food cluster diets, based on estimated STMRs were 0–0% of the maximum ADI of 4 mg/kg bw (Annex 3). The Meeting concluded that the long-term dietary exposure of residues of oxathiapiprolin from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term dietary exposure

The Meeting decided that an ARfD is unnecessary and concluded that the short-term dietary exposure to residues of oxathiapiprolin, from uses considered by the current Meeting, are unlikely to present a public health concern.