The International Estimated Short-Term Intakes (IESTI) of fenpyrazamine were calculated for /commodities using HRs/HR-Ps and STMRs/STMR-Ps estimated by the current Meeting (see Annex 4). The calculated IESTIs were 0–40% of the ARfD for the general population and 0–30% of the ARfD for children. The Meeting concluded that the short-term dietary exposure to residues of fenpyrazamine, when used in ways that have been considered by the JMPR, is unlikely to present a public health concern.

5.14 FENPYROXIMATE (193)

TOXICOLOGY

Fenpyroximate is the International Organization for Standardization (ISO)–approved common name for *tert*-butyl (E)-alpha-(1,3)-dimethyl-5-phenoxy-1 *H* -pyrazol-4-yl methyleneamino-oxy)- *para*-toluate (International Union of Pure and Applied Chemistry), with Chemical Abstracts Service number 134098-61-6 (E isomer) and 111812-58-9 (unspecified stereochemistry).

Fenpyroximate is a phenoxypyrazole acaricide for application to leaves infested with phytophagous mites. Fenpyroximate inhibits mitochondrial NADH-coenzyme Q reductase of the electron transport chain in mites.

Fenpyroximate was evaluated by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) in 1995, when an acceptable daily intake (ADI) of 0–0.01mg/kg bw was established based upon a no-observed-adverse-effect level (NOAEL) of 1 mg/kg bw per day in a 104-week study in rats and a safety factor of 100. The critical effect in that study was a reduction in body weight gain and plasma protein concentration. Fenpyroximate was re-evaluated by the 2004 JMPR in order to determine an acute reference dose (ARfD). The ARfD of 0.01mg/kg bw was established based on the marginal lowest-observed-adverse-effect level (LOAEL) of 2 mg/kg bw per day for the marginal induction of diarrhoea at the beginning of the 13- week toxicity study in dogs using a safety factor of 200 as no NOAEL was identified in the study. The ARfD was re-evaluated by the 2007 JMPR. The 2007 Meeting established an ARfD of 0.02 mg/kg bw based on the NOAEL of 2 mg/kg bw identified from a study of fenpyroximate, where diarrhoea was observed after a single dose in dogs, and using a safety factor of 100. Furthermore, the Meeting also stated that it remained unclear whether the diarrhoea observed in dogs was the result of fenpyroximate being a direct irritant or its pharmacological effects; it was not possible to consider a modification in the safety factor.

Fenpyroximate was reviewed by the present Meeting under the periodic review programme of Codex Committee on Pesticide Residues (CCPR). New studies included a phototoxicity study, acute and short-term neurotoxicity studies in rats, immunotoxicity study, single and repeated-dose toxicity studies in dogs, gene mutation studies on the parent and metabolites and an in vitro metabolism study.

All studies evaluated in this monograph were performed by laboratories that were certified for good laboratory practice (GLP) and that complied, where appropriate, with the relevant Organisation for Economic Co-operation and Development (OECD) test guidelines or similar guidelines of the European Union or United States Environmental Protection Agency, unless otherwise indicated. A search of the open literature did not reveal any relevant publications.

Biochemical aspects

Based on biliary excretion studies using [pyrazole-^{14}C]fenpyroximate and [benzyl-^{14}C]fenpyroximate (2 mg/kg bw) in rats, oral absorption of fenpyroximate was about 60% of the administered dose considering bile excretion (47–55%) and urinary excretion (5–10%) within 48 hours. Oral administration of single or repeated doses of 2 mg/kg bw and 400 mg/kg bw dose of either [pyrazole-^{14}C]fenpyroximate or [benzyl-^{14}C]fenpyroximate resulted in approximately 70–92% of the applied dose being excreted via faeces and approximately 9.0–18% via urine in male and female rats. In the low-dose group (2 mg/kg bw), radioactivity in blood increased slowly with time to reach T_{max} values of about 11.0 hours after applying the pyrazole-labelled compound and about 7.0 after applying the benzyl-labelled compound. Radioactivity declined with half-lives between 6.1 and 8.9 hours for both labelled compounds. The mean concentration of radioactivity had decreased to or below the limit of detection (LOD) after 72 hours for pyrazole-labelled fenpyroximate and 48 hours for benzyl-labelled fenpyroximate.

At 400 mg/kg bw, radioactivity increased slowly with a T_{max} value of about 90.0 hours after administration of pyrazole-labelled fenpyroximate or 29.0 hours for males and 86.0 hours for females after administration of benzyl-labelled fenpyroximate. Radioactivity declined with $t_{½}$ between 35.4 and 48.7 hours for both labels. The mean concentration of radioactivity had decreased to or below the

LOD after 216 hours and 168 hours for the pyrazole-labelled fenpyroximate and for the benzyl-labelled fenpyroximate, respectively.

The high number of identified fenpyroximate metabolites indicates that fenpyroximate was extensively metabolized by, for example, hydrolytic cleavage of the oxime bond, hydrolysis of the tert-butyl ester moiety, oxidation of the tert-butyl group, hydroxylation of the phenoxy ring and 3-methyl group, by isomerization, *N*-demethylation and conjugation.

The major urinary metabolites were M-8 (1,3-dimethyl-5-phenoxypyrazole-4-carboxylic acid) and M-21 (4-cyano-1-methyl-5-phenoxypyrazole-3-carboxylic acid); they were also excreted via faeces but not in large amounts. Fenpyroximate represents the major compound in faeces; M-3 ((*E*)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoic acid) and M-22 ((*E*)-2-[4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoyloxy]-2-methylpropanoic acid) were also excreted in faeces; metabolites of minor abundance were the Z-isomer of fenpyroximate (metabolite M-1; tert-butyl (*Z*)-α-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethyleneamino-oxy)-*p*-toluate), M-6 (1,3-dimethyl-5-phenoxypyrzole-4-carbaldehyde) and M-11 (1,3-dimethyl-5-phenoxypyrazole-4-carbonitrile). There were no changes in the metabolic profile of [pyrazole-^{14}C]fenpyroximate or [benzyl-^{14}C]fenpyroximate upon repeated dosing or after applying the low or the high dose.

Toxicological data

In rats, the acute oral LD_{50} was 480 and 245 mg/kg bw for males and females, respectively, the acute dermal LD_{50} was greater than 2000 mg/kg bw and the acute inhalation LC_{50} was 0.21 and 0.33 mg/L for male and female, respectively. Fenpyroximate was not irritating to the skin of rabbits and mildly irritating to the eyes of rabbits. It was sensitizing to the skin of guinea pigs, as determined by the Magnusson-Kligman test, and negative for skin sensitization in the Buehler test. Fenpyroximate was not phototoxic.

In repeated-dose toxicity studies, diarrhoea and decreased body weights in dogs, and decreased in body weights and liver effects in rats were the key findings.

In a 13-week toxicity study in rats using dietary fenpyroximate concentrations of 0, 20, 100 or 500 ppm (equal to 0, 1.3, 6.57 and 35.2 mg/kg bw per day for males and 0, 1.65, 8.29 and 38.6 mg/kg bw per day for females, respectively), the NOAEL was 20 ppm (equal to 1.3 mg/kg bw per day) based on decreased body weight and body weight gains, reduced feed consumption and minimal hepatocytic hypertrophy in both sexes at 100 ppm (equal to 6.57 mg/kg bw per day).

In a single dose oral toxicity study in dogs, fenpyroximate was administered as a bolus gavage dose of 0, 2 or 5 mg/kg bw. As diarrhoea was seen at all dose levels, the NOAEL could not be identified.

In a dose escalation oral toxicity study in the same dogs, fenpyroximate was administered via bolus gavage dose of 2, 5, 20 and 25 mg/kg bw. The NOAEL was 2 mg/kg bw per day based on diarrhoea seen at 5 mg/kg bw per day.

In a 90-day oral toxicity study in dogs using oral (capsule) fenpyroximate doses of 0, 2, 10 or 50 mg/kg bw per day, the LOAEL was 2 mg/kg bw per day, the lowest dose tested, based on slight bradycardia and an increased incidence of diarrhoea in both sexes (weekly observations) and reduced feed consumption, body weight and body weight gain and increased emaciation and torpor in females only.

In a 1-year oral toxicity study in dogs using oral (capsule) fenpyroximate doses of 0, 0.5, 1.5, 5.0 or 15.0 mg/kg bw per day, the NOAEL was 1.5 mg/kg bw per day based on increased incidences of diarrhoea at 5 mg/kg bw per day.

In a 78-week carcinogenicity study in mice using dietary fenpyroximate concentrations of 0, 25, 100, 400 or 800 ppm (equal to 0, 2.46, 9.47, 38.0 and 69.6 mg/kg bw per day for males and 0, 2.46, 10.2, 41.5 and 73.1 mg/kg bw per day for females, respectively), the NOAEL was 25 ppm

(equal to 2.43 mg/kg bw per day) based on decreased body weights and feed consumption at 100 ppm (equal to 9.47 mg/kg bw per day). There were no treatment-related neoplastic findings.

In a 2-year chronic toxicity and carcinogenicity study in rats using dietary fenpyroximate concentrations of 0, 10, 25, 75 or 150 ppm (equal to 0, 0.4, 0.97, 3.00 and 6.20 mg/kg bw per day for males and 0, 0.49, 1.21, 3.18 and 8.01 mg/kg bw per day for females, respectively), the NOAEL was 25 ppm (equal to 0.97 mg/kg bw per day) based on decreased body weights, feed consumption and feed conversion ($p < 0.01$) and decreased plasma total protein at 75 ppm (equal to 3.0 mg/kg bw per day). There were no neoplastic findings that were related to treatment.

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

Fenpyroximate was tested for genotoxicity in an adequate range of assays, both in vitro and in vivo. No evidence of genotoxicity was found.

The Meeting concluded that fenpyroximate 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 fenpyroximate is unlikely to pose a carcinogenic risk to humans.

In a two-generation reproductive toxicity study in rats using dietary fenpyroximate concentrations of 0, 10, 30 or 100 ppm (equal to 0, 0.67, 1.99 and 6.59 mg/kg bw per day for males and 0, 0.83, 2.44 and 8.60 mg/kg bw per day for females, respectively), the NOAEL for reproductive toxicity was 100 ppm (equal to 6.59 mg/kg bw per day). The NOAEL for parental toxicity was 30 ppm (equal to 1.99 mg/kg bw per day) based on decreased body weights, decreased feed consumption and increased absolute testicular and epididymal weights (absolute and relative to body weight) in males at 100 ppm (equal to 6.59 mg/kg bw per day). The NOAEL for offspring toxicity was 30 ppm (equal to 1.99 mg/kg bw per day) based on decreased pup body weight at 100 ppm (equal to 6.59 mg/kg bw per day).

In a developmental toxicity study in rats using oral gavage fenpyroximate doses of 0, 1.0, 5.0 or 25 mg/kg bw per day, the NOAEL for maternal toxicity was 25 mg/kg bw per day, the highest dose tested. The NOAEL for embryo/fetal toxicity was 5 mg/kg bw per day, based on increases in the number of thoracic ribs at 25 mg/kg bw per day.

In a developmental toxicity study in rabbits using oral gavage fenpyroximate doses of 0, 1.0, 2.5 or 5 mg/kg bw per day, the NOAEL for maternal toxicity was 2.5 mg/kg bw per day, based on reduced body weights, feed and water consumption and faecal output at 5 mg/kg bw per day. The NOAEL for embryo/fetal toxicity was 2.5 mg/kg bw per day, based on elevations in the frequency of unilateral and bilateral slightly folded retinas (variations) at 5 mg/kg bw per day.

The Meeting concluded that fenpyroximate is not teratogenic.

In an acute neurotoxicity study in rats administered a single oral gavage dose of fenpyroximate at 0, 37.5, 150 or 300 mg/kg bw, the NOAEL for general toxicity was 37.5 mg/kg bw based on decreased motor activity (total activity counts and total time spent in movement) in both sexes and a reduction in auditory startle response in females at 24 hours post dose, and mild dehydration in males, reduced feed consumptions (about 60%) and statistically significant decreased in body weights and body weight gains in first 3 days in males and females, at 150 mg/kg bw. The marginal decreases in motor activity and reduction in auditory response were considered to be effects secondary to the excessive general toxicity rather than neurotoxic effects. The Meeting noted that the 150 mg/kg bw effect level in this study is approximately 65% of the LD_{50} value for fenpyroximate in females.

In a 90-day study of neurotoxicity in rats given diets containing fenpyroximate at a concentration of 0, 30, 100 or 300 ppm (equal to 0, 1.8, 6.1 and 16.4 mg/kg bw per day for males and 0, 2.0, 6.6 and 18.4 mg/kg bw per day for females, respectively), the NOAEL for general toxicity was 30 ppm (equal to 1.8 mg/kg bw per day) based on clinical signs consisting of an increased incidence of chromorhinorrhea and dehydration in both sexes at 100 ppm (equal to 6.1 mg/kg bw per day). The NOAEL for neurotoxicity was 300 ppm (equal to 16.4 mg/kg bw per day), the highest dose tested.

No evidence of delayed neurotoxicity was seen in an acute delayed neurotoxicity study in hens at doses up to 5000 mg/kg bw.

The Meeting concluded that fenpyroximate is not neurotoxic.

No evidence of immunotoxicity was observed in an immunotoxicity study in male and female rats administered fenpyroximate in the diet at a dose level of 0, 30, 100 or 300 ppm (equal to 0, 2.2, 7.1 and 18.4 mg/kg bw per day for males and 0, 2.6, 7.9 and 21.4 mg/kg bw per day for females, respectively) for 28 days.

The Meeting concluded that fenpyroximate is not immunotoxic.

Toxicological data on metabolites and/or degradates

The acute oral LD_{50} value for M-1 metabolite (animal and plant metabolite; tert-butyl (*Z*)-α-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethyleneamino-oxy)-*p*-toluate) in rats was 500–700 mg/kg bw for males and 607 mg/kg bw for females. M-1 was negative for mutagenicity in the bacterial gene mutation assay, mammalian cytogenetic assay in Chinese hamster V79 lung cells, mammalian cytogenetic assay using mouse lymphoma cells and in vivo micronucleus in mice.

The acute oral LD_{50} value for animal and plant metabolite M-12 (tert-butyl (E)-4-[(3-methyl-5-phenoxypyrazole-4-yl) methyleneaminooxymethyl] benzoate) rats was greater than 5000 mg/kg bw in male rates. M-12 was negative for mutagenicity in the Ames test.

The animal and plant metabolite M-3 was negative for mutagenicity in the bacterial gene mutation assay, mammalian cytogenetic assay in Chinese hamster V79 lung cells and mammalian cytogenetic assay using mouse lymphoma cells.

The major goat metabolite Fen-OH (2-hydroxymethyl-2-propyl (E)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)-methylenaminooxymethyl]benzoate) was not found in rats. However, it is plausible that Fen-OH occurs as an unstable intermediate metabolite in the rat when the parent is oxidized at its t-butyl moiety to give M-22. No toxicological data were available on Fen-OH but an additional hydroxy group usually renders a molecule more likely to undergo further phase II metabolism and be more rapidly excreted.

The Meeting concluded the toxicity of plant and livestock metabolites M-1, M-3, M-5, M-21, M-22, and Fen-OH would be covered under the toxicity of the parent compound since these metabolites were also detected in rats at significant levels.

Human data

No adverse health effects were reported in workers in fenpyroximate-manufacturing plants. Eye and skin irritation was reported in some workers in charge of manufacturing fenpyroximate or its 5% soluble concentrate formulation and also in some farm workers handling 5% soluble concentrate formulation.

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

Toxicological evaluation

The Meeting withdrew the existing ARfD and established an ARfD of 0.01 mg/kg bw on the basis of the LOAEL of 2 mg/kg bw for the induction of diarrhoea seen in a newly submitted single bolus gavage study and 13-week study of toxicity in dogs. A safety factor of 200 was used since no NOAEL was identified. It was unclear whether the diarrhoea was the result of a direct irritant or pharmacological effect of fenpyroximate; however, histopathological examination of gastrointestinal tract did not reveal any evidence of irritation in the available database.

This ADI and ARfD can be applied to M-1, M-3, M-5, M-21, M-22 and Fen-OH.

A toxicological monograph was prepared.

Levels relevant to risk assessment of fenpyroximate

Species	Study	Effect	NOAEL	LOAEL
Mouse	Two-year study of toxicity and carcinogenicity[a]	Toxicity	25 ppm, equal to 2.43 mg/kg bw per day	100 ppm, equal to 9.47 mg/kg bw per day
		Carcinogenicity	800 ppm, equal to 69.63 mg/kg bw per day[b]	–
Rat	Acute neurotoxicity study[c]	Neurotoxicity	300 mg/kg bw per day[b]	---
	90-day neurotoxicity study[a]	Neurotoxicity	300 ppm, equal to 16.4 mg/kg bw per day[b]	
	Two-year studies of toxicity and carcinogenicity[a,d]	Toxicity	25 ppm, equal to 0.97 mg/kg bw per day	75 ppm, equal to 3.0mg/kg bw per day
		Carcinogenicity	150 ppm, equal to 6.20 mg/kg bw per day[b]	–
	Two-generation study of reproductive toxicity[a]	Reproductive toxicity	100 ppm, equal to 6.59mg/kg bw per day[b]	—
		Parental toxicity	30 ppm, equal to 1.99 mg/kg bw per day	100 ppm, equal to 6.59 mg/kg bw per day
		Offspring toxicity	30 ppm, equal to 1.99 mg/kg bw per day	100 ppm, equal to 6.59 mg/kg bw per day
	Developmental toxicity study[c]	Maternal toxicity	25 mg/kg bw per day[b]	
		Embryo/fetal toxicity	5 mg/kg bw per day	25 mg/kg bw per day
Rabbit	Developmental toxicity study[c]	Maternal toxicity	2.5 mg/kg bw per day	5 mg/kg bw per day
		Embryo/fetal toxicity	2.5 mg/kg bw per day	5 mg/kg bw per day
Dog	Single dose, escalating-dose study, and 13-week study[c,d,e]	Toxicity		2 mg/kg bw per day

[a] Dietary administration.

[b] Highest dose tested.

[c] Gavage administration.

[d] Two or more studies combined.

[e] Capsule administration.

Estimate of acceptable daily intake (ADI; applies to fenpyroximate and to M-1, M-3, M-5, M-21, M-22 and Fen-OH, expressed as fenpyroximate)

0–0.01mg/kg bw

Estimate of acute reference dose (ARfD; applies to fenpyroximate and to M-1, M-3, M-5, M-21 M-22 and Fen-OH, expressed as fenpyroximate)

0.01 mg/kg bw

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 fenpyroximate

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Approximately 60%, based on excretion via bile (47–55%) and urine (5–10%) within 48 hours; T_{max} about 11 and 90 hrs at 2 mg/kg bw and 400 mg/kg bw, respectively
Dermal absorption	No data
Distribution	Widely distributed, the highest amounts of radioactivity was found in the gastrointestinal tract, liver, fat and kidney; 168 h after administration tissue residues below LOD
Potential for accumulation	No evidence of significant accumulation
Rate and extent of excretion	Rapid and complete within 48 h at 2 mg/kg bw, mainly in bile
Metabolism in animals	Extensive; cleavage of the benzyl moiety from the pyrazole ring with further oxidation, oxime hydrolysis, ester hydrolysis and other pathways of metabolism were 4-hydroxylation of the 5-phenoxy ring and oxidation of the t-butyl moiety
Toxicologically significant compounds in animals and plants	Parent and M-1
Acute toxicity	
Rat, LD_{50}, oral	480 and 245 for male and female, respectively
Rat, LD_{50}, dermal	>2 000 mg/kg bw
Rat, LC_{50}, inhalation	0.21 and 0.33 mg/L male and female, respectively
Rabbit, dermal irritation	Non-irritating
Rabbit, ocular irritation	Mildly irritating
Guinea pigs, dermal sensitization	Sensitizing (Magnusson-Kligman) and non-sensitizing (Buehler)
Short-term studies of toxicity	
Target/critical effect	Reduced feed intake, decreased body weight gain (rat); diarrhoea, salivation, emesis, bradycardia (dogs)
Lowest relevant oral NOAEL	1.3 mg/kg bw per day (rat); 1.5 mg/kg bw per day (dog)
Lowest relevant dermal NOAEL	300 mg/kg bw per day (rat)[b]
Lowest relevant inhalation NOAEC	2.0 mg/m^3 (rat)

Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Lower body weight gain, feed intake and feed conversion efficiency; decreased total protein
Lowest relevant NOAEL	0.97 mg/kg bw per day (rat)
Carcinogenicity	Not carcinogenic in mice or rats[a]
Genotoxicity	
	No evidence of genotoxicity[a]
Reproductive toxicity	
Target/critical effect	None
Lowest relevant parental NOAEL	1.99 mg/kg bw per day (rat)
Lowest relevant offspring NOAEL	1.99 mg/kg bw per day (rat)
Lowest relevant reproductive NOAEL	6.59 mg/kg bw per day (rat)[b]
Developmental toxicity	
Target/critical effect	Increased incidence of slightly folded retinas in rabbits
Lowest relevant maternal NOAEL	2.5 mg/kg bw per day (rabbit)
Lowest relevant embryo/fetal NOAEL	5.0 mg/kg bw per day (rabbit)
Neurotoxicity	
Acute neurotoxicity NOAEL	300 mg/kg bw (rat) [b]
Subchronic neurotoxicity NOAEL	16.4 mg/kg bw per day (rat)[b]
Delayed neurotoxicity NOAEL	5 000 mg/kg bw (hen)[b]
Other toxicological studies	
Immunotoxicity	18.4 mg/kg bw per day (rat)[b]
Studies on toxicologically relevant metabolites	
M-1	Oral LD_{50}: 500 and 607 mg/kg bw for males and females, respectively (rats)
	Ames test, mammalian cytogenetic assay in Chinese hamster lung cells, mouse lymphoma assay and micronucleus test: negative
M-3	Bacterial gene mutation assay, mammalian cytogenetic assay in Chinese hamster lung cells and mouse lymphoma
M-12	Oral LD_{50}: >5000 mg/kg bw for males rats
	Negative for mutagenicity in the bacterial gene mutation assay
Human data	
	Eye and skin irritation reported in workers at manufacturing plants and agricultural workers

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

[b] Highest dose tested.

Summary

	Value	Study	Safety factor
ADI[a]	0–0.01 mg/kg bw	104-study of toxicity(rats)	100
ARfD[a]	0.01 mg/kg bw	Single dose toxicity and 13-week dog toxicity study	200

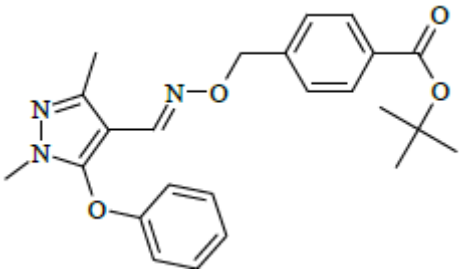
[a] Applies to fenpyroximate and to M-1, M-3, M-5, M-21, M-22 and Fen-OH, expressed as fenpyroximate

RESIDUE AND ANALYTICAL ASPECTS

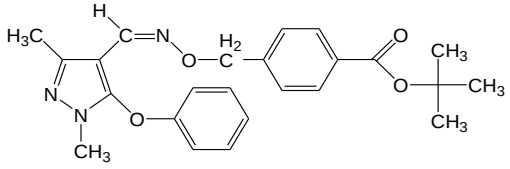
Fenpyroximate is a pyrazole non-systemic selective acaricide/insecticide for the control of mites and hoppers in a wide range of crops including fruits and vegetables. It was first evaluated by JMPR in 1995 and then in 1999 and 2010 for maximum residue levels, and in 2004 and 2007 for toxicology.

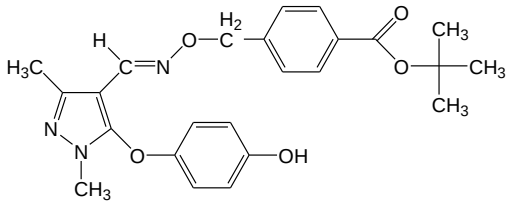
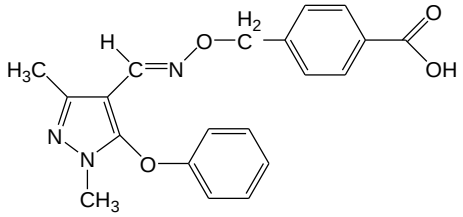
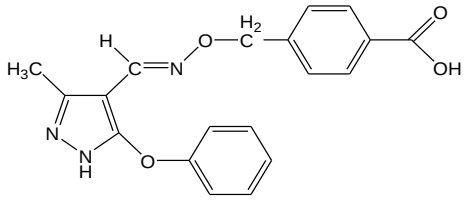
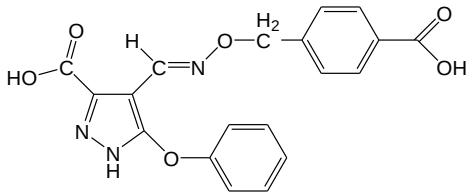
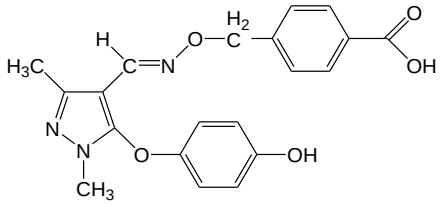
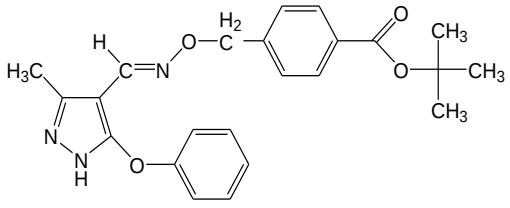
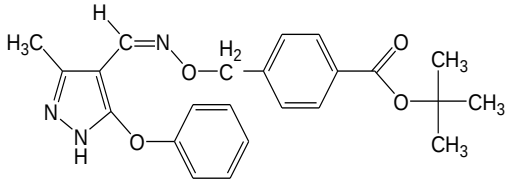
Fenpyroximate was scheduled at the 48th Session of the CCPR for Periodic Re-evaluation for residues and toxicology by 2017 JMPR. The meeting received information from manufacturer on the metabolism of fenpyroximate in citrus, apple, grape, snap beans, cotton, Swiss chard and lactating goat, as well as rotational crop studies, environmental fate in soil and water, method of residue analysis, stability in stored analytical samples, use patterns, supervised residue trials, fate of residue during storage and processing, and livestock feeding studies.

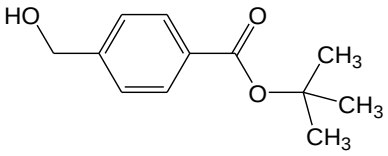
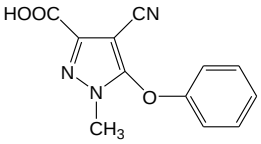
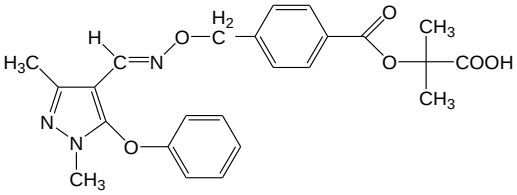
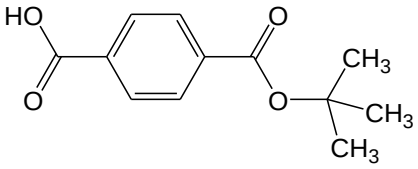
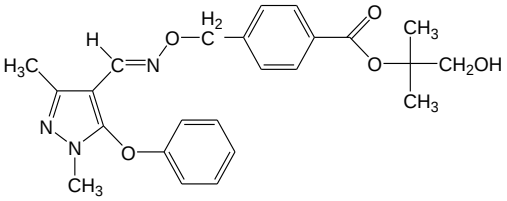
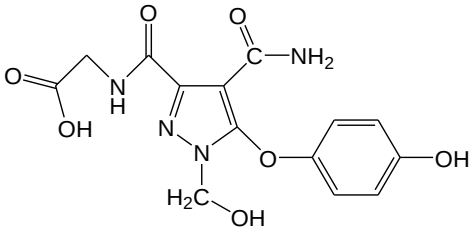
The IUPAC name of fenpyroximate is tert-butyl (E)-alpha-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethyleneamino-oxy)-*p* toluate.



The following abbreviations are used for the metabolites discussed in the appraisal:

Code Number (Synonyms)	Description	Structure
M-1 (*Z*-isomer)	IUPAC: tert-butyl (*Z*)-α-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethyleneamino-oxy)-*p*-toluate CAS: 1,1-dimethylethyl (*Z*)-4-[[[[(1,3-dimethyl-5-phenoxy-1*H*-pyrazol-4-yl)methylene]amino]oxy]methyl]benzoate	

Code Number (Synonyms)	Description	Structure
M-2	Tert-butyl (*E*)-4-{[1,3-dimethyl-5-(4-hydroxyphenoxy)pyrazol-4-yl]-methyleneaminooxymethyl}benzoate	
M-3	(*E*)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoic acid	
N-desmethyl M-3	(*E*)-4-[(3-methyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoic acid	
N-desmethyl M-3 acid	(*E*)-4-[(3-carboxy-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoic acid	
M-5	(*E*)-4-{[(1,3-dimethyl-5-(4-hydroxyphenoxy)pyrazol-4-yl]methyleneaminooxymethyl}benzoic acid	
M-12	Tert-butyl (*E*)--4-[(3-methyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoate	
M-12 isomer	Tert-butyl (*Z*)-4-[(3-methyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoate	

Code Number (Synonyms)	Description	Structure
M-15	Tert-butyl 4-hydroxymethylbenzoate	
M-21	4-cyano-1-methyl-5-phenoxypyrazole-3-carboxylic acid	
M-22	(*E*)-2-[4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoyloxy]-2-methylpropanoic acid	
MTBT	Mono-(tert-butyl) terephthalate	
Fen-OH	2-hydroxymethyl-2-propyl (*E*)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)-methylenaminooxymethyl]benzoate	
Metabolite 2	2-(5-(4-hydroxyphenoxy)-1-(hydroxymethyl)-1H-pyrazole-4-carbamoyl-3-carbonylamino)acetic acid	

Studies on the metabolism in plants, livestock and environmental fate utilised either [pyrazole-3-^{14}C]-fenpyroximate or [benzyl-(U)-^{14}C]-fenpyroximate.

Plant metabolism

The meeting received plant metabolism studies with fenpyroximate following foliar application (representative use patterns) to citrus, apples, grapes (Fruit crop group), snap beans and cotton (Pulses and Oilseeds crop group) and Swiss chard (Leafy crop group).

Citrus

In a study, outdoor mandarin tangerine trees were treated with [pyrazole-^{14}C] fenpyroximate at a rate of 22.4±1.5 mg/tree or 33.5±0.5 mg /tree. The residues in pulp were less than 0.03 mg/kg (LOD) at 0–28 DAT or less than 0.01 mg/kg at maturity (137 DAT), therefore no characterization or identification was conducted. 67–89% radioactive residues in leaves and more than 92% in rind were extracted with acetone/methanol. Fenpyroximate (33% TRR, 0.12 mg eq/kg), M-12 (17% TRR, 0.06 mg eq/kg) and M-1 (6% TRR, 0.02 mg eq/kg) were identified as major residues in rind at harvest.

Fenpyroximate (18% TRR, 0.24 mg eq/kg), M-1 (9% TRR, 0.13 mg eq/kg) and M-12 (6% TRR, 0.08 mg eq/kg) were the major components of radioactive residues in leaves.

The polar metabolites were enzyme hydrolysed with β-glucosidase or cellulose, and M-20 glucoside and several other glucosides were found in leaves and the fruit rind.

In the second study, outdoor mandarin trees were treated with [benzyl-^{14}C]-fenpyroximate at a rate of 21 mg/tree. Citrus leaves and fruits were sampled from two trees at 0, 3, 7, 14, 28 and 98 DAT. The radioactive residues in pulps were all less than 0.01 mg/kg, and no further characterization or identification were conducted. The radioactive residues in rinds were 0.21 mg eq/kg at maturity (98 DAT), and 81–99% radioactive residues in rind were extracted with acetone/methanol (1:1). The residue of fenpyroximate in the rind was 1.1 mg eq/kg (99% TRR) just after application and 0.09 mg eq/kg (43% TRR) at maturity (98 DAT). The major metabolites in rind were M-1 and M-12. M-1 in rind were less than 4% TRR (0.01–0.04 mg eq/kg) in all samples. M-12 level in rind was 11–12% TRR (0.10–0.12 mg eq/kg) at 7–28 DAT, and 19% TRR (0.04 mg eq/kg) at maturity.

The radioactive residues in leaves were 4.2, 2.5 and 0.86 mg eq/ kg at 14, 28 and 98 DAT (maturity). 72–100% of radioactive residues in leaves were extracted with acetone/methanol (1:1). The residues of fenpyroximate in the leaves were 9.8 mg eq/kg (100% TRR) just after application, 1.1 mg eq/kg (43% TRR) at 28 DAT and 0.21 mg eq/kg (24% TRR) at maturity (98 DAT). The major metabolites in leaves were M-1 and M-12. M-1 level in leaves was 20–32% TRR (0.49–2.03 mg eq/kg) from 7 to 28 DAT, and was 16% TRR (0.14 mg eq/kg) at 98 DAT. M-12 level in leaves was less than 5% TRR (0.09–0.21 mg eq/kg) at 3–28 DAT, and 8% TRR (0.07 mg eq/kg) at maturity. Two new metabolites, M-15 in leaves was at maximum of 0.04 mg eq/kg (< 1% TRR) at 7 DAT, and M-17 in leaves was at maximum of 0.16 mg eq/kg (4% TRR) at 14 DAT.

The polar metabolites were enzyme hydrolysed with β-glucosidase or cellulose, M-15 glucoside and several unknown glucosides were detected at a level of less than 0.01 mg eq/kg in the leaves and rind at 98 DAT.

In the third study, outdoor Dancy tangerine trees were treated with [pyrazole-^{14}C] fenpyroximate at the rates of 21 mg/tree (harvest at day 0–28) or 32 mg/tree (harvest at day 65). No radioactive residues were detected in pulps from trees treated with 21 mg/tree at 0–28 DAT (LOD was 0.13 mg eq/kg). Radioactive residue levels in pulps were 0.022 mg eq/kg at harvest (65 DAT).

The radioactive residue levels were 0.96–1.4 mg eq/kg in rind from trees treated with 21 mg/tree. Radioactive residue levels in rind were 1.0 mg eq/kg at the time of harvest (65 DAT). 90% of radioactivity from rind were extracted with acetone/methanol. The residues of fenpyroximate, M-1, M-12 and M-3 in rind were 0.60 mg eq/kg (58% TRR), 0.13 mg eq/kg (13% TRR), 0.04 mg eq/kg (4% TRR) and 0.04 mg eq/kg (4%TRR) at harvest (65 DAT). M-6 was detected at 0.02 mg eq/kg (2%TRR) and other metabolites (M-3, M-8, M-9, M-11, M-13 and M-19) were < 0.02 mg eq/kg (<2% TRR).

The radioactive residue levels were 11–14 mg eq/kg in leaves from trees treated with 21 mg/tree (0–28 DAT). Radioactive residue levels in leaves were 14 mg eq/kg from trees treated with 32 mg eq/tree (65 DAT). 71–96% of radioactivity from leaves were extracted with acetone/methanol. Residues of fenpyroximate in leaves were 3.6–12 mg eq/kg from 0–28 DAT. The residues of fenpyroximate, M-1 and M-12 in leaves at harvest (65 DAT) were 4.4 mg eq/kg (31% TRR), 1.7 mg eq/kg (12% TRR) and 0.41 mg eq/kg (3% TRR). Polar Radioactive residues accounted for 1.93 mg eq/kg (14% TRR) and other metabolites were < 0.02 mg eq/kg (< 2% TRR).

Apple

The meeting received information on 2 metabolism studies of fenpyroximate in/on apple.

In the studies, apple trees were treated once by foliar spraying with [pyrazole-^{14}C] or [benzyl-^{14}C]-fenpyroximate at rate of 7.5 g ai/100 L. The residues in apple fruits were 0.12–0.13 mg eq/kg at day 0 and 0.032–0.036 mg eq/kg at harvest. More than 97% radioactive residues in fruit was extracted with acetone/water (1:1). The major components of radioactive residues in fruits were fenpyroximate and M-1. The residues of fenpyroximate and M-1 in fruit were 0.015–0.017 mg eq/kg (47% TRR) and 0.005–0.007 mg eq/kg (18–19% TRR) at harvest. The other metabolites were all below 0.01 mg eq/kg in fruits.

Radioactive residues in leaves amounted to 10–12 mg eq/kg at day 0 and decreased to 0.51–0.63 mg eq/kg at harvest (57 DAT). More than 94% radioactive residues in leaves was extracted with acetone/water (1:1). The major components of radioactive residues in leaves were fenpyroximate and M-1. The residues of fenpyroximate and M-1 in leaves were 1.3–1.6 mg eq/kg (53–59% TRR) and 0.50–0.61 mg eq/kg (19–25% TRR) at 28 DAT, and decreased to 0.22 mg eq/kg (35–43% TRR) and 0.091–0.16 mg eq/kg (18–26% TRR) at harvest. The other metabolites were all below 0.01 mg eq/kg in leaves.

Grape

The meeting received information on 2 metabolism studies of Fenpyroximate in/on grape.

In the studies, grapevines was once treated by hand spraying with [pyrazole-^{14}C] or [benzyl-^{14}C]-fenpyroximate at rate of 7.5 g ai/100L.The radioactive residues in grape juice were lower than 0.01mg eq/kg over the whole sampling period, and no further characterization or identification was conducted. The radioactive residues in grape berries were 0.086–0.097 mg eq/kg at day 0 and 0.060–0.081 mg eq/kg at harvest. More than 93% of radioactive residues in berries were extracted with acetone/methanol (1:1). The major components of radioactivity in berries were fenpyroximate and M-1. The residues of fenpyroximate and M-1 were 0.027–0.031 mg eq/kg (38–45% TRR) and 0.004–0.006 mg eq/kg (5–10% TRR) in grape berry at harvest. Other metabolites identified in grape berry were less than 0.01 mg eq/kg.

The radioactive residues in leaves amounted to 6.2–7.5 mg eq/kg at day 0 and decreased to 0.97–1.2 mg eq/kg at harvest (57 DAT). 83–99% of radioactive residues in leaves was extracted with acetone/methanol (1:1). The major components of radioactivity were fenpyroximate and M-1. The residues of fenpyroximate and M-1 were 0.33–0.64 mg eq/kg (34–56% TRR) and 0.052–0.054 mg eq/kg (5% TRR) in leaves at harvest (57 DAT). Minor metabolites identified were M-9 (0.01 mg eq/kg), M-12 (0.01 mg eq/kg) and M-19 (0.02 mg eq/kg) in leaves at harvest.

Snap bean

The snap bean plants (*Phaseolus vulgaris*, field grown) were treated with [Pyrazole-^{14}C] - fenpyroximate at rate of 104 g/ha or [Benzyl-^{14}C]-fenpyroximate at rate of 105 g/ha. Snap beans were harvested 7 days after application. The total radioactive residues in beans were 0.11 to 0.12 mg eq/kg. More than 99% of the radioactive residues was extracted with acetonitrile: water. The primary components of the residues were fenpyroximate and M-1. The residues of fenpyroximate accounted for 86 to 89% TRR (0.095–0.106 mg eq/kg). The residues of M-1 accounted 4.0 to 4.7% TRR (0.005 mg eq/kg). Other minor components were less than 10% TRR or 0.01 mg eq/kg.

Swiss chard

Swiss Chard plants were treated once with [pyrazole-^{14}C] or [benzyl-^{14}C]-fenpyroximate at rate of 102 g ai/ha. Samples of stem, leaves from 0, 14 and 35 DAT and root at 35 DAT were collected. Radioactive residues in stems and leaves at 0–35 DAT were up to 6.5 mg eq/kg for [pyrazole-^{14}C] fenpyroximate and up to 7.7 mg eq/kg for [benzyl ring -^{14}C] fenpyroximate. The majority of the radioactivity (96 to 100% of TRR) was extracted with acetonitrile/distilled water (4/1, v/v) and acetonitrile/ 0.1N hydrochloric acid (4/1, v/v). The most prominent residue in stems and leaves was

fenpyroximate (0.34–7.6 mg eq/kg, 37–99% TRR). High polar radioactivity (retained at TLC origin) accounted for 31 to 49% TRR (0.43–0.68 mg eq/kg), which consisted of a number of individual metabolites with each individually below 8.5% TRR. . M-1 was less than 3.8% TRR (0.04 mg eq/kg).

Cotton

The cotton plants were treated once with [pyrazole-^{14}C] fenpyroximate as a foliar spray at a rate of 194 g ai/ha. The cotton forage of immature plants was harvested 1 DAT. Mature plants were harvested after boll opening (30 DAT) and were separated into seed, lint and gin trash. The major parts of the treated radioactivity were recovered from rinses and extracts (68–126% of TRR) in the forage, seed kernel, lint/hull, leaves and gin trash. The radioactive residues in post-extraction solid (PES) was < 10% of TRR except in seed kernels (28% TRR) and lint/hulls (15% TRR). However, the levels of radioactivity in PES of seed kernel and lint/hull were very low (0.002–0.003 mg eq/kg). The radioactive residues were 9.2 mg eq/kg in gin trash, 3.6 mg eq/kg in forage, 0.021 mg eq/kg in lint/hull, and 0.008 mg eq/kg in seed kernel.

Fenpyroximate and M-1 (approximately equal amounts) were the major components in leaves, the immature cotton (forage), cotton seed, and the cotton gin trash. . The residues of fenpyroximate and M-1 were 2.5 mg eq/kg (70% of TRR) and 1.2 mg eq/kg (32% of TRR), respectively, in immature cotton (forage), and for both fenpyroximate and M1, 0.003 mg eq/kg (38% TRR) in cottonseed (kernel), and 3.4 mg eq/kg (37% of TRR) in Gin trash. A number of other metabolites detected were less than 10% TRR or 0.01 mg/kg.

In summary, following foliar spray application of fenpyroximate, radioactive residues mainly remained on plant surfaces, and the parent fenpyroximate and M-1 were the major components of residues. All metabolites above 0.01 mg/kg in plants were also found in rats. Primary metabolic pathways of fenpyroximate in plants included conversion of fenpyroximate to Z-isomer (M-1) and hydrolysis of ester, oxime ether cleavage, N-demethylation, oxidation or conjugation to polar metabolites

Confined rotational crop studies

The meeting received information on two confined rotational crop studies.

In the first study, radish, lettuce and wheat were sown as rotational crops at intervals of 30, 120 and 365 days following treatment of sandy loam soil with [pyrazole-^{14}C] fenpyroximate at a rate of 224 g ai/ha. Lettuce and radish were harvested at maturity. Wheat was sampled at the forage and hay growth stages, and at maturity for collection of grain, straw and chaff. Residues in lettuce were ≤0.002 mg eq/kg. Residues in radish root and leaves ranged from 0.001 to 0.008 mg eq/kg. Residues wheat forage and hay ranged from 0.005 to 0.047 mg eq/kg. Residues in straw and chaff taken at maturity were 0.018 to 0.11 mg eq/kg and residues in grain were 0.004 to 0.01 mg eq/kg.

All individual metabolite residues were < 0.01 mg eq/kg. The residues of fenpyroximate in radish root was 0.001 mg eq/kg, and other two metabolites were less than 0.002 mg eq/kg. The residues of three metabolites in radish foliage were 0.001–0.002 mg eq/kg.

Wheat forage from the 120 day plant back contained M-5, M-3 and 4 other metabolites (0.001–0.005 mg eq/kg). All metabolites in hay extracts from all plant back groups were 0.001–0.007 mg eq/kg. M-21 in the 30 day plant back hay, and M-8, M-5 and M-3 in hay extracts from 120 and 365 day plant back were identified. Residues of metabolites in wheat chaff were 0.001–0.006 mg eq/kg.

The extracted residues in wheat straw from the 30, 120 and 365 day plant back intervals were 0.052, 0.081 and 0.025 mg eq/kg. Straw from the 30 day plant back contained a polar unknown (0.022 mg eq/kg, 32% TRR), M-8 (0.008 mg eq/kg, 12% TRR), and 5 other metabolites. Straw from the 120 day plant back contained M-8 (0.011 mg eq/kg, 14% TRR) and other 3 metabolites above 0.01 mg eq/kg. These included a polar unknown and 2 mid polarity metabolites.

In another study, radish, spinach, and wheat were sown as rotational crops at intervals of 30, 120 and 270 days following treatment of sandy loam soil with [benzyl-^{14}C]-fenpyroximate at a rate of

111 g ai/ha. The plants were harvested at immaturity and maturity. Total radioactive residues in all crop matrices were very low. Wheat hay, straw and grain from Day 31, and wheat straw and grain from Day 118 had TRR equal to or more than 0.01 mg/kg. TRRs in all crops at 270 days were below 0.01 mg/kg.

Extraction of radioactivity accounted for between 69–87% TRR (0.010–0.033 mg/kg) for Day 31 (grain, hay and straw) and 24–39% TRR (0.002–0.005 mg/kg) for Day 118 grain and straw. All individual metabolites in wheat straw at the 31 day plant-back interval were less than 0.001 mg eq/kg.

In summary, fenpyroximate related residues in soil are unlikely to result in significant levels in rotational crops following application at maximum seasonal rates of up to 224 g ai/ha for non-permanent crops.

Animal metabolism

Lactating goats

Two studies on lactating goat metabolism were available for the meeting. In the first study, a lactating goat was orally administered [pyrazole-^{14}C]-fenpyroximate by capsule twice daily for 3 consecutive days at a dose of 10 ppm in the diet, corresponding to 0.5 mg/kg bodyweight/day. Milk samples were collected twice daily during the dosing period. The treated goat was sacrificed approximately 22 hours after the final dose.

The majority of radioactive residues was recovered in the excreta (urine 32% AD, faeces 33% AD) and in the gastrointestinal tract (11% AD). For tissues, radioactive residues were highest in liver (1.2 mg eq/kg), followed by kidney (1.1 mg eq/kg), muscle (0.021 mg eq/kg) and fat (0.082 mg eq/kg). TRR in milk reached 0.037 mg eq/kg before the end of dosing.

More than 67% of the TRR in milk and tissues was extracted with solvent. The residues of fenpyroximate in milk were 0.001–0.008 mg eq/kg. The major metabolites in milk were M-21 (0.011–0.015 mg eq/kg, 37–55% TRR) and Fen-OH (0.001–0.003 mg eq/kg, 3–12% TRR). The residues of fenpyroximate were highest in fat (0.035 mg/kg, 42% TRR), followed by muscle (0.006 mg eq/kg, 25% TRR) and kidney (0.005 mg eq/kg, 1% TRR). N-desmethyl M-3 (0.27–0.31 mg eq/kg, 21–28% TRR) and M-3 (0.46–0.61 mg eq/kg, 42–50% TRR) were the major metabolites detected in kidney and liver, Fen-OH (0.014–0.029 mg eq/kg, 35–58% TRR) was the major metabolite detected in fat and muscle, while other metabolites were less than 10% TRR in tissues. No M-1 was detected in tissues and only a very low level in milk (0.001 mg eq/kg, 3% TRR).

In another study, a lactating goat was orally administered by capsule with [benzyl -^{14}C]-fenpyroximate for 3 consecutive days at a rate of 10 ppm in diet, corresponding to 0.3 mg/kg bodyweight/day. Milk samples were collected twice daily during the dosing period. The treated goat was sacrificed approximately 22 hours after the final dose.

The majority of the radioactive residues were recovered in the excreta (urine 12% AD, faeces 45% AD) and in the gastrointestinal tract (22% AD, unexcreted). For tissues, radioactive residues were highest in kidney (2.1 mg eq/kg), followed by liver (1.3 mg eq/kg) with fat (0.14 mg eq/kg) and muscle (0.027 mg eq/kg). TRR in milk reached the plateau of 0.031 mg eq/kg at 24–32 hours after first dosing.

More than 85% of the TRR in milk and tissues was extracted with solvent. The residues of fenpyroximate in milk were 0.003–0.008 mg eq/kg (13–26% TRR). The major metabolites in milk were M-22 (0.003–0.007 mg eq/kg, 16–27% TRR). Fen-OH was detected only in milk (0.002 mg eq/kg, 8% TRR) at 23–32 hour and M-21 (0.005 mg eq/kg, 38% TRR) was only detected in milk at 8–24 hours. The residues of fenpyroximate was highest in fat (0.049 mg eq/kg, 36% TRR), followed by kidney (0.022 mg eq/kg, 1% TRR) and muscle (0.002 mg eq/kg, 7% TRR). M-5 Glucuronide (0.25–0.55 mg eq/kg, 20–26% TRR), Fen-OH (0.741–0.98 mg eq/kg, 47–59% TRR) were the major metabolites in kidney and liver, M-22 (0.020 mg eq/kg, 74% TRR), Fen-OH (0.009 mg eq/kg, 33% TRR) were major metabolites in muscle. Fen-OH (0.019 mg eq/kg, 14% TRR) and M-22 (0.024 mg eq/kg, 17% TRR) were detected in fat. M-1 was detected in kidney

(0.140 mg eq/kg, 5% TRR) and liver (0.073 mg eq/kg, 6% TRR). Other metabolites detected were less than 10% TRR in tissues.

Environmental fate

Aerobic metabolism in soil

The Meeting received information on soil aerobic metabolism, photolysis and aqueous hydrolysis properties of [^{14}C]-fenpyroximate.

The degradation of fenpyroximate in soil incubated under dark aerobic conditions was moderate to slow with DT_{50} values of 23–254 days, indicating moderate persistence in soil. The parent fenpyroximate was the predominant radioactive residue in soil from day 0 to day 219. The major degradation products formed in soil treated with [benzyl (U)-^{14}C]-fenpyroximate were M-3 with maximum value of 29% AR, while other minor degradation products including M-1 and M-15 were less than 5% AR. The major degradation products formed in soil treated with [pyrazole-3-^{14}C]-fenpyroximate were M-3 (maximum 17% AR), M-8 (maximum 16% AR), and M-11 (maximum 9.6% AR), with less than 5% AR of other minor degradation products including M-1, M-6 and M-13.

In summary, fenpyroximate degraded steadily to major metabolites M-3, M-8 and M-11, minor metabolites M-1 and M-6, bound residue and carbon dioxide.

Soil photolysis

The soil photolysis of fenpyroximate in wet soils was investigated. Irradiation enhanced the degradation of fenpyroximate on wet soils. The DT_{50} values for the irradiated soil samples (equivalent to natural sunlight at 30–50°N) were 43 and 35 days for [benzyl-^{14}C] and [pyrazole-^{14}C] fenpyroximate, respectively. While the DT_{50} values for the dark soil samples were 91 and 69 days for [benzyl-^{14}C] and [pyrazole -^{14}C] fenpyroximate, respectively. Major degradation products observed in irradiated soil samples were M-1 (maximum 17% AR), M-12 (maximum 5.5% AR), M-12 isomer (maximum 5.1% AR) and MTBT (maximum 8.3% AR). M-3 (maximum 14% AR) was the only degradation product observed in the dark soil sample.

Hydrolysis

Fenpyroximate degradation was very slow at pH 5, 7, and 9 at 25 °C. The half-life for the hydrolytic degradation of [pyrazole-^{14}C]-fenpyroximate was calculated to be 180 days for pH 5, 226 days for pH 7 and 221 days for pH 9, indicating hydrolysis plays a negligible role in its degradation under environmental conditions. M-1 (maximum 7% AR) was only observed at pH 5 and pH 9. The principal hydrolysis product observed at each pH was M-3 (maximum 10% AR).

Methods of analysis

The Meeting received description and validation data for analytical methods for residues of fenpyroximate, M-1, M-3 and de-methyl fenpyroximate in plant matrices, livestock matrices and soil. The recoveries were within 70–120% with RSD less than 20%, the validated methods were considered suitable for data generation.

For most data gathering methods, residues are extracted with acetonitrile, acetone or methanol. Extracted residues undergo clean-up by silica gel/alumina column, GPC or dispersive SPE with primary/secondary amine (PSA). The residue separation and analysis is by GC-FTD, GC-N-FID, LC-UV, GC-MS, LC-MS, or LC-MS/MS, using internal standards or matrix matched standards. For most matrices, the limits of quantification (LOQ) for each analyte is 0.01 mg/kg.

For livestock matrices, the residues are extracted with acetone: water (2:1, v/v), acetonitrile, or acetonitrile: water (8:2. v/v), cleaned up by SPE or GPC, and analysed with GC or LC-MS. The LOQs for fenpyroximate are 0.01 mg/kg in milk and tissues (liver, kidney, muscle and fat).

Multi-residue methods (QuEChERS) for enforcement are also validated for fenpyroximate and M-1 in plant matrices, fenpyroximate and M-3 in livestock matrices.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of fenpyroximate in various matrices on freezer storage (-18 °C). The periods of demonstrated stability cover the frozen storage intervals used in the residue studies on crops.

Residues of fenpyroximate and M-1 were stable in lettuce at least 9 months, in apple at least 18 months, in orange at least 9 months, in hops at least 24 months, in sunflower at least 9 months and in potato at least 9 months. Residues of fenpyroximate were stable in grape for at least 12 months. Residues of M-1 were stable in grape for at least 36 months

The stability of fenpyroximate in animal commodities was studied in the lactating goat residue transfer study with fortified samples stored for the same intervals as in studies. The residues of fenpyroximate and M-1 were stable in muscle at least 56 days, kidney at least 53 days, fat at least 54 days, milk at least 79 days and liver at least 53 days.

Definition of the residue

Following application of fenpyroximate to crops, the parent compound and its Z isomer (M-1) were the major residues from the day of application until harvest (7–137 days after treatment). With the exception of M-12 in citrus rind (19% TRR, 0.04 mg eq/kg), other metabolites were less than 10% TRR or less than 0.01 mg eq/kg. Residues of fenpyroximate were consistently two to ten times greater than M-1 across all crops in the metabolism studies, and residues of M-1 were frequently below the LOQ in crop field trials. Therefore, the Meeting decided that fenpyroximate is a suitable marker for enforcement in plants.

In deciding if additional compounds should be included in the residue definition for risk assessment, the Meeting considered the likely occurrence of the compounds and the toxicological properties of those compounds. M-1 is found in metabolism studies and crop field trials at levels that are not negligible relative to parent compound in some samples and is considered to have equal toxicity to parent fenpyroximate. Therefore, M-1 should be included for risk assessment. The only other candidate compound is M-3, which formed under conditions simulating pasteurization, brewing/baking/boiling, and sterilisation. M-3 comprised from 41% (pasteurisation) to 89% (sterilisation) of the applied radioactivity in that study. M-3 was observed in the rat metabolism study and its toxicity is considered to be covered by that of fenpyroximate. Processing studies that included these conditions were conducted with exaggerated residues of fenpyroximate (relative to field trial residues) in RAC commodities of apple, bean, grape, strawberry, maize, and tea. Residues of M-3 were < 0.01 mg/kg in all processed commodities except canned beans (up to 0.07 mg/kg) and strawberry jam (0.02 mg/kg). These levels of M-3 were less than 15% of the residues of parent compound. Therefore, the Meeting decided that M-3 did not contribute significantly to the total exposure of fenpyroximate through the diet. The residue definition for assessing dietary exposure from plant commodities is the sum of fenpyroximate and M-1, expressed as fenpyroximate.

In goats, the residue profile varied by matrix. The Fen-OH metabolite was consistently observed as a major residue across all matrices (12% TRR milk, 58% TRR muscle, 35% TRR fat, 59% TRR liver, and 47% TRR kidney). Additional residues observed across multiple matrices at greater than 10% TRR were fenpyroximate (26% TRR milk, 43% TRR fat), M-5 glucuronide (20% TRR liver, 26% TRR kidney), M-3 (50% TRR liver, 42% TRR kidney), M-21 (26–55% TRR in milk, and M-22 (74% TRR muscle, 17% TRR fat). A QuEChERS method was validated for analysis of fenpyroximate and M-3 in milk, fat, muscle, and offal. Based on structural similarities between fenpyroximate, M-3 and Fen-OH, the Meeting noted that the method is likely to be suitable for analysis of Fen-OH. Given the toxicity of Fen-OH is considered to be covered by that of fenpyroximate, the Meeting decided that the sum of fenpyroximate, Fen-OH and M-3, expressed as fenpyroximate is a suitable marker for compliance in livestock commodities.

In addition to the residues for compliance, dietary exposure from consumption of livestock commodities may occur for M-5-glucuronide for liver (20% TRR, 0.25 mg eq/kg) and kidney (26% TRR, 0.55 mg eq/kg), for M-21 in milk (37% TRR, 0.011 mg eq/kg), and M-22 in muscle (74% TRR,

0.02 mg eq/kg). The toxicity of M-5- glucuronide, M-21 and M-22 are covered by parent fenpyroximate. Since M-21 and M-22 were not detected in the feeding study, the Meeting decided that they do not need to be included for assessing dietary exposure. The Meeting decided that definition for dietary assessment is the sum of fenpyroximate, Fen-OH, M-3, and M-5 (free and conjugated), expressed as fenpyroximate, in livestock commodities.

The Log Pow of fenpyroximate is above 5. The ratio of residues of fenpyroximate in fat and muscle in metabolism studies is 5.8 to 24.5, and the total residues in fat is 3.4–5.1 times higher than residues in muscle. On the weight of evidence, the Meeting decided the residue is fat soluble.

The residue definition of fenpyroximate for plant commodities for compliance with the MRL is fenpyroximate, and for dietary assessment is the sum of fenpyroximate and M-1 (Z isomer).

Residue definition of fenpyroximate for animal commodities for compliance with MRL is sum of fenpyroximate, Fen-OH and M-3, expressed as fenpyroximate, for dietary assessment is sum of fenpyroximate, Fen-OH, M-3, and M-5 (free and conjugated), expressed as fenpyroximate.

The residues of fenpyroximate, sum of fenpyroximate, Fen-OH and M-3 are fat soluble.

Results of supervised trials on crops

Supervised residue trial data were available for fenpyroximate on citrus (oranges, mandarin, lemons, grapefruit, natsudaidai, tangor), pome fruit (apples, pears), stone fruit (cherries, peaches, apricot, plums), berries and other small fruits (grape, raspberries, strawberries), assorted tropical and subtropical fruits-inedible peel (avocado, papaya), cucurbits (cucumber, melon, courgette, watermelon, cantaloupe), fruit vegetables other than cucurbits (tomatoes, pepper), legume vegetables (beans), root and tuber vegetables (potatoes), cereal grain (maize), tree nuts (almond, pecan, walnut), hops, coffee and tea.

Citrus fruits

The critical GAP for citrus in the USA is two foliar applications at 235 g ai/ha with a PHI of 14 days. The maximum rate per growing season is 471 g ai/ha. The Meeting received supervised residue trial data for fenpyroximate on citrus fruit from the USA, EU and Japan.

In trials approximating critical GAP in the USA, residues in citrus fruit were:

Lemons: residues of fenpyroximate (n=4) 0.017, 0.15, 0.17 and 0.18 mg/kg, residues of fenpyroximate and M-1 (n=4) 0.16, 0.18, 0.19 and 0.2 mg/kg.

Grapefruit: residues of fenpyroximate (n=4) < 0.01, 0.017, 0.017 and 0.073 mg/kg, residues of fenpyroximate and M-1 (n=4) 0.025, 0.047, 0.077 and 0.081 mg/kg

Oranges: residues of fenpyroximate (n=8) 0.011, 0.018, 0.039, 0.066, 0.13, 0.1332, 0.15 and 0.26 mg/kg, the residues of fenpyroximate and M-1 (n=8) 0.074, 0.089, 0.14, 0.15, 0.16, 0.18, 0.19 and 0.27 mg/kg.

The Meeting noted that median residues following two foliar applications to lemon, grapefruit and orange are within a 5-fold range and a Kruskal-Wallis H-test suggest the residues in lemon, grapefruit and orange are from similar populations. The Meeting decided to combine the data to estimate a maximum residue level for the citrus group. The combined residue data of fenpyroximate (n=16) are: < 0.01, 0.011, 0.017(3), 0.018, 0.039, 0.066, 0.073, 0.13, 0.13, 0.15, 0.15, 0.17, 0.18 and 0.26 mg/kg. The combined residue data of fenpyroximate and M-1 (n=16) 0.025, 0.047, 0.074, 0.077, 0.081, 0.089, 0.17, 0.15, 0.16, 0.16, 0.18, 0.18, 0.19, 0.19, 0.20 and 0.27 mg/kg.

In trials conducted on tangor, satsuma, Chin citron natsudaidai and orange with approximate application rate, the residues in flesh was 13% of that of fruit. The Meeting recommended a maximum residue level of 0.6 mg/kg, and STMR of 0.020 mg/kg and HR of 0.0364 (highest individual) mg/kg respectively for citrus group, and replace the previous recommendation of 0.5 mg/kg for citrus fruits.

Pome fruits

Apple

The critical GAP for apple in Greece is one foliar application at 106 g ai/ha with a PHI of 7 days.

In trials conducted in EU member states approximating critical GAP, the residues of fenpyroximate in apples were: (n=10) 0.04, 0.06, 0.07(2), 0.08, 0.11(2), 0.12(2) and 0.14 mg/kg, the residues of fenpyroximate and M-1 in apples were: (n=10) 0.05, 0.07, 0.08(2), 0.09, 0.12(2), 0.13, 0.14 and 0.19 mg/kg.

The meeting noted that the cGAP gave rise to residues that exceeded the ARfD (110% for children in Canada) and therefore a public health concern could not be excluded. For this reason, the alternative GAP from Belgium was considered. The GAP in Belgium is one foliar application at 76.5 g ai/ha with a PHI of 7 days. Ten trials conducted in the EU are available at over dosed rates compared to the GAP and where scaled using the proportionality principle.

Residues of fenpyroximate in apple in rank order (n=10) were: 0.01, 0.04, 0.06, 0.07, 0.08, 0.09, 0.10, 0.12, 0.14 and 0.19 mg/kg.

Residues of fenpyroximate in apple (scaled using factors ranging from 1.42 – 2.35) in rank order (n=10) were: 0.028, 0.039, 0.049, 0.055, 0.062, 0.068, 0.073, 0.077, 0.081 and 0.095 mg/kg.

Residues of fenpyroximate and M-1 in apples were: (n=10) 0.038, 0.049, 0.059, 0.065, 0.072, 0.078, 0.083, 0.087, 0.1 and 0.15 mg/kg.

The Meeting recommended maximum residue level, STMR and HR of 0.2, 0.075 and 0.15 mg/kg respectively for apples.

Pears

The critical GAP for pears in US (pome fruit) is one foliar application at 117 g ai/ha with a PHI of 14 days. In trials conducted in USA approximating critical GAP in USA, France and New Zealand, residues of fenpyroximate in pears were: (n=6) 0.04, < 0.05, 0.07, 0.086, 0.051 and 0.14 mg/kg. The residues of fenpyroximate an M-1 in pears were: (n=6): 0.05, 0.07, < 0.10, 0.101, 0.136 and 0.14 mg/kg.

In trials conducted in USA with nominal rate of 450 g ai/ha with a PHI of 14 days were considered, the residues of fenpyroximate in pears were: (n=6) 0.073, 0.13, 0.16, 0.18, 0.24 and 0.28 mg/kg. The residues of fenpyroximate and M-1 in pears were: (n=6) 0.12, 0.18, 0.22, 0.23, 0.30 and 0.35 mg/kg.

The scaled residues (117/450=0.26) of fenpyroximate were: (n=6) 0.019, 0.033, 0.043, 0.047, 0.063, 0.072 mg/kg. The scaled residues (0.26) of fenpyroximate and M-1 were: (n=6) 0.032, 0.048, 0.056, 0.060, 0.077 and 0.090 mg/kg

Taking the proportionality approach into consideration, the Meeting agreed to make estimation based on combined data. The Meeting recommended maximum residue level of 0.2 mg/kg, STMR of 0.078 mg/kg and HR of 0.14 mg/kg for pears.

The Meeting withdrew the previous recommendations of 0.3 mg/kg for pome fruits.

Stone fruits

The critical GAP in USA for stone fruits is two applications at 117 g ai/ha with a PHI of 7 days.

Cherry

In trials conducted in the USA approximating critical GAP, the residues of fenpyroximate in cherries were: (n=8) 0.26, 0.34, 0.36, 0.46, 0.66, 0.79, 0.93 and 0.99 mg/kg. The residues of fenpyroximate and M-1 were: 0.31, 0.39, 0.41, 0.51, 0.66, 0.79, 0.93 and 0.99 mg/kg. The Meeting recommended maximum residue level, STMR and HR of 2, 0.585 and 0.99 mg/kg respectively for Cherry. The

Meeting noted that the GAP in USA is for group of stone fruits, and decided to extrapolate to subgroup of cherries.

Short term dietary exposure assessment showed that residues in cherry exceed the acute reference dose (ARfD) of 0.01 mg/kg bw, at 110% of ARfD for children (Denmark, Germany). No alternative GAP with sufficient data for cherry was available.

Peach

In trials conducted in the USA approximating critical GAP, the residues of fenpyroximate in peaches were (n=10): 0.073, 0.075, 0.086, 0.098, 0.11, 0.13, 0.13, 0.15, 0.18 and 0.20 mg/kg. The residues of fenpyroximate and M-1 were: 0.12, 0.12, 0.14, 0.15, 0.16, 0.18, 0.18, 0.20, 0.23, 0.25 mg/kg. The Meeting recommended maximum residue level, STMR and HR of 0.4, 0.17 and 0.25 mg/kg respectively for peaches.

Short term dietary exposure assessment showed that residues in peach exceed the acute reference dose (ARfD) of 0.01 mg/kg bw, at 130% of ARfD for children (Japan, Canada). No alternative GAP with sufficient data for peach was available.

However, as there was no exceedance of the ARfD for apricot, therefore, the Meeting estimated the maximum residue level, STMR and HR of 0.4, 0.17 and 0.25 mg/kg respectively for apricot.

Plum

In trials conducted in the USA approximating critical GAP, residues of fenpyroximate in plums were (n=6): < 0.05(2), 0.08 0.13, 0.20 and 0.27 mg/kg. The residues of fenpyroximate and M-1 were: < 0.1(2), 0.13, 0.18, 0.25 and 0.32 mg/kg. The Meeting estimated the maximum residue level, STMR and HR of 0.8, 0.155 and 0.33 mg/kg respectively for plums. The Meeting noted that the GAP in USA is for group of stone fruits, and decided to extrapolate to peaches.

Short term dietary exposure assessment showed that residues in plum dried exceed the acute reference dose (ARfD) of 0.01 mg/kg bw, at 270% of ARfD for children (Australia). No alternative GAP with sufficient data for plum was available.

The Meeting withdrew the previous recommendations of 0.4 mg/kg for stone fruits.

Berries and other small fruits

Raspberry

The critical GAP in the USA on raspberries is two applications at 117 g ai/ha with a PHI of 1 days. No trials were provided matching the critical GAP.

The registered use of fenpyroximate for raspberry in Austria allows one application at rate of 76.5 g ai/ha with a PHI of 14 days. In trials conducted in matching GAP, the residues of fenpyroximate in raspberry were: 0.01 0.04, 0.08 and 0.10 mg/kg. The residues of fenpyroximate and M-1 were: 0.02, 0.05, 0.09 and 0.11 mg/kg. The Meeting estimated a maximum residue level, STMR and HR of 0.2, 0.07 and 0.11 mg/kg respectively for raspberry.

Grape

The critical GAP in USA for grape is two applications at 117 g ai/ha with a PHI of 14 days.

In trials conducted in the Germany (two applications at rate of 135 g ai/ha with PHI of 14 days) approximating critical GAP, the residues of fenpyroximate in grapes were (n=2): 0.11, 0.40 mg/kg. The residues of fenpyroximate and M-1 were: (n=2) 0.12 and 0.41 mg/kg.

The registered use of fenpyroximate for vine in Spain allows one application at rate of 50 g ai/ha with a PHI of 28 days. In trials conducted in EU matching the GAP, the residues of fenpyroximate in grape were: (n=12) < 0.01(2), 0.01(2), 0.02(2), 0.03, 0.04(3), and 0.05(2) mg/kg.

The residues of fenpyroximate and M-1 were: (n=12) < 0.02(2), 0.02(2), 0.03(2), 0.04(3) 0.05 and 0.06(2) mg/kg.

The Meeting recommended maximum residue level of 0.1 mg/kg, STMR of 0.035 mg/kg and HR of 0.06 mg/kg for grapes.

Strawberries

The Critical GAP in the USA on low growing berries including strawberries (USA subgroup 13-07G) is two applications at a rate of 117 g ai/ha with a PHI of 1 days.

In trials conducted in USA approximating critical GAP, the residues of fenpyroximate in strawberries were: (n=8) 0.06, 0.07, 0.19(2), 0.24, 0.24, 0.28 and 0.53 mg/kg. The residues of fenpyroximate and M-1 were: (n=8) 0.06, 0.08, 0.20, 0.22, 0.24, 0.27, 0.33 and 0.56 mg/kg.

The meeting noted that the cGAP gave rise to residues that lead to an exceedance of the ARfD (130% for children in France) and therefore a public health concern could not be excluded. The Meeting considered the alternative GAP for strawberries in Germany and Austria. The GAP in Germany and Austria is one foliar application at 102 g ai/ha with a PHI of 7 days. Sixteen trials support the GAP.

Residues of fenpyroximate in strawberries in rank order (n=16) were: < 0.01 (2), 0.01 (2), 0.02, 0.03, 0.05 (3), 0.06, 0.07 (2), 0.08, 0.10, 0.13, 0.19 mg/kg

Residues of fenpyroximate and M1 in strawberries in rank order (n=16) were: 0.02 (4), 0.03, 0.04, 0.06 (3), 0.07, 0.08 (2), 0.09, 0.11, 0.14, 0.20 mg/kg.

The Meeting recommended maximum residue level of 0.3 mg/kg, STMR of 0.06 mg/kg and HR of 0.2 mg/kg for strawberries.

Assorted tropical and sub-tropical fruit – inedible peel

Avocado

The Critical GAP in the USA on avocado is two applications at a rate of 117 g ai/ha with a PHI of 1 days.

In trials conducted in USA approximating critical GAP, the residues in avocado were: (n=5) < 0.05, < 0.05, < 0.05, 0.06 and 0.10 mg /kg. The Meeting noted that the avocado is minor crop, and agreed to estimate a maximum residue level, STMR and HR of 0.2, 0.05 and 0.1 mg/kg respectively.

Papaya

The critical GAP in Brazil is three applications at rates of up to 40 g ai/ha with a PHI of 3 days.

The Meeting was was unable to estimate a maximum residue level as no trials were provided matching the critical GAP.

Cucurbit vegetable

Cucumber

The critical GAP in the USA on cucumber is two applications at a rate of 117 g ai/ha with a PHI of 1 days. In trials conducted in USA matching the cGAP, residues of fenpyroximate in cucumber were: (n=7) < 0.05, 0.08 (2), 0.063, 0.065, 0.11 and 0.17 mg/kg. The residues of fenpyroximate and M-1 were: < 0.10, 0.113, 0.115, 0.13(2), 0.16 and 0.22 mg/kg. The Meeting estimated the maximum residue level, STMR and HR of 0.3, 0.13 and 0.24 (highest individual) mg/kg for cucumber, to replace previous recommendation of 0.3 mg/kg.

Summer Squash

The registered uses of fenpyroximate for zucchini in Germany allows one application at rate of 46–92 g ai/ha with PHI of 3 days, In trials conducted in France and Italy matching the GAP, residues of fenpyroximate in courgettes were: (n=6) < 0.01, 0.01(2), 0.02(2) and 0.03 mg/kg. The residues of fenpyroximate and M-1 were: < 0.02, 0.02(2), 0.03(2) and 0.04 mg/kg. The Meeting estimated the maximum residue level, STMR and HR of 0.06, 0.025 and 0.04 mg/kg for summer squash.

Melons, except Watermelon

The GAP in the USA on cantaloupe (included in USA crop subgroup 9A) is two applications at rate of 117 g ai/ha with a PHI of 3 days.

In trials conducted in USA matching the GAP, the residues of fenpyroximate, fenpyroximate and M-1 in cantaloupe were: (n=8) < 0.05 (8) mg ai/ha.

In trials conducted in Spain and Italy (one application of 110 g ai/ha, 3 days PHI), the residues of fenpyroximate in melons were : (n=4) < 0.01, 0.01, 0.02 and 0.08 mg/kg, residues of fenpyroximate and M-1 were: < 0.02, 0.02, 0.03 and 0.09 mg/kg.

The Meeting noted the application in trials on cantaloupe was 12–12 days, and decided to combine the data to estimate a maximum residue level, STMR and HR of 0.2, 0.05 and 0.09 mg/kg respectively for melon except watermelon, replaced the previous recommendation of 0.05 mg/kg).

Watermelon

The GAP in the USA on watermelon (included in USA crop subgroup 9A) is two applications at rate of 117 g ai/ha with a PHI of 3 days. In trials conducted in USA (2 application at rate of 110 g ai/ha, PHI of 1day), the residues of fenpyroximate in watermelon fruit were: (n=4) < 0.05 (4). The residues of fenpyroximate and M-1 were < 0.1 (4).

The Meeting agreed to estimate the maximum residue level, STMR and HR of 0.05, 0.1 and 0.1 mg/kg.

Short term dietary exposure assessment showed that residues in watermelon exceed the acute reference dose (ARfD) of 0.01 mg/kg bw, at 190% of ARfD for children (Canada). No alternative GAP with sufficient data for watermelon was available.

Fruiting vegetables other than Cucurbit

Peppers

The critical GAP in USA on pepper (included in US crop group 8–10) is two applications at rate of 117 g ai/ha with a PHI of 1 day.

In trials conducted in USA matching the cGAP, residues of fenpyroximate, fenpyroximate and M-1 in peppers were: (n=16) < 0.05(9), 0.05, 0.054, 0.07(2), 0.012 and 0.13 mg/kg. The Meeting estimated the maximum residue level, STMR and HR of 0.2, 0.05 and 0.13 mg/kg for bell and non-bell pepper. The Meeting noted that the GAP in USA is for US crop group 8–10, The Meeting agreed to extrapolate to subgroup of peppers except martynia, okra and roselle.

The Meeting withdraw the previous recommendation for chill pepper, dry of 1 mg/kg.

Tomato

The Critical GAP in the USA on tomato (for USA crop group 8-10) is two applications at rate of 117 g ai/ha with a PHI of 1 days.

In trials conducted in USA approximating critical GAP, the residues of fenpyroximate in tomato were: (n=19) < 0.05 (9), 0.05, 0.07, 0.08 (3), 0.09 (3), 0.11 and 0.12 mg/kg. The residues of fenpyroximate and M-1 were: < 0.1(9), 0.1, 0.12, 0.13(3), 0.14(3), 0.16 and 0.17 mg/kg. As residues in cherry tomato is normally higher than that in tomato, the Meeting estimated a maximum residue

level, STMR and HR of 0.3, 0.10 and 0.17 mg/kg respectively for cherry tomato and tomato. The Meeting noted that the GAP in USA is for US crop group 8-10, and agreed to extrapolate to subgroup of eggplants.

Short term dietary exposure assessment showed that residues in tomato dried exceed the acute reference dose (ARfD) of 0.01 mg/kg bw, at 310% of ARfD for general population (Australia). No alternative GAP with sufficient data for tomato was available.

The Meeting withdrew the previous recommendation for fruiting vegetables other than cucurbits of 0.2 mg/kg.

Beans with pods

The GAP in the USA on bean is two applications at rate of 117 g ai/ha with a PHI of 1 days. In trials conducted in USA matching the US GAP, residues of fenpyroximate in bean with pod were: (n=8) < 0.05(2), 0.09(3), 0.15, 0.18, 0.19 mg/kg. The residues of fenpyroximate and M-1 were: < 0.1(2), 0.14(3), 0.20, 0.24 and 0.24 mg/kg.

The GAP in the Spain on bean is one application at rate of 102 g ai/ha with a PHI of 7 days. In trials conducted in Greece, France and Italy approximating the Spain GAP, residues in bean with pod were: (n=16) 0.02, 0.03(4), 0.06(3), 0.07, 0.08(2), 0.1, 0.13, 0.14, 0.23 and 0.41 mg/kg. The residues of fenpyroximate and M-1 were: 0.03, 0.04(4), 0.07(3), 0.08, 0.09(2), 0.11, 0.14, 0.15, 0.24 and 0.42 mg/kg. The Meeting noted that the residues from trial approximating the Spain GAP were higher than residues from trials in US, and agree to estimate the maximum residue level, STMR and HR of 0.5, 0.075 and 0.42 mg/kg for bean with pod based on trials in Europe, and extrapolated the estimates to subgroup of beans with pods. Furthermore, the Meeting withdraws its previous recommendation of 0.4 mg/kg for common bean (pods and/or immature seeds).

Potato

GAP in US is two applications at rate of 117 g ai/ha with a PHI of 7 days. In trials conducted in USA matching the GAP, residues of fenpyroximate in potato tubers were: (n=16) < 0.05(16) mg/kg. The Meeting noted that residues of fenpyroximate or M-1 from trials at 5 times rate were < 0.05 mg/kg, and estimated the maximum residue level, STMR and HR of 0.05*, 0 and 0 mg/kg respectively for potatoes.

Maize

The GAP in the USA on maize is two applications at rate of 117 g ai/ha with a PHI of 14 days. In trials conducted in USA matching the US GAP, residues of fenpyroximate or M-1 in maize grain were: (n=10) < 0.01(10). The Meeting estimated the maximum residue level, STMR of 0.01*, 0.01 mg/kg respectively for maize.

Tree nuts

GAP in US on tree nut (US crop group 14) is two applications at rate of 117 g ai/ha with a PHI of 14 days. In trials on almond (5), pecan (5) and walnut (3) conducted in USA with exaggerated rate (one application of 450 g ai/ha 14 days PHI), residues of fenpyroximate or M-1 in tree nut meats were: (n=13) < 0.05(13) mg/kg. The Meeting estimated the maximum residue level, STMR and HR of 0.05*, 0 and 0 mg/kg respectively for tree nuts.

Coffee

GAP in Brazil on coffee is two applications at rate of 50–100 g ai/ha with a PHI of 15 days. In trials on coffee conducted in Brazil matching the GAP, residues in coffee beans were: (n=8) < 0.01(3), < 0.025(3), 0.03 and 0.04 mg/kg. The Meeting estimated the maximum residue level, STMR and HR of 0.07, 0.025 and 0.04 mg/kg respectively for coffee bean.

Hops

GAP in Europe (Austria) on hop is one application at rate of 76.8–268.8 g ai/ha with a PHI of 21 days. In trials conducted in Germany and Japan approximating the Austrian GAP, residues of fenpyroximate in dried hops were: (n=6) 1.2, 3.7, 4.3, 5.0, 7.4 and 8.2 mg/kg. The residues of fenpyroximate and M-1 were: 2.2, 4.7, 5.0, 5.3, 7.4 and 8.2 mg/kg. The Meeting estimated the maximum residue level, STMR of 15, 5.15 mg/kg respectively for hops, dry, and replaced the previous recommendation of 10 mg/kg.

Tea

GAP in India on tea is one application at rate of 25 g ai/ha with a PHI of 7 days. In trials conducted in India approximating Indian GAP, residues of fenpyroximate in tea leaves were (n=10): 0.3, 0.68, 0.93, 0.95, 1.2, 1.4, 1.8, 3.01, 3,7 and 3.9 mg/kg. The residues of fenpyroximate and M-1 were: 0.33, 0.71, 0.98(2), 1.3, 1.5, 1.8, 3.0, 3.8 and 4.1 mg/kg. The Meeting estimated the maximum residue level and STMR of 8 and 1.4 mg/kg, respectively, for tea, green, black, dry.

Animal feed items

Bean forage

The GAP in the USA on bean is two applications at rate of 117 g ai/ha with a PHI of 1 days. In trials conducted in USA matching the US GAP, residues of fenpyroximate and M-1 in forage of bean were: (n=8) < 0.1(2), 1.2, 2.6, 3.0, 3.1, 4.5 and 6.8 mg/kg. The Meeting estimated the median residues and high residues of 2.8 and 7.5 (highest individual) mg/kg for bean forage.

Maize forage and stover

The GAP in the USA on maize is two applications at rate of 117 g ai/ha with a PHI of 14 days.

In trials conducted in USA matching the US GAP, residues of fenpyroximate and M-1 in maize forage were: (n=9) 0.31, 0.32, 0.33, 0.37, 0.38, 0.47, 0.58, 0.81 and1.12 mg/kg. The residues of fenpyroximate in maize stover were: (n=10) 0.17, 1.0, 1.0, 1.1, 1.1, 1.5, 1.6, 1.6, 1.8 and 2.2 mg/kg. The residues of fenpyroximate and M-1 in maize stover were: (n=10) 0.30, 1.4, 1.4, 1.6, 1.9, 2.2, 2.5, 3.0, 3.3 and 3.9 mg/kg. The Meeting estimated the median residues and highest residue of 0.38 and 1.3 (highest individual) mg/kg for maize forage, maximum residue level of 5 mg/kg, median residue of 2.05 and highest residue of 4.1 mg/kg (highest individual) for maize fodder.

Maize silage

GAP in Europe on maize is one applications at rate of 50 g ai/ha with a PHI of 28 days. In trials conducted in Hungary matching the GAP, residues in maize silage grains were: (n=2) 0.24 and 0.90 mg/kg. Two trials are not sufficient for recommendation.

Almond hulls

GAP in US on tree nut (US crop group 14) is two applications at rate of 117 g ai/ha with a PHI of 14 days. In trials on almond conducted in USA with exaggerated rate (one application of 450 g ai/ha 14 days PHI), residues in almond hull were: (n=5) 0.76, 0.92 1.2, 1.3, 1.4 mg/kg. No trials conducted matching GAP.

Fate of residues during processing

The Meeting received information on the fate of incurred residues of fenpyroximate during the processing of beans, apples, tomatoes, grapes strawberries and orange.

Hydrolysis

The Meeting received information on the nature of the residues of fenpyroximate under simulated processing conditions (pasteurization: 20 minutes at 90 °C and pH 4, baking/brewing/boiling: 60

minutes at 100 °C and pH 5, sterilization: 20 minutes at 120 °C and pH 6), fenpyroximate was not hydrolytically stable under processing conditions representative of sterilisation, pasteurisation, and brewing, baking and boiling. M-3 (41–89%) was detected as predominant product of hydrolysis in all conditions, with M-6 (< 3%) as minor hydrolysis products. M-1(< 2%) was only detected in under pasteurisation condition.

The fate of fenpyroximate residues has been investigated in a number of studies simulating household or commercial processing of beans, apples, tomatoes, grapes, strawberries, potatoes, orange, maize and tea. Residues of M-3 were < 0.01 mg/kg in all processed commodities except canned beans (up to 0.07 mg/kg) and strawberry jam (0.02 mg/kg).

Processing studies were conducted with exaggerated residues of fenpyroximate (relative to field trial residues) in RAC commodities of apple, bean, grape, strawberry, maize, and tea. Residues of M-3 were < 0.01 mg/kg in all processed commodities except canned beans (up to 0.07 mg/kg) and strawberry jam (0.02 mg/kg). These levels of M-3 were less than 15% of the residues of parent compound. Therefore, the Meeting decided that M-3 were not included in calculation for processing factor.

The residues of fenpyroximate increase in some dried or concentrated commodities (apple pomace, dry apple, grape raisin, aspirated grain fraction of maize, orange oil and dry orange)

Processing factors calculated from sum of fenpyroximate and M-1, and estimated STMR-P and HR-P

	Processed Fraction	Processing Factor	Best estimate PF	RAC STMR or STMR-P*	RAC HR or HR-P*
Beans	Fresh beans (RAC)			0.08	0.42
	Washed beans	1.2, 0.89	1.045	0.084	0.44
	Cooked beans	0.73, 0.47	0.6	0.048	0.25
	Canned beans	0.42, 0.46	0.44	0.035	0.18
Apples	Fresh apple (RAC)			0.075	0.15
	Washed fruits	0.71, 1.1	0.905	0.679	0.136
	Wet Pomace	2.2, 5.5	3.85	0.289	
	Dry Pomace	5.1, 12.0	8.55	0.641	
	Pasteurised juice	0.18, 0.14	0.16	0.012	
	Pasteurised sauce	0.18, 0.18	0.18	0.0135	
	Dried apples	3.8, 5.0	4.4	0.33	0.66
Tomatoes	Whole tomato (RAC)			0.1	0.17
	Washed tomatoes	0.92, 0.83	0.875	0.088	0.15
	Tomato juice	0.85, 0.42	0.635	0.064	
	Canned tomatoes	0.54, 0.25	0.395	0.04	0.067
	Puree	0.76, 0.67	0.715	0.072	
Grapes	Whole fruit (RAC)			0.035	0.06
	Wet pomace	4.7, 5.1	4.9	0.19	
	Wine	0.27, 0.04	0.155	0.005	
	Pasteurised juice	0.27, 0.04	0.155	0.005	
	Washed grapes	0.82, 0.60	0.71	0.025	0.043
	Raisins	2.9, 1.1	2	0.07	0.12
Strawberries	Whole fruit (RAC)			0.06	0.2
	Washed fruit	0.53, 0.58	0.555	0.0333	0.111
	Canned fruit	0.05, 0.19	0.12	0.0072	
	Jam	0.19, 0.38	0.285	0.0171	
Orange	Fresh fruits (RAC)			0.15	0.28
	Juice	< 0.019, < 0.044	0.032	0.0048	
	Molasses	0.093, 0.046	0.07	0.011	
	Oil	72.2, 13.3	43	6.5	
	Dried fruit	5.3, 5.0	5.2	0.78	1.5
Tea	Dry tea leave			1.5	4.1
	infusion	0.0069, 0.0068 0.013, 0.019 0.0069, 0.0070 0.0088	0.0098	0.015	0.04

	Processed Fraction	Processing Factor	Best estimate PF	RAC STMR or STMR-P*	RAC HR or HR-P*
Maize	Grains (RAC)			0.01	
	Grits	0.016	0.016	0.00016	
	Meal	0.15	0.15	0.0015	
	Flour	0.37	0.37	0.0037	
	Refined oil (dry milling)	0.99	0.99	0.0099	
	Refined oil (wet milling)	0.31	0.31	0.0031	
	Aspirated grain fraction	86	86	0.86	

*: STMR-P or HR-P was calculated by processing factor of fenpyroximate and M-1.

Processing factors calculated from fenpyroximate for estimation of MRL

	Processed Fraction	Processing Factor	Best estimate PF	MRL*
Apples	RAW			0.2
	Dried apples	3.8, 4,9	4.4	1
Grapes	RAW			0.1
	Raisins	2.9, 1.04	2.0	0.2
Orange	Fresh fruits (RAC)			0.6
	Oil	74, 4,7	39	25

*MRL for processed commodities was calculated by processing factor of fenpyroximate.

As residues in dried apple are higher than residues in apple fruit, the Meeting estimated a maximum residue level of 1 (0.2×4.4) mg/kg for dried apples.

As residues in orange oil are higher than residues in orange fruit, the Meeting estimated a maximum residue level of 25 (0.6×39) mg/kg for citrus oil.

As residues in grape raisin are higher than residues in grape berry, the Meeting estimated a maximum residue level of 0.2 (0.1×2) mg/kg for grape, dry, and replaced the previous recommendation of 0.3 mg/kg.

Residues in animal commodities

Farm animal feeding studies

The Meeting received information on the residue levels in tissues and milk of dairy cows dosed with fenpyroximate at the equivalent of 1.0, 3.0 and 10 ppm in the feed for 28 consecutive days.

Residues of fenpyroximate/Fen-OH and M-3 in milk from high dose group reached plateau of 0.017 mg/kg at 3 days after the first dose and were 0.010 mg/kg at day 28. Residues of fenpyroximate/Fen-OH and M-3 in milk from high dose group were 0.006–0.022 mg/kg, from low and median dose group were < 0.008 mg/kg for all samples. Other minor metabolites were < 0.005mg/kg.

Residues of fenpyroximate/Fen-OH and M-3 in liver from high dose group were 0.71–0.911 mg/kg, 0.28–0.42 mg/kg from median, 0.16–0.22 from low dose group. Other metabolites were less than 0.01 mg/kg from high dose group or undetected.

Residues of fenpyroximate/Fen-OH and M-3 in kidney from high dose group were 0.359–0.459 mg/kg, 0.24–0.36 mg/kg from median dose group, and 0.18–0.23 mg/kg from low dose group. Other metabolites were either less than 0.01 mg/kg or undetected.

Residues of fenpyroximate/Fen-OH and M-3 in muscle from high, median and low dose group were 0.025–0.059, 0.012–0.017 and < 0.01 mg/kg, with other metabolites (including M-3) less than 0.01mg/kg or undetected.

Residues of fenpyroximate/Fen-OH and M-3 in fat from high, median and low dose group were 0.046–0.169, 0.035–0.083 and 0.01–0.018 mg/kg, with no other metabolites above 0.01mg/kg.

A laying hens feeding study was not available.

Estimation of livestock dietary burdens

Potential cattle feed items include: bean forage, corn, corn forage and stover, apple pomace and dry citrus pulp. Dietary burden calculations for beef cattle and dairy cattle and poultry are provided below. The dietary burdens were estimated using the OECD diets listed in Appendix IX of the 2017 edition of the FAO Manual.

Summary of livestock dietary burden (ppm fenpyroximate equivalents of dry matter diet) (to be finished)

	US-Canada		EU		Australia(		Japan	
	Max	Mean	Max	mean	max	Mean	max	Mean
Beef cattle	0.885	0.524	3.49	1.625	14.8 (3.503)	5.812 (1.595)	0.009	0.009
Dairy cattle	1.956	0.905	6.89	2.81	16.5 (3.503)[AB]	6.36 (1.595)[CD]	1.63	0.48
Broilers	0.00852	0.00852	0.01	0.01			0.01	0.01
Layers	0.00852	0.00852	0.5(0.502)[E]	0.26(0.255)[F]			0.01	0.01

[A] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat

[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 meat.

[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 meat and eggs

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

The Meeting noted that the calculated maximum animal burden (16.5 ppm) was from Australia (mainly from bean forage). As fenpyroximate is not registered for use in bean in Australia and Australia doesn't import any forage, the meeting decided to refine the animal burden calculation (to exclude bean forage). The refined calculation of Dietary burden for beef cattle and dairy cattle for Australia is shown in (parentheses).

Animal commodity maximum residue levels

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

	Feed level ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues (mg/kg)			
				Muscle	liver	Kidney	Fat
MRL (mg/kg), beef or dairy cattle							
Feeding study	3	0.005	3	0.017	0.42	0.36	0.083
	10	0.013	10	0.059	0.91	0.459	0.169
Dietary burden and high residue estimation	3.503	0.0056	3.503	0.020	0.455	0.367	0.089
STMR (mg/kg), beef or dairy cattle							
Feeding study	1	0	1	< 0.01	0.19	0.20	0.015
	3	0.005		3	0.015	0.30	0.066
Dietary burden and median residue estimated	1.595	0.0015	1.595	0.011	0.24	0.23	0.03

The Meeting estimated a maximum residue level of 0.01* mg/kg for fenpyroximate for milk, of 0.1 mg/kg for mammalian meat (fat), of 0.5 mg/kg for edible offal (mammalian) and 0.1 mg/kg for mammalian fats. The Meeting estimated an STMR of 0.0015 mg/kg for milk, of 0.011 mg/ kg for mammalian meat, 0.24 mg/kg for edible offal (mammalian) and 0.03 mg/kg for mammalian fat.

Since neither feeding study nor metabolism study on laying hens was available, the Meeting was unable to estimate maximum residue level for poultry commodities.

RECOMMENDATIONS

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

Definition of the residue (for compliance with MRLs) for plant commodities: *fenpyroximate.*

Definition of the residue (for dietary risk assessment) for plant commodities: *sum of parent fenpyroximate and itert-butyl (Z)-α-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethyleneamino-oxy)-p-toluate (its Z-isomer M-1), expressed as fenpyroximate.*

Definition of the residue (for compliance with the MRL) for animal commodities: *sum of fenpyroximate, 2-hydroxymethyl-2-propyl (E)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)-methylenaminooxymethyl]benzoate(Fen-OH), and (E)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoic acid(M-3), expressed as fenpyroximate*.

Definition of the residue (for dietary risk assessment) for animal commodities: *sum of fenpyroximate, 2-hydroxymethyl-2-propyl (E)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)-methylenaminooxymethyl]benzoate(Fen-OH), (E)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoic acid(M-3), and (E)-4-{[(1,3-dimethyl-5-(4-hydroxyphenoxy)pyrazol-4-yl]methyleneaminooxymethyl}benzoic acid (M-5, free and its conjugates), expressed as fenpyroximate.*

The residue is fat soluble.

Desirable information

Information on feeding study and metabolism on laying hen is desired for estimation of maximum residue level for poultry commodities.

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The IEDI of fenpyroximate based on the STMRs estimated by this Meetings for the 17 GEMS/Food regional diets were 3–10% of the maximum ADI of 0.01 mg/kg bw. The Meeting concluded that the long-term dietary intake of residues of fenpyroximate is unlikely to present a public health concern.

Short-term dietary exposure

An ARfD for fenyroximate is 0.01 mg/kg bw. The Meeting estimated the International Estimated Short-Term Intake (IESTI) of fenpyroximate for commodities for which STMR, HR and maximum residue levels were estimated by the current Meeting. The IESTI were less than 100% of a maximum ARfD for the commodities estimated, except for cherry (110% for children from Netherland and Denmark), peach (130% for children from Japan and Canada), watermelon (190% for children from Canada), dried tomato (310% the for general population from Australia), and dried plums (270% for children from Australia). The Meeting concluded that the short-term intake of fenpyroximate residues from uses considered by the current Meeting may present a public health concern for these commodities.