5.20 FLUXAPYROXAD (256)

TOXICOLOGY

Fluxapyroxad is the ISO-approved name for 3-(fluoromethyl)-1-methyl-*N*-(3′,4′,5′-trifluoro[1,1′-biphenyl]-2-yl)-1H-pyrazole-4-carboxamide (IUPAC) (CAS No. 907204-31-3). It is a fungicide that belongs to the carboxamide class. Its proposed fungicidal mode of action is inhibition of succinate dehydrogenase, resulting in the inhibition of the citric acid cycle and mitochondrial electron transport pathways.

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

All the critical studies contained certificates of compliance with GLP.

Biochemical aspects

In rats, ^{14}C-labelled fluxapyroxad was rapidly and moderately well absorbed from the gastrointestinal tract following oral dosing. The extent of absorption was approximately 65–80% of the administered dose, independent of dose and sex. Maximum concentrations of radioactivity in plasma were observed within 1 hour of dosing for the low-dose group (5 mg/kg bw), 8 hours for the mid-dose group (50 mg/kg bw) and 24 hours for the high-dose group (500 mg/kg bw). In another study in rats, maximum tissue concentrations occurred within 1 hour post-dosing at the low dose (7.5 mg/kg bw) and 16 hours post-dosing at the high dose (150 mg/kg bw), with higher concentrations of radioactivity found in liver, thyroid and adrenals. Very little fluxapyroxad was present in other tissues at the end of the study (7 days). There were no major sex-related differences in the pattern of excretion. Faecal excretion was the primary route of elimination, and excretion was rapid, with the majority of the administered dose (61–83%) excreted by all routes within 48 hours after dosing.

The main biotransformation mechanisms of fluxapyroxad in rats are hydroxylation at the biphenyl ring, *N*-demethylation at the pyrazole ring, loss of a fluorine atom at the biphenyl ring and conjugation with glucuronic acid or glutathione, yielding about 50 metabolites.

Toxicological data

The LD_{50} in rats treated orally or dermally with fluxapyroxad was greater than 2000 mg/kg bw. The LC_{50} in rats treated by inhalation was greater than 5.1 mg/L of air. Fluxapyroxad was minimally irritating to the skin of rabbits, not irritating to the eyes of rabbits and not sensitizing in guinea-pigs under the conditions of the maximization test.

Following repeated gavage or dietary dosing, the liver was the main target organ in mice, rats and dogs. In general, the main effects in mice and rats were increased liver weight, liver enlargement and centrilobular hepatocellular hypertrophy, as well as alterations in clinical chemistry. In the dog, increased liver weights and alterations in clinical chemistry were accompanied by fibrosis. The thyroid was also a target in mice and rats, with effects including increased thyroid weight, changes in hormone levels (thyroxine and thyroid stimulating hormone) and thyroid follicular cell hypertrophy and hyperplasia. Other treatment-related effects at higher doses consisted of siderosis and impaired iron storage in rats and dogs, as well as teeth whitening and shortened prothrombin time in rats only.

The NOAEL in a 90-day rat study was 100 ppm (equal to 7.3 mg/kg bw per day), based on liver and thyroid effects in females (increased absolute and relative liver weights, increased incidences of centrilobular hepatocellular hypertrophy and hypertrophy/hyperplasia of thyroid follicular cells) at 500 ppm (equal to 35.1 mg/kg bw per day). The NOAEL in a 90-day mouse study was 2000 ppm (equal to 390 mg/kg bw per day), based on decreased body weight and multifocal necrosis in the liver in males at 6000 ppm (equal to 1136 mg/kg bw per day). The NOAEL in a 1-year dog study was 300 ppm (equal to 9 mg/kg bw per day), based on clinical chemistry alterations and fibrosis in the liver in females at 1500 ppm (equal to 43 mg/kg bw per day).

In an 18-month carcinogenicity study in mice, the NOAEL was 750 ppm (equal to 107 mg/kg bw per day), based on decreased body weight gain at 3000 ppm (equal to 468 mg/kg bw per day). There was no evidence of carcinogenicity in mice.

In a 2-year rat study, the NOAEL was 50 ppm (equal to 2.1 mg/kg bw per day), based on reduced body weight gain in the absence of an effect on feed consumption at 250 ppm (equal to 11 mg/kg bw per day). The incidence of combined hepatocellular adenomas and carcinomas in males was increased at the top two doses of 1500 ppm (equal to 68 mg/kg bw per day) and 3000 ppm (equal to 145 mg/kg bw per day), and there was an increased incidence of hepatocellular adenomas in females at the highest dose (3000 ppm, equal to 145 mg/kg bw per day); this incidence also slightly exceeded the historical control range. There was a small increase in the incidence of thyroid follicular cell adenomas and carcinomas in males at the highest dose tested; this incidence was within the historical control range (4–30%), but above the historical control mean (15%). The incidence and severity of follicular cell hyperplasia were increased starting at 1500 ppm (equal to 68 mg/kg bw per day). The Meeting concluded that high doses of fluxapyroxad caused an increased incidence of hepatocellular adenomas and carcinomas in males, hepatocellular adenomas in females, and follicular cell adenomas and carcinomas combined in the thyroid in males.

Special studies were conducted to examine liver effects in the rat. These studies showed that fluxapyroxad increased microsomal protein levels and cytochrome P450 activity, specifically benzyloxyresorufin *O*-dealkylase and pentoxyresorufin *O*-dealkylase, and cell proliferation in the liver of rats. The Meeting concluded that for the liver tumours in rats, there was sufficient evidence to support the proposed mitogenic mode of action associated with induction of CYP2B-type cytochrome P450. Special studies on the mode of action in the thyroid produced equivocal results.

Fluxapyroxad was adequately tested for genotoxicity in vitro and in vivo in a range of assays and was not found to be genotoxic.

The Meeting concluded that fluxapyroxad was unlikely to be genotoxic.

On the basis of the lack of genotoxicity, the absence of carcinogenicity in mice and the presence of liver and thyroid follicular cell tumours in rats only at high doses, the Meeting concluded that fluxapyroxad is unlikely to pose a carcinogenic risk to humans at anticipated dietary residue levels.

No effects on reproduction were noted in a multigeneration reproductive toxicity study in the rat. However, there was a decrease in body weight and increased incidences of hepatocellular hypertrophy and thyroid follicular cell hypertrophy/hyperplasia in the offspring in both generations at 50 mg/kg bw per day and above. The marginal increase in the incidence of very slight hepatocellular hypertrophy at 10 mg/kg bw per day in F_1 offspring was not considered to be toxicologically relevant. At the high dose only, whitening of the incisors due to a decrease in iron-containing pigment in ameloblasts was observed. The NOAEL for parental toxicity was 10 mg/kg bw per day, based on decreased body weight gain and effects on the liver and thyroid at 50 mg/kg bw per day. The NOAEL for offspring toxicity was 10 mg/kg bw per day, based on reduced body weight and body weight gain and liver effects at 50 mg/kg bw per day. The NOAEL for reproductive toxicity was 300 mg/kg bw per day, the highest dose tested.

In a developmental toxicity study in rats, there were no effects on development observed when pregnant rats were administered doses up to 1000 mg/kg bw per day. There was a transient decrease in body weight gain from GD 6 to GD 8 in dams at and above 200 mg/kg bw per day. Increased liver and thyroid weights and increased incidences of thyroid follicular hypertrophy/hyperplasia were observed in maternal animals at 1000 mg/kg bw per day. The NOAEL for maternal toxicity in rats was 25 mg/kg bw per day, and the NOAEL for developmental toxicity was 1000 mg/kg bw per day, the highest dose tested. In rabbits, there was an increase in early resorptions, as well as one abortion, and a decrease in fetal weight at the high dose (60 mg/kg bw per day), which occurred in the presence of a marked reduction in feed consumption and body weight. Fetal weights were also reduced, and there was an increased incidence of paw hyperflexion at the high dose. The NOAEL for maternal and developmental toxicity in rabbits was 25 mg/kg bw per day.

The Meeting concluded that fluxapyroxad was not teratogenic in rats or rabbits.

In an acute neurotoxicity study in rats, the NOAEL was 125 mg/kg bw, based on decreased motor activity and rearing at a dose of 500 mg/kg bw. There was no histological evidence of damage to the central or peripheral nervous system. There was no evidence of neurotoxicity in a 90-day neurotoxicity study in rats.

In a 4-week immunotoxicity study in mice, no adverse effects were observed at any dose up to 6000 ppm (equal to 1323 mg/kg bw per day), the highest dose tested.

Three minor metabolites in rats that are also found in plants and soil were assessed for toxicity. The oral LD_{50} in rats for the metabolite M700F001 was greater than 2000 mg/kg bw. In a 90-day feeding study in rats, the NOAEL for M700F001 was 954 mg/kg bw per day, the highest dose tested. The metabolite was not genotoxic in any of an adequate range of in vitro and in vivo genotoxicity assays. In a developmental toxicity study in rabbits, the maternal and developmental NOAEL was 250 mg/kg bw per day, the highest dose tested.

The oral LD_{50} in rats for the metabolite M700F002 was greater than 2000 mg/kg bw. In a 28-day dietary study of M700F002 in rats, the NOAEL was 1165 mg/kg bw per day, the highest dose tested. In a 90-day feeding study in rats, the NOAEL for M700F002 was 958 mg/kg bw per day, the highest dose tested. This metabolite was not genotoxic in any of an adequate range of in vitro and in vivo genotoxicity assays. In a developmental toxicity study in rabbits, the maternal and developmental NOAEL was 300 mg/kg bw per day, based on increased maternal mortality, abortions and stomach erosions as well as decreased body weight gain at 1000 mg/kg bw per day.

The oral LD_{50} in rats for the metabolite M700F048 was greater than 2000 mg/kg bw. In a 28-day dietary study of M700F048 in rats, the NOAEL was 189 mg/kg bw per day, based on decreased body weight gain at 1478 mg/kg bw per day. This metabolite was not genotoxic in any of an adequate range of in vitro and in vivo genotoxicity assays. In a developmental toxicity study in rabbits, the maternal and developmental NOAEL was 30 mg/kg bw per day, based on increased maternal mortality, abortions, late resorptions and stomach erosions as well as decreased body weight gain at 100 mg/kg bw per day.

The metabolites were not considered to be more toxic than fluxapyroxad.

There was no information available on adverse health effects in manufacturing plant personnel or in operators and workers exposed to fluxapyroxad formulations during their use. There are no reports of poisoning with fluxapyroxad.

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

Toxicological evaluation

The Meeting established an ADI of 0–0.02 mg/kg bw on the basis of the NOAEL of 2.1 mg/kg bw per day in the 2-year rat combined chronic toxicity/carcinogenicity study for body weight effects in both sexes in the absence of effects on feed consumption. A safety factor of 100 was applied.

The Meeting established an ARfD of 0.3 mg/kg bw on the basis of the NOAEL of 25 mg/kg bw per day in the developmental toxicity study in rabbits for early resorptions and the rat developmental toxicity study based on a transient decrease in body weight gain from GD 6 to GD 8. A safety factor of 100 was applied.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Eighteen-month study of toxicity and carcinogenicity[a]	Toxicity	750 ppm, equal to 107 mg/kg bw per day	3000 ppm, equal to 468 mg/kg bw per day

Species	Study	Effect	NOAEL	LOAEL
		Carcinogenicity	6000 ppm, equal to 1119 mg/kg bw per day[b]	—
Rat	Two-year study of toxicity and carcinogenicity[a]	Toxicity	50 ppm, equal to 2.1 mg/kg bw per day	250 ppm, equal to 11 mg/kg bw per day
		Carcinogenicity	250 ppm, equal to 11 mg/kg bw per day	1500 ppm, equal to 68 mg/kg bw per day
	Two-generation study of reproductive toxicity[a]	Reproductive toxicity	300 mg/kg bw per day[b]	—
		Parental toxicity	10 mg/kg bw per day	50 mg/kg bw per day
		Offspring toxicity	10 mg/kg bw per day	50 mg/kg bw per day
	Developmental toxicity study[c]	Maternal toxicity	25 mg/kg bw per day	200 mg/kg bw per day
		Embryo and fetal toxicity	1000 mg/kg bw per day[b]	—
Rabbit	Developmental toxicity study[c]	Maternal toxicity	25 mg/kg bw per day	60 mg/kg bw per day
		Embryo and fetal toxicity	25 mg/kg bw per day	60 mg/kg bw per day
Dog	One-year study of toxicity[a]	Toxicity	300 ppm, equal to 9 mg/kg bw per day	1500 ppm, equal to 43 mg/kg bw per day

[a] Dietary administration.

[b] Highest dose tested.

[c] Gavage administration.

Estimate of acceptable daily intake for humans

0–0.02 mg/kg bw

Estimate of acute reference dose

0.3 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 fluxapyroxad

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid; to a moderate extent
Dermal absorption	Not available
Distribution	Widely distributed; highest concentrations in liver, thyroid and adrenals
Potential for accumulation	No evidence of accumulation
Rate and extent of excretion	Largely complete within 24 h; primarily via faeces (70–85%, bile 30–54%) and to a lesser extent urine (8–17%)
Metabolism in animals	Extensive
Toxicologically significant compounds in animals, plants and the environment	Parent compound, M007F048
Acute toxicity	
Rat, LD_{50}, oral	> 2000 mg/kg bw
Rat, LD_{50}, dermal	> 2000 mg/kg bw

Rat, LC_{50}, inhalation	> 5.1 mg/L
Rabbit, dermal irritation	Minimally irritating
Rabbit, ocular irritation	Not irritating
Dermal sensitization	Not sensitizing (Magnusson & Kligman)
Short-term studies of toxicity	
Target/critical effect	Liver (clinical chemistry changes), thyroid (hypertrophy/hyperplasia)
Lowest relevant oral NOAEL	7.3 mg/kg bw per day (rats)
Lowest relevant dermal NOAEL	1000 mg/kg bw per day (rats)
Lowest relevant inhalation NOAEC	No data
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Body weight
Lowest relevant NOAEL	2.1 mg/kg bw per day (rats)
Carcinogenicity	Liver and thyroid tumours observed in rats at high doses; unlikely to pose a carcinogenic risk to humans at anticipated dietary intake levels
Genotoxicity	
	Not genotoxic
Reproductive toxicity	
Target/critical effect	No effect on fertility at highest dose tested; decrease in body weight, liver and thyroid effects in pups at parentally toxic dose
Lowest relevant parental NOAEL	10 mg/kg bw per day
Lowest relevant reproductive NOAEL	300 mg/kg bw per day (highest dose tested)
Lowest relevant offspring NOAEL	10 mg/kg bw per day
Developmental toxicity	
Target/critical effect	Decreased fetal weight and paw hyperflexion at maternally toxic dose (rabbits)
Lowest relevant maternal NOAEL	25 mg/kg bw per day (rats and rabbits)
Lowest relevant developmental NOAEL	25 mg/kg bw per day (rabbits)
Neurotoxicity	
Target/critical effect	Decreased motor activity and rearing
Acute neurotoxicity NOAEL	125 mg/kg bw (rats)
Immunotoxicity	
	1323 mg/kg bw per day (highest dose tested; mice)
Other toxicological studies	
	Toxicity studies on metabolites Special studies on liver and thyroid tumour modes of action
Medical data	
	No reports received

Summary

	Value	Study	Safety factor
ADI	0–0.02 mg/kg bw	Two-year toxicity/carcinogenicity study (rat)	100
ARfD	0.3 mg/kg bw	Developmental toxicity studies (rat and rabbit)	100

RESIDUE AND ANALYTICAL ASPECTS

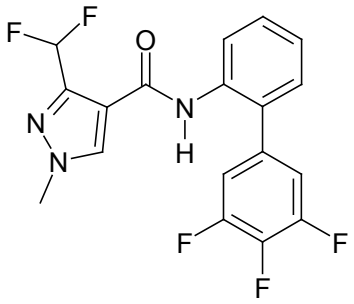
Residue and toxicological aspects of fluxapyroxad were considered for the first time by the present Meeting. The toxicological and residue evaluation was scheduled by the Forty-second Session of the CCPR[1].

[1] ALINORM 10/33/24

Fluxapyroxad is a new active ingredient developed to control a broad spectrum of fungal diseases. It belongs to the carboxamide class of chemicals and its mode of action is inhibition of succinate dehydrogenase in complex II of the mitochondrial respiratory chain, which results in inhibition of spore germination, germ tubes and mycelial growth within the fungus target species.

The manufacturer supplied information on identity, metabolism and environmental fate, methods of residue analysis, freezer storage stability, registered use patterns, supervised residue trials, fate of residues in processing and farm animal feeding studies.

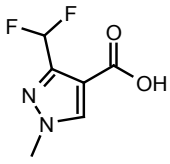
The IUPAC name is 3-(difluoromethyl)-1-methyl-N- (3′,4′,5′-trifluoro [1,1′-biphenyl]-2-yl)-1H-pyrazole-4-carboxamide.



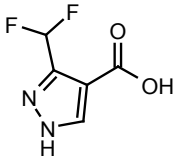
Fluxapyroxad

The 2012 JMPR established an ADI for fluxapyroxad of 0–0.02 mg/kg bw and an ARfD of 0.3 mg/kg bw.

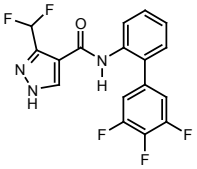
The structures of key metabolites discussed are listed below:



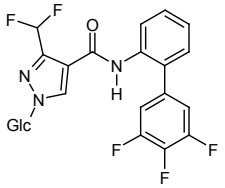
M700F001



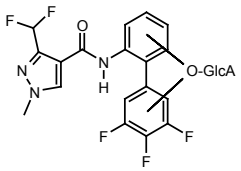
M700F002



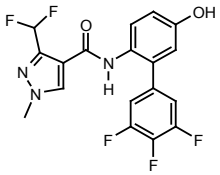
M700F008



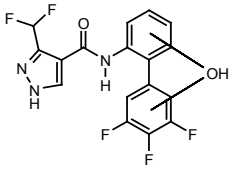
M700F048



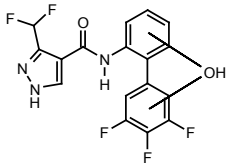
M700F004



M700F005



M700F009



M700F010

Animal metabolism

The Meeting received animal metabolism studies with fluxapyroxad in rats, hens and goats.

Rats

Evaluation of the metabolism studies in rats, which was carried out by the WHO Core Assessment Group, showed that ^{14}C-labelled fluxapyroxad was rapidly and moderately well absorbed from the gastrointestinal tract of rats following oral dosing. The extent of absorption was approximately 65–80% of the administered dose, independent of dose and sex. Very little fluxapyroxad was retained in the tissues. There were no major sex-related differences in the pattern of excretion. Faecal excretion was the primary route of elimination, and excretion was rapid, with the majority excreted by all routes 48 hours after dosing (61–83%). Fluxapyroxad in rats is metabolized mainly by hydroxylation at the

biphenyl moiety (sometimes repeated), loss of a fluorine atom at the biphenyl ring, N-demethylation at the pyrazole moiety, conjugation of the hydroxyl-groups with glucuronic acid or with sulfate and conjugation with glutathione derivatives.

Goats - Fluxapyroxad

Fluxapyroxad labelled in the aniline or pyrazole ring was orally administered by gavage to lactating goats at 11.33–11.75 ppm in the feed or 0.39–0.44 mg/kg bw/day for 8 consecutive days. Milk was sampled twice daily (in the morning before administration of the test substance and in the afternoon). Animals were sacrificed approximately 24 hours after the last dose.

Overall, ≥ 80% of the total administered dose was eliminated in excreta. In milk, 0.09–0.10% of the administered dose was detected. A plateau was reached within 24 hours after administration. Tissues and organs retained < 0.4% of the administered dose. TRRs were 0.007–0.009 mg/kg equiv. in muscle, 0.021–0.025 mg/kg equiv. in fat, 0.036–0.078 mg/kg equiv. in kidney and 0.35–0.56 mg/kg equiv. in liver. The extractability of the radioactive residues in methanol or acetonitrile was ≥ 79% for all tissues other than liver. In liver, extractability was 30–34%. A major proportion of the residual radioactive residues (polar components, probably bound to proteins) was released from extracted liver tissue after incubation with protease.

Fluxapyroxad represented one of the major residues in milk (13–20% of the TRRs, 0.0015–0.0033 mg/kg equiv.), muscle (12%, 0.0009 mg/kg equiv., aniline label only) and fat (34–44% of the TRRs, 0.0084–0.0092 mg/kg equiv.), while accounting for minor proportions in liver and kidney (3–7% of the TRRs, 0.0025–0.020 mg/kg equiv.). The other predominant compound was the desmethyl metabolite M700F008, representing a main proportion in milk (24–25% of the TRRs, 0.0027–0.0043 mg/kg equiv.), muscle (55–83% of the TRRs, 0.0041–0.0078 mg/kg equiv.), fat (26% of the TRRs, 0.0054–0.0064 mg/kg equiv.), liver (13–17% of the TRRs, 0.058–0.071 mg/kg equiv.) and kidney (23–26% of the TRRs, 0.0093–0.017 mg/kg equiv).

Further metabolites at > 10% of the TRRs were detected in milk, kidney and fat. In milk, the metabolite M700F010 was found at levels of 12–15% of the TRRs (≤ 0.0025 mg/kg). The metabolite M700F005 was present in fat at 14% of the TRRs (0.0034 mg/kg equiv.) and in kidney at 19% of the TRRs (0.015 mg/kg equiv.), with pyrazole label only. The metabolite M700F004 was present in kidney at levels of 12–13% of the TRRs (≤ 0.010 mg/kg equiv.).

With both labels, comparable metabolic pathways were observed. Hydrolytic cleavage of fluxapyroxad at the carboxamide bond was not seen. Fluxapyroxad was metabolized *via* two main transformation reactions, N-demethylation of the pyrazole moiety and hydroxylation of the biphenyl moiety. These reactions, occurring also in combination, followed by conjugation with glucuronic acid, led to the main metabolites. Several minor metabolic routes, i.e., hydroxylation at the pyrazole ring, conversion of the pyrazole CHF_2 group into a carboxy group, N-glucuronidation of the desmethyl metabolite and removal of an aromatic fluorine substituent, led to a range of minor components.

Goats – M700F002

Since the metabolite M700F002 was observed in soya bean seed and in confined rotational crop matrices at levels > 10% of the TRRs, livestock metabolism studies were conducted with this compound.

The test item ^{14}C-labelled on the carbon of the pyrazole ring bearing the carboxyl group, was fed to two lactating goats for eight consecutive days at 11.0–12.5 ppm in the feed, 0.38–0.42 mg/kg bw/day. Milk was collected in the morning before administration of the test item and in the afternoon. Animals were sacrificed approximately 4 hours after the final dose. Of the applied dose, 32% was found in urine and 54% in faeces. Milk contained 0.05% of the applied dose. Residues remaining in whole organs accounted for < 0.04% of the administered dose. Residues were 0.006 mg/kg equiv. in fat, 0.012 mg/kg equiv. in muscle, 0.023 mg/kg equiv. in liver and 0.146 mg/kg equiv. in kidney. In total, 98% of the applied dose could be recovered. In goat, the test item M700F002 was the only

radioactive component detected in the matrices analysed, indicating that M700F002 is not significantly transformed in the goat.

Goats – M700F048

Metabolism studies were also conducted on lactating goats with M700F048, a plant metabolite of fluxapyroxad which was not observed in animals. ^{14}C-M700F048, labelled in the aniline moiety was fed to two lactating goats at doses of 12.94 and 12.80 ppm in the feed, 0.39 and 0.40 mg/kg bw/day, for ten consecutive days. Milk was collected in the morning before administration of the test item and in the afternoon. Animals were sacrificed within 20 hours after the last dose. Excreta accounted for 92.4% of the M700F048 administered. The pooled milk sample (Day 4–10) contained 0.045% of the applied dose. Overall, < 0.5% of the total administered dose was found in tissues and organs. The TRRs in organs and tissues amounted to 0.575 mg/kg equiv. for liver, 0.075 mg/kg equiv. for kidney, 0.033 mg/kg equiv. for fat and 0.011 mg/kg equiv. for muscle.

M700F048 was found at ≤ 3% of the TRRs in milk and tissues. In muscle and liver, no M700F048 was detected. One of the main components identified in all matrices was the deglycosylated metabolite M700F008, accounting for 14–54% of the TRRs. Further biotransformation products were the biphenyl-hydroxylated metabolites M700F009 and M700F010. M700F010 was the main metabolite identified in milk (32% of the TRRs) and was also detected in higher portions in kidney (14% of the TRRs).

The main biotransformation reactions were deglycosylation of M700F048 and hydroxylation at the biphenyl moiety. Further biotransformation reactions observed were hydroxylation at the pyrazole ring, replacement of an aromatic fluorine atom, presumably by a hydroxy group and oxidation and hydrolysis of the CHF_2 group (forming a carboxy group) with subsequent protein conjugation.

Hens – Fluxapyroxad

Fluxapyroxad labelled in the aniline ring was orally administered by gavage to 12 laying hens at 11.5 ppm in the feed or 0.76 mg/kg bw (1.59 mg/animal/day) for 12 consecutive days. Eggs were collected twice daily (in the afternoon after administration of the test substance and the morning before subsequent administration). Animals were sacrificed approximately 23 hours after the last dose.

Overall, ≥ 86% of the total administered dose was eliminated in excreta. In eggs, 0.18% of the administered dose was detected. A plateau was reached at Day 9 of the dosing period. Tissues and organs (with the exception of the GI tract) retained < 0.5% of the administered dose. TRRs were 0.010 mg/kg equiv. in leg muscle, 0.059 mg/kg equiv. in fat and 0.210 mg/kg equiv. in liver. The extractability of the radioactive residues was ≥ 79% for all tissues other than liver. In liver, extractability was 68%. A significant proportion of the residual radioactive residue, probably bound to proteins, was released from extracted liver tissue after incubation with protease.

Fluxapyroxad was one of the major residues in egg (14% of the TRRs, 0.009 mg/kg equiv.), leg muscle (18% of the TRRs, 0.0011 mg/kg equiv.), fat (63% of the TRRs, 0.023 mg/kg equiv.) and was observed in minor amounts in liver (1% of the TRRs, 0.002 mg/kg equiv.). The other predominant compound was the desmethyl metabolite M700F008, being a large proportion in egg (50% of the TRRs, 0.033 mg/kg equiv.), leg muscle (together with M700F016 amounting to 26% of the TRRs, 0.0016 mg/kg equiv.), and fat (25% of the TRRs, 0.009 mg/kg equiv.). M700F008 was detected in minor amounts in liver.

The metabolism of fluxapyroxad in laying hens mainly proceeds *via* hydroxylation at the biphenyl moiety, loss of a fluorine atom at the biphenyl ring (presumably by substitution with a hydroxyl–group), conjugation of the hydroxyl groups with glucuronic acid, and demethylation at the pyrazole ring. Additionally, conjugates with glutathione derivatives were identified.

Hens – M700F002

Labelled ^{14}C–M700F002 was fed to 10 laying hens at 13.1 ppm in the feed, 0.84 mg/kg bw/day or 1.66 mg/animal/day for ten consecutive days. Eggs were sampled in the morning before administration of the test substance and in the afternoon. Animals were sacrificed approximately 23 hours after the last dose. In excreta, 82% of the applied dose was found. Eggs contained 0.009% of the applied dose. Residues were 0.0041 mg/kg in liver, 0.0022 mg/kg in breast muscle, 0.0030 mg/kg in leg muscle, 0.0023 mg/kg for abdominal fat and 0.0058 mg/kg for body fat. In total, 84% of the applied dose was recovered in excreta, eggs, blood, tissues, GI tract and cage wash. The unchanged test item M700F002 was the only component identified in the extracts of egg, tissues and excreta and the only component detected in the methanol extracts of liver, leg muscle, body fat and excreta. It was concluded that the test item M700F002 is not considerably metabolized in laying hens.

Hens – M700F048

^{14}C–M700F048, labelled in the aniline moiety was fed to 12 laying hens at 12.9 ppm feed or 0.78 mg/kg bw/day for 11 consecutive days. Eggs were collected in the afternoon after administration of the test item and in the morning before the subsequent administration. Animals were sacrificed 18–22 hours after the last dose.

Overall, excreta contained 91.8% of the M700F048 administered, and excreta and cage wash together amounted to 94.1% of the total administered dose. In eggs, 0.15% of the total radioactivity administered was found. Total radioactive residues in eggs increased until day 8 and thereafter remained unchanged until day 11. At sacrifice, 18–22 hours after the last administration, organ and tissues were pooled from all animals. In total, < 0.5% of the total administered dose could be found in the tissues and organs. The residue levels in edible tissues and organs were 0.187 mg/kg equiv. for liver, 0.0079 mg/kg equiv. for breast muscle, 0.0091 mg/kg equiv. for leg muscle, 0.033 mg/kg equiv. for abdominal fat, and 0.032 mg/kg equiv. for body fat.

The unchanged test item M700F048 was present in only minor amounts in eggs and tissues (< 4% of the TRRs). The main metabolite in eggs and all tissues was the deglycosylated component M700F008, accounting for ≥ 67% of the TRRs (except in liver, where it accounted for 23% of the TRRs).

The results show that M700F048 is metabolized in hens mainly by the splitting-off of the sugar moiety. All metabolites identified in edible matrices (M700F008, M700F047, M700F009 and M700F010) were also found upon administration of M700F048 to rats.

Summary of animal metabolism

The metabolic pathways of fluxapyroxad in rats, goats and poultry were similar. The metabolism of fluxapyroxad mainly proceeds *via* hydroxylation at the biphenyl moiety, loss of a fluorine atom at the biphenyl ring, conjugation of the hydroxyl groups with glucuronic acid and demethylation at the pyrazole ring. Additionally, conjugates with glutathione derivatives were identified in rat and hen metabolism. The metabolism of rats was more complex than the metabolism of goats and hens, with a much larger number of metabolites observed.

Plant metabolism

The metabolism of fluxapyroxad was investigated in soya beans, tomato and wheat.

Aniline or pyrazole labelled fluxapyroxad was applied by foliar methods to tomatoes at a rate of 100 g ai/ha. Three applications took place 17, 10 and 3 days before harvest (55, 62 and 69 days after planting). Ripe tomato fruit were sampled 3 days after the last treatment. Other green parts of the plants (stem, panicles and leaves – referred to as tomato leaves) were also sampled.

Aniline or pyrazole labelled fluxapyroxad was applied by foliar methods to soya beans at a rate of 60 g ai/ha. Three applications were made at BBCH 16/17, 51–59 and 71–75. Samples of soya bean forage were taken after the first application (0 days after treatment; DAT) and immediately before the third application (21 days after the first treatment; 14 days after the second treatment). Soya

bean hay, straw, hulls and seed were harvested at BBCH 89, approximately a month after the third application.

Parent compound was generally the main component of the TRR. In the tomato and foliar wheat studies, parent was the only component observed at > 10% of the TRR. In tomatoes parent accounted for > 94% of the TRR in fruit (0.156 mg/kg equiv.) and > 90% TRR (6.039 mg/kg equiv.) in leaves. In wheat parent accounted for 60–91% of the TRR after foliar treatment and 58–79% TRR for forage, hay, straw and chaff after seed treatment, but only 7–17% TRR in grain after seed treatment. The group of metabolites M700F008, M700F043, M700F041 and M700F006 was found to occur in all wheat matrices after foliar treatment as the second most predominant component of radioactivity, representing 2–7% of the TRRs. After seed treatment, M700F008 was observed in all wheat matrices for both labels as the second most predominant component, representing 2–11% of the TRRs.

Aniline or pyrazole labelled fluxapyroxad was applied by foliar methods to spring wheat at a rate of 125 g ai/ha. Two applications were made at BBCH 30/35 and 69. Wheat forage samples were collected 36 days after the first application at BBCH 59. Wheat hay was sampled at 4 DALA (BBCH 73–75); straw, chaff and grain samples were collected at 34 and 35 DALA for the aniline and pyrazole label, respectively (BBCH 89).

Aniline or pyrazole labelled fluxapyroxad was applied as a seed treatment to spring wheat at a rate of 75 g ai/100 kg seed (equivalent to an application rate of 135g ai/ha). Wheat forage samples were collected at BBCH 59, wheat hay was sampled at BBCH 73–75 while straw, chaff and grain samples were collected at BBCH 89.

In the soya bean studies, parent accounted for 54–98% of the TRR in all matrices except seed, where it accounted for 7–21% of the TRR. The major metabolite in soya bean seed was M700F002 at 33% of the TRR (0.087 mg/kg equiv.) which is specific for the pyrazole label only. The corresponding cleavage product was not observed for the aniline label. An additional metabolite, M700F048 accounted for 9–20% (0.023 mg/kg equiv.) of the TRR in soya bean seed.

Two plant metabolites which were not observed in the animal metabolism studies with fluxapyroxad were M700F002 and M700F048. For M700F048, separate goat and hen metabolism studies have confirmed that M700F048 follows the same route of metabolism as fluxapyroxad. Both fluxapyroxad and M700F048 are degraded to the common metabolite M700F008, followed by hydroxylation of the biphenyl moiety and conjugation steps. Separate goat and hen metabolism studies for M700F002 have shown that M700F002 is not significantly transformed in the goat or the hen.

Confined Rotational Crops

Studies of residues in confined rotational crops have been submitted in which soil was treated at 250g ai/ha, followed by soil aging at 30, 120/149 and 365 days (aniline and pyrazole ^{14}C labels respectively). Representative succeeding crops of spinach (leafy vegetable), radish (root vegetable) and wheat (cereal grain) were planted at the above intervals to determine whether fluxapyroxad residues or degradates appear in follow crops. At all three plant-back intervals significant translocation of radioactivity from soil to plant was observed with radioactive residues in wheat straw up to 2.65 mg/kg and spinach up to 0.18 mg/kg. Lower residues were observed in radish roots (maximum of 0.015 mg/kg) and wheat grain (maximum of 0.043 mg/kg).

The metabolite pattern was similar to that observed for primary crops. No metabolites specific to rotational crops were observed. As observed in foliar treated plants, fluxapyroxad was the main component of the residue in both studies. It was the major residue observed in almost every matrix and every plant back interval. Major metabolites observed include M700F008 and M700F048 and in the pyrazole label only, M700F001 and M700F002. The latter two metabolites were observed in soil metabolism studies with fluxapyroxad.

Environmental Fate in Soil

The Meeting received information on soil photolysis, aerobic and anaerobic soil metabolism, field dissipation and adsorption/ desorption behaviour in different soils. Only those studies relevant to the current evaluation were considered.

Light was found to have little influence on the behaviour and degradation of fluxapyroxad in soils. Fluxapyroxad was found to be stable in aqueous solution at pH 4, 5, 7 and 9 (50 °C) for five days.

Under aerobic laboratory conditions at 20–27 °C fluxapyroxad degrades at a moderate to slow rate with DT_{50} values ranging from 69 to 689 days and DT_{90} values from >120 to >1000 days. There was no apparent correlation between half–lives and soil characteristics of pH and organic carbon. Cleavage of the carboxamide bridge produced M700F001, followed by demethylation to form M700F002. Both metabolites were observed at levels greater than 10% applied radioactivity in some soils and both declined over time. Laboratory aerobic soil degradation studies were conducted on both metabolites. Metabolite M700F001 degraded rapidly with DT_{50} values ranging from 2–9 days while DT_{50} values for M700F002 ranged from 77–197 days.

Field dissipation studies were carried out at six European sites, five sites in the USA and one in Canada. In general the field behaviour of fluxapyroxad was consistent with the model developed from the laboratory studies. Fluxapyroxad dissipated by aerobic soil processes and formed M700F001 and M700F002. These metabolites also dissipated, presumably metabolized to CO_2 and/or incorporated into soil organic fractions as observed in radiolabelled laboratory studies.

Fluxapyroxad dissipated with DT_{50} values of 9.9 to 370 days in the field studies. European field dissipation studies carried out on M700F002 at four sites showed DT_{50} values ranging from 26–39 days.

Generally the DT_{50} and DT_{90} values and residues at the end of study periods indicated that fluxapyroxad has a potential for residue carry over to the following cropping season if application is performed annually.

Methods of analysis

The Meeting received information on analytical methods for the determination of residues of the active substance, fluxapyroxad and the metabolites M700F002, M700F008 and M700F048 in plant matrices and animal matrices.

The methods used are based on HPLC/MS-MS and UPLC/MS-MS for plant matrices and HPLC/MS-MS for animal matrices. All methods involve extraction with either methanol/water (plant matrices) or acetonitrile/water (animal matrices). All methods have been adequately validated with LOQs of 0.01 mg/kg for fluxapyroxad, M700F002, M700F008 and M700F048 in plant matrices and LOQs of 0.01 mg/kg for bovine muscle, liver, kidney and fat or 0.001 mg/kg for milk, milk products and egg in animal matrices.

Radio-validation of the plant matrices method was carried out during the soya bean, tomato and wheat metabolism studies and the animal matrices method during the laying goat and hen metabolism studies. No multi–residue method was submitted for evaluation.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the freezer storage stability of fluxapyroxad and the metabolites M700F002, M700F008 and M700F048 in plant and animal commodities.

Freezer storage stability studies showed that fluxapyroxad, M700F002 and M700F048 were stable for up to 24, 27 and 24 months in a variety of matrices. M700F008 was found to be stable for up to 24 months in wheat straw and dried pea seed. A decrease in stability was observed after 3 months for the other four matrices tested, i.e., wheat whole plant, wheat grain, lemon fruit and soya bean seed. The recoveries observed for storage intervals between 4–24 months did not show any subsequent significant decrease.

Samples from the fluxapyroxad wheat and soya bean metabolism studies were re–analysed after a storage interval of approximately 37 months to investigate the stability of incurred residues of M700F008 in wheat forage (pyrazole label), wheat straw (aniline label), wheat grain (pyrazole label) and soya bean seed (aniline label). Recoveries of M700F008 in these matrices after approximately 37–39 months were shown to be similar to those obtained in the original study.

Fluxapyroxad and the metabolites M700F002, M700F008 and M700F048 were demonstrated to be stable in extracts of animal matrices under refrigerator conditions for 7 days at the time of the validation of Method L01040/02.

In the hen metabolism study for fluxapyroxad a comparison of the extractabilities and metabolite patterns (HPLC chromatograms) showed no relevant changes in the nature of the radioactive residues during sample storage over approximately 16 months.

In the goat metabolism study for fluxapyroxad the stability of the residues in acetonitrile and methanol extracts was demonstrated for the whole period of metabolite investigation. Extracts which were obtained after storage of the matrices for about 18 months (milk, kidney and muscle) or 10–23 months (fat) showed concentrations and metabolite patterns comparable to data generated during earlier workups.

For the study of the metabolism of metabolite M700F002 in goat, the radiochemical stability of the test item over the 8 day dosing period was confirmed. Extractions were performed several times during the course of the study. No differences in the extraction characteristics at approximately 2–5 months after sampling were observed. The stability of radioactivity in extracts stored in a refrigerator was also proven for up to 83 days of storage by comparison of the HPLC chromatograms.

Residue Definition

Animals

In the goat metabolism studies, fluxapyroxad represented one of the major residues in milk, muscle and fat (12–44% of the TRRs), while accounting for minor proportions in liver and kidney (3–7% of the TRRs). The other predominant compound was the desmethyl metabolite M700F008, representing a main proportion in milk, muscle, fat, liver and kidney (13–83% of the TRRs). The dairy cow feeding study showed that levels of M700F008 in milk were generally of the same order as fluxapyroxad. Residues in fat were lower than fluxapyroxad residues, while those in liver and kidney were somewhat higher than fluxapyroxad residues.

In the hen metabolism study, fluxapyroxad represented one of the major residues in egg (14% leg muscle and fat (14–63% of the TRRs) and was observed in minor amounts in liver (1% of the TRRs). The other predominant compound was the desmethyl metabolite M700F008, representing a main proportion in egg, leg muscle and fat (25–50% of the TRRs). M700F008 was detected at minor amounts (4% of the TRRs) in liver (0.009 mg/kg). The laying hen feeding study showed that levels of M700F008 in egg were higher than fluxapyroxad. Residues of M700F008 were observed in liver at the two highest feeding levels (1.8 and 6.0 ppm), but fluxapyroxad residues were not observed. Residues in fat were lower than fluxapyroxad residues (both only observed at 6.0 ppm).

Two plant metabolites which were not observed in the animal metabolism studies with fluxapyroxad were M700F002 and M700F048. For M700F048 separate goat and hen metabolism studies have confirmed that M700F048 follows the same route of metabolism as fluxapyroxad. Both fluxapyroxad and M700F048 are degraded to the common metabolite M700F008 followed by hydroxylation of the biphenyl moiety and conjugation steps.

In residue field trials M700F048 was usually only found in minor proportions compared to parent or was found at low absolute levels. It is therefore not necessary to include M700F048 in the residue definition for animal commodities. Similarly the metabolite M700F002 was not detected in most residues trials provided (maximum observation across all trials was 0.02 mg/kg). In the animal feeding studies M700F002 was not seen above the LOQ in any animal matrix at any dose level. It is therefore not necessary to include M700F002 in the residue definition for animal commodities.

It is considered that a residue definition of parent is appropriate for commodities of animal origin for compliance with MRLs (enforcement). Parent fluxapyroxad and M700F008 are of comparable toxicity and because M700F008 is detected as a predominant compound in a number of animal matrices, a residue definition of parent plus M700F008 (expressed as parent equivalents) is appropriate for commodities of animal origin for risk assessment.

Plants

In the plant metabolism studies parent was generally the main component of the TRR. In the tomato and foliar wheat studies, parent was the only component observed at > 10% of the TRR (58 to > 94% TRR in tomato fruit and leaves and all wheat matrices). After wheat seed treatment parent accounted for 58–79% TRR in forage, hay, straw and chaff but only 7–17% TRR in grain. A group of metabolites that includes M700F008 was found to occur in all wheat matrices after foliar treatment as the second most predominant component of radioactivity, representing 2–7% of the TRRs. After seed treatment, M700F008 was observed in all wheat matrices for both labels as the second most predominant component, representing 2–11% of the TRRs.

In the soya bean studies, parent accounted for 54–98% of the TRR in all matrices except seed, where it accounted for 7–21% of the TRR. The major metabolite in soya bean seed was M700F002 at 33% of the TRR (0.087 mg/kg equiv.) which is specific for the pyrazole label only. An additional metabolite, M700F048 accounted for 9–20% (0.023 mg/kg equiv.) of the TRR in soya bean seed.

No metabolites specific to rotational crops were observed. As observed in foliar treated plants, fluxapyroxad was the main component of the residue. Major metabolites observed include M700F008 and M700F048 and in the pyrazole label only, the soil metabolites M700F001 and M700F002.

Residues trials over a wide variety of crops (pome fruit, stone fruit, fruiting vegetables other than cucurbits, legume vegetables, pulses, root and tuber vegetables, cereal grains, oilseeds and various animal feeds) as well as rotational crop studies were submitted in which the residues of parent fluxapyroxad, M700F002, M700F008, M700F048 were determined. In general detectable residues of M700F002 were very rarely observed and then at very low levels. It is considered unnecessary to include M700F002 in the residue definition for plant commodities.

M700F008 and M700F048 were observed more frequently than M700F002 in plants but parent fluxapyroxad was almost always present when detectable residues were observed in either M700F008 or M700F048 and was, in the vast majority of cases, the significantly dominant residue. However in stone fruit (particularly cherries) and in canola, M700F008 and M700F048 were significant residues while M700F008 was also a significant residue in peppers and soya beans.

It is considered that a residue definition of parent only is appropriate for fluxapyroxad in plant commodities for compliance against MRLs as parent is present in most plant matrices. Fluxapyroxad and the metabolites M700F008 and M700F048 are of comparable toxicity and as the metabolites are present in significant amounts in some plant matrices, it is considered that a residue definition of fluxapyroxad + M700F008 + M700F048 (fluxapyroxad total residues expressed as parent equivalents) is appropriate for risk assessment.

The log K_{ow} of fluxapyroxad (log K_{ow} 3.13, pH 7) suggests that fluxapyroxad might be moderately fat-soluble.

The ratio of fluxapyroxad residues in muscle and fat observed in the livestock metabolism and feeding studies (*e.g.* in the lactating dairy cow feeding study: up to 14× higher in fat based on mean residues) support the conclusion that fluxapyroxad is fat-soluble.

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

Definition of the residue (for estimation of dietary intake for plant commodities): *Sum of fluxapyroxad and 3-(difluoromethyl)- N-(3',4',5'-trifluoro[1,1'-biphenyl]-2-yl)-1H-pyrazole-4-*

carboxamide (M700F008) and 3–(difluoromethyl)- 1-(ß-D-glucopyranosyl)-N-(3',4',5'-triflurobipheny-2-yl)-1H-pyrzaole-4-carboxamide (M700F048) and expressed as parent equivalents

Definition of the residue (for estimation of dietary intake for animal commodities): *Sum of fluxapyroxad and 3-(difluoromethyl)- N-(3',4',5'-trifluoro[1,1'-biphenyl]-2-yl)-1H-pyrazole-4-carboxamide (M700F008) and expressed as parent equivalents*

The residue is fat-soluble.

Results of supervised residue trials on crops

Supervised trials were available for the use of fluxapyroxad on numerous crops: apples, pears, cherries, peaches, plums, tomatoes, bell and non-bell peppers, sweet corn, peas, beans, soya beans, potatoes, sugar beet, barley, field corn, oats, rice, sorghum, triticale, wheat, canola, sunflowers, cotton and peanuts.

After sampling, if a higher residue level was observed at a longer PHI than the GAP, the higher value has been used in maximum residue level estimation.

In trials where duplicate field samples from replicated or unreplicated plots were taken at each sampling time and analysed separately, the mean was taken as the best estimate of the residue. Where residues have been reported as < LOD (less than the limit of detection) the values have been considered as < LOQ (< 0.01 mg/kg) for the purposes of maximum residue level estimation.

The OECD calculator was used as a tool to assist in the estimation of maximum residue levels from the selected residue data set obtained from the supervised residue trials. As a first step, the Meeting reviewed all relevant factors related to each data set in arriving at a best estimate of the maximum residue using expert judgement. Then the OECD calculator was employed. If the statistical calculation spreadsheet suggested a different value from that recommended by the Meeting, a brief estimation of the deviation was supplied.

For dietary intake assessment the residues are expressed as the sum of fluxapyroxad + M700F008 + M700F048 expressed as fluxapyroxad (referred to as "total"). In most cases the metabolites were tabulated as mg/kg of specific analyte, so the M700F008 and M700F048 amounts were converted to fluxapyroxad by multiplying by 1.038 and 0.72 respectively. The treatment of values at < LOQ is illustrated below. Residues data for most crops show that the metabolites M700F008 and M700F048 are commonly < LOD. Although this is expressed as < LOQ for the purposes of maximum residue level estimation, it is considered appropriate that when one component is above the LOQ and the others are below the LOQ, that the combined residue is assumed to be equal to the main component.

Fluxapyroxad	M700F008	M700F048	Total Residues (mg/kg) (Sum of fluxapyroxad + M700F008 + M700F048)
0.10	< 0.01	< 0.01	0.10
< 0.01	< 0.01	< 0.01	< 0.01
< 0.01	0.03	< 0.01	0.03

Product labels were available from Australia, Brazil, France, Germany, United Kingdom and the United States of America.

Pome Fruits

Residue trials were conducted in apples according to the GAP in the USA for pome fruit (4 applications at 97–100g ai/ha, 0 day PHI). Applications were made using either concentrate or dilute spray volumes.

Residues of fluxapyroxad in apples from supervised trials matching US GAP, in ranked order, were: 0.14, 0.15, 0.21, 0.24, 0.25, 0.26, 0.28, 0.31, 0.35, 0.36 and 0.37 mg/kg.

The ranked order of total residues in apples from supervised trials according to GAP were: 0.14, 0.15, 0.21, 0.24, 0.25, 0.26, 0.31, 0.35, 0.36, 0.36 and 0.37 mg/kg

Residue trials were conducted in pears in the USA and Canada according to GAP in the USA (4 applications at 97–100 g ai/ha, 0 day PHI). Applications were made using either concentrate or dilute spray volumes.

Residues of fluxapyroxad in pears from supervised trials according to US GAP, in ranked order, were: 0.18, 0.20, 0.23, 0.29, 0.34, 0.38, 0.45 and 0.47 mg/kg.

The total residues in pears from supervised trials according to GAP, in ranked order were: 0.18, 0.20, 0.23, 0.30, 0.34, 0.38, 0.46 and 0.47 mg/kg.

The use pattern in the USA is for pome fruit. The Meeting noted that the USA and Canadian datasets matching US GAP for apples and pears resulted in similar residues (Mann-Whitney U-Test). The Meeting decided to combine the data for apples and pears to increase the data set for the purposes of estimating a maximum residue level, STMR, HR and to make a recommendation for pome fruit.

The ranked order of residues of fluxapyroxad in apples and pears from supervised trials according to GAP were: 0.14, 0.15, 0.18, 0.20, 0.21, 0.23, 0.24, 0.25, 0.26, 0.28, 0.29, 0.31, 0.34, 0.35, 0.36, 0.37, 0.38, 0.45 and 0.47 mg/kg.

The ranked order of total residues in apples and pears from supervised trials according to GAP were: 0.14, 0.15, 0.18, 0.20, 0.21, 0.23, 0.24, 0.25, 0.26, 0.30, 0.31, 0.34, 0.35, 0.36, 0.36, 0.37, 0.38, 0.46 and 0.47 mg/kg.

The Meeting estimated maximum residue level, STMR and HR values for fluxapyroxad in pome fruit of 0.9, 0.30 and 0.47 mg/kg respectively.

Stone Fruits

Residue trials were conducted in cherries in the USA and Canada matching the GAP in the USA for stone fruit (3 applications at 121–123 g ai/ha, 0 day PHI). Applications were made using either concentrate or dilute spray volumes.

The ranked order of residues of fluxapyroxad in cherries from supervised trials according to GAP were: 0.26, 0.31, 0.55, 0.56, 0.59, 0.82, 1.10 and 1.87 mg/kg.

The ranked order of total residues in cherries from supervised trials according to US GAP were: 0.37, 0.50, 0.72, 0.73, 0.78, 1.13, 1.38 and 2.32 mg/kg.

Residue trials were conducted in peaches in the USA and Canada matching to the GAP in the USA for stone fruit (3 applications at 121–123g ai/ha, 0 day PHI).

The ranked order of residues of fluxapyroxad in peaches from supervised trials according to GAP were: 0.28, 0.30, 0.32, 0.33, 0.34, 0.43, 0.45, 0.55, 0.57, 0.58, 0.59 and 0.63 mg/kg.

The total residues in peaches from supervised trials according to GAP, in ranked order were: 0.30, 0.31, 0.33, 0.34, 0.35, 0.45, 0.48, 0.58, 0.62, 0.63, 0.66 and 0.66 mg/kg.

Residue trials were conducted in plums in the USA and Canada matching the GAP in the USA for stone fruit (3 applications at 121–123g ai/ha, 0 day PHI).

The ranked order of residues of fluxapyroxad in plums from supervised trials according to GAP were: 0.23, 0.24, 0.27, 0.37, 0.38, 0.49, 0.55, 0.56, 0.64 and 0.95 mg/kg.

The total residues in plums from supervised trials according to GAP, in ranked order were: 0.23, 0.24, 0.27, 0.38, 0.39, 0.49, 0.55, 0.56, 0.64 and 0.95 mg/kg.

The use pattern in the USA is for stone fruit. The Meeting noted that the USA and Canadian datasets matching GAP for cherries, peaches and plums resulted in similar residues. The Meeting decided to combine the data for cherries, peaches and plums to increase the database for the purposes of estimating a maximum residue level and STMR and to make a recommendation for stone fruit.

The ranked order of residues of fluxapyroxad in cherries, peaches and plums from supervised trials according to GAP were: 0.23, 0.24, 0.26, 0.27, 0.28, 0.30, 0.31, 0.32, 0.33, 0.34, 0.37, 0.38, 0.43, 0.45, 0.49, 0.55, 0.55, 0.55, 0.56, 0.56, 0.57, 0.58, 0.59, 0.59, 0.63, 0.64, 0.82, 0.95, 1.10 and 1.87 mg/kg.

The ranked order of total residues in cherries, peaches and plums from supervised trials according to GAP were: 0.23, 0.24, 0.27, 0.30, 0.31, 0.33, 0.34, 0.35, 0.37, 0.38, 0.39, 0.45, 0.48, 0.49, 0.50, 0.55, 0.56, 0.58, 0.62, 0.63, 0.64, 0.66, 0.66, 0.72, 0.73, 0.78, 0.95, 1.13, 1.38 and 2.32 mg/kg.

The Meeting estimated maximum residue level, STMR and HR values for fluxapyroxad in stone fruits of 2, 0.525 and 2.3 mg/kg, respectively.

Fruiting Vegetables, other than Cucurbits

Residue trials were conducted in tomatoes in the USA and Canada matching to the GAP of the USA for fruiting vegetables other than cucurbits (3 applications at 97–101g ai/ha with a 7 day PHI). In addition two trials were carried out in cherry tomatoes in California according to the same USA GAP. Each trial was also carried out with 2 applications of fluxapyroxad to tomatoes. The highest residue observations, regardless of whether 2 or 3 applications of fluxapyroxad were made, will be considered for the purpose of estimating a maximum residue level.

The ranked order of residues of fluxapyroxad in tomatoes from supervised trials according to the GAP were: 0.03, 0.04, 0.0455, 0.05, 0.06, 0.07, 0.07, 0.07, 0.07, 0.08, 0.09, 0.11, 0.13, 0.27 and 0.44 mg/kg.

The total residues in tomatoes from supervised trials according to GAP, in ranked order were: 0.03, 0.04, 0.045, 0.055, 0.06, 0.07, 0.07, 0.07, 0.07, 0.08, 0.09, 0.11, 0.13, 0.27 and 0.44 mg/kg.

Residue trials were conducted in bell peppers in the USA and Canada according to the GAP of the USA for fruiting vegetables other than cucurbits (3 applications at 97–101g ai/ha, 7 day PHI).

The ranked order of residues of fluxapyroxad in bell peppers from supervised trials according to the GAP were: < 0.01, 0.01, 0.01, 0.02, 0.04, 0.09, 0.09 and 0.24 mg/kg.

The total residues in bell peppers from supervised trials according to GAP, in ranked order were: < 0.01, 0.01, 0.03, 0.03, 0.06, 0.15, 0.16 and 0.37 mg/kg.

Residue trials were conducted in chili peppers at two locations in the USA matching the critical GAP of the USA for fruiting vegetables other than cucurbits (3 applications at 97–101g ai/ha, 7 day PHI).

The residues of fluxapyroxad in non-bell chili peppers from supervised trials according to the GAP were: 0.02 and 0.30 mg/kg.

The total residues in non-bell chili peppers from supervised trials according to GAP, in ranked order were: 0.03 and 0.32 mg/kg.

The use pattern in the USA is for Fruiting vegetables (eggplant, ground cherry, pepino, pepper (all varieties), tomatillo and tomato). The Meeting noted that the USA and Canadian datasets matching GAP for tomatoes and peppers resulted in similar residues (Mann-Whitney U-Test). The Meeting decided to combine the data in estimating a maximum residue level and STMR for fruiting vegetables other than cucurbits (except mushrooms and sweet corn).

Residues of fluxapyroxad in tomatoes and peppers from supervised trials according to the GAP were: < 0.01, 0.01, 0.01, 0.02, 0.02, 0.03, 0.04, 0.04, 0.04, 0.05, 0.06, 0.07, 0.07, 0.07, 0.07, 0.08, 0.09, 0.09, 0.09, 0.11, 0.13, 0.24, 0.27, 0.30 and 0.44 mg/kg.

The total residues in tomatoes and peppers from supervised trials according to GAP, in ranked order were: < 0.01, 0.01, 0.03, 0.03, 0.03, 0.03, 0.04, 0.04, 0.05, 0.06, 0.06, 0.07, 0.07, 0.07, 0.07, 0.08, 0.09, 0.11, 0.13, 0.15, 0.16, 0.27, 0.32, 0.37 and 0.44 mg/kg.

The Meeting estimated maximum residue level, STMR and HR values for fluxapyroxad in fruiting vegetables other than cucurbits (except mushrooms and sweet corn) of 0.6, 0.07 and 0.44 mg/kg, respectively.

On the basis of the STMR and HR for fruiting vegetables other than cucurbits and the dehydration factor of 10, an STMR and HR were calculated as 0.70 and 4.4 mg/kg respectively for chili peppers. Based on the estimated maximum residue level for fruiting vegetables other than cucurbits, the Meeting recommended a maximum residue level of 6 mg/kg for chili peppers (dry).

Sweet corn, corn-on-the-cob

Residue trials were conducted in field corn (four trials) and sweet corn (five trials) at various locations in the USA and Canada matching the GAP in the USA (2 applications at 97–100g ai/ha, 7 day for sweet corn). Samples were taken to measure residues in kernels + cobs with husks removed samples.

The ranked order of highest residues of fluxapyroxad (and total residues) in kernels + cobs with husks removed samples from supervised trials collected 5–7 days after the last application was < 0.01 (8) and 0.08 mg/kg.

The Meeting estimated maximum residue level, STMR and HR values for fluxapyroxad in sweet corn (corn-on-the-cob) of 0.15, 0.01 and 0.08 mg/kg respectively.

Legume vegetables

Edible podded peas and beans

Registered use patterns in legumes exist for edible podded legume vegetables and succulent shelled peas and beans.

Residue trials were conducted in peas generally according to the critical GAP in the USA for edible podded legumes (2 applications at 97–101g ai/ha, 7 day PHI).

The ranked order of residues of fluxapyroxad in pea succulent seed with pods from supervised trials according to GAP were: 0.22, 0.23, 0.39, 0.65, 0.66, 0.73 and 0.74 mg/kg.

The ranked order of total residues in pea succulent seed with pods from supervised trials according to GAP were: 0.24, 0.24, 0.40, 0.65, 0.68, 0.73 and 0.74 mg/kg.

The Meeting estimated maximum residue level, STMR and HR values for fluxapyroxad in pea succulent seed with pods of 2, 0.65 and 0.74 mg/kg respectively.

The Meeting decided to extrapolate the maximum residue level and STMR and HR value for pea succulent seed with pods to Beans, except broad bean and soya bean.

Residue trials were conducted in soya beans generally according to the GAP in the USA for edible podded legumes (2 applications at 97–100g ai/ha, 7 day PHI).

The ranked order of residues of fluxapyroxad in soya bean succulent seed with pods from supervised trials according to GAP was 0.10, 0.10, 0.11, 0.11, 0.18, 0.20, 0.21, 0.27, 0.29, 0.29, 0.46, 0.69 and 0.69 mg/kg.

The ranked order of total residues in soya bean succulent seed with pods from supervised trials according to GAP was 0.11, 0.12, 0.12, 0.13, 0.20, 0.21, 0.24, 0.28, 0.31, 0.34, 0.52, 0.71 and 0.74 mg/kg.

The Meeting estimated maximum residue level, STMR and HR values for fluxapyroxad in soya bean (young pods) of 1.5, 0.24 and 0.74 mg/kg, respectively.

Edible peas and beans without pods

Residue trials were conducted in peas at 8 locations in the USA and Canada (9 trials) generally according to the critical GAP in USA for succulent shelled peas and beans (2 applications at 97–101 g ai/ha, 7 day PHI).

Residues of fluxapyroxad in pea succulent seed without pods from supervised trials according to GAP were: < 0.01, 0.03, 0.03, 0.03, 0.03, 0.04 and 0.04 mg/kg.

The total residues in pea succulent seed without pods from supervised trials according to GAP, in ranked order, were: < 0.01, 0.03, 0.03, 0.03, 0.03, 0.04 and 0.04 mg/kg.

The Meeting estimated maximum residue level, STMR and HR values for fluxapyroxad in pea, shelled (succulent seed) of 0.09, 0.03 and 0.04 mg/kg, respectively.

The Meeting decided to extrapolate the maximum residue level and STMR and HR value for pea, shelled (succulent seed) to Beans, shelled.

Residue trials were conducted in soya beans in the USA and Canada matching the GAP in the USA for succulent shelled peas and beans (2 applications at 97–100g ai/ha, 7 day PHI).

The ranked order of residues of fluxapyroxad in soya bean succulent seed without pods from supervised trials according to GAP were: < 0.01 (5), 0.01, 0.01, 0.02, 0.03, 0.04, 0.04, 0.11 and 0.37 mg/kg.

The total residues in soya bean succulent seed without pods from supervised trials according to GAP, in ranked order, were: < 0.01 (5), 0.01, 0.01, 0.03, 0.04, 0.04, 0.04, 0.12 and 0.37 mg/kg.

The Meeting estimated maximum residue level and STMR values for fluxapyroxad in soya beans (immature seeds) of 0.5, 0.01 and 0.37 mg/kg respectively.

Pulses

Soya bean, dry

Residue trials were conducted in soya bean in Brazil, in which four applications were made at 50 g ai/ha at 15 day intervals. Sampling was performed at a 14 day PHI in two trials and 0, 7, 14, 21 and 30 day PHI in two decline trials. The GAP in Brazil is up to 4 applications at 60g ai/ha, 14 day PHI, 10–20 day interval between applications).

The residues of fluxapyroxad (and total residues) in soya bean seeds from supervised trials collected 14 days after the last application were: < 0.01 (4) and 0.03 mg/kg.

Residue trials were conducted in soya bean in the USA and Canada according to the GAP in the USA (2 applications at 97–101g ai/ha, 21 day PHI).

The ranked order of residues of fluxapyroxad in dried soya bean seed from supervised trials collected 20–22 days after the last application were: < 0.01 (10), 0.01, 0.03, 0.04 and 0.10 mg/kg.

The ranked order of total residues in dried soya bean seed from supervised trials collected 20–22 days after the last application were: < 0.01 (10), 0.01, 0.03, 0.04 and 0.11 mg/kg.

Based on the USA and Canadian residues data the Meeting estimated maximum residue level and STMR values for fluxapyroxad in soya bean (dry) of 0.15 and 0.01 mg/kg, respectively.

Dried Shelled Peas and Beans

Residue trials were conducted in peas (dry) in the USA and Canada according to the GAP in the USA (2 applications at 97–101g ai/ha, 21 day PHI).

The ranked order of residues of fluxapyroxad (and total residues) in dried pea seed from supervised trials collected 21–22 days after the last application were: < 0.01, < 0.01, 0.02, 0.02, 0.04, 0.09, 0.11, 0.15 and 0.16 mg/kg.

The Meeting estimated maximum residue level and STMR values for fluxapyroxad in peas (dry) of 0.4 and 0.04 mg/kg respectively.

The Meeting decided to extrapolate the maximum residue level and STMR value for peas (dry) to lentils and chickpeas.

Residue trials were conducted in beans in the USA matching the GAP in the USA (2 applications at 195–200g ai/ha, 21 day PHI).

The ranked order of residues of fluxapyroxad in bean seed from supervised trials approximating GAP were: 0.01, 0.01, 0.02, 0.03, 0.03, 0.04, 0.04, 0.05, 0.05, 0.07 and 0.21 mg/kg.

The ranked order of total residues in bean seed from supervised trials approximating GAP were: 0.01, 0.01, 0.02, 0.03, 0.03, 0.04, 0.05, 0.05, 0.06, 0.07 and 0.25 mg/kg.

The Meeting estimated maximum residue level and STMR values for fluxapyroxad in beans (dry) of 0.3 and 0.04 mg/kg, respectively.

Potatoes

Residue trials were conducted in potatoes in the USA and Canada according to the critical GAP in the USA (3 applications at 97–101g ai/ha, 7 day PHI).

The ranked order of residues of fluxapyroxad (and total residues) in potatoes from supervised trials collected 7 days after the last application were: < 0.01 (17), 0.02 and 0.02 mg/kg.

The Meeting estimated maximum residue level, STMR and HR values for fluxapyroxad in potatoes of 0.03, 0.01 and 0.02 mg/kg respectively.

Sugar beet

Residue trials were conducted in sugar beet in the USA and Canada according to the critical GAP in USA (3 applications at 97–101g ai/ha, 7 day PHI).

The ranked order of residues of fluxapyroxad (and total residues) in sugar beet roots from supervised trials collected 7 days after the last application were: 0.01, 0.01, 0.03, 0.03, 0.03, 0.04, 0.04, 0.04, 0.05, 0.05, 0.06 and 0.06 mg/kg.

The Meeting estimated maximum residue level, STMR and HR values for fluxapyroxad in sugar beet of 0.15, 0.04 and 0.06 mg/kg respectively.

Cotton seed

Residue trials were conducted in cotton in the USA according to the critical GAP in USA (seed treatment application at 20g ai/100 kg seed).

No detectable residues of fluxapyroxad or any metabolite were observed from supervised trials collected 155–193 days after the seed treatment application. In addition, two trials were carried out at 5× the GAP application rate in which no residues were detectable.

The Meeting estimated maximum residue level and STMR values for fluxapyroxad in cotton seed of 0.01* and 0 mg/kg.

Peanuts

Residue trials were conducted in peanuts in the USA according to the critical GAP in USA (3 applications at 97g ai/ha, 7 day PHI).

No residues of fluxapyroxad were observed in peanut nutmeat from supervised trials collected 7 days (3 days in one trial) after application. One decline trial in which residues observations were taken at 0, 4, 7, 14 and 21 days PHI gave fluxapyroxad residues at < 0.01 mg/kg at all sampling intervals. Finite residues of metabolite M700F008 were observed at all sampling times in one trial.

Residues of fluxapyroxad in peanut nutmeat from supervised trials according to GAP were < 0.01 (12) mg/kg.

Total residues in peanut nutmeat from supervised trials according to GAP were: < 0.01 (11) and 0.08 mg/kg.

The Meeting estimated maximum residue level and STMR values for fluxapyroxad in peanut nutmeat of 0.01 and 0.01 mg/kg.

Oilseed - Rape seed and Sunflower seed

Residues observed in rape and sunflowers were higher than those observed in cottonseed and peanuts and were therefore considered separately.

Residue trials were conducted in rape seed (canola) in the USA and Canada matching the GAP in the USA (2 applications at 97–101g ai/ha, 21 day PHI).

The ranked order of residues of fluxapyroxad in rape seed from supervised trials according to GAP were: 0.02, 0.02, 0.04, 0.05, 0.09, 0.09, 0.12, 0.16, 0.19, 0.22 and 0.73 mg/kg.

The total residues in rape seed from supervised trials according to GAP were: 0.02, 0.02, 0.04, 0.05, 0.11, 0.11, 0.15, 0.18, 0.25, 0.27 and 0.83 mg/kg.

Residue trials were conducted in sunflower in the USA and Canada according to the GAP in the USA (2 applications at 97–101g ai/ha, 21 day PHI).

The residues of fluxapyroxad (and total residues) in sunflower seed from supervised trials according to GAP, in ranked order, were: 0.02, 0.02, 0.05, 0.06, 0.09 and 0.11 mg/kg.

The use pattern in the USA is for oilseeds. The Meeting noted that the USA and Canadian datasets, matching GAP for rape seed and sunflower seed, resulted in similar residues (Mann-Whitney U-Test). The Meeting decided to combine the data for rape seed and sunflower seed to increase the dataset for the purposes of estimating a maximum residue level, STMR, HR and to make a recommendation for oilseeds.

The ranked order of residues of fluxapyroxad in rape seed and sunflower seed from supervised trials according to GAP were: 0.02, 0.02, 0.02, 0.02, 0.04, 0.05, 0.05, 0.06, 0.09, 0.09, 0.09, 0.11, 0.12, 0.16, 0.19, 0.22 and 0.73 mg/kg.

The ranked order of total residues in rape seed and sunflower seed from supervised trials according to GAP were: 0.02, 0.02, 0.02, 0.02, 0.04, 0.05, 0.05, 0.06, 0.09, 0.11, 0.11, 0.11, 0.15, 0.18, 0.25, 0.27 and 0.83 mg/kg.

The Meeting estimated maximum residue level and STMR values for fluxapyroxad in oilseeds (except peanuts and cotton) of 1.5 and 0.09 mg/kg, respectively.

Cereals

Barley

Residue trials were conducted in barley in Brazil matching the GAP in Brazil (2 applications at 60 g ai/ha, 30 day PHI, 15–20 day interval between applications).

The residues of fluxapyroxad in barley grain from supervised trials according to the GAP in Brazil were: 0.09, 0.14, 0.15 and 0.28 mg/kg.

The ranked order of total residues of fluxapyroxad in barley grain from supervised trials according to the GAP in Brazil were: 0.09, 0.14, 0.15 and 0.30 mg/kg.

Residue trials were conducted in barley in various European countries (Germany, the Netherlands, France, the UK, Greece, Spain and Italy) in each of two growing seasons, according to the GAP in Europe. (GAP in European countries is 2 applications at 125g ai/ha, 35 day PHI (France) or in the United Kingdom not required if application is at or before GS 69). Trials were also run at a lower rate of application (77–90g ai/ha). Residues data were collected at PHIs ranging from 29–63 days.

The ranked order of residues of fluxapyroxad in barley grain, from supervised trials in Europe collected 35–63 days after the last application, were: 0.02, 0.05, 0.08, 0.09, 0.09, 0.10, 0.10, 0.13, 0.15, 0.17, 0.18, 0.19, 0.23, 0.23, 0.24 and 0.41 mg/kg.

The ranked order of total residues in barley grain, from supervised trials in Europe collected 29–63 days after the last application, were: 0.02, 0.05, 0.08, 0.09, 0.09, 0.10, 0.10, 0.13, 0.16, 0.17, 0.18, 0.19, 0.23, 0.23, 0.24 and 0.45 mg/kg.

Residue trials were conducted in barley in Australia according to the GAP in Australia (2 applications at 62.5g ai/ha).

The residues of fluxapyroxad (and total residues) in barley grain from supervised trials collected at harvest were 0.03 and 0.05 mg/kg.

Residue trials were conducted in barley in the USA and Canada according to the critical GAP in the USA (2 applications at 97–100g ai/ha, 21 day PHI).

The residues of fluxapyroxad in barley grain from supervised trials approximating GAP, in ranked order, were: < 0.01, 0.39, 0.39, 0.41, 0.50, 0.52, 0.52, 0.54, 0.82, 0.87, 1.02 and 1.22 mg/kg.

The total residues in barley grain from supervised trials approximating US GAP were: < 0.01, 0.39, 0.41, 0.44, 0.51, 0.53, 0.54, 0.54, 0.84, 0.87, 1.02 and 1.26 mg/kg.

The data from the USA and Canada were used to estimate a maximum residue level and STMR for barley grain.

The Meeting estimated maximum residue level and STMR values for fluxapyroxad in barley grain of 2 and 0.535 mg/kg respectively.

Oats

Residue trials were conducted in oats in Brazil according to the GAP in Brazil (2 applications at 60 g ai/ha, 30 day PHI, 15–20 day interval between applications).

The residues of fluxapyroxad and (total residues) in oat grain from supervised trials collected 30 days after the last application were < 0.01, < 0.01, 0.05 and 0.28 mg/kg.

The Meeting considered that there were insufficient data reflecting the GAP for fluxapyroxad on oats in Brazil to estimate an appropriate maximum residue level. In addition the GAP in Brazil is less critical than the GAP in the USA (2 applications at 97–100g ai/ha, 21 day PHI).

The Meeting recognized that barley and oats share an identical GAP and normally show comparable residues. It was therefore decided to apply the maximum residue level and STMR recommended for fluxapyroxad on barley to oats (2 and 0.535 mg/kg respectively).

Maize

Residue trials were conducted in maize in Brazil according to the GAP in Brazil (2 applications at 60g ai/ha, 45 day PHI, 15–20 days between applications).

No detectable residues of fluxapyroxad or metabolites in corn grain were observed in samples from supervised trials collected 45 days after the last application.

Residue trials were conducted in maize in the USA and Canada according to the critical GAP in USA (2 applications at 97–100g ai/ha, 21 day PHI).

No residues of fluxapyroxad or the metabolites M700F008 or M700F048 were detected in corn grain (maize) from supervised trials approximating GAP.

The Meeting estimated maximum residue level and STMR values for fluxapyroxad in maize (corn grain) of 0.01* and 0.01 mg/kg respectively.

Rice

Residue trials were provided for rice but none of the submitted labels had a use pattern. As no GAP is available it was not possible to estimate a maximum residue level for the use of fluxapyroxad on rice.

Sorghum

Residue trials were conducted in sorghum in the USA in which two applications were made at 97–104 g ai/ha (6–7 day retreatment interval) with a 20–23 day PHI. It was not possible to establish a maximum residue level based on any label use of fluxapyroxad on sorghum as the submitted residue trial data did not correspond to any label GAP.

Wheat and triticale

Residue trials were conducted in wheat in Brazil, in which three applications were made at 60 g ai/ha at 15 day intervals. Sampling was performed at a 30 day PHI in two trials and 0, 7, 15, 30 and 45 day PHI in two decline trials. The GAP in Brazil is 3 or 4 applications at 60 g ai/ha, 30 day PHI, 15–20 day interval between applications).

The ranked order of residues of fluxapyroxad (and total residues) in wheat grain from supervised trials collected 30 days after the last application were: 0.02, 0.03, 0.04 and 0.08 mg/kg.

Residue trials were conducted in wheat or triticale in various countries in Europe (Germany, the UK, France, Spain and Italy) in each of two growing seasons, matching a GAP in Europe. (GAP in various European countries is 2 applications at 125g ai/ha, 35 day PHI (France) or in the United Kingdom no PHI required if application is at or before GS 69). Residues data were collected at PHIs ranging from 34–60 days.

The ranked order of residues of fluxapyroxad (and total residues) in wheat or triticale (t) grain, from supervised trials in Europe collected 34–60 days after the last application, were: < 0.01 (t), 0.01, 0.01, 0.01, 0.01, 0.02 (t), 0.02 (t), 0.02, 0.02, 0.03 (t), 0.03, 0.03, 0.04, 0.04, 0.05 and 0.06 mg/kg.

Residue trials were conducted in wheat at four locations in Australia in which 2 applications were made at 61–62g ai/ha or 122–124g ai/ha. There is no corresponding GAP.

Residue trials were conducted in wheat in the USA and Canada according to the GAP in the USA (2 applications at 97–100g ai/ha, 21 day PHI). The residues of fluxapyroxad in wheat grain from supervised trials corresponding to GAP, in ranked order, were: 0.03, 0.03, 0.05, 0.05, 0.05, 0.05, 0.06, 0.06, 0.06, 0.07, 0.08, 0.09, 0.10, 0.11, 0.11, 0.12, 0.12, 0.13, 0.19 and 0.21 mg/kg.

The total residues in wheat grain from supervised trials corresponding to GAP, in ranked order were: 0.03, 0.03, 0.05, 0.05, 0.05, 0.06, 0.06, 0.06, 0.07, 0.08, 0.09, 0.09, 0.11, 0.11, 0.12, 0.13, 0.13, 0.15, 0.19 and 0.21 mg/kg.

The data from the USA and Canada were used to estimate a maximum residue level and STMR for wheat grain.

The Meeting estimated maximum residue level and STMR values for fluxapyroxad in wheat grain of 0.3 and 0.085 mg/kg respectively.

The Meeting recognized that wheat, rye and triticale share an identical GAP and normally show comparable residues. The Meeting agreed to apply the maximum residue level and STMR recommended for fluxapyroxad from wheat to rye and triticale.

Animal feeds

The Meeting received supervised trials data for a variety of animal feeds (pea vines and hay, soya bean forage and hay, sugar beet tops, barley forage, straw, hay, whole plant without roots, ears and rest of plant without roots, corn forage and stover, rice straw, sorghum forage and stover, wheat forage, straw, hay, whole plant without roots, ears and rest of plant without roots, cotton gin by–products and peanut hay).

Moisture content percentages for animal feeds have been determined for selected samples (usually control samples). Where available these values have been used to calculate dry weight residues values from residues observations from the same trials, which were then used in calculation of suitable maximum residue levels of the animal feeds. Where these values were not determined, the

values from the FAO Manual on the Submission and Evaluation of Pesticides Residues Data for the feeds, has been used to convert wet weight residues values to dry weight residues values.

Pea vines

Residue trials were conducted in peas in the USA and Canada according to the GAP in USA (2 applications at 97–101g ai/ha, 7 day PHI and a 7 day PHI for pea vines).

The ranked order of total residues in pea vines (wet weight) from supervised trials collected 6–8 days after the last application were: 0.83**,** 1.62**,** 1.76, 2.85**,** 2.90**,** 3.23 and 3.35 mg/kg.

The ranked order of total residues in pea vines (dry weight) from supervised trials collected 6–8 days after the last application were: 4.69, 6.78, 11, 11.6, 12.9, 14.8, 22.9 mg/kg.

The Meeting did not estimate a maximum residue level for pea vines as it is understood the commodity is not normally traded internationally. The Meeting estimated median and highest residues values for fluxapyroxad in pea vines of 12 and 23 mg/kg respectively.

Pea hay

Residue trials were conducted in peas in the USA and Canada according to the GAP in the USA (2 applications at 97–101g ai/ha, 7 day PHI and a 7 day PHI for pea hay).

The residues of fluxapyroxad in pea hay (fresh weight) from supervised trials collected 6–8 days after the last application, ranked order were: 4.53, 6.01, 7.20, 9.18, 9.49, 10.8 and 12.1 mg/kg.

The residues of fluxapyroxad in pea hay (dry weight) from supervised trials collected 6–8 days after the last application, ranked order were: 5.21, 6.87, 10.8, 11.1, 11.3, 16.0 and 17.4 mg/kg.

The total residues in pea hay (fresh weight) from supervised trials collected 6–8 days after the last application, in ranked order were: 4.61, 6.12, 7.22, 9.38, 9.56, 10.8 and 12.2 mg/kg.

The total residues in pea hay (dry weight) from supervised trials collected 6–8 days after the last application, ranked order were: 5.30, 6.99, 11.0, 11.2, 11.3, 16.2 and 17.4 mg/kg.

The Meeting estimated maximum residue level, median and highest residues values for fluxapyroxad in pea hay of 40, 11 and 17 mg/kg respectively.

Soya bean forage

Residue trials were conducted in soya beans in the USA and Canada according to the GAP in the USA (2 applications at 97–101g ai/ha, 7 day PHI and a 7 day PHI for bean forage).

The ranked order of total residues in soya bean forage (fresh weight) from supervised trials collected 6–8 days after the last application were: 0.87, 0.96, 1.18, 1.20, 1.70, 1.98, 2.24, 2.25, 2.31, 2.43, 2.95, 3.31 and 6.56 mg/kg.

The ranked order of total residues in soya bean forage (dry weight) from supervised trials collected 6–8 days after the last application were: 3.88, 4.90, 5.31, 5.39, 6.42, 7.70, 7.71, 7.86, 8.01, 8.78, 11.0, 12.4 and 25.9 mg/kg.

Meeting did not estimate a maximum residue level for soya bean forage as it is understood the commodity is not traded internationally. The Meeting estimated median and highest residues values for fluxapyroxad in soya bean forage of 7.7 and 26 mg/kg.

Soya bean hay

Residue trials were conducted in soya beans at 14 locations in the USA and Canada (15 trials) according to the critical GAP in USA (2 applications at 97–101g ai/ha, 7 day PHI and a 7 day PHI for bean hay).

The ranked order of residues of fluxapyroxad in soya bean hay (fresh weight) from supervised trials collected 6–8 days after the last application were: 0.54, 1.79, 2.33, 3.60, 3.64, 4.39, 4.60, 4.79, 5.20, 5.87, 6.32, 6.44 and 16.25 mg/kg.

The ranked order of residues of fluxapyroxad in soya bean hay (dry weight) from supervised trials collected 6–8 days after the last application were: 1.36, 3.94, 4.57, 5.21, 5.91, 7.27, 7.38, 7.39, 7.63, 8.58, 9.09, 9.77 and 19.6 mg/kg.

The ranked order of total residues in soya bean hay (fresh weight) from supervised trials collected 6–8 days after the last application were: 0.56, 1.87, 2.38, 3.73, 3.79, 4.49, 4.67, 4.83, 5.30, 5.99, 6.51, 6.60 and 16.45 mg/kg.

The ranked order of total residues in soya bean hay (dry weight) from supervised trials collected 6–8 days after the last application were: 1.41, 4.77, 4.15, 5.32, 5.96, 7.43, 7.58, 7.61, 7.79, 8.80, 9.27, 9.92 and 19.9 mg/kg.

The Meeting estimated maximum residue level, median and highest residues values for fluxapyroxad in soya bean fodder of 30, 7.6 and 20 mg/kg respectively.

Sugar beet tops

Residue trials were conducted in sugar beet in the USA and Canada according to the critical GAP in USA (3 applications at 97–101g ai/ha, 7 day PHI for leaves, roots and tops).

The ranked order of total residues in sugar beet tops (fresh weight) from supervised trials collected 7–8 days after the last application were: 0.76, 0.84, 1.18, 1.84, 2.11, 2.17, 2.59, 3.01, 3.43, 3.84, 3.88 mg/kg.

The ranked order of total residues of fluxapyroxad in sugar beet tops (dry weight) from supervised trials collected 7–8 days after the last application were: 3.30, 3.65, 5.13, 8.00, 9.17, 9.43, 11.3, 13.1, 14.9, 16.7 and 16.9 mg/kg.

Meeting did not estimate a maximum residue level for the commodity as it is not traded internationally. The Meeting estimated median and highest residues values for fluxapyroxad in sugar beet tops of 9.4 and 17 mg/kg respectively.

Maize forage and stover

Residue trials were conducted in maize (corn) in the USA and Canada according to the critical GAP in USA (2 applications at 97–100g ai/ha, harvest 21 day PHI, forage 7 days).

The ranked order of total residues of fluxapyroxad in maize forage (fresh weight) from supervised trials collected 6–8 days after the last application were: 0.23, 0.36, 0.42, 0.48, 0.68, 0.69, 0.73, 0.81, 0.88, 0.88, 0.95, 1.07 and 1.38 mg/kg.

The ranked order of total residues of fluxapyroxad in maize forage (dry weight) from supervised trials collected 6–8 days after the last application were: 0.84, 1.42, 1.62, 1.80, 2.10, 2.74, 2.82, 3.02, 3.08, 3.23, 3.45, 3.59 and 3.62 mg/kg.

Meeting did not estimate a maximum residue level for the commodity as it is not traded internationally. The Meeting estimated median and highest residues values for fluxapyroxad in maize forage of 2.8 and 3.6 mg/kg respectively.

The residues of fluxapyroxad in maize stover (fresh weight) from supervised trials collected 20–22 days after the last application, in ranked order, were: 0.23, 0.39, 0.59, 0.60, 0.93, 0.96, 1.43, 1.45, 2.12, 2.13, 2.21, 2.22 and 3.57 mg/kg.

The residues of fluxapyroxad in maize stover (dry weight) from supervised trials collected 20–22 days after the last application, in ranked order, were: 0.80, 0.96, 1.12, 1.70, 2.30, 2.65, 3.57, 4.37, 4.45, 4.64, 5.04, 5.89 and 6.44 mg/kg.

The ranked order of total residues of fluxapyroxad in maize stover (wet weight) from supervised trials collected 20–22 days after the last application were: 0.25, 0.39, 0.62, 0.63, 0.98, 1.01, 1.45, 1.48, 2.17, 2.19, 2.25, 2.25 and 3.64 mg/kg.

The ranked order of total residues of fluxapyroxad in maize stover (dry weight) from supervised trials collected 20–22 days after the last application were: 0.87, 0.96, 1.18, 1.81, 2.42, 2.74, 3.62, 4.50, 4.54, 4.71, 5.15, 6.00 and 6.57 mg/kg.

The Meeting estimated maximum residue level, median and highest residues values for fluxapyroxad in maize fodder of 15, 3.6 and 6.6 mg/kg respectively.

Rice Straw

Residue trials were provided for rice but none of the submitted labels have a use pattern.

Sorghum Forage and Hay

Residue trials were conducted in sorghum at 9 locations in the USA in which two applications were made at 97–104 g ai/ha (6–7 day retreatment interval). Forage data was collected at a 7 day PHI and stover data at a 20 to 23 day PHI.

It is not possible to estimate a maximum residue level for sorghum as the submitted data did not correspond to any label GAP.

Barley and wheat forage, hay and straw

Barley animal feed data (whole plant no roots, straw, ears, rest of plants without roots) were collected in the trials carried out in various European countries (Germany, the Netherlands, France, the UK, Greece, Spain and Italy) in the 2008 and 2009 growing seasons (2 applications at either 77–90 g ai/ha or 121–135 g ai/ha) which approximates the UK GAP (2 applications at 125g ai/ha – used up to and including flowering GS 69 with no restrictions on animal feeding).

The ranked order of total residues in barley rest of plant no roots (forage) samples collected 27–48 days after the second application (fresh weight) at the GAP application rate were: 0.11, 0.13, 0.17, 0.22, 0.24, 0.25, 0.27, 0.50, 0.70, 0.78, 0.97 and 1.33 mg/kg.

The ranked order of total residues in barley rest of plant no roots (forage) dry weight samples after applications at the higher (GAP) rate were: 0.37, 0.43, 0.57, 0.73, 0.80, 0.83, 0.90, 1.67, 2.33, 2.6, 3.23 and 4.43 mg/kg.

Residue trials were conducted in barley at two locations in Australia in which 2 applications were made at 61–62g ai/ha or 122–123g ai/ha. There is a 14 day restriction on grazing or using for stock feed. Forage data was nominally collected at 0, 7 and 14 days after the first application and immediately before the second application. In one trial forage was collected at 14 days after the first application and at -0, 0, 8 and 15 days after the second application.

The ranked order of total residues in barley forage (dry weight) from supervised trials collected at 14/15 days only in each trial was 2.46 (after 1st application) and 3.39 (after 1st application) mg/kg for the trials at the lower rate.

The residues of fluxapyroxad in barley straw (dry weight) from supervised trials collected at harvest were 1.07 and 2.57 mg/kg for the trials at the lower rate.

The total residues in barley straw (dry weight) from supervised trials collected at harvest were 1.13 and 2.67 mg/kg for the trials at the lower rate.

Residue trials were conducted in barley in the USA and Canada matching the critical GAP in the USA (2 applications at 97–100g ai/ha, harvest 21 day PHI, barley hay or green chopped wheat 7 days). Barley hay and straw samples were obtained at six of the trial sites.

Barley hay was obtained for samples collected at a 20–26 day PHI except for one trial (RCN R080746) at which sampling occurred at 20, 21, 25, 27 and 31 day PHIs. As the GAP for hay is a 7

day PHI, these data could be utilized to estimate an appropriate maximum residue level for fluxapyroxad in barley hay.

Barley straw was obtained for samples collected at a 20–26 day PHI except for one trial (RCN R080746) at which sampling occurred at 20, 21, 25, 27 and 31 day PHIs.

The residues of fluxapyroxad in barley straw (fresh weight) from supervised trials collected 20–22 days after the last application, in ranked order were: 0.72, 3.17, 3.45, 3.89, 5.43 and 9.52 mg/kg.

The residues of fluxapyroxad in barley straw (dry weight) from supervised trials collected 20–22 days after the last application, in ranked order were: 1.61, 5.78, 6.73, 7.79, 9.92 and 14.1 mg/kg.

The total residues in barley straw (fresh weight) from supervised trials collected 20–22 days after the last application, in ranked order were: 0.84, 3.48, 3.60, 3.96, 5.49 and 9.82 mg/kg.

The total residues in barley straw (dry weight) from supervised trials collected 20–22 days after the last application, ranked order were: 1.88, 5.88, 7.02, 8.55, 10.0 and 14.6 mg/kg.

Wheat animal feed data (whole plant no roots, straw, ears, rest of plants without roots) were collected in the trials carried out in Europe (Germany, he UK, France, Spain and Italy) in the 2008 and 2009 growing seasons (2 applications at 116–135g ai/ha) which approximated the UK GAP (2 applications at 125 g ai/ha and use up to GS 67). The labels for European GAP have no restrictions on animal feeding.

The ranked order of total residues in wheat rest of plant no roots (forage) samples collected 34–49 days after the second application (wet weight) at the GAP application rate were: 0.22, 0.25, 0.33, 0.39, 0.53, 0.61, 0.64, 0.77, 1.23, 2.56 and 5.05 mg/kg.

The total residues in wheat rest of plant no roots (forage) dry weight samples after applications at the higher (GAP) rate, in ranked order were: 0.88, 1.00, 1.32, 1.56, 2.12, 2.44, 2.56, 3.08, 4.92, 10.2 and 20.2 mg/kg.

The ranked order of residues of fluxapyroxad in wheat straw samples collected 34–60 days PHI (wet weight – highest value taken in each trial when readings at various PHIs) were: 0.32, 0.44, 0.46, 0.49, 0.55, 0.55, 0.64, 1.00, 1.00, 1.02, 1.19, 1.55, 1.80, 2.58, 2.78 and 6.05 mg/kg.

The ranked order of residues of fluxapyroxad in wheat straw samples collected 34–60 days PHI (dry weight – highest value taken in each trial when readings at various PHI) were: 0.36, 0.50, 0.52, 0.56, 0.63, 0.63, 0.73, 1.14, 1.14, 1.16, 1.35, 1.76, 2.05, 2.93, 3.16 and 6.88 mg/kg.

The ranked order of total residues in wheat straw samples collected 34–60 days PHI (fresh weight – highest value taken in each trial when readings at various PHIs) were: 0.35, 0.51, 0.53, 0.56, 0.58, 0.61, 0.68, 1.08, 1.08, 1.12, 1.31, 1.62, 1.96, 2.85, 2.92 and 6.24 mg/kg.

The ranked order of total residues of wheat straw samples collected 34–49 days PHI (dry weight – highest value taken in each trial when readings at various PHIs) were: 0.39, 0.58, 0.59, 0.64, 0.66, 0.69, 0.77, 1.23, 1.23, 1.27, 1.49, 1.8, 2.23, 3.24, 3.32 and 7.09 mg/kg.

Residue trials were conducted in wheat at four locations in Australia in which 2 applications were made at 61–62g ai/ha or 122–124g ai/ha. There is no corresponding GAP.

Residue trials were conducted in wheat at 22 locations in the USA and Canada (25 trials) generally according to the GAP in USA (2 applications at 97–100g ai/ha, harvest 21 day PHI, wheat hay or green chopped wheat 7–days). Observations from trials, in which, sampling took place at 25 and 27 days PHI, were not considered for the purposes of estimating a maximum residue level for straw.

The ranked order of total residues of fluxapyroxad in wheat forage (fresh weight) from supervised trials collected 6–8 days after the last application were: 0.10, 0.19, 0.21, 0.25, 0.32, 0.36, 0.57, 0.60, 0.64, 0.81, 0.85, 0.89, 0.95, 0.99, 1.19, 1.23, 1.40, 3.45, 3.60, 3.71, 4.80 and 9.27 mg/kg.

The ranked order of total residues of fluxapyroxad in wheat forage (dry weight) from supervised trials collected 6–8 days after the last application were: 0.64, 0.99, 1.09, 1.25, 1.84, 2.37, 3.33, 3.37, 3.39, 3.64, 3.73, 3.90, 4.52, 4.76, 5.34, 5.65, 6.26, 9.28, 12.1, 17.9, 19.4 and 40.66 mg/kg.

There is no necessity to estimate a maximum residue level for forage as it is not traded. Although the UK GAP is the critical GAP (application rates higher and no restrictions on animal feeding), on the basis that the residues are substantially higher in the USA trials, the highest and median residues will be taken from the USA trials. The Meeting estimated median and highest residues values for fluxapyroxad in wheat forage of 3.8 and 41 mg/kg.

The ranked order of fluxapyroxad in wheat straw (fresh weight) from supervised trials collected 20–22 days after the last application were: 0.75, 0.78, 0.80, 0.85, 0.97, 0.99, 1.07, 1.08, 1.24, 1.92, 2.29, 2.56, 3.08, 3.40, 4.61, 5.14, 6.39, 6.53, 7.16 and 7.29 mg/kg.

The ranked order of fluxapyroxad in wheat straw (dry weight) from supervised trials collected 20–22 days after the last application were: 1.24, 1.40, 1.46, 1.57, 1.61, 1.66, 1.72, 1.90, 2.07, 3.40, 4.01, 4.12, 4.28, 4.36, 5.26, 5.60, 7.33, 8.35, 8.47 and 10.1 mg/kg.

The ranked order of total residues of fluxapyroxad in wheat straw (wet weight) from supervised trials collected 20–22 days after the last application were: 0.91, 0.97, 1.00, 1.05, 1.09, 1.21, 1.25, 1.29, 1.65, 2.09, 2.79, 2.87, 3.59, 4.13, 4.79, 5.40, 6.41, 7.03, 7.61 and 8.00 mg/kg.

The ranked order of total residues of fluxapyroxad in wheat straw (dry weight) from supervised trials collected 20–22 days after the last application were: 1.25, 1.80, 1.83, 1.86, 1.89, 1.90, 2.31, 2.40, 2.75, 3.70, 4.37, 4.52, 5.16, 5.47, 5.85, 5.89, 7.35, 8.88, 9.29 and 10.8 mg/kg.

The ranked order of residues of fluxapyroxad in wheat hay (wet weight) from supervised trials collected 6–8 days after the last application were: 0.33, 0.37, 0.51, 0.51, 1.38, 1.42, 2.09, 2.12, 2.24, 2.58, 2.64, 2.72, 2.74, 2.86, 2.87, 3.29, 4.80, 5.75, 6.68, 5.97, 7.46 and 9.60 mg/kg.

The ranked order of residues of fluxapyroxad in wheat hay (dry weight) from supervised trials collected 6–8 days after the last application were: 0.65, 0.69, 0.76, 0.90, 2.58, 2.66, 3.00, 3.03, 3.33, 3.53, 3.73, 4.18, 4.61, 4.79, 7.21, 8.48, 8.59, 9.42, 9.83, 13.8, 15.7 and 17.6 mg/kg.

The ranked order of total residues of fluxapyroxad in wheat hay (wet weight) from supervised trials collected 6–8 days after the last application were: 0.35, 0.42, 0.54, 0.56, 1.42, 1.53, 2.19, 2.34, 2.35, 2.74, 2.74, 2.88, 2.97, 2.98, 3.13, 3.41, 4.99, 5.91, 6.17, 7.01, 7.56 and 9.93 mg/kg.

The ranked order of total residues of fluxapyroxad in wheat hay (dry weight) from supervised trials collected 6–8 days after the last application were: 0.68, 0.78, 0.81, 0.99, 2.78, 2.95, 3.12, 3.14, 3.48, 3.75, 3.86, 4.34, 4.84, 4.98, 7.49, 8.59, 9.01, 9.73, 10.1, 15.1, 17.2 and 18.3 mg/kg.

The Meeting used the wheat hay data to estimate maximum residue level, median and highest residues values for fluxapyroxad in wheat straw and fodder (dry) of 30, 4.1 and 18 mg/kg.

In practical conditions it is difficult to distinguish between forage and fodder of various cereal grains. The Meeting decided to use the wheat forage data to establish dietary parameters for barley. The Meeting estimated median and highest residues values for fluxapyroxad in wheat forage of 3.8 and 41 mg/kg and will extrapolate these values to barley forage. Similarly the wheat straw and fodder (dry) maximum residue level, STMR and HR will be extrapolated to barley.

The wheat and barley straw and fodder (dry) maximum residue level, median and highest residues and wheat and barley forage median and highest residues are also recommended for oats, rye and triticale as residues in these crops are not expected to significantly differ.

Cotton gin by–products (gin trash)

Residue trials were conducted in cotton at seven locations in the USA according to the critical GAP in USA (seed treatment application at 20 g ai/100 kg seed). No residues were detected in any sample. In addition two trials were carried out at 5× the GAP application rate in which no residues were detectable.

The Meeting estimated a maximum residue level for fluxapyroxad on cotton gin by-products of 0.01* mg/kg. The median residues are 0 mg/kg.

Peanut Hay

Residue trials were conducted at 12 different sites in the USA, matching the US GAP (3 applications at 97g ai/ha – maximum of 2 consecutive with a 7 day PHI). However the following restraint applies, "DO NOT graze or harvest for forage use".

Although residues data for peanut hay were submitted (sampling at 7, 14 and 21 days in 10 trials and sampling at either 3, 10 and 17 days or 0, 4, 7, 14 and 21 days in the other two trials, these data were not used to estimate a maximum residue level, as there is no GAP on which to base a recommendation.

Rotational Crops

Residues of fluxapyroxad are persistent in soil and may be taken up by following crops. In the USA the total seasonal application rate for crops apart from pome fruit, stone fruit and fruiting vegetables other than cucurbits is 200 g ai/ha. In Europe the total seasonal rate for cereals is 250 g ai/ha. In Australia the total seasonal rate for barley is 125 g ai/ha and in Brazil the total seasonal rate for cereals is up to 240 g ai/ha.

Field rotational crop studies conducted in the USA (one study) and Europe (four studies) have been made available to this Meeting.

Plots received either 2 applications to bare soil at 99–101 g ai/ha (198 g ai/season) or 1 application at 250 g ai/ha. Carrot/radish, potato and sugar beet, cauliflower/broccoli and lettuce, corn and wheat and canola and sunflower, were planted at various plant back intervals from 29–30 to 365 DALA). Another study was conducted in Germany and the UK where applications was made twice to barley (Germany) or wheat (UK) at a single rate equivalent to 125 g ai/ha. After harvest of the cereals, the rotational crops lettuce, radish and carrots were cultivated as secondary crops.

In general, residues of fluxapyroxad were observed more frequently than M700F008, while residues of M700F048 were rarely observed.

If the highest field rate is considered (250 g ai/ha) and a DT_{50} of 370 days (the highest in the field), then a plateau of residues in the soil will be reached after approximately 5 years. If it is considered that 50% of this residue is captured by plants, then the rotational crop studies can be considered to be reflective of practical conditions.

The Meeting considered that residues of fluxapyroxad may occur in succeeding crops but at insignificant levels in most crops, apart for cereal straw. Therefore, the Meeting considered it unnecessary to change or estimate new maximum residue levels to account for any uptake of residues of fluxapyroxad *via* the roots. For cereal straw, for which there is the possibility of an additional uptake of up to 0.6 mg/kg, it is considered that this is not significant in comparison with the residues in cereal straw from direct foliar treatment.

Fate of residues during processing

The Meeting received processing studies for apples, plums, tomatoes, soya bean, potatoes, sugar beet, barley, wheat, corn, sorghum, rice, peanuts, rape seed, sunflower seed and cotton seed. The table summarizes STMR-P and HR-P values calculated on the determined processing factors. In addition the following maximum residue levels were proposed.

Plums, based on the processing factor of 2.81 for dried prunes and the plum HR of 0.95 mg/kg, the Meeting estimated a maximum residue level for fluxapyroxad in prunes of 5 mg/kg.

Soya beans, based on the processing factor of 1.15 for soya bean hulls and the soya bean (dry) maximum residue level estimate of 0.15, the Meeting recommended a maximum residue level for fluxapyroxad in soya bean hulls of 0.3 mg/kg.

Wheat, based on the processing factor of 2.90 for wheat bran and the wheat grain maximum residue level estimate of 0.3 mg/kg the Meeting recommended a maximum residue level for fluxapyroxad in wheat bran of 1 mg/kg.

Barley, based on the processing factor of 1.89 for barley bran and the barley grain maximum residue level estimate of 2 mg/kg, the calculated expected highest residues in barley bran are 3.78 mg/kg. The Meeting recommended a maximum residue level for fluxapyroxad in barley bran of 4 mg/kg.

The processing factors derived from the processing studies and the resulting recommendations for STMR-Ps, HR-Ps, and/or maximum residue levels are summarized in the table below.

Processing Factors from the Processing of Raw Agricultural Commodities (RACs) with Field–Incurred Residues from Foliar Treatment with Fluxapyroxad

RAC	Processed Commodity	Processing Factor	RAC Maximum residue level	Processed Commodity Maximum residue level	RAC STMR	Processed Commodity STMR–P	RAC HR	Processed Commodity HR–P
Apple	Juice	0.21	0.9	–	0.26	0.05	0.37	0.08
	Pomace, wet	4.60		–		1.20		1.70
	Apple sauce	0.24		–		0.06		0.09
	Canned apples	0.22		–		0.06		0.08
	Dried apples	0.54		–		0.14		0.20
Plum	Washed plums	0.77	2	–	0.44	0.34	0.95	0.73
	Puree	0.83		–		0.37		0.79
	Jam	0.41		–		0.18		0.39
	Dried Prunes	2.81		5		1.23		2.66
Tomatoes	Canned tomatoes	0.19	0.6	–	0.07	0.013	0.44	0.08
	Paste	0.73		–		0.051		0.32
	Puree	0.37		–		0.026		0.16
	Raw juice	0.18		–		0.013		0.08
	Tomato peel	2.37		–		0.17		1.04
	Pomace, wet	3.40		–		0.24		1.50
Soya bean seed	Flour	0.50	0.15	0.3	0.01	0.005	0.11	0.055
	Hulls	1.15		–		0.012		0.13
	Meal	0.50		–		0.005		0.055
	Miso	0.50		–		0.005		0.055
	Refined oil	0.55		–		0.055		0.061
	Soy milk	0.50		–		0.005		0.055
	Soy sauce	0.50		–		0.005		0.055
	Tofu	0.50		–		0.005		0.055
	Aspirated grain fractions	158				1.58		17.38
Potato	Granules/flakes	0.5	0.03	–	0.01	0.005	0.02	0.01
	Chips	0.5		–		0.005		0.01
	Peel, wet	5.0		–		0.05		0.1
	Peeled potatoes	0.5		–		0.005		0.01
	Boiled potatoes (unpeeled)	0.5		–		0.005		0.01
	Microwave, boiled potatoes (unpeeled)	0.5		–		0.005		0.01
	Baked potato (unpeeled)	0.5		–		0.005		0.01
	Fried potato (unpeeled)	0.5		–		0.005		0.01

RAC	Processed Commodity	Processing Factor	RAC Maximum residue level	Processed Commodity Maximum residue level	RAC STMR	Processed Commodity STMR–P	RAC HR	Processed Commodity HR–P
	Process waste	0.5		–		0.005		0.01
	Dried pulp	7.0		–		0.07		0.14
Sugar beet	Refined sugar	0.17	0.15	–	0.04	0.007	0.06	0.010
	Dried pulp	1.75		–		0.07		0.11
	Molasses	0.80		–		0.032		0.048
	Thick juice	0.75		–		0.03		0.045
	Ensiled pulp	0.37		–		0.015		0.022
Wheat	Bran	2.90	0.3	1	0.085	0.25	0.21	0.61
	Flour	0.16		–		0.014		0.032
	Middlings	0.36		–		0.031		0.076
	Shorts	0.50		–		0.043		0.11
	Germ	1.22		–		0.10		0.26
	Bread (white)	0.12		–		0.010		0.03
	Whole meal	0.96		–		0.082		0.20
	Bread whole meal	0.64		–		0.054		0.13
	Aspirated grain fractions	220		–		18.7		46.2
Barley	Pot barley	0.16	2	–	0.535	0.086	1.26	0.20
	Bran	1.89		4		1.01		2.38
	Flour	0.15		–		0.080		0.19
	Brewing malt	0.01		–		0.0054		0.013
	Spent grain	0.25		–		0.13		0.32
	Beer	0.02		–		0.011		0.025
Maize	Meal	0.7	0.01	–	0.01	0.007	0.01	0.007
	Flour	0.9		–		0.009		0.009
	Grits	0.3		–		0.003		0.003
	Starch	0.1		–		0.001		0.001
Canola seed	Meal	0.42	1.5	–	0.11	0.046	0.83	0.35
	Refined oil	0.23		–		0.025		0.19
Sunflower seed	Meal	0.12	1.5	–	0.055	0.006	0.11	0.013
	Refined oil	0.08		–		0.004		0.008

Processed commodity STMR–Ps and HR–Ps were calculated on the basis of the total residues (fluxapyroxad + M700F008 + M700F048) process factor.

Residues in Animal Commodities

Estimated maximum and mean dietary burdens of farm animals

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 2009 edition of the FAO Manual.

Potential cattle feed items include: apple pomace, tomato pomace, oat grain, sugar beet tops, sugar beet dried pulp, sugar beet ensiled pulp, sugar beet molasses, barley grain, forage, hay and straw, brewer's grain, wheat grain, forage, hay and straw, wheat milled by-products, wheat aspirated grain fractions, maize grain fodder and forage, maize meal, maize milled by-products, potato culls and dried pulp (potato process waste), sunflower meal, barley bran, sugar beet tops, cotton seed, cotton seed meal and hulls, cotton gin by-products, soya bean forage and fodder (hay), soya beans, soya bean meal and hulls, soya bean aspirated grain fractions, bean and pea seed, bean vines and pea vines and hay/ fodder and canola meal.

Summary of livestock dietary burden for fluxapyroxad (ppm of dry matter diet)

	US–Canada		EU		Australia		Japan	
	max	mean	max	mean	max	mean	max	mean
Beef cattle	4.61	2.25	19.3	5.51	40.7a	11.4c	0.60	0.60
Dairy cattle	18.4	4.17	18.8	5.78	39.2b	9.37d	3.93	1.77

[a] Highest maximum beef or dairy cattle dietary burden suitable for HR and maximum residue level estimates for mammalian meat

[b] Highest maximum dairy cattle dietary burden suitable for HR and maximum residue level estimates for mammalian milk

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

[s] Highest mean dairy cattle dietary burden suitable for STMR estimates for mammalian milk

Potential poultry feed items include: apple pomace, tomato pomace, oat grain, sugar beet tops, sugar beet dried pulp, sugar beet ensiled pulp, sugar beet molasses, barley grain, forage, hay and straw, brewer's grain, wheat grain, forage, hay and straw, wheat milled by-products, maize grain fodder and forage, maize meal, maize milled by-products, potato culls and dried pulp (potato process waste), sunflower meal, barley bran, sugar beet tops, cotton seed, cotton seed meal and hulls, cotton gin by-products, soya bean forage and fodder (hay), soya beans, soya bean meal and hulls, soya bean aspirated grain fractions, bean and pea seed, bean vines and pea vines and hay/ fodder and canola meal.

Summary of poultry dietary burden for fluxapyroxad (ppm of dry matter diet)

	US–Canada		EU		Australia		Japan	
	max	mean	max	mean	max	mean	max	mean
Poultry Broiler	0.53	0.53	0.50	0.50	0.18	0.18	0.079	0.079
Poultry Layer	0.53	0.53	7.14[a]	2.10[b]	0.18	0.18	0.14	0.14

[a] Highest maximum poultry dietary burden suitable for HR and maximum residue level estimates for poultry meat and eggs

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

Farm Animal Dietary Burden

The Meeting received a lactating dairy cow feeding study which provided information on residues of fluxapyroxad, M700F002 and M700F048 arising in tissues and milk when dairy cows were dosed with fluxapyroxad and metabolite M700F002 for 28 days, at target feeding levels equivalent to 3, 6, 18 and 60 ppm (fluxapyroxad) and 0, 0.1, 0.3 and 1 ppm (M700F002) in the diet. A depuration period of 7 days followed.

Residues of fluxapyroxad and M700F008 were observed in milk at all feeding levels although in the lowest dose group most milk samples showed fluxapyroxad residues below LOQ. Residues of fluxapyroxad and M700F008 in the higher dose groups reached a plateau after five to seven days. Analysis of milk samples from depuration animals showed no fluxapyroxad or M700F008 residues above LOQ were detectable after four days of withdrawal. Generally residue levels of M700F008 in milk were similar to the fluxapyroxad residue levels. The highest total residues (fluxapyroxad + M700F008) in milk at the highest dosing regime were 0.054 mg/kg (mean 0.031 mg/kg). Residues were demonstrated to concentrate into cream. The highest total residues (mean in brackets) in liver, kidney, fat and muscle were 0.45 (0.35), 0.098 (0.067), 0.264 (0.260) and 0.045 (0.036) mg/kg respectively. Analysis of the depuration tissue samples showed no residues of fluxapyroxad or M700F008 above LOQ after two days of withdrawal.

No residues of M700F002 above LOQ (0.001 mg/kg) were detected in any milk or tissue samples from any dose group.

The Meeting also received information on the residue levels arising in tissues and eggs when laying hens were dosed with fluxapyroxad and metabolite M700F002 for 28 days, at target feeding levels equivalent to 0.3, 0.6, 1.8 and 6 ppm (fluxapyroxad) and 0.025, 0.05, 0.15 and 0.5 ppm (M700F002) in the diet. A depuration period of 14 days followed.

Residues of fluxapyroxad were observed in egg at all feeding levels although in the lowest dose group all but one mean egg samples showed fluxapyroxad residues below LOQ and all egg samples showed M700F008 residues below LOQ. In the highest dose group fluxapyroxad and M700F008 residues reached a plateau at five days. No residues of either fluxapyroxad or M700F008 were detected at the highest feeding level in muscle and skin with fat. The highest total residues (mean in brackets) in liver and fat were 0.029 (0.025) and 0.042 (0.040) mg/kg respectively.

No residues of M700F002 above LOQ (0.001 mg/kg) were detected in any egg or tissue samples from any dose group.

Analysis of the depuration egg samples showed that residues of fluxapyroxad and M700F008 were < LOQ after four and eight days of withdrawal respectively and not detectable after eight and ten days of withdrawal respectively. Analysis of the depuration tissue samples showed that residues of fluxapyroxad and M700F008 were < LOQ after three days of withdrawal.

Animal commodity maximum residue levels

Cattle STMR and HR

For highest residue level estimation, the high residues in the cattle tissues were calculated by interpolating the maximum dietary burden for beef cattle (40.7 ppm) between the relevant feeding levels (18.2 and 60.3) in the dairy cow feeding study and using the highest tissue concentrations (fluxapyroxad + M700F008) from individual animals within those feeding groups. For highest residue level estimation, the high residues in the cattle milk were calculated by interpolating the maximum dietary burden for dairy cattle (39.2 ppm) between the relevant feeding levels (18.2 and 60.3) in the dairy cow feeding study and using the highest mean milk concentrations (fluxapyroxad + M700F008) from those feeding groups.

The STMR values for the tissues were calculated by interpolating the mean dietary burden for beef cattle (11.4 ppm) between the relevant feeding levels (6.1 and 18.2 ppm) from the dairy cow feeding study and using the mean tissue concentrations (fluxapyroxad + M700F008) from those feeding groups. The STMR values for the milk were calculated by interpolating the mean dietary burden for dairy cattle (9.37 ppm) between the relevant feeding levels (6.1 and 18.2 ppm) from the dairy cow feeding study and using the mean milk concentrations (fluxapyroxad + M700F008) from those feeding groups.

Fluxapyroxad Feeding Study	Feed Level (ppm) for milk residues	Residues (mg/kg) in milk	Feed Level (ppm) for tissue residues	Residues (mg/kg)			
				Muscle	Liver	Kidney	Fat
HR Determination (beef or dairy cattle)							
Feeding Study	18.2 60.3	0.0099 0.031	18.2 60.3	< 0.02 0.045	0.15 0.45	0.032 0.098	0.077 0.264
Dietary burden and estimate of highest residue	39.2	0.020	40.7	0.033	0.31	0.067	0.176
STMR Determination (beef or dairy cattle)							
Feeding Study	6.1 18.2	0.0032 0.0078	6.1 18.2	< 0.02 < 0.02	0.052 0.12	0.021 0.027	0.029 0.070
Dietary burden and estimate of highest residue	9.37	0.004	11.4	< 0.02	0.081	0.024	0.047

The Meeting estimated the following STMR values: milk 0.004 mg/kg; muscle < 0.02 mg/kg; edible offal (based on liver) 0.081 mg/kg and fat 0.047 mg/kg.

The Meeting estimated the following HR values: milk 0.020 mg/kg; muscle 0.033 mg/kg; edible offal (based on liver) 0.31 mg/kg and fat 0.18 mg/kg.

At various dosing levels (day 21) the mean residues observed in cream were up to 9× the mean residues in milk. It is therefore calculated that maximum residues in cream will be 0.18 mg/kg and STMR is 0.036.

It is assumed that cream is 40% fat, therefore the estimated highest residue and STMR for milk fats for dietary purposes are 0.45 and 0.09 mg/kg.

Cattle – maximum residue level

For maximum residue level estimation, the high residues in the cattle tissues were calculated by interpolating the maximum dietary burden (40.7 ppm) between the relevant feeding levels (18.2 and 60.3) in the dairy cow feeding study and using the highest tissue concentrations (fluxapyroxad) from individual animals within those feeding groups. For maximum residue level estimation, the high residues in the milk were calculated by interpolating the maximum dietary burden (39.2 ppm) between the relevant feeding levels (18.2 and 60.3) in the dairy cow feeding study and using the highest mean milk concentrations (fluxapyroxad) from those feeding groups.

Fluxapyroxad Feeding Study	Feed Level (ppm) for milk residues	Residues (mg/kg) in milk	Feed Level (ppm) for tissue residues	Residues (mg/kg)			
				Muscle	Liver	Kidney	Fat
Maximum residue level determination (beef or dairy cattle)							
Feeding Study	18.2 60.3	0.0052 0.015	18.2 60.3	< 0.01 0.012	0.032 0.094	< 0.01 0.019	0.059 0.171
Dietary burden and estimate of highest residue	39.2	0.010	40.7	0.011	0.065	0.015	0.119

The Meeting estimated the following highest residues for the purposes of maximum residue level estimation: milk 0.010 mg/kg; muscle 0.011 mg/kg; edible offal (based on liver) 0.065 mg/kg and fat 0.12 mg/kg.

At various dosing levels (day 21) the mean residues observed in cream were up to 10.5× the mean residues in milk. It is therefore calculated that maximum residues in cream will be 0.11 mg/kg.

It is assumed that cream is 40% fat, therefore the estimated highest residue for milk fats is 0.26 mg/kg.

The Meeting estimated the following maximum residue level values: milk 0.02 mg/kg; milk fats 0.5 mg/kg; meat (mammalian except marine) (fat) 0.2 mg/kg and edible offal (mammalian) 0.1 mg/kg.

Poultry STMR and HR

For highest residue level estimation, the high residues in the hen tissues and eggs were calculated by extrapolating the maximum dietary burden (7.1 ppm) with the highest feeding level (6.0 ppm) in the laying hen feeding study and using the highest tissue concentrations (fluxapyroxad + M700F008) from individual animals within that feeding group and using the highest mean egg concentration (fluxapyroxad + M700F008) from that feeding group.

The STMR values for the tissues and eggs were calculated by interpolating the mean dietary burden (2.1 ppm) between the relevant feeding levels (1.8 and 6.0 ppm) from the poultry feeding study and using the mean tissue and egg concentrations (fluxapyroxad + M700F008) from those feeding groups.

Fluxapyroxad Feeding Study	Feed Level (ppm) for egg residues	Residues (mg/kg) in egg	Feed Level (ppm) for tissue residues	Residues (mg/kg)			
				Muscle	Liver	Skin with Fat	Fat
HR Determination (poultry broiler or layer)							
Feeding Study	6.0	0.020	6.0	< 0.02	0.029	< 0.02	0.042
Dietary burden and estimate of highest residue	7.1	0.023	7.1	< 0.024	0.034	< 0.024	0.050
STMR Determination (poultry broiler or layer)							
Feeding Study	1.8 6.0	0.0053 0.014	1.8 6.0	< 0.02 < 0.02	0.021 0.025	< 0.02 < 0.02	< 0.02 0.040
Dietary burden and estimate of highest residue	2.1	0.006	2.1	< 0.02	0.021	< 0.02	0.021

The Meeting estimated the following STMR values: egg 0.006 mg/kg; muscle 0.02 mg/kg; edible offal (based on liver) 0.021 mg/kg and fat 0.021 mg/kg.

The Meeting estimated the following HR values: egg 0.023 mg/kg; muscle 0.024 mg/kg; edible offal (based on liver) 0.034 mg/kg and fat 0.050 mg/kg.

Poultry maximum residue level

For maximum residue level estimation, the high residues in the hen tissues and eggs were calculated by extrapolating the maximum dietary burden (7.1 ppm) with the highest feeding level (6.0 ppm) in the laying hen feeding study and using the highest tissue concentrations (fluxapyroxad) from individual animals within that feeding group and using the highest mean egg concentration (fluxapyroxad) from that feeding group.

Fluxapyroxad Feeding Study	Feed Level (ppm) for egg residues	Residues (mg/kg) in egg	Feed Level (ppm) for tissue residues	Residues (mg/kg)			
				Muscle	Liver	Skin with Fat	Fat
Maximum residue level determination (poultry broiler or layer)							
Feeding Study	6.0	0.0065	6.0	< 0.01	< 0.01	< 0.01	0.028
Dietary burden and estimate of highest residue	7.1	0.0077	7.1	< 0.012	< 0.012	< 0.012	0.033

The Meeting estimated the following highest residue values for the purpose of maximum residue level estimation: egg 0.0077 mg/kg; muscle 0.012 mg/kg; liver 0.012 mg/kg, skin with fat 0.012 mg/kg and fat 0.033 mg/kg.

The Meeting estimated the following maximum residue levels: poultry meat 0.02 mg/kg; poultry fats 0.05 mg/kg, poultry edible offal 0.02 mg/kg and eggs 0.02 mg/kg.

DIETARY RISK ASSESSMENT

Long-term intake

The evaluation of fluxapyroxad has resulted in recommendations for maximum residue levels and STMRs for raw and processed commodities. Consumption data were available for 36 food commodities and were used in the dietary intake calculation. The results are shown in Annex 3. The

International Estimated Daily Intakes for the 13 GEMS/Food regional diets, based on estimated STMRs were in the range 1–10% of the maximum ADI of 0.02 mg/kg bw (Annex 3).

The Meeting concluded that the long-term intake of residues of fluxapyroxad from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The International Estimated Short-term Intake (IESTI) for fluxapyroxad was calculated for the food commodities (and their processing fractions) for which maximum residue levels and HRs were estimated and for which consumption data were available. The results are shown in Annex 4. The IESTI of fluxapyroxad varied from 0–20% of the ARfD (0.3 mg/kg bw).

The Meeting concluded that the short-term intake of residues of fluxapyroxad from uses that have been considered by the JMPR is unlikely to present a public health concern.