5.13 Kresoxim-methyl (199)

RESIDUE AND ANALYTICAL ASPECTS

Kresoxim-methyl is a strobilurin fungicide, acting by inhibiting mitochondrial respiration.

Kresoxim-methyl was first evaluated for toxicology and residues by JMPR in 1998 and a periodic evaluation was conducted by the 2018 JMPR. An ADI of 0-0.3 mg/kg bw was established and an ARfD was not considered necessary.

For plant commodities, the definition of the residue for compliance with the MRL is: k*resoxim-methyl* and for dietary risk asessment is: *Sum of kresoxim-methyl and metabolites (2E)-(methoxyimino){2-[(2-methylphenoxy)methyl]phenyl}acetic acid (490M1), and (2E)-{2-[(4-hydroxy-2-methylphenoxy)methyl]phenyl}(methoxyimino)acetic acid (490M9) including their conjugates, expressed as kresoxim-methyl*

For animal commodities, the definition of the residue for compliance with the MRL and for dietary risk assessment is: *Sum of metabolites (2E)-(methoxyimino){2-[(2-methylphenoxy)methyl]phenyl}acetic acid (490M1), and (2E)-{2-[(4-hydroxy-2-methylphenoxy)methyl]phenyl}(methoxyimino)acetic acid (490M9), expressed as kresoxim-methyl*

The residue is not fat-soluble.

The 2018 JMPR also noted that if future uses of kresoxim-methyl result in an increase of the dietary exposure to metabolite 490M2, to more than the threshhold of toxicological concern (TTC) for a Cramer Class III compound, a reconsideration of the residue definition for dietary exposure may be necessary.

Kresoxim-methyl was scheduled at the Fiftieth Session of the CCPR for evaluation of additional uses by the 2019 JMPR. The Meeting received new GAP information and new supporting residue information for pome fruit.

Results of supervised residue trials on crops

New supervised trials from Canada and the USA were available for the use of kresoxim-methyl on pome fruit. The analytical methods used in these trials were reviewed by the 2018 JMPR and the demonstrated stability of residues in frozen samples (12 months) covered the storage intervals in the trials considered by the Meeting.

Product labels were available from Australia, Belgium, Canada, France, the Netherlands, Spain, the UK and the USA.

For dietary risk assessment, 'total residues' refers to the sum of kresoxim-methyl and metabolites 490M1 and 490M9, expressed as kresoxim-methyl. The parent-equivalent conversion factors were 1.047 (409M1) and 0.994 (490M9).

Pome fruit

The critical GAP for kresoxim-methyl on pome fruit is in the USA, with a maximum of 4 foliar applications of 0.22 kg ai/ha, a minimum retreatment interval of 7 days and a pre-harvest interval of 30 days.

In trials from Canada and the USA on apples and pears, matching the GAP in the USA, residues of kresoxim-methyl in apples were: < 0.05 (8), 0.05 (2), 0.06 (3), 0.07 and 0.08 (3) mg/kg (n = 17) and in pears were: < 0.05 (6), 0.06 and 0.09 mg/kg (n = 8).

For maximum residue level estimation, the combined kresoxim-methyl data set for apples and pears, matching the critical GAP for pome fruit in the USA is: < 0.05 (14), 0.05 (2), 0.06 (4), 0.07, 0.08 (3) and 0.09 mg/kg (n = 25).

For dietary risk assessment, total residues (parent, 490M1 and 490M9, expressed as kresoxim-methyl) in apples from trials matching the GAP in the USA were: < 0.1 (7), 0.1 (2), 0.11 (2), 0.12 (2), and 0.13 (4) mg/kg and in pears were: < 0.1 (2), 0.11 (2), 0.13, 0.14, 0.19 and 0.2 mg/kg.

The combined data set for total residues in apples and pears, matching the GAP in the USA is: < 0.1 (9), 0.1 (2), 0.11 (4), 0.12 (2), 0.13 (5), 0.14, 0.19 and 0.2 mg/kg (n = 25).

The Meeting estimated a maximum residue level of 0.15 mg/kg for kresoxim-methyl and an STMR of 0.11 mg/kg for total residues in pome fruit except persimmon, Japanese to replace the previous recommendation for pome fruit.

Fate of residues during processing

The 2018 JMPR reviewed information on the fate of kresoxim-methyl and metabolites 490M1 and 490M9 residues during processing of apples.

Table 1 Processing factors for total residues in apple commodities estimated by the 2018 JMPR for dietary exposure estimation

Raw commodity [STMR]	Processed commodity	Individual processing factors	Mean or best estimate processing factor	STMR-P = $STMR_{RAC}$ × PF (mg/kg)	Median residue = $STMR_{RAC}$ × PF (mg/kg)
Apple [0.11 mg/kg]	Apple sauce	0.23, 0.26, 0.27, 0.29, 0.31, 0.50, 0.63	0.29	0.032	
	Wet pomace	0.31, 0.47, 1.4, 2.1, 2.2, 2.6, 2.7, 4.0	2.2		0.24
	Apple juice	0.10, 0.10, 0.12, 0.13, 0.26, 0.30, 0.31, 0.63	0.2	0.022	
	Dried apples	0.23, 0.30, 0.42, 0.61	0.39	0.043	
	Dried pomace	4.5, 8.7, 9.1, 16	8.9		0.98

Residues in animal commodities

Farm animal dietary burden

Dietary burdens were calculated for beef cattle, dairy cattle, broilers and laying poultry based on feed items evaluated by the JMPR in 2018 and by the current Meeting.

The additional residue burdens arising from the consumption of wet apple pomace do not change the conclusions of the 2018 JMPR. For beef and dairy cattle, the maximum and mean dietary burdens remain at 3.2 ppm and 1.5 ppm, respectively.

Wet apple pomace is not a component of the poultry diets, and maximum and mean dietary burdens for poultry estimated by the 2018 JMPR remain unchanged.

Animal commodity maximum residue levels

The Meeting agreed that since the kresoxim-methyl maximum and mean livestock dietary burdens have not changed, the 2018 JMPR recommendations for animal commodities need not be revised.

RECOMMENDATIONS

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

Definition of the residue for compliance with the MRL for plant commodities: *Kresoxim-methyl*

Definition of the residue for dietary risk assessment for plant commodities: *Sum of kresoxim-methyl and metabolites (2E)-(methoxyimino){2-[(2-methylphenoxy)methyl]phenyl}acetic acid (490M1), and (2E)-{2-[(4-hydroxy-2-methylphenoxy)methyl]phenyl}(methoxyimino)acetic acid (490M9) including their conjugates, expressed as kresoxim-methyl*

Definition of the residue for compliance with the MRL and dietary risk assessment for animal commodities: *Sum of metabolites (2E)-(methoxyimino){2-[(2-methylphenoxy)methyl]phenyl}acetic acid (490M1), and (2E)-{2-[(4-hydroxy-2-methylphenoxy)methyl]phenyl}(methoxyimino)acetic acid (490M9), expressed as kresoxim-methyl*

The residue is not fat-soluble.

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The ADI for kresoxim-methyl (and applying to metabolites 490M1 and 490M9) is 0–0.3 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for kresoxim-methyl were estimated for the 17 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by the JMPR. The results are shown in Annex 3 of the 2019 JMPR Report.

The IEDIs ranged from 0–0.4% of the maximum ADI. The Meeting concluded that long-term dietary exposure to residues of kresoxim-methyl from uses considered by the JMPR is unlikely to present a public health concern.

Acute dietary exposure

The 2018 JMPR decided that an ARfD for kresoxim-methyl is unnecessary. The Meeting therefore concluded that the acute dietary exposure to residues of kresoxim-methyl from the uses considered is unlikely to present a public health concern.

Threshold of toxicological concern (TTC) consideration for metabolites

Metabolite 490M2

The 2018 JMPR applied the TTC approach to assess the metabolite 490M2 and concluded that the maximum long-term dietary exposure (0.30 µg/kg bw per day) was below the 1.5 µg/kg bw per day threshold for a Cramer Class III compound.

The current Meeting noted that with the additional residue contribution from the pome fruit commodities considered by the Meeting, the maximum long-term dietary exposure for metabolite 490M2 increased to 0.34 µg/kg bw per day. The Meeting concluded that dietary exposure to residues of 490M2 in food commodities considered by the current and previous Meetings is unlikely to present a public health concern.