FENTHION (039)

EXPLANATION

Fenthion was first evaluated in 1971 and has been reviewed several times since, most recently in 1995 as part of the CCPR Periodic Review Programme. On the basis of the results from supervised trials, the 1995 JMPR withdrew the previous recommendations for MRLs except those for cherries, olives, and husked rice. It recommended new MRLs for mandarins and sweet and sour oranges to replace the MRL for citrus fruit, and proposed an amended MRL for virgin olive oil.

The 29th CCPR decided to retain the CXLs for meat and milk for 4 years according to the Periodic Review procedure until results of animal feeding studies were available.

At the 30th Session of the CCPR, it was noted that ingestion of up to 200 ml virgin olive oil containing fenthion residues at the level of the MRL would not lead to exposure exceeding the acute RfD of 0.01 mg/kg bw. The CCPR noted that new GAP for olives was being developed in the European Union and consequently new data were to be expected. The 31st Session of the CCPR was informed that animal feeding studies and new data on olives, oranges and mandarins would be available for the 2000 JMPR. It retained the draft MRLs for mandarins and sweet and sour oranges at Step 7 (7B), awaiting the residue evaluation by the 2000 JMPR.

The 32nd Session of the CCPR was informed that animal feeding studies had been provided for evaluation by the 2000 JMPR and agreed to extend the 4-year period under the Periodic Review procedure for the MRLs for meat and milks pending the evaluation.

The 1995 JMPR had listed as desirable full details of olive trials in Greece begun in May 1995, additional information on residues in treated animal feeds and on residues in meat and offal arising either from dermal treatment or consumption of fenthion-treated animal feeds in transfer studies. Information on the measured octanol/water partition coefficients of the oxidative metabolites of fenthion was also requested.

The manufacturer reported new residue trials on peaches and olives in support of pending GAP within the European Union and also resubmitted the 1968 results of trials on cherries in Germany, but these results could not be evaluated as the relevant GAP is still pending.

Information on current GAP, the fate of residues in processing peaches, apples and olives, the octanol/water partition coefficients of the oxidative metabolites, methods of residue analysis, an animal feeding study and residues in food in commerce or at consumption was also provided.

Information on national MRLs and GAP was provided by the governments of Australia, Germany and The Netherlands as follows.

Information was submitted on the octanol/water partition coefficients of fenthion and its oxidative metabolites. Measurements were made at octanol:water volume ratios of 1:1 and 1:10 as listed below.

	log P_{ow}	
	O/W* = 1	O/W = 1/10
Fenthion	4.04 ± 0.05	4.06 ± 0.04
Fenthion sulfoxide	1.98 ± 0.04	1.93 ± 0.03
Fenthion sulfone	2.02 ± 0.02	2.17 ± 0.02

*octanol/water (v/v)

USE PATTERN

The manufacturer reported registered world-wide uses of fenthion on cherries, peaches, citrus fruit and olives.

The Meeting was informed that fenthion was under review in the European Union and revised GAP was pending. Information on current GAP was provided by the manufacturer and the governments of Germany and Australia. Product labels were supplied by the manufacturer and the government of Australia.

The external application of fenthion to animals is no longer registered in Europe, and it is no longer used on lactating dairy cattle in Australia. The current MRL for residues of fenthion in milk (0.2 mg/kg) was set as a temporary standard until August 2001.

Table 1. Registered use of fenthion in Australia for direct animal treatment.

	Form	Liveweight, kg	Application		Withholding period
			Dose, ml/animal	Dose, mg/kg bw	
Beef cattle	Spot-on	up to 110	2.5	4.5	10 days
		110 to 220	5	9-4.5	
Non-lactating dairy cattle		220 to 550	10	9-3.6	
		Over 550	20	7	

Farm animal feeding studies

Fenthion is not directly applied to fodder plants, but fenthion residues may occur in plant parts or processed plant products, e.g. from rice or citrus, that are used as animal feeding stuffs.

The 1995 JMPR concluded that additional information on residues in meat and offal arising either from dermal treatment or consumption of fenthion-treated animal feeds in transfer studies was desirable. In response, a cattle feeding trial was reported to the Meeting (Phillips *et al*., 1996).

Nine Holstein dairy cows each weighing 539-632 kg were dosed orally with gelatin capsules of fenthion for 28 consecutive days. Three cows were dosed with fenthion at each level: 0.075 mg/kg bw, 0.23 mg/kg bw and 0.75 mg/kg bw, equivalent to 1.9 ppm, 7.6 ppm, and 20 ppm fenthion in the feed. An additional cow served as the control.

Organs, tissues and milk were analysed for fenthion, fenoxon and their sulfoxides and sulfones. No significant effect on body weight, feed intake, or milk production was observed at any dosage. The cows were milked twice daily on days (-1), 1, 7, 14, 21, 26, 27, and 28, and tissue samples were collected from each cow not more than 24 hours after the last dose.

At the highest dose the total residues of fenthion in the liver ranged from <0.05 mg/kg to 0.07 mg/kg and in composite perirenal, omental and subcutaneous fat from <0.05 to 0.12 mg/kg. The residues in the kidneys and in composite round, flank and loin muscle were below the LOD of 0.05 mg/kg. Residues in liver and fat were below the LOD of 0.05 mg/kg in the 0.23 mg/kg bw group. Kidneys and muscle of this group and all tissues of the 0.075 dose group were not analysed because no residues were detected at the higher dose level.

Table 2. Total fenthion residues in the edible tissues of dairy cattle after daily dosing with fenthion for 28 consecutive days.

Feeding level, ppm	Dose, mg/kg bw	Total residues, mg/kg							
		Liver		Kidneys		Composite muscle		Composite fat	
		Range	Av.	Range	Av.	Range	Av.	Range	Av.
1.9	0.075	NA		NA		NA		NA	
7.6	0.23	<0.05	<0.05	NA		NA		<0.05	<0.05
20	0.75	<0.05-0.07	0.06	<0.05	<0.05	<0.05	<0.05	<0.05-0.12	0.09

NA not analysed LOD 0.05 mg/kg

Residues in the milk at the 0.75 mg/kg bw dose level were 0.02, 0.04, 0.03, 0.04, and 0.04 mg/kg (average) at days 1, 7, 14, 21, and 28 respectively. A plateau of about 0.04 mg/kg was reached for total residues of fenthion in the cows dosed at 0.75 mg/kg bw within 7 days. At the 0.23 and 0.075 mg/kg bw dose levels the residues in the milk were below the LOD of 0.01 mg/kg (Table 3).

Table 3. Fenthion residues in the milk from dairy cattle after daily dosing with fenthion for 28 days.

Feeding level, ppm	Dose, mg/kg bw	Days	Total fenthion residues, mg/kg	
			Range	Average
20	0.75	1	0.02	0.02
		7	0.03-0.047	0.039
		14	0.025-0.034	0.03
		21	0.037-0.043	0.04
		28	0.036-0.042	0.041
7.6	0.23	28	<0.01	<0.01
1.9	0.075	28	<0.01	<0.01

LOD = 0.01 mg/kg

FATE OF RESIDUES IN STORAGE AND PROCESSING

The Meeting received information on the fate of incurred residues of fenthion during the processing of apples, peaches, oranges and olives. Processing studies on apples, oranges and olives were evaluated by the 1995 JMPR. Although maximum residue levels were not estimated for apples, peaches and olives because GAP was only pending, processing factors for apples and peaches were calculated. Processing factors for the production of crude olive oil were reported in 1995.

Peaches. Three trials were conducted in Spain in 1994 and 1995. Fenthion was applied twice to peach trees at 1.1 kg ai/ha. The water volume was 1500 l/ha, corresponding to a spray concentration of 0.075% ai. Fruits were sampled 28 days after the last application from the treated and untreated plots.

The peaches were washed in running water with slow movement in all the processes and stoned. Jam was made from peeled and stoned peaches by household preparation. The processing into preserve and juice in the laboratory simulated industrial practice (Figure 1).

Table 4. Total fenthion residues in peaches and their processed commodities from supervised trials in Spain (Heinemann and Ohs, 1997).

Country, year (variety)	Application					PHI, days	Commodity	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	Water, l/ha	No.				
Spain, 1995 (Miraflores)	500 EC	1.125	0.075	1500	2	28	whole fruit washed fruit juice jam preserve	0.03 0.01 0.02 <0.01 <0.01	*RA-3013/95* 0385-94 403857 (Heinemann and Ohs, 1997)
Spain, 1995 (Gladis)	500 EC	1.125	0.075	1500	2	28	whole fruit washed fruit juice jam preserve	0.13 0.06 <0.01 <0.01 0.01	*RA-3013/95* 0242-95 502421 (Heinemann and Ohs, 1997)

Figure 1. Processing of peaches to jam.

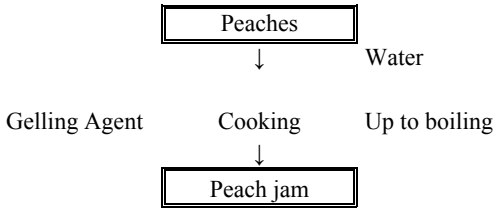


Figure 2. Processing of peaches to preserve.

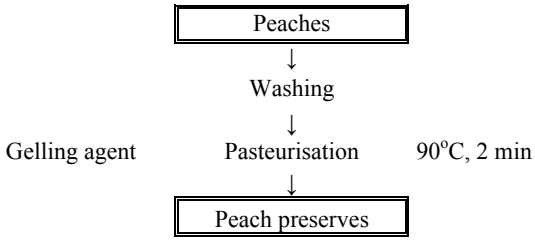
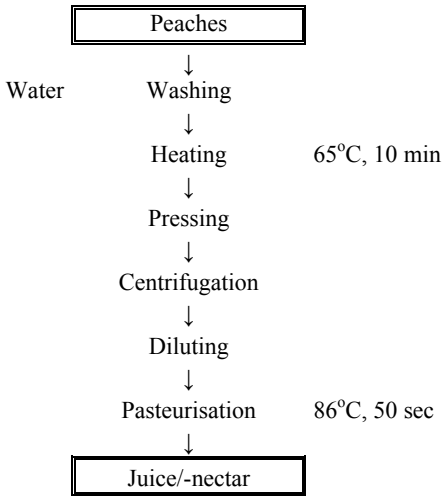


Figure 3. Processing of peaches to juice/-nectar.



Processing factors

Table 5. Processing factors calculated from unrounded residues of fenthion and of combined fenthion and fenthion sulfone expressed as fenthion.

Commodity	Residues, mg/kg			Processing factors			
	Trial A	Trial B	Trial C	Trial A	Trial B	Trial C	Mean
Apples, 18 days PHI	0.22			-			
Apples, washed	0.12			0.5			0.5
Sauce, raw	0.15			0.7			0.7
Sauce	0.11			0.5			0.5
Juice, raw	0.20			0.9			0.9
Juice	0.18			0.8			0.8
Pomace, dry	0.96			4.4			4.4
Peaches, 28 days PHI	0.17	0.03	0.13				
Peaches, washed	0.40	0.01	0.06	2.4	0.33	0.46	1.06
Jam	0.06	< 0.01	< 0.01	0.35	0.33	0.08	0.25
Preserve	< 0.01	< 0.01	0.01	0.06	0.33	0.08	0.16
Juice	0.06	0.02	< 0.01	0.35	0.67	0.08	0.37

APPRAISAL

Fenthion was first evaluated by the Joint Meeting in 1971 and has been reviewed several times since, most recently in 1995 within the Periodic Review Programme of the CCPR. On the basis of data on residues found in supervised trials, the 1995 JMPR agreed to withdraw the previous recommendations for all MRLs except those for cherries, olives, and husked rice, which were confirmed. The 1995 JMPR recommended new MRLs for mandarins and sweet and sour oranges, replacing the existing MRL for citrus fruit, and amended the MRL for virgin olive oil.

At its twenty-ninth Session, the CCPR decided to retain the Codex MRLs for meat and milk for 4 years until data from animal feeding studies became available. At its thirtieth session, the CCPR noted that ingestion of up to 200 ml of virgin olive oil containing fenthion residues at the MRL would not exceed the acute RfD of 0.01 mg/kg bw. The Committee recognized that new GAP for olives was being developed within the European Union and, consequently, new data were to be expected. At its thirty-first Session, the CCPR was informed that the results of animal feeding studies and new data on olives, oranges, and mandarins would be available for the 2000 JMPR. The CCPR decided to retain the draft MRLs for mandarins and sweet and sour oranges to Step 7 (7B) until the residue evaluation of the 2000 JMPR became available. At its thirty-second Session, the CCPR was informed that the results of animal feeding studies had been provided to the 2000 JMPR and agreed to extend the 4-year extension for the MRLs for meat and milks, pending the review of the 2000 JMPR.

The 1995 JMPR considered that it would be desirable to have full details of the trials on olives conducted in Greece and additional information on residues in treated animal feeds and in meat and offal from animals treated externally or which had consumed fenthion-treated feeds in transfer studies. Information on the measured octanol-water partition coefficients of the oxidative metabolites of fenthion was also considered desirable.

The manufacturer provided new studies of residues in peaches and olives, to support pending GAP within the European Union, and data on cherries from a trial conducted in Germany in 1968 which had been submitted to the Meeting previously. These data were not considered, as the related GAP in the European Union is pending. In addition, information on current GAP, the fate of residues during the processing of peaches, apples, and olives, octanol-water partition coefficients for the

oxidative metabolites, methods of analysis for residues, an animal transfer study, and residues in food in commerce or at consumption were provided. Information on national MRLs and GAP was provided by Australia, Germany and The Netherlands.

Octanol-water partition coefficients

The manufacture submitted data on the octanol-water partition coefficients of fenthion, fenthion sulfoxide, and fenthion sulfone. The log P_{OW} for fenthion is 4.04 and 4.06 at *n*-octanol:water ratios of 1 and 0.1, respectively. The two metabolites are polar, with log P_{OW} values for fenthion sulfoxide of 1.98 and 1.93 and for fenthion sulfone of 2.02 and 2.17 at *n*-octanol:water ratios of 1 and 0.1, respectively.

Residues in animal commodities

Exposure to fenthion residues may occur during consumption of rice. In the evaluation of fenthion use on rice made by the Meeting in 1995, the concentrations of total fenthion residues in rice in the trials conducted according to GAP (median values in italics) were <0.001 (17 trials), <0.002 (2 trials), 0.008, 0.009, 0.01 (2 trials), 0.012, *<0.014* (8 trials), *<0.015* (17 trials), <0.016 (2 trials), <0.017, 0.018, <0.019 (2 trials), <0.02, <0.023, <0.024 (5 trials), and <0.028 (2 trials) mg/kg. The current Meeting estimated an STMR value of 0.0145 mg/kg.

The Meeting received data on the processing of oranges, which could have been used to assess the dietary burden from consumption of dried orange pulp; however, residues in this animal feed commodity were not determined, and the report was submitted as a summary. The Meeting decided that it was inadequate.

The Meeting considered that husked rice is a minor animal feed commodity and is therefore not suitable for calculating the dietary burden of fenthion residues in farm animals.

A study of transfer of fenthion residues in lactating dairy cows was made available to the Meeting. Encapsulated fenthion was given for 28 days to groups of three cows at a dose of 0.075, 0.23, or 0.75 mg/kg bw. The only edible tissues in which residues of fenthion were detected were liver and composite fat, and only in cows at the highest dose. In liver, the concentration of residues ranged from <0.05 to 0.07 mg/kg. In composite fat (perirenal, omental, subcutaneous), the concentration ranged from <0.05 to 0.12 mg/kg. The concentrations in kidney and composite muscle (round, flank, loin) were below the LOQ of 0.05 mg/kg. At 0.23 mg/kg bw, the concentration of total residues in liver and composite fat was below the LOQ. Kidney and muscle of cows at this dose and all tissues of cows at 0.075 mg/kg were not analysed because no residues were expected on the basis that none were found at the higher dose. The concentration of total residues of fenthion in milk reached a plateau in the cows given 0.75 mg/kg bw within 7 days, well before the 28-day slaughter. At the two lower doses, the concentration in milk was below the LOQ of 0.01 mg/kg.

The Meeting noted that, although the results of an animal feeding study had been submitted, the calculated dietary burden of fenthion residues in animal commodities was an underestimate. GAP exists for direct use of fenthion on animals, but data on dermal application to animals were not available. The Meeting was therefore unable to estimate maximum residue levels for fenthion in animal commodities. It confirmed the 1995 JMPR recommendation to withdraw the maximum residue levels for meat (of mammals other than marine mammals) and milk.

The Meeting received information on the fate of incurred residues of fenthion during the processing of apples, peaches, oranges, and olives, and processing factors were calculated for apples and peaches. Processing factors for olives were calculated by the 1995 JMPR. The processing data for oranges were not evaluated as the report submitted was inadequate.

RECOMMENDATIONS

The 1995 recommendation to withdraw the MRLs for meat (from mammals other than marine mammals) and milks is confirmed.

Definition of the residue for compliance with MRLs and estimation of dietary intake: sum of fenthion, its oxygen analogue and their sulfoxides and sulfones, expressed as fenthion.

The residue is fat-soluble.

Dietary risk assessment

Chronic intake

STMR values were estimated by the present Meeting for husked rice. When data on consumption were available, the STMR value was used with the existing MRLs and draft MRLs for six other food commodities in estimating dietary intake.

The dietary intakes from the five GEMS/Food regional diets, based on new and existing STMR values and MRLs, represented 1-12% of the ADI. The Meeting concluded that the dietary intake of fenthion residues would not exceed the ADI in any GEMS/Food regional diet (Annex 3). The estimates of dietary intake will be further refined during the next periodic review of residues.

Short-term intake

The acute RfD for fenthion established by the present Meeting is 0.01 mg/kg bw. The IESTIs for husked rice (Annex 3) was 0.0009 mg/kg bw (1% of the acute RfD) for aduts and 0.00018 mg/kg bw (2% of the acute RfD) for children. The Meeting concluded that it is highly unlikely that the short-term intake of fenthion would exceed the acute RfD. The lack of STMR values, except for husked rice, for fenthion in food commodities precluded a risk assessment for short-term intake, which will be assessed during the next periodic review of residues.

REFERENCES

Heinemann, O and P. Ohs. 1997. Determination of residues of Lebaycid 500 EC on peach following spray application in peaches. Bayer Report RA-3013/95. Unpublished

Philips, J.D., L.L. Roesel, C.D. Chickering and R.R. Gronberg. 1966. A 28-day feeding study of fenthion in dairy cattle. Bayer Report No. 107313.