5.17 METHOXYFENOZIDE (209)

RESIDUE AND ANALYTICAL ASPECTS

Methoxyfenozide was evaluated by the JMPR for residues and toxicology in 2003, when an ADI of 0-0.1 mg/kg bw and an ARfD of 0.9 mg/kg bw were established and maximum residue levels, supervised trial median residues and highest residues were recommended for a number of commodities. The residue was defined as methoxyfenozide for compliance with MRLs and for dietary intake estimation in both plant and animal commodities. The residue is fat-soluble, but is not classed as fat-soluble with respect to its distribution in milk.

Additional residue data and information on use patterns as well as residue analytical methods were submitted for evaluation by the present meeting on citrus fruits, small fruits and berries, tropical fruits with inedible peel, cucurbits, legume vegetables, pulses, and root and tuber vegetables.

Methods of Analysis

The fully validated analytical methods used in the supervised trials were based on LC/MS/MS detection. The average recovery values reported at various fortification levels were between 76 and 107%. The LOQ values ranged from 0.01 mg/kg to 0.07mg/kg.

The tests for stability of residues under deep-frozen conditions were performed in oranges, orange processed fractions, peas, radishes, sugar beets, sweet potatoes and peanuts. They indicated that the residues were stable during the deep-frozen storage intervals.

Results of supervised trials on crops

Most of the supervised trials were conducted within the programme of IR-4 in the USA where the maximum total seasonal application rate is 1.12 kg ai/ha. Some trials were from Europe and residue data on soybean was obtained from trials carried out by Dow AgroScience in the USA.

The NAFTA calculator was used as a tool in the estimation of the maximum residue level from the selected residue data set obtained from trials conducted according to GAP. As a first step, the Meeting reviewed all relevant factors related to each data set in arriving at the best estimate of the maximum residue level using expert judgement. Then, the NAFTA calculator was employed. If the statistical calculator spreadsheet suggested a different value from that recommended by JMPR, a brief explanation of the deviation was supplied. Some common factors that may lead to rejection of the statistical estimate include when the number of data points in a data set is < 15 or when there are a large number of values < LOQ.

Citrus fruit

Supervised trials were conducted on oranges (2) lemons (2) and grapefruit (2) in California and Texas during the 2005 and 2006 growing seasons that complied with the registered use patterns in the USA (dosage rate 0.134–0.28 kg ai/ha with 4 applications at 14–17 days intervals and PHI of 1 day.) The residues in whole fruits were: grapefruit: 0.12, 0.28 mg/kg; orange: 0.17, 1.7 mg/kg; lemon: 0.41, 0.93 mg/kg.

Nine supervised trials were performed on oranges in Greece, Italy, Portugal and Spain. The use pattern is 0.144–0.192 kg ai/ha with 2 applications at 10-day intervals and PHI of 14 days in Greece, Portugal and Spain. The Italian trials were also evaluated according to the use pattern in the other South European countries. The residues in whole orange were in rank order: 0.06, 0.13, 0.14, 0.16, 0.18, 0.19, 0.21, and 0.34 mg/kg.

Eight residue trials were performed on mandarins in South Europe, which were evaluated according to the GAP in Greece, Portugal and Spain (dosage of 0.144–0.192 kg ai/ha with 2 applications at 10 day interval, PHI of 14 days) taking into account the dosage at the last application. The residues in whole mandarin were in rank order: 0.11, 0.16, 0.21, 0.24, 0.27, 0.30, 0.35 and 0.45 mg/kg.

The Mann-Whitney U-test indicated that residue distributions in orange and mandarin were not significantly different and they can be combined: 0.06, 0.11, 0.13, 0.14, 0.16, 0.16, 0.18, 0.19, 0.21, 0.21, 0.24, 0.27, 0.3, 0.34, 0.35, and 0.45 mg/kg.

In the same trials, the residues in 17 orange and mandarin pulp samples 14 days after the last application were: < 0.05 mg/kg. As the residue data from US trials are not sufficient for estimation of maximum residue levels for citrus fruits, and the US GAP is quite different from that in South Europe, the Meeting estimated the following residue levels in citrus fruits based on the European GAP and residue data: maximum residue level of 0.7 mg/kg, median residue and HR of 0.05 mg/kg. The value derived from use of the NAFTA calculator was 0.7 mg/kg which corresponds to the maximum residue level of 0.7 mg/kg estimated by the current Meeting.

Blueberry

Eight field trials were performed in USA with three foliar applications of the test substance 6–9 days apart at rates ranged from 0.27 to 0.30 kg ai/ha per application (US GAP: dosage rate 0.134–0.28 kg ai/ha with 3 applications at 7 day interval and PHI of 7 days.). Samples were collected 6–7 days after last application. The residues measured in six independent trials were in rank order: 0.54, 0.85, 1.1, 1.4, 1.8, and 2.0 mg/kg.

The Meeting estimated a maximum residue level of 4 mg/kg, median residue of 1.25 mg/kg, HR of 2 mg/kg. The value derived from use of the NAFTA calculator was 3.5 mg/kg which, after rounding up to one figure, agrees with the maximum residue level of 4 mg/kg estimated by the current Meeting.

Cranberry

The trials evaluated by the 2006 JMPR were submitted again. The results were not evaluated by this meeting.

Strawberry

Eight field trials were conducted in USA with four or five foliar applications at a rate of approximately 0.28 kg ai/ha (1.33 times maximum US GAP: dosage 0.1/0.21 kg/ha at 14 day intervals, PHI of 3 days) amounting to a total seasonal rate of approximately 1.12 kg ai/ha. Samples were collected at 2–4 days after the final application. The residues were: 0.18, 0.20, 0.21, 0.24, 0.43, 0.49 and 1.2 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, median residue of 0.24 mg/kg and HR of 1.2 mg/kg. The value derived from use of the NAFTA calculator was 1.7 mg/kg which, after rounding up to one significant figure, was in agreement with the maximum residue level of 2 mg/kg estimated by the current Meeting.

Avocado

Six trials were conducted in the USA with four applications corresponding to maximum US GAP (dosage rate 0.18–0.28 kg ai/ha with five applications at 6 day intervals, PHI of 2 days and total seasonal rate of 1.12 kg ai/ha.).

The residues in five independent trials were 0.06, 0.08, 0.13, 0.16 and 0.41 mg/kg.

The Meeting estimated maximum, HR and median residues of 0.7 mg/kg, 0.41 and 0.13 mg/kg. The value derived from use of the NAFTA calculator was 0.7 mg/kg which was in agreement with the maximum residue level estimated by the current Meeting.

Papaya

Four trials were conducted in the USA at maximum US label rate (GAP: dosage rate 0.21–0.28 kg ai/ha with maximum five applications at 10-day intervals, PHI is 3 days). Samples taken from independent trials 3–4 days after last application contained residues: 0.18, 0.31 and 0.33 mg/kg. The residue in samples taken from a replicate plot was 0.17 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg, median residue of 0.31 and high residue of 0.33 mg/kg. The value derived from use of the NAFTA calculator was 0.6 mg/kg. However, the Meeting considered this value too low, as previously evaluated data sets indicate that two times the median value would cover only less than 70% of the residues derived from trials performed with various compounds at maximum GAP in commodities belonging to the Codex commodity group of 'Assorted tropical fruits – inedible peel' (FI).

Fruiting vegetables, Cucurbits

Cantaloupe

Seven trials were conducted in the USA with application rates of 1.55 times maximum US GAP (dosage rate 0.067–0.18 kg/ha, four applications at 7 day intervals, with a PHI of 3 days).

As the application rate did not match the GAP, the Meeting could not estimate a maximum residue level.

Cucumber

Eight trials were conducted in the USA with application rates of 1.55 maximum US GAP (dosage rate 0.067–0.18 kg/ha, four applications at 7 days intervals, PHI 3 days).

As the application rate did not match the GAP, the Meeting could not estimate a maximum residue level.

Squash, Summer

Six trials were conducted in the USA with application rates of 1.55 maximum US GAP (dosage rate 0.067–0.18 kg/ha, four applications at 7 days intervals, PHI 3 days).

As the application rate did not match the GAP, the Meeting could not estimate a maximum residue level.

Legume vegetables

Beans (in pods)

Six field trials were conducted in the USA with maximum US GAP (4 × 0.28 kg ai/ha, 7–14 days apart, PHI 7 days). The samples collected7–8 days after last application contained residues of: < 0.05, < 0.05, < 0.05, 0.079, 0.62 and 0.99 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, median residue of 0.065 mg/kg and HR of 0.99 mg/kg. The value derived from use of the NAFTA calculator was 0.45 mg/kg. However, it was considered too low as 2 of 6 valid residue values were higher.

Beans and peas succulent shelled

Seven field trials were conducted on beans in the USA with four or five foliar applications corresponding to maximum US GAP (4 × 0.28 kg ai/ha at 7–14 days, PHI of 7 days). The Meeting considered that an early application did not have any influence on the residues in shelled beans and evaluated the residue data together. Two trials were performed at the same site using different varieties. The residues measured in shelled beans after 6–7 days PHI were: < 0.05 (4), 0.052, 0.086 and 0.14 mg/kg.

Eight field trials were conducted on peas according to maximum US GAP (4 × 0.28 kg ai/ha at 7–14 days, PHI of 7 days). Two field trials conducted on the same site were not considered independent and only the highest residue was used for evaluation. The residues found in the independent trial samples were: < 0.05 (3), 0.058, 0.12, 0.14, and 0.18 mg/kg.

The Meeting noted that the residue populations in shelled beans and peas were not significantly different and can be combined: < 0.05 (7), 0.052, 0.058, 0.086, 0.12, 0.14, 0.14 and 0.18 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg, median residue of 0.05 mg/kg and HR of 0.18 mg/kg for shelled succulent beans and peas. The value derived from use of the NAFTA calculator was 0.3 mg/kg which was in agreement with the maximum residue level estimated by the present Meeting.

Pulses

Dry beans

Thirteen field trials were conducted in the USA according to maximum US GAP (4 × 0.28 kg ai/ha at 7–14 days, with a PHI of 7 days).

Several trials were conducted at the same site. The residues in independent trials were < 0.05 (9) and 0.22. No explanation as to the cause of the high detectable residue could be found in the trial report.

The Meeting noted that the residue distribution in succulent beans and peas support the residue distribution in dry beans and peas, and estimated a maximum residue level of 0.5 mg/kg, and median residue of 0.05 mg/kg. The NAFTA calculator was not used due to the large proportion of values below the LOQ.

Cowpea (Black eyed pea), dry

Six field trials were conducted in the USA according to maximum US GAP (4 × 0.28 kg ai/ha at 7–14 days, 7 day PHI). After harvest, the peas were dried for up to 11 days and shelled. Two trials were conducted at the same site approximately 20 days apart.

The residues in independent trials were 0.13, 0.17, 0.56, 0.67, and 3.4 mg/kg

The Meeting estimated a maximum residues level of 5 mg/kg, and median residue of 0.56 mg/kg. The value derived from use of the NAFTA calculator was 5 mg/kg which was in agreement with the maximum residue level estimated by the present Meeting.

Soya bean

Sixteen residue trials, including two decline and three bridging studies, were conducted in the USA with 4 applications over double the label rate each with a PHI of 14–15 days instead of the registered 7 days. In addition to the parent compound, the residues of OH-methoxyfenozide and the total sugar conjugates of methoxyfenozide (G-methoxyfenozide) were also determined.

As the trial conditions did not match the US label rate and PHI, the Meeting could not make and estimation or recommendation of a maximum residue level.

Root and tuber vegetables

Carrot

Seven field trials were conducted in the USA according to maximum US GAP (0.28 kg ai/ha, with a 14 day PHI). The residues measured were < 0.05, 0.057, 0.084, 0.13, 0.14, 0.16, and 0.31 mg/kg.

The Meeting estimated a maximum residues level of 0.5 mg/kg, median residue of 0.13 mg/kg and an HR of 0.31 mg/kg. The value derived from use of the NAFTA calculator was 0.5 mg/kg which was in agreement with the maximum residue level estimated by the present Meeting.

Radish

Five field trials were conducted in USA according to maximum US GAP (2 × 0.28 kg ai/ha, at 14 days, with a PHI of 14 days). The residues in radish were: < 0.05, <0.05, 0.08, 0.10 and 0.12 mg/kg

The Meeting estimated a maximum residues level of 0.4 mg/kg, median residue of 0.08 mg/kg and an HR of 0.12 mg/kg for radish. The value derived from use of the NAFTA calculator was 0.35 mg/kg which was comparable with the maximum residue level estimated by the present Meeting.

The residues in radish tops with leaves were: 0.33, 0.34, 0.75, 1.8, and 4.0 mg/kg.

The Meeting estimated a maximum residues level of 7 mg/kg, median residue of 0.75 mg/kg and an HR of 4.0 mg/kg for radish leaves including tops. The value derived from use of the NAFTA calculator was 7 mg/kg which was in agreement with the maximum residue level of 7 mg/kg estimated by the present Meeting.

Sugar beet

Eleven field trials were conducted in the USA according to maximum US GAP (0.28 kg ai/ha with a PHI of 7 days). The residues measured in roots were: < 0.05(3), 0.066, 0.092, 0.11, 0.13, 0.14, 0.14, 0.17, and 0.18 mg/kg.

The Meeting estimated a maximum residues level of 0.3 mg/kg, median residue of 0.11 mg/kg and an HR of 0.18 mg/kg. The value derived from use of the NAFTA calculator was 0.3 mg/kg which agreed with the maximum residue level of 0.3 mg/kg estimated by the current Meeting.

Sweet potato

Nine field trials were conducted in the USA according to maximum US GAP (3 × 0.18 kg ai/ha at 14 days, 7 days PHI). The residues measured in roots were < 0.01 (8) and 0.012 mg/kg.

The Meeting estimated a maximum residues level of 0.02 mg/kg, median residue of 0.01 mg/kg and an HR of 0.012 mg/kg for sweet potato. The NAFTA calculator was not used due to the large proportion of values below LOQ.

Peanut

Supervised field trials on peanut were conducted in Maryland, Colorado, Georgia (four trials at the same site), North Carolina (four trials at the same site), and Texas (two trials at the same site) according to maximum US GAP (3 × 0.10-0.18 at 7-day intervals, PHI of 7 days). The varieties were

also the same in the trials in Texas. The residues were below the LOQ in all trials except one where 0.011 and 0.016 mg/kg were measured in replicate samples of peanut meat.

The Meeting estimated a maximum residues level of 0.03 mg/kg, median residue of 0.01 mg/kg and an HR of 0.016 mg/kg. The NAFTA calculator was not used due to the large proportion of values below LOQ.

Fate of residues during processing

The fate of methoxyfenozide residues during processing was examined in oranges, peanut and sugar beet in processing studies simulating the industrial processing as far as possible. The marmalade was prepared according to household practice. Estimated processing factors and STMR-Ps are summarised below.

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors	PF (Mean, median or best estimate)	RAC-STMR (mg/kg)	STMR-P (mg/kg)
Orange	Orange peel	2.884, 4.201, 4.0	4.0		
	Orange pulp dry	< 0.253, < 0.223, < 0.385, 1.098	1.1	0.2	0.22
	Marmalade	0.505, 1.067, 0.769	0.77		
	Orange juice	0.253, 0.223	0.22	0.05	0.011
	Orange oil	42.5	42.5		
Peanuts	Peanut oil	2.89	2.89	0.01	0.0289
Sugar beet	Sugar beet molasses	1.143	1.14	0.11	0.126
	Refined sugar	0.071	0.071		

Based on the processing factors, the Meeting estimated STMR values of 0.22 mg/kg for dry orange pulp (based on median residue of 0.2 mg/kg in whole fruits), 0.011 mg/kg for citrus juice, 0.0289 for refined peanut oil, and 0.126 mg/kg for sugar beet molasses.

On processing peanuts, methoxyfenozide concentrated in the oil. The Meeting decided to estimate a maximum residue level for peanut oil refined of 0.1 mg/kg based on a highest residue for peanuts of 0.016 mg/kg and a processing factor of 2.89 (0.016 mg/kg × 2.89 = 0.05 mg/kg).

Residues in animal feed

The residues in animal feed were measured in crops derived from supervised trials conducted according to maximum US GAPs which are reported above under individual commodities.

Residues in/on bean foliage treated with methoxyfenozide at maximum GAP were: 3.4, 4.6, 5.3, 6.6, 16, and 32 mg/kg.

The Meeting estimated a highest residue of 32 mg/kg and a median residue of 5.95 mg/kg.

Residues in sugar beet tops were: 0.85, 0.85, 1.9, 2.6, 3.3, 3.6, 3.8, 4.7, 4.9, 9.5 and 10 mg/kg.

The Meeting estimated a highest residue of 10 mg/kg and a median residue of 3.8 mg/kg.

Residues in peanut hay were: 0.22, 0.3, 0.46, 1.1, 9.0, 13, 14, 17, 27, 29, 33, and 51 mg/kg

The Meeting estimated, respectively maximum, highest and median residue levels of 80mg/kg, 60 mg/kg and 16 mg/kg based on dry weight basis (85% dry matter) corresponding to 70 mg/kg on peanut hay, highest residue of 51 mg/kg and a median residue of 13.5 mg/kg for peanut fodder as received. (NAFTA calculator indicates 50 mg/kg maximum residue for commodity as received. However, it was considered too low as previously evaluated data sets indicate that 4 times the median value would cover only less than about 60% of the residues derived from trials performed

with various pesticides at maximum GAP in commodities belonging to the Codex commodity group of Legume animal feeds (AL)).

Residues were reported in soya bean forage and hay. As the application conditions did not match GAP, the residues were recorded in the monograph but not evaluated.

Residues in animal commodities

Estimated maximum and mean dietary burdens of farm animals

Dietary burden calculations for beef cattle, dairy cattle are provided in Annex 6.

		Animal dietary burden, methoxyfenozide [ppm] in dry matter diet		
		US-Canada	EU	Australia
Beef cattle	max	47.92	44.65	78.86
	mean	12.30	10.62	16.55
Dairy cattle	max	30.41	40.76	82.00[a]
	mean	9.61	9.74	16.66[b]

[a] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat and milk.

[b] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat and milk.

The 2003 JMPR estimated maximum dietary burdens of methoxyfenozide for beef cattle, dairy cattle, and poultry of 26 ppm, 31 ppm, and 0.07 ppm, and median dietary burdens of 7.5 ppm, 7.8 ppm, and 0.07 ppm, respectively. The maximum and mean dietary burdens for beef and dairy cattle based on the new OECD feed consumption figures and the residue levels estimated by the present Meeting are 82 ppm and 16.66 ppm, respectively.

Farm animal feeding studies

The 2003 JMPR reported feeding studies on cows, where three cows at each level were dosed orally with the equivalent of 16, 54, or 180 ppm in the diet for 28 consecutive days. Milk was collected daily and analysed on days 1, 2, 4, 7, 10, 14, 17, 21, 24, and 28. The cows were slaughtered within 24 h of the last dose, and tissues were collected and analysed for methoxyfenozide and the glucuronide conjugate of the A-ring phenol.

The residues [mg/kg] detected in various tissues at feeding levels given are summarised below:

Tissue	Residue level	16 ppm	54 ppm	180 ppm
Milk	Max	< 0.01	< 0.01	0.1
	Average	< 0.01	< 0.01	0.028
Muscle	Max	< 0.003	< 0.003	0.1
	Average	< 0.003	0.028	0.073
Fat	Max	0.011	0.082	0.44
	Average	< 0.01	0.041	0.28
Liver	Max	< 0.003	0.03	0.15
	Average		0.028	0.13
Kidney	Max	< 0.01	< 0.01	0.034
	Average	< 0.01	< 0.01	0.026

The Meeting interpolated the residues measured following feeding with 54 ppm and 180 ppm methoxyfenozide in the diet. The calculated maximum and average (in brackets) residues were: milk: 0.03 mg/kg, (0.014 mg/kg), muscle: 0.025 mg/kg (0.019 mg/kg), fat: 0.162 mg/kg (0.094 mg/kg), liver: 0.057 mg/kg (0.051 mg/kg), and kidney: 0.015 mg/kg (0.014 mg/kg)

The Meeting estimated a maximum residue level, HR and median residue, respectively, 0.1 mg/kg, 0.057 mg/kg, 0.051 mg/kg for edible offal; of 0.2 mg/kg, 0.162 mg/kg, 0.094 mg/kg for meat from mammals other than marine mammals (based on fat) and maximum residue level and median residues of 0.05 mg/kg, 0.03 mg/kg for whole milk. .

The new maximum or median level recommendations do not affect the dietary burden of poultry. The residue levels estimated by the 2003 JMPR remain the same.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDI) for methoxyfenozide was calculated from recommendations for STMRs for raw commodities in combination with consumption data for corresponding food commodities. The results are shown in Annex 3.

The International Estimated Daily Intakes (IEDI) of methoxyfenozide in the 13 GEMS/Food Consumption Cluster Diets, based on the STMRs estimated by the 2003 and 2009 JMPR were in the range 0–8% of the maximum ADI of 0.1 mg/kg bw. The Meeting concluded that the long-term intake of residues of methoxyfenozide from uses considered by the Meeting is unlikely to present a public health concern.

Short-term intake

The International Estimated Short Term Intake (IESTI) for methoxyfenozide was calculated for the food commodities for which STMRs or HRs were estimated by the present Meeting and for which consumption data were available. The results are shown in Annex 4.

The International Estimated Short Term Intake (IESTI) varied from 0–2% of the ARfD (0.9 mg/kg bw) for the general population. The IESTI varied from 0–6% of the ARfD for children 6 years and below. The Meeting concluded that the short-term intake of residues of methoxyfenozide from uses considered by the present Meeting is unlikely to present a public health concern.