5.24 METHOXYFENOZIDE (209)

RESIDUE AND ANALYTICAL ASPECTS

Methoxyfenozide was evaluated for residues and toxicology by the 2003 JMPR. The 2003 Meeting established an ADI of 0–0.1 mg/kg bw and an ARfD of 0.9 mg/kg bw, and made a number of maximum residue level recommendations. The 2009 JMPR also recommended a number of maximum residue levels. 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 classified as fat-soluble with respect to its distribution in milk.

The current Meeting evaluated residue trial data for various crops including field accumulation data in rotational crops, analytical methods, and storage stability tests.

Methods of analysis

Analytical methods used in field trials, based on LC-MS/MS detection, were fully validated for representative samples of high and low-moisture content crops. Recoveries of methoxyfenozide ranged between 69% and 113% at fortification levels of 0.02–1.0 mg/kg.

The LOQ of 0.02 mg/kg was also confirmed by independent validation.

Stability of residues in stored analytical samples

The tests for stability of residues under frozen conditions were performed in guava, litchi, papaya, spring onion, cucumber, pea (pods and vines) and globe artichoke. They indicated that the residues were stable during the frozen storage intervals prevailed in the field trials. Residues in non-tested commodities were also considered stable. The results conform to previous JMPR reviews indicating that methoxyfenozide residues are stable for 1–2 years in various matrices under frozen conditions.

Results of supervised residue trials on crops

The Meeting received information on supervised field trials in citrus fruits, guava, litchi, papaya, spring onion, melons, cucumber, summer squash, spinach, common bean, pea (pods), pea (dry), globe artichoke, alfalfa and clover.

As a representative residue value for each field trial, the mean of replicate samples was used for estimation of a maximum residue level.

The OECD MRL calculator was used as a tool in estimation of the maximum residue level. Where different estimates were made, the reasons are indicated under corresponding recommendations.

Citrus fruits

The 2009 JMPR estimated a maximum residue level of 0.7 mg/kg on citrus based on the European GAP. The present Meeting received new residue information on US citrus trials matching the GAP of the USA.

The maximum US GAP for citrus fruits is a rate of 0.28 kg ai/ha, four applications at 14–17 days intervals with a 1 day PHI.

Residues from nine trials on oranges, in ranked order, were: 0.16, 0.21, 0.25, 0.26, 0.28, 0.32, 0.32, 0.55, and 1.7 mg/kg.

For grapefruits, residues for six trials, in ranked order, were: 0.12, 0.15, 0.22, 0.26, 0.27, and 0.28 mg/kg.

For lemon, residues from five trials were: 0.21, 0.33, 0.35, 0.39 and 0.79 mg/kg.

As the residue distributions in oranges, grapefruits and lemon were not significantly different, the datasets could be combined (n=20): 0.12, 0.15, 0.16, 0.21, 0.21, 0.22, 0.25, 0.26 (2), 0.27, 0.28, 0.28, 0.32, 0.32, 0.33, 0.35, 0.39, 0.55, 0.79 and 1.7 mg/kg. The Meeting decided to estimate a group MRL for citrus fruits. Based on the residues the Meeting estimated a maximum residue level of 2 mg/kg, an STMR of 0.28 mg/kg and an HR of 1.7 mg/kg for citrus fruits. The Meeting agreed to withdraw its previous maximum residue level of 0.7 mg/kg for citrus fruits.

Assorted tropical and sub-tropical fruits-edible peel

Guava

The GAP in the USA consists of six applications at a rate of 0.18–0.28 kg ai/ha with 6 day intervals, total seasonal rate of 1.12 kg ai/ha, and a 3 day PHI. Three trials were conducted in the USA matching maximum US GAP, in which methoxyfenozide was applied four times at a rate of 0.28–0.29 kg ai/ha, at 7–8 day intervals and 3–4 day PHI.

The Meeting decided the trials were not independent as they were conducted at the same site, same variety and with only few days' difference in treatment dates. As a result the Meeting considered them insufficient to estimate a maximum residue level.

Assorted tropical and sub-tropical - fruits-inedible peel

Litchi

The GAP in the USA consists of five applications at rate of 0.18–0.28 kg ai/ha, 10 day intervals, and a 14 day PHI. Three trials were conducted in the USA matching maximum US GAP (0.25–0.33 kg ai/ha with six applications, at 9–16 interval days, 13 day PHI).

However, as the trials were conducted with the same variety at neighbouring locations with application dates 0–7 days apart the Meeting judged the trials not to be independent. As a result the Meeting considered them insufficient to estimate a maximum residue level.

Mango and Pomegranate

The 2009 JMPR recommended maximum residue levels of 1 mg/kg for papaya and 0.7 mg/kg for avocado. The present Meeting received a request of extrapolating existing information for papaya and avocado to mango and pomegranate.

According to US GAP, the four crops have different PHIs (2 days for avocado, 3 days for papaya and mango and 7 days for pomegranate). As the GAPs are different, the Meeting could not consider the extrapolation of residue data from papaya and avocado to mango and pomegranate.

Spring onion

The GAP in the USA is for six applications at 0.21 kg ai/ha, total seasonal rate of 1.12 kg ai/ha and a 1 day PHI. Five trials were conducted in the USA with application rates of 4 × 0.28 kg ai/ha, which is 1.33 times higher than maximum US GAP rate. The residues, in ranked order, were: 0.060, 0.50, 0.60, 1.6, and 3.5 mg/kg.

The lack of two applications early in the growing season was considered non-influential on the final residue levels. The Meeting applied the proportionality principle and used the scaling factor of 0.8. The resultant scaled residue values were: 0.048, 0.40, 0.48, 1.3, and 2.8 mg/kg.

The Meeting estimated a maximum residue level of 6 mg/kg, an STMR of 0.48 mg/kg and an HR of 2.8 mg/kg for spring onion.

Fruiting vegetables, Cucurbits

Melons, except watermelon

Seven field trials conducted in the USA in 1999 on cantaloupe were re-submitted. The use of proportionality approach was considered by this Meeting for estimating a maximum residue level.

The 2009 Meeting did not estimate a maximum residue level, as the trials did not match US GAP. The treatment rate in the trials was 1.55 times the maximum US GAP (4 × 0.18 kg ai/ha at 7 day, PHI of 3 days) and resulted in which were: 0.071, 0.11, 0.13, 0.13, 0.15, 0.19, and 0.21 mg/kg.

The Meeting noted that other residue information on melons was not available. The Meeting agreed to use a proportionality approach with a scaling factor of 0.7 (rounded value for 0.60–0.67). The adjusted residue values were: 0.050, 0.077, 0.091, 0.091, 0.11, 0.13, and 0.15 mg/kg at maximum US GAP.

Cucumber

Eight trials conducted in cucumber in the USA in 1999 were re-submitted. The application of proportionality for estimating a maximum residue level was considered by this Meeting.

The 2009 Meeting did not estimate a maximum residue level as the trials did not match US GAP. The residue concentrations in cucumber were: 0.011, 0.019, 0.026, 0.033, 0.033, 0.048, 0.051, and 0.052 mg/kg, at dosage rate of 1.55 times maximum US GAP (4 × 0.18 kg ai/ha at 7 day, PHI of 3 days).

The Meeting noted that other residue information on cucumber was not available. In addition, it was considered that the proportionality approach could be applied. The Meeting decided to use the proportionality approach and estimate a scaling factor.

Using a scaling factor of 0.7 (rounded value for 0.60–0.67), the adjusted residue values were: < 0.01, 0.013, 0.018, 0.023, 0.023, 0.034, 0.036, and 0.036 mg/kg at maximum US GAP.

Squash, summer

Six trials conducted in the USA in 1999 were re-submitted. The application of proportionality in estimating a maximum residue level was considered by this Meeting.

The 2009 Meeting did not estimate a maximum residue level as the trials did not match US GAP. The residue concentrations were: < 0.02, 0.02, 0.034, 0.089, 0.10, and 0.16 mg/kg, at 1.55 times the maximum US GAP rate (4 × 0.18 kg ai/ha at 7 day, PHI of 3 days).

Other residue information on cucumber was not available. The Meeting agreed to apply a proportionality approach and estimate a scaling factor.

Using the scaling factor of 0.7 (rounded from 0.64–0.67), adjusted residue values were: < 0.02, < 0.02, 0.024, 0.062, 0.070, and 0.11 mg/kg at maximum US GAP.

Taking into account that GAPs for melons, cucumber, and summer squash are the same, the Meeting decided to estimate a group maximum residue level of 0.3 mg/kg for fruiting vegetables, cucurbits, except watermelon based on residues in melons. For dietary intake purposes of cucurbits except watermelon, the Meeting estimated an STMR 0.091 mg/kg and an HR of 0.15 mg/kg.

Leafy vegetables

Spinach

The current Meeting received residue information for three new trials. As the GAP was not changed, the Meeting also considered the residue data evaluated by the 2003 JMPR and combined the data, thus residues are in rank order: *5.5,10, 10*, 11, 12, 14, 18, 23, and 43 mg/kg (*new data in italic*).

The Meeting maintained its previous estimates for the maximum residue level of 50 mg/kg, the HR of 43 mg/kg, and estimated an STMR of 12 mg/kg.

Legume vegetables

Common bean (pods and/or immature seeds)

The Meeting received two new trials which were assessed with six trials previously evaluated by the 2009 JMPR. All trials were conducted at maximum US GAP (4 × 0.28 kg ai/ha at 7 days, with a PHI of 7 days). Residues were: < 0.05 (4), *0.075, 0.10*, 0.57, and 0.81 mg/kg (*new data in italic*). The new trials did not affect the estimates made by 2009 JMPR.

Peas (pods and succulent=immature seeds)

Three trials were conducted in the USA according to maximum US GAP (4 × 0.28 kg ai/ha at 7 days, with a PHI of 7 days). The residues in peas with pods were: 0.11, 0.13, and 0.42 mg/kg.

The Meeting considered the similarity of common bean and pea crops, and noted that three residue data measured in peas were in the range of those in common beans. The combined data base of residues in common bean and peas (pods) supports the estimation of maximum residue level of 2 mg/kg, an STMR of 0.10, an HR of 0.81 mg/kg for peas *(pods and succulent=immature seeds).*

Thus, the Meeting agreed to recommend a maximum residue level of 2 mg/kg, an STMR of 0.10 mg/kg and an HR of 0.81 mg/kg for peas *(pods and succulent=immature seeds).*

Peas (dry)

Six trials were conducted in the USA. Four trials matched maximum US GAP (4 × 0.28 kg ai/ha at 7 day intervals, a PHI of 7 days.

Residue concentrations from the four trials were: 0.068, 0.097, 0.17, and 0.17 mg/kg.

The 2009 Meeting evaluated data in cowpea, in which residues were: 0.13, 0.17, 0.56, 0.67, and 3.4 mg/kg.

As the GAPs for pea (dry) and cowpea are the same, the Meeting decided to estimate a group maximum residue level. The combined residues were: 0.068, 0.097, 0.13, 0.17 (n=3), 0.56, 0.67, and 3.4 mg/kg. The Meeting estimated a maximum residue level of 5 mg/kg and an STMR of 0.17 mg/kg for peas (dry), based on the combined dataset. The Meeting withdrew its previous recommendation for a maximum residue level of 5 mg/kg for cowpea (dry).

Artichoke, globe

Three trials conducted in the USA matched maximum US GAP (4 × 0.28 kg ai/ha at PHI of 4 days and total seasonal rate of 1.12 kg ai/ha). The residues were: 0.97, 1.1, and 1.2 mg/kg.

The trials were not independent as they were conducted at the same site using the same variety with the same dates of application.

The Meeting did not consider the data sufficient to estimate a maximum residue level for globe artichoke.

Legume animal feeds

Alfalfa (forage and fodder)

Nine trials for alfalfa forage and fodder each were conducted in the USA (US GAP: at a rate of 0.13 kg ai/ha, one application per cutting, and 0 day PHI for forage, 7 day PHI for fodder).

The treatment regime in the forage trials differed from the US GAP (4 × 0.14 kg ai/ha per cutting and a 0 day PHI). For the fodder trials the PHI also differed from the US GAP (4 × 0.14 kg ai/ha per cutting and 3 day PHI).

As the alfalfa trials did not match US GAP the Meeting did not estimate a maximum residue level for alfalfa fodder.

Clover (forage and hay)

Nine trials for clover forage and hay each were conducted in the USA (US GAP: a dosage rate of 0.13 kg ai/ha, one application per cutting, and 0 day PHI for forage, 7 day PHI for hay).

The treatment regime in the forage trials differed from the US GAP (4 × 0.14 kg ai/ha per cutting and a 0 day PHI). For the hay trials the PHI also differed from the US GAP (4 × 0.14 kg ai/ha per cutting and 3 day PHI).

As the clover trials did not match US GAP the Meeting did not estimate a maximum residue level for clover hay.

Bean forage

The residues were measured in bean foliage derived from supervised trials conducted according to maximum US GAP for the common bean commodity described previously.

Residues from eight trials conducted according to maximum US GAP were: 3.3, 3.6, 4.1, 4.6, 5.1, 5.8, 15, and 26 mg/kg. The Meeting estimated a median residue of 4.9 mg/kg and the highest residue of 26 mg/kg.

Pea vines

The residues in pea foliage were derived from the supervised trials for pea (pods), which were conducted according to maximum US GAP as described previously under the common bean commodity: 3.5, 6.1, and 8.6 mg/kg.

The Meeting decided to combine the data for bean forage, beans and peas for mutual support. The resulting residues were: 3.3, 3.5, 3.6, 4.1, 4.6, 5.1, 5.8, 6.1, 8.6, 15, and 26 mg/kg.

The Meeting estimated a median residue of 5.1 mg/kg and the highest residue of 26 mg/kg for bean forage and pea vines and withdrew its previous recommendations for bean forage.

Fate of residues during processing

The 2009 JMPR estimated processing factors for orange products. Taking into account the STMR for citrus fruits estimated by the present Meeting, new STMR-Ps for citrus products were calculated. The STMR-P values are summarized below.

Raw agricultural commodity (RAC)	Processed commodity	Processing factor	RAC-STMR (mg/kg)	STMR-P (mg/kg)
Citrus	Citrus juice	0.22	0.28	0.062
	Marmalade	0.77	0.28	0.22
	Citrus oil	42.5	0.28	12
	Citrus dry pulp	1.1	0.28	0.31

Residues in animal commodities

Estimated dietary burdens of farm animals

The Meeting estimated the dietary burden of methoxyfenozide residues by applying the OECD feed table for maximum proportion of agricultural commodities in animal feed (FAO Manual 2nd ed. 2009, Appendix IX).

Dietary burden calculations for beef cattle, dairy cattle are provided in Annex 6. A mean and maximum dietary burden for livestock, based on methoxyfenozide use, is shown below.

	Livestock dietary burden, methoxyfenozide, ppm of dry matter diet							
	US-Canada		EU		Australia		Japan	
	max	mean	max	mean	max	mean	max	mean
Beef cattle	16.97	9.01	110.8	48.19	110.8	48.25	0.0222	0.0222
Dairy cattle	66.10	29.57	96.57	38.40	110.8[a]	48.25[b]	56.30	27.54
Poultry, broilers	0.0923	0.0923	0.321	0.171	0.0668	0.0668	0.0159	0.0159
Poultry, layers	0.0923	0.0923	24.03[c]	8.058[d]	0.0668	0.0668	0.0182	0.0182

[a] Highest maximum beef or dairy cattle dietary burden suitable for maximum residue level estimates for mammalian meat, edible offal and milk

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

[c] Highest maximum broiler or layer poultry dietary burden suitable for maximum residue level estimates for poultry meat, edible offal and eggs

[d] Highest mean broiler or layer poultry dietary burden suitable for STMR estimates for poultry meat, edible offal and eggs

Farm animal feeding studies

The present Meeting used the feeding studies utilized by the 2003 and 2009 JMPR. In the studies, cows at each level were dosed orally at feeding levels of 16, 54 or 180 ppm for 28 consecutive days. The methoxyfenozide residues detected in various tissues are summarized below.

Tissue	Feeding level in cows					
	16 ppm		54 ppm		180 ppm	
	Maximum Res [a], mg/kg	Average Res, mg/kg	Maximum Res, mg/kg	Average Res, mg/kg	Maximum Res, mg/kg	Average Res, mg/kg
Milk	< 0.01	< 0.01	< 0.01	< 0.01	0.1	0.028
Muscle	< 0.003	< 0.003	< 0.003	< 0.003	0.01	0.0073
Fat	0.011	< 0.01	0.082	0.041	0.44	0.28
Liver	< 0.01	< 0.01	0.03	0.028	0.15	0.13
Kidney	< 0.01	< 0.01	< 0.01	< 0.01	0.034	0.026

[a] Methoxyfenozide

Estimated residues in animal commodities

The residues in animal commodities were estimated based on the calculated animal dietary burden and by interpolating with feeding study residues. The following table shows the expected residues in animal commodities.

	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues (mg/kg) in			
				Muscle	Liver	Kidney	Fat
Maximum residue level beef or dairy cattle							
Feeding study [a]	54 180	< 0.01 0.028	54 180	< 0.003 0.01	0.03 0.15	< 0.01 0.034	0.082 0.44
Dietary burden and residue estimate	110.8	0.018	110.8	0.0062	0.096	0.021	0.24
STMR beef or dairy cattle							
Feeding study [b]	16 54	< 0.01 < 0.01	16 54	< 0.003 < 0.003	< 0.01 0.028	< 0.01 < 0.01	< 0.01 0.041
Dietary burden and residue estimate	48.3	< 0.01	48.3	< 0.003	0.025	< 0.01	0.036

[a] Highest residues for tissues and mean residue for milk

[b] Mean residues for tissues and milk

For meat from mammals other than marine mammals, the Meeting estimated a maximum residue level of 0.3 mg/kg, an STMR of 0.036 mg/kg and an HR of 0.24 mg/kg, based on fat, and an STMR of < 0.003 mg/kg and an HR of 0.0062 mg/kg, based on muscle. For edible offal from mammals, the Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR of 0.025 mg/kg

and an HR of 0.096 mg/kg, based on residues in liver. In addition, the Meeting withdrew its previous estimates for those commodities. The maximum residue levels for milk, as recommended by the 2009 JMPR, remained the same.

Estimated STMRs or HRs for the poultry commodities based on present animal burden calculation did not affect previous JMPR recommendations.

DIETARY RISK ASSESSMENT

Long –term intake

The ADI for methoxyfenozide is 0–0.1 mg/kg bw. The International Estimated Daily Intakes (IEDI) for methoxyfenozide were estimated for the 13 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by the previous and present JMPR. The results are shown in Annex 3. The IEDI ranged 0–5% of the maximum ADI. The Meeting concluded that the long-term intake of residues of methoxyfenozide from uses considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The ARfD for methoxyfenozide is 0.9 mg/kg bw. 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 IESTI varied from 0–10% of the ARfD.

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