FLUDIOXONIL (211)

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EXPLANATION

Fludioxonil (4-(2,2-difluoro-1,3-benzodioxol-4-yl)pyrrole-3-carbonitrile), a fungicide, was first evaluated by the 2004 JMPR. The Meeting recommended the following residue definitions for fludioxonil:

For plant commodities for compliance with the MRL and estimation of dietary intakes: *fludioxonil*

For animal commodities for compliance with the MRL and estimation of dietary intakes: *sum of fludioxonil and its benzopyrrole metabolites, determined as 2,2-difluorobeno[1,1]dioxole-4-carboxylic acid and expressed as fludioxonil*

Fludioxonil is fat-soluble

The 2004 JMPR recommended 48 MRLs for a variety of commodities and an ADI of 0–0.4 mg/kg bw. ARfD was considered unnecessary.

Fludioxonil was reviewed also by the 2006 and 2010 JMPR which together recommended six additional MRLs and replaced two previous MRLs.

After the 2010 JMPR, a post-harvest use of fludioxonil on mangoes was proposed and supported by Australia. Residue trials were conducted to support this use on mangoes and their results were provided to the current Meeting along with information on methods of analysis for fludioxonil on mangoes.

METHODS OF RESIDUE ANALYSIS

Analytical methods

GC/MS Method AG-664

Method AG-664, which has not been evaluated by JMPR, was used with minor modifications for the determination of fludioxonil residues in mangoes in supervised residue trials conducted in Australia in 2008.

Method AG-664 was originally developed to analyse fludioxonil in seeds following seed treatment application (Mauli and Skinner, 1996, AG-664). Minor modifications to the method have been made to enable selective mass spectrometric detection for the analysis of fludioxonil residues in mango fruit and pulp samples (Keets, 2009, SYN0904).

Method AG-664 involves extraction of samples with methanol/water (90:10 v/v). Extracts are centrifuged and an aliquot is diluted with ultra-pure water and water saturated with sodium chloride. Sample clean-up is carried out by partition with dichloromethane. The organic phase is collected, evaporated and the residue is dissolved in acetone. The final extract is analysed by gas chromatography using a mass spectrometer detector (GC/MS). The quantitative determination is carried out by external standardization using SIR mode (parent ion 248 m/z plus three quantifier ions 127, 154 and 182 m/z).

The linearity of the detector response was assessed using four standard solutions of fludioxonil (injected in duplicate) in the range 10–400 ng/mL. Typical correlation coefficients (R^2)

were in the range 0.9987–0.9993 and hence it is considered that analyte concentrations are determined in the dynamic range of the instrument.

Method AG-664 was validated for the determination of fludioxonil in mango pulp at the following fortification levels: the proposed LOQ of the method (0.01 mg/kg) and 20× LOQ (0.20 mg/kg). The method was also validated for mango peel at following fortification levels: 0.01 mg/kg (LOQ) and 800× LOQ (8 mg/kg). Satisfactory recoveries (mean 87–88%) were demonstrated at all fortification levels in both matrices. RSD was less than 20% in both matrices indicating that repeatability was also acceptable. The reported LOQ for fludioxonil was 0.01 mg/kg in both matrices.

Table 1 Recoveries by Method AG-664 for the determination of fludioxonil in mango pulp and peel (SYN0904)

Matrix	Fortification level (mg/kg)	Mean recovery rate (%)	RSD (%)	n
Mango pulp	0.01–0.20	88	5.4	9
Mango peel	0.01–8.00	87	14	9

HPLC/UV Method REM 133.04

Method REM 133.04 (Mair, 1993, REM-133.04), which was evaluated by JMPR, was used with minor modifications for the determination of fludioxonil residues in mangoes in supervised residue trials conducted in South Africa in 2004.

The 2004 JMPR concluded that Method REM 133-04 is fully validated for a range of crops and crop types (grapes and wine, tomatoes, strawberries, corn on the cob and eggplant (Mair, 1993), and apples, strawberries, grapes and wine, and wheat grain (Tribolet, 2001, 210/01)) and is suitable for the determination of fludioxonil in samples of plant origin.

In each study (Gill and Gardinal, 2007a-d, 03-6093, 03-6094, 04-6000 and 04-6001), the linearity of the detector response was confirmed over the range 2.5-1000 ng fludioxonil/mL using six calibration solutions. In the studies, correlation coefficients (R^2) were found to be at least 0.999 and the intercepts did not differ significantly from zero.

Method REM-133.04 was validated for the determination of fludioxonil in mango pulp at the fortification levels of 0.02 and 0.1 mg/kg and in mango peel at 1.0 and 10 mg/kg. Satisfactory recoveries (mean 92–102%) were demonstrated at all fortification levels in both matrices. RSD was less than 20% in both matrices indicating that repeatability was also acceptable.

Table 2 Recoveries by Method REM 133.04 for the determination of fludioxonil in mango pulp and peel

Matrix	Fortification level (mg/kg)	Recovery rate (%)					RSD (%)
		03-6093	03-6094	04-6000	04-6001	Mean	
Mango pulp	0.02	103	97	82	86	92	11
	0.1	108	101	98	102	102	4.1
	0.02–0.1	86–108					9.1
Mango peel	1.0	99	91	–	–	95	6.0
	10	94	85	–	–	90	7.1
	1.0–10	85–99				92	6.3

HPLC/MS/MS Method REM 133.06

Method REM 133.06, which has not been reviewed by JMPR, was used with minor modifications for the determination of fludioxonil in mangoes in supervised residue trials conducted in South Africa in 2008.

Method REM 133.06 is an adaptation of Method REM 133.04 in that a much reduced sample clean-up in combination with tandem mass spectrometric detection is utilized (Nichols, 2006, REM 133.06). Its procedures are summarized below.

Crop samples were extracted with methanol. Extracts were centrifuged and aliquots were diluted with acetonitrile:water (30:70 v/v). Final determination is by HPLC with tandem mass spectrometric detection.

Method REM 133.06 was validated for the determination of fludioxonil in six crops at the various fortification levels: the proposed LOQ of 0.01 mg/kg and the levels expected in supervised residue trials. Mean recoveries of fludioxonil at each fortification level and overall for all matrices were within the acceptable range of 70% to 110% with an RSD < 20% for all six matrices with sufficient repeatability (Anderson and Nichols, 2006, RJ3773B)

Table 3 Recoveries by Method REM 133.06 for determination of fludioxonil

Matrix	Fortification level (mg/kg)	Recovery rate (%)		RSD (%)	n
		Individual results	Mean		
Determination using primary MRM transition 247.0> 179.9 m/z					
Orange fruit	0.01	107, 112, 109, 115, 102	109	5	5
	10.0	100, 96, 98, 100, 98	99	2	5
	Overall	96–115	104	6	10
Kiwi fruit	0.01	98, 92, 82, 81, 84	87	8	5
	20.0	86, 88, 88, 87, 84	87	2	5
	Overall	81–98	87	6	10
Lettuce	0.01	97, 101, 110, 103, 99	102	5	5
	5.0	88, 89, 92, 90, 92	90	2	5
	Overall	88–110	96	7	10
Wheat grain	0.01	106, 102, 109, 101, 98	103	4	5
	0.1	86, 99, 97, 94, 81	91	8	5
	Overall	86–109	97	9	10
Wheat straw	0.01	88, 96, 103, 106, 91	97	8	5
	0.1	105, 98, 97, 94, 96	98	4	5
	Overall	88–106	97	6	10
Grape	0.01	92, 86, 99, 110, 114	100	12	5
	3.0	99, 107, 96, 106, 101	102	4	5
	Overall	86–110	101	8	10
Wine	0.01	99, 119, 107, 91, 103	104	10	5
	0.1	114, 100, 93, 99, 100	101	3	5
	Overall	81–119	102	9	10
Sunflower seed	0.01	91, 92, 91, 97, 81	90	7	5
	0.1	83, 83, 82, 80, 83	82	1	5
	Overall	80–97	86	7	10
Determination using confirmatory MRM transition 247.0> 126.1 m/z					
Orange fruit	0.01	104,108, 110, 100, 100	105	4	5
	10.0	100, 96, 96, 99, 97	98	2	5
	Overall	96–110	101	5	10
Kiwi fruit	0.01	95, 84, 81, 76, 76	83	9	5
	20.0	86, 88, 88, 89, 84	87	2	5
	Overall	76–95	87	6	10
Lettuce	0.01	98, 111, 106, 94, 95	101	7	5
	5.0	91, 93, 92, 90, 91	91	1	5
	Overall	90–111	96	7	10
Wheat grain	0.01	88, 121, 89, 105, 102	101	13	5
	0.1	92, 100, 102, 100, 90	97	5	5
	Overall	88–121	99	10	10
Wheat straw	0.01	103, 93, 81, 96, 90	92	9	5
	0.1	89,86, 95, 97, 97	93	5	5
	Overall	81–103	93	7	10
Grape	0.01	123, 112, 120, 89, 104	109	12	5
	3.0	98, 100, 93, 102, 101	99	3	5
	Overall	89–123	104	10	10

Matrix	Fortification level (mg/kg)	Recovery rate (%)		RSD (%)	n
		Individual results	Mean		
Wine	0.01	86, 109, 98, 91, 107	98	9	5
	0.1	103, 98, 96, 102, 109	101	3	5
	Overall	86–109	100	7	10
Sunflower seed	0.01	89, 76, 78. 99, 80	85	11	5
	0.1	76, 84, 79, 78, 79	79	4	5
	Overall	76–99	82	9	10

Re-analysis of sunflower, orange fruit, straw and lettuce primary extracts stored at < 7°C after 7 ± 1 and 28 ± 1 days demonstrated that fludioxonil gave recoveries comparable to the original results, and within the acceptable range. Re-analysis of the orange analytical solution after 8 days of storage gave higher than expected recoveries (95–122%) but the primary orange extracts stored for 28 days were further stored for 7 days, re-analysed, and an acceptable recovery range of 93–110% was determined.

LC-MS/MS with two transitions is considered to be highly selective and the method is therefore specific. Matrix effects were assessed by comparing the mean instrumental response to five injections of a standard prepared in acetonitrile:ultrapure water (30:70 v/v) as in the method with the mean response to five injections of standard prepared in matrix. Some suppression or enhancement of LC-MS/MS response to fludioxonil in the presence of matrix was demonstrated but this was less than 10% for most matrices so that samples may be quantified using non-matrix matched standards. The greatest matrix effects were observed with sunflower matrix, but recovery results were still within the acceptable range (mean recovery 70–110% with RSD < 20%).

The method was considered to be selective for fludioxonil.

Detector response using either the primary or confirmatory transition was tested in the range from 0.05 to 12.0 ng/mL (equivalent to 1.0–240 pg injected using a 20 µL injection volume). The regressions of concentration on detector response were linear (R^2 = 1.000) and the intercepts not significantly different from zero (p = 0.05) for both transitions tested. Thus residues from 0.01 mg/kg to 1.0 mg/kg may be analysed directly (without additional dilution) while remaining within at least ± 20% of the linear range of the instrument. It is therefore considered acceptable to use single point calibration for residue calculations for each of the matrices tested. It is considered that analyte concentrations are determined in the dynamic range of the instrument.

The LOQ for fludioxonil in the crop matrices tested using Method REM 133.06 was established as 0.01 mg/kg. Residues of fludioxonil measured in control samples were < 30% of the LOQ during method validation.

In addition to above, the method was validated for determination of fludioxonil in mango fractions during the supervised residue trial study (Jones, 2009, T011308-06-PHA) to confirm the reliability of the analytical method for the determination of fludioxonil residues in mangoes.

Table 4 Recoveries by Method REM 133.06 for determination of fludioxonil in mangoes

Matrix	Fortification level (mg/kg)	Recovery rate (%)		RSD (%)
		Individual value	Mean	
Mango Peel	0.01	116		
	0.01	107		
	0.01	109		
	1.0	83		
	1.0	101		
	10.0	82 [a]		
	Overall		100	14
Mango Pulp	0.01	80		
	0.01	98		
	0.10	94		
	1.0	108 [a]		
	Overall		95	12

[a] mean of replicate injections

In the South African 2008 residue study, the linearity of the detector response was confirmed over the range 0.05-5 ng/mL using five calibration solutions. The correlation coefficient (R^2) was found to be 0.9994 and the intercept did not to differ significantly from zero.

Stability of residues in stored analytical samples

The 2004 JMPR and 2010 JMPR evaluated the study results on stability of residues and concluded that fludioxonil is stable in an array of stored frozen commodities. Fludioxonil is stable in frozen samples for the longest periods tested: 24 months in apples and grapes; 427 days in whole grapefruit; 303 days in lemon pulp; and 3 months in frozen samples of peaches, plums, cherries and blueberries.

USE PATTERNS

Fludioxonil is registered globally as a fungicide and has many uses. The current Meeting received information on the post-harvest use of fludioxonil on mangoes in South Africa, which is summarized in Table 5. The target fungal pest controlled is stem-end rot (*Lasiodiplodia theobromae, Botryodiplodia theobromae*). The recommended maximum use pattern is to prepare a 34.5 g ai/hL solution (150 mL product/hL), for use as a hot dip. Mature fruits are dipped into the fludioxonil solution at a temperature of 52 ºC for at least 30 seconds and up to 5 minutes.

Table 5 Registered post-harvest use of fludioxonil on mango in South Africa

Crop	Country	Formulation	Application				PHI days
			Method	Maximum Rate g ai /hL	Maximum number	Interval days	
Mango	South Africa	230 g ai/L SC	Hot dip (52 °C, min 30 sec, max 5 min)	34.5 (150 mL product/hL)	1	na	Na

na = not applicable

Residues Resulting From Supervised Trials on Crops

The Meeting received information on fludioxonil supervised field trials on mangoes conducted in Australia and South Africa as shown in Table 6.

Six supervised residue trials were conducted in Australia in 2008, four in South Africa in 2004 and six in 2008 also in South Africa. From each site, mango fruits were treated post-harvest by hot dip in fungicide solution at 52 °C for up to 5 minutes at a concentration equivalent to 29.6–34.5 g ai/hL.

A variety of decline trials were undertaken in which samples of fruit were taken for analysis either immediately after the treatment had dried or at various time points after treatment (between 0 to 61 days) to demonstrate. In all trials, residues in pulp and peel were determined separately and whole fruit residue values were calculated from these data.

The samples were packed, transported and stored frozen prior to analysis. Samples were stored deep-frozen for a maximum of 8 months.

Residues in all control samples were less than the limit of quantification for fludioxonil.

In order to provide the worst case situation, the highest residues determined in trials in which mangoes were dipped at rates of 29.6–34.5 g ai/hL were selected to estimate a maximum residue level. The relevant results are underlined in Table 6.

The laboratory reports include batch recovery data at residue levels comparable to those occurring in the samples from the supervised trials. The field reports provide data on the dates of

treatments, methods used and sampling dates. Dates of analyses or duration of residue sample storage are also provided. Residue data are not adjusted for percentage recovery.

Mangoes

Table 6 Residues resulting from post-harvest application of fludioxonil to mango in Australia and South Africa

MANGO Location Year Variety	Number of applications (growth stage at application)	Rate (g ai/hL)	DAD (days after dipping)	Crop Part	Fludioxonil Residue (mg/kg)	Author, Date, Study No. Trial Ref.
AUSTRALIA						
North Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 14.8 g ai/hL	0	Peel	1.40	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S1/T2
				Pulp	< 0.01	
				Whole fruit	0.16	
Far North Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 29.6	0	Peel	3.43	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S1/T3
				Pulp	< 0.01	
				Whole fruit	0.42	
Far North Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 14.8	0	Peel	0.93	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S2/T2
				Pulp	< 0.01	
				Whole fruit	0.10	
			7	Peel	0.84	
				Pulp	< 0.01	
				Whole fruit	0.05	
			14	Peel	0.69	
				Pulp	< 0.01	
				Whole fruit	0.07	
			28	Peel	0.76	
				Pulp	< 0.01	
				Whole fruit	0.07	
			35	Peel	0.52	
				Pulp	< 0.01	
				Whole fruit	0.03	
Far North Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 29.6	0	Peel	2.48	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S2/T3
				Pulp	< 0.01	
				Whole fruit	0.29	
			7	Peel	2.21	
				Pulp	< 0.01	
				Whole fruit	0.29	
			14	Peel	1.72	
				Pulp	< 0.01	
				Whole fruit	0.21	
			28	Peel	1.85	
				Pulp	< 0.01	
				Whole fruit	0.18	
			35	Peel	1.21	
				Pulp	< 0.01	
				Whole fruit	0.13	
North Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 14.8	0	Peel	3.37	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S3/T2
				Pulp	< 0.01	
				Whole fruit	0.33	
North Queensland 2009	Mature fruit post-harvest	Hot dip 29.6	0	Peel	5.78	Keats A 2009 SYN0904
				Pulp	< 0.01	
				Whole fruit	0.67	

MANGO Location Year Variety	Number of applications (growth stage at application)	Rate (g ai/hL)	DAD (days after dipping)	Crop Part	Fludioxonil Residue (mg/kg)	Author, Date, Study No. Trial Ref.
Mango						A9859A_10043 Trial SYN0904/S3/T3
North Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 14.8	0	Peel	2.69	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S4/T2
				Pulp	< 0.01	
				Whole fruit	0.20	
			7	Peel	2.57	
				Pulp	< 0.01	
				Whole fruit	0.23	
			14	Peel	1.77	
				Pulp	< 0.01	
				Whole fruit	0.09	
			28	Peel	0.88	
				Pulp	< 0.01	
				Whole fruit	0.14	
			35	Peel	1.11	
				Pulp	< 0.01	
				Whole fruit	0.08	
Far North Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 29.6	0	Peel	4.25	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S4/T3
				Pulp	< 0.01	
				Whole fruit	0.26	
			7	Peel	3.39	
				Pulp	< 0.01	
				Whole fruit	0.36	
			14	Peel	3.80	
				Pulp	< 0.01	
				Whole fruit	0.27	
			28	Peel	3.80	
				Pulp	< 0.01	
				Whole fruit	0.25	
			35	Peel	2.57	
				Pulp	< 0.01	
				Whole fruit	0.14	
South East Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 14.8	0	Peel	2.75	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S5/T2
				Pulp	< 0.01	
				Whole fruit	0.27	
			7	Peel	2.42	
				Pulp	< 0.01	
				Whole fruit	0.22	
			14	Peel	2.46	
				Pulp	< 0.01	
				Whole fruit	0.17	
			28	Peel	2.46	
				Pulp	< 0.01	
				Whole fruit	0.23	
			35	Peel	1.73	
				Pulp	< 0.01	
				Whole fruit	0.10	
South East Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 29.6	0	Peel	6.50	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S5/T3
				Pulp	< 0.01	
				Whole fruit	0.74	
			7	Peel	4.76	
				Pulp	< 0.01	
				Whole fruit	0.43	
			14	Peel	5.40	
				Pulp	< 0.01	
				Whole fruit	0.43	
			28	Peel	3.73	

MANGO Location Year Variety	Number of applications (growth stage at application)	Rate (g ai/hL)	DAD (days after dipping)	Crop Part	Fludioxonil Residue (mg/kg)	Author, Date, Study No. Trial Ref.
				Pulp	< 0.01	
				Whole fruit	0.29	
			35	Peel	2.94	
				Pulp	< 0.01	
				Whole fruit	0.18	
South East Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 14.8	0	Peel	2.30	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S6/T2
				Pulp	< 0.01	
				Whole fruit	0.15	
			7	Peel	1.95	
				Pulp	< 0.01	
				Whole fruit	0.18	
			14	Peel	1.84	
				Pulp	< 0.01	
				Whole fruit	0.19	
			28	Peel	1.86	
				Pulp	< 0.01	
				Whole fruit	0.13	
			35	Peel	1.58	
				Pulp	< 0.01	
				Whole fruit	0.11	
South East Queensland 2009 Mango	Mature fruit post-harvest	Hot dip 29.6	0	Peel	4.08	Keats A 2009 SYN0904 A9859A_10043 Trial SYN0904/S6/T3
				Pulp	< 0.01	
				Whole fruit	0.31	
			7	Peel	2.98	
				Pulp	< 0.01	
				Whole fruit	0.18	
			14	Peel	2.52	
				Pulp	< 0.01	
				Whole fruit	0.24	
			28	Peel	2.50	
				Pulp	< 0.01	
				Whole fruit	0.26	
			35	Peel	2.01	
				Pulp	< 0.01	
				Whole fruit	0.17	
SOUTH AFRICA						
2004 Mango (Kent)	BBCH 81 post-harvest	(dip) 30	0	Flesh	< 0.02	Gardinal P,, Gill P 2004 03-6093 CGA173506/7336 Trial 03-6093 Plot 1
				Peel	2.68	
				Whole fruit	0.42	
			7	Flesh	< 0.02	
				Peel	3.86	
				Whole fruit	0.49	
			14	Flesh	< 0.02	
				Peel	2.67	
				Whole fruit	0.36	
			30	Flesh	< 0.02	
				Peel	2.05	
				Whole fruit	0.26	
			61	Flesh	< 0.02	
				Peel	1.27	
				Whole fruit	0.14	
2004 Mango (Kent)	BBCH 81 post-harvest	(drench) 30	0	Flesh	< 0.02	Gardinal P,, Gill P 2004 03-6093 CGA173506/7336 Trial 03-6093 Plot 2
				Peel	1.77	
				Whole fruit	0.28	
			7	Flesh	< 0.02	
				Peel	1.37	
				Whole fruit	0.2	
			14	Flesh	< 0.02	

MANGO Location Year Variety	Number of applications (growth stage at application)	Rate (g ai/hL)	DAD (days after dipping)	Crop Part	Fludioxonil Residue (mg/kg)	Author, Date, Study No. Trial Ref.
				Peel	1.04	
				Whole fruit	0.17	
			30	Flesh	< 0.02	
				Peel	0.97	
				Whole fruit	0.12	
			61	Flesh	< 0.02	
				Peel	0.42	
				Whole fruit	0.06	
2004 Mango (Kent)	BBCH 81 post-harvest	(dip) 30	0	Flesh	< 0.02	Gardinal P,, Gill P 2004 03-6094 CGA173506/7337 Trial 03-6094 Plot 1
				Peel	8.54	
				Whole fruit	0.66	
			7	Flesh	< 0.02	
				Peel	5.66	
				Whole fruit	0.56	
			14	Flesh	< 0.02	
				Peel	5.79	
				Whole fruit	0.59	
			30	Flesh	< 0.02	
				Peel	4.8	
				Whole fruit	0.5	
			61	Flesh	< 0.02	
				Peel	3.81	
				Whole fruit	0.40	
2004 Mango (Kent)	BBCH 81 post-harvest	(drench) 30	0	Flesh	< 0.02	Gardinal P,, Gill P 2004 03-6094 CGA173506/7337 Trial 03-6094 Plot 2
				Peel	4.86	
				Whole fruit	0.42	
			7	Flesh	< 0.02	
				Peel	5.25	
				Whole fruit	0.51	
			14	Flesh	< 0.02	
				Peel	4.36	
				Whole fruit	0.46	
			30	Flesh	< 0.02	
				Peel	4.16	
				Whole fruit	0.37	
			61	Flesh	< 0.02	
				Peel	3.1	
				Whole fruit	0.30	
2004 Mango (Kent)	BBCH 81 post-harvest	(dip) 30	0	Flesh	< 0.02	Gardinal P,, Gill P 2004 04-6000 CGA173506/7338 Trial 04-6000 Plot 1
				Peel	2.61	
				Whole fruit	0.34	
2004 Mango (Kent)	BBCH 81 post-harvest	(drench) 30	0	Flesh	< 0.02	Gardinal P,, Gill P 2004 04-6000 CGA173506/7338 Trial 04-6000 Plot 2
				Peel	2.62	
				Whole fruit	0.32	
2004 Mango (Kent)	BBCH 81 post-harvest	(dip) 30	0	Flesh	< 0.02	Gardinal P,, Gill P 2004 04-6001 CGA173506/7339 Trial 04-6001 Plot 1
				Peel	5.19	
				Whole fruit	0.37	
2004 Mango (Kent)	BBCH 81 post-harvest	(drench) 30	0	Flesh	< 0.02	Gardinal P,, Gill P 2004 04-6001 CGA173506/7339 Trial 04-6001 Plot 2
				Peel	4.15	
				Whole fruit	0.31	

MANGO Location Year Variety	Number of applications (growth stage at application)	Rate (g ai/hL)	DAD (days after dipping)	Crop Part	Fludioxonil Residue (mg/kg)	Author, Date, Study No. Trial Ref.
Tzaneen 2008 Mango (Tommy Atkins)	BBCH 81 post-harvest	(dip) 34.	0	Flesh	0.03	Jones S 2008 S08-02598 CGA173506_11412 Trial ZA 14RF001 2008 Plot 2
				Peel	3.14	
				Whole fruit	0.60	
			7	Flesh	0.03	
				Peel	2.74	
				Whole fruit	0.54	
			14	Flesh	0.04	
				Peel	2.33	
				Whole fruit	0.52	
			28	Flesh	0.04	
				Peel	2.81	
				Whole fruit	0.50	
			35	Flesh	0.04	
				Peel	3.03	
				Whole fruit	0.62	
Tzaneen 2008 Mango (Tommy Atkins)	BBCH 81 post-harvest	(dip)	0	Flesh	0.04	Jones S 2008 S08-02598 CGA173506_11412 Trial ZA 14RF001 2008 Plot 3
				Peel	4.42	
				Whole fruit	0.88	
			7	Flesh	0.04	
				Peel	3.23	
				Whole fruit	0.76	
			14	Flesh	0.07	
				Peel	3.96	
				Whole fruit	0.75	
			28	Flesh	0.07	
				Peel	3.85	
				Whole fruit	0.92	
			35	Flesh	0.05	
				Peel	3.52	
				Whole fruit	0.83	
Tzaneen 2008 Mango (Tommy Atkins)	BBCH 81 post-harvest	(dip) 34.5	0	Flesh	0.09	Jones S 2008 S08-02598 CGA173506_11412 Trial ZA 14RF002 2008 Plot 2
				Peel	5.01	
				Whole fruit	1.23	
			7	Flesh	0.08	
				Peel	3.84	
				Whole fruit	0.85	
			14	Flesh	0.09	
				Peel	6.18	
				Whole fruit	1.06	
			28	Flesh	0.08	
				Peel	2.94	
				Whole fruit	0.92	
			35	Flesh	0.08	
				Peel	2.49	
				Whole fruit	1.09	
Tzaneen 2008 Mango (Tommy Atkins)	BBCH 81 post-harvest	(dip) 34.5	0	Flesh	0.04	Jones S 2008 S08-02598 CGA173506_11412 Trial ZA 14RF003 2008 Plot 2
				Peel	5.08	
				Whole fruit	1.07	
			7	Flesh	0.04	
				Peel	3.87	
				Whole fruit	0.80	
			14	Flesh	0.03	
				Peel	4.07	
				Whole fruit	0.78	
			28	Flesh	0.04	
				Peel	4.79	
				Whole fruit	0.95	
			35	Flesh	0.06	

MANGO Location Year Variety	Number of applications (growth stage at application)	Rate (g ai/hL)	DAD (days after dipping)	Crop Part	Fludioxonil Residue (mg/kg)	Author, Date, Study No. Trial Ref.
				Peel	3.71	
				Whole fruit	0.94	
Tzaneen 2008 Mango (Tommy Atkins)	BBCH 81 post-harvest	(dip) 34.5	0	Flesh	0.01	Jones S 2008 S08-02598 CGA173506_11412 Trial ZA 14RF004 2008 Plot 2
				Peel	1.99	
				Whole fruit	0.46	
			7	Flesh	< 0.01	
				Peel	1.97	
				Whole fruit	0.43	
			14	Flesh	< 0.01	
				Peel	2.18	
				Whole fruit	0.41	
			28	Flesh	0.01	
				Peel	1.83	
				Whole fruit	0.43	
			35	Flesh	0.02	
				Peel	2.22	
				Whole fruit	0.59	

"0" indicates 0 day after dipping.

Residues in animal commodities

As mango or its by-products are not included in the OECD animal feed table, the Meeting concluded that there is no need to calculate animal dietary burden this time.

APPRAISAL

Fludioxonil (4-(2,2-difluoro-1,3-benzodioxol-4-yl)pyrrole-3-carbonitrile) was first evaluated by the 2004 JMPR. The 2004 JMPR recommended 48 maximum residue levels for a variety of commodities and an ADI of 0–0.4 mg/kg bw. ARfD was considered unnecessary. The 2004 JMPR recommended the residue definition for plant commodities (for both compliance with the MRL and estimation of dietary intakes) should be fludioxonil. Fludioxonil is considered fat-soluble.

Fludioxonil was reviewed also by the 2006 and 2010 JMPR which together recommended six additional maximum residue levels and withdrew two previous maximum residue levels. At the Forty-third Session, CCPR included fludioxonil in the Priority List for review by the current Meeting for an additional MRL.

After the 2010 JMPR, a post-harvest use of fludioxonil on mango was approved and the label was available to the current Meeting from South Africa. The current Meeting received information on residue trials conducted in Australia and South Africa to support this use, along with information on methods of analysis for fludioxonil in mango.

Methods of analysis

The Meeting received information on validation of three methods of analysis used in the supervised field trial studies, HPLC/UV method already reviewed by the 2008 JMPR and two new methods, GC/MS method and HPLC/MS/MS method, for determination of fludioxonil in mango. These methods were satisfactorily validated for determination of fludioxonil in mango pulp and peel with mean recoveries within a range of 70–110% and RSD less than 20%.

Stability of residues in stored analytical samples

The 2004, 2006 and 2010 JMPR concluded that fludioxonil is stable when stored frozen for at least the following periods: 24 months in apple and grape; 14 months in grapefruit; and 10 months in lemon pulp and potato. In supervised trials, samples were stored deep-frozen for a maximum of 8 months.

Results of supervised residue trials on crops

The Meeting received information on supervised post-harvest trials of fludioxonil on mango.

The OECD MRL 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 trial conditions and other relevant factors related to each data set to arrive at a best estimate of the maximum residue level using expert judgement. Then, the OECD calculator was employed. If the statistical calculation spreadsheet suggested a different value, a brief explanation of the derivation was supplied.

Mango

A number of trials were conducted in Australia and South Africa. The registered post-harvest use of fludioxonil on mango in South Africa allows hot dip at 52 °C for a minimum of 30 seconds to a maximum of 5 minutes at the maximum rate of 34.5 g ai/hL. As the intended use was post-harvest application, the trials conducted in Australia and those in South Africa using post-harvest application were considered together.

Residues in whole fruit (including stone) from trials conducted in Australia and South Africa using post-harvest application following GAP in South Africa were in rank order (14): 0.29, 0.31, 0.34, 0.36, 0.37, 0.42, 0.49, 0.59, 0.62, 0.66, 0.67, 0.74, 1.1 and 1.2 mg/kg.

Corresponding residues in pulp, in rank order were (n = 14): < 0.01 (6), < 0.02(4), 0.02, 0.04(2), and 0.09 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg and an STMR of 0.02 mg/kg.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the residue levels listed below are suitable for establishing maximum residue limits and for IEDI and IESTI assessment.

Definition of residue for compliance with the MRLs and estimation of dietary intake in plant commodities*: fludioxonil*

Definition of residue for compliance with the MRLs and estimation of dietary intake: *sum of fludioxonil and its benzopyrrole metabolites, determined as 2,2-difluorobeno[1,1]dioxole-4-carboxylic acid and expressed as fludioxonil.*

The residue is fat-soluble.

Commodity		Recommended MRL, mg/kg		STMR/STMR-P mg/kg	HR/HR-P mg/kg
CCN	Name	New	Previous		
FI 0345	Mango	2	–	0.02	–

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDIs) of fludioxonil were calculated for the 13 GEMS/Food cluster diets using STMRs and STMRPs estimated by the 2004, 2006, 2010 and current Meetings (Annex 3 of the 2012 JMPR Report). The ADI is 0–0.4 mg/kg bw and the calculated IEDIs

were 0–2% of the maximum ADI. The Meeting concluded that the long-term intake of residues of fludioxonil resulting from the uses considered by the 2004, 2006, 2010 and current JMPR is unlikely to present a public health concern.

Short-term intake

The 2004 JMPR concluded that an ARfD for fludioxonil is unnecessary. The Meeting therefore concluded that the short-term intake of fludioxonil residues is unlikely to present a public health concern.

REFERENCES

Code	Author(s)	Year	Title, Institute, Report reference
	FAO/WHO	2005	Pesticide Residues in Food 2004, Evaluations 2004, Part I Residues
AG-664	Manuli M, Skinner D	1996	Analytical method for the determination of residues of difenoconazole, fludioxonil, fluxofenim, mefanoxam and metalaxyl in seed by capillary gas chromatography. Syngenta Reference No.: CGA48988/4190
SYN0904	Keats A	2009	Determination of CGA173506 (Fludioxonil) residues in mangoes following an application of A-9859-A as a post-harvest dip. Syngenta Reference No.: A9859A_10043
REM 133.06	Nichols, C	2006	Analytical Method for the Determination of Residues of Fludioxonil (CGA173506) in Crop Matrices. Final Determination by LC-MS/MS. Syngenta Method No. REM 133.06, Syngenta File No. CGA173506/6932
RJ3773B	Anderson, L, Nichols, C	2006	Fludioxonil (CGA173506): Validation of Residue Analytical Method REM 133.06 for the Determination of Residues in Crops. Final Determination by LC-MS/MS. Syngenta File No. CGA173506/6933
T011308-06-PHA	Jones, S	2009	Fludioxonil: Residue study on fludioxonil as a post-harvest use on Mangos in South Africa, Final Report. Syngenta File No CGA173506-11412
03-6093	Gardinal P, Gill P	2007a	Fludioxonil (CGA173506): Residue study in or on Mangos in South Africa—Post-harvest application, Final Report. Syngenta File No. CGA173506/7336
03-6094	Gardinal P, Gill P	2007b	Fludioxonil (CGA173506): Residue study in or on Mangos in South Africa—Post-harvest application, Final Report. Syngenta File No. CGA173506/7337
04-6000	Gardinal P, Gill P	2007c	Fludioxonil (CGA173506): Residue study in or on Mangos in South Africa—Post-harvest application, Final Report. Syngenta File No. CGA173506/7338
04-6001	Gardinal P, Gill P	2007d	Fludioxonil (CGA173506): Residue study in or on Mangos in South Africa—Post-harvest application, Final Report. Syngenta File No. CGA173506/7339