THIABENDAZOLE (065)

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EXPLANATION

Thiabendazole is a benzimidazole compound used as a systemic fungicide in agriculture, and also as a broad-spectrum anthelmintic in various animal species. It was first evaluated by JMPR in 1970, and the latest evaluation was conducted in 2006 (T, R).

The residue definitions for thiabendazole are for compliance with MRL and for dietary risk assessment for plant commodities: *thiabendazole.*

For compliance with MRL for animal commodities: *sum of thiabendazole and 5-hydroxythiabendazole*

And for dietary risk assessment for animal commodities: *sum of thiabendazole, 5-hydroxythiabendazole and its sulfate conjugate*.

The compound was scheduled at the Fiftieth Session of the CCPR for the evaluation of additional uses by the 2019 Extra JMPR. Plant metabolism studies, analytical methods and residue trials on mango, beans, peas and sweet potato, and processing studies were submitted to the Meeting.

Plant metabolism

Two plant metabolism studies not previously evaluated by the Meeting were submitted, one study investigated the metabolism of thiabendazole in oranges treated post-harvest and one in maize when used as a seed treatment.

Orange, post-harvest

In the study conducted by Piskorski (2012), [Phenyl-U-^{14}C]-thiabendazole was applied to orange fruits in a single dose at 0.2 kg ai/hL prior to storage in the dark at approximately 5 °C and at a relative humidity of about 85%, and oranges sampled and analysed directly after application and at intervals of 8 and 16 weeks. At each timepoint, radioactive residues were extracted from the fruit surface with acetonitrile and the washed oranges were separated into peel and flesh, which were milled and then homogenized under liquid nitrogen prior to combustion/LSC analysis. Radioactivity of orange flesh was always < 0.01 mg eq/kg, and only the homogenised, washed peel were sequentially shaken with 1N NaOH/phosphate buffer pH 8, extracted with ethyl acetate, phosphate buffer pH 8 again and then with acetonitrile. The liquid and solid phases were separated by centrifugation and the supernatant was filtered, the radioactivity in each extract quantified by LSC, and further concentrated for TLC and HPLC analysis for residues identification and characterization. Aliquots of the post extraction debris were analysed by combustion/LSC. Analysis of samples was completed within six months of each sampling date and therefore no storage stability analysis was required. The results are shown in Tables 1 and 2.

Table 1 Summary of total radioactive residues and extractability in mature oranges treated post-harvest with [^{14}C]thiabendazole

Period of storage	Initial Fruit Wash		Washed Fruit Peel				Flesh		TRR[a]
			Extracted Radioactivity		Non-extracted Radioactivity				
	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	mg eq/kg
0 days	94.35	4.982	4.37	0.231	1.24	0.066	0.04	0.002	5.280
8 weeks	80.93	4.379	14.02	0.759	4.92	0.266	0.14	0.007	5.411
16 weeks	72.59	3.001	22.51	0.931	4.78	0.198	0.11	0.005	4.134

[a] The total radioactive residue (mg/kg) is calculated by the summation of the radioactivity present in the initial fruit surface wash, extract and debris generated from analysis of the washed peel and the direct combustion of orange flesh.

Table 2 Summary of identification and characterization of residues found in orange peel washes

		Day 0		8 weeks of storage		16 weeks of storage	
TRR by summation (mg/kg)		5.280[a]		5.411[a]		4.134[a]	
TRR by direct quantification (mg eq/kg)		5.333[b]		5.556[b]		4.207[b]	
Percentage of TRR for chromatography (%)on a conveyor belt		98.72		94.94		95.11	
Origin of component	Component	% TRR	Residue (mg eq/kg)	% TRR	Residue (mg eq/kg)	% TRR	Residue (mg eq/kg)
Chromato-graphed	Thiabendazole	98.56	5.204	92.30	4.994	89.91	3.717
	5-hydroxythiabendazole	N/D	N/D	0.34	0.018	0.39	0.016
	Benzimidazole	N/D	N/D	0.04	0.002	ND	ND
	Benzimidazole-COOH	N/D	N/D	0.30	0.016	0.30	0.012
	Unassigned [c]	0.02	0.001	1.65	0.089	2.28	0.094
	Baseline	0.20	0.011	0.31	0.017	2.22	0.092
	Unextracted (peel)	1.24	0.066	4.92	0.266	4.78	0.198
	Unextracted (flesh)	0.04	0.002	0.14	0.007	0.11	0.005
	Total	100	5.28	100	5.41	100	4.13

ND: Not detected;

[a] TRR determined by summation of radioactivity present in the surface wash, solvent extracts of washed peel, debris following solvent extraction of washed peel and combusted flesh;

[b] The radioactive residue determined by summation of radioactivity present in the surface wash and direct quantification from washed fruit (separately peel and flesh) employing combustion/LSC;

[c] Unassigned radiocomponents which chromatographed away from the origin in 2D-TLC SSA. For the day 0 samples this consists of 2 components, none > 0.01%TRR (<0.001 mg/kg); for week 8 samples this consists of 9 components, none > 0.53% TRR (0.029 mg/kg); for week 16 samples, this consists of 7 components, none > 1.13%TRR (0.047 mg/kg);

Maize, seed treatment

[Phenyl-U-^{14}C]-thiabendazole, formulated as a suspension concentrate, was applied as a single seed dressing to maize seeds at the maximum rate of 0.09 mg/seed (MacKinnon, 2005). Treated maize was grown under glasshouse conditions with plants harvested at growth stages representing commercial forage, sweet corn and maturity. Samples of forage were taken at the growth stage of V12 or BBCH 19, 81 days after sowing. Samples of forage, cobs and kernels were taken at the sweet corn stage of R4 or BBCH 83–85, 101 days after sowing and at maturity growth stage R6 or BBCH 89, 116 days after sowing. All samples were stored frozen at ≤ -20 °C.

No residues were detected in the cobs or kernels from the sweet corn or at maturity growth stages. TRR of foliage from the sweet corn stage and at maturity were < 0.01 mg eq/kg (0.005 and 0.002 mg eq/kg, respectively, and were not analysed. Foliage from the forage stage sample had TRR of 0.014 mg eq/kg and was extracted with acetonitrile:water (8:2), dried and reconstituted with acetone:water (3:2). After filtration, the solution was reduced to dryness and reconstituted with acetone:water (1:1), resulting in a bi-phasic system of organic and aqueous fractions. 42.5% of the TRR (0.006 mg/kg) were extracted and 55.5% remained unextracted (0.008 mg/kg). Aliquots of the organic and aqueous fractions submitted to normal and reversed-phase TLC. TRR were characterised to be composed of multiple minor metabolites without the presence of thiabendazole. No further attempt was made to extract and characterise the post extraction solid residue.

RESIDUE ANALYSIS

Analytical methods

In Method GRM040.01A, samples are extracted with aqueous phosphate buffer (pH 6) and partitioned against ethyl acetate (McLean and Nelson, 2008). Any conjugates of thiabendazole or benzimidazole were extracted with ethyl acetate following the addition of a glucosidase enzyme to the aqueous phase. The ethyl acetate phase was analysed by LC-MS/MS, with a LOQ of 0.01 mg/kg for each analyte. Table 3 shows the recovery data of this procedure.

Table 3 Recoveries of thiabendazole from crops using method GRM040.01A

Commodity	Compound	Fortification level, mg/kg	No.	Mean recovery (%)	RSD (%)	Mean recovery (%)	RSD (%)
				Primary transition		Confirmatory transistion	
Spinach (leaves)	Thiabendazole (m/z = 202 → 131)	0.01	5	101	2	102	2
		0.1	5	97	2	98	1
	Benzimidazole	0.01	5	87	2	87	1
	(m/z = 119 → 92)	0.10	5	88	3	87	3
Wheat (grain)	Thiabendazole (m/z = 202 → 131)	0.01	5	94	2	94	2
		0.1	5	94	2	93	2
	Benzimidazole (m/z = 119 → 92)	0.01	5	92	2	96	2
		0.10	5	92	2	94	2
Wheat (straw)	Thiabendazole (m/z = 202 → 131)	0.01	5	95	3	95	2
		0.1	5	94	2	93	1
	Benzimidazole (m/z = 119 → 92)	0.01	5	87	2	90	2
		0.10	5	89	1	88	2
Carrot (roots)	Thiabendazole (m/z = 202 → 131)	0.01	5	105	1	105	2
		0.1	5	96	1	96	2
	Benzimidazole (m/z = 119 → 92)	0.01	5	93	2	94	1
		0.10	5	89	1	89	2
Bean (with pods)	Thiabendazole (m/z = 202 → 131)	0.01	3	98	2.4		
		1.0	3	96	6.2		
	Benzimidazole (m/z = 119 → 92)	0.01	3	95	1.4		
		1.0	3	85	8.8		
Pea (vines)	Thiabendazole (m/z = 202 → 131)	0.01	3	89	1.4		
		1.0	3	92	1.9		
	Benzimidazole (m/z = 119 → 92)	0.01	3	75	1.8		
		1.0	3	76	4.3		
Sweet potato (roots)	Thiabendazole (m/z = 202 → 131)	0.01	3	85	4.1		
		0.1	3	84	14		
		10	3	75	2.0		
	Benzimidazole (m/z = 119 → 92)	0.01	3	90	7.1		
		0.10	3	88	12		
		10	3	73	2.2		
Sweet potato (chips)	Thiabendazole (m/z = 202 → 131)	0.01	3	86	3.6		
		1.0	3	82	1.9		
		10	3	67	3.1		
	Benzimidazole (m/z = 119 → 92)	0.01	3	83	2.6		
		1.0	3	81	0.1		
		10	3	68	6.8		
Sweet potato (flakes)	Thiabendazole (m/z = 202 → 131)	0.01	3	89	4.5		
		1.0	3	91	9.5		
		10	3	73	17		
	Benzimidazole (m/z = 119 → 92)	0.01	3	80	7.9		
		1.0	3	72	6.4		
		10	3	65	32		

In Method GRM046.04A, samples were extracted twice with ethyl acetate, centrifuged and purified using a cation exchange SPE cartridge (Crook, 2012). The purified extracts were quantified by LC-MS/MS, monitoring for the primary transition (m/z = 202→175) and the confirmatory transition (m/z = 202→131). The response of the LC-MS/MS was shown to be linear for both primary and confirmatory transitions for thiabendazole over a concentration range of between 30% LOQ and 20% above the upper fortification level, with correlation coefficients > 0.99. Insignificant enhancement or suppression (< 20%) of detector response was observed for both analytes and all the matrices. The recovery data are shown in Table 4.

Table 4 Recoveries of thiabendazole from crops using method GRM046.04A

Commodity	Fortification level (mg/kg)	No.	Mean recovery (%)	RSD (%)	Mean recovery (%)	RSD (%)
			m/z = 202→175		*m/z* = 202→131	
Lettuce	0.01	5	90	5.0	92	3.4
	0.1	5	81	13.5	82	14.2
Tomato	0.01	5	88	7.7	88	7.7
	0.1	5	82	11.4	83	11.7
Orange	0.01	5	80	7.7	86	9.7
	0.10	5	81	2.7	79	7.2
Potato	0.01	5	90	4.9	90	2.7
	0.1	5	83	8.6	83	8.3
Avocado	0.01	5	86	4.4	85	4.7
	0.10	5	87	5.0	88	4.7
Maize (whole cob)	0.01	5	93	1.9	94	1.2
	0.10	5	78	11.8	79	12.0
Mango (peel)	0.01	5	87	6.4	-	-
	0.1	5	88	7.7	-	-
	1.0	5	92	4.0	-	-
	20	5	86	4.1	-	-
Mango (pulp)	0.01	5	79	5.6	-	-
	0.01	5	84	4.6	-	-
	1.0	5	103	5.8	-	-

The extraction efficiency of the methods used in the trials was shown by analysing oranges treated with [Phenyl-U-^{14}C]-thiabendazole from the metabolism study (Piskorski, 2012). The results are shown in Table 5.

Table 5 Comparison of solvent extractabilities of thiabendazole residues from whole fruit orange from metabolism and residue analytical methods

Method	Radioactivity extracted		Relative efficiency (%)[1]	Thiabendazole		Relative thiabendazole recovery (%)[a]
	%TRR	mg eq/kg		%TRR	mg/kg	
Metabolism extraction[b]	95.1	3.931	N/A	89.9	3.717	N/A
M-046[c]	81.8	1.849	86.0	80.8	1.827	89.9
M-049[c]	68.1	1.538	71.6	67.2	1.519	74.7
Modified M-049[c]	70.1	1.585	73.7	66.7	1.508	74.2

N/A - Not applicable;

[a] (Residue method %TRR extracted/metabolism method %TRR extracted) × 100%;

[b] Results from oranges stored for 16 weeks; sum of washed and extracted radioactivity from the orange peel. The flesh was not extracted as the radioactive residue present was only 0.005 mg/kg;

[c] Mean values of 2 replicates.

A QuEChERS method (EN 15662:2009-02 or L-00.00-115) was validated for thiabendazole in crop commodities (Class and Bacher, 2012). A sample aliquot (5 or 10 g) is extracted with acetonitrile:water. magnesium sulphate, sodium chloride, sodium citrate tribasic dihydrate and sodium citrate dibasic sesquihydrate are added, the mixture is shaken, centrifuged and transferred to a dispersive SPE (dSPE) clean-up tube. If necessary, the upper acetonitrile phase is stored frozen for approximately three hours to remove fat or waxes. Thiabendazole is determined by LC-MS/MS, at a LOQ of 0.01 mg/kg. The recovery results are shown in Table 6.

Table 6 Recovery of thiabendazole from crops using the QuEChERS method

Commodity	Fortification level (mg/kg)	No.	Mean recovery (%)	RSD (%)	Mean recovery (%)	RSD (%)
			m/z=202→175		m/z=202→131	
Lettuce	0.01	5	101	3	101	4
	0.1	5	103	2	102	2
Orange (whole fruit)	0.01	5	99	4	101	5
	0.1	5	97	5	99	4
Wheat (grain)	0.01	5	88	5	87	4
	0.1	5	89	4	89	3
Olives	0.01	5	80	8	84	9
	0.1	5	83	4	85	4

The LC-MS/MS response was shown to be linear over the range from ≤ 20% of the LOQ to 20 × LOQ for both primary and confirmatory transitions, with correlation coefficients (r) ≥ 0.99. Significant matrix effects (> 20%) were observed for orange, wheat grain and olive matrices, and matrix-matched standards were used for quantification. A method validation was conducted by an independent laboratory, and the data are presented in Table 7 (Amic, 2012).

Table 7 Recovery of thiabendazole from crops using the QuEChERS method

Commodity	Fortification level (mg/kg)	No.	Mean recovery (%)	RSD (%)	Mean recovery (%)	RSD (%)
			m/z=202→175		m/z=202→131	
Lettuce	0.01	5	94	2	92	2
	0.1	5	93	1	93	1
Olives	0.01	5	90	3	93	2
	0.1	5	92	2	83	5

The QuEChERS method was also validated for thiabendazole and 5-hydroxy-thiabendazole in animal matrices and the recovery results are shown in Table 8 (Class and Backer, 2012; Watson, 2014).

Table 8 Recovery of thiabendazole and 5-hydroxy-thiabendazole in animal commodities using the QuEChERS method

Commodity	Compound	Fortification level (mg/kg)	No.	Range of Recovery (%)	Mean recovery (%)	RSD (%)
Primary transition						
Muscle	Thiabendazole (m/z=202→175)	0.01	5	93-99	97	2.5
		0.1	5	90-96	92	2.5
	5-Hydroxy-thiabendazole (m/z=218→147)	0.01	5	70-79	75	5.9
		0.1	5	77-82	80	2.3
Fat	Thiabendazole (m/z=202→175)	0.01	5	95-105	101	3.9
		0.1	5	98-103	100	1.9
	5-Hydroxy-thiabendazole (m/z=218→147)	0.01	5	96-106	100	4.5
		0.1	5	90-99	94	3.8
Liver	Thiabendazole (m/z=202→175)	0.01	5	87-93	90	2.7
		0.1	5	86-88	87	0.9
	5-Hydroxy-thiabendazole (m/z=218→147)	0.01	5	70-80	75	5.3
		0.1	5	70-72	71	1.2
Milk	Thiabendazole (m/z=202→175)	0.01	5	93-98	96	1.9
		0.1	5	91-95	93	1.9
	5-Hydroxy-thiabendazole (m/z=218→147)	0.01	5	82-93	88	4.7
		0.1	5	82-89	85	3.4
Egg	Thiabendazole (m/z=202→175)	0.01	5	86-94	92	3.5
		0.1	5	98-103	101	2.3

Commodity	Compound	Fortification level (mg/kg)	No.	Range of Recovery (%)	Mean recovery (%)	RSD (%)
	5-Hydroxy-thiabendazole (m/z=218→147)	0.01	5	69-86	79	8.5
		0.1	5	91-98	95	2.9
Confirmatory transition						
Muscle	Thiabendazole (m/z=202→131)	0.01	5	92-100	94	3.4
		0.1	5	90-97	93	2.7
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	74-87	81	6.0
		0.1	5	75-79	77	1.9
Fat	Thiabendazole (m/z=202→131)	0.01	5	99-106	101	2.6
		0.1	5	99-106	102	2.9
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	95-103	99	3.8
		0.1	5	90-97	93	3.0
Liver	Thiabendazole (m/z=202→131)	0.01	5	87-91	89	1.9
		0.1	5	85-87	86	0.9
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	71-78	75	3.5
		0.1	5	71-74	72	1.8
Milk	Thiabendazole (m/z=202→131)	0.01	5	92-99	96	2.6
		0.1	5	94-97	95	1.2
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	79-91	85	5.1
		0.1	5	84-90	87	3.1
Egg	Thiabendazole (m/z=202→131)	0.01	5	84-95	91	4.9
		0.1	5	99-105	102	2.4
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	71-86	80	7.4
		0.1	5	91-97	95	2.2

The QuEChERS method for animal commodities was validated by an independent laboratory (Amic, 2012), and recovery data are shown in Table 9.

Table 9 Recovery of thiabendazole and 5-hydroxy-thiabendazole in animal commodities obtained by an independent laboratory

Commodity	Compound	Fortification level (mg/kg)	No.	Range of Recovery (%)	Mean recovery (%)	RSD (%)
Primary transition						
Muscle	Thiabendazole (m/z=202→175)	0.01	5	119-122	120	1
		0.1	5	96-102	99	2
	5-Hydroxy-thiabendazole (m/z=218→147)	0.01	5	92-103	99	4
		0.1	5	72-78	75	3
Fat	Thiabendazole (m/z=202→175)	0.01	5	103-110	107	2
		0.1	5	92-105	99	5
	5-Hydroxy-thiabendazole (m/z=218→147)	0.01	5	110-114	111	2
		0.1	5	94-107	100	5
Liver	Thiabendazole (m/z=202→175)	0.01	5	97-103	99	3
		0.1	5	89-98	94	4
	5-Hydroxy-thiabendazole (m/z=218→147)	0.01	5	71-80	75	4
		0.1	5	66-73	70	4
Milk	Thiabendazole (m/z=202→175)	0.01	5	92-103	96	5
		0.1	5	96-104	100	3
	5-Hydroxy-thiabendazole (m/z=218→147)	0.01	5	68-87	78	9
		0.1	5	84-93	89	4
Egg	Thiabendazole (m/z=202→175)	0.01	5	90-100	96	4
		0.1	5	96-101	98	2
		0.01	5	77-96	86	8

Commodity	Compound	Fortification level (mg/kg)	No.	Range of Recovery (%)	Mean recovery (%)	RSD (%)
	5-Hydroxy-thiabendazole (m/z=218→147)	0.1	5	80-95	87	7
Confirmatory transition						
Muscle	Thiabendazole (m/z=202→131)	0.01	5	115-121	119	2
		0.1	5	96-100	97	2
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	92-101	97	4
		0.1	5	71-80	75	5
Fat	Thiabendazole (m/z=202→131)	0.01	5	102-109	106	3
		0.1	5	90-103	97	5
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	106-114	110	3
		0.1	5	94-106	100	4
Liver	Thiabendazole (m/z=202→131)	0.01	5	93-102	97	3
		0.1	5	89-97	93	4
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	73-83	78	5
		0.1	5	69-73	71	3
Milk	Thiabendazole (m/z=202→131)	0.01	5	90-105	97	6
		0.1	5	96-104	100	3
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	65-81	74	8
		0.1	5	83-90	87	4
Egg	Thiabendazole (m/z=202→131)	0.01	5	88-98	93	4
		0.1	5	94-100	97	2
	5-Hydroxy-thiabendazole (m/z=218→191)	0.01	5	76-93	88	8
		0.1	5	79-93	87	7

Stability of pesticide residues in stored analytical samples

Homogenised samples aliquots were fortified with known amounts of either thiabendazole or benzimidazole in methanol at 0.1 mg/kg. The solvent was allowed to evaporate and the samples sealed and stored in a freezer at -20 ± 5 °C (Manson, 2014). The initial concentration was determined by analysis of two freshly-prepared samples fortified with both thiabendazole and benzimidazole using Method GRM040.01A, with acceptable procedural recoveries. The results are shown in Table 10.

Table 10 Storage stability data for thiabendazole and benzimidazole residues in frozen plant matrices

Matrix	Analyte	Interval (days/months)	Fortification level (mg/kg)	Residue level in freezer storage	
				mg/kg	% remaining (mean)
Navy beans (dry seed)	Thiabendazole	0 / 0	0.1	0.090, 0.091	90, 91 (91)
		132 / 4	0.1	0.083, 0.080	83, 80 (82)
		300 / 10	0.1	0.089, 0.092	89, 92 (91)
		377 / 12	0.1	0.094, 0.094	94, 94 (94)
		544 / 18	0.1	0.083, 0.080	83, 80 (82)
		743 / 24	0.1	0.093, 0.090	93, 90 (92)
	Benzimidazole	0 / 0	0.1	0.077, 0.081	77, 81 (79)
		132 / 4	0.1	0.066, 0.064	66, 64 (65)
		300 / 10	0.1	0.092, 0.094	92, 94 (93)
		377 / 12	0.1	0.084, 0.080	84, 80 (82)
		544 / 18	0.1	0.066, 0.072	66, 72 (69)
		743 / 24	0.1	0.087, 0.081	87, 81 (84)
Soya bean (Seed)	Thiabendazole	0 / 0	0.1	0.088, 0.088	88, 88 (88)
		100 / 3	0.1	0.085, 0.080	85, 80 (83)
		275 / 9	0.1	0.077, 0.074	77, 74 (76)
		379 / 12	0.1	0.082, 0.084	82, 84 (83)
		544 / 18	0.1	0.066, 0.075	66, 75 (71)

Matrix	Analyte	Interval (days/months)	Fortification level (mg/kg)	Residue level in freezer storage	
				mg/kg	% remaining (mean)
		730 / 24	0.1	0.083, 0.080	83, 80 (82)
	Benzimidazole	0 / 0	0.1	0.077, 0.073	77, 73 (75)
		100 / 3	0.1	0.073, 0.074	73, 74 (74)
		275 / 9	0.1	0.077, 0.076	77, 76 (77)
		379 / 12	0.1	0.064, 0.061	64, 61 (63)
		544 / 18	0.1	0.058, 0.054	58, 54 (56)
		730 / 24	0.1	0.072, 0.069	72, 69 (71)
Spinach (leaves)	Thiabendazole	0 / 0	0.1	0.090, 0.092	90, 92 (91)
		91 / 3	0.1	0.077, 0.080	77, 80 (79)
		271 / 9	0.1	0.070, 0.068	70, 68 (69)
		371 / 12	0.1	0.083, 0.085	83, 85 (84)
		544 / 18	0.1	0.079, 0.091	79, 91 (85)
		740 / 24	0.1	0.088, 0.087	88, 87 (88)
	Benzimidazole	0 / 0	0.1	0.081, 0.075	81, 75 (78)
		91 / 3	0.1	0.058, 0.056	58, 56 (57)
		271 / 9	0.1	0.056, 0.056	56, 56 (56)
		371 / 12	0.1	0.048, 0.047	48, 47 (48)
		544 / 18	0.1	0.042, 0.047	42, 47 (45)
		740 / 24	0.1	0.036, 0.035	36, 35 (36)
Barley (grain)	Thiabendazole	0 / 0	0.1	0.091, 0.096	91, 96 (94)
		91 / 3	0.1	0.081, 0.078	81, 78 (80)
		271 / 9	0.1	0.072, 0.075	72, 75 (74)
		371 / 12	0.1	0.088, 0.084	88, 84 (86)
		544 / 18	0.1	0.070, 0.068	70, 68 (69)
		747 / 25	0.1	0.085, 0.085	85, 85 (85)
	Benzimidazole	0 / 0	0.1	0.071, 0.076	71, 76 (74)
		91 / 3	0.1	0.070, 0.069	70, 69 (70)
		271 / 9	0.1	0.075, 0.074	75, 74 (75)
		371 / 12	0.1	0.076, 0.075	76, 75 (76)
		544 / 18	0.1	0.061, 0.064	61, 64 (63)
		747 / 25	0.1	0.079, 0.079	79, 79 (79)
Orange (whole fruit)	Thiabendazole	0 / 0	0.1	0.095, 0.098	95, 98 (97)
		100 / 3	0.1	0.093, 0.090	93, 90 (92)
		275 / 9	0.1	0.068, 0.074	68, 74 (71)
		392 / 13	0.1	0.098, 0.105	98, 105 (102)
		544 / 18	0.1	0.082, 0.084	82, 84 (83)
		730 / 24	0.1	0.092, 0.093	92, 93 (93)
	Benzimidazole	0 / 0	0.1	0.081, 0.070	81, 70 (76)
		100 / 3	0.1	0.070, 0.068	70, 68 (69)
		275 / 9	0.1	0.076, 0.074	76, 74 (75)
		392 / 13	0.1	0.079, 0.077	79, 77 (78)
		544 / 18	0.1	0.073, 0.082	73, 82 (78)
		730 / 24	0.1	0.084, 0.081	84, 81 (83)

USE PATTERNS

Table 11 shows the use patterns of thiabendazole for the crops and treatments relevant to this evaluation.

Table 11 Registered uses of thiabendazole using SC formulation for seed and post harvest treatments

Crop	Country	Application	kg ai/tonne	kg ai/hL	PHI (days)
Beans [a] (except soya bean)	USA	Seed treatment	0.55	-	-
Chickpea	USA	Seed treatment	0.65	-	-
Lentil	USA	Seed treatment	0.34	-	-

Crop	Country	Application	kg ai/tonne	kg ai/hL	PHI (days)
Peas [1)]	USA	Seed treatment	0.33	-	-
Mango	Belize, Costa Rica, Dominican Republic, Guatemala, Honduras, Panama and Nicaragua,	Dip (post-harvest)	-	0.24	0
	Brazil	Post-harvest	-	0.19	0
Soya bean	USA	Seed treatment	0.20	-	-
Sweet potato	USA	Dip (post-harvest)	-	0.16	0
		Spray (post-harvest), in a conveyor line	0.006		0

[a] According to USA. Crop Group 6: Legume Vegetables (Succulent or Dried);

RESULTS OF SUPERVISED RESIDUE TRIALS ON CROPS

Mango

Eight post-harvest trials were conducted on mango in Brazil in 2017, using either a dip or a spray application. Samples were maintained in frozen storage prior to extraction for periods of up to 60 days. The results are summarized in Table 12.

Table 12 Residues of thiabendazole on mango from post-harvest trials conducted in 2017 with dip or spray applications in Brazil (Report: LBS17004)

Location (variety)	Application Rate (kg ai/hL)	PHI (days)	Crop Part	Residue (mg/kg) Thiabendazole	Trial
Taquaritinga, São Paulo (Palmer)	0.25 dip	0	Peel Pulp Whole fruit [a]	8.3, 7.2 (7.7) 0.025, 0.030 (0.027) 2.4	LBS17004-01
	0.097 spray	0	Peel Pulp Whole fruit [a]	8.9, 7.6, 5.9, 5.6, 6.2 (6.8) <0.01, <0.01 (<0.01) 2.3	
Juazeiro, Bahia (Keit)	0.25 dip	0	Peel Pulp Whole fruit [a]	15, 16, 13, 14, 14 (14) 0.011, 0.013 (0.012) 4.5	LBS17004-02
	0.097 spray	0	Peel Pulp Whole fruit [a]	8.2, 7.3 (7.7) <0.01, <0.01 (<0.01) 2.5	
Casa-Nova, Bahia (Kent)	0.25 dip	0	Peel Pulp Whole fruit [a]	11, 11, 12, 12 (11) 0.010, <0.01 (0.01) 3.4	LBS17004-03
	0.097 spray	0	Peel Pulp Whole fruit [a]	10, 7.9 (9.0) <0.01, <0.01 (<0.01) 2.6	
Petrolina, Pernambuco (Tommy)	0.25 dip	0	Peel Pulp Whole fruit [a]	10, 8.1 (9.1) 0.021, 0.025 (0.023) 2.6	LBS17004-04
	0.097 spray	0	Peel Pulp Whole fruit [a]	8.0, 7.7 (7.8) <0.01, <0.01 (<0.01) 2.1	

[a] Calculated from residues in the pulp and in the peel

Twelve trials were conducted on fresh beans in the USA in 2013/14 with seed-treated bean seeds. The results are summarized in Table 13.

Table 13 Residues of thiabendazole on green beans with or without pods from seed treatment trials conducted in the USA in 2013 (Report: TK0180600)

Region (Variety)	Application Rate (kg ai/ton seed)	DAT (days)	Crop Part	Residues, mg/kg	Trial
Germansville, PA (Provider)	0.62	47	Beans with pods	<0.01, <0.01 (<0.01)	TK0180600-01
Chula, GA (Provider)	0.62	61	Beans with pods	<0.01, <0.01 (<0.01)	TK0180600-02
Athens, GA (Provider)	0.62	48	Beans with pods	<0.01, <0.01 (<0.01)	TK0180600-03
Richland, IA (Provider)	0.62	60	Beans with pods	<0.01, <0.01 (<0.01)	TK0180600-04
Geneva, MN (Provider)	0.62	67	Beans with pods	<0.01, <0.01 (<0.01)	TK0180600-05
Paso Robles, CA (Provider)	0.62	84	Beans with pods	<0.01, <0.01 (<0.01)	TK0180600-06
Athens, GA (Fordhook 242)	0.21	91	Beans green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-07
Seven Springs (Fordhook 242)	0.21	142	Beans green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-08
Lenexa, KS (Fordhook 242)	0.21	104	Beans green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-10
Chico, CA (Fordhook 242)	0.21	135	Beans green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-11
Parkdale, OR (Fordhook 242)	0.21	132	Beans green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-12
Chula, GA (Jackson Wonder)	0.42	75	Beans green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-41

Nine supervised harvest trials were conducted on fresh peas in the U.S.A. in 2013/14 with thiabendazole treated pea seeds, three trials on peas with pods and six trials on peas without pods. The results are summarized in Table 14.

Table 14 Residues of thiabendazole on green peas with or without pods from seed treatment trials conducted in the USA in 2013-21014 (Report: TK0180600)

Country (Region)	Application rate (kg ai/ton seed)	DAT (days)	Crop Part	Residues (mg/kg)	Trial
Germansville, PA (Sugar Ann)	0.99	51	Peas with pods	<0.01, <0.01 (<0.01)	TK0180600-13
Athenas, GA (Sugar Ann)	1	53	Peas with pods	<0.01, <0.01 (<0.01)	TK0180600-14
Lenexa, KS (Sugar Ann)	0.99	53	Peas with pods	<0.01, <0.01 (<0.01)	TK0180600-15
Northwood, ND (Premium)	1.2	49	Peas green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-17
Verona, WI (Premium)	1.2	51	Peas green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-18
Parkdale, OR (Premium)	1.2	71	Peas green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-19
Payette, ID (Premium)	1.2	54	Peas green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-20
Hilsboro, OR (Premium)	1.2	61	Peas green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-21

Country (Region)	Application rate (kg ai/ton seed)	DAT (days)	Crop Part	Residues (mg/kg)	Trial
Lenexa, KS (Premium)	1.2	38	Peas green w/o pods	<0.01, <0.01 (<0.01)	TK0180600-39

Nine supervised trials were conducted on dry beans in the U.S.A. in 2013 following thiadendazole treatment of bean seeds. The results are summarized in Table 15.

Table 15 Residues of thiabendazole on dry beans, following seed-treatment conducted in the USA in 2013 (Report: TK0180600)

Region (Variety)	Application rate (kg ai/ton seed)	DAT (days)	Residue (mg/kg)	Trial
Verona, WI (Lariat)	0.44	109	<0.01, <0.01 (<0.01)	TK0180600-22
Royalton, MN (Lariat)	0.44	117	<0.01, <0.01 (<0.01)	TK0180600-23
York, NE (Lariat)	0.44	102	<0.01, <0.01 (<0.01)	TK0180600-24
Geneva, MN (Lariat)	0.44	104	<0.01, <0.01 (<0.01)	TK0180600-25
Grand Island (Red Hawk)	0.41	107	<0.01, <0.01 (<0.01)	TK0180600-26
San Angelo, TX (Red Hawk)	0.41	167	<0.01, <0.01 (<0.01)	TK0180600-27
Jerome, ID (Red Hawk)	0.41	95	<0.01, <0.01 (<0.01)	TK0180600-28
Chico, CA (Red Hawk)	0.41	94	<0.01, <0.01 (<0.01)	TK0180600-29
American Falls (Red Hawk)	0.41	110	<0.01, <0.01 (<0.01)	TK0180600-30

Ten supervised harvest trials were conducted on dry peas in the U.S.A. with thiabendazole treated pea seeds in 1996 or 2013. The results are summarized in Table 16.

Table 16 Residues of thiabendazole on dry peas after seed treatment from trials conducted in the USA in 1996 and 2013.

Region (Variety)	Application rate (kg ai/ton seed)	DAT (days)	Residue (mg/kg)	Report, Trial - Year
Prosser, WA (SS Alaska Dry Pea)	0.9	83	<0.05, <0.05 (<0.05)	IR-4 06532, 96-WA85 - 1996
Prosser, WA (Umatilla Dry Pea)	0.9	83	<0.05, <0.05 (<0.05)	IR-4 06532, 96-WA84 – 1996
Prosser, WA (Columbia Dry Pea)	0.9	83	<0.05, <0.05 (<0.05)	IR-4 06532, 96-WA83 – 1996
Kimberly, ID (Umatilla Dry Pea)	0.9	87	<0.05, <0.05 (<0.05)	IR-4 06532, 96-ID09 – 1996
Kimberly, ID (Columbia Dry Pea)	0.9	90	<0.05, <0.05 (<0.05)	IR-4 06532, 96-ID10 -1996
Ephrata, WA (Montex 4153)	0.8	98	<0.01, <0.01 (<0.01)	TK0180600 TK0180600-31 – 2013
Parkdale, OR (Montex 4153)	0.8	93	<0.01, <0.01 (<0.01)	TK0180600 TK0180600-32 – 2013
American Falls (Montex 4153)	0.8	105	<0.01, <0.01 (<0.01)	TK0180600 TK0180600-33 – 2013
Chubbuck, ID (Montex 4153)	0.8	105	<0.01, <0.01 (<0.01)	TK0180600 TK0180600-34 - 2013
Payette, ID (Montex 4153)	0.8	81	<0.01, <0.01 (<0.01))	TK0180600 TK0180600-35 - 2013

Sweet Potato

Eight residue trials relevant to the use of thiabendazole on sweet potato were conducted in the USA in 2016. The results are summarized in Table 17.

Table 17 Residues of thabendazole on sweet potato from post-harvest trials in USA in 2016 (IR-4 Project No. 11859)

Region (variety)	Application rate (kg ai/tone)	Application rate (kg ai/hL)	DAT (days)	Residue (mg/kg)	Trial
Kibler, AR	0.006 (spray)	-	0	0.382, 0.368 (0.38)	AR499
(Beauregard)	-	0.16 (dip)	0	4.68, 4.85 (4.8)	
Parlier, CA	0.006 (spray)	-	0	1.32, 1.08 (1.2)	CA498
(Covington)	-	0.16 (dip)	0	2.84, 2.60 (2.7)	
Parlier, CA (Covington)	-	0.16 (dip)	0	4.4	CA525
Tifton, GA	0.006 (spray)	-	0	0.26, 0.250 (0.26)	GA*503
(Beauregard)	-	0.16 (dip)	0	5.22, 5.85 (5.5)	
Tifton, GA	0.006 (spray)	-	0	0.201, 0.219 (0.21)	GA*504
(Covington)	-	0.16 (dip)		4.93, 5.89 (5.4)	
Clinton, NC	0.006 (spray)	-	0	0.452, 0.462 (0.46)	NC500
(Covington)	-	0.18 (dip)	0	6.97, 5.55 (6.3)	
Fremont, OH	0.006 (spray)	-	0	0.531, 0.491 (0.51)	OH*502
(Beauregard)	-	0.16 (dip)	0	4.29, 4.79 (4.5)	
Weslaco, TX	0.006 (spray)	-	0	0.549, 0.526 (0.54)	TX501
(Beauregard)	-	0.16 (dip)	0	4.62, 4.61 (4.6)	

Animal feedstuffs

Table 18 Residues of thiabendazole on dry peas vines and hay from seed treatment trials conducted in the USA in 2013 Report: TK0180600

Region (Variety)	Application rate (kg ai/ton seed)	DAT (days)	Crop Part	Residue (mg/kg)	Trial
Ephrata, WA (Montex 4153)	0.8	71 71	Vines Hay	0.010, 0.022 (0.02) 0.064, 0.089 (0.08)	TK0180600-31
Parkdale, OR (Montex 4153)	0.8	56 59	Vines Hay	0.015, 0.024 (0.02) 0.056, 0.051 (0.05)	TK0180600-32
American Falls (Montex 4153)	0.8	64 70	Vines Hay	<0.01, <0.01 (<0.01) 0.015, <0.01 (0.01)	TK0180600-33 2013
Chubbuck, ID (Montex 4153)	0.8	64 69	Vines Hay	<0.01, <0.01 (<0.01) <0.01, <0.01 (<0.01)	TK0180600-34
Payette, ID (Montex 4153)	0.8	55 59	Vines Hay	0.013, <0.01 (0.01) 0.018, 0.056 (0.04)	TK0180600-35

Table 19 Residues of thiabendazole on cowpea (California Black Eyed #5) animal feed after seed treatment in the USA in 2013. Report: TK0180600

Region	Application rate (kg ai/ton seed)	DAT (days)	Crop Part	Residue (mg/kg)	Trial
Blackville, SC	0.8	46 50	Forage Hay	<0.01, <0.01 (<0.01) <0.01, <0.01 (<0.01)	TK0180600-36
Blackville, SC	0.8	70 75	Forage Hay	<0.01, <0.01 (<0.01) <0.01, <0.01 (<0.01)	TK0180600-37

Region	Application rate (kg ai/ton seed)	DAT (days)	Crop Part	Residue (mg/kg)	Trial
Hinton, OK	0.8	62 65	Forage Hay	<0.01, <0.01 (<0.01) <0.01, <0.01 (<0.01)	TK0180600-38

FATE OF RESIDUES DURING PROCESSING

Effects on the nature of the residues during processing

A study on the nature of residues in processed commodities was submitted to the Meeting (Adam, 1999). Individual aqueous solutions of [phenyl-U-^{14}C]-thiabendazole were prepared in sterile buffer solutions, and duplicate samples were incubated under different conditions and the recovered in Table 20. The actual concentrations of [phenyl-U-^{14}C]-thiabendazole was in average 5.3 mg/L. For each sample to be analysed the ^{14}C-activity was measured by LSC after the samples were taken, the pH of the solution measured at ambient temperature and thereafter, the samples neutralised to pH 7. Subsamples of the neutralised test solutions were directly analysed by HPLC and 2D-TLC for test substance and degradation products. HPLC and TLC analysis of the radioactivity in the neutralised, aqueous buffer solutions after incubation revealed only parent compound at all three pH-values tested. The results of the radioactivity recovered at each condition is also shown in Table 20.

Table 20 Hydrolytic conditions simulating processing and % of radioactive recovery for thiabendazole

Process represented	Temperature (°C)	Time (min)	pH	Radioactive recovery, thiabendazole (%)
Pasteurisation	90	20	4	103.5, 103.3 (103.4)
Baking, Brewing, Boiling	100	60	5	99.9, 102.5 (101.2)
Sterilisation	120	20	6	99.8, 98.9 (99.4)

Effects on the level of the residues during processing

Sweet potato

Samples from the field phase of post-harvest trial CA525 (dip application) were used for processing of sweet potato roots into flakes, chips, baked sweet potatoes and French fries (Jolly, 2018). Treated sweet potatoes were batch-tub washed for 5 minutes before submitted to processing.

Sweet potato flake: Sweet potatoes were batch steam-peeled for ~ 45 seconds, scrubbed and a sample of the steam-peeled sweet potatoes was analysed. The remaining were cut into slabs, which were spray-washed in water for ~ 30 seconds to remove free starch, pre-cooked at 70–77 °C for 20 minutes and cooled for about 20 minutes in water. The sweet potato slabs were steam-cooked at 94–100 °C for 30 minutes, mashed using a modified meat grinder, and the mash/puree analysed. An aliquot of the sweet potato mash was mixed with an emulsion of pre-weighed food additives and fed onto a drum dryer to dry into a thin sheet, which were fed into a hammer mill for uniform milling of the finished sweet potato flakes.

Sweet potato chip: Washed sweet potatoes were peeled, cut into thin slices (~ 0.16 cm) using a restaurant-style cutter/slicer and discharged into a tub of hot water to remove free starch. The slices were drained and fried in a restaurant-style deep fat fryer at about 165–191 °C for ~60 seconds. The fried sweet potato chips were drained, salted and analysed.

Baked sweet potato: Washed sweet potatoes were punctured with a fork or knife then placed in a preheated oven at 220 °C and baked for about 1 hour to reach an internal temperature of about 88–92 °C, allowed to cool and analysed.

Sweet potato fries: Fries were produced by first slicing washed, unpeeled sweet potatoes into strips (approx. 1 cm) using a French fry cutter, the strips were fried in a deep fat fryer for about 2.5 minutes at 180 °C, the fries were allowed to drain and cool and analysed.

Residues of thiabendazole in samples of sweet potato RAC roots prior to processing and after processing, and the processing factors are shown in Table 21.

Table 21 Processing study on sweet potato with thiabendazole

	Residues (mg/kg)	Processing factor
RAC roots before processing	3.76	-
Washed roots	0.989	0.26
Raw washed & peeled roots	0.124	0.03
Wet Peel	0.013	0.003
Baked washed with peel	1.06	0.28
Chips	0.092	0.02
Puree	0.060	0.02
Fries	0.437	0.12
Flakes	0.319	0.08

APPRAISAL

Thiabendazole, a benzimidazole fungicide, was first evaluated by JMPR in 1970, and the latest residue evaluation was conducted in 2006 (T, R).

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) established an ADI of 0–0.1 mg/kg and the 2006 JMPR established an ARfD of 0.3 mg/kg bw for women of childbearing age and of 1 mg/kg bw for the general population.

The residue definitions for thiabendazole for compliance with the MRL and dietary risk assessment for plant commodities: *thiabendazole.*

The residue definitions for thiabendazole for compliance with the MRL for animal commodities: *sum of thiabendazole and 5-hydroxythiabendazole.*

The residue definitions for thiabendazole for dietary risk assessment for animal commodities: *sum of thiabendazole, 5-hydroxythiabendazole and its sulfate conjugate*.

The compound was scheduled at the Fiftieth Session of the CCPR for the evaluation of additional uses by the 2019 Extra JMPR. Plant metabolism studies on orange (post-harvest) and maize (seed treatment), analytical methods and residue studies on mango, beans, peas and sweet potato, and processing studies were submitted to the Meeting.

Plant metabolism

[Phenyl-U-^{14}C]-thiabendazole was applied post-harvest to orange fruits in a single dose at 0.2 kg ai/hL prior to storage in the dark at 5 °C, and samples were analysed just after application, 8 and 16 weeks later. Radioactivity was extracted from the fruit surface with acetonitrile, and oranges separated into peel and flesh. Radioactivity in orange flesh was < 0.01 mg eq/kg (0.002–0.007 mg/kg eq) and was not further investigated. From 94 (day 0) to 73% (16 weeks) of TRR were recovered from the fruit surface. About 98% TRR in the orange peel on day 0 was thiabendazole (5.2 mg/kg), with residues dropping to 90%TRR after 16 weeks (3.7 mg/kg). Only minor metabolites of thiabendazole were observed in orange peel, arising via hydroxylation of the phenyl ring to produce 5-hydroxy-thiabendazole (~0.02 mg eq/kg), and elimination of the thiazole ring to produce benzimidazole (0.002 mg/kg at 8 weeks) and carboxylated benzimidazole (0.02 mg eq/kg at 8 weeks).

[Phenyl-U-^{14}C]-thiabendazole was applied to maize seed at 0.09 mg/seed. Treated maize was grown under glasshouse and plants were harvested at stages representing commercial forage, sweet corn and maturity. No residues were found in cobs and kernels. The TRRs of foliage from the sweet corn stage and maturity were 0.005 and 0.002 mg eq/kg, respectively. Only the foliage from the forage stage had TRR > 0.01 mg eq/kg (0.014 mg eq/kg), from which 55.5% remained unextracted (0.008 mg eq/kg). Extracted residues in forage were composed of multiple minor metabolites without the presence of thiabendazole. No further attempt was made to characterise the unextracted residue.

In summary, thiabendazole was the only relevant residue found in orange after post-harvest treatment and no thiabendazole related residues were found in maize commodities after seed treatment.

Methods of analysis

Additional methods of analysis and validation data for crop commodities were submitted to the Meeting. In general, samples are extracted with ethyl acetate, cleaned-up with cation exchange SPE and analysed by LC-MS/MS with a LOQ of 0.01 mg/kg. In another LC-MS/MS method, conjugates of thiabendazole or benzimidazole are extracted with ethyl acetate following addition of glucosidase enzyme to the aqueous phase (LOQ of 0.01 mg/kg). The efficiency of ethyl acetate extraction was confirmed with orange (whole fruit) treated post-harvest from the metabolism study. Additionaly, the QuEChERS method was validated for thiabendazole in crop commodities and for thiabendazole and 5-hydroxy thiabendazole in animal commodities, with a LOQ of 0.01 mg/kg in all cases.

Storage stability of residues under frozen conditions

Stability studies conducted with beans (dry seed), soya beans, spinach, barley and oranges showed that residues were stable under frozen conditions (-20 ºC) for at least 24 months.

Results of supervised residue trials on crops

Mango

Thiabendazole is registered for post-harvest use in a dip solution at a concentration of 0.24 kg ai/hL in Central American countries and 0.19 kg ai/hL in Brazil. In four trials conducted in Brazil according to central American GAP, residues were 2.4, 2.6, 3.4 and 4.5 mg/kg in the whole fruit and 0.01, 0.012, 0.023, and 0.027 (highest individual level of 0.030) mg/kg in the pulp.

The Meeting agreed that four trials were enough to make a recommendation for mango due to the lower variability of the residues in post-harvest treatment, using the mean + 4×SD approach.

The Meeting estimated a maximum residue level of 7 mg/kg (Po), a STMR of 0.0175 mg/kg and a HR of 0.030 mg/kg for thiabendazole in mango.

Succulent beans and peas subgroups

Thiabendazole is registered in the USA as a seed treatment in beans (succulent and dry, except soya bean) at 0.55 kg ai/tonne seed. The GAP for soya bean is 0.20 kg ai/tonne seed. In seven bean trials conducted in the USA approximating the GAP, residues in beans with pods were < 0.01 (6) mg/kg and residues in bean without the pods in one trial were < 0.01 mg/kg.

The GAP rate for peas (succulent and dry) in the USA is 0.33 kg ai/tonne seed. In nine trials conducted in peas at about 3–4 times the GAP rate, residues in the peas without the pods were < 0.01 (9) mg/kg.

As the trials conducted with beans at GAP and the trials conducted with peas at a rate higher than the GAP gave no quantified residues, and the GAP for soya bean is lower, the Meeting agreed that the residue data provided support a recommendation for the subgroups of succulent beans and peas.

The Meeting estimated a maximum residue level of 0.01(*) mg/kg, a STMR and HR of 0 mg/kg for thiabendazole for the subgroups of Beans with pods, Peas with pods, Succulent beans without pods and Succulent peas without pods

Dry beans and peas, subgroups

Thiabendazole is registered in the USA as a seed treatment in beans (succulent and dry, except soya bean) at 0.55 kg ai/tonne seed. The GAP for soya bean is 0.20 kg ai/tonne seed. In nine trials conducted approximating the GAP in the USA, residues in dry beans were < 0.01 (9) mg/kg.

The GAP rate for peas (succulent and dry) in the USA is 0.33 kg ai/tonne seed. In 10 trials conducted with peas using at least 2.4 times the GAP rate, residues in dry peas were < 0.01 (5) and < 0.05 (5) mg/kg.

As the trials conducted with beans at GAP and the trials conducted with peas at a higher rate than the GAP gave no quantified residues, and the GAP for soya bean is lower, the Meeting agreed that the residue data provided support a recommendation for the subgroups of dry beans and peas.

The Meeting estimated a maximum residue level of 0.01(*) mg/kg and a STMR of 0 mg/kg for thiabendazole for the subgroups of Dry beans and Dry peas.

Sweet potato

Thiabendazole is registered in the USA as post-harvest dip in a 0.16 kg ai/hL solution or spray (on a conveyor belt) at 0.006 kg ai/tonne.

In seven trials conducted according to the spray GAP, residues were 0.21, 0.26, 0.38, 0.46, 0.51, 0.54 and 1.2 mg/kg.

In eight trials conducted according to the dip GAP, residues were 2.7, 4.4, 4.5, 4.6, 4.8, 5.4, 5.5, and 6.3 (highest individual level of 6.97) mg/kg.

Based on the dip trials, which gives the highest residues, and on the mean + (4×SD) approach, the Meeting estimated a maximum residue level of 9 mg/kg (Po), a STMR of 4.7 mg/kg and a HR of 6.97 mg/kg for thiabendazole in sweet potato.

Animal feedstuffs

The GAP rate for peas (succulent and dry) in USA is 0.33 kg ai/tonne seed. In the trials conducted with pea in the USA at 2.4 times the GAP, residues ranged from < 0.01 to 0.02 mg/kg in the vines and from < 0.01 to 0.08 mg/kg in the hay. In three trials conducted with cowpea beans at 1.4 times the USA GAP for beans, residues in vines and hay were < 0.01 mg/kg.

As no trials were conducted according to GAP, no recommendations were made for thiabendazole in legume animal feeds.

Fate of residues during processing

In a study to simulate the hydrolysis of thiabendazole under different temperature/time and pH conditions, 99-103% of the applied radioactivity was recovered.

Sweet potatoes treated post-harvest with a dipping solution were processed to flake, chip, baked and fries. The processing factors and estimated STMRs for the processed commodities are shown below.

Crop	PF	STMR/STMR-P, mg/kg	HR/HR-P, mg/kg
Raw sweet potato	-	4.7	6.97
Baked washed with peel	0.28	1.3	1.95
Chips	0.02	0.094	0.139
Puree	0.02	0.094	0.139
Fries	0.12	0.564	0.836
Flakes	0.08	0.376	0.558

Residues in animal commodities

The estimations conducted by the present Meeting do not impact the previous calcutated dietary burden of thiabendazole and do not affect the recommendations made by the JMPR for animal commodities

RECOMMENDATIONS

On the basis of the data obtained 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 the residue for compliance with the MRL and dietary risk assessment for plant commodities: *thiabendazole*

Definition of the residue for compliance with the MRL for animal commodities: *sum of thiabendazole and 5-hydroxythiabendazole*

Definition of the residue for dietary risk assessment for animal commodities: *sum of thiabendazole, 5-hydroxythiabendazole and its sulfate conjugate*.

CCN	Commodity	Recommended Maximun residue level (mg/kg)		STMR or STMR-P (mg/kg)	HR or HR-P (mg/kg)
		New	Previous		
FI 0345	Mango	7 (Po)	5 (Po)	0.0175	0.030
VP 2060	Beans with pods	0.01*		0	0
VP 2061	Peas with pods	0.01*		0	0
VP 2062	Succulent beans without pods	0.01*		0	0
VP 2063	Succulent peas without pods	0.01*		0	0
VD 2065	Dry beans	0.01*		0	
VD 2066	Dry peas	0.01*		0	
VR 0508	Sweet potato	9 (Po)		4.7	6.97
	Sweet potato Baked washed with peel			1.3	1.95
	Sweet potato Chips			0.094	0.139
	Sweet potato Puree			0.094	0.139
	Sweet potato Fries			0.564	0.836
	Sweet potato Flakes			0.376	0.558

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The ADI for thiabendazole is 0–0.1 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for thiabendazole were estimated for the 17 GEMS/Food Consumptiion Cluster diets using the STMR or STMR-P values estimated by the JMPR. The results are shown in Annex 3 of the 2019 Extra JMPR Report.

The IEDIs accounted for 2 to 10% of the maximum ADI. The Meeting concluded that the long-term dietary exposure to residues of thiabendazole from uses considered by the JMPR is unlikely to present a public health concern.

Acute dietary exposure

The ARfDs for thiabendazole is 1 mg/kg bw for the general population and 0.3 mg/kg bw for women of child-bearing age. The International Estimate of Short Term Intakes (IESTIs) for thiabendazole were calculated for the food commodities for which HRs/HR-Ps or STMRs/STMR-Ps were estimated by the present Meeting and for which consumption data were available. The results are shown in Annex 4 of the 2019 Extra JMPR Report.

The IESTIs were 0–20% (children) and 0–7% (general population) of the ARfD for the general population; and from 0–9% of the ARfD for women of child bearing age. The Meeting concluded that the acute dietary exposure to residues of thiabendazole from uses considered by the present Meeting is unlikely to present a public health concern.

REFERENCES

Study	Author(s)	Year	Study Title
TK0023758	Piskorski R	2012	Thiabendazole - Metabolism in Oranges during Post Harvest Storage. Report Number 115 01 191. Innovative Environmental Services (IES) Ltd, Benkenstrasse 260, CH-4108 Witterswil, Switzerland. Study Dates: Feb. 2011 – March 2012. Syngenta report No. TK0023758. Syngenta File No. 10466C_10086. GLP, unpublished
25080	MacKinnon I.M.R	2005	The Metabolism of [^{14}C]-Thiabendazole Applied as a Seed Dressing in Maize. Inveresk, UK. Study Dates: September 2004 - June 2005. Inveresk Study Number 805464. Syngenta File No. MK360/0921. GLP, unpublished
GRM040.01A	McLean N., Nelson S.	2008	Thiabendazole: Residue Method for the Determination of Thiabendazole and Benzimidazole in Crops. Syngenta Method GRM040.01A. Syngenta File No. MK360_50008. non-GLP, unpublished
S11-00514-INT	Ellis C.	2012	Thiabendazole - Residue Study on Rotational Crops in the United Kingdom in 2011 and 2012. Syngenta report No. S11-00514-INT. Syngenta File No. 10466C_10090. GLP, unpublished
TK0180600	Oakes T.L.	2015	Thiabendazole 340-F (A10466G) - Magnitude of the residues in or on representative crops of Legume vegetables, Crop Group 6 (Except Soybeans) and Crop Group 7 USA 2013. Syngenta report No. TK0180600. Syngenta File No. A10466G_50059. GLP, unpublished
11859	Jolly C.	2018	Thiabendazole: Magnitude of the residue on sweet potato (post-harvest) IR-4 Report No. 11859. Syngenta File No. MK360_50995. GLP, unpublished
GRM046.04A	Crook S.	2012	Thiabendazole - Analytical Method GRM046.04A for the Determination of Thiabendazole (MK360) in Crops. Analytical Method No. GRM046.04A Syngenta File No.: MK360_11457. GLP, unpublished
S14-00940	Watson G.	2014	Thiabendazole – Validation of Analytical Method GRM046.04A for the Determination of Thiabendazole in Plant Matrices by LC-MS/MS. Syngenta Report No. S14-00940. Syngenta File No. MK360_11640. GLP, unpublished
LBS17004	Becker, G.	2018	A10466 - Magnitude of the residues of thiabendazole in mango fruits - , 2017-18. Syngenta Report No. LBS17004. Syngenta File No. A10466C_10727 GLP, unpublished
B 2445 G	Class T., Bacher R.	2012	Thiabendazole - Validation of the QuEChERS Method for the Determination of Residues of Thiabendazole in Crop and Animal Matrices by LC-MS/MS - Validation Report. Syngenta report No. B 2445 G. Syngenta File No. K360_11470. GLP, unpublished
S11-04024	Amic S.	2012	Thiabendazole - Independent Laboratory Validation of the QuEChERS Method for the Determination of Thiabendazole in Crop and Animal Matrices by LC-MS/MS. Syngenta report No. S11-04024. Syngenta File No. MK360_11484. GLP, unpublished
S14-00723	Watson G.	2014	Thiabendazole - Validation of the QuEChERS Analytical Method for Determination of Residues of Thiabendazole and its 5-hydroythiabendazole Metabolite in Animal Matrices. Syngenta report N. S14-00723. Syngenta File No.: MK360_11618. GLP, unpublished
S15-05865	Amic S.	2016	Thiabendazole – Independent Laboratory Validation of the QuEChERS Method for Determination of Residues of Thiabendazole and it's 5-Hydroythiabendazole Metabolite in Animal Matrices by LC-MS/MS. Syngenta report No. S15-05865. Syngenta File No.: MK360_11369. GLP, unpublished
66879	Mason B.J.	2014	Thiabendazole – Stability of Thiabendazole and Benzimidazole Residues in Representative Crop Raw Agricultural Commodities Under Freezer Storage Conditions. IR-4 PR No. 66879. Syngenta File No MK360_50594. GLP, unpublished
LBS17004	Becker, G.	2018	A10466 - Magnitude of the residues of thiabendazole in mango fruits - , 2017-18.Syngenta Report No. LBS17004. Syngenta File No. A10466C_10727 GLP, unpublished

Study	Author(s)	Year	Study Title
LBS17007	Becker, G.	2018	A10466 - Magnitude of the residues of thiabendazole in mango fruits - , 2017-18. Syngenta Report No. LBS17007. Syngenta File No. A10466C_10728. GLP, unpublished
06532	Thompson D.C.	2000	Thiabendazole: Magnitude of Residue on Pea (Dry). Syngenta Report No. 06532. Syngenta File No. 403940. GLP, unpublished
TK0180600	Oakes T.L.	2015	Thiabendazole 340-F (A10466G) - Magnitude of the residues in or on representative crops of Legume vegetables, Crop Group 6 (Except Soybeans) and Crop Group 7 USA 2013. Syngenta Report No. TK0180600. Syngenta File No. A10466G_50059. GLP, unpublished
11859	Jolly C.	2018	Thiabendazole: Magnitude of the residue on sweet potato (post-harvest). IR-4 Report No. 11859. Syngenta File No.MK360_50995. GLP, unpublished
06532	Adam D.	1999	Hydrolysis of ^{14}C-Labelled MK 360 / CGA 28020 under Processing Conditions; Syngenta Report No. 99DA03; Syngenta File No. MK360/0534
11859	Jolly C.	2018	Thiabendazole: Magnitude of the residue on sweet potato (post-harvest), IR-4 Report No. 11859. Syngenta File No. MK360_50995, GLP, unpublished