DITHIOCARBAMATES (105) - MANCOZEB (050)

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EXPLANATION

Mancozeb was evaluated in 1993 in the CCPR periodic review programme. Since then, in 2012, the Meeting evaluated residue data on mancozeb and maneb, however, made no recommendation for MRLs. Currently, a number of MRLs for dithiocarbamates are established based on the residue data derived from use of mancozeb, maneb, metiram, thiram, ziram and propineb.

The 1993 JMPR evaluated several dithiocarbamate fungicides for toxicology and residues when the Meeting established an ADI of 0–0.03 mg/kg bw (group or in any combination) for ethylene-bis-dithiocarbamates (EBDCs: mancozeb, maneb, metiram and zineb). In addition, for their metabolite ethylenethiourea (ETU), the Meeting established an ADI of 0–0.004 mg/kg bw. At present, there are no ARfDs established by the JMPR for ethylene-bis-dithiocarbamates or ETU.

The mancozeb residue is defined as total dithiocarbamates, determined as CS_2, evolved during acid digestion and expressed as mg CS_2/kg, for compliance with MRLs in plant and animal commodities. Dithiocarbamate residues are not fat soluble.

Dithiocarbamates-Mancozeb was listed by the Forty-fifth Session of the CCPR (2013) for the evaluation of additional MRL in 2014 JMPR. Further, it was requested by the Session that 2014 JMPR evaluate monitoring data on spices produced by India for additional MRLs. The Meeting received supervised residue trial data from Thailand (chili pepper) and the Republic of Korea (ginseng and the processed products). From India, monitoring data on spices (cardamom, coriander, cumin, fennel and black pepper) were submitted.

RESIDUE ANALYSIS

Analytical methods

The analytical method used for determination of dithiocarbamates in chili pepper was based on the Dutch manual of analytical methods (Ministry of Welfare, Health and Cultural Affairs, 1988), which was reviewed in 1995 by JMPR: dithiocarbamates are converted to CS_2 by treatment with hydrochloric acid in the presence of stannous chloride. The CS_2 in the head-space is determined by GC with either ECD or FPD. For analysis of dithiocarbamates in chili pepper, ECD was used. The limit of quantification was 0.05 mg/kg as CS_2. Recovery tests were performed at five levels of 0.05–5.0 mg CS_2/kg (n=3 at each level). The average recoveries were in the range of 71–101%. In procedural recovery tests conducted at a fortified level of 0.1 mg CS_2/kg, the average recoveries (n=3) were 81–100% with an acceptable RSDs. ETU residue was not analysed.

Information on an analytical method ABY0064 with a validation study was submitted, for the analysis of mancozeb in ginseng and the processed products. This method is based on the direct determination, by HPLC-MS/MS, of a derivatized EBDC (EBDC-dimethyl produced by *S*-methylation). In the mass analysis, individual EBDCs are distinguished using compound-specific transition ions.

The validation study was performed with orange, olive and their products. An aliquot of extracting solvent and iodomethane were added to sample (2 g). The extracting solvent was a mixture of disodium EDTA (ethylenediaminetetraacetic acid), NaOH, L-cysteine, water and methanol. The sample extract was cleaned up using C_{18} SPE cartridge with an eluting solvent of water:methanol (40:60, v:v). Residues were quantified with by HPLC-MS/MS (MRM *m*/*z* 241 > 134). The responses of the HPLC/MS/MS systems were linear over the range 0.1 to 5 ng/mL (r^2, > 0.99). At the fortification levels of 0.01 and 0.1 mg/kg of mancozeb, individual recoveries were in the range of 70% to 108% (RSD, < 15%). The limit of quantification was 0.01 mg/kg in all matrices (Table 1).

In the validation study, additionally, a method for ETU analysis was tested for its performance. The method involved extraction with dichloromethane, clean-up by liquid-liquid partition with hexane and quantification by HPLC-MS/MS (MRM *m*/*z* 103 > 44 for ETU; MRM *m*/*z* 107 > 48 for internal standard, ETU D4). The linearity was over the range 2.5 to 100 ng/mL. At the fortification levels of 0.01 and 0.1 mg/kg of ETU, individual recoveries were in the range of 79% and 109% (CV, < 12%). The limit of quantification was 0.01 mg/kg in the all matrices (Table 2).

The control sample extracts from all matrices (oranges, olives and their by-products) were fortified with mancozeb (as the methylated derivative) or ETU, the residues in the final extracts were stable for seven days stored at approximately -20 °C. The storage period was sufficient to cover the maximum storage period of the extracts from this validation study.

Table 1 Recoveries of mancozeb in orange, olive and the processed products using the method ABY0064

Matrix	Fortification, mg/kg	No.	Range of recoveries, %	Mean recovery, %	CV, %
Orange pulp	0.01	5	73-98	82	12.5
	0.1	5	71-76	73	2.6
Orange peel	0.01	5	96-101	97	2.3
	0.1	5	96-104	101	3.6
Orange juice	0.01	5	85-95	90	4.4
	0.1	5	75-78	77	2.0
Orange oil	0.01	5	97-103	94	14.7
	0.1	5	98-108	101	4.4
Orange wet pomace	0.01	5	80-100	90	7.9
	0.1	5	80-93	88	5.9
Orange dry pomace	0.01	5	70-84	74	7.8
	0.1	5	71-81	76	6.8
Olive oil	0.01	5	72-85	78	7.0
	0.1	5	70-86	78	9.6

Mancozeb was not detected (< 0.01 mg/kg) in control samples.

Table 2 Recoveries of ETU from oranges, olives and the processed by-products

Matrix	Fortification, mg/kg	No.	Range of recoveries, %	Mean recovery, %	CV, %
Orange whole fruit	0.01	5	79-98	88	9.5
	0.1	5	94-106	100	4.4
Orange pulp	0.01	5	94-107	103	5.0
	0.1	5	97-107	102	3.7
Orange peel	0.01	5	88-104	97	7.0
	0.1	5	89-95	92	2.4
Orange juice	0.01	5	80-103	89	12.4
	0.1	5	96-109	104	5.0
Orange oil	0.01	5	88-93	89	5.4
	0.1	5	80-92	87	5.4
Orange wet pomace	0.01	5	91-100	96	3.5
	0.1	5	99-104	102	2.3
Orange dry pomace	0.01	5	90-109	98	7.7
	0.1	5	100-106	103	2.5
Olive whole fruit	0.01	5	79-109	98	12.3
	0.1	5	95-108	103	5.4

Matrix	Fortification, mg/kg	No.	Range of recoveries, %	Mean recovery, %	CV, %
Olive oil	0.01	5	85-94	91	4.7
	0.1	5	89-98	94	3.7

ETU was not detected (< 0.01 mg/kg) in control samples.

Analyses of mancozeb and ETU in ginseng and the processed products were conducted by the analytical methods mentioned above, except minor modifications in certain trials, e.g., use of HLP SPE instead of C18 SPE or without involvement of internal standard in ETU analysis. LOQ of mancozeb in fresh ginseng by HPLC-MS/MS was 0.01 mg/kg and 0.02 mg/kg for the other matrices (dried ginseng, red ginseng, water extract of dried ginseng and water extract of red ginseng). For ETU, the LOQs were 0.01mg/kg or 0.02 mg/kg in fresh ginseng and 0.02 mg/kg in dried and red ginseng. In the ginseng matrices (fresh and processed), individual procedural recoveries (n=3 or 5) for mancozeb and ETU were between 70% and 120% (RSD, <20%) at the various fortification levels (0.01–1.0 mg/kg in mancozeb; 0.02–1.0 mg/kg in ETU).

In the analysis of dithiocarbamates in spices employed in monitoring, spectrometry was used. The samples (10–20 g) were hydrolysed with hydrochloric acid and stannous chloride solution at elevated temperature, and the evolved carbon disulphide (CS_2) passed through two gas washing tubes in series containing lead acetate and sodium hydroxide solutions and an absorption tube containing an ethanolic solution of cupric acetate and diethanol amine. Formed two cupric complexes of N,N-bis (2-hydroxyethly) dithiocarbamic acid were measured by spectrometry at 453 nm (Kepple G.E. J AOAC 54, 528-532, 1971). LOQs of dithiocarbamates in spices (cardamom, coriander, cumin, fennel and pepper) were 0.1 mg CS_2/kg. At fortification levels of 0.1–1.0 mg CS_2/kg, recoveries were 90–110% in cumin, coriander and fennel and 88-107% in cardamom and black pepper.

Stability of residues in stored analytical samples

In ginseng trials, fortified control samples were concurrently treated with the field trial samples during storage and analysis. The ginseng samples (fresh and processed) fortified with mancozeb and ETU were stored together with the field trial samples at -20 °C or below until analysis. Recoveries of mancozeb in fresh ginseng were 81–92% (0.1 mg/kg, n=5) at 56 days or 86–94% (0.1–0.5 mg/kg, n=6) at 103 days. In the processed ginseng, recoveries of mancozeb were 81–117% (0.2 mg/kg, n=20 for all processed types) at 11–56 days or 78–94% (0.2–1.0 mg/kg, n=6 for dried ginseng) at 100 days. For ETU, the recoveries in fresh ginseng were 84–92% (0.2 mg/kg, n=5) at 71 days or 85–96% (0.1–0.5 mg/kg, n=6) at 103 days; in the processed, 83–96% (0.2 mg/kg, n=10 for dried and red ginseng) at 55–62 days or 90–96% (0.2–1.0 mg/kg, n=6 for dried ginseng) at 100 days. The days refer to mean storage days of fortified samples and covered the actual storage days of the samples, except for two cases in fresh ginseng, analysis of mancozeb (max. actual storage 76 days over test 56 days,) and analysis of ETU (max. actual storage 92 days over test 71 days). Based on the results, it is considered that the residues were stable during the study period.

As the analysis of mancozeb residues in chili peppers was undertaken on the day of harvest, storage stability tests were not conducted.

USE PATTERN

Mancozeb is a protective fungicide effective against a wide range of foliar fungal diseases. The registered uses on ginseng, chili pepper, cumin and black pepper are summarized in Table 3.

Table 3 Registered uses of mancozeb submitted for evaluation

Crop	Country	Formulation	Application					PHI, days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hl	No.	Interval days	
Chili pepper	Thailand	80% WP	Foliar spraying	2.0[a]	0.4	3	5	7
Ginseng	Rep. of Korea	75% WP	Foliar spraying	2.4[b]	0.12	5	10	45

Crop	Country	Formulation	Application					PHI, days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hl	No.	Interval days	
Cumin	India	75% WP	Foliar spraying		0.30			1
Pepper, black	India	64% WP [c]	Foliar spraying		0.09			21
Pepper, black	India	64% WP [c]	Soil drenching		0.036			21

WP: Wettable powder
[a] The spray volume of 500 L/ha is recommended by an authority.
[b] Calculated value based on a spray volume of 2,000 L/ha from agricultural practices
[c] Mix formulation with metalaxyl 8%

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The Meeting received information on supervised field trials for ginseng and chili pepper.

Crop group	Commodity	Table No.
Fruiting vegetables, other than Cucurbits	Peppers, Chili	4
Root and tuber vegetables	Ginseng	5

Submitted residue trials were not performed in compliance with GLP principles, but conducted under the supervision of study director.

In handling replicate samples, the mean value was calculated. From trials carried out side-by-side, the higher residue was chosen.

Fruiting vegetables, other than Cucurbits

Peppers, Chili

Six residue trials were conducted in Thailand in 2005-2008. Mancozeb WP 80% was applied to chili pepper as a foliar application three times at a spray concentration of 0.32 kg ai/hL with 6-8 day intervals. Spray volumes were between 500 L/ha and 643 L/ha. After the last application, mature fruits of 1-1.5 kg were collected from each plot of three plots at 0, 1, 3, 5, 7, 9, 12 and 15 days.

Whole fruit sample was analysed on the harvest day. Mancozeb residue was determined as CS_2. In control samples, the residue concentrations were less than < 0.05 mg/kg as CS_2.

Table 4 Mancozeb residues in chili pepper from supervised trials performed in Thailand

Location Year (Variety)	Application					DAT, days	Residue [a], mg/kg as CS_2	Report No.
	kg ai/ha	n	Interval days	L/ha	kg ai/hL			
GAP	2.0	3	5	500	0.40	7		
Kanchanaburi 2008 (n.r.)	1.6	3	7-8	504	0.32	0	4.0	MA-CH-01
						1	3.4	
						3	3.0	
						5	2.7	
						7	1.7	
						9	1.4	
						12	1.2	
						15	0.79	
Ratchaburi 2008 (n.r.)	2.0	3	6-7	637	0.32	0	5.6	MA-CH-02
						1	4.8	
						3	2.8	
						5	1.6	
						7	1.2	

Location Year (Variety)	Application					DAT, days	Residue [a], mg/kg as CS_2	Report No.
	kg ai/ha	n	Interval days	L/ha	kg ai/hL			
						9	1.2	
						12	1.0	
						15	0.46	
Ratchaburi 2005 (n.r.)	2.0	3	7	637	0.32	0	2.3	MA-CH-03
						1	1.6	
						3	1.3	
						5	1.0	
						7	0.80	
						9	0.69	
						12	0.21	
						15	0.083	
Kanchanaburi 2005 (n.r.)	2.0	3	7	635	0.32	0	3.2	MA-CH-04
						1	2.3	
						3	1.4	
						5	1.1	
						7	0.75	
						9	0.49	
						12	0.21	
						15	0.13	
Ratchaburi 2007 (n.r.)	2.1	3	7	643	0.32	0	1.1	CY-CH-05
						1	0.88	
						3	0.68	
						5	0.31	
						7	0.31	
						9	0.20	
						12	0.28	
						15	0.22	
Rachaburi 2007 (n.r.)	2.0	3	7-8	614	0.32	0	0.61	
						1	1.5	
						3	0.79	
						5	0.70	
						7	0.48	
						9	0.20	
						12	0.23	
						15	0.17	

Chili pepper: Capsicum annuum Linn. var. *acuminatum* Fingerh
WP 80% formulation was used.
Portion analysed: whole fruit without stem
[a] The residue value is an average of analytical results for three harvested samples.

Root and tuber vegetables

Ginseng

Four residue trials were conducted in the Republic of Korea in 2013. Mancozeb WP 75% formulation was applied five times (10 day intervals) to four-year old ginseng as a foliar application. Three trials of which were decline trials. The concentration in spray solution was 0.12 kg ai/hL and a spray volume of 2,000 L/ha was used. The calculated dose rate of each application was 12-13 kg ai/ha. Ginseng was collected at 45 days (0, 25, 35, 45, 55 days in the decline trials) after the last application. Foliage and stem were removed before shipment to an analytical laboratory. After removing the soil particles on ginseng roots by washing with tap water, it was blended and stored at -20℃or -60℃until analysis. The mass of sample was more than 2 kg.

The residues from application of mancozeb formulation were analysed for both mancozeb and ETU. In control samples, no residue was not detected (< LQO). Ginseng processing studies were also conducted. These are described in the following section.

Table 5 Mancozeb and ETU residues in ginseng from supervised trials performed in the Republic of Korea

Location Year (Variety)[a]	Application[b]				DAT, days	Residue[c], mg/kg		Study No. or ID
	kg ai/ha	n	Interval days	kg ai/hL		Mancozeb	ETU	
GAP		5	10	0.12	45			
Yeongju 2013	2.4-2.6	5	10	0.12	45	0.05	0.01	MFDS13162FS009
Geumsan 2013	2.4-2.5	5	10	0.12	0[e]	0.19	0.04	MFDS13162FS009
					25	0.09	0.04	
					35	0.07	0.08	
					45	0.07	0.04	
					55	0.11	0.04	
Sunheung[d] 2013	2.5	5	10	0.12	0[e]	0.03	< 0.01	CRI-2013-C-1
					25	0.02	< 0.01	
					35	0.05	< 0.01	
					45[f]	0.02	< 0.01	
					45	0.02	< 0.01	
					55	0.02	< 0.01	
Punggi[d] 2013CRI-2013-C-1	2.5	5	10	0.12	0[e]	0.03	< 0.01	CRI-2013-C-1
					25	0.02	< 0.01	
					35	0.03	< 0.01	
					45[e,f]	0.05	< 0.01	
					45	0.03	< 0.01	
					55	0.02	< 0.01	

[a] *Panax ginseng* C.A. Mey (Violet-stem variant)
[b] WP 75% formulation was used.
[C] The residue value is an average of analytical results for three harvested samples.
[d] The two trials were not independent. These were conducted in an adjacent location of 8 km distance and by the same application method and on the same days.
[e] In the trial conducted in Sunheung, analysis of control sample was performed only at 0 day; while for trial conducted in Punggi only at 0 and 45 days.
[f] At 45 days, duplicate samples were collected.

Spices

Spices (cardamom, coriander, cumin, fennel and black pepper) were collected from the retail outlets during 2009–2014 in India. About 20–500 g of sample of each spice was collected and out of which10–20 g of homogenized sample was taken for the analysis.

Table 6 Dithiocarbamate residues in spices monitored in India during 2009-2014

Spice		No. of samples	Residues (mg CS_2/kg)		
Group	Name		Median	Max	Detections
Seed	Cumin	384	3.6	17	0.11, 0.12, 0.14, 0.15, 0.26, 0.27, 0.29 (2), 0.31, 0.36, 0.41, 0.46, 0.53, 0.54, 0.55, 0.60 (2), 0.61, 0.63, 0.64, 0.65 (2), 0.69, 0.71, 0.73, 0.74 0.75, 0.76 (2), 0.78 (2), 0.79, 0.81(2), 0.82(2), 0.83 (2), 0.85, 0.88, 0.90 (2), 0.92, 0.93, 0.94, 0.97 (2), 0.98, 1.00, 1.02, 1.04 (2), 1.05, 1.07 (2), 1.08, 1.11, 1.14, 1.19, 1.20, 1.23, 1.25, 1.27, 1.28, 1.30, 1.33, 1.35, 1.37, 1.41, 1.43 1.45, 1.48, 1.50 (2), 1.51, 1.53, 1.57, 1.60, 1.69, 1.70 (2), 1.71, 1.79, 1.80, 1.83, 1.87, 1.92, 1.96, 1.97 (2), 1.98, 2.01 (2), 2.02, 2.05, 2.06, 2.09, 2.10, 2.13 (2), 2.15, 2.16,

Spice		No. of samples	Residues (mg CS_2/kg)		
Group	Name		Median	Max	Detections
					2.20 (2), 2.23, 2.35, 2.36, 2.39, 2.40, 2.42 (3), 2.44 (2), 2.47, 2.55, 2.62, 2.66 (2), 2.67 (4), 2.70, 2.72, 2.73, 2.74, 2.76 (3), 2.79, 2.80, 2.88 (4), 2.89, 2.90 (3), 2.93 (2), 2.94, 2.95, 2.99 (2), 3.00, 3.01, 3.02, 3.04 (3), 3.07, 3.09, 3.10 (2), 3.14, 3.18, 3.20 (2), 3.23, 3.29, 3.30 (2), 3.32 (3), 3.33 (2), 3.36 (4), 3.40 (4), 3.42, 3.44, 3.47, 3.49 (2), 3.50 (3), 3.52, 3.55, 3.59, 3.60 (2), 3.61, 3.62, 3.67, 3.68, 3.73, 3.80 (3), 3.82, 3.84, 3.89, 3.92, 3.98, 4.01, 4.03, 4.10 (2), 4.13 (2), 4.16, 4.20, 4.34, 4.36, 4.38, 4.48, 4.63, 4.64, 4.67, 4.68, 4.75, 4.80 (3), 4.85, 4.90, 4.91, 5.00, 5.09, 5.10, 5.11, 5.15, 5.20 (2), 5.22, 5.30, 5.38, 5.40 (2), 5.56, 5.60 (3), 5.62, 5.70 (2), 5.72, 5.78, 5.80, 6.01 (2), 6.05, 6.07, 6.10 (2), 6.11, 6.14, 6.16, 6.20 (6), 6.27, 6.30 (4), 6.32, 6.38 (2), 6.40 (2), 6.41, 6.43, 6.44, 6.50 (7), 6.60 (2), 6.65 (4), 6.70, 6.80 (3), 6.82, 6.84, 6.88, 6.90 (3), 6.91, 6.94, 6.96, 7.04, 7.10 (3), 7.20 (10), 7.30 (2), 7.31 (2), 7.40 (4), 7.50 (2), 7.59 (2), 7.60 (5), 7.70, 7.77, 7.84, 7.90 (2), 8.01, 8.03, 8.10, 8.13, 8.20 (3), 8.30 (2), 8.40 (3), 8.41, 8.57, 8.60 (2), 8.70 (2), 8.90 (3), 9.04, 9.10, 9.28, 9.35, 9.39, 9.40 (2), 9.43 (2), 9.88 (2), 9.98, 10.20, 10.69 (2), 11.38, 11.44, 12.53, 13.17, 13.32, 14.54, 15.47, 16.88, 17.20
Fruit or berry	Cardamom	1,037	< 0.1	< 0.1	0
Seeds	Coriander	248	< 0.1	0.4	0.4
Fruit or berry	Black pepper	272	< 0.1	< 0.1	0
Seeds	Fennel	286	2.0	2.8	1.06, 2.01, 2.83

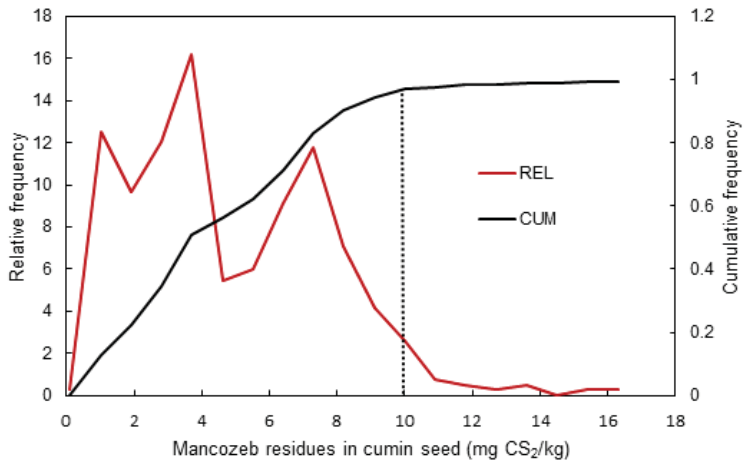

Figure 1 Distribution of mancozeb residues in cumin seed (n=383)

Dotted line indicates that the residue value (10 mg CS_2/kg) covers at least 99th percentile of residues.

FATE OF RESIDUES IN STORAGE AND PROCESSING

In processing

The Meeting received information on the fate of mancozeb residues during the processing of ginseng.

Ginseng

Four-year old ginseng cultivated under shaded conditions was treated five times with a 75% WP formulation at a spray concentration of 0.12 kg ai/hL (12–13 kg ai/ha per application) with 10 day treatment intervals. The fresh ginseng was collected 45 days or decline days (0, 25, 35, 45, and 55 days) after the last application. The harvested ginseng was treated with tap water to remove the soil particles and then dried.

To produce dried ginseng, the washed fresh ginseng was air-dried at 60 °C. Red ginseng was prepared by steaming fresh ginseng for three hours at 98 °C and then by air-drying at 65 °C and further drying under the sunlight. The dried or red ginseng were cut and extracted three times by refluxing in water at 85 °C. The extract was concentrated to 72° Brix. Dried ginseng, red ginseng and the water extracts were packed in inert plastic bottles and stored at -20 °C until analysis.

Water contents in fresh ginseng, dried ginseng, red ginseng, water extract of dried ginseng and water extract of red ginseng were 71%, 8%, 9%, 47% and 52%, respectively.

Table 7 Mancozeb and ETU residues in processing ginseng products

Location Year (Variety)	Application, WP 75%			PHI, days	Sample analysed	Residues, mg/kg		Pf		Study No. or ID
						Mancozeb	ETU	Mancozeb	ETU	
	kg ai/ha	n	kg ai/hL							
GAP		5	0.12	45						
Yeongju 2013	2.4-2.6	5	0.12	45	Fresh ginseng	0.05	0.01			
					Dried ginseng	0.14	0.05	2.8	1.75	MFDS1316 2FS009
					Red ginseng	0.08	0.12	1.6	4.2	
					Water extract of dried ginseng	< 0.02	n.a.	< 0.4		
					Water extract of red ginseng	< 0.02	n.a.	< 0.4		
Sunheung 2013	2.5	5	0.12	0	Fresh ginseng	0.03	< 0.01			
					Dried ginseng	0.04	< 0.02	1.3		CRI-2013-C-1
				25	Fresh ginseng	0.02	< 0.01			
					Dried ginseng	0.04	< 0.02	2.0		
				35	Fresh ginseng	0.05	< 0.01			
					Dried ginseng	0.06	< 0.02	1.2		
				45	Fresh ginseng	0.02	< 0.01			
					Dried ginseng	0.04, 0.04	< 0.02	2.0		
				55	Fresh ginseng	0.02	< 0.01			
					Dried ginseng	0.04	< 0.02	2.0		
Punggi 2013	2.5	5	0.12	0	Fresh ginseng	0.03	< 0.01			CRI-2013-C-1
					Dried ginseng	0.04	< 0.02	1.3		
				25	Fresh ginseng	0.02	< 0.01			
					Dried ginseng	< 0.02	< 0.02	<1.0		
				35	Fresh ginseng	0.03	< 0.01			
					Dried ginseng	0.04	< 0.02	1.3		
				45	Fresh ginseng	0.04	< 0.01			
					Dried ginseng	0.04, 0.07	< 0.02	1.4		
				55	Fresh ginseng	0.02	< 0.01			
					Dried ginseng	0.04	< 0.02	2.0		

Processing studies were performed once in the Yeongj location and three times in Sunheung and Punngi location each. Pre-processing samples were not analysed. Residue values for fresh ginseng were taken from field trial data.

n.a.: not analysed
Ginseng variety: Panax ginseng C.A. Mey (Violet-stem variant)
Processing factors were calculated:
For mancozeb, the concentration of mancozeb in dried ginseng was divided by the concentration of mancozeb in fresh ginseng.
For ETU, the concentration of ETU in dried ginseng was divided by the sum of ETU and mancozeb (expressed as ETU equivalents by multiplying 0.378 of conversion factor) in fresh ginseng in order to account for mancozeb as a potential source of ETU during processing.

Table 8 Summary of processing factors for mancozeb in ginseng (RAC)

Processed commodity	Calculated processing factors		Pf, best estimate	
	Mancozeb	ETU	Mancozeb	ETU
Dried ginseng	< 1.0, 1.2, 1.3, 1.3, 1.3, 1.4, 2.0, 2.0, 2.0, 2.0, 2.8	1.75		
Red ginseng	1.6	4.2		
Ginseng, dried including red ginseng	< 1.0, 1.2, 1.3, 1.3, 1.3, 1.4, 1.6, 2.0, 2.0, 2.0, 2.0, 2.8	1.75, 4.2	1.5	4.2
Water extract of dried ginseng	< 0.4			
Water extract of red ginseng	< 0.4			
Ginseng, extracts	< 0.4, < 0.4		< 0.4	

APPRAISAL

Mancozeb was evaluated in 1993 in the CCPR periodic review programme. Since then, in 2012, the Meeting evaluated residue data on mancozeb and maneb, however, made no recommendation for MRLs. Currently, a number of MRLs for dithiocarbamates are established based on the residue data derived from use of mancozeb, maneb, metiram, thiram, ziram and propineb.

Dithiocarbamates-Mancozeb was listed by the Forty-fifth Session of the CCPR (2013) for the evaluation of additional MRL in 2014 JMPR. The Meeting received supervised residue trial data from Thailand (chili pepper) and the Republic of Korea (ginseng and the processed products). In addition, India submitted monitoring data on spices (cardamom, coriander, cumin, fennel and black pepper).

The mancozeb residue is defined as total dithiocarbamates, determined as CS_2, evolved during acid digestion and expressed as mg CS_2/kg, for compliance with MRLs. Dithiocarbamate residues are not fat soluble.

In 1993, the JMPR established a group (or in any combination) ADI of 0–0.03 mg/kg bw for ethylene-bis-dithiocarbamates (EBDCs: mancozeb, maneb, metiram and zineb) and an ADI of 0–0.004 mg/kg bw for their metabolite ethylenethiourea (ETU). The parent EBDC and ETU are defined as the residues for evaluating dietary intake. The Meeting is assessing combined residues of mancozeb and ETU using the ratio of the ADIs (7.5) to express residues in terms of mancozeb-toxicity-equivalents (MTE).

Methods of analysis

The analytical method used for the determination of dithiocarbamates in chili pepper was considered by the JMPR in 1995. According to the method, dithiocarbamate residues in chili pepper were converted to CS_2 by treatment with hydrochloric acid in the presence of stannous chloride. The CS_2 in the head-space was determined by GC-ECD and the limit of quantification was 0.05 mg CS_2/kg. The validity of the analytical results was supported by a set of recovery test and procedural recoveries.

Mancozeb and ETU in ginseng and its processed products were directly measured using analytical method ABY0064.

The method ABY0064 is based on the direct determination, by HPLC-MS/MS, of a derivatized EBDC (EBDC-dimethyl produced by *S*-methylation). In the method, disodium EDTA and iodomethane are used for decomposing and methylating EBDC compounds, and then the extracts are cleaned up with C_{18} SPE cartridge. In the mass analysis, individual EBDCs are distinguished using compound-specific transition ions.

The method ABY0064 was fully validated with analytical matrices of orange, olive and their processed products. The recoveries of mancozeb were within an acceptable range (70–120%) at fortification levels of 0.01 mg/kg and 0.1 mg/kg. The LOQs were 0.01 mg/kg. In ginseng residue trials, procedural recoveries were acceptable and the LOQs were 0.01 mg/kg or 0.02 mg/kg.

A method developed for determination of ETU was fully validated for the same matrices used in a validation study of ABY0064. The recoveries and RSDs were within an acceptable range at fortification levels of 0.01 mg/kg and 0.1 mg/kg and the LOQs were 0.01 mg/kg. In ginseng residue trials, procedural recoveries were acceptable and the LOQs were 0.01 mg/kg.

Spectrometry was used for the analysis of dithiocarbamates in spices. Dithiocarbamate residues in spices were converted to CS_2 and two cupric complexes of N,N-bis (2-hydroxyethly) dithiocarbamic acid, which were measured at 453 nm. LOQs of dithiocarbamates in spices (cardamom, coriander, cumin, fennel and pepper) were 0.1 mg/kg. At fortification levels of 0.1–1.0 mg CS_2/kg, recoveries were 88–110% in cumin, coriander, fennel, cardamom and black pepper.

Stability of residues in stored analytical samples

Storage stability tests for ginseng samples were performed simultaneously with freezer storage of field trial samples or processed samples. Mancozeb and ETU residues were stable during the study period, 103 days until analysis of mancozeb and ETU for fresh ginseng and 11–100 days (mancozeb analysis) or 55–100 days (ETU analysis) for the processed products.

In residue trials of chili pepper, analysis of mancozeb, as CS_2, was conducted on the day the samples were harvested.

Results of supervised trials on crops

The MRLs for mancozeb are expressed as CS_2. For trials using the headspace method, residues are reported in terms of CS_2. For trials using the HPLC-MS/MS method, residues are reported as mancozeb and ETU. For those trials, maximum residue estimates are made by converting mancozeb to CS_2-equivalents.

To estimate dietary intakes, residues are expressed in terms of mancozeb toxicity-equivalents (MTE). The conversion factor for ETU to MTE is the ratio of the ADI for mancozeb to that of ETU, which is 7.5. Thus, when residues were measured as mancozeb and ETU, the total MTE was estimated by multiplying the ETU residue by 7.5 and adding the result to the measured mancozeb residue. The resulting ETU-equivalent was then converted to MTE using the 7.5 factor. The molecular weights of these compounds are CS_2=76.1 g/mol, ETU=102.2 g/mol, and mancozeb=541.0 g/mol, assuming that the 2 moles of ETU are formed from one mole of mancozeb, leading to the following conversion factors:

CS_2 mancozeb equivalent: $541.045/(4\times76.139)= 1.777 \times CS_2$ mg/kg

Mancozeb MTE equivalent is: mancozeb mg/kg (measured as mancozeb)

MTE for ETU = 7.5×ETU mg/kg

MTE for combined residues of mancozeb measured as CS_2 mg/kg and ETU mg/kg:

$MTE_{(MCZ+ETU)} = 1.777\times CS_2$ mg/kg + 7.5× ETU mg/kg

Fruiting vegetables, other than Cucurbits

Peppers, Chili

Mancozeb is registered in Thailand for use on chili peppers at a GAP of 3 x 0.4 kg ai/hL, with 5 day intervals and a PHI of 7 days. A total of six trials were conducted in Thailand in 2005–2008, matching the GAP.

The residues, as CS_2 were (n=6): 0.31, 0.48, 0.75, 0.80, 1.2 and 1.7 mg CS_2/kg.

The Meeting estimated a maximum residue level of 3 mg CS_2/kg, an STMR of 1.4 mg MTE/kg and an HR of 3.0 mg MTE/kg for chili pepper. Using the default factor of 7 for dried chili pepper, the Meeting estimated a maximum residue level of 20 mg CS_2/kg, a STMR-P of 9.8 mg MET/kg and an HR-P of 21 mg MET/kg for dried chili pepper.

Root and tuber vegetables

Ginseng

Mancozeb is registered in the Republic of Korea for use on ginseng at a GAP of 5×0.12 kg ai/hL, with 10 day intervals and a PHI of 45 days. Four trials matching the GAP conducted in the Republic of Korea in 2013 were submitted. Two trials were conducted on the same dates of application in sites closely located and with the same application method; therefore, the trials are not considered to be independent. Only three trials could be considered for estimation of a maximum residue level.

The measured concentrations of mancozeb in ginseng were (n=3): 0.05, 0.05 and 0.11 mg/kg, which is equivalent to 0.028, 0.028 and 0.062 mg/kg as CS_2.

The measured concentrations of ETU in ginseng were (n=3): < 0.01, 0.01 and 0.04 mg/kg.

The Meeting estimated a maximum residue level of 0.15 mg CS_2/kg.

For dietary intake, the STMR is 0.125 mg MTE/kg and the HR is 0.41 mg MTE/kg.

Results of monitoring studies on spices

Monitoring of spices was conducted for dithiocarbamates in India during 2009–2014. Residues in spices came from the use of mancozeb and other dithiocarbamates. Spice samples were analysed based on the determination of CS_2.

The numbers of samples analysed were: 383 for cumin seed, 1,037 for cardamom, 248 for coriander seed, 272 for black pepper and 286 for fennel seed.

In all of the cardamom (1,037 samples) and black pepper (272 samples), CS_2 residues were < 0.1 mg/kg.

In coriander seed, CS_2 residues were < 0.1 (247), 0.4 mg CS_2/kg.

In fennel seed, CS_2 residues were < 0.1 (283), 1.1, 2.0 and 2.8 mg CS_2/kg.

In cumin seed (383 samples), CS_2 residues ranged from 0.11 mg/kg to 17 mg CS_2/kg, with a median of 3.6 mg CS_2/kg.

For compliance, the Meeting estimated maximum residue levels of 0.1 mg CS_2/kg for black pepper, cardamom, coriander seed, and fennel seed, and 10 mg CS_2/kg for cumin seed. The Meeting noted that the maximum residue estimate covers at least 98% of the observed residues.

For dietary intake, the Meeting estimated STMRs of < 0.18 mg MTE/kg for black pepper, cardamom, coriander seed, and fennel seed, and 6.4 mg MTE/kg for cumin seed.

Fate of residues during processing

The Meeting received information on the fate of mancozeb residues during the processing of ginseng. Conversion of residues to their CS_2, mancozeb, and/or ETU equivalents was done, as needed, as described above for supervised residue trials.

RAC and processed	Pf, best estimate		STMRRAC		Median-P		HRRAC		Highest residue-P	
	mancozeb	ETU*	mancozeb (mg/ kg)	ETU (mg/kg)	mancozeb (mg /kg)	ETU equiv. (mg/kg)	mancozeb (mg/ kg)	ETU (mg/kg)	mancozeb (mg /kg)	ETU equiv. (mg/kg
Ginseng			0.05	0.01			0.11	0.04		
Ginseng, dried including red ginseng	1.5	4.2			0.075	0.1197			0.17	0.3389

* Fraction yield of ETU = $[ETU]_{proc}/([ETU]_{rac} + 0.378\times[mancozeb]_{rac})$

In dried ginseng, each processing factor for mancozeb, ETU and CS_2 residue was calculated as follows:

For mancozeb, the concentration of mancozeb in dried ginseng was divided by the concentration of mancozeb in fresh ginseng.

For ETU, the concentration of ETU in dried ginseng was divided by the sum of ETU and mancozeb (expressed as ETU equivalents) in fresh ginseng in order to account for mancozeb as a potential source of ETU during processing. The stoichiometric conversion factor for mancozeb to ETU is 0.377 (102.2 g ETU/mol ÷ 271.2 g mancozeb/mol).

For compliance, the Meeting estimated a maximum residue level of 0.3 mg CS_2/kg, based on a maximum residue level of 0.15 mg CS_2/kg for ginseng and the processing factor of dried ginseng, 1.5 (1.5×0.15=0.225 mg/kg).

For dietary intake, the Meeting estimated an STMR-P of 0.075+7.5×0.1197=0.97 mg MTE/kg and an HR-P of 0.17+7.5×0.33894=2.71 mg MTE/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.

The mancozeb residue is defined as total dithiocarbamates, determined as CS_2, evolved during acid digestion and expressed as mg CS_2/kg, for compliance with MRLs in plant and animal commodities.

For estimation of dietary intake in plant and animal commodities, the residue definition is mancozeb and ETU.

Dithiocarbamate residues are not fat soluble.

DIETARY RISK ASSESSMENT

Long-term intake

A group ADI (or in any combination) for ethylene-bis-dithiocarbamates (EBDCs: mancozeb, maneb, metiram and zineb) is 0–0.03 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for mancozeb were estimated based on the 17 GEMS/Food Consumption Cluster Diets using only the STMR or STMR-P values estimated by the current JMPR. The results are shown in Annex 3 of the 2014 JMPR Report. The IEDIs ranged 0-6% of the maximum ADI. The Meeting concluded that the

long-term intake of residues of mancozeb from uses added by the current JMPR is unlikely to present a public health concern.

Short-term intake

The ARfD for mancozeb and its metabolite ETU is not available currently. The Meeting noted that the dithiocarbamates were last evaluated in 1993 before the ARfD established by the JMPR.

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