Food and Agriculture Organization of the United Nations

World Health Organization

JOINT FAO/WHO MEETING ON PESTICIDE RESIDUES

SUMMARY REPORT

ACCEPTABLE DAILY INTAKES, ACUTE REFERENCE DOSES, RESIDUE DEFINITIONS, RECOMMENDED MAXIMUM RESIDUE LIMITS, SUPERVISED TRIALS MEDIAN RESIDUE VALUES AND OTHER VALUES RECORDED

BY THE 2021 MEETING
6–17 September 2021; 4 and 7 October 2021

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The following extracts of the results of the 2021 Joint FAO/WHO Meeting on Pesticide Residues (JMPR) are provided to make them accessible to interested parties at an early date.

The Meeting evaluated 15 pesticides. The Meeting estimated maximum residue levels, which it recommended for use as maximum residue limits (MRLs) by the CCPR. It also estimated supervised trials median residue (STMR) and highest residue (HR) levels as a basis for estimation of the dietary exposure to residues of the pesticides reviewed. The allocations and estimates are shown in the table.

Pesticides for which the estimated dietary exposures might, on the basis of the available information, exceed their Acceptable Daily Intakes (ADIs) are marked with footnotes, which are also applied to specific commodities when the available information indicated that the Acute Reference Dose (ARfD) of a pesticide might be exceeded when the commodity was consumed.

The table includes the Codex reference numbers of the compounds and the Codex classification numbers (CCNs) of the commodities, to facilitate reference to the Codex maximum limits for pesticide residues (Codex Alimentarius, Vol. 2B) and other documents and working documents of the Codex Alimentarius Commission. Both compounds and commodities are listed in alphabetical order.

Apart from the abbreviations indicated above, the following qualifications are used in the Table.

* (following recommended MRL)	At or about the limit of quantification
as	The median or highest residue is reported at the moisture content of the feed commodity "as received"
dw	The value is reported in the dry weight of the feed commodity
HR-P	Highest residue in a processed commodity, in mg/kg, calculated by multiplying the HR in the raw commodity by the processing factor
Po	The recommendation accommodates post-harvest treatment of the commodity.
PoP (following recommendation for processed foods) (classes D and E in the Codex classification)	The recommendation accommodates post-harvest treatment of the primary food commodity.
STMR-P	An STMR for a processed commodity calculated by applying the concentration or reduction factor for the process to the STMR calculated for the raw agricultural commodity.
W (in place of a recommended MRL)	The previous recommendation is withdrawn, or withdrawal of the recommended MRL or existing Codex or draft MRL is recommended.

Pesticide acceptable daily intakes, acute reference doses, residue definitions, recommended maximum residue limits, supervised trials median residue and highest residue values recorded by the 2021 meeting.

Note: No new recommendations were made for dimethoate, ethoxyquin and guazatine, therefore they do not appear in the table below.

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
Afidopyropen (312) ADI: 0–0.08 mg/kg bw ARfD: 0.2 mg/kg bw (for women of child-bearing age) ARfD: 0.3 mg/kg bw (for general population)	Definition of the residue for compliance with the MRL for plant commodities: *Afidopyropen* Definition of the residue for dietary risk assessment for plant commodities: *the sum of afidopyropen + dimer of [(3R,6R,6aR,12S,12bR)-3-[(cyclopropanecarbonyl)oxy]-6,12-dihydroxy-4,6a,12b-trimethyl-11-oxo-9-(pyridin-3-yl)-1,3,4,4a,5,6,6a,12,12a,12b-decahydro-2H,11H-naphtho[2,1-b]pyrano[3,4-e]pyran-4-yl]methyl rac-cyclopropanecarboxylate (M007)* Definition of the residue for compliance with the MRL for animal commodities: *Afidopyropen* Definition of the residue for dietary risk assessment for animal commodities, excluding liver: *Afidopyropen + (3S,4R,4aR,6S, 6aS, 12R,12aS,12bS)-3,6,12-trihydroxy-4-(hydroxymethyl)-4,6a, 12b-trimethyl--9-(pyridin-3-yl)-1, 3,4,4a,5,6,6a,12, 12a,12b-decahydro-2H,11H-benzo- [f] pyrano[4,3-b]chromen-11-one (M001) + Cyclopropane carboxylic acid (CPCA/M061) and (2R)-3-carboxy-2- [(cyclopropylcarbonyl)oxy]- N, N, N-trimethylpropan-1-aminium chloride (CPCA-carnitine conjugate/M060), expressed as afidopyropen*. Definition of the residue for dietary risk assessment for animal commodities, liver: *Afidopyropen + (3S,4R,4aR,6S, 6aS, 12R,12aS,12bS)-3,6,12-trihydroxy-4-(hydroxymethyl)-4,6a, 12b-trimethyl--9-(pyridin-3-yl)-1, 3,4,4a,5,6,6a,12, 12a,12b-decahydro-2H,11H-benzo- [f] pyrano[4,3-b]chromen-11-one (M001) + Cyclopropane carboxylic acid (CPCA/M061) and (2R)-3-carboxy-2- [(cyclopropylcarbonyl)oxy]- N, N, N-trimethylpropan-1- aminium chloride (CPCA-carnitine conjugate/M060) + [(3S,4R,4aR,6S,6aS,12R,12aS,12bS)-3-(cyclopropylcarbonyl)oxy]-6,12-dihydroxy-4,6a,12b-trimethyl-9-(1-oxidopyridin-3-yl)-11-oxo-1,3,4,4a,5,6,6a,12,12a,12b-decahydro-2H, 11H-benzo[f]pyrano[4,3-b]chromen-4-yl]methyl cyclopropane-carboxylate (M017), expressed as afidopyropen*. *The residue is not fat-soluble.*					
Fenpyroximate (193) [b] ADI: 0–0.005 mg/kg bw ARfD: 0.005 mg/kg bw	FC 0001	Citrus Fruit, Group of	W	0.6		
	FC 0002	Lemons and Limes (including Citron), Subgroup of	1	-	0.37 (RAC)	0.59 (RAC)
					0.085 (flesh)	0.14 (flesh)
	FC 0003	Mandarins (including Mandarin-like hybrids), Subgroup of	1 [a]	-	0.37 (RAC)	0.59 (RAC)
					0.085 (flesh)	0.14 (flesh)
	FC 0004	Oranges, sweet, sour (including orange-like hybrids), Subgroup of	0.7 [a]	-	0.225 (RAC)	0.48 (RAC)
					0.052 (flesh)	0.11 (flesh)
	FC 0005	Pummelo and Grapefruits (including Shaddock-like hybrids), Subgroup of	0.5	-	0.19 (RAC)	0.32 (RAC)
					0.044 (flesh)	0.074 (flesh)
	FS 0014	Plums (including fresh Prunes), Subgroup of	0.05	0.8	0.025 (RAC)	0.040 (RAC)
	FB 0272	Raspberries, Red, Black	W	0.2		

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
	FB 2005	Cane berries, Subgroup of	3 [a]	-	0.84	1.4
	FB 2006	Bush berries, Subgroup of	2 [a]	-	0.8	1.2
	VC 0424	Cucumber	W	0.3		
	VC 0431	Squash, summer	W	0.06		
	VC 2039	Cucumbers and Summer squashes, Subgroup of	0.3 [a]	-	0.12	0.24
	VP 2062	Succulent beans without pods, Subgroup of	0.05*	-	0.1	0.1
	VS 2080	Stems and petioles, Subgroup of	3 [a]	-	0.845	2.1
	ML 0106	Milks	0.01	0.01	0.005	-
	MM 0095	Meat (from mammals other than marine mammals)	0.2 (fat)	0.1 (fat)	0.015 (muscle)	0.041 (muscle)
					0.063 (fat)	0.13 (fat)
	MF 0100	Mammalian fats (except milk fats)	0.2	0.1	0.063	0.13
	MO 0105	Edible offal (mammalian)	0.8	0.5	0.4	0.77
		Subgroup of Succulent beans without pods, cooked			0.06	0.06
		Subgroup of Succulent beans without pods, canned			0.044	0.044
		Subgroup of Lemons and Limes, juice			0.037	-
		Subgroup of Mandarins, juice			0.037	-
		Subgroup of Oranges, juice			0.022	-
		Subgroup of Pummelo and Grapefruits, juice			0.019	-
		Subgroup of Lemons and Limes, marmalade			0.018	-
		Subgroup of Mandarins, marmalade			0.018	-
		Subgroup of Oranges, marmalade			0.011	-
		Subgroup of Pummelo and Grapefruits, marmalade			0.0094	-
	OR 0004	Orange oil, edible	W	25		
		Subgroup of Lemons and Limes, oil	150		58	
		Subgroup of Mandarins, oil	150		58	
		Subgroup of Oranges, oil	100		35	
		Subgroup of Pummelo and Grapefruits, oil	80		30	
		Subgroup of Plums, dried (prunes)	0.15		0.05	0.08
		Subgroup of Plums, juice			0.012	
		Subgroup of Plums, jam			0.012	
		Subgroup of Plums, puree			0.012	
		Subgroup of Lemons and Limes, dried pulp	6 (dw)		1.8	-
		Subgroup of Oranges, dried pulp	4 (dw)		1.1	-
		Subgroup of Pummelo and Grapefruits, dried pulp	3 (dw)		0.95	-
	RAC: Raw Agricultural Commodity					

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
	[a] ***On the basis of the information provided to the JMPR it was concluded that the estimated acute dietary exposure to residues of fenpyroximate for the consumption of commodities from the subgroups of Mandarins, Oranges, sweet, sour, Cane berries, Bush berries, Cucumbers and Summer squash, and Stems and Petioles may present a public health concern.***					
	[b] ***As the current Meeting revised the ARfD for fenpyroximate, a new acute dietary risk assessment for all recommendations made by the 2017 and 2018 JMPRs was conducted in addition to those commodities considered by the current Meeting.*** ***Based on the revised ARfD, the current Meeting confirmed the 2017 JMPR conclusion that the estimated acute dietary exposure to residues of fenpyroximate for the consumption of commodities from FS 0013 Subgroup of cherries, FS 0247 Peach, VC 0432 Watermelon may present a public health concern. Alternative GAP data were available for plums, so the 2017 JMPR exceedances noted for FS 0014 Plums and dried plum no longer exist.*** ***In addition, the current Meeting also concluded, based on the revised ARfD, that the estimated acute dietary exposure to residues of fenpyroximate for the consumption of commodities FP 0226 Apple, FP 0230 Pear, FS 0240 Apricot, VC 0046 Melons (except watermelon), VO 2045 Subgroup of Tomatoes, VO 2046 Subgroup of Eggplants, VP 2060 Subgroup of Beans with pods as previously considered by the 2017 and 2018 JMPRs may present a public health concern.***					
	Definition of the residue for compliance with the MRL for plant commodities: f*enpyroximate* Definition of the residue for dietary risk assessment for plant commodities and for dietary burden calculations: *Sum of parent fenpyroximate and tert-butyl (Z)-α-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethyleneamino-oxy)-p-toluate (its Z-isomer M-1), expressed as fenpyroximate*. Definition of the residue for compliance with the MRL for animal commodities: *Sum of fenpyroximate and (E)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl) methyleneaminooxymethyl]benzoic acid (M-3), expressed as fenpyroximate*. Definition of the residue for dietary risk assessment for animal commodities: *Sum of fenpyroximate, 2-hydroxymethyl-2-propyl (E)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)-methylenaminooxymethyl]benzoate (Fen-OH), 2-hydroxy-2-methylpropyl (E)-α-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethyleneamino-oxy)-p-toluate (R-UL-1) and (E)-4-[(1,3-dimethyl-5-phenoxypyrazol-4-yl)methyleneaminooxymethyl]benzoic acid (M-3), expressed as fenpyroximate.* *The residue is fat-soluble.*					
Fipronil (202)** [a] ADI: 0–0.0002 mg/kg bw ARfD: 0.03 mg/kg bw	FI 0327	Banana	0.004 *	0.005	0	0
	GC 0640	Barley	W	0.002*		
	GC 2087	Barley, similar grains, and pseudocereals with husks, Subgroup of	0.004 *		0.00536	
	AS 0640	Barley, straw and fodder dry *Barley, hay and/or straw* [#]	0.07 dw			
	HH 0722	Basil, leaves	0.8	1.5	0.23	0.57
	VD 2065	Dry beans, Subgroup of (except soya beans)	0.01		0.002	
	VB 0041	Cabbage, head	W	0.02		
	MO 1280	Cattle, kidney	W	0.02		
	MO 1281	Cattle, liver	W	0.1		
	MM 0812	Cattle meat	W	0.5 (fat)		
	ML 0812	Cattle milk	W	0.02		
	SO 0691	Cottonseed	0.01		0.002	

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
	PE 0112	Eggs	0.04	0.02	0.0358	0.06141
	VB 0042	Flowerhead Brassicas, Subgroup of	W	0.02		
	VL 0053	Leafy vegetables, Group of	0.01 [b]		0	0.02919
	VP 2060	Beans with pods, Subgroup of	0.01		0.008	0.0099
	GC 0645	Maize	W	0.01		
	GC 2091	Maize cereals, Subgroup of	0.01		0.004	
	AS 0645	Maize fodder (dry)	W	0.1 dw		
	GC 0647	Oats	W	0.002*		
	AS0647	Oat straw and fodder dry	0.07 dw			
	AS 3554 #	*Oat, hay and/or straw #*				
	VA 0385	Onion, bulb	0.03		0.02	0.033
	VR 0589	Potato	0.05	0.02	0.00493	0.0296
	PF 0111	Poultry fats	0.07	0.02	0.04698	0.1006
	PM 0110	Poultry meat	0.007	0.01*	0.00486 muscle 0.04698 fat	0.01169 muscle 0.1006 fat
	PO 0111	Poultry, Edible offal of	0.03	0.02	0.03227 Liver	0.04231 Liver
	GC 0649	Rice	W	0.01		
	GC 2088	Rice cereals, Subgroup of	0.4		0.00411	
	CM 0649	Rice, husked	0.4		0.0023	
	CM 1205	Rice, polished	0.15		0.002	
	CM 1206	Rice bran, unprocessed	2		0.00323	
	CM 1207	Rice hulls	2			
	AS 0649	Rice straw and fodder, Dry	0.6 dw	0.2 dw		
		Rice, hay and/or straw #				
	VR 0075	Root and Tuber vegetables, Group of (except potato and sugar beet)	0.002[b]		0	0.00212
	GC 0650	Rye	W	0.002*		
	AS 0650	Rye straw and fodder dry	0.05 dw			
	AS 3555#	*Rye, hay and/or straw #*				
	VD 0541	Soya bean (dry)	0.01		0.00411	
	AB 0541	Soya bean hulls	0.06			
	AL 3538 #					
	AS 0081#	Straw and fodder (dry) of cereal grains (except of barley, oats, rice, rye, triticale and wheat)	0.03 [b] dw			
	VR 0596	Sugar beet	0.01	0.2	0.003	
	GS 0659	Sugar cane	0.01		0.00304	0.00815
	SO 0702	Sunflower seed	W	0.002*		
	SO 2091	Sunflower seeds, Subgroup of	0.004 *		0.008	
	VO 2045	Tomato, Subgroup of	0.01 *		0.008	0.008
	GC 0653	Triticale	W	0.002*		
	AS 0653	Triticale straw and fodder dry	0.05 dw			
		Triticale, hay and/or straw #				
	GC 0654	Wheat	W	0.002*		
	GC2086	Wheat, similar grains, and pseudocereals with husks, Subgroup of	0.004 *		0.008	
	AS 0654	Wheat straw and fodder dry	0.05 dw			

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
		Wheat, hay and/or straw [#]				
	MO 0105	Edible offal (Mammalian)	0.1		0.09145 Liver	0.32752 Liver
	MF 0100	Mammalian fats (except milk fats)	0.4		0.17625	0.65651
	MM 0095	Meat (from mammals other than marine mammals)	0.03		0.0085 muscle 0.17625 fat	0.04926 muscle 0.65651 fat
	ML 0106	Milks	0.03		0.00845	0.04321
	FM 0183	Milk fats	0.3		0.12	0.59
	OC 0541	Soya bean oil, crude	0.05		0.01808	
		Potato washed			0.00244	0.01465
		Potato peeled			0.00158	0.00947
		Potato, cooked peeled			0.00121	0.00725
		Potato, microwave unpeeled			0.00333	0.01998
		Potato, French fries			0.00182	0.01095
		Potato flakes			0.00222	
	DV 0589[#]	*Potato, flakes/granules*				
	CF 3513	Rice, flour			0.00053	
		Rice, polished cooked			0.00016	
		Rice polished steamed			0.00012	
		Sake			0.00008	
		Sugarcane juice			0.00182	
	DM 0659	Sugar cane molasses			0.00007	
	DM3524	Sugar cane, sugar refined			0.00007	
	OC 0691	Cotton seed oil, crude			0.0008	
	OR 0691	Cotton seed oil, edible			0.0006	
	[a] ***On the basis of the information provided to the JMPR it was concluded that the estimated long-term dietary exposure to residues of fipronil may present a public health concern***. [b] residues resulting from rotational cropping					
	[#] *New codes and/or commodity names as agreed by CCPR 52 and proposed for adoption by CAC 43*;					
	Definition of the residue for compliance with the MRL for plant and animal commodities: *Sum of fipronil and 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonylpyrazole (MB46136) expressed in terms of fipronil*. Definition of the residue for dietary risk assessment for plant and animal commodities: *Sum of fipronil and 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonylpyrazole (MB46136), 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (MB45950) and 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylpyrazole (MB46513) expressed in terms of fipronil.* *The residue is fat-soluble*.					
Fluensulfone (265) ADI: 0–0.01 mg/kg bw ARfD: 0.3 mg/kg bw	FP 0009	Pome fruits, Group of (except Persimmon, Japanese)	0.3	0.2	0	0
	Definition of the residue for compliance with the MRL for plant commodities: *the sum of fluensulfone and 3,4,4-trifluorobut-3-ene-1-sulfonic acid (BSA), expressed as fluensulfone*					

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
	equivalents. Definition of the residue for compliance with the MRL for animal commodities: *fluensulfone* Definition of the residue for dietary risk assessment for plant and animal commodities: *fluensulfone* *The residue is fat-soluble.*					
Flutianil (319)*	FP 0226	Apple	0.15	-	0.047	
ADI: 0–0.8 mg/kg bw	FS 0013	Cherries, Subgroup of	0.4	-	0.11	
ARfD: Unnecessary	FB 2008	Small fruit vine climbing, Subgroup of	0.7	-	0.075	
	JF 0226	Apple, juice			0.005	
	JF 0269	Grape, juice			0.05	
	DF 0269	Grape, dried (=Currants, Raisins and Sultanas)			0.09	
	Definition of the residue for compliance with the MRL for plant and animal commodities: *Flutianil* Definition of the residue for dietary risk assessment for plant commodities: *Sum of flutianil and 2-fluoro-5-(trifluoromethyl)benzenesulfonic acid (OC 56635), expressed as flutianil* *The residue is fat-soluble.*					
Isoprothiolane (299)						
ADI: 0–0.1 mg/kg bw ARfD: Unnecessary						
Mefentrifluconazole (320)*						
ADI: 0–0.04 mg/kg bw ARfD: 0.3 mg/kg bw						
Metalaxyl (138)** [a]	FP 0226	Apple	0.02* (MM)		0	0
ADI: 0–0.08 mg/kg bw [b]	VS 0621	Asparagus	W	0.05*		
ARfD: 0.5 mg/kg bw [b]	FI 0326	Avocado	W	0.2		
	VB 0400	Broccoli	W	0.5		
	VB 0402	Brussels sprouts	0.15 (M)	0.2	0.44	0.77
	VB 0041	Cabbages, Head	0.08 (MM)	0.5	0.22	0.44
	SB 0715	Cacao bean	W	0.2		
	VR 0577	Carrot	0.02* MM)	0.05*	0.02	0.02
	VB 0404	Cauliflower	W	0.5		
	GC 0080	Cereal grains	W	0.05		
	FC 0001	Citrus fruits, Group of	W	5		
	SO 0691	Cottonseed	W	0.05*		
	VC 0424	Cucumber	W	0.5		
	VB 0042	Flowered brassicas, Subgroup of	0.2 (M)		0.275	1.21
	VC 0425	Gherkin	W	0.5		
	VR 0604	Ginseng	0.03* (MM)		0.03	0.03
	FB 0269	Grapes	1.5 (MM)	1	0.182	0.884

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
	JF 0269	Grape, juice			0.073	
		Grape wine			0.138	
	DH 1100	Hops, dry	W	10		
	VL 0482	Lettuce, head	W	2		
	VL 0483	Lettuce, leaf	1.5 (M)		1.43	8.14
	VC 0046	Melons, except Watermelon	0.15 (MM)	0.2	0.013	0.026
	VA 0385	Onion, Bulb	0.03 (MM)	2	0.02	0.02
	FC 0004	Oranges, Sweet, Sour, Subgroup of	0.7 (M)		0.013 (flesh) 0.338 (RAC)	0.026 (flesh) 0.39 (RAC)
	JF 0004	Orange juice			0.016	
		Orange marmalade			0.101	
	OR 0004	Orange oil, edible	7		3.04	
	SO 0697	Peanut	W	0.1		
	FP 0230	Pear	0.02* MM)		0	0
	VP 0064	Peas, shelled (succulent seeds)	W	0.05*		
	VO 0051	Peppers	W	1		
	HS 0790	Pepper, black, White, pink, green	2 (MM)		0.455	
	VO 0444	Peppers Chili, dried	W	10		
	FP 0009	Pome fruits	W	1		
	VR 0589	Potato	0.02 (M)	0.05*	0.01	0.02
	FB 0272	Raspberries, red, black	W	0.2		
	VD 0451	Soya bean (dry)	W	0.05*		
	HS 0190	Spices, seeds	W	5 (Mt)		
	VL 0502	Spinach	0.02* MM)	2	0.22	0.22
	VC 0431	Squash, summer	W	0.2		
	VR 0596	Sugar beet	W	0.05*		
	SO 0702	Sunflower seed	0.01* (MM)	0.05*	0	
	VO 0448	Tomato	W	0.5		
	VO 2045	Tomatoes, Subgroup of	0.3 (MM)		0.058	0.234
	VC 0432	Watermelon	W	0.2		
	VC 0433	Winter squash	W	0.2		
	RAC: Raw Agricultural Commodity					
	[a] Residue data that was the basis for the estimation: metalaxyl (M), metalaxyl-M (MM) or monitoring (Mt) [b] Applies to metalaxyl and metalaxyl-M (alone or in combination)					
	Residue definition for metalaxyl and metalaxyl-M for compliance with the MRL for plant commodities: *metalaxyl (sum of enantiomers)*. Residue definition for metalaxyl and metalaxyl-M for dietary risk assessment in plant commodities: *metalaxyl (sum of enantiomers) and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester (M8; free and conjugated; sum of enantiomers), expressed as metalaxyl*. Residue definition for metalaxyl and metalaxyl-M for compliance with the MRL in animal commodities is: *the sum of metalaxyl (sum of enantiomers) and metabolites (free + conjugated) M3 (N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)alanine methyl ester) and M8 (N-(2-*					

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
	hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester (sum of enantiomers), expressed as metalaxyl. Residue definition for metalaxyl and metalaxyl-M for dietary risk assessment in animal commodities is: *the sum of metalaxyl (sum of enantiomers) and metabolites (free + conjugated) M1 (N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine), M3 (N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)alanine methyl ester), M6 (N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)alanine), M7 (N-(2,6-dimethyl- 5-hydroxyphenyl)-N-(methoxyacetyl)alanine methyl ester) and M8 (N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester (sum of enantiomers), expressed as metalaxyl.* *The residue is not fat-soluble.*					
Metalaxyl-M (212) ADI: 0–0.08 mg/kg bw [b] ARfD: 0.5 mg/kg bw [b]	FP 0226	Apple	W	0.02 *		
	SB 0715	Cacao beans	W	0.02		
	FB 0269	Grapes	W	1		
	VL 0482	Lettuce, head	W	0.5		
	VA 0385	Onion, bulb	W	0.03		
	VO 0445	Peppers, sweet (including pimento or pimiento)	W	0.5		
	VR 0589	Potato	W	0.02 *		
	VL 0502	Spinach	W	0.1		
	SO 0702	Sunflower seed	W	0.02 *		
	VO 0448	Tomato	W	0.2		
	[b] Applies to metalaxyl and metalaxyl-M (alone or in combination)					
	Residue definition for metalaxyl and metalaxyl-M for compliance with the MRL for plant commodities: *metalaxyl (sum of enantiomers).* Residue definition for metalaxyl and metalaxyl-M for dietary risk assessment in plant commodities: *metalaxyl (sum of enantiomers) and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester (M8; free and conjugated; sum of enantiomers), expressed as metalaxyl.* Residue definition for metalaxyl and metalaxyl-M for compliance with the MRL in animal commodities is: *the sum of metalaxyl (sum of enantiomers) and metabolites (free + conjugated) M3 (N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)alanine methyl ester) and M8 (N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester (sum of enantiomers), expressed as metalaxyl.* Residue definition for metalaxyl and metalaxyl-M for dietary risk assessment in animal commodities is: *the sum of metalaxyl (sum of enantiomers) and metabolites (free + conjugated) M1 (N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine), M3 (N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)alanine methyl ester), M6 (N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)alanine), M7 (N-(2,6-dimethyl- 5-hydroxyphenyl)-N-(methoxyacetyl)alanine methyl ester) and M8 (N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester (sum of enantiomers), expressed as metalaxyl.* *The residue is not fat-soluble.*					
Metconazole (313) ADI: 0–0.04 mg/kg bw ARfD: 0.04 mg/kg bw Triazole alanine and Triazole acetic ADI: 0–1 mg/kg bw ARfD: Unnecessary 1,2,4-triazole	GC 0654	Wheat	0.15		0.035	
	GC 0653	Triticale	0.15		0.035	
	CM 0654	Wheat bran, unprocessed	0.3		0.067	
	CF 1212	Wheat, wholemeal			0.026	
	CF 1211	Wheat, flour			0.008	
	CF 1210	Wheat, germ			0.035	

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
ADI: 0–0.2 mg/kg bw ARfD: 0.3 mg/kg bw	CP 1211	White bread			0.021	
	Definition of the residue for compliance with the MRL for plant and animal commodities: *Metconazole (sum of cis and trans isomer)*. Definition of the residue for dietary risk assessment for plant commodities: *Metconazole (sum of cis and trans isomer)*. Definition of the residue for compliance with the MRL and dietary risk assessment for animal commodities: *Sum of metconazole (cis and trans-isomer) and metabolites (1SR,2SR,5RS)-5-(4-chlorobenzyl)-2-(hydroxymethyl)-2-methyl-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol (M1; free and conjugated) and (1RS,2SR,3RS)-3-(4-chlorobenzyl)-2-hydroxy-1-methyl-2-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanecarboxylic acid (M12; free and conjugated), expressed as metconazole*. *The residue is not fat-soluble*				
Pendimethalin (292) ADI: 0–0.1 mg/kg bw ARfD: 1 mg/kg bw	FB 0269	Grapes	0.05*	-	0.05	0.05
	VA 0384	Leek	0.3	-	0.02	0.23
	VB 0042	Flowerhead Brassicas, Subgroup of	0.01*	-	0	0
	VO 0050	Fruiting vegetables, other than Cucurbits, Group of	0.05*	-	0.05	0.05
	VD 0541	Soya bean (dry)	0.05*	-	0.05	-
	GC 0654	Wheat	0.01*	-	0.01	-
	GC 0649	Rice	0.01*	-	0	-
	GC 0645	Maize	0.05*	-	0.05	-
	GS 0659	Sugar cane	0.01*		0	-
	SO 0702	Sunflower Seed	0.05*		0.05	-
	HH 0740	Parsley, leaves	1.5		0.305	0.76
	AS 0654	Wheat straw and fodder dry *Wheat, hay and/or straw #*	0.3		0.05	0.17
	AS 0649	Rice straw and fodder, dry *Rice, hay and/or straw #*	0.01*		0	0
	AS 0645 *AS 3552 #*	Maize fodder (dry) *Maize, hay and/or straw #*	0.05*		0.05	0.05
	# New codes and/or commodity names as agreed by CCPR 52 and proposed for adoption by CAC43					
	Definition of the residue for compliance with the MRL and dietary risk assessment for plant and animal commodities: *Pendimethalin*. *The residue is fat-soluble*.					
Pyrasulfotole (321)* ADI: 0–0.01 mg/kg bw ARfD: Unnecessary	GC 0640	Barley	0.03		0.02	
	AS 0640	Barley straw and fodder, dry *Barley, hay and/or straw #*	0.8 (dw)		0.21 [a] Hay (dw) 0.105 [a] Straw (dw)	0.50 [b] Hay (dw) 0.38 [b] Straw (dw)
	MO 0105	Edible offal (Mammalian)	0.5		0.084	
	PE 0112	Eggs	0.02*		0	

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
	MF 0100	Mammalian fats (except milk fats)	0.02*		0.02	
	MM 0095	Meat (from mammals other than marine mammals)	0.02*		0.02 muscle 0.02 fat	
	ML 0106	Milks	0.01*		0.01	
	GC 0647	Oats	0.15		0.02	
	AS 0647	Oat straw and fodder, dry	0.8 (dw)		0.21 [a] Hay (dw)	0.50 [b] Hay (dw)
	AS 3554 [#]	*Oat, hay and/or straw [#]*			0.105 [a] Straw (dw)	0.38 [b] Straw (dw)
	PM 0110	Poultry meat	0.02*		0.02 muscle 0.02 fat	
	PO 0111	Poultry, Edible offal of	0.05		0.02	
	PF 0111	Poultry fats	0.02*		0.02	
	GC 0650	Rye	0.02*		0.02	
	AS 0650	Rye, straw and fodder, dry	0.8 (dw)		0.105 [a] Straw (dw)	0.38 [b] Straw (dw)
		Rice, hay and/or straw [#]				
	GC 0651	Sorghum Grain	0.5		0.091	
	GC 0653	Triticale	0.02*		0.02	
	AS 0653	Triticale, straw and fodder, dry	0.8 (dw)		0.21 [a] Hay (dw)	0.50 [b] Hay (dw)
		Triticale, hay and/or straw [#]			0.105 [a] Straw (dw)	0.38 [b] Straw (dw)
	CM 0654	Wheat bran, unprocessed	0.03		0.028	
	GC 0654	Wheat	0.02*		0.02	
	AS 0654	Wheat straw and fodder, dry	0.8 (dw)		0.21 [a] Hay (dw)	0.50 [b] Hay (dw)
		Wheat, hay and/or straw [#]			0.105 [a] Straw (dw)	0.38 [b] Straw (dw)
	CF 1211	Wheat, flour			0.02	
	CF 1210	Wheat germ			0.016	
	[#] New codes and/or commodity names as agreed by CCPR 52 and proposed for adoption by CAC43					
	[a] Median [b] Highest					
	Definition of the residue for compliance with the MRL and for dietary risk assessment for plant commodities: *Sum of pyrasulfotole and desmethyl-pyrasulfotole and its conjugates, expressed as pyrasulfotole*. Definition of the residue for compliance with the MRL and for dietary risk assessment for animal commodities: *Sum of pyrasulfotole and desmethyl-pyrasulfotole, expressed as pyrasulfotole.* *The residue is not fat-soluble*.					

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
Pyraziflumid (322)* ADI: 0–0.02 mg/kg bw ARfD: 2 mg/kg bw	FP 0226	Apple	1.5		0.36	0.73
	JF 0226	Apple juice			0.036	-
	DF 0269	Grape, dried (=Currants, Raisins and Sultanas)	6		1.14	1.96
	MO 0105	Edible offal (mammalian) [a]			0.005	0.005
	FB 0269	Grapes	3		0.57	0.98
	JF 0269	Grape juice			0.057	-
	MF 0100	Mammalian fats (except milk fats) [a]			0.002	0.002
	MM 0095	Meat (from mammals other than marine mammals) [a]			0.0005 (muscle)	0.0005 (muscle)
					0.002 (fat)	0.002 (fat)
	ML 0106	Milks [a]			0.0001	-
	FP 0230	Pear	1.5		0.36	0.73
	FP 0307	Persimmon, Japanese	1.5		0.36	0.73
	[a] **No maximum residue level recommendation due to the absence of an enforcement method**					
	Definition of the residue for compliance with the MRL for plant commodities: *pyraziflumid*. Definition of the residue for dietary risk assessment for plant commodities: *pyraziflumid*. Definition of the residue for compliance with the MRL for animal commodities: *Pyraziflumid and its pyraziflumid-4'-OH metabolite (free), expressed as pyraziflumid.* Definition of the residue for dietary risk assessment for animal commodities*: pyraziflumid and its pyraziflumid-4'-OH metabolite (free and conjugated), expressed as pyraziflumid*. *The residue is fat-soluble*.					
Spiropidion (323)* ADI: 0–0.02 mg/kg bw ARfD: 0.3 mg/kg bw	VC 0424	Cucumber	0.8		0.34	0.7
	VC 0046	Melons (except watermelon)	0.9		0.25	0.91
	VC 0429	Pumpkins	0.9		0.25	0.91
	VC 0432	Watermelon	0.9		0.25	0.91
	VC 0433	Winter squash	0.9		0.25	0.91
	VO 0448	Tomato	0.8		0.245	0.7
	VO 0051	Peppers, Subgroup of (except martynia, okra, roselle)	1		0.49	1.2
	HS 0444	Peppers, Chili, dried	7		2.905	7
	VD 0541	Soya bean (dry)	3		0.49	
	VW 0448	Tomato paste	1.5		0.46 paste 0.27 puree	
	DM 0448#	*Tomato, puree#*				
	VR 0589	Potato	1.5		0.28	0.98
	DV 0448	Tomato (dried)	7		1.7	4.8
		Soya flour	5		0.79	
	AB 1265	Soya bean meal	5		0.62	
	AL 3539 #					
		Potato, flakes	5		0.67	
	DV 0589#	*Potato, flakes/granules#*				

Pesticide (Codex reference number)	CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P	HR or HR-P
			New	Previous	mg/kg	mg/kg
	MO 0105	Edible offal (mammalian)	0.2		0.098 kidney	0.2 kidney
	MF 0100	Mammalian fats (except milk fats)	0.025		0.013	0.021
	MM 0095	Meat (from mammals other than marine mammals)	0.012 *		0.0065 muscle 0.013 fat	0.01 muscle 0.021 fat
	ML 0106	Milks	0.012 *		0.0057	
	PE 0112	Eggs	0.012 *		0.00089	0.00089
	PM 0110	Poultry meat	0.012 *		0.00041 muscle 0.00035 fat	0.00041 muscle 0.00035 fat
	PO 0111	Poultry, edible offal of	0.012 *		0.0033	0.0033
	PF 0111	Poultry fat	0.012 *		0.00035	0.00035
	JF 0448	Tomato juice			0.19	
		Canned tomatoes (peeled)			0.15	0.44
	OR 0541	Soya bean oil, refined			0.01	
		Soya milk			0.039	
		Tofu			0.051	
		Soy sauce			0.02	
		Miso			0.098	
		Potato (peeled)			0.37	1.3
		Potato crisps			0.23	
		Potato (baked, with peel)			0.55	2
		Potato fries (without peel)			0.2	
		Potato starch			0.16	
	# New codes and/or commodity names as agreed by CCPR 52 and proposed for adoption by CAC 43;					
	Definition of the residue for compliance with the MRL for plant commodities*: the sum of spiropidion and spiropidion-enol (SYN547305) expressed as spiropidion* Definition of the residue for dietary risk assessment for plant commodities: *the sum of spiropidion, spiropidion-enol (SYN547305), 3-(4-chloro-2,6-dimethyl-phenyl)-4-hydroxy-8-methoxy-1,8-diazaspiro[4.5]dec-3-en-2-one (SYN547435) and 3-(4-chloro-2,6-dimethyl-phenyl)-4-hydroxy-1-methyl-1,8-diazaspiro[4.5]dec-3-en-2-one (SYN548430), expressed as spiropidion.* Definition of the residue for compliance with the MRL for animal commodities: *spiropidion-enol (SYN547305) expressed as spiropidion.* Definition of the residue for dietary risk assessment for animal commodities: *free and conjugated spiropidion-enol (SYN547305) expressed as spiropidion.* *The residue is not fat-soluble.*					
Tetraniliprole (324)*						
ADI: 0–2 mg/kg bw ARfD: Unnecessary						

2. General considerations

2.1 Benefits and challenges to virtual JMPR meetings

The Meeting acknowledged the significant additional efforts made by the FAO and WHO secretariats to overcome challenges and logistical complexity for the 2021 JMPR meeting.

With restrictions still in place due to the ongoing COVID-19 pandemic, the 2021 JMPR was conducted in a virtual environment. As with the Extra 2021 Meeting, which was also held virtually, organizers needed to accommodate a 16-hour range in time zones for the individual experts. The meeting was originally scheduled for a two-week period, with meeting times set for three hours per day in an attempt to minimise unsocial hours across time zones, although that was frequently extended on an as-needed basis. At the end of the scheduled two-week period, additional discussion was needed on a number of topics, and two additional days were added. The follow-up meeting days were scheduled after a two-week break to allow participants time to advance the work under consideration.

Whereas the Extra Meeting focused on new uses, which did not involve establishing health-based guidance values or determining residue definitions, this Meeting focused on new compounds and compounds under the periodic review programme, for which more extensive reviews and discussions were required. The consideration of new compounds and those under periodic review are the most difficult and time-intensive topics that the JMPR handles as part of its regular business.

The WHO group has had positive experiences over the last 3 years in the use of virtual video/teleconference pre-meeting discussions and recognises their value as an additional tool to help streamline and enhance the efficiency of the physical meeting. The Meeting agreed that the virtual meeting format may be more beneficial for facilitating meeting planning and initiating pre-meeting discussions to advance decision making for certain topics than for conducting in-depth reviews of new compounds or periodic reviews. The Meeting noted the time commitments devoted to pre-meeting preparations and peer review even with the current reduced agenda were significant.

The Meeting agreed that there are some advantages to the virtual meeting format, including the absence of time lost in transit. While not aware of the details, the Meeting assumed that a virtual meeting can be accomplished at a lower financial cost to meeting organisers with a particular reduction in travel costs compared to an in-person meeting. The Meeting considered that this was at the expense of output, with the current Meeting considering 15 compounds on the agenda where 12 detailed evaluations were conducted for residues, toxicology or both, while for comparison a typical JMPR agenda would have in the region of 35 agenda items on average, so a significant reduction on a typical JMPR agenda[1]. It was recognised that there was increased pressure on meeting participants resulting in additional costs for individuals and (where relevant) their organisations to cover the additional time commitments.

The virtual meeting environment presented many challenges, including the need for adequate and mutually compatible IT resources (for individual experts and FAO/WHO), competing demands for expert's time and attention, limited time to discuss issues and reach consensus, lack of side discussions (e.g. over lunch), and in many cases significant personal sacrifice for experts needing to work outside of normal business hours. These aspects were noted by the 2021 Extra Meeting, which elaborated on these challenges in more detail[2].

The Meeting agreed that conducting business by a virtual meeting platform provides a realistic way to accomplish some aspects of the work that needs to be addressed and is better than not meeting

[1] Agenda items: JMPR 2019 (29), 2018 (38) and 2017 (38)

[2] Section 2.1 of the JOINT FAO/WHO Meeting on Pesticide Residues Summary Report Acceptable Daily Intakes, Acute Reference Doses, Residue Definitions, Recommended Maximum Residue Limits, Supervised Trials Median Residue values and other values recorded by the 2021 Extra Meeting 17–21 May and 7–11 June 2021; Issued July 2021; http://www.fao.org/3/cb5358en/cb5358en.pdf

when there are extraordinary circumstances that prevent an in-person meeting. Overall, however, the virtual format is not favourable to the efficient completion of much of the work of the JMPR, especially aspects requiring in depth scientific discussions involving a number of contributors. A comparison of the agenda for this Meeting versus other recent annual meetings clearly demonstrates the restricted amount of work that JMPR was able to complete via the virtual format. The Meeting reiterated the conclusion from the 2021 Extra Meeting that "*… continuation of the online-only meeting format is expected to give only limited benefits which overall are outweighed by counterproductive aspects which do not aid future JMPR decision making*."

2.2 International estimate of short-term intakes (IESTI) equations

The Joint FAO/WHO Meeting on Pesticide Residues (JMPR) derives acute dietary exposure estimates to carry out dietary risk assessments for compounds where an acute reference dose (ARfD) for a pesticide has been considered necessary and, since 1999, has used international estimate of short-term intake (IESTI) equations to make those estimates. Following its initial development, the methodology has been modified several times by the JMPR, but not all modifications have been adopted at a national level.

Following the EFSA/FAO/WHO workshop held in 2015 where modifications to the IESTI equations were discussed (EFSA 2015), the workshop outcomes were considered by the 2015 JMPR and a recommendation was made to CCPR that an FAO/WHO working group be established to compare results from the current and the proposed IESTI equations. In 2016, CCPR initiated an assessment of the IESTI equations in terms of their advantages, challenges, impact on risk management, consumer protection goals and trade. Four working papers on the IESTI equations have been considered by subsequent CCPR meetings. CCPR52 forwarded the most recent discussion paper (CCPR52 CX/PR 21/52/15) to the JMPR for consideration of the following topics:

- *Benefits/advantages and challenges* of *the current IESTI methodology* – consider a possible way forward to address the challenges identified in Table 2 of the discussion paper on issues that fall under the remit of JMPR.
- *Benchmarking of IESTI calculations against probabilistic exposure estimates* – consider comments submitted in response to CL 2021/42-PR and the final version of the acute probabilistic exposure assessment published in the paper by Crépet *et al* .(2021).
- *Review of the parameters of the IESTI equations: findings of FAO/WHO and published in peer reviewed literature* – discuss the need for developing further guidance on how to derive certain input values such as large portion, unit weight and the variability factor (LP, U, U_e, VF).
- *Information on bulking and blending relevant for IESTI Case 3* – The information should support discussions in JMPR to decide whether the list of commodities for which the exposure calculation is performed according to IESTI Case 3 needs to be revised.

Benefits/advantages and challenges of the current IESTI methodology

The CCPR working paper recognized the benefits of the current IESTI equation:

> *"they are transparent, easy to undertake, reproducible and use conservative assumptions that take national food consumption patterns into account. From a risk management perspective use of the IESTI equations provides a clear answer as to whether there is an expected risk of acute exposures to a pesticide residue exceeding the relevant ARfD due to consumption of specific commodities for which an MRL is recommended."*

The challenges identified were:

> *'the level of uncertainty in data for variables used in the IESTI equations, difficulties in risk communication and the fact that national MRLs may not be fully harmonised with Codex MRLs (CXLs)'.*

The 2019 JMPR considered the IESTI equations as appropriate and fit for the purpose of estimating acute dietary exposure as part of its evaluation of pesticide residues. The Meeting acknowledged that the quality of the input information could be improved. Changes to the IESTI equations proposed by different countries, such as the removal of the unit weight (U_e) parameter and use of the MRL as the residue level instead of the highest residue from the field trial data (HR), could be further considered by the JMPR, pending output from the proposed FAO/WHO working group described below.

Conservative assumptions are used in IESTI equations to ensure that all populations considered in the risk assessment are sufficiently protected. For pesticides with an ARfD, the IESTI is calculated separately for each pesticide residue/commodity combination where a maximum residue level is estimated by the JMPR. Selection of the appropriate IESTI equation (Cases 1, 2a, 2b, 3) depends on the unit weight of raw fruit or vegetable commodities, pesticide treatment (pre- or post-harvest) and the level of bulking and blending of the commodity premarket. These are simple deterministic calculations in that they utilize single data points for food consumption and pesticide residue concentration rather than distributional data, and information cannot be provided on the distribution of dietary exposures nor can the uncertainty of the exposure estimate be quantified (FAO/WHO 2020).

Benchmarking of IESTI calculations against probabilistic exposure estimates

To investigate the extent to which the current IESTI equations provide sufficient consumer protection, results from a separate FAO/WHO research study were considered. This study by Crépet *et al*. (2021) was undertaken to benchmark the IESTI equations against probabilistic acute exposure estimates. The Meeting noted that to date the CCPR, as risk managers, have not nominated a specific level of protection to be met in pesticide residue risk assessments undertaken by the JMPR.

Crépet et al. assessed acute dietary exposure to pesticide residues from all commodities likely to contain the residue by undertaking a probabilistic dietary exposure assessment. The study was based on national food consumption and residue monitoring data, which served as a second tier, 'real world' estimate of the actual acute dietary exposure. Forty-seven pesticides with Codex MRLs (CXLs), an ARfD and the same residue definition for enforcement and dietary risk assessment were initially selected for inclusion in the study. Acute dietary exposure estimates for adults and children in eight countries were reported for 38 pesticides with adequate residue monitoring data.

The aim of the study was not to provide a comprehensive assessment for countries in all regions. Crépet et al. demonstrated that it is possible to conduct a more refined acute dietary exposure assessment that incorporated contributions from all commodities containing the residue of interest, despite some of the food consumption data sets for the countries included being incomplete.

Crépet *et al.* (2021) indicated that the probability of acute dietary exposures exceeding the relevant ARfD was null for all countries and populations considered (whole population, consumers only at the 97.5th percentile of exposure), even with a very conservative scenario based on assumed 100% usage of each pesticide in all foods in which it was permitted for use. Based on the probabilistic acute risk assessment results, the study authors concluded there was no appreciable risk to the population of adults or children in the eight countries studied. The results of the benchmarking study are supported by previous research studies, for example a study using US EPA pesticide residue monitoring data (Cleveland *et al.* 2019), where the study authors concluded that:

> *"alternate methodology choices are not expected to impact the large margins observed between the probabilistic estimates and the IESTI equations or to change the overall conclusion that existing IESTI equations are conservative and health-protective."*

A level of protection (LoP) analysis was also performed in Crépet *et al.* (2021) using the same consumption data as for the acute dietary exposure estimates, but assuming that all food consumed contained pesticide residues at the Codex MRL for each of the 47 pesticides selected. The LoP was defined by the study authors as the percentage of person × days with acute exposure estimates from all food sources at or below the ARfD when the residue occurs at the level of the MRL, which is highly unlikely to occur. In this analysis the LoP was almost always 100%, with only a few exceptions for a small number

of age groups in some countries (see Table 5 in Crépet *et al.* 2021). The Meeting concluded that based on the very conservative assumptions used in the model, this would not constitute a public health concern.

The Meeting confirmed the 2019 JMPR conclusion that, based on the benchmarking study report, the current IESTI equations were considered protective for acute risk.

The Meeting noted that probabilistic estimates of acute dietary exposure would generally be used post-regulation to verify that pesticide standards such as the Codex MRLs are providing acceptable levels of consumer protection. The Meeting considered that it would be inappropriate to undertake probabilistic assessments pre-regulation because there are only limited analytical results available from supervised field trials.

Review of the parameters of the IESTI equations

In terms of providing guidance on input parameters for IESTI equations, the Meeting proposed an FAO/WHO expert group be established to ensure the most appropriate and scientifically robust input parameters (LP, U, VF) are used in IESTI assessments. This FAO/WHO expert group could, for example, discuss the following issues:

- Use of the LP_{bw} (g/kg body weight) calculated from single consumer day dietary records, expressed on an individual body weight basis rather than the LP (g/day) and generic body weight data.
- Determination of the minimum number of food consumption data points required for the derivation of a 97.5th percentile food consumption value with a 95th confidence interval for consumers of the commodity can be derived, noting research studies indicate that at least 120 data points are needed (Hamilton *et al*. 2004, EFSA 2014, Ambrus and Szenczi-Cseh 2017).
- Development of options for deriving the LP or LP_{bw} for infrequently consumed foods where the food consumption data do not support the derivation of a valid high-percentile consumption amount for a single food owing to a small data set (FAO/WHO, 2020).
- Confirmation of standard data formats for the submission of consumption and body weight data at an individual record level (rather than summary data) by countries to FAO/WHO, including details on how food consumption data for raw agricultural commodities have been derived from records of foods actually consumed.
- Development of agreed procedures for linking the food codes used in the WHO food consumption database (FoodEx2 food classification system) to the Codex food classification system, including use of recipes to disaggregate composite foods to ingredients, so that residue levels can be assigned in a consistent manner.
- Development of options for deriving and using unit weights of raw commodities, including exploration of the option of removing this parameter from the IESTI equations. In practice, as many countries do not submit unit weight data, the unit weight is often derived by JMPR from limited data for a few countries.
- Review of the available literature on residue variability in crops. JMPR currently supports the use of a single variability factor of three as it is based on a substantial amount of research data from a number of countries and pesticide applications in supervised trials that measured pesticide residues in single units in a number of different crops (Hamilton *et al*., 2004; EFSA 2015; Ambrus and Szenczi-Cseh 2017).

One of the modifications to the current IESTI equations outlined in the 2015 EFSA/WHO/FAO report was to replace the HR level with the proposed MRL, which would result in a more conservative estimate than using the HR. The Meeting acknowledged that the limited number of residue data points submitted in supervised trial studies contribute to a level of uncertainty in the HR variable. In contrast, the MRL takes into account the distribution of all selected field trial residue values as calculated by the OECD MRL calculator (OECD 2020). The Meeting noted that the overall impact of modifying several

parameters in the IESTI equations has been investigated in several studies (Breysse *et al*. 2018, Richter *et al*. 2018, van der Velde-Koerts *et al*. 2018). These indicate that using MRLs as the high residue level, in combination with other modifications, such as removing the unit weight parameter from the Case 2a equation, compensated each other numerically to some extent. Research into the impact of substituting the MRL for the STMR/STMR-P value in the IESTI Case 3 equation indicates that the current IESTI Case 3 equation makes a conservative assumption about the residue level in bulked and/or blended commodities, and is adequate for consumer protection purposes. Substituting the MRL for the STMR/STMR-P value would result in a potentially unnecessary and appreciable over-estimation of acute dietary exposure for these commodities (van der Velde-Koerts *et al*., 2018). The Meeting noted that the impact of changing the IESTI equation as outlined in the 2015 EFSA/WHO/FAO report would be larger for those compound/commodity combinations where the acute dietary exposure estimate approaches the level of the ARfD.

Information on bulking and blending relevant for IESTI Case 3

For assessing acute dietary exposure to pesticide residues in most commodities the JMPR uses the highest residue (HR) derived from residue studies. Exceptions to this are commodities that are: [1] treated pre-harvest and are sufficiently bulked and blended from multiple producers prior to consumption, and [2] processed commodities which are sufficiently bulked/blended prior to or during processing.

For these commodities, the use of a central-tendency residue level is more appropriate for assessing exposure, and the JMPR uses a median residue level (STMR or, for processed commodities, STMR-P). In 2018, CCPR50 agreed:

> *"to gather relevant information on bulking and blending, in order to feed into the risk assessors' work through the JMPR Secretariat"*

as part of ongoing work to evaluate the need for changes to the equations used to derive International estimated short-term intake (IESTI). Subsequently, CCPR52 (2021) agreed to provide:

> *"information on bulking and blending relevant for IESTI Case 3 […] to JMPR for further evaluation/consideration. The information should support discussions in JMPR to decide whether the list of commodities for which the exposure calculation is performed according to IESTI Case 3 needs to be revised".*

The Meeting welcomed the opportunity to review the data on bulking and blending and to incorporate any findings into its dietary risk assessment practices. However, only a listing of the available data was made available to the Meeting. This issue will be considered when the data have been provided to the JMPR.

Conclusion

The Meeting confirmed the 2019 JMPR conclusion that, on the basis of the probabilistic benchmark study of acute dietary exposures for high consumers (97.5th percentile of consumer-only exposure), the current IESTI equations used as part of JMPR risk assessments are fit for the purpose of ensuring consumer protection and provide confidence that adoption of recommended MRLs is not expected to result in a public health concern.

The Meeting noted that the modifications to the IESTI equations discussed at the 2015 EFSA/FAO/WHO meeting are not expected to change the conclusions of the risk assessment in terms of consumer protection, but introduce an additional degree of conservatism based on the benchmarking analysis. The Meeting further noted that the absence of quantitative consumer protection goals clearly formulated by CCPR does pose a challenge for determining the appropriate level of conservatism of the IESTI equation.

The Meeting proposed that FAO/WHO establish an expert working group to develop guidance that ensures the most appropriate and scientifically robust data for the input parameters is available for use in IESTI equations, and to further consider the impact of possible modifications to the IESTI equations in relation to the unit weight and residue level parameters.

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2.3 First considerations on a possible need for amendments to EHC 240 guidance on appropriate use of toxicological historical control data (HCD)

The meeting discussed a fundamental set of principles that, it was proposed, needed to be established before guidance for harmonized use of HCD could be drafted. Among other things, the discussions pointed to the need for a detailed delineation of the possible causes of study-to-study variability, which may be due to different study conditions and thus different influencing factors. Based on such a consolidated cause–effect analysis, criteria should be developed that enable decisions regarding in which circumstances and for which endpoints the use of HCD can serve as a basis for assessment, and the

circumstances/endpoints where it cannot.

The Meeting was informed about an ongoing project launched by the European Food Safety Authority (EFSA; scheduled to last until Autumn 2022), the aim of which is to collate all relevant information on stakeholder experience, knowledge and understanding of the use and interpretation of HCD when evaluating toxicity studies. The FAO/WHO Joint Meeting on Pesticide Residues (JMPR), as one of the relevant stakeholders, will be approached to participate in the planned survey and in the workshop, to be held in Spring 2022.

It was agreed that that the JMPR will actively participate in the above mentioned survey and the workshop, and that the possibility of developing JMPR Guidance on HCD would be discussed at the next Meeting, taking into account progress of the EFSA project.

2.4 Guidance on the assessment and interpretation of non-linear dispositional kinetics

Following the recommendation of the 2019 Joint FAO/WHO Meeting on Pesticide Residues (JMPR), the Joint Secretariat convened a group of experts to undertake preparatory work for the development of a guidance on the assessment and interpretation of non-linear dispositional kinetics (the kinetically derived maximum dose; KMD)-based evaluation of pesticide residues.

In guideline toxicology studies, chemicals (including pesticides) are evaluated using a dose-selection protocol that includes either a maximum tolerated dose (MTD) or a limit dose, designed to maximize the detection of any toxicity due to the treatment , observed in experimental. The introduction of concurrent in-life toxicokinetics into repeat-dose studies has revealed that in toxicity studies the dispositional kinetics at high dose levels may exhibit dose-related non-linearity. Information derived at such dose levels may be less useful, more difficult to interpret in relation to human exposures to chemicals, and may not be compatible with modern animal welfare considerations.

Non-linear kinetics can result from the saturation of absorption, distribution, metabolism or excretion, or any combination of such saturations. Adding to this complexity, non-linear kinetics can apply to the parent, its metabolites or both.

The KMD approach, which is based on evidence of dose-associated dispositional non-linear kinetics (dose non-proportionality), is now being used by sponsors as an alternative to the MTD approach for setting the dose range and top dose in animal toxicity studies. The KMD approach is likely to contribute particularly to the evaluation of the carcinogenicity observed at high doses and the results of teratogenicity studies conducted using oral gavage. As a result, the Meeting agreed that guidance on the integration of the KMD approach into JMPR evaluations is needed, and that such guidance should not focus specifically on KMD but more generally on the interpretation of non-linearity in the dispositional kinetics of pesticides.

Such guidance on the interpretation of toxicology studies is needed to increase the scientific quality, consistency and transparency of JMPR assessments. Currently it is proposed that any guidance on these issues should focus on JMPR's terms of reference, which relate to the risks from residues of pesticides in food, rather than hazard classification. A partial list of questions that the proposed guidance could consider includes:

- How should non-linearity be interpreted and evaluated?
- What is the minimum data base need to sufficiently evaluate issues pertaining to non-linearity?
- Does the presence of non-linearity sufficiently justify not investigating the effect of higher doses, and should the proposed electronic working group recommend a cut-off based on the occurrence of non-linear kinetics?
- Should non-linear absorption, non-linear target tissue exposure and other non-linear events be considered separately?

- Can guidance be provided on the design and interpretation of in vitro evidence of non-linearity in kinetic processes?

The Meeting agreed the composition of an Electronic Working Group and charged the group to prepare draft guidance for discussion at a future JMPR meeting.

2.5 Recommendations for use of leafy vegetables to extrapolate residues to the Subgroup 027A Herbs (herbaceous plants).

Some delegations at the Fifty-second Session of the CCPR expressed concerns that the 2019 JMPR had utilised residues in mustard greens to extrapolate to herbs rather than using leaf lettuce and spinach, the representative commodities recommended by CCPR in "Principles and Guidance on the Selection of Representative Commodities for the Extrapolation of Maximum Residue Limits for Pesticides to Commodity Groups (CXG 84-2012)".

The Meeting recalled that CXG 84-2012 allows for the use of alternative representative commodities provided these can be justified. The following provides the justification used by the JMPR in selecting mustard greens to extrapolate residues to the Sub-group 027A Herbs.

The principles used for the selection of representative commodities listed in CXG 84-2012 are:

- A representative commodity is most likely to contain the highest residues.
- A representative commodity is likely to be major in terms of production and/or consumption.
- A representative commodity is most likely similar in morphology, growth habit, pest problems and edible portion to the related commodities within a group or subgroup.

To provide an evidence-based justification for extrapolation, a review was conducted of the residue potential of crops in the Subgroup 027A, Herbs (herbaceous plants).

Residues of foliar applied pesticides are to a large extent governed by the initial spray deposits which in turn depend on a number of plant parameters including the relative surface area of the leaves and stems, the wettability of the leaf surfaces (waxy surface versus hairy surface etc.) as well as crop morphology.

Residues on the day of application of foliar sprays provide a good indication of relative residue potential for different commodities, with the ranking of residue potential largely preserved with increasing time after application even with relative differences in growth dilution within a group or subgroup and the potential impact on residues at longer post-application intervals.

A measure of the initial spray deposits can be gained by collating residue levels in the commodities on the day of application following a single spray. To expand the database, the Meeting considered that data from trials where more than one spray had been applied could be used provided there was sufficient evidence to conclude that the earlier spray did not contribute significantly to the observed residue. The Meeting utilised JMPR evaluations in the period 1993 to 2019 and supplemented these with other publicly available information such as published scientific papers and EU draft Assessment Reports to assemble a database of initial residue levels normalised to an application rate of 1 kg ai/ha.

As only a small number of trials were located, where decline information was available this was used to correct for the contribution to the terminal residue (day 0) from earlier sprays and thus further expand the database.

A summary of the initial residue deposits for the different commodities is shown in Figure 1 in the form of box-plots. The boxes cover 50% of values (25^{th} to 75^{th} percentiles) while the whiskers cover 95% of values with the median represented by the dark horizontal lines.

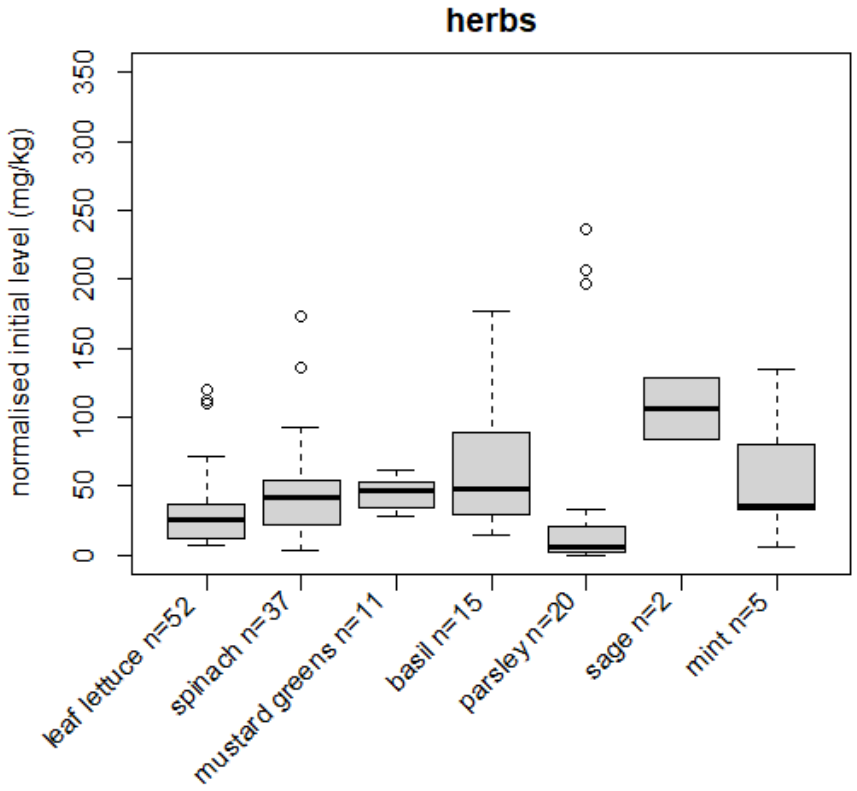

Figure 1 Initial residue (normalised to an application rate of 1 kg ai/ha) for herbs and for leaf lettuce, spinach and mustard greens

Table 1 provides a summary of the mean and median normalised residues observed for each crop.

Table 1 Day-0 residues normalised for application rate

Commodity	n	Median (mg/kg)	Mean (mg/kg)
Basil	15	47.9	64.5
Mint	5	36.3	58.0
Parsley	20	5.7	38.5
Sage	2	-	106
Leaf lettuce	52	26.4	31.3
Spinach	37	42.0	46.5
Mustard greens	11	46.9	44.9

Basil: clethodim[20], cyazofamid[14], lambda-cyhalothrin[14], oxathiapiprolin[15], spirotetramat[20]

Mint: abamectin[15], clethodim[20], spirotetramat[20]

Parsley: acetamiprid[2], azoxystrobin[19], chlorpyrifos-methyl[18], cypermethrin[19], deltamethrin[19], difenoconazole[19], dimethoate[18], imidacloprid[2], iprodione[18], lambda-cyhalothrin[19], metalaxyl-M[18,19], permethrin[18], pirimicarb[19], propargite[18], spinosad[19], spirotetramat[21], tebuconazole[19], thiacloprid[19]

Sage: clethodim[20], spirotetramat[20]

Leaf lettuce: beta-cypermethrin[23], butocarboxin[3], chlorantraniliprole[11], chlorothalonil[23], chlorpyrifos[22,23], cyantraniliprole[13], alpha-cypermethrin[11], zeta-cypermethrin[11], deltamethrin[23], dimethoate[6,11,23], fluopyram[12], iprodione[5], pirimicarb[10], thiamethoxam[12], trichlorfon[23]

Mustard greens: Spinosad[8], thiamethoxam[12]

Spinach: chlorantraniliprole[11], chlorpyrifos[17], alpha-cypermethrin[11], deltamethrin[9], diazinon[4], dimethoate[6], fluazifop-P-butyl[17], lambda-cyhalothrin[17], metalaxyl[17], methomyl[8], mevinphos[7], thiamethoxam[12], thiophanate-methyl[16]

Normalised day-0 residues for single residue trials on coriander[1], dill[1], marjoram[24] and thyme[24] were 13.4, 21.1, 43.6 and 51.2 mg/kg, respectively.

The available trials on basil, parsley, sage and mint demonstrate that residue levels in herbs from Subgroup 027A are closer to those of mustard greens than those of leaf lettuce. The Meeting confirmed that mustard greens and spinach are suitable representative crops for extrapolation from a leafy vegetable to Subgroup 027A Herbs.

The JMPR encourages the CCPR and its members to consider the above evidence-based approach in the selection of representative crops for establishing MRLs.

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3. Responses to specific concerns raised by the Codex Committee on Pesticide Residues (CCPR)

3.1 Afidopyropen (312)

Concern #1 – On the inclusion of M007 in the residue definition of risk assessment of plant commodities

Background

Afidopyropen was evaluated as a new compound by the 2019 JMPR for toxicity and residues.

The following residue definitions were established for afidopyropen in plant commodities:

For compliance with the MRL: *afidopyropen*

For dietary risk assessment: *sum of afidopyropen + M007, expressed as afidopyropen.*

The toxicity of the dimer M440I007 (M007) was evaluated by the 2019 JMPR. It was concluded that "*The dimer was not considered to be of greater toxicity than the parent. The ADI and ARfD cover both parent and the dimer*."

The current Meeting received a concern form from the Delegation of the United States of America (USA), relating to the residue definition for dietary risk assessment for plant commodities. The delegation noted that addition of M440I007 in the risk assessment definition does not reflect the known significantly lower toxicity of the M440I007 metabolite; it is very conservative to add the parent and M440I007 metabolite and then assess against the parent health-based guidance values (especially for the ARfD, where there is no evidence of acute toxicity). A clearer explanation addressing this point was requested from the JMPR.

Comments by the JMPR

Despite the claim from the manufacturer that this metabolite is less toxic than the parent, the WHO concluded that M007 is "of similar toxicity" to the parent. The WHO based this conclusion on the common finding of changes in the myocardium. These changes were also seen at the highest dose tested in the short-term study with M007, but the authors didn't do a histopathological assessment of the lower doses. Consequently, the WHO could not establish whether this effect did not occur at lower levels and subsequently could only conclude that M007 is "of similar toxicity". No new information on the toxicity of

the dimer was provided to the current Meeting with the concern form.

The dimer is not observed in the rat metabolism and as such, the toxicity of the dimer is not "covered by parent". NOAELs/LOAELs for parent (in mg/kg bw) and for M007 (in mg/kg bw) for the critical effects are very close (same effect at the same dose). Since in this case both parent and the dimer are of similar toxicity (in terms of dose per kg bw), the dimer does not need to be normalized to parent equivalents as is usually done for metabolites that are covered by parent.

As such, the residue definition proposed by the 2019 JMPR as "S*um of afidopyropen + M007, expressed as afidopyropen"* was imprecise and should have been "S*um of afidopyropen + M007*". In this case, stoichiometric correction to parent compound equivalents (× 2) and for molecular weight (× 0.5) would result in an overall factor of 1 and lead to a simple summation of residue concentrations.

The toxicity data provided on the dimer M007 are insufficient to conclude that it is of lower toxicity than the parent. To justify the use of a lowering potency factor or even exclusion of the dimer from the residue definition, supportive data are needed. A histopathological examination of the relevant (myocardial) tissues for the mid and low-dose groups could prove that M007 is "of less toxicity". The manufacturer is kindly asked to submit this data.

The Meeting decided to rephrase the residue definition for dietary risk assessment for plant commodities to *the sum of afidopyropen + dimer of [(3R,6R,6aR,12S,12bR)-3-[(cyclopropanecarbonyl)oxy]-6,12-dihydroxy-4,6a,12b-trimethyl-11-oxo-9-(pyridin-3-yl)-1,3,4,4a,5,6,6a,12,12a,12b-decahydro-2H,11H-naphtho[2,1-b]pyrano[3,4-e]pyran-4-yl]methyl rac-cyclopropanecarboxylate (M007)*.

The change in the residue definition for dietary risk assessment does not impact the previous estimates of dietary exposure calculated by the 2019 JMPR because in the previous evaluation the residue concentrations were added without further adjustment in agreement with the corrected expression of the definition.

Concern #2 – On the low MRL for milk

Background

A second concern was raised by the Delegation of the USA regarding the very low maximum residue level recommendation drafted for milk at 0.001 mg/kg. It was indicated that, though supported by current methods, this value is very low for practical monitoring in trade. A typical default of 0.01* mg/kg would be better harmonized with enforcement practices and more useful to the international trading community and it was recommended that this 0.01* mg/kg CXL value, be used instead.

Response of the JMPR

The JMPR acknowledges that the maximum residue level for milk is low but is indeed supported by current analytical methods. Furthermore, the use of (very) low maximum residue levels in milk is observed for many other active substances. The JMPR always recommends maximum residue levels based on expected residues in food or feed commodities and the technical capabilities of validated analytical methodologies.

3.2 Benomyl (069), carbendazim (072), thiophanate-methyl (077)

The Delegation of the European Union (EU) submitted a concern form at the Fifty-second CCPR relating to benomyl, carbendazim and thiophanate-methyl is in reference to these substances' status in terms of priority listing and scheduling for periodic review by the JMPR. The JMPR acknowledges receipt of the concern form, however, priority listing and scheduling is the responsibility of the CCPR. The JMPR refers this matter to the CCPR for resolution.

3.3 Chlorothalonil (081)

Concern #1 Concern was raised by the European Union (EU)

A potential public health concern was raised by the European Union (EU) about a number of metabolites of chlorothalonil which meant the consumer risk assessment could not be finalized and new toxicological studies had been submitted to the EU which had not been evaluated by JMPR. According to an evaluation by the European Food Safety Authority (EFSA) published in 2018, the specific concerns related to:

- EFSA was unable to conclude on toxicological reference values for metabolite R182281 (SDS-3701), there being concerns over potential genotoxicity;
- Metabolite R613636 was formed under processing conditions and genotoxic potential could not be excluded by EFSA;
- Metabolite R417888, a soil metabolite, had not been investigated in rotational crop residue trials and genotoxic potential could not be excluded by EFSA.

The EU has set an ARfD for chlorothalonil of 0.05 mg/kg body weight (bw) per day based on body weight loss at the start of dosing at 10 mg/kg bw per day in a study of developmental toxicity in rabbits. The previous EU ARfD was 0.6 mg/kg bw per day.

JMPR last reviewed chlorothalonil for toxicology in 2009, establishing an ADI of 0–0.02 mg/kg bw based on the NOAEL for kidney toxicity in a two-year study in rats, and an ARfD of 0.6 mg/kg bw, based on the NOAEL for kidney toxicity in acute toxicity studies in rats.

In addition, the 2010 JMPR evaluated data on soil metabolite R611965 and concluded it was of lower toxicity than chlorothalonil and covered by the ADI and ARfD for chlorothalonil.

In the 2019 Extra JMPR the dietary risk from metabolites R613636 and R417888 was considered.

The EU concern form does not identify the types of new toxicological studies submitted, nor whether they had identified effects critical to the consumer risk assessment that were not covered by the existing database. As the new EU ADI and ARfD are based on studies evaluated previously by JMPR, it appears unlikely that the new toxicology studies would be critical to the consumer risk assessment.

Regarding the specific concerns:

The 2009 JMPR evaluated an extensive database on SDS-3701 concluding that it was more toxic than chlorothalonil and established an ADI of 0–0.008 mg/kg bw and an ARfD of 0.03 mg/kg bw. A positive result in an in vitro chromosomal aberration study was not confirmed in vivo and the Meeting concluded that SDS-3701 was not genotoxic.

The 2019 Extra JMPR considered genotoxicity data and data on the formation of R613636. Results were negative in two gene mutation tests. Although a positive response was found in the chromosomal aberration test R613636 was negative for genotoxicity in an in vivo mouse micronucleus test. The Meeting concluded that R613636 was unlikely to be genotoxic in vivo and could be assessed using the TTC approach in Cramer class III.

Metabolite R613636 was primarily found in processed foods and is formed from parent chlorothalonil during sterilization at 120 °C (but not during pasteurization or cooking). The metabolite was assessed under the TTC approach as a Cramer class III compound. Since the current international estimated dietary intake (IEDI) model does not sufficiently address the percentage of processed foods in the daily diet, a conservative approach was selected by multiplying the maximum IEDI of 9.3 µg/kg bw for parent chlorothalonil by a factor of 0.23 (representing the percentage of total radioactive residues [TRR] recovered as R613636 in simulated hydrolysis studies). In the absence of more detailed data on the consumption of sterilized foods, the Meeting decided that the gap between the

maximum IEDI for R613636 of 2.37 µg/kg bw and the Cramer class III threshold of 1.5 µg/kg bw is small and it would be very unlikely that the majority of foods (> 50%) would be subject to sterilization treatment.

The 2021 Meeting concluded that R613636 is unlikely to present a public health concern.

The 2019 Extra JMPR Meeting considered genotoxicity, toxicity and formation data on R417888. It gave a positive response in the chromosomal aberration assay without metabolic activation and in one mouse lymphoma assay with metabolic activation, but it was negative in a repeat mouse lymphoma assay at higher concentrations. R417888 was negative for genotoxicity in vivo in a mouse micronucleus test and for unscheduled DNA synthesis. The Meeting concluded R417888 was unlikely to be genotoxic in vivo and would be covered by the ARfD and ADI of chlorothalonil because of its lower acute and repeat-dose toxicity in comparison with the parent compound.

Metabolite R417888 was not identified in the residue data package received by the Meeting for the last periodic review. It was noticed that in the EU re-assessment report an additional confined rotational crop study by Rizzo was described, showing residues for "metabolites R611965 and R417888, accounting for 59%, 66% and 51% TRR for the 30, 120 and 365 plant-back intervals" in carrot roots. However, both compound co-eluted in the thin-layer chromatography (TLC) system used, and specific analysis revealed that "the majority of the residue was due to metabolite R611965 (51% TRR, 0.14 mg/kg)" in the 30-days sample. The toxicity of R611965 itself was also considered by the JMPR 2019 Extra Meeting, which concluded that "it would be covered by the ADI and ARfD of chlorothalonil, but noted that it is at least 10 times less potent than chlorothalonil." Consequently, the relevance of R417888 to consumer exposure was considered low. Although the data on R417888 were missing, its potentially small contribution to the TRR in rotational crops also suggests low significance for consumer exposure.

The JMPR 2009 monograph cites body weight loss at 20 mg/kg bw per day as the basis for the NOAEL in the rabbit study, used by the EU to derive its ARfD, but JMPR did not consider this finding applicable to the derivation of the ARfD.

The Meeting concluded that, based on the information presented in the EU documentation, the potential public health concerns raised by the EU over dietary exposures to chlorothalonil and its metabolites had not been substantiated and that they did not merit any review in advance of the normal periodic review.

Concern #2 Concern raised by the United Kingdom acute intake assessment for the metabolite R613636 in cranberry

Background

Chlorothalonil was reviewed by the JMPR in 2009 (T) and 2010 (T, R) within the periodic review program and evaluated for an additional use in cranberry at the 2019 Extra JMPR. The 2010 Meeting identified a hydrolysis product, R613636, that formed primarily during conditions simulating sterilisation (pH 6, 120 °C, 20 minutes; approximately 23% of total residue), with lesser amounts formed during conditions similar to baking, brewing, and boiling (pH 5, 100 °C, 60 minutes; approximately 3.4% of total residue). Furthermore, the 2010 Meeting noted that temperature, and not pH, appears to be the key variable in the formation of R613636.

The United Kingdom submitted a concern form at the Fifty-second CCPR stating that the exposure estimated for R613636 from cranberry exceeded the threshold of toxicological concern for Cramer class III, that the overall chronic exposure to R613636 from all commodities had not been addressed, and that the acute exposure to R613636 from cranberry had not been addressed.

Comment by the JMPR

The 2019 Extra Meeting agreed that R613636 could be assessed using the TTC approach as a Cramer Class III compound (1.5 µg/kg per day). As the consumption data within the IEDI model used to assess long-term dietary exposure does not allow specifically for assessment of sterilised foods, the Meeting

decided to apply the factor of 0.23 to the maximum IEDI of 9.33 µg/kg bw for chlorothalonil to assess exposure to R613636. The estimated exposure was 2.37 µg/kg bw. While this estimate is greater than the threshold of 1.5 µg/kg per day, the Meeting noted that the estimate assumes that all foods are sterilised, and that it is very unlikely that all foods would be subjected to such high-temperature (120°C) treatment. The 2019 Extra Meeting concluded that long-term exposure to R613636 was unlikely to present a public health concern.

The current Meeting received processing studies on barley, wheat grain, cabbage, beans with pod (*Phaseolus vulgaris*) and tomato that include analysis for R613636. A cursory review of the results indicates that in all cases, residues of R613636 in processed commodities subject to heating were < 0.01 mg/kg and that overall it was only observed in one sample of wheat germ at 0.02 mg/kg. As the IEDI inputs for parent chlorothalonil were generally much greater than 0.02 mg/kg, it is likely that the new data will result in a much lower exposure estimate than was made by the 2019 Extra Meeting; however, time and resource constraints did not allow for a full evaluation of the data by the current Meeting. The Meeting agreed to evaluate the new data on processed commodities and to re-assess exposure to R613636 at its next meeting.

With regard to acute exposure to R613636 in cranberry juice, the 2019 Extra Meeting, in keeping with then-current practice, did not make an acute assessment by TTC due to lack of an agreed-upon threshold for assessing acute exposure. The current Meeting examined the acute exposure to R613636 in cranberry juice. The STMR and HR for cranberry are 3.0 and 7.7 mg/kg, respectively. A processing study on cranberry was not available. The Meeting agreed to apply the processing factors of 0.14 for unpasteurised grape juice and 0.26 for raisins (2010 JMPR) to derive estimates for cranberry juice and dried cranberry, respectively. As no processing factors were available to refine residue estimates for other processed cranberry commodities, the Meeting used the STMR/HR from the RAC. Residue estimates of chlorothalonil for all processed commodities were then adjusted to R613636 using the factor of 0.23 discussed above. Residues of R613636 used in the acute assessment for cranberry were: raw with skin, 0 mg/kg; canned/preserved, 1.77 mg/kg (7.7 mg/kg × 0.23); dried, 0.46 mg/kg (7.7 mg/kg × 0.26 × 0.23); juice, 0.0966 mg/kg (3 mg/kg × 0.14 × 0.23); jam, sauce/puree, and unspecified processed, 0.69 mg/kg (3 mg/kg × 0.23). The Meeting noted that (1) none of the processed cranberry commodities experience conditions similar to sterilisation; therefore, these are very conservative estimates and (2) the new data on residues of R613636 will likely support lower estimates than those calculated above.

The resulting maximum IESTI for cranberry (all commodities) was 3.51 µg/kg bw. A single-exposure TTC for Cramer class III compounds of 5 µg/kg bw was proposed by the European Food Safety Authority (EFSA 2012). The Meeting considered that this is precautionary and appropriate for use in assessing acute intakes of R613636. As a result, the acute exposure to R613636 in cranberry commodities is not expected to be a public health concern.

References

EFSA (2012). Scientific opinion on the evaluation of the toxicological relevance of pesticide metabolites for dietary risk assessment. EFSA Panel on Plant Protection Products and their Residues (PPR). *EFSA J*., 10(7):2799 [187 pp.]. doi:10.2903/j.efsa.2012.2799.

3.4 Chlorpyrifos (017) and Chlorpyrifos-methyl (090)

Chlorpyrifos

A potential public health concern was raised by the European Union (EU) about the potential for chlorpyrifos to be genotoxic, damage DNA and affect neurodevelopment in children. Based on a statement published in 2019 by the European Food Safety Authority (EFSA), the concern form was triggered by studies in the published literature and new evaluations of an unpublished developmental neurotoxicity study. The concern form noted that the last JMPR review of chlorpyrifos for toxicology was in 1999.

The 2019 JMPR Meeting had been aware of the availability of new information on chlorpyrifos and the outcomes of the EFSA review (see Section 2.6 of the JMPR 2019 Report). The 2019 Meeting strongly recommended that given the 20-year gap since chlorpyrifos was last reviewed by the JMPR and the magnitude of potential concerns identified by the EU, chlorpyrifos be prioritized for periodic re-evaluation. It was noted that aspects of epidemiology should be included.

Given the concerns identified by the 2019 JMPR the current Meeting urged that chlorpyrifos should be re-evaluated as soon as possible. It was noted that findings from recent epidemiology studies would need to be assessed. The Meeting noted that CCPR has scheduled chlorpyrifos and chlorpyrifos-methyl for periodic evaluation by the 2024 JMPR.

The JMPR Joint Secretariats are currently investigating the most efficient ways to re-evaluate chlorpyrifos and chlorpyrifos-methyl for toxicology and residues, taking into account the size and complexity of their dossiers, and the aspects they have in common.

Chlorpyrifos-methyl

A potential public health concern was raised by the European Union (EU) about the potential for chlorpyrifos-methyl to be genotoxic, damage DNA and affect neurodevelopment in children. Based on a statement published in 2019 by the European Food Safety Authority (EFSA), the concern form was triggered by studies in the published literature and findings in the developmental neurotoxicity studies with chlorpyrifos-methyl and the closely related compound chlorpyrifos. The concern form noted that the last JMPR review of chlorpyrifos-methyl for toxicology was in 2001.

The Meeting noted that CCPR has scheduled chlorpyrifos and chlorpyrifos-methyl for periodic evaluation by the 2024 JMPR. The JMPR Joint Secretariats are currently investigating the most efficient ways to re-evaluate chlorpyrifos and chlorpyrifos-methyl for toxicology and residues, taking into account the size and complexity of their dossiers, and the aspects they have in common.

3.5 Fluensulfone (265)

Background

Fluensulfone was evaluated by the 2019 JMPR for additional uses in a range of commodities, including pome fruit and citrus.

The current Meeting received a concern form from the Delegation of the USA, relating to the proposed maximum residue level for pome fruit and also on the decision not to calculate a processing factor for citrus juice.

For pome fruit, the Delegation of the USA advised that in one of the pear trials used for estimating the maximum residue level, the reported residue values were incorrect, and that based on the corrected values, a higher maximum residue limit should be estimated.

For citrus juice, the Delegation of the USA proposed that since detectable residues of the BSA metabolite of fluensulfone were present in orange juice, processing factors for total residues (parent plus BSA) could be calculated from the two processing studies, and since the higher of these factors was very similar to that calculated for apple juice, the apple juice processing factor should be considered the appropriate processing factor for calculating the MRL for citrus/orange juice.

Comments by the JMPR

Pome fruit

For pome fruit, the 2019 JMPR estimated a maximum residue level of 0.2 mg/kg for fluensulfone (sum of fluensulfone + BSA metabolite, expressed as fluensulfone) in pome fruit (except persimmon,

Japanese) based on the residues reported in 16 trials on apples and 8 trials on pears matching the critical GAP (USA) for a pre-flowering soil application of 3.92 kg ai/treated ha (broadcast, banded or by chemigation).

The current Meeting reviewed the study reports of the pome fruit residue trials and confirmed that in one of the pear trials (Ref: R-35572: PR-WA), there was a transcription error in the 2019 Fluensulfone Evaluation Table 13. The corrected values (after rounding) for this trial are reported below and the residue selected for maximum residue level estimation is underlined:

Table 1: Residues in pear trial Ref: R-35572: PR-WA

POME FRUIT Country, Year Location (variety) Reference	Application				DALA	Matrix	Residues, mg/kg [mean]		
	No.	Type	Kg ai/ treated ha	Water (L/ha)			Fluensulfone	BSA	Total [a]
GAP: USA	2	Chemi gation	3.92		Up to flower bud swell and/or after harvest (max 3.92 kg ai/ha/year)				
PEAR									
USA, 2015 Ephrata, WA (D'Anjou) R-35572	1	Band spray	4.00	18947	114	Pear	ND, ND [ND]	0.13, 0.15 [0.14]	0.2, 0.24 [0.22]
					121 (NCH)		ND, ND [ND]	0.13, 0.14 [0.13]	0.21, 0.22 [0.21]
					128		ND, ND [ND]	0.14, 0.13 [0.13]	0.22, 0.21 [0.22]
					135		ND, ND [ND]	0.11, 0.12 [0.12]	0.18, 0.2 [0.19]

ND = <0.003 mg/kg, with a value of 0.01 mg/kg used for calculating Total residues and a value of 0 mg/kg used for dietary exposure estimation

[a] Total residues, expressed as parent = Sum of fluensulfone + (BSA×1.53) mg/kg.

The corrected data sets for <u>total residues</u> in apples and pears from trials matching the critical GAP for fluensulfone on pome fruit are:

Apples: < 0.025 (10), 0.028 (3), 0.031, 0.037 and 0.16 mg/kg (n = 16)

Pears: < 0.025 (4), 0.026, 0.11, 0.17 and 0.22 mg/kg (n = 8).

Noting that the residues arising from early season soil applications to apple and pear trees were not statistically different (Kruskal-Wallis), the Meeting agreed to estimate a group maximum residue level based on a combined total residue data set of: < 0.025 (14), 0.026, 0.028 (3), 0.031, 0.037, 0.11, 0.16, 0.17, and 0.22 mg/kg (n = 24). Corresponding residues of fluensulfone (parent only) were all below the detection limit.

The Meeting estimated a maximum residue level of 0.3 mg/kg for fluensulfone (fluensulfone+BSA metabolite), an STMR of 0 mg/kg and an HR of 0 mg/kg for fluensulfone (parent only) in pome fruit (except persimmon, Japanese) to replace the previous recommendation.

Because the STMR and the HR remain unchanged, no refinement of the dietary exposure estimation was needed. Based on the 2019 JMPR conclusion that any uptake of the metabolite MeS from permanent crops would be insignificant, the current Meeting considered it unnecessary to revisit the Cramer class III TTC assessment for MeS (2-Methylsulfonylthiazole).

Citrus juice

For citrus juice, the 2019 JMPR reviewed the two citrus processing studies evaluated by the 2017 JMPR, where fluensulfone was applied as a soil-irrigated treatment matching the critical GAP but at an exaggerated (2×) rate of 8.1 kg ai/ha and agreed that since fluensulfone residues were not detected in whole fruit (RAC), processing factors could not be calculated.

The current Meeting noted that for apple, plum and grape commodities, where fluensulfone residues were also not detectable in the RAC or the processed commodities, fluensulfone residues in fruit from field trials matching GAP were also <LOQ, and the processing studies reflecting this 'no parent residue' situation were able to be used to estimate processing factors based on the transfer of the BSA metabolite residues.

However, for citrus, since measurable residues of fluensulfone (up to about 0.05 mg/kg) were observed in supervised field trials matching GAP, the citrus processing studies were not suitable for estimating processing factors as they did not address the behaviour of fluensulfone during processing.

The Meeting confirmed the 2019 JMPR conclusion that a processing factor for citrus juice could not be calculated.

3.6 Metconazole (313)

Background

Metconazole was evaluated as a new compound by the 2019 JMPR and maximum residue levels were estimated for a range of commodities. In evaluating metconazole residues in wheat, the 2019 JMPR concluded that no maximum residue level could be estimated due to an insufficient number of trials matching the GAP with regards to the PHI.

The current Meeting received a concern raised by the Delegation of the USA that only four residue trials with pre-harvest intervals (PHIs) longer than 21 days were considered to approximate the GAP PHI of 30 days ± 25%, despite PHIs in most of the trials being 20–22 days. It was noted that the 2019 JMPR applied a tolerance of ± 25% to the PHI parameter itself, rather than the expected residue concentrations.

Comments by the JMPR

The current Meeting re-evaluated the decline trials for wheat, as well as for rye, barley and oat. For wheat, two decline trials were provided. The first trial (R05047) did not show a typical decline pattern and was considered inconclusive. However, the second trial (R05050) showed declining residues. The decline rate was estimated by using 14 DALT data as the starting point following normalisation. Wheat samples taken at 19 DALT or later are not expected to result in a greater than 25% change in the residue concentration compared to the label PHI of 30 days. In addition, with consideration of decline trials for rye (R05147), barley (R05156) and oat (R05132), the mean relative decline showed that a ± 25% change in the residue concentration is not expected for samples collected between 12 and 48 DALT (Figure 1).

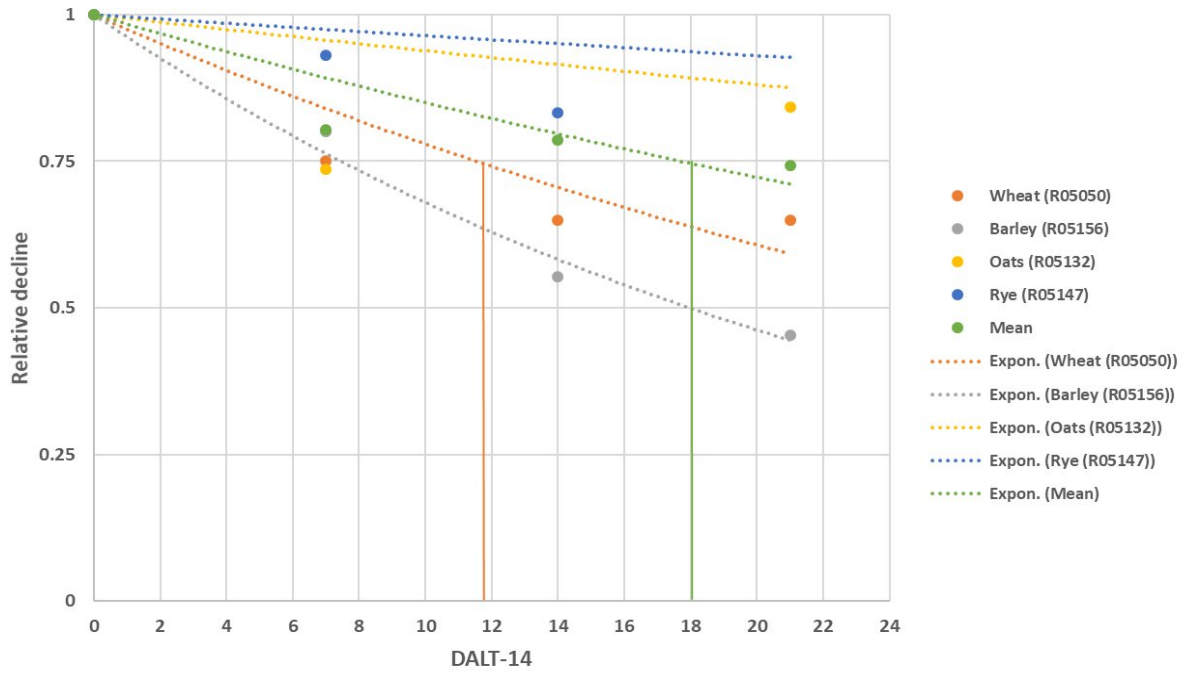

Figure 1 Relative decline of metconazole in wheat, barley, oat and rye

The Meeting noted that the expected change in residue concentration is less than 25% for samples taken at PHIs of 20–22 days compared to the 30-day label PHI and decided to use these trials to estimate a maximum residue level for wheat.

The ranked order of residues in wheat following applications of metconazole approximating the GAP, for estimating maximum residue levels and dietary risk assessment, were (n = 15): 0.011, 0.013, 0.015, 0.019, 0.023, 0.027, 0.028, 0.035, 0.036, 0.040, 0.048, 0.051, 0.054, 0.094, and 0.096 mg/kg.

The Meeting estimated a maximum residue level of 0.15 mg/kg and an STMR of 0.035 mg/kg for metconazole in wheat and decided to extrapolate its recommendation to triticale.

The fate of metconazole residues has been examined under conditions simulating household and commercial processing of wheat. These trials were evaluated by the 2019 JMPR. Estimated processing factors for the commodities considered at this Meeting are summarised below.

Table 1 Estimated processing factors for maximum residue level and dietary exposure estimations for processed wheat commodities according to the residue definition metconazole (sum of cis and trans isomer)

Crop	Residue (mg/kg) in RAC			Processed commodity	Individual PF	Median or best estimate PF	Residue (mg/kg) in processed commodity		
	MRL	STMR	HR				MRL-P	STMR-P	HR-P
Wheat	0.15	0.035	-	Coarse bran	1.6, 1.8, 2.0, 2.1	1.9	0.3	0.067	
			-	Whole meal flour	0.39, 0.60, 0.88, 0.91	0.74	-	0.026	
			-	Flour	0.18, 0.21, 0.24, 0.42	0.23	-	0.008	
			-	Germ	0.64, 0.92, 1.1, 1.2	1.0	-	0.035	
			-	Bread	0.44, 0.58, 0.63, 0.70	0.61	-	0.021	-

The addition of wheat, triticale and their processed commodities that may be used as animal feed items did not significantly change the livestock dietary burden. The Meeting agreed that a revision of the previously estimated maximum residue level recommendations for animal commodities was unnecessary.

RECOMMENDATIONS

Table 2 Residue levels suitable for establishing maximum residue limits and for IEDI and IESTI assessments

Commodity		Recommended maximum residue level, mg/kg		STMR or STMR-P, mg/kg	HR or highest residue, mg/kg
CCN	Name	New	Previous		
GC 0654	Wheat	0.15		0.035	
GC 0653	Triticale	0.15		0.035	
CM 0654	Wheat bran, unprocessed	0.3		0.067	
CF 1212	Wheat, wholemeal			0.026	
CF 1211	Wheat, flour			0.008	
CF 1210	Wheat, germ			0.035	
CP 1211	Wheat white bread			0.021	

Dietary risk assessment

Long-term dietary exposure

The ADI for metconazole is 0–0.04 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for metconazole were estimated for the 17 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by the JMPR. The results are shown in Annex 3 of the 2021 JMPR Report.

The IEDIs ranged from 0–2% of the maximum ADI. The Meeting concluded that long-term dietary exposure to residues of metconazole from uses considered by the JMPR is unlikely to present a public health concern.

Acute dietary exposure

The ARfD for metconazole is 0.04 mg/kg bw. The International Estimate of Short Term Intakes (IESTIs) for metconazole were calculated for the food commodities and their processed commodities for which HRs/HR-Ps or STMRs/STMR-Ps were estimated by the current Meeting and for which consumption data were available. The results are shown in Annex 4 of the 2021 JMPR Report.

The IESTIs varied from 0–3% of the ARfD for children and 0–1% of the ARfD for the general population. The Meeting concluded that acute dietary exposure to residues of metconazole from uses considered by the current Meeting is unlikely to present a public health concern.

References

FAO and WHO. 2019. Pesticide Residues in Food - Report 2021 – Joint FAO/WHO Meeting on Pesticide Residues. Rome.

3.7 Propiconazole (160)

A potential public health concern was raised by the European Union (EU) about a number of aspects of propiconazole, which had resulted in differences between JMPR and EU in respect of the ADI and ARfD, the residue definition and consideration of metabolites. According to communication from the European Food Safety Authority (EFSA), the concern form related to the following:

- the ADI and ARfD values established by EFSA are lower than those of the JMPR;

- EFSA was unable to conclude on the toxicity of some metabolites;
- EFSA was unable to conclude on endocrine disrupting potential;
- EFSA was unable to conclude on the residue definition and consumer dietary intake assessment;
- acute intake concerns were cited with respect to some CXLs.

JMPR reviewed propiconazole in 2004, establishing an ADI of 0–0.07 mg/kg (bw) (not 0.7 mg/kg bw as stated in the concern form), based on the NOAEL from a two-generation study of reproductive toxicity, and an ARfD of 0.3 mg/kg bw, based on the NOAEL from a rat developmental toxicity study, applying a safety factor of 100.

Regarding the specific concerns

1a. The EU ADI of 0.04 mg/kg bw per day is derived from the NOAEL from a two-year study of chronic toxicity and carcinogenicity. The JMPR Meeting noted that from the values in Tables B-6.5-3 and 4 of the EU RAR this NOAEL is based on slight (< 5%) reductions in adrenal weights in males and slight (< 10%) reductions in body weight gain in females at some time points, but not over the entire duration of the study. The JMPR considers such slight reductions in adrenal weight and body weight gains, in the absence of any related findings, as not adverse. If the EU have scientific evidence to support the consideration of such minor changes as adverse, it would be helpful if this could be made available for consideration by JMPR.

1b. The EU ARfD of 0.1 mg/kg bw is derived from the same study and NOAEL (30 mg/kg bw per day) as that of the JMPR but applying a safety factor of 300 to maintain a margin of 900 to the LOAEL for developmental effects (90 mg/kg bw per day). The JMPR 2004 Meeting of considered that the margin between the ARfD of 0.3 mg/kg bw and the LOAEL for the severe effect of cleft palate and maternal toxicity at 300 mg/kg bw per day was adequate.

2. The EU concern form does not identify for which metabolites conclusions on toxicity cannot be made, exactly why the residue definition cannot be finalized nor which CXLs present acute intake concerns. Without this information JMPR cannot comment on these generic EU concerns. The JMPR has noted that the list of end-points for the EFSA conclusion cites that a number of metabolites of propiconazole yielded negative Ames tests, indicating they are unlikely to be DNA reactive, and therefore conclusions on them could be made based on a threshold of toxicological concern (TTC) assessment.

3. The Meeting noted that, within the EU legislative framework, endocrine disruption is a hazard identification process with direct risk management consequences, while JMPR includes these aspects as part of the risk assessments as a means to understand mode of action for certain apical effects, if relevant. The JMPR 2004 Meeting concluded that the available database on propiconazole was adequate to characterize the potential hazards to fetuses, infants and children.

4. The Meeting concluded that based on the information presented in the EU documentation, the concerns identified about dietary exposures to propiconazole and metabolites were insufficiently precise, and no conclusions could be made as to whether they represent a public health concern. It should also be noted that in the absence of clear marker components, the JMPR decided to define the residue both for MRLs and for the estimation of the dietary exposure as “propiconazole plus all metabolites convertible to 2,4-dichlorobenzoic acid, expressed as propiconazole”. This common moiety approach covers the majority of residues for parent propiconazole and its metabolites in plant and animal commodities and represents a conservative estimate on the exposure in terms of propiconazole equivalents.

The Meeting concluded that based on the information presented in the EU documentation, the potential concerns identified about dietary exposures to propiconazole and its metabolites were not substantiated and did not merit any review in advance of the normal periodic review.