The definition of the residue (for dietary intake estimation) for animal commodities*: the sum of prothioconazole-desthio, prothioconazole-desthio-3-hydroxy, prothioconazole-desthio-4-hydroxy and their conjugates expressed as prothioconazole-desthio*.

The residue is not fat soluble.

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The International Estimated Daily Intakes (IEDI) for prothioconazole-desthio was calculated from recommendations for STMRs for raw and processed commodities in combination with consumption data for corresponding food commodities. The results are shown in Annex 3 to the 2017 JMPR Report.

The IEDI of the 17 GEMS/Food cluster diets, based on the estimated STMRs represented 0–3% of the maximum ADI of 0.01 mg/kg bw/day. The Meeting concluded that the long-term dietary exposure to residues of prothioconazole from uses considered by the JMPR is unlikely to present a public health concern.

Short-term dietary exposure

The International Estimated Short term Intake (IESTI) for prothioconazole-desthio was calculated for all food commodities and their processed fractions for which maximum residue levels were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI for women of child bearing age is 0–30% of the ARfD of 0.01 mg/kg bw. The IESTI for children and general population is 0% of the ARfD of 1 mg/kg bw. The Meeting concluded that the short-term dietary exposure to residues of prothioconazole, when used in ways that have been considered by the current JMPR, is unlikely to present a public health concern.

5.32 QUINCLORAC (287)

RESIDUE AND ANALYTICAL ASPECTS

Quinclorac is a systemic herbicide used with uptake through roots and foliage and used to control annual grass and broadleaf weeds. It was evaluated by the 2015 JMPR for the first time for toxicology and for residues. The 2015 JMPR allocated an ADI of 0–0.4 mg/kg bw, and an ARfD of 2 mg/kg bw. It also determined that the definition of residue for plant commodities was quinclorac plus quinclorac conjugates for compliance with MRLs and quinclorac plus quinclorac conjugate plus quinclorac methyl ester expressed as quinclorac for estimation of dietary intake, and the definition of residue for animal commodities was quinclorac plus quinclorac conjugates for compliance with MRLs and for estimation of dietary intake. It recommended maximum residue levels for cranberry and rhubarb.

Quinclorac was included on the priority list by the CCPR at the 48th Session in 2016 for evaluation for additional uses by the current Meeting. The current Meeting received information on analytical methods, use patterns and supervised residue trials to support estimation of maximum residue levels for rice and rape seed.

Methods of analysis

The Meeting received a new analytical method D1607/01 developed in 2016 for more precise accounting of quinclorac and quinclorac methyl ester in rape seed. The method D1607/01 did not convert quinclorac methyl ester back into quinclorac.

The total residues of quinclorac in rape seed and forage were determined in three consecutive extraction procedures. For the 1st extraction, samples were extracted with acetonitrile/water (1/1). Parent quinclorac and quinclorac methyl ester were determined using LC-MS/MS. For the 2nd extraction, the seed and forage marc with aqueous phase from the 1st extraction were extracted with acetone/10 mM phosphate buffer at pH 7 (1/1) and with acetone, respectively. Parent quinclorac and quinclorac methyl ester were determined using LC-MS/MS. For the 3rd extraction, the marc from the 2nd extraction was treated with 1N NaOH at 100°C for 1 hour. This harsh hydrolysis to release quinclorac conjugates was used in the plant metabolism study for rape seed. Quinclorac and quinclorac conjugates were determined as quinclorac using LC-MS/MS. After each sample extraction and clean-up, residues are determined by LC-MS/MS, monitoring ion transitions at m/z 242→224 (quantitation) and m/z 242→161 (confirmation) for quinclorac, and m/z 256→224 (quantitation) and m/z 256→161 (confirmation) for quinclorac methyl ester. Total residues of quinclorac were reported as the sum from each extraction procedure. Similarly, the total residues of quinclorac methyl ester were determined in two consecutive extraction procedures and reported as the sum from each extraction procedure. The LOQ for residues of quinclorac and quinclorac conjugates was 0.01 mg/kg, and the LOQ for residues of quinclorac methyl ester was 0.01 mg/kg in/on rape seed and forage.

The Meeting also received a multi-residue analytical method D1502/1 for quinclorac in plant matrices and for quinclorac methyl ester in rape seed.

Parent quinclorac residues in/on homogenized plant samples (5 g each) - except dry matrices and rape seed – were extracted with acetonitrile and cleaned-up by a mixture of "QuEChERS" salts ($MgSO_4$, NaCl, trisodium citrate dihydrate and disodium hydrogen citrate sesquihydrate). The residues in the organic phase were diluted with acetonitrile/water (10/90, v/v) and analysed by LC-MS/MS. For dry/low-moisture content matrices (wheat grain, bean seed, rape seed), and for the separate analysis of quinclorac methyl ester in/on rape seed, the homogenized samples (5 g each) after hydration with water were extracted and partitioned, as described above, and re-extracted with acetonitrile. The residues in an aliquot of the combined acetontrile extracts were further purified with the addition of the second "QuEChERS" salt mixture (described above). The residues in the organic phase were diluted with acetonitrile/water (10/90, v/v) for quinclorac analyses, or with methanol/water (1/1, v/v) for quinclorac methyl ester analyses, and determined by LC-MS/MS. The LOQ for residues of quinclorac and quinclorac methyl ester in/on plant commodities is 0.01 mg/kg.

The methods are suitable for the analysis of quinclorac and quinclorac methyl ester residues in rape seed and forage.

Stability of residues in stored analytical samples

The freezer storage stability studies were reported on rice (grain and straw) and rape seed samples to the 2015 JMPR. Storage stability results indicated that quinclorac residues were stable for at least 38 months in rice (grain and straw) and at least 22 months in rape seed, and quinclorac methyl ester residues were stable for at least 22 months in rape seed. The periods of storage stability studies generally cover the sample storage intervals of residue trials.

Residues resulting from supervised residue trials on crops

The Meeting received supervised trial data for the broadcast spray application of quinclorac on rice and oilseed rape from the USA.

Labels were available from Canada and the USA describing the registered uses of quinclorac.

The 2015 JMPR noted that quinclorac methyl ester has a toxicological potency up to 10 times that of quinclorac. In calculating residue values for dietary intake estimation the Meeting agreed to use the following formula: residues = (quinclorac + quinclorac conjugate) + 10 × quinclorac methyl ester.

The 2015 JMPR also noted quinclorac methyl ester in cereals at levels up to 10 percent of quinclorac in the metabolism study and agreed to use to the following formula to estimate levels for use in dietary intake calculations:

HR/STMR = (quinclorac + quinclorac conjugate) + 10 × 0.1 (quinclorac + quinclorac conjugate)

= 2 × (quinclorac + quinclorac conjugate)

Rice

The supervised trials were conducted on rice in the USA during the 1996 (submitted to the 2015 JMPR) and 2016 growing seasons.

The GAP on rice in the USA is one broadcast application at a maximum rate of 0.50 kg ai/ha from at least the 2-leaf stage to before heading with a PHI of 40 days.

Quinclorac residues (quinclorac + quinclorac conjugate) in rice grains from independent trials in the USA matching GAP for maximum residue level estimation were (n=12): 0.11, 0.26, 0.38, 0.49, 0.56, 0.71, 0.77, 1.1, 1.7, 1.8, 3.3 and 7.9 mg/kg.

Based on the quinclorac residues for rice grains from trials in the USA, the Meeting estimated a maximum residue level of 10 mg/kg and a median residue value for livestock feed of 0.74 mg/kg for quinclorac in rice.

Residues for dietary intake estimation (2 × (quinclorac + quinclorac conjugate)) in rice grains were (n=12): 0.22, 0.52, 0.76, 0.98, 1.1, 1.4, 1.5, 2.2, 3.4, 3.6, 6.6 and 16 mg/kg.

Based on the residues for dietary intake estimation in rice grains, the Meeting estimated an STMR value of 1.45 mg/kg for rice.

Rape seed

Data were available from supervised trials on oilseed rape in Canada and the USA. Residues of quinclorac and quinclorac methyl ester in oilseed rape samples were analysed using the new analytical method D1607/1.

The GAP on oilseed rape of Canada is one broadcast application at rate of 0.10 kg ai/ha and a PHI of 60 days.

Quinclorac residues (quinclorac + quinclorac conjugate) in rape seeds from independent trials in Canada and the USA matching GAP for a maximum residue level estimation were (n=9): < 0.01, 0.01, 0.015 (2), 0.017, 0.022, 0.033, 0.055 and 0.10 mg/kg.

Based on the quinclorac residues for rape seeds from trials in Canada and the USA, the Meeting estimated a maximum residue level of 0.15 mg/kg and a median residue value for livestock feed of 0.017 mg/kg for quinclorac in rape seed.

Quinclorac methyl ester residues expressed as quinclorac equivalents in rape seeds from independent trials in Canada and the USA matching GAP were (n=9): < 0.01, 0.022, 0.029, 0.050, 0.062, 0.082, 0.13, 0.11 and 0.19 mg/kg.

Residues for dietary intake estimation ((quinclorac + quinclorac conjugate) + 10 × quinclorac methyl ester) in rape seeds were (n=9): < 0.11, 0.23, 0.31, 0.52, 0.64, 0.84, 1.2, 1.3 and 2.0 mg/kg.

Based on the residues for dietary intake estimation in rape seeds, the Meeting estimated an STMR value of 0.64 mg/kg for rape seed.

Animal feedstuffs

Rice straw and fodder, dry

Data were available from supervised trials on rice in the USA during the 1996 (submitted to the 2015 JMPR) and 2016 growing seasons.

The GAP on rice of the USA is one broadcast application at a maximum rate of 0.50 kg ai/ha from at least the 2-leaf stage to before heading and a PHI of 40 days.

Quinclorac residues (quinclorac + quinclorac conjugate) in rice straw (as received) from independent trials in the USA matching GAP were (n=12): 0.36, 0.39, 0.70, 0.84, 0.96, 1.2 (2), 1.3, 1.8, 2.5, 3.4 and 4.4 mg/kg.

Based on the quinclorac residues for rice straw, the Meeting estimated a median residue value of 1.2 mg/kg and a highest residue value of 4.4 mg/kg on an "as received" basis and after correction for an average 90% dry matter content, estimated a maximum residue level of 8 mg/kg for quinclorac in rice straw.

Rape forage

Data were available from supervised trials on oilseed rape in Canada and the USA.

The GAP on oilseed rape in Canada is one broadcast application at a rate of 0.10 kg ai/ha and a PHI of 60 days. Grain and meal from treated oilseed rape can be fed to livestock, while other portions of the treated oilseed rape must not be grazed or fed to livestock.

Since the Canadian GAP does not allow grazing or feeding rape forage to livestock, the Meeting agreed not to estimate a median residue value and a highest residue value for rape forage.

Fate of residues during processing

Residues in processed commodities

The 2015 JMPR received information on the fate of incurred residues of quinclorac during the processing of rice and rape seed. Residues of quinclorac and quinclorac methyl ester were determined in rape seed, meal and refined oil using analytical method D9708/1 (quinclorac) and D9806 (quinclorac methyl ester). Method D9708/1 is not suitable of the determination of quinclorac in rape seed because extraction with acetone/0.1 M NaOH converts quinclorac methyl ester partly into parent quinclorac. However, since the ratios of the residues in processed commodities were estimated as processing factors, the results of the study using method D9708/1 were acceptable.

Estimated processing factors and the derived STMR-Ps are summarized in the Table below.

Processing factors, STMR-P for food and feed

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factor	RAC STMR or median residue (mg/kg)	STMR-P (mg/kg)	Median residue (mg/kg)
Rice	Husked rice	1.0	1.45 (STMR)	1.45	-
	Polished rice	0.76		1.1	-
	Husked rice	1.0	0.74 (median residue)	-	0.74
	Hulls	1.1		-	0.81
	Bran, unprocessed	3		-	2.2

Raw agricultural commodity (RAC)	Processed commodity	Processing factor (PF)				**RAC**	
		Quinclorac + quinclorac conjugate		(Quinclorac + quinclorac conjugate) + 10 × quinclorac methyl ester		STMR (mg/kg)	median residue (mg/kg)
		Calculated [a]	PF [b]	Calculated [a]	PF [b]		
Rape seed	Meal	0.36, <1, 1.6, 2.2	1.3	-	-	-	0.017
	Refined oil	-	-	0.64, 1.0, 1.2, 1.3	1.1	0.64	-

[a] Each value represents a separate study. The factor is the ratio of the residue in the processed commodity divided by the residue in the RAC.

[b] Mean or best estimate

The Meeting estimated a maximum residue level of 10 mg/kg (10 × 1.0 = 10 mg/kg) for husked rice and 8 mg/kg (10 × 0.76 = 7.6 mg/kg) for polished rice.

The Meeting estimated an STMR value of 0.70 mg/kg (0.64×1.1 = 0.70 mg/kg) for rape seed refined oil and a median residue value of 0.022 mg/kg (0.017×1.3 = 0.022 mg/kg) for rape seed meal.

Residue in animal commodities

Farm animal dietary burden

The Meeting estimated the dietary burden of quinclorac in farm animals on the basis of the diets listed in Appendix IX of the FAO Manual third edition, 2016. Calculations from the highest residue, STMR (some bulk commodities) and STMR-P values provide levels in feed suitable for estimating MRLs, while calculations using STMR and STMR-P values for feed are suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed on a dry weight basis.

Estimated maximum and mean dietary burdens of farm animals

The calculations were made according to the animal rations from US-Canada, EU, Australia and Japan in the Table (Appendix IX of the FAO manual).

Potential feed items include: rice grains, rice hulls, rice bran, rice straw and rape seed meal.

Livestock dietary burden, quinclorac, ppm of dry matter diet								
	US-Canada		EU		Australia		Japan	
	Max	Mean	Max	Mean	Max	Mean	Max	Mean
Beef cattle	0.535	0.535	0.494	0.138	**3.91[a]**	**1.78[b]**	3.18	1.23
Dairy cattle	0.535	0.535	0.736	0.558	**2.13[c]**	**1.42[d]**	1.47	0.584
Poultry – broiler	0.413	0.413	0.244	0.244	0.911	0.911	0.123	0.123
Poultry – layer	0.413	0.413	0.125	0.125	**0.911[e]**	**0.911[f]**	0.493	0.493

[a] Highest maximum beef cattle dietary burden suitable for MRL estimates for mammalian meat, fat and edible offal

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

[c] Highest maximum dairy cattle dietary burden suitable for MRL estimates for milk

[d] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk

[e] Highest maximum layer poultry dietary burden suitable for MRL estimates for poultry meat, fat, edible offal and eggs

[f] Highest mean layer poultry dietary burden suitable for STMR estimates for poultry meat, fat, edible offal and eggs

Farm animal feeding studies

The 2015 JMPR received lactating dairy cow and laying hen feeding studies using quinclorac, which provided information on likely residues resulting in animal commodities and milk from quinclorac residues in the animal diet.

Animal commodities maximum residue levels

For MRL estimation, the residue in the animal commodities is quinclorac and quinclorac conjugates.

Residues in tissues and milk at the expected dietary burden for beef and dairy cattle are shown in the Table below. Residues of quinclorac in milk were only detected at levels of 500 ppm in the diet.

	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues (mg/kg) in			
				Muscle	Liver	Kidney	Fat
MRL beef or dairy cattle							
Feeding study	1 10	< 0.05 < 0.05	1 10	< 0.05 < 0.05	< 0.05 < 0.05	< 0.05 0.082	< 0.05 < 0.05
Dietary burden and residue estimate	2.13	< 0.05	3.91	< 0.05	< 0.05	0.060	< 0.05
STMR beef or dairy cattle							
Feeding study	1 10	< 0.05 < 0.05	1 10	< 0.05 < 0.05	< 0.05 < 0.05	< 0.05 0.073	< 0.05 < 0.05
Dietary burden and residue estimate	1.42	< 0.05	1.78	< 0.05	< 0.05	0.052	< 0.05

Based on the highest estimated residue in milk (< 0.05 mg/kg), the Meeting estimated a maximum residue level of 0.05 (*) mg/kg in milk.

Based on the highest estimated residue in fat (< 0.05 mg/kg), the Meeting estimated a maximum residue level of 0.05 (*) mg/kg in mammalian fat and meat (fat).

Based on the highest estimated residue in kidney (0.060 mg/kg), the Meeting estimated a maximum residue level of 0.1 mg/kg in mammalian edible offal.

Based on the highest estimated residues in tissues, the Meeting estimated HR values of 0 mg/kg in mammalian muscle, 0.060 mg/kg in mammalian edible offal and 0.05 mg/kg in mammalian fat.

Based on the mean estimated residues in tissues and milk, the Meeting estimated STMR values of 0 mg/kg in milk, 0 mg/kg in mammalian muscle, 0.052 mg/kg in mammalian edible offal and 0.05 mg/kg in mammalian fat.

Residues in tissues and eggs at the expected dietary burden for broiler and layer poultry are shown in the Table below.

	Feed level (ppm) for egg residues	Residues (mg/kg) in eggs	Feed level (ppm) for tissue residues	Residues (mg/kg) in			
				Muscle	Liver	Kidney	Skin & Fat
MRL broiler or layer poultry							
Feeding study	1	< 0.05	1	< 0.05	< 0.05	< 0.05	< 0.05
Dietary burden and residue estimate	0.911	< 0.05	0.911	< 0.05	< 0.05	< 0.05	< 0.05
STMR broiler or layer poultry							
Feeding study	1	< 0.05	1	< 0.05	< 0.05	< 0.05	< 0.05
Dietary burden and residue estimate	0.911	< 0.05	0.911	< 0.05	< 0.05	< 0.05	< 0.05

Based on the highest estimated residue in eggs (< 0.05 mg/kg), the Meeting estimated a maximum residue level of 0.05 (*) mg/kg in eggs.