



### 5.31 PROTHIOCONAZOLE (232)

#### RESIDUE AND ANALYTICAL ASPECTS

Prothioconazole is a systemic triazolinethione fungicide that is used for the control of diseases caused by *Ascomycetes*, *Basidiomycetes* and *Deuteromycetes* in a range of crops. It was first evaluated by JMPR for toxicology and residues in 2008. The residue definition for plant commodities for enforcement and dietary risk assessment is prothioconazole-desthio. The residue definition for animal commodities for enforcement is prothioconazole-desthio and for dietary risk assessment is 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.

The 2008 JMPR established, for prothioconazole-desthio, an ADI of 0–0.01 mg/kg bw and ARfD of 0.01 mg/kg bw for women of child bearing age and 1 mg/kg bw for the general population. Prothioconazole was listed by the 48<sup>th</sup> Session of the CCPR for the evaluation of additional MRLs. The Meeting received information on the GAP and supervised residue trials on cotton conducted in Brazil and the USA.

##### *Results of supervised residue trials on crops*

The current meeting received information on the use pattern and supervised residue trials for foliar application of prothioconazole on cotton conducted in Brazil and the USA. For estimating HR or highest residue, the highest individual residue value from the trials conducted in accordance with GAP was used.

##### *Oilseeds*

###### *Cotton seeds*

Twelve supervised trials were conducted in the USA included plots which were treated according to the GAP for cotton in the USA (US GAP: 3 times 0.20–0.21 kg ai/ha at 14 days intervals, 30-day PHI). Prothioconazole-desthio residue concentrations on cotton based on the USA GAP are: < 0.018 (3), 0.028, 0.031, 0.033, 0.070, 0.075, 0.079, 0.081, 0.083 and 0.18 mg/kg.

The Meeting estimated a maximum residue level, and STMR at 0.3 and 0.052 mg/kg, respectively, for prothioconazole in cotton seed.

##### *Animal feedstuffs*

###### *Cotton gin by-products*

Six supervised trials were conducted in the USA included plots which were treated according to the GAP for cotton in the USA (US GAP: 3 times 0.20–0.21 kg ai/ha at 14 days intervals, 30-day PHI). Prothioconazole-desthio residue concentrations on cotton gin by-products based on the USA GAP are: 0.43, 0.78, 1.1, 1.1, 1.2 and 1.8 mg/kg (n=6).

The Meeting estimated the median residue of 1.1 mg/kg and the highest residue of 1.8 mg/kg in cotton gin trash for estimating livestock dietary burden.

##### *Fate of residues during processing*

###### *High temperature hydrolysis*

A hydrolysis study representative of core processing procedures was previously evaluated by the 2008 JMPR. The 2008 meeting concluded that prothioconazole degraded slightly (< 11%) to prothioconazole-desthio at 120 °C at pH6.

A further hydrolytic degradation study was conducted on the metabolite prothioconazole-desthio.

Prothioconazole-desthio did not show any sign of decomposition when exposed to sets of conditions representing pasteurization (pH 4, 90 °C), baking, brewing and boiling (pH 5, 100 °C) and sterilization (pH 6, 120 °C).

For prothioconazole-desthio, the nature of the residue in the processed commodity is expected to be identical with that in the raw agricultural commodity for all three types of food processing operations examined.

#### *Residues in processed commodities*

Field cotton was treated at 5× total seasonal rate. Subsamples of undelinted seed, the raw agricultural commodity (RAC), were separated after ginning, and used to generate the processed commodities of meal, hulls, refined oil (bleached and deodorized (RBD oil)), solvent extracted crude oil, pre-clarified crude oil, and neutralized crude oil. Processing was performed using procedures that simulated commercial practices.

Based on the results of processing studies conducted in the USA in combination with the residues from supervised trials, the estimated processing factors and the derived STMR-Ps are summarized in the Table below.

Raw Agricultural commodity (RAC)	Processed Fractions	Prothioconazole-desthio		STMR/ STMR-P	MRL <sup>b</sup>
		Processing factor <sup>a</sup>	PF (mean)		
Cotton seed	seed, undelinted	--		0.052	0.3
	meal	< 0.10, 0.10	0.1	0.005	-
	hull	0.28, < 0.04	0.16	0.008	-
	crude oil, preclarified	< 0.10, < 0.04	< 0.07	0.004	-
	oil, solv. extracted	< 0.10, < 0.04	< 0.07	0.004	-
	crude oil, neutralized	< 0.10, 0.11	0.1	0.005	-
	oil, refined	< 0.10, 0.28	0.19	0.01	-

<sup>a</sup> The calculated processing factors are the ratio of the residue in the processed commodity divided by the residue in the RAC.

<sup>b</sup> MRLs in processed commodities are only proposed where they are higher than the raw grain

The prothioconazole-desthio residue did not concentrate (processing factor < 1×) in meal, hulls, refined oil (bleached and deodorized), solvent extracted crude oil, pre-clarified crude oil, or neutralized crude oil.

#### *Residues in animal commodities*

##### *Farm animal dietary burdens*

The Meeting estimated the dietary burden of prothioconazole in farm animals on the basis of the diets listed in Appendix IX of the FAO Manual 2016. Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are presented in Annex 6 and are summarized below.

	US-Canada		EU		Australia		Japan	
	Max	Mean	Max	Mean	Max	Mean	Max	Mean
Beef cattle	1.99	1.45	14.01	5.78 <sup>b</sup>	21.60 <sup>a</sup>	5.44	0.04	0.04
Dairy cattle	8.64	3.26	13.91	5.32	18.42 <sup>c</sup>	5.44 <sup>d</sup>	4.52	2.82
Poultry broilers	0.04	0.04	0.04	0.04	0.05	0.05	0.005	0.005
Poultry layers	0.04	0.04	3.05 <sup>e</sup>	0.92 <sup>f</sup>	0.05	0.05	0.02	0.02

<sup>a</sup> suitable for estimating maximum residue levels for meat, fat and edible offal of cattle.

<sup>b</sup> suitable for estimating STMR for meat, fat and edible offal of cattle.

<sup>c</sup> suitable for estimating maximum residue levels for Milk.

<sup>d</sup> suitable for STMR levels for Milk.

<sup>e</sup> suitable for estimating maximum residue levels for poultry meat, offal and eggs.

<sup>f</sup> suitable for STMR levels for poultry meat, offal and eggs.

#### *Animal commodity maximum residue levels*

Residue levels of prothioconazole-desthio included in the residue definition in milk and tissues were obtained by extrapolation between the 4 and 25 ppm feeding level in the dairy cow feeding study.

Prothioconazole feeding study	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues (mg/kg)			
				Muscle	Liver	Kidney	Fat
<b>MRL beef or dairy cattle</b>							
Feeding study1	4.00 25.00	< 0.004 < 0.004	4.00 25.00	< 0.01 < 0.01	0.05 0.26	0.04 0.17	< 0.01 0.02
Dietary burden and high residue	18.42	< 0.004	21.60	< 0.01	0.226	0.149	0.018
<b>STMR beef or dairy cattle</b>							
Feeding study2	4.00 25.00	< 0.004 < 0.004	4.00 25.00	< 0.01 < 0.01	0.04 0.22	0.02 0.14	< 0.01 0.01
Dietary burden and residue estimate	5.44	< 0.004	5.78	< 0.01	0.055	0.03	0.01

Residues of prothioconazole-desthio expected in cattle milk and tissues for use in estimating maximum residue levels are: 0.018 mg/kg (fat), 0.01 mg/kg (muscle), 0.226 mg/kg (liver) and 0.149 mg/kg (kidney) and the mean residue for milk is < 0.004 mg/kg.

The Meeting estimate the maximum residue levels of 0.3 mg/kg for edible offal, 0.01 mg/kg for meat, 0.02 for mammalian fat and 0.004\* mg/kg for milk.

Estimated STMRs for dietary intake estimation are 0.01 mg/kg for meat and fat, 0.055 mg/kg for liver, 0.03 mg/kg for kidney and 0.004 mg/kg for milk.

For poultry, no new feeding study was submitted. From the metabolism study on laying hens with the parent prothioconazole at an exaggerated rate of 171 mg/kg feed indicated a total residue of 4, 0.036, 0.45 and 0.089 mg/kg for liver, eggs, subcutaneous fat, and muscle respectively. Assuming a proportional residue level the 3.05 mg/kg residue in feed would result in 0.071, 0.0006 (LOQ=0.005), 0.008 (LOQ=0.01) and 0.0016 (LOQ= 0.01) mg/kg residue in liver, eggs, subcutaneous fat, and muscle respectively.

The Meeting estimate maximum residue levels of 0.1 (for poultry edible offal), 0.005\* (eggs), 0.01\* (fat), and 0.01\* (muscle) mg/kg.

The Meeting estimated STMRs and HRs for dietary intake estimation of 0.071 mg/kg for liver, 0.0006 mg/kg for eggs, 0.008 mg/kg for fat and 0.0016 mg/kg for muscle.

#### **RECOMMENDATION**

On the basis of the data from supervised trials the Meeting concluded that the residue levels listed in Annex 1 are suitable for establishing maximum residue limits and for IEDI and IESTI assessment.

Definition of the residue (for compliance with the MRL and estimation of dietary intake) for plant commodities: *prothioconazole-desthio*.

Definition of the residue (for compliance with MRLs) for animal commodities: *prothioconazole-desthio*; and