

PROTHIOCONAZOLE (232)

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EXPLANATION

Prothioconazole is a systemic triazolinthione fungicide that is used for the control of diseases caused by *Ascomycetes*, *Basidiomycetes* and *Deuteromycetes* in a range of crops first evaluated by JMPR for toxicology and residues in 2008, which recommended limits for barley, oats, rye, triticale and wheat grain and straw, peanut, rape seed and for meat, mammalian fats, edible offal and milks. Furthermore, the 2008 Meeting concluded that 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 2009 JMPR reviewed existing US field trial data, together with any additional residues data, on pulses, sugar beet, wheat and barley grain, canola (rape seed), soya bean and cereal forages/straw.

Prothioconazole was subsequently evaluated by the 2014 JMPR, which recommended maximum residue limits for blueberry, corn, cranberry, cucurbits, potato and sweet corn; as well as peanut and soya bean.

Prothioconazole was listed by the 48th 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 the USA and Brazil.

RESIDUE ANALYSIS

The Meeting received no additional information on analytical methods for the determination of residues of prothioconazole. The trials carried out in Brazil on cotton used method 00598 or method 01013, which were already evaluated during previous JMPR submissions. The trials carried out in the USA on cotton used method JA-001-P04-02, which was already evaluated during the previous JMPR submission.

Stability of Residues in Stored Samples

The stability of residues of prothioconazole and its metabolites in stored samples was evaluated by the 2008 and 2014 JMPR. The previously submitted stability studies are considered adequate to cover the sample storage intervals in the residue trials submitted to the current Meeting; no further stability data were submitted.

USE PATTERNS

The authorized uses relevant to the supervised trial data submitted to the current Meeting are summarized in Table 1.

Table 1 Registered Uses of Prothioconazole

Crop	Country	Formulation	Application			PHI days
			Method	Rate, g ai/ha	No. or max (g ai/ha/ season)	
Oilseeds						
Cotton	USA	500SC	Foliar	46	3 (138)	30
Cotton	USA	480SC	Foliar	200	3 (600)	30
Cotton	Brazil	250 EC	Foliar	125	3(375)	30
Cotton	Brazil	325SC	Foliar	87.5	4(350)	30

RESULTS OF SUPERVISED RESIDUE TRIALS ON CROPS

The Meeting received residue data from supervised field trials conducted in the USA and Brazil involving foliar applications of prothioconazole on cotton.

Trials were well documented with the results of the laboratory analysis and field reports. The former included method validation including recoveries with spiking at residue levels similar to those occurring in samples from the supervised trials. Dates of analyses or duration of residue sample storage were also provided. Although trials included control plots, no control data are recorded in the Tables because no residues in control samples exceeded the LOQ. The residues definition for monitoring and risk assessment in plant commodities is prothioconazole-desthio only. However for consistency with previous JMPR evaluations, for trials conducted in the USA, the tables show residues of prothioconazole sulfonic acid (JAU 6476 sulfonic acid), prothioconazole-desthio (JAU 6476 desthio) and total prothioconazole (JAU 6476). For trials conducted in Brazil, the tables show residues of parent prothioconazole (JAU 6476), prothioconazole-desthio (JAU 6476 desthio) and sometimes total prothioconazole (JAU 6476). Only the residues of prothioconazole-desthio have been used for calculation of MRL, HR and STMR values for plant commodities. Unless otherwise indicated, residues of prothioconazole-desthio are expressed as mg prothioconazole-desthio equivalents/kg (mg eq/kg).

In the trials where multiple analyses are conducted on a single sample, the mean value is reported. Where multiple samples were taken from a single plot, the mean residue value is reported in accordance with the OECD MRL Calculator. Where results from separate plots with distinguishing characteristics such as different formulations, varieties or treatment schedules were reported, results are listed for each plot.

Results have not been corrected for concurrent method recoveries. Residues and application rates have generally been rounded to two significant figures or, for residues near the LOQ, to one significant figure. Residue values from the trials conducted according to the maximum GAP were used for the estimation of maximum residue levels. Those results included in the tables are underlined.

The results of these supervised trials are summarized in the tables listed below

Crop Group	Commodity	Country, year of trials	Table No.
Oilseeds	Cotton	USA 2013	Table 2
Oilseeds	Cotton	USA 2013	Table 3
Oilseeds	Cotton	Brazil, 2005	Table 4
Oilseeds	Cotton	Brazil, 2006, 2011, 2012, 2013	Table 5

Oilseeds

Cotton seed

Twelve supervised trials were conducted in 2013 in the major cotton-producing states in the USA (Netzband and Jerkins, 2015, RAJAN029). The trials were carried out according to the critical GAP in the USA. Three of the trials were decline trials and the rest were at harvest trials. Three applications of an SC formulation containing 480 g/L prothioconazole were made at 14 day intervals and samples of cotton were taken from each plot at the PHI of 30 days (actual PHI 27-31 days). In the three decline trials, additional samples were collected at 23–26, 34–36, 38–40 and 43–44 days after the last application.

Three types of plots were investigated: Plot TRTD1 (present in all trials) received 3 equivalent foliar spray applications of 480 SC tank-mixed with 500 SC (SC formulation containing trifloxystrobin). For all applications, individual application rates ranged from 0.20 to 0.21 kg/ha for prothioconazole. Intervals between applications ranged from 12 to 15 days, and applications were

made when the cotton plants were between BBCH 65 and 89. Total seasonal application rates for TRTD1 ranged from 0.60 to 0.61 kg/ha for prothioconazole.

Plot TRTD2 (present in all trials except JA016-13DA) received a single in-furrow application of prothioconazole 480 SC formulation at planting followed by two non-equivalent foliar applications of prothioconazole 480 SC formulation. Rates for the in furrow application (made at BBCH 00, dry seed) were 0.25 kg prothioconazole/ha. The interval between the in furrow application and the first foliar application (second application total) ranged from 76 to 181 days. Actual rates for the second application were 0.15 kg prothioconazole/ha. The interval between the two foliar applications was 13 to 14 days. Actual rates for the third application were between 0.20 and 0.21 kg prothioconazole/ha. Both foliar applications were made between BBCH 71 and 88. Total seasonal application rates for TRTD2 were 0.60 kg prothioconazole/ha.

Plot TRTD3 (present only in the three bridging trials, JA007-13HA, JA011-13HA, and JA015-13HA) received only cotton seeds treated with Prothioconazole 480 SC formulation at a rate of 30 g prothioconazole per 100 kg seed leading to a seasonal application rate of 0.006 kg prothioconazole/ha (data not shown).

All samples were frozen within 4 hours of collection and shipped frozen from the field site except the bulk stripper cotton samples, which were stored at ambient temperature and shipped at ambient temperature by the next business day. When the samples were stored at ambient temperature longer than 24 hours (trial JA012-13DA), fans were used to prevent overheating. The maximum period of storage was 448 days (14.9 months), which falls within the stability period of 3 years as confirmed by previous studies with prothioconazole and prothioconazole-desthio.

Residues of prothioconazole on cotton were determined by high performance liquid chromatography – electrospray ionization tandem mass spectrometry (LC-MS/MS). The method JA-001-P04-02, which was used for the analysis, was validated with an LOQ of 0.02 mg/kg for prothioconazole-sulfonic acid, 0.02 mg/kg for prothioconazole-desthio (expressed as parent; or 0.018 mg/kg expressed at itself) and 0.04 mg/kg for total prothioconazole.

At each sampling interval, duplicate composite samples (two separate runs through the plot) of seed cotton raw agricultural commodities (RAC) were harvested from the treated plots when the RAC(s) were at commercial maturity.

Procedural recoveries for cotton seed at fortification levels of 0.02–1.0 mg/kg were within the acceptable range of 70–120% for prothioconazole-desthio, prothioconazole-sulfonic acid and prothioconazole, with the exception of 2 individual recoveries for prothioconazole at 0.02 mg/kg (67% and 69%). The prothioconazole recovery was the sum of prothioconazole-desthio and prothioconazole-sulfonic acid from recovery samples fortified with prothioconazole only. The results are summarized in the table below.

Procedural recoveries for cotton gin by-products at fortification levels of 0.02–2.5 mg/kg were within the acceptable range of 70–120% for prothioconazole-desthio, prothioconazole-sulfonic acid and prothioconazole, with the exception of 2 individual recoveries for prothioconazole at 0.02 mg/kg and 2.5 mg/kg (68% and 66%, respectively); 2 individual recoveries for prothioconazole sulfonic acid at 0.02 mg/kg and 2.5 mg/kg (69% and 68%, respectively); and 1 individual recovery for prothioconazole-desthio at 0.02 mg/kg (69%). The prothioconazole recovery was the sum of prothioconazole-desthio and prothioconazole-sulfonic acid from recovery samples fortified with prothioconazole only.

Results of supervised trials conducted in cotton seed in the USA were < 0.018–0.18 mg/kg (TRTD1) and < 0.018–0.095 mg/kg (TRTD2) for prothioconazole-desthio, < 0.020–0.063 mg/kg (TRTD1) and < 0.020–0.036 mg/kg (TRTD2) for prothioconazole-sulfonic acid, and < 0.040–0.26 mg/kg (TRTD1) and < 0.040–0.13 mg/kg (TRTD2) for total prothioconazole.

Results of supervised trials conducted in gin by-products in the USA were 1.05–1.15 mg/kg (TRTD1) and 0.43–0.78 mg/kg (TRTD2) for prothioconazole-desthio, 0.10–0.17 mg/kg (TRTD1) and

0.082–0.094 mg/kg (TRTD2) for prothioconazole-sulfonic acid, and 1.3–1.4 (TRTD1) and 0.57–0.94 mg/kg (TRTD2) for total prothioconazole.

The results of the trials from Plot TRTD1 are summarized in Table 2 and the results of the trials from Plot TRTD2 are summarized in Table 3.

Table 2 Prothioconazole residues in cotton resulting from supervised trials in the USA (TRTD1)

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 sulfonic acid mg/kg	JAU 6476 desthio mg/kg	JAU 6476 total mg/kg	Reference
	Formulation (g ai/L)	g ai/ha	g ai/hL	Water (L/ha)	No						
GAP, USA	480 g/L SC	200			3	30					
JA005-13HA-TRTD1 Alabama, USA 2013 (DPL 1050)	480 g/L SC	198-201	71.2-109	183-278	3	29	seed, undelinted	0.048	<u>0.033</u>	0.084	Netzband and Jerkins, 2015, RAJAN029
JA006-13HA-TRTD1 Mississippi, USA 2013 (Phytogen 499)	480 g/L SC	198-204	144-153	133-140	3	31	seed, undelinted	< 0.020	<u>< 0.018</u>	< 0.040	Netzband and Jerkins, 2015, RAJAN029
JA007-13HA-TRTD1 Arkansas, USA 2013 (FM1944GLB2)	480 g/L SC	199-200	193-210	96-103	3	30	seed, undelinted	< 0.020	<u>< 0.018</u>	< 0.040	Netzband and Jerkins, 2015, RAJAN029
JA008-13DA-TRTD1 Arkansas, USA 2013 (DynaGro2570 B2RF)	480 g/L SC	200-201	189-210	97-106	3	25	seed, undelinted	< 0.020	0.027	0.05	Netzband and Jerkins, 2015, RAJAN029
						29		< 0.020	<u>< 0.018</u>	< 0.040	
						35		< 0.020	<u>< 0.018</u>	< 0.040	
						40		< 0.020	< 0.018	< 0.040	
						44		< 0.020	< 0.018	< 0.040	
JA009-13DA-TRTD1 Texas, USA 2013 (DPL 0912 B2RF)	480 g/L SC	200-201	178-179	112-113	3	23	seed, undelinted	< 0.020	0.019	0.041	Netzband and Jerkins, 2015, RAJAN029
						29		< 0.020	0.021	0.043	
						34		< 0.020	< 0.018	< 0.040	
						38		< 0.020	<u>0.028</u>	0.051	
						44		< 0.020	< 0.018	< 0.040	
						23	gin by-products	0.25	1.56	2	
						29		0.17	<u>1.15</u>	1.4	
						34		0.097	0.48	0.63	
						38		0.083	0.38	0.5	
44	0.076	0.32	0.43								
JA010-13HA-TRTD1 Texas, USA 2013 (DP0912 B2RF)	480 g/L SC	203-206	144	141-143	3	28	seed, undelinted	0.024	<u>0.083</u>	0.12	Netzband and Jerkins, 2015, RAJAN029
JA011-13HA-TRTD1 Texas, USA 2013 (FM1944GLB2)	480 g/L SC	200-203	144	139-141	3	28	seed, undelinted	< 0.020	<u>0.075</u>	0.1	Netzband and Jerkins, 2015, RAJAN029
JA012-13DA-TRTD1 Oklahoma, USA 2013 (FM 1960 B2F)	480 g/L SC	198-200	103-132	150-194	3	26	seed, undelinted	< 0.020	0.02	0.042	Netzband and Jerkins, 2015, RAJAN029
						30		< 0.020	0.022	0.045	
						36		< 0.020	0.023	0.045	
						40		< 0.020	<u>0.031</u>	0.054	

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 sulfonic acid mg/kg	JAU 6476 desthio mg/kg	JAU 6476 total mg/kg	Reference
	Formulation (g ai/L)	g ai/ha	g ai/hL	Water (L/ha)	No						
						43		< 0.020	0.023	0.045	
						26	gin by- products	0.11	1.13	1.4	
					30	0.1		1.05	1.3		
					36	0.084		0.84	0.99		
					40	0.08		0.82	0.98		
						43		0.078	0.81	1	
JA013-13DA- TRTD1 Texas, USA 2013 (FM 1944 GLB2)	480 g/L SC	198- 202	146- 150	132- 138	3	27	seed, undelinted	< 0.020	0.07	0.1	Netzband and Jerkins, 2015, RAJAN029
						27	gin by- products	0.19	1.76	2.1	
JA014-13HA- TRTD1 California, USA 2013 (DP 399)	480 g/L SC	196- 206	70.9- 71.3	275- 289	3	28	seed, undelinted	0.063	0.18	0.26	Netzband and Jerkins, 2015, RAJAN029
JA015-13HA- TRTD1 California, USA 2013 (FM1944GLB2)	480 g/L SC	200- 206	76.9- 85.1	235- 268	3	29	seed, undelinted	< 0.020	0.079	0.11	Netzband and Jerkins, 2015, RAJAN029
JA016-13HA- TRTD1 California, USA 2013 (Phytogen 499)	480 g/L SC	200- 202	71.6- 85.5	234- 282	3	25	seed, undelinted	0.031	0.24	0.3	Netzband and Jerkins, 2015, RAJAN029
						30		0.043	0.081	0.13	

JAU 6476 = prothioconazole. Total residues expressed as mg prothioconazole equivalents/kg.

JAU 6476 desthio = prothioconazole-desthio. Residues expressed as mg prothioconazole-desthio/kg.

JAU 6476 sulfonic acid = prothioconazole-sulfonic acid. Residues expressed as mg prothioconazole/kg.

Table 3 Prothioconazole residues in cotton resulting from supervised trials in the USA (TRTD2)

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 sulfonic acid mg/kg	JAU 6476 desthio mg/kg	JAU 6476 total mg/kg	Reference
	Formulation (g ai/L)	g ai/ha	g ai/h L	Water (L/ha)	No						
GAP, USA	480 g/L SC	200			3	30					
JA005- 13HA- TRTD2 Alabama, USA 2013 (DPL 1050)	480 g/L SC	148- 250	53.2- 260	97-278	3	29	seed, undelinted	0.036	0.058	0.1	Netzband and Jerkins, 2015, RAJAN029
JA006- 13HA- TRTD2 Mississippi, USA 2013 (Phytogen 499)	480 g/L SC	148- 254	106- 450	56-140	3	31	seed, undelinted	< 0.020	< 0.018	< 0.040	Netzband and Jerkins, 2015, RAJAN029

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 sulfonic acid mg/kg	JAU 6476 desthio mg/kg	JAU 6476 total mg/kg	Reference
	Formulati on (g ai/L)	g ai/ha	g ai/h L	Water (L/ha)	No						
JA007- 13HA- TRTD2 Arkansas, USA 2013 (FM1944GL B2)	480 g/L SC	152- 250	160- 225	96-111	3	30	seed, undelinted	< 0.020	< 0.018	< 0.040	Netzband and Jerkins, 2015, RAJAN029
JA008- 13DA- TRTD2 Arkansas, USA 2013 (DynaGro25 70 B2RF)	480 g/L SC	152- 251	160- 224	97-112	3	25	seed, undelinted	< 0.020	< 0.018< 0.018< 0. 018< 0.01 8< 0.018	< 0.040	Netzband and Jerkins, 2015, RAJAN029
						29		< 0.020		< 0.040	
						35		< 0.020		< 0.040	
						40		< 0.020		< 0.040	
						44		< 0.020		< 0.040	
JA009- 13DA- TRTD2 Texas, USA 2013 (DPL 0912 B2RF)	480 g/L SC	150- 253	133- 270	95-113	3	23	seed, undelinted	< 0.020	0.019	0.04	Netzband and Jerkins, 2015, RAJAN029
						29		< 0.020	< 0.018	< 0.040	
						34		< 0.020	0.02	0.042	
						38		< 0.020	< 0.018	< 0.040	
						44		< 0.020	0.092	0.12	
						23	gin by- products	0.11	0.55	0.72	
						29		0.094	0.43	0.57	
						34		0.078	0.34	0.46	
						38		0.065	0.21	0.29	
						44		0.093	0.33	0.46	
JA010- 13HA- TRTD2 Texas, USA 2013 (DP0912 B2RF)	480 g/L SC	148- 252	106- 540	47-140	3	28	seed, undelinted	< 0.020	0.031	0.054	Netzband and Jerkins, 2015, RAJAN029
JA011- 13HA- TRTD2 Texas, USA 2013 (FM1944GL B2)	480 g/L SC	149- 248	106- 530	47-142	3	28	seed, undelinted	< 0.020	0.059	0.086	Netzband and Jerkins, 2015, RAJAN029
JA012- 13DA- TRTD2 Oklahoma, USA 2013 (FM 1960 B2F)	480 g/L SC	149- 251	81.0 -216	116- 195	3	26	seed, undelinted	< 0.020	< 0.018	< 0.040	Netzband and Jerkins, 2015, RAJAN029
						30		< 0.020	< 0.018	< 0.040	
						36		< 0.020	< 0.018	< 0.040	
						40		< 0.020	0.032	0.056	
						43		< 0.020	0.028	0.051	
						26	gin by- products	0.07	0.66	0.8	
						30		0.072	0.66	0.8	
						36		0.082	0.78	0.94	
						40		0.07	0.72	0.86	
						43		0.073	0.65	0.79	
JA013- 13DA- TRTD2	480 g/L SC	148- 252	113- 260	98-135	3	27	seed, undelinted	< 0.020	0.043	0.068	Netzband and Jerkins, 2015,

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 sulfonic acid mg/kg	JAU 6476 desthio mg/kg	JAU 6476 total mg/kg	Reference
	Formulation (g ai/L)	g ai/ha	g ai/h L	Water (L/ha)	No						
Texas, USA 2013 (FM 1944 GLB2)						27	gin by- products	0.167	1.09	1.4	RAJAN029
JA014- 13HA- TRTD2 California, USA 2013 (DP 399)	480 g/L SC	150- 247	53.8 - 84.9	279- 291	3	28	seed, undelinted	0.025	0.086	0.12	Netzband and Jerkins, 2015, RAJAN029
JA015- 13HA- TRTD2 California, USA 2013 (FM1944GL B2)	480 g/L SC	151- 248	58.1 - 260	95-260	3	29	seed, undelinted	< 0.020	0.095	0.13	Netzband and Jerkins, 2015, RAJAN029

JAU 6476 = prothioconazole. Total residues expressed as mg prothioconazole equivalents/kg.

JAU 6476 desthio = prothioconazole-desthio. Residues expressed as mg prothioconazole-desthio/kg.

JAU 6476 sulfonic acid = prothioconazole-sulfonic acid. Residues expressed as mg prothioconazole /kg.

A total of six trials were conducted in 2005 on cotton in Brazil (Galhiane, M. S.; de Sousa, S. L., 2005, UNESP RA-954-05, UNESP RA-955-05 and UNESP RA-956-05). Three trials were performed according to the GAP in Brazil (3×125 g/ha, PHI=30 days), and three according to twice the GAP (3×250 g/ha, PHI=30 days).

The maximum period of storage was 55 days (1.8 months), which falls within the stability period of 3 years as confirmed by previous studies with prothioconazole and prothioconazole-desthio.

Residues of prothioconazole-desthio were determined by HPLC-MS/MS using method 00598. The LOQ was 0.01 mg/kg. Procedural recoveries at fortification levels of 0.01–0.1 mg/kg were within the acceptable range of 70–120%, RSD < 20%, for prothioconazole-desthio.

Residue levels of prothioconazole-desthio were always < 0.01 mg/kg when applied at 3×125 g/ha, and ranged from < 0.01 to 0.02 mg/kg when applied at 3×250 g/ha (double the GAP). The results of these trials are summarized in Table 4.

Table 4 Prothioconazole residues in cotton resulting from supervised trials in the Brazil with 250EC formulation

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 mg/kg	JAU 6476 desthio mg/kg	Reference
	Formulation (g ai/L)	g ai/ha	g ai/hL	Water (L/ha)	No					
GAP, Brazil	250 g/L EC	125			3	30				
UNESP RA- 954/05 FR05BRA006 BRA- FR05BRA006- P1-A	250 g/L EC	130	63	200	3	30	seed	n.d.	< 0.01	Galhiane and de Sousa, 2005, UNESP RA-954-05

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 mg/kg	JAU 6476 desthio mg/kg	Reference
	Formulation (g ai/L)	g ai/ha	g ai/hL	Water (L/ha)	No					
Paulinia, SP Brazil 2005; (Delta Pine)										
UNESP RA- 955/05 FR05BRA006 BRA- FR05BRA006- P2-A Rio Verde, Brazil 2005; (Fibermax 966)	250 g/L EC	130	63	200	3	30	seed	n.d.	< 0.01	Galhiane and de Sousa, 2005, UNESP RA-955-05
UNESP RA- 956/05 FR05BRA006 BRA- FR05BRA006- P3-A Maracaju - MS, Brazil 2005; (Delta Opal)	250 g/L EC	130	63	200	3	30	seed	n.d.	< 0.01	Galhiane and de Sousa, 2005, UNESP RA-956-05
UNESP RA- 954/05 FR05BRA006 BRA- FR05BRA006- P1-B Paulinia, SP Brazil 2005; (Delta Pine)	250 g/L EC	250	125	200	3	30	seed	< 0.01	0.01	Galhiane and de Sousa, 2005, UNESP RA-954-05
UNESP RA- 955/05 FR05BRA006 BRA- FR05BRA006- P2-B Rio Verde, Brazil 2005; (Fibermax 966)	250 g/L EC	250	125	200	3	30	seed	< 0.01	0.02	Galhiane and de Sousa, 2005, UNESP RA-955-05
UNESP RA- 956/05 FR05BRA006 BRA- FR05BRA006- P3-B Maracaju - MS, Brazil 2005; (Delta Opal)	250 g/L EC	250	125	200	3	30	seed	< 0.01	< 0.01	Galhiane and de Sousa, 2005, UNESP RA-956-05

JAU 6476 = prothioconazole. Total residues expressed as mg prothioconazole equivalents/kg.

JAU 6476 desthio = prothioconazole-desthio. Residues expressed as mg prothioconazole-desthio/kg.

JAU 6476 = prothioconazole. Residues expressed as mg prothioconazole/kg

n.d.: not detected

A total of eighteen supervised trials were conducted in 2006, 2011, 2012 and 2013 on cotton in Brazil (Galhiane, M. S.; de Sousa Santos, L., 2007, UNESP RA-1223/07, UNESP RA-1224/07, UNESP RA-1225/07, UNESP RA-1226/07; Resende, G., 2011, F11-017; Resende, G., 2012, F12-010

and Resende, G., 2013, F13-004). Ten trials were decline trials. All trials were carried out according to the GAP in Brazil, except for the four trials performed in 2006 (Galhiane, M. S.; de Sousa Santos, L., 2007) where the PHI was 21–22 day instead of 30 days.

In studies Galhiane, M. S.; de Sousa Santos, L., 2007, UNESP RA-1223/07 (one trial), UNESP RA-1224/07 (one trial), UNESP RA-1225/07 (one trial) and UNESP RA-1226/07 (one trial), an SC formulation containing 175 g/L prothioconazole and 150 g/L trifloxystrobin was applied four times to cotton at 88 g prothioconazole/ha, with an interval of 12 days between applications, and a PHI of 21–22 days.

The maximum period of storage was 246 days (8.2 months), which falls within the stability period of 3 years as confirmed by previous studies with prothioconazole and prothioconazole-desthio.

Residues of prothioconazole-desthio were determined by HPLC/MS/MS using method 00598. The LOQ was 0.01 mg/kg. Procedural recoveries at fortification levels of 0.01–0.1 mg/kg were within the acceptable range of 70–120%, RSD < 20%, for all analytes.

In study Resende, G., 2011, F11-017 (four trials), an SC formulation containing 175 g/L prothioconazole and 150 g/L trifloxystrobin was applied four times to cotton at 84–96 g prothioconazole/ha, with an interval of 10 days between applications.

The maximum period of storage was 233 days (7.8 months), which falls within the stability period of 3 years as confirmed by previous studies with prothioconazole and prothioconazole-desthio.

Residues of prothioconazole-desthio were determined by HPLC-MS/MS using method 01013. The LOQ was 0.01 mg/kg. Procedural recoveries at fortification levels of 0.01–1.0 mg/kg were within the acceptable range of 70–120%, RSD < 20%, for all analytes.

In studies Resende, G., 2012, F12-010 (5 trials) and Resende, G., 2013, F13-004 (5 trials), an SC formulation containing 175 g/L prothioconazole, 125 g/L bixafen (BYF 00587) and 150 g/L trifloxystrobin was applied four times to cotton at 84–92 g prothioconazole/ha, with an interval of 14 days between applications.

The maximum period of storage was 192 days (6.4 months), which falls within the stability period of 3 years as confirmed by previous studies with prothioconazole and prothioconazole-desthio.

Residues of prothioconazole-desthio were determined by HPLC-MS/MS using method 01013. The LOQ was 0.01 mg/kg. Procedural recoveries at fortification levels of 0.01–1.0 mg/kg (and 0.01–3.0 mg/kg for prothioconazole) were within the acceptable range of 70–120%, RSD < 20%, for all analytes.

Residue levels of prothioconazole-desthio ranged from < 0.01 to 0.16 mg/kg when applied at 4×88 g/ha, and a 30-d PHI (the GAP). The results of these trials are summarized in Table 5.

Table 5 Prothioconazole residues in cotton resulting from supervised trials in the Brazil

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 mg/kg	JAU 6476 desthio mg/kg	JAU 6476 total mg/kg	Reference
	Formulation (g ai/L)	g ai/ha	g ai/hL	Water (L/ha)	No						
GAP, Brazil	175 g/L	88			4	30					
UNESP RA-1223/07 FR06BRA015 BRA-FR06BRA015- P1 Paulinia SP, Brazil, 2006 (Delta Opal)	175	88	44	200	4	21	Seed	< 0.01	< 0.01	< 0.02	Galhiane, and de Sousa Santos, 2007, UNESP RA-1223/07
UNESP RA-1224/07 FR06BRA015 BRA-FR06BRA015- P2 Rondonopolis MT, Brazil, 2006 (Delta	175	88	44	200	4	21	Seed	n.d.	n.d.	n.d.	Galhiane, and de Sousa Santos, 2007, UNESP RA-1224/07

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 mg/kg	JAU 6476 desthio mg/kg	JAU 6476 total mg/kg	Reference
	Formulation (g ai/L)	g ai/ha	g ai/hL	Water (L/ha)	No						
Opal)											
UNESP RA-1225/07 FR06BRA015 BRA-FR06BRA015- P3 Costa Rica MS, Brazil, 2006 (Delta Opal)	175	88	44	200	4	21	Seed	n.d.	< 0.01	< 0.01	Galhiane, and de Sousa Santos, 2007, UNESP RA-1225/07
UNESP RA-1226/07 FR06BRA015 BRA-FR06BRA015- P4 Rio Verde, Brazil, 2006 (FMX 966)	175	88	44	200	4	22	Seed	n.d.	n.d.	n.d.	Galhiane, and de Sousa Santos, 2007, UNESP RA-1226/07
F11-017 F11-017-01, Ituverava, Brazil 2011; (Monsanto DP 604)	175	90.4- 92.4	45.2- 46.2	200	4	25 29 35	Seed	0.02 < 0.01 < 0.01	0.21 0.16 0.06	0.25 0.19 0.08	Resende, 2011, F11-017
F11-017 F11-017-02, Uberlandia, Brazil 2011; (Fiber Max 966 LL)	175	84.6- 94.4	42.3- 47.2	200	4	25 30 35	Seed	< 0.01 < 0.01 < 0.01	0.07 0.05 0.05	0.09 0.07 0.07	Resende, 2011, F11-017
F11-017 F11-017-03, Jaboticabal, Brazil 2011; (IMA CD 6001 LL)	175	84.6- 96.3	42.3- 48.2	200	4	30	Seed	< 0.01	0.08	0.10	Resende, 2011, F11-017
F11-017 F11-017-04, Rio Verde, Brazil 2011; (FM 966 LL)	175	83.4- 89.8	41.7- 44.9	200	4	30	Seed	< 0.01	0.08	0.10	Resende, 2011, F11-017
F12-010 F12-010-01, Paulinia, Brazil 2012; (FM 966 LL)	175	83.7- 92.2	41.8- 46.1	200	4	25 30 35	Seed	< 0.01 < 0.01 < 0.01	< 0.01 0.01 0.01	< 0.02 0.02 0.02	Resende, 2012, F12-010
F12-010 F12-010-02, Ribeirão Preto, Brazil 2012; (FM 966 LL)	175	87.5- 91.2	43.8- 45.6	200	4	25 30 34	Seed	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01	< 0.02 < 0.02 < 0.02	Resende, 2012, F12-010
F12-010 F12-010-03, Uberlândia, Brazil 2012; (Fm 966 LL)	175	87.5- 89.4	43.8- 44.7	200	4	25 30 35	Seed	< 0.01 < 0.01 < 0.01	0.01 < 0.01 < 0.01	0.02 < 0.02 < 0.02	Resende, 2012, F12-010
F12-010 F12-010-04, Jaboticabal, Brazil 2012; (FM 966 LL)	175	87.5- 90.5	43.8- 45.2	200	4	30	Seed	< 0.01	< 0.01	0.02	Resende, 2012, F12-010
F12-010 F12-010-05, Ituverava, Brazil 2012; (NU OPAL RR)	175	86.1- 88.9	43.1- 44.5	200	4	30	Seed	< 0.01	0.01	< 0.02	Resende, 2012, F12-010
F13-004 F13-004-01, Paulinia, Brazil 2012; (FM 966 LL)	175	87.5- 88.0	43.8- 0.0440	200	4	15 20 25 30 35	Seed	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	0.01 0.01 0.01 0.01 < 0.01	0.02 0.02 0.02 0.02 < 0.02	Resende, 2013, F13-004
F13-004 F13-004-02, Ribeirao Preto, Brazil 2012; (FB 966 LL)	175	87.5- 91.9	43.8- 45.9	200	4	15 19 25 30 35	Seed	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	0.018 < 0.01 < 0.01 < 0.01 < 0.01	0.03 < 0.02 < 0.02 < 0.02 < 0.02	Resende, 2013, F13-004
F13-004 F13-004-03,	175	86.5- 89.8	43.4- 44.9	200	4	15 19	Seed	< 0.01 < 0.01	0.036 0.036	0.05 0.05	Resende, 2013, F13-004

COTTON Trial Country, year (Variety)	Application					PHI days	Commodity	JAU 6476 mg/kg	JAU 6476 desthio mg/kg	JAU 6476 total mg/kg	Reference
	Formulation (g ai/L)	g ai/ha	g ai/hL	Water (L/ha)	No						
Uberlandia, Brazil 2012; (FM 966 LL)						25 30 35		< 0.01 < 0.01 < 0.01	0.036 0.036 0.054	0.05 0.05 0.07	
F13-004 F13-004-04, Cravinhos, Brazil 2012; (FB 966 LL)	175	86.8- 88.9	43.4- 44.0	200	4	15 20 24 30 35	Seed	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.02 < 0.02 < 0.02 < 0.02 < 0.02	Resende, 2013, F13-004
F13-004 F13-004-05, Trindade, Brazil 2012; (FM 975 WS)	175	84.2- 92.1	42.1- 45.7	200	4	15 18 25 30 35	Seed	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.02 < 0.02 < 0.02 < 0.02 < 0.02	Resende, 2013, F13-004

JAU 6476 desthio = prothioconazole-desthio. Residues expressed as mg prothioconazole-desthio/kg.

JAU 6476 = prothioconazole. Residues expressed as mg prothioconazole/kg.

n.d.: not detected

FATE OF RESIDUES IN STORAGE AND IN PROCESSING

In stored commodities

No data regarding use of prothioconazole in stored commodities were presented to the Meeting.

In processing

The Meeting received information on high temperature hydrolysis of prothioconazole and the fate of prothioconazole residues during the processing of cotton seeds.

Cotton seed is processed prior to consumption. Processing factors have been calculated for prothioconazole residues in cotton seeds.

High-temperature hydrolysis

A hydrolysis study representative of core processing procedures was previously evaluated by the 2008 JMPR and reported in the 2008 JMPR Evaluation (Prothioconazole – Table 79). The 2008 meeting concluded that prothioconazole degraded slightly ($\leq 11\%$) to prothioconazole-desthio at 120 °C at pH 6.

A further hydrolysis study (Gilges, 2001, MR-106/00) was conducted on prothioconazole-desthio. The hydrolytic degradation of the metabolite prothioconazole-desthio in buffered drinking water has been investigated in order to determine whether the nature of the residue found in processed agricultural commodities is likely to be different from that in raw agricultural commodities. The test substance was exposed to three sets of conditions each of them being representative for a typical food processing operation.

Radiolabelled [phenyl-UL-¹⁴C] prothioconazole-desthio was dissolved at concentrations of approximately 5 mg/L in citrate buffers which were incubated at 90 °C for 20 min (pH 4), 100 °C for 60 min (pH 5) and 120 °C for 20 min (pH 6). After incubation the samples were analysed by liquid scintillation counting to establish recoveries of radioactivity and by HPLC for determination of concentrations of test substance and hydrolysis products. A set of control solutions was used to obtain zero-time values.

Recoveries of radioactivity were found to be 99.4%, 99.9% and 100.3% of applied radioactivity for the three experiments. Prothioconazole-desthio did not show any sign of decomposition if exposed to the sets of conditions representing pasteurization (pH 4, 90 °C), baking, brewing and boiling (pH 5, 100 °C) and sterilization (pH 6, 120 °C).

Conditions	Recoveries of radioactivity ([phenyl-UL- ¹⁴ C] prothioconazole- desthio)	Unknown	Reference
90 °C for 20 min (pH 4.0)	99.4%	< 0.5%	Gilges, 2001, MR-106/00
100 °C for 60 min (pH 5.0)	99.9%	< 0.5%	
120 °C for 20 min (pH 6.0)	100.3%	< 0.5%	

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. The experiments showed that prothioconazole-desthio was stable under hydrolytic conditions at high temperatures. No degradates were detected at any of the investigated pH and temperature ranges.

Cotton seeds

A processing study was conducted on cotton in the USA to determine the potential for concentration of residues of prothioconazole in cotton processed fractions (Veal, 2015, RAJAN030). The SC formulation containing 480 g prothioconazole/L was applied to cotton with three broadcast foliar sprays at the exaggerated rates of 1 kg ai/ha equivalent to 5× the maximum total seasonal rate for prothioconazole on cotton.

Plots TRT5X received 3 equivalent foliar spray applications of Proline 480 SC mixed with Gem 500 SC (an SC formulation containing trifloxystrobin). Individual application rates ranged from 0.99 to 1.05 kg prothioconazole/ha. The interval between applications was 13 to 15 days. Total seasonal application rates for the 5× plots ranged from 2.99 to 3.12 kg prothioconazole/ha. The first application was made between BBCH growth stage 65 and 69. The spray volume ranged from 194 to 262 L/ha.

Plot TRT3× received 3 equivalent foliar spray applications of Proline 480 SC mixed with Gem 500 SC (n SC formulation containing trifloxystrobin). Individual application rates ranged from 0.60 to 0.64 kg prothioconazole/ha. The interval between applications was 14 to 15 days. Total seasonal application rates for the 3× plots ranged from 1.81 to 1.86 kg prothioconazole/ha. These plots were reserve plots that were not harvested.

All applications were made using ground-based equipment. The adjuvant, INDUCE PH 0.125% v/v, was used in all applications.

Single composite seed cotton samples were harvested at a 28 to 29-day pre-harvest interval (PHI) from the TRT5X plots. Single composite samplers of seed cotton samples were harvested from the control plots on the same day the respective samples were collected from the treated plots.

After ginning, triplicate subsamples of undelinted seed, the raw agricultural commodity (RAC), were separated, and the remaining undelinted seed was 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.

Storage stability studies indicate that prothioconazole and desthio-prothioconazole residues are stable in cotton commodities during frozen storage for at least 36 months prior to analysis. The maximum storage period of frozen samples in this study for prothioconazole was 216 days (7.2 months) for cotton seed and 187 days (6.2 months) for cotton processed commodities.

Residues of prothioconazole on cotton were determined by high performance liquid chromatography – electrospray ionization tandem mass spectrometry (LC/MS/MS). The method JA-001-P04-02, which was used for the analysis, was validated with an LOQ of 0.02 mg/kg for prothioconazole-sulfonic acid, 0.02 mg/kg for prothioconazole-desthio (expressed as parent; or 0.018 mg/kg expressed at itself) and 0.04 mg/kg for total prothioconazole.

Procedural recoveries at fortification levels of 0.02–0.75 mg/kg were within the acceptable range of 70–120% for prothioconazole-desthio, prothioconazole-sulfonic acid and prothioconazole in each matrix, with the exception of:-

- One recovery of prothioconazole sulfonic acid in undelinted seed (69%);
- One recovery of prothioconazole-desthio in undelinted seed (69%);
- Two recoveries of prothioconazole in meal (69% and 66%);
- Two recoveries of prothioconazole in hull (65% and 66%);
- One recovery of prothioconazole-desthio in hull (66%);
- Two recoveries of prothioconazole in neutralized crude oil (65% and 66%);
- One recovery of prothioconazole-desthio in neutralized crude oil (66%);
- One recovery of prothioconazole in preclarified crude oil (66%);
- One recovery of prothioconazole-desthio in preclarified crude oil (66%).

The prothioconazole recovery was the sum of prothioconazole-desthio and prothioconazole-sulfonic acid from recovery samples fortified with prothioconazole only. The results are summarized in Table 6.

Table 6 Validation recovery data for prothioconazole, prothioconazole-desthio and prothioconazole sulfonic acid in cotton undelinted seed and cotton processed commodities for study RAJAN030

Crop matrix	Analyte	Fortification Level [mg/kg]	n	Recovery in validation samples			
				Single Values		Mean [%]	RSD [%]
				[%]			
Undelinted seed	Prothioconazole	0.020	3	72,82,75		77	6.7
		0.750	3	78,84,78		80	4.3
		Overall	6			78	5.6
	Prothioconazole sulfonic acid	0.020	4	76,75,75,69		74	4.3
		0.750	3	80,83,87		83	4.2
		Overall	7			78	7.7
	Prothioconazole-desthio	0.020	5	85,73,83,72,69		76	9.3
		0.750	3	82,83,88		84	3.8
		Overall	8			79	8.8
crude oil, preclarified	Prothioconazole	0.020	3	73,66,71		70	5.2
		1.00	3	88,82,101		90	10.8
		Overall	6			80	16.1
	Prothioconazole sulfonic acid	0.020	4	87,91,87,96		90	4.7
		1.00	3	90,98,91		93	4.7
		Overall	10			91	4.6
	Prothioconazole-desthio	0.020	4	66,74,80,105		81	20.7
		1.00	3	88,101,87		92	8.5
		Overall	7			86	16.3
meal	Prothioconazole	0.020	4	83,69,84,66		76	12.4
		1.00	3	84,90,82		85	4.9
		Overall	7			80	11.0
	Prothioconazole sulfonic acid	0.020	3	90,92,90		91	1.3
		1.00	3	85,89,89		88	2.6
		Overall	6			89	2.6
	Prothioconazole-desthio	0.020	3	93,101,99		98	4.3
		1.00	3	82,87,82		84	3.5
		Overall	6			91	9.2
oil, refined	Prothioconazole	0.020	3	90,83,90		88	4.6
	Prothioconazole sulfonic acid	0.020	4	87,97,110,87		95	11.4
	Prothioconazole-desthio	0.020	3	81,85,72		79	8.4

Crop matrix	Analyte	Fortification Level [mg/kg]	n	Recovery in validation samples			
				Single Values		Mean [%]	RSD [%]
				[%]			
Solvent extracted oil	Prothioconazole	0.020	3	76,81,78		78	3.2
		1.00	3	80,73,83		79	6.5
		Overall	6			79	4.6
	Prothioconazole sulfonic acid	0.020	4	86,89,87,93		89	3.5
		1.00	3	89,92,89		90	1.9
		Overall	7			89	2.8
	Prothioconazole-desthio	0.020	3	76,82,82		80	4.3
		1.00	3	80,76,89		82	8.2
		Overall	6			81	6.0
crude oil, neutralised	Prothioconazole	0.020	4	73,70,65,66		69	5.4
		1.00	3	80,80,77		79	2.2
		Overall	7			73	8.6
	Prothioconazole sulfonic acid	0.020	4	72,78,77,76		76	3.5
		1.00	3	84,89,85		86	3.1
		Overall	7			80	7.5
	Prothioconazole-desthio	0.020	3	72,74,86		77	9.8
		1.00	3	83,74,66		74	11.4
		Overall	6			76	9.7
hull	Prothioconazole	0.020	4	65,71,88,79		76	13.2
		0.200	3	66,79,86		77	13.2
		Overall	7			76	12
	Prothioconazole sulfonic acid	0.020	3	74,81,78		78	4.5
		0.200	5	78,80,81,83,85		81	3.3
		Overall	8				
	Prothioconazole-desthio	0.020	3	66,79,83		76	11.7
		0.200	5	77,77,78,86,85		81	5.6
		Overall	8			79	8.0

RSD: Relative Standard Deviation

The average prothioconazole-desthio and the average total prothioconazole residue did not concentrate (processing factor <1×) in meal, hulls, refined oil (bleached and deodorized), solvent extracted crude oil, pre-clarified crude oil, and neutralized crude oil. The results are summarized in Table 7 and 8.

Table 7 Residues of prothioconazole-desthio in cotton and cotton processed fractions

COTTON Trial Country, year (Variety)	Processed Fractions	Prothioconazole-desthio (mean) mg/kg	Processing factor	Reference
JA017-13PA JA017-13PA-TRT5X Louisiana, USA 2013 (Phytogen 499 WRF)	seed, undelinted	0.180	--	Veal, 2015, RAJAN030
	meal	< 0.018	< 0.10	
	hull	0.050	0.28	
	crude oil, preclarified	< 0.018	< 0.10	
	oil, solv. extracted	< 0.018	< 0.10	
	crude oil, neutralized	< 0.018	< 0.10	
	oil, refined	< 0.018	< 0.10	
JA018-13PA JA018-13PA-TRT5X Texas, USA 2013 (DP0912 B2RF)	seed, undelinted	0.494	--	
	meal	0.051	0.10	
	hull	< 0.018	< 0.04	
	crude oil, preclarified	< 0.018	< 0.04	
	oil, solv. extracted	< 0.018	< 0.04	
	crude oil, neutralized	0.055	0.11	
	oil, refined	0.137	0.28	

Table 8 Residues of total prothioconazole in cotton and cotton processed fractions

COTTON Trial Country, year (Variety)	Processed Fractions	Total Prothioconazole (mean) mg/kg	Processing factor	Reference
JA017-13PA JA017-13PA-TRT5X Louisiana, USA 2013 (Phytogen 499 WRF)	seed, undelinted	0.227	--	Veal, 2015, RAJAN030
	meal	< 0.040	< 0.18	
	hull	0.075	0.33	
	crude oil, preclarified	< 0.040	< 0.18	
	oil, solv. extracted	< 0.040	< 0.18	
	crude oil, neutralized	< 0.040	< 0.18	
	oil, refined	< 0.040	< 0.18	
JA018-13PA JA018-13PA-TRT5X Texas, USA 2013 (DP0912 B2RF)	seed, undelinted	0.661	--	
	meal	0.077	0.12	
	hull	< 0.040	< 0.06	
	crude oil, preclarified	< 0.040	< 0.06	
	oil, solv. extracted	< 0.040	< 0.06	
	crude oil, neutralized	0.080	0.12	
	oil, refined	0.171	0.26	

Residues in animal commodities

Farm animal feeding studies

Animal feeding studies were evaluated by the 2008 Meeting. No additional information is provided concerning feeding studies.

APPRAISAL

Prothioconazole is a systemic triazolinthione 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 48th 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 ($\leq 11\%$) 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 ^b
		Processing factor ^a	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	-

Raw Agricultural commodity (RAC)	Processed Fractions	Prothioconazole-desthio		STMR/ STMR-P	MRL ^b
		Processing factor ^a	PF (mean)		
	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	-

^a The calculated processing factors are the ratio of the residue in the processed commodity divided by the residue in the RAC.

^b 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 ^b	21.60 ^a	5.44	0.04	0.04
Dairy cattle	8.64	3.26	13.91	5.32	18.42 ^c	5.44 ^d	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 ^e	0.92 ^f	0.05	0.05	0.02	0.02

^a suitable for estimating maximum residue levels for meat, fat and edible offal of cattle.

^b suitable for estimating STMR for meat, fat and edible offal of cattle.

^c suitable for estimating maximum residue levels for Milk.

^d suitable for STMR levels for Milk.

^e suitable for estimating maximum residue levels for poultry meat, offal and eggs.

^f 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
MRL beef or dairy cattle							
Feeding study1	4.00	< 0.004	4.00	< 0.01	0.05	0.04	< 0.01
	25.00	< 0.004	25.00	< 0.01	0.26	0.17	0.02
Dietary burden and high residue	18.42	< 0.004	21.60	< 0.01	0.226	0.149	0.018
STMR beef or dairy cattle							
Feeding study2	4.00	< 0.004	4.00	< 0.01	0.04	0.02	< 0.01
	25.00	< 0.004	25.00	< 0.01	0.22	0.14	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 below 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

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.

CCN	Commodity	Proposed MRL (mg/kg)	STMR or STMR-P (mg/kg)	HR or HR-P (mg/kg)
SO 0691	Cotton seed	0.3	0.052	
ML 0106	Milks	0.004*	0.004	0.004
MF 0100	Mammalian fats (except milk fats)	0.02	0.01	0.018
MM 0095	Meat (from mammals other than marine mammals)	0.01	0.01	0.01
MO 0105	Edible offal (mammalian)	0.3	Kidney: 0.03, Liver: 0.055	Kidney: 0.15, Liver: 0.23
PE 0112	Eggs	0.005*	0.0006	0.0006
PO 0111	Poultry edible offal	0.1	0.071 (liver)	0.071 (liver)
PF 0111	Poultry fats	0.01*	0.008	0.008
PM 0110	Poultry meat	0.01*	0.0016	0.0016

For calculating animal dietary burdens

CCN	Commodity	Proposed MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
SO 0691	Cotton gin by-products		1.1	1.8

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The International Estimated Daily Intakes (IEDI) for prothioconazole-dethio 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-dethio 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 to the 2017 JMPR Report.

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.

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