Profenofos (171)

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EXPLANATION

Profenofos is an organophosphorus insecticide. The mode of action is via the inhibition of the acetylcholinesterase enzyme.

It was first evaluated by the JMPR in 1990 as a new compound. It was re-evaluated at the 2007 JMPR for toxicology and the 2008 JMPR for residues. The 2007 JMPR evaluated profenofos for toxicology under the Periodic Review Programme and recommended the current ADI of 0–0.03 mg/kg bw and ARfD of 1 mg/kg bw.

The 2008 JMPR evaluated profenofos for residues under the Periodic Review Programme and concluded that the definition of the residue for compliance with the MRL and dietary risk assessment was profenofos.

Profenofos was scheduled at the Forty-ninth Session of the CCPR for the evaluation of additional uses by the 2018 JMPR. The current Meeting received residues data for green coffee beans.

RESIDUE ANALYSIS

Analytical methods

Data generation methods

Two methods were used to determine residues of profenofos in green coffee beans.

Method POPIT MET.011 REV00

Residues of profenofos were extracted from coffee bean with methanol. An aliquot of the extract was partitioned against a saturated sodium chloride, water and hexane solution (2:1:1, v/v/v). The hexane phase was added to a silica solid phase extraction (SPE) column. The aqueous phase was partitioned with a further portion of hexane and the hexane phase added to the same SPE column. Profenofos was eluted in hexane/ethyl acetate (4:1, v/v), concentrated and re-dissolved in hexane. Final determination was by GC-NPD. The method has an LOQ of 0.02 mg/kg. The method was validated in conjunction with the analyses of the residue trial samples. The linearity of the detector response covered a working range of 0.01–0.32 µg/mL. Recovery data are outlined in Table 1.

Table 1 Recovery data for method POPIT MET.011 REV00

Matrix	Fortification level [mg/kg]	Individual recoveries [%]	Range of recoveries [%]	Mean recovery [%]	RSD [%]
Green coffee bean	0.02	104, 108, 97, 98, 94, 92, 92	92–108	98	6
	0.23	87, 109, 94	87–109	97	12

Method POPIT MET.061. REV06

Residues of profenofos were extracted from green coffee bean with methanol. An aliquot of the extract was partitioned against a saturated sodium chloride, water and hexane solution (2:1:1, v/v/v). The hexane phase was added to a silica solid phase extraction (SPE) column. The aqueous phase was partitioned with a further portion of hexane and the hexane phase added to the same SPE column. Profenofos was eluted in hexane/ethyl acetate (4:1, v/v), concentrated and re-dissolved in hexane for further purification by gel permeation chromatography (GPC). The eluate was concentrated and dissolved in water:acetonitrile (1:1, v/v). Final determination was by LC-MS/MS with quantification achieved using the ion transition m/z 374.90 → m/z 304.70. The method has an LOQ of 0.01 mg/kg. The linearity of the detector response covered a working range of 0.5–17 ng/mL. The method was validated for coffee beans as well as other crops. Recovery data are outlined in Table 2.

Table 2 for Recovery data Method POPIT MET.061. REV06

Matrix	Fortification level [mg/kg]	Individual recoveries [%]	Range of recoveries [%]	Mean recovery [%]	RSD [%]
Green coffee bean (high oil content)	0.01	81, 85, 104, 88, 91, 108, 92	81–108	93	11
	0.1	106, 106, 106, 97, 106	97–106	104	4

Matrix	Fortification level [mg/kg]	Individual recoveries [%]	Range of recoveries [%]	Mean recovery [%]	RSD [%]
Cotton (high oil content)	0.01	73, 82, 80, 72, 68, 69, 74, 78	68–82	75	7
	0.1	73, 82, 77, 73, 75, 76	73–82	76	4
	0.4	86, 71, 85, 81, 91, 92	81–92	84	9
	1.0	70, 86, 79, 72, 70	70–86	75	9
Peanut (high oil content)	0.01	96, 98, 100, 91, 93, 92, 89, 95	89–100	94	4
	0.1	84, 81, 85, 97, 101, 105	81–105	92	11
Sunflower (high oil content)	0.01	72, 71, 75, 71, 73, 77, 69, 73	69–77	73	3
	0.1	68, 68, 74, 70, 69, 72	68–74	70	3
Cabbage (high water content)	0.01	89, 88, 91, 73, 89, 90, 91, 92	73–92	88	7
	0.1	79, 91, 94, 90, 98, 105	79–105	93	9
	1.0	93, 93, 93, 91, 94, 93	91–94	93	1
Corn (maize) grain (high starch content)	0.01	76, 77, 82, 94, 93, 87, 92, 98	76–98	87	9
	0.1	82, 86, 101, 102, 93, 95	82–102	93	9

Enforcement method

The Meeting received information from a literature review (Harmoko, Kartasamita & Tresnawati, 2015) on the validation of the QuEChERs method for the determination of profenofos in coffee. Quantification was achieved using LC-MS/MS and the ion transition m/z 327.9 → m/z 302.9. The validation data are summarized in Table 3.

Table 3 Summary of validation data for the determination of profenofos in green coffee beans

Commodity	LOQ (mg/kg)	Fortification level (mg/kg)	Mean recoveries (%) for n=6	RSD (%)	Linearity (mg/kg)
Green coffee beans	0.05	0.01	118	3	0.005–0.05 R^2 = 0.997
		0.05	90	7	
		0.1	84	6	

USE PATTERN

Table 4 lists the additional uses of profenofos submitted to the 2018 JMPR.

Table 4 Summary of the additional GAP submitted for consideration in this Meeting

Crop	Country	Indoor/ outdoor	Type	Timing of application	Rate (g ai/ha)	No. of appl (interval)	PHI (days)
Coffee	Brazil	Outdoor	EC	-	400	2 (30 days)	7

Hyphen means “not specified” or “not defined”.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

Coffee bean

Ten residue trials were conducted in Brazil in 2001 and 2006 using an EC formulation.

Within the trials a number of different application patterns were undertaken:

- Four trials were conducted with two foliar applications at a rate of 400 g ai/ha. Samples were collected 3, 7 and 10 days after the last application.
- Three trials were conducted with two foliar applications at a rate of 300 g ai/ha. In addition, at each trial site at the same time, trials were also conducted with two foliar applications of 600 g ai/ha. Samples were collected from 0–32 days after the last application.

- Three trials were conducted with one foliar application of 240 g ai/ha. In addition, at each trial site at the same time, trials were also conducted with one foliar application of 480 g ai/ha. Samples were collected from 25–35 days after the last application.

  After collection, the samples were subjected to different processing procedures prior to storage and analysis:

Study M0535

After collection, the samples were dried either in the sun (trials M05035-JJB1 and M05035-JJB2), in an oven for 7 days then at room temperature (trial M05035-LZF1), or just at room temperature (trial M05035-LZF2). After drying, the samples were processed, where the beans were separated from the shells (via removal of the exocarp, mesocarp and endocarp from the bean). The processing took place within a single day. The beans were packed in HDPE plastic bags. The bags were labelled and stored in a freezer, where they remained until dispatched to the laboratory.

Study M00095

No details on the processing procedures undertaken prior to storage and analysis are available in the study. The sponsor has indicated that normal commercial practices would have been followed i.e. duration of any drying is typically dependent on time taken to reach a lower bean moisture content (c. 11%). This lower moisture content facilitates the removal of the exocarp, mesocarp and endocarp.

Study M05015

Following harvest the samples were sundried outdoors (trials M05015-JJB1 and M05015-JJB2) or in a greenhouse (trial M05015-LZF). After drying, the samples were processed, where the beans were separated from the shells (via removal of the exocarp, mesocarp and endocarp from the bean). The beans were packed in HDPE plastic bags. The bags were labelled and stored in a freezer, where they remained until the samples were submitted to the laboratory.

After the drying steps and the procedures to remove the coffee beans from their skins, the samples were stored frozen prior to extraction and analysis for up to 445 days.

Residues of profenofos in coffee (green beans) were determined using analytical methods POPIT MET.011. Rev 00 or POPIT MET.061. Procedural recoveries were conducted at fortification levels ranging from 0.01 mg/kg to 0.1 mg/kg with acceptable recoveries obtained.

Table 5 Residues of profenofos in green coffee bean from supervised trials in Brazil

Location, Country Year, Crop/Variety	Rate (g ai/ha)	Interval (days)	Growth stage at application	DALA (days)	Crop part	Profenofos (mg/kg)	Reference
GAP Brazil	400 ai/ha × 2 or 240 g ai/ha x1	30 -	- -	7 30	-	-	-
Monte Carmelo, Minas Gerais Brazil 2006 Coffee/Mundo Novo	400 400	30	BBCH 85 BBCH 89	3 7 10	Bean	<0.01 <0.01 <0.01	Report: M05035 Study: M05035 Trial: M05035-JJB1 - Complied with GLP principles and national regulations
Indianopolis, Minas Gerais Brazil 2006 Coffee/Mundo Novo	400 400	30	BBCH 85 BBCH 89	3 7 10	Bean	<0.01 <0.01 <0.01	Report: M05035 Study: M05035 Trial: M05035-JJB2 - Complied with GLP principles and national regulations

Location, Country Year, Crop/Variety	Rate (g ai/ha)	Interval (days)	Growth stage at application	DALA (days)	Crop part	Profenofos (mg/kg)	Reference
Holambra, São Paulo Brazil 2006 Coffee/Mundo Novo	400 400	30	BBCH 73–77 BBCH 85–87	3 7 10	Bean	0.03 0.02 0.02	Report: M05035 Study: M05035 Trial: M05035-LZF1 - Complied with GLP principles and national regulations
Santa Amelia, Paraná Brazil 2006 Coffee/Obata	400 400	30	BBCH 73–77 BBCH 85–87	3 7 10	Bean	<0.01 <0.01 <0.01	Report: M05035 Study: M05035 Trial: M05035-LZF2 - Complied with GLP principles and national regulations
Santo Antonio da Posses, SP Brazil 2001 Coffee/Mundo Novo	300 300	21	BBCH 81–82 BBCH 85–88	2 7 14 21 30	Bean	<0.02 <0.02 <0.02 <0.02 <0.02	Report: M00095 Study: M00095 Trial: M00095-JJB1 - Complied with GLP principles and national regulations
	600 600	21	BBCH 81–82 BBCH 85–88	2 7 14 21 30	Bean	<0.02 <0.02 <0.02 <0.02 <0.02	
Guaxupe, MG Brazil 2001 Coffee/Mundo Novo	300 300	21	BBCH 83–84 BBCH 85–86	0 7 14 21 30	Bean	<0.02 <0.02 <0.02 <0.02 <0.02	Report: M00095 Study: M00095 Trial: M00095-JJB2 - Complied with GLP principles and national regulations
	600 600	21	BBCH 83–84 BBCH 85–86	0 7 14 21 30	Bean	<0.02 <0.02 <0.02 <0.02 <0.02	
Ocaucu, SP Brazil 2001 Coffee/Ubata	300 300	21	BBCH 79 BBCH 81	0 7 14 21 32	Bean	0.11 <0.02 <0.02 <0.02 <0.02	Report: M00095 Study: M00095 Trial: M00095-LZF - Complied with GLP principles and national regulations
	600 600	21	BBCH 79 BBCH 81	0 7 14 21 32	Bean	0.15 <0.02 0.08 0.06 <0.02	
Monte Carmelo, MG Brazil 2006 Coffee/Mondo Novo	240	-	BBCH 81	25 30 35	Bean	<0.01 <0.01 <0.01	Report: M05015 Study: M05015 Trial: M05015-JJB1 - Complied with GLP principles and national regulations
	480	-	BBCH 81	25 30 35	Bean	<0.01 <0.01 <0.01	

Location, Country Year, Crop/Variety	Rate (g ai/ha)	Interval (days)	Growth stage at application	DALA (days)	Crop part	Profenofos (mg/kg)	Reference
Idianopolis, MG Brazil 2006 Coffee/Mundo Novo	240	-	BBCH 85	25 30 35	Bean	<0.01 <0.01 <0.01	Report: M05015 Study: M05015 Trial: M05015-JJB2 - Complied with GLP principles and national regulations
	480	-	BBCH 85	25 30 35	Bean	<0.01 <0.01 <0.01	
Holambra, SP Brazil 2006 Coffee/Mundo Novo	240	-	BBCH 73–77	25 30 35	Bean	<0.01 <0.01 <0.01	Report: M05015 Study: M05015 Trial: M05015-LZF - Complied with GLP principles and national regulations
	480	-	BBCH 73–77	25 30 35	Bean	<0.01 <0.01 <0.01	

APPRAISAL

Profenofos is an organophosphorus insecticide. The mode of action is via the inhibition of the acetylcholinesterase enzyme.

It was first evaluated by the JMPR in 1990 as a new compound. It was re-evaluated in the 2007 JMPR for toxicology and the 2008 JMPR for residues. The 2007 JMPR evaluated profenofos for toxicology under the Periodic Review Programme and recommended the current ADI of 0–0.03 mg/kg bw and ARfD of 1 mg/kg bw.

The 2008 JMPR evaluated profenofos for residue under the Periodic Review Programme and concluded that the definition of residue for compliance with MRL and for dietary risk assessment was profenofos.

Profenofos was re-evaluated by the 2011 and 2015 JMPR for additional uses.

Profenofos was scheduled at the Forty-ninth Session of the CCPR for the evaluation of additional uses in the 2018 JMPR. The current Meeting received residues data for green coffee beans.

Methods of analysis

The Meeting received two new methods for the determination of profenofos in green coffee bean. The two data generation methods involved extraction with methanol followed by sample clean up by SPE. Final determination was achieved using either GC-NPD or LC-MS/MS; the LOQ for profenofos was either 0.01 mg/kg or 0.02 mg/kg respectively.

The Meeting concluded that suitable methods are available for the determination of profenofos in green coffee beans.

For enforcement, a review of the literature demonstrated that residues of profenofos in green coffee beans can be determined using the QuEChERs method with an LOQ of 0.01 mg/kg.

Stability of residues in stored analytical samples

Data were previously evaluated by the 2008 JMPR for crops with high oil content. The Meeting concluded that the demonstrated storage stability for various cotton fractions was sufficient to support the maximum length of storage of the green coffee beans (445 days prior to analysis).

Results of supervised residue trials on crops

The Meeting received residue trials data for profenofos on green coffee beans.

Coffee beans

The critical GAP in Brazil, is for two foliar applications of 400 g ai/ha, a re-treatment interval of 30 days and a PHI of 7 days.

A total of seven supervised residue trials, conducted in Brazil on green coffee beans following normal agricultural practices, supported the critical GAP.

Residues in green coffee beans in rank order (n=7) were: < 0.01, < 0.01, < 0.01, < 0.02, < 0.02, < 0.02 and 0.02 mg/kg.

The Meeting estimated a maximum residue level of 0.04 mg/kg and a STMR of 0.02 mg/kg for green coffee beans.

RECOMMENDATIONS

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

CCN	Commodity name	Recommended maximum residue level, mg/kg		STMR or STMR- P, mg/kg
		New	Previous	
SB 0716	Coffee beans	0.04	-	0.02

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The ADI for profenofos is 0–0.03 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for profenofos 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 2018 JMPR Report. The IEDIs ranged from 0–20% of the maximum ADI.

The Meeting concluded that long-term dietary exposure to residues of profenofos from uses considered by the JMPR is unlikely to present a public health concern.

Acute dietary exposure

The ARfD for profenofos is 1 mg/kg bw. The International Estimate of Short Term Intakes (IESTIs) for profenofos were calculated for the food commodities and their processed commodities for which HRs/HR-Ps or STMRs/STMR-Ps were estimated by the present Meeting and for which consumption data were available. The results are shown in Annex 4 of the 2018 JMPR Report. The IESTI was 0% of the ARfD.

The Meeting concluded that acute dietary exposure to residues of profenofos from the use considered by the present Meeting is unlikely to present a public health concern.

REFERENCES

Author	Report No./Trial ID	Year	Title, Institute
Casagrande, C., Afonso, K.	M05015	2007	Polytrin 400/40 EC- Magnitude of profenofos and cypermethrin residues in coffee beans - Brazil, 2006. Report No. M05015 Not to GLP (To local Brazilian agricultural practices), Unpublished Syngenta File No. A6465F_1000
Francisco, E., Marconi, F.	M00095	2002	Curyom 550 EC- Magnitude of profenofos and lufenuron residues in coffee - Brazil, 2001. Report No. M00095 GLP, Unpublished Syngenta File No. CGA15324/1754
Mantovani, V.	POPIT MET.061.Rev06	2006	Determination of profenofos residues (CGA 15324) in plant samples by LC/MS/MS. Report No. POPIT MET.061.Rev06 GLP, Unpublished Syngenta File No. CGA015324_10001
Marconi, F., Afonso, K.	M05035	2007	Curyom 550 EC- Magnitude of profenofos and lufenuron residues in coffee - Brazil, 2006. Report No. M05035 GLP, Unpublished Syngenta File No. A9441A_10000
Harmoko, Kartasamita and Tresnawati	-	2015	QuEChERS Method for the Determination of Pesticide Residues in Indonesian Green Coffee Beans using Liquid Chromatography Tandem Mass Spectrometry. Journal of Mathematical and Fundamental Sciences, [S.I.], v. 47, n. 3, p. 296–308, dec. 2015. ISSN 2338-5510.