METHOPRENE (147)

First draft prepared by Dr R Scrivens, Health and Safety Executive, York, United Kingdom

EXPLANATION

Methoprene is an insect growth regulator classified as a juvenile hormone mimic. It has insecticidal activity against a variety of insect species. Methoprene is used to control infestations in post-harvest stored cereal grain commodities and other stored commodities (sunflower and peanuts).

Methoprene was first evaluated by the JMPR in 1984 and re-evaluated for residues several times. The most recent residues evaluation was conducted in 2016. The ADI of 0–0.09 mg/kg bw was established for racemic methoprene (R and S enantiomers in ratio 1:1); a separate ADI of 0–0.05 mg/kg bw was established for S-methoprene (2001). An ARfD was unnecessary. The residue definition for methoprene and for S-methoprene for plant and animal commodities, for both compliance with MRLs and dietary risk assessment is methoprene. The residue is fat soluble.

At the Fiftieth Session of the CCPR (2018), methoprene was scheduled for evaluation of additional use patterns by the 2019 Extra JMPR. The current Meeting received residue data for post-harvest use on stored peanuts.

RESIDUE ANALYSIS

Analytical methods

The Meeting received recovery data (generated concurrently to the analysis of the residue trial samples) for the analytical method employed in the analysis of stored peanut commodities (CAP 427.05). This method was previously evaluated by the 2016 JMPR, validated for the determination of methoprene in sunflower seeds by reverse-phase HPLC with UV detection at 264 nm. Prior to analysis, samples were extracted with 100 mL methanol by shaking the unshelled peanut samples for a minimum of 5 hours. Samples were allowed to sit or shake for 19 additional hours, after which 5 mL of dibutyl phthalate (DBP) was added as an internal standard. Mean procedural recoveries for unshelled peanuts analysed using CAP 427.05 were approximately 100% with a relative standard deviation of approximately 6% (Table 1), and a lowest limit of method validation of 1.3 mg/kg.

Table 1 Procedural recovery data for method CAP 427.05

Matrix	Analyte	Fortification level (approx.) [mg/kg]	Individual recoveries [%]	Range of recoveries [%]	Mean recovery [%]	RSD [%]
Unshelled peanuts	Methoprene	1.3	100, 107, 114, 115, 118	100-118	111	6.6
		2.7	100, 104, 104, 106, 109, 111, 111, 114, 115, 119,	100-119	109	5.4

Stability of pesticide residues in stored analytical samples

No new storage stability data were submitted to the current Meeting.

USE PATTERN

The additional (peanut) GAP submitted for consideration in the current Meeting is summarized in Table 2. Whilst the formulation may be diluted in water or oil for other stored commodities, for peanuts the label states to dilute with water only.

Table 2 List of additional uses of S-methoprene submitted in 2019

Crop	Country	Formulation		Application		WHP [a] (days)
		Type	Conc.	Rate	No.	
Peanuts	USA	EC	288 g/L	max 34.6 g ai/1000 bushels [b] (up to 4.5 g ai/t)	ns	ns

[a] WHP=withholding period

[b] 1000 bushels (USA) 7.7 t is the weight/volume (t/1000 bushels) for Virginia type and 9.5 t is for south-eastern runners (unshelled) peanuts

ns: not stated

RESULTS OF SUPERVISED RESIDUE TRIALS ON CROPS

Peanuts

Five residue trials were conducted in the USA in 2015.

Commercially grown unshelled peanuts from three different farm locations were harvested, bagged, and sent to the testing facility for treatment and residue analysis. Each farm location submitted 13 to 45 kg unshelled peanuts. One of the farms provided three different varieties for testing. Each of the trials consisted of two untreated controls and two treated samples of 2.3 kg size. At a single location, the formulation containing S-methoprene was applied at 7.5 mL product/US ton which equates to 2.4 g ai/t by admixture to the peanuts while being turned in a cement mixer, this occurred for each trial. Water was used as the diluent in line with the label recommendation for peanuts. The cement mixer was used to simulate peanuts flowing through a grain auger. Prior to the application, excess dust was collected from the cement mixer using a dust collection device. Although the intended product can be used with dust-controlling oils this physical removal of dust is not usual label recommended practice prior to application with S-methoprene. Despite this, the intention was to remove excess dust to prevent S-methoprene adhering to dust, and is therefore likely to be worst case (in terms of residue levels on the target peanut lots). Treated samples were taken one day after treatment and placed into frozen storage where they were maintained frozen for periods of up to 149 days prior to extraction and analysis.

Residues following application of S-methoprene were determined as methoprene in peanuts following the method CAP 427.05 using reverse-phase HPLC with UV detection. Procedural recoveries from spiking at similar levels to those occurring in the samples from the supervised trials were reported (see Table 1).

The results of the supervised trials are presented in Table 3. No residues were found in the untreated controls (< 0.01 mg/kg). Residue results have been presented uncorrected for recovery. Residue values which have been used for the estimation of maximum residue levels and STMRs are underlined.

These trials can be regarded as independent trials, as the application of S-methoprene was made separately for each trial, and the trials themselves did not involve storing the peanuts for a period of storage under normal commercial food handling conditions. The aim being to analyse a situation in which the highest likely residues from label use might arise, i.e., where no pre-harvest interval is specified. As a result residues of methoprene in peanuts were determined shortly after treatment (after one day) for all trials.

Table 3 Residues in Peanuts from supervised trials in the USA involving S-methoprene as a post-harvest application

Year, Variety (source of peanuts)	Application			DALA days	Residues determined as methoprene (mg/kg)	Reference
	Form.	g ai/1000 bushels (g ai/t) unshelled peanuts	no.			
GAP USA: Peanuts	EC	up to4.5 g ai/t 34.6 g ai/1000 bushels	ns ns	ns ns		
2015 Peanuts (unshelled)/ GA 06G Peanuts sourced from Newton, Alabama, USA	EC	22.1 (2.4)	1	1	2.2, 1.9 mean = 2.0 (LOD = 0.007)	5189 Haas and Witte, 2016
2015 Peanuts (unshelled)/ Spanish (Organic) Peanuts sourced from Wellman, Texas, USA	EC	26.2 (2.4)	1	1	2.2, 2.1 mean = 2.1 (LOD = 0.006)	
2015 Peanuts (unshelled)/ Runner Peanuts sourced from Wellman, Texas, USA	EC	23.8 (2.4)	1	1	1.7, 1.9 mean=1.8 (LOD = 0.004)	
2015 Peanuts (unshelled)/ Virginia Peanuts sourced from Wellman, Texas, USA	EC	22.8 (2.4)	1	1	2.0, 2.0 mean=2.0 (LOD = 0.003)	
2015 Peanuts (unshelled)/ OG6 Peanuts sourced from Ashburn, Georgia, USA	EC	26.2 (2.4)	1	1	1.9, 2.1 mean=2.0 (LOD = 0.002)	

FATE OF RESIDUES DURING PROCESSING

No new data were received on the fate of S-methoprene residues on processing.

APPRAISAL

Methoprene, an insect growth regulator, was first evaluated by the JMPR in 1984 and evaluated for residues several times. The most recent residues evaluation was conducted in 2016. The ADI of 0–

0.09 mg/kg bw was established for racemic methoprene (R and S enantiomers in ratio 1:1); a separate ADI of 0–0.05 mg/kg bw was established for S-methoprene (2001). An ARfD was unnecessary. The residue definition for methoprene and for S-methoprene for plant and animal commodities, for both compliance with MRLs and dietary risk assessment, is methoprene. The residue is fat soluble.

At the Fiftieth Session of the CCPR (2018), methoprene was scheduled for evaluation of additional use patterns by the 2019 Extra JMPR. The current Meeting received residue data for post-harvest use on stored peanuts.

Methods of analysis

Residues of methoprene were determined in peanuts using an HPLC-UV analytical method that was previously evaluated by the 2016 JMPR. New data validating the method for peanuts was received by the Meeting with the lower and upper levels of fortification validated being 1.3 and 2.7 mg/kg. Based on the residue levels found in the trials, the Meeting concluded that the available validation data are adequate to ensure the validity of the results.

Stability of residues in stored analytical samples

The 2005 Meeting concluded that "numerous laboratory and field trials have shown long term stability of methoprene in stored grain, not only at -20 °C but even at room temperature". Noting that residues of methoprene in wheat grain trials evaluated by the JMPR in 2005 remained stable over 180 days of ambient storage, the Meeting concluded that residues of methoprene in samples from the peanut supervised trials would be stable over the periods of frozen storage of up to 149 days.

Results of supervised residue trials on crops

Peanut

The critical GAP in the USA is application of S-methoprene at up to 36.4 g ai/1000 bushels (corresponding to up to 4.5 g ai/t) with no withholding period specified. Five residue trials from the USA at dose rates (2.4 g ai/t; 64, 66, 69, 76 and 76% of GAP rate in g ai/1000 bushels) below the critical GAP were provided to the Meeting.

Residues in peanuts in rank order (n=5) were: 1.8, 2.0 (3), and 2.1 mg/kg.

As in the trials, where S-methoprene was applied separately to different peanut lots simulating commercial application practice, the results reflected a high recovery of applied methoprene (75 to 88% of the 2.4 g ai/t applied in all the trials), the Meeting decided that the application rate determined the level of residue expected at the zero day withholding period of the GAP.

Based on the GAP, and with an anticipated variation in weights of different peanut varieties per 1000 bushels (the label expression reflecting amount of S-methoprene applied to 1000 bushels of peanuts), the Meeting considered that residues of up to about 4.5 mg/kg can be anticipated.

The Meeting estimated a maximum residue level of 5 (Po) mg/kg and a STMR of 5 mg/kg.

Residues in animal commodities

Peanut meal can be fed to livestock. The 2016 JMPR evaluated residues of methoprene in cereal grains and oilseeds (except for peanuts). Estimation by the present Meeting, now including peanuts, does not significantly increase the previously estimated (2016) maximum dietary burdens of 13.46 ppm in the diet of cattle and 10.62 ppm for poultry. The Meeting confirmed its previous conclusions for animal commodities.

RECOMMENDATIONS

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

Definition of the residue for compliance with the MRL and dietary risk assessment for plant commodities: methoprene

Definition of the residue for compliance with the MRL and dietary risk assessment for animal commodities: methoprene

The residue is fat-soluble.

CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P mg/kg	HR or HR-P mg/kg
		New	Previous		
SO 0703	Peanut whole	5 Po	-	5	-

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The ADI for S-methoprene is 0–0.05 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for methoprene 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 2019 Extra JMPR Report.

Assuming the residues are S-methoprene, the IEDIs ranged from 10–60% of the maximum ADI. The Meeting concluded that long-term dietary exposure to residues of methoprene from uses considered by the JMPR is unlikley to present a public health concern.

Acute dietary exposure

The 2001 JMPR decided that an ARfD for methoprene was unnecessary. The Meeting therefore concluded that the acute dietary exposure to residues of methoprene from the uses considered is unlikely to present a public health concern.

REFERENCES

Author	Report No./Trial ID	Year	Title, Institute
Haas, K.L. and Witte, J.	5189	2016	(S)-Methoprene: Residues on Peanuts The above report contains methods of analyses CAP 414 and CAP 427.05 as appendices