5.23 PROPAMOCARB (148)

RESIDUE AND ANALYTICAL ASPECTS

Propamocarb is a systemic carbamate fungicide, which was first evaluated in 1984. It was evaluated under the periodic review program in 2005 for toxicology and 2006 for residues. It was last evaluated by the 2014 JMPR, which recommended maximum residue levels for additional uses. The ADI and ARfD are established as 0–0.4 mg/kg bw and 2 mg/kg bw, respectively. The residue definition for plant and animal commodities is propamocarb (free base) for both enforcement of MRLs and dietary exposure assessment. The residue is not fat-soluble.

At the Forty-ninth Session of the CCPR (2017), propamocarb was scheduled for the evaluation of a new livestock feeding study by the 2018 JMPR and consideration of maximum residue levels for mammalian commodities. The Meeting received a dairy cow feeding study, analytical method and storage stability study from the manufacturer.

Methods of analysis

The Meeting received a new analytical method for the determination of propamocarb and its metabolites (propamocarb N-oxide, 2-hydroxypropyl propamocarb, propamocarb oxazolidinone and propamocarb glucuronide) in animal matrices. For extraction of residues, either 0.1% 1 N acetic acid in methanol for propamocarb glucuronide or acetonitrile for all other analytes were used. LC-MS/MS was used for the determination of the analytes. This method was successfully validated and the LOQ levels achieved for all analytes were 0.010 mg/kg in milk and 0.020 mg/kg in tissues (muscle, fat, liver and kidney), as parent equivalents.

Stability of residues in stored analytical samples

Analysis for propamocarb was completed within one month of sampling.

Residues in animal commodities

Farm animal feeding studies

The Meeting received information on the residue levels in milk and tissues of dairy cows administered propamocarb (as propamocarb-HCl) at doses equivalent to of 13.6, 26.3 and 138 ppm in the feed for 29 consecutive days.

In milk, parent compound was found only at the highest dose (138 ppm) at the level of 0.015 mg/kg (< 0.01 mg/kg at the medium dose, 26.3 ppm).

In tissues, mean (maximum) concentrations of parent were at the lowest, medium and the highest doses, respectively: for muscle, < 0.02 (< 0.02) mg/kg, 0.02 (0.020) mg/kg and 0.077 (0.088) mg/kg; for fat, < 0.02 (< 0.02) mg/kg, < 0.02 (< 0.02) mg/kg and 0.029 (0.042) mg/kg; for liver, 0.23 (0.28) mg/kg, 0.38 (0.50) mg/kg and 1.3 (1.3) mg/kg; for kidney, 0.49 (0.57) mg/kg, 0.92 (1.1) mg/kg and 3.4 (3.7) mg/kg.

During the depuration phase for cows dosed at 138 ppm, residue levels of parent declined rapidly. In milk (3 days) and tissues (7 days) after the cessation of dosing, the residue levels of parent were all below LOQs.

Animal commodity maximum residue levels

The 2014 JMPR estimated the propamocarb dietary burdens for the calculation of mammalian commodity maximum residue levels and STMRs as 31.55 ppm and 10.7 ppm, respectively. The calculations used to

estimate maximum residue levels, STMR and HR values for cattle matrices (based on the dietary burdens and feeding study results described above) is shown below.

	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Propamocarb (mg/kg)			
				Muscle	Liver	Kidney	Fat
Maximum residue level (mg/kg), beef or dairy cattle							
Feeding study	26.3	< 0.01	26.3	0.020	0.50	1.1	0.02
	138	0.015	138	0.088	1.3	3.7	0.042
Dietary burden and high residue estimation	31.55	0.010	31.55	0.023	0.54	1.2	0.021
STMR (mg/kg), beef or dairy cattle							
Feeding study	13.6	< 0.01	13.6	0.020	0.28	0.57	0.02
Dietary burden and median residue estimation	10.7	< 0.01	10.7	0.016	0.22	0.45	0.016

The Meeting estimated a maximum residue level of 0.01(*) mg/kg and a STMR of 0 mg/kg for milks. For tissues, the Meeting estimated maximum residue levels of 0.03 mg/kg for meat (from mammals other than marine mammals) and mammalian fat (except milk fats) and 1.5 mg/kg for edible offal (mammalian) based on residues in kidney. The Meeting estimated STMR and HR values of 0.016 mg/kg and 0.023 mg/kg for muscle, 0.016 mg/kg and 0.021 mg/kg for fat and 0.45 mg/kg and 1.2 mg/kg for edible offal, respectively.

RECOMMENDATIONS

On the basis of the available data, 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 dietary risk assessment for plant and animal commodities: *propamocarb*.

The residue is not fat-soluble.

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The ADI for propamocarb is 0–0.4 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for propamocarb 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 0–2% of the maximum ADI.

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

Acute dietary exposure

The ARfD for propamocarb is 2 mg/kg bw. The International Estimate of Short Term Intakes (IESTIs) for propamocarb 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 IESTIs were 0% of the ARfD for children and varied from 0–1% for the general population.

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

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