5.23 PROPAMOCARB (148)

RESIDUE AND ANALYTICAL ASPECTS

Propamocarb is a systemic carbamate fungicide with specific activity against Oomycete species that cause seed, seedling, root, foot and stem rots and foliar diseases in a number of edible crops. The compound was first evaluated by the JMPR in 1984, and was then reviewed by JMPR in 1986, 1987 and 2005, an ADI of 0–0.4 mg/kg bw and an ARfD of 2 mg/kg bw were established in 2005. Propamocarb was evaluated within the periodic review programme for residue and analytical aspects by JMPR in 2006.

The residue definition in plant and animal products for both enforcement and dietary intake purposes is propamocarb (free base. Propamocarb is not considered fat soluble.

The meeting received information on GAP and supervised residue trials in/on onion, leek, broccoli, cauliflower, Brussels sprouts, head cabbage, kale and lima bean. A new analytical method was provided for propamocarb in animal matrices, as well as new studies in laying hen metabolism, feeding studies on lactating cow and laying hens, rotational crops and processed commodities.

Animal metabolism

Laying hen

A metabolism study with propamocarb in laying hens was received by the Meeting. Laying hens were orally dosed via capsule with [14C] propamocarb hydrochloride at a rate of approximately 19 ppm in the feed (1.0 mg/kg body weight) once daily for fourteen consecutive days. The majority of the residues (92% to 99% of the TRR) in the egg and tissues could be extracted.

The TRR in eggs increased from day-1 through too day-7 and reached a plateau, at day-8, of about 0.25 mg eq./kg. The TRR in the tissue samples were highest in liver (0.492 mg/kg) with 0.14 mg/kg in leg muscle, 0.12 mg/kg in breast muscle and 0.042 mg/kg in fat (0.065 mg/kg in renal fat).

The major residues in the eggs and tissues were parent propamocarb (2% in fat, 5% in muscle, 9% in liver and 12% in eggs) and desmethyl propamocarb (6% in fat, 22% in liver, 29% in muscle, and 45% in eggs). The minor residues found in the eggs and tissues were bis-desmethyl-propamocarb (< 1% to 7%) and propamocarb-N-oxide (< 1%).

In summary, the metabolic degradation of propamocarb is rapid and extensive in laying hens with desmethyl-propamocarb and propamocarb being the major residues in all tissues (mostly in liver, eggs and muscle). Demethylation is the main route of metabolism for the parent compound. A minor route of metabolism involves oxidation of the tertiary nitrogen to form propamocarb-N-oxide. The pathway and metabolism profile found in laying hen is consistent to that of the lactating cow metabolism study evaluated by 2006 JMPR.

Field crop rotational studies

Rotational crop studies were conducted in Germany and France during 2002/2003. Four applications of 72.2, 36.1, 3.61 and 3.61 kg ai/ha propamocarb were applied to cabbage as the primary crop, and Lamb's lettuce and wheat were grown as rotational crops with a plant-back interval (PBI) of 52–102 days. No residues of Propamocarb were found above LOQ in Lamb's lettuce, wheat grain, wheat (green material) and wheat straw.

Four rotational crop studies were conducted in the Netherlands, France, Spain and Italy from 2008 to 2010 .Three spray applications of 1.325 kg ai/ha. propamocarb with 7–13days interval were applied to lettuce as primary crop, and carrots, lettuce and wheat or barley were grown as rotational

crops, with plant-back intervals (PBI) of 26–46 days. No residues of propamocarb were found above LOQ in any of these rotational crops.

In rotational field studies with wheat, sugar beet, table beet, dry bean and soya beans conducted in USA in 1997 (four applications at rates of 1.68 kg ai/ha.), which was evaluated by 2006 JMPR, there was no residues detected in wheat grain and straw, soya bean seed, beetroot and beet tops and dry bean from a 30 day PBI, and residues were in the range of 0.229 to 0.51 mg/kg only in wheat hay and forage from a 30 day PBI.

The meeting noted that the GAP of propamocarb (3–4 applications of 1 kg ai/ha.) approximates the application rate in the new studies and was lower than in the 1997 studies. The Meeting agreed that no residue in food and feed commodities are expected from rotational crops following the registered uses.

Methods of analysis

The meeting received the information on multiresidue QuEChERS Method (BCS method ID 01205) for analysis of residues of propamocarb in meat (cattle), liver (cattle), kidney (cattle), fat (cattle), milk (cattle) and egg (chicken) (mass transitions at m/z 102 and 74). The limit of quantification (LOQ) was at 0.01 mg/kg in meat, liver, kidney, fat, milk and egg. The method was confirmed by results of an independent laboratory validation which repeated mean recovery rates of 80–88% in all matrices.

Stability of residues in stored analytical samples

The meeting received information on storage stability of propamocarb in frozen cabbage samples. Propamocarb hydrochloride was stable for a period of at least 39 months.

Results of supervised residue trials on crops

The meeting received supervised residue trial data for propamocarb in/on bulb onion, leek, broccoli, cauliflower, Brussels sprouts, head cabbage, kale and lima bean.

Bulb vegetables

Bulb onion

In 21 trials conducted in Europe according to GAP in Italy (three foliar applications of 1.0 kg ai/ha, 7days PHI), residues were < 0.01(2), 0.01, 0.02(4), 0.03, 0.04, 0.05(5), 0.07, 0.21, 0.41, 0.52, 0.86, 1.3 and 1.4 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg, a STMR of 0.05 mg/kg and a HR of 1.4 mg/kg for propamocarb in onion bulb.

Leek

In 12 trials conducted in Europe according to GAP in Albania (four foliar applications at 1.0 kg ai/ha, 14days PHI), residues were 0.24, 0.74, 0.9, 1.1(2), 2.4, 2.6, 4.0, 4.4, 5.5, 11 and 15 mg/kg. The meeting estimated a maximum residue level of 30 mg/kg, a STMR of 2.5 mg/kg and a HR of 15 mg/kg for propamocarb in leek.

Brassica vegetables

Broccoli

In ten trials conducted in Europe according to GAP in Spain (three foliar applications of 1.0 kg ai/ha, 14 days PHI), residues were 0.01, 0.16, 0.17, 0.21, 0.29(2), 0.32, 0.63, 0.97 and 1.7 mg/kg. The

meeting estimated a maximum residue level of 3 mg/kg, a STMR of 0.29 mg/kg and a HR of 1.7 mg/kg for propamocarb in broccoli.

Cauliflower

In ten trials conducted in Europe according to GAP in Greece (three foliar applications of 1.0 kg ai/ha, 14 days PHI), residues were < 0.01, 0.01, 0.02(2), 0.03, 0.04, 0.06, 0.08, 0.20 and 0.82 mg/kg. The meeting estimated a maximum residue level of 2 mg/kg, a STMR of 0.035 mg/kg and a HR of 0.82 mg/kg for propamocarb in cauliflower to replace the previous recommendation of 0.2 mg/kg.

Brussels sprouts

In eight trials conducted in Europe matching the GAP of Belgium (three foliar applications of 1.0 kg ai/ha, 14 days PHI), residues were 0.20, 0.25, 0.24, 0.46, 0.48, 0.49, 0.64 and 1.3 mg/kg. The meeting estimated a maximum residue level of 2 mg/kg, a STMR of 0.47 mg/kg and a HR of 1.3 mg/kg for propamocarb in Brussels sprouts.

Head cabbage

In 12 trials conducted in Europe matching the GAP of Spain (three foliar applications at 1.0 kg ai/ha, 14 days PHI), residue were 0.02, 0.03, 0.06, 0.08, 0.13, 0.18, 0.21, 0.23, 0.24, 0.28, 0.32 and 0.36 mg/kg. The meeting estimated a maximum residue level of 1 mg/kg, a STMR of 0.195 mg/kg and a HR of 0.36 mg/kg for propamocarb in head cabbage.

Leafy vegetables

Kale

In nine trials conducted in Europe matching the GAP of Belgium (three foliar applications of 1.0 kg ai/ha, 14 days PHI), residues were 0.33, 0.39, 0.46, 3.9, 4.0, 4.0, 5.2, 10.7 and 11.8 mg/kg. The meeting estimated a maximum residue level of 20 mg/kg, a STMR of 4.0 mg/kg and a HR of 11.8 mg/kg for propamocarb in kale.

Legume vegetables

Lima Beans

In three trials conducted in the United States according to US GAP (four foliar applications at 1.0 kg ai/ha, 0 days PHI), residues in seed without pods were 0.26, 0.42 and 0.43 mg/kg, residues in forage were 40.6, 83.6 and 47.4 mg/kg. As only three trials were conducted according to GAP the meeting could not recommend a maximum residue level for propamocarb in lima bean seed without pods.

Fate of residues during processing

The Meeting received information on the fate of propamocarb residues during the processing of tomatoes, spinach and lettuce, and a study on the nature of residues in processed commodities. Propamocarb hydrochloride was stable under all conditions of processing tested (pasteurisation, baking, brewing, boiling and sterilisation). Processing factors based on the residue of propamocarb are listed in table below. Using the STMR-RAC obtained from propamocarb use, the Meeting estimated STMR-P values for processed commodities to be used in dietary intake calculations and/or livestock dietary burden calculations.

Summary of the processing studies in tomato, spinach and lettuce

Commodity	Processed commodity	Processing factors Residue: PCB	Processing factor(PF) (Mean or best estimate)	STMR-P= STMRRAC × PF(mg/kg)
Tomato 0.515 mg/kg [a]	Juice	0.43, 0.44, 0.46, 0.53, 0.59, 0.68, 0.86	0.53	0.27
	Preserve	0.27, 0.31, 0.34, 0.40, 0.41,0.50, 0.59	0.40	0.21
	Puree	0.32, 0.40, 0.64, 0.65, 0.71, 0.83, 1.1 [a], 1.4 [a], 1.4 [a], 2.6	0.77	0.40
	Paste [a]	3.0, 3.2, 3.0	3.1	1.54
Spinach 11.2 mg/kg [a]	Leaf, cooked	0.86, 0.87, 0.88, 0.93	0.88	9.9

[a] Data from 2006 JMPR evaluation

Farm animal feeding studies

The meeting received information on feeding studies with lactating cows and laying hens.

Dairy cow feeding study

No measurable residues of propamocarb or its metabolites 2-hydroxy-propamocarb, propamocarb-N-oxide, and oxazolidine-2-one propamocarb were detected in milk or edible tissues of cattle exposed to propamocarb at levels of 0.8, 2.4 or 8 ppm administrated daily for 28 days, except for milk, where levels of up to 0.019 mg/kg of 2-hydroxy-propamocarb were found in the highest dose group (8 ppm).These residues were equally distributed between the milk fat and the skim milk. LOQs were 0.01 mg/kg (milk) and 0.05 mg/kg (tissues).

Laying hen feed study

A residue transfer study of propamocarb was conducted in laying hens. Hens were dosed orally for 35 consecutive days at the rates of 1.2 ppm (0.3×), 4.1 ppm (1×), 12.3 ppm (3×), and 41.1 ppm (10×) in the feed.

The mean (maximum) propamocarb residues in the egg samples from 1× and 0.3× feeding levels were: 0.0047 mg/kg (0.005 mg/kg) and 0.012 mg/kg (0.013 mg/kg) at Day 35.

In fat, the mean (maximum) propamocarb residues at Day 35 were < LOD (0.0014 mg/kg) in 1× and 0.3× dose groups.

In liver, the mean (maximum) propamocarb residues at Day 35 were 0.0037 mg/kg (0.0055 mg/kg) in the 1× dose group, and 0.0019 mg/kg (0.0021 mg/kg) in the 0.3× dose group.

In muscle, the mean (maximum) propamocarb residues at Day 35 were 0.0022 mg/kg (0.0028 mg/kg) in the 1× dose group, and 0.001 mg/kg (0.001 mg/kg) in the 0.3× dose group.

Animal commodity maximum residues levels

The dietary burdens were estimated using the OECD diets listed in Appendix IX of the 2009 Edition of FAO Manual. Potential cattle feed items include: cabbage, kale and potatoes (including by-products). Dietary burden calculations for beef cattle and dairy cattle and poultry are provided below.

Summary of livestock dietary burden (ppm of dry matter diet)

	US-Canada		EU		Australia		Japan	
	max	mean	max	mean	max	mean	max	mean
Beef cattle	0.38	0.20	16.16	5.58	0.11	0.05	0.00	0.00
Dairy cattle	0.13	0.07	16.11	5.53	31.55 [a, b]	10.70 [c, d]	0.00	0.00

	US-Canada		EU		Australia		Japan	
	max	mean	max	mean	max	mean	max	mean
Poultry-broiler	0.00	0.00	0.10	0.04	0.00	0.00	0.00	0.00
Poultry-layer	0.00	0.00	4.03[e]	1.37[f]	0.00	0.00	0.00	0.00

[a] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat
[b] Highest maximum dairy cattle dietary burden suitable for MRL estimates for mammalian milk
[c] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat
[d] Highest mean dairy cattle dietary burden suitable for STMR estimates for mammalian milk
[e] Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs
[f] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs

The propamocarb dietary burden for animal commodity MRL and STMR estimation (residue levels in animal feed expressed on dry weight) are 31.55 and 10.7 ppm for mammalian products (based primarily on the new use on kale), and the maximum and mean dietary burdens are 4.03 and 1.37 ppm for poultry products.

Mammalian products

The Meeting noted that the maximum cattle dietary burden was about 3–4 times higher than the dose level (8 ppm) in the feeding study and the metabolism study of lactating cow (11.5 ppm), and could not estimate maximum residue levels for mammalian commodities. The Meeting agreed to withdraw the previous MRLs of 0.01* mg/kg for milk, meat from mammals other than marine mammals, and edible offal, mammalians.

Poultry products

The MRLs for poultry products were estimated using the maximum dietary burden and the highest residues obtained from the laying hen feeding study. For the estimation of the STMRs, the mean dietary burden and mean residues on poultry products from the feeding study were used.

The maximum dietary burden of 4.03 ppm DM matches the 1× dose level of the laying hen feeding study. Therefore, the residue levels reported in the feeding study were used as a direct estimate of the residue levels in poultry muscle, fat, liver and eggs resulting from the dietary burden. Similarly, the STMR of 1.37 ppm approximates the lowest dose level of the feeding study (1.2 ppm). Therefore, as an estimate for the STMR in the poultry products, the mean residue levels from the feeding study at this level were used. The estimated MRLs and STMRs are summarized in following table.

	Feed level	Residues	Feed level	Residues (mg/kg) in		
	(ppm) for egg residues	(mg/kg) in egg	(ppm) for tissue residues	Muscle	Liver	Fat
MRL poultry						
Feeding study [a]	4.1	0.005	4.1	0.0028	0.0055	< LOD [c]
Dietary burden and high residue	4.03	0.005	4.03	0.0028	0.0055	< LOD [c]
STMR poultry						
Feeding study [b]	1.2	0.0012	1.2	0.0010	0.0019	< LOD [c]
Dietary burden and residue estimate	1.37	0.0012	1.37	0.0010	0.0019	< LOD [c]

[a] Highest residues for tissues and highest residues for eggs
[b] Mean residues for tissues and mean residues for eggs
[c] LOD in fat was 0.0014 for propamocarb

The meeting estimated the following STMR values: eggs 0.001 mg/kg, muscle 0.001 mg/kg, liver 0.002 mg/kg and fat 0.001 mg/kg. The following HR values are also estimated: eggs of 0.005 mg/kg, muscles of 0.003 mg/kg, liver of 0.006 mg/kg and fat of 0.001 mg/kg.

The meeting recommended the maximum residue levels of 0.01* mg/kg for poultry fat, and confirmed it previous recommendation for maximum residue levels of 0.01* mg/kg for eggs, poultry meat, and poultry, edible offal of.

DIETARY RISK ASSESSMENT

Long-term intake

The long-term dietary intake for propamocarb (ADI 0–0.4 mg/kg bw) was calculated for the 17 regional diets on the basis of the STMRs estimated by the JMPR in 2006 and the current meeting. The results are shown in Annex 3 of the 2014 Report.

The International Estimated Daily Intakes (IEDI) of propamocarb were 0–1% of the maximum ADI (0.4 mg/kg bw). The Meeting concluded that the long-term intake of residues of propamocarb from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The ARfD for propamocarb is 2 mg/kg bw. The International Estimated Short Term Intake (IESTI) of propamocarb was calculated for the commodities for the commodities for which residue levels were estimated. The results are shown in Annex 4 of the 2014 Report.

The IESTI of propamocarb calculated were up to 20% of the ARfD (2 mg/kg bw) for children and general population. The Meeting concluded that the short-term intake of residues of propamocarb resulting from uses that have been considered by current meeting is unlikely to present a public health concern.