

CARBOFURAN (096)

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EXPLANATION

Carbofuran was first reviewed in 1976 and most recently in 1997, when the Meeting recommended the withdrawal of MRLs for a number of commodities. At the 31st Session of the CCPR, the delegation from Thailand reported that new data would be available on rice, maize, sweet corn, and dry and immature soya beans. The CCPR also noted that data on carrots, cotton seed, egg plant, maize and maize fodder, tomatoes, wheat, grapes, peanuts, peppers, sunflower seed and turnips would also be reported and decided to maintain the CXLs for these for four years pending evaluation by the 2002 JMPR.

The manufacturer reported information on GAP, fate of residues in processing, residues in food in commerce or at consumption, national MRLs, and residue data (including analytical methods) for cereals, oil seeds (cotton seed, rape seed) and sweet corn. Residue data were reported by the government of Thailand on soya beans, rice, and sweet corn and by the government of Poland on sugar beet, horse beans and maize. The governments of Germany, The Netherlands, Thailand and Poland reported information on GAP and/or national MRLs

RESIDUE ANALYSIS

Analytical methods

Carbofuran and its metabolite 3-hydroxy-carbofuran (3-OH-carbofuran) are extracted from vegetables by refluxing with 0.25 M HCl. After filtration the extract is cleaned up on a C-18 SPE column, followed by an aminopropyl column eluted with 1% methanol in dichloromethane for analysis by HPLC, with fluorescence detection after post-column treatment by alkaline hydrolysis and derivatization with *o*-phthaldehyde and 2-mercaptoethanol. In another method the compounds are quantified by HPLC with tandem coupled mass spectrometers. In both methods the limit of detection (LOD) is 0.01 mg/kg and of quantification (LOQ) 0.05 mg/kg. Validations were presented in the reports, and recoveries at fortifications from 0.05 to 1 mg/kg varied from 62 to 125%.

In a method used in India, the acid extract is cleaned up on C-18 and Florisil SPE columns and quantified by HPLC with a UV-visible detector. The LOQ was 0.1 mg/kg and recoveries at fortifications of 0.1, 0.5 and 1 mg/kg carbofuran and 3-OH-carbofuran ranged from 71 to 91%.

USE PATTERN

Carbofuran is registered in many countries for the control of insects and nematodes in various crops. The manufacturer submitted product labels from Brazil, Colombia, India, South Korea, Poland and the USA. Information on the crops with data evaluated at this Meeting is summarized in Table 1.

Table 1. Registered uses of carbaryl.

Crop	Country	Form.	Application				PHI days
			Method	kg ai/ha	spray conc., kg ai/hl	No.	
Cotton	Brazil	50G	In furrow	1.5-3	NA	1	45
	Colombia	3SC	Foliar	0.54-0.73	NA	1	NS
			At plant/banded	0.66-0.99	NA	1	NS
Field corn (Maize)	Brazil	50G	Soil, at planting	1-1.75	NA	1	30
	Colombia	3SC	Seed, at planting	0.825	NS	1	NS
	Germany	GR	Seed, soil covering	0.0375 g/m	NA	1	
	India	3G	NS	0.50-1.0	NA		NS
	Maize	GR	During bowing of seeds	0+75	NA	NS	NS
	Thailand	GR	On top of young plant	1.5	NA	1	35
	USA	4F	Foliar	0.14-1.1	1.2-12 ¹	1-2 ²	30
			In furrow/banded	1.1	NA	1	30
Horse bean	Poland	350FS	Seed dressing	9.8 g/kg seed	NA	NS	NS
Rape seed	Poland	35LS	Seed treatment	5.25g/kg seed	NA	1	NS
Rice	Brazil	50G	Broadcast ³	0.75-1	NA	1	30
	Colombia	3GR	Broadcast	0.6-0.9	NA	1	NS
	India	3G	Broadcast	0.75-2.0	NA	NS	NS
	South Korea	3GR	In furrow	0.9-1.2	NA	3	45
	Thailand	GR	broadcast	0.563-0.938		1-2	60-80
Soya bean	Thailand	GR	Seeding bed	0.75-1.125	NA	1	80-110
Sugar beet	Poland	350FS	Seed dressing	1.2 g/kg seed	NA	NS	NS
Sweet corn	USA	4F	Foliar	0.56	1.2-6 ¹	1-2 ²	7
			In furrow/banded	1.1	NA	1	30
	Thailand	GR	On top of young plant	1.5	NA	1	35

NA: not applicable

NS: not specified

LS: liquid seed treatment

¹ Lower number ground applications, higher aerial

² Only two foliar, or one banded and one foliar, applications per season

³ Apply after flooding and hold water for 48 hours or when pest appears.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The results of supervised trials in Asia, Europe, Latin America and the USA are shown in Tables 2-8. All trials included treated and control plots. When residues were undetected they are shown as below the LOD or LOQ (e.g. <0.01 mg/kg). Residues were rounded to two significant figures, but those near the LOQ to one significant figure. Double-underlined values are from treatments according to maximum GAP ($\pm 30\%$) and were considered for the estimations of maximum residue levels and STMRs.

Reports according to GLP requirements included method validation, dates of analyses of samples, sprayers used and their calibration, plot size, sample size and sampling method. Residue data were not corrected for percentage recoveries. Data submitted only in summary were not evaluated.

Vegetables:	Table 2 – Sweet corn
Cereals:	Table 3 – Field corn (maize) Table 4– Rice
Oil seeds:	Table 5 – Cotton seed Table 6 – Rape seed
Animal feed:	Table 7 – Maize forage and stover (fodder) Table 8 – Rice straw

In each evaluated trial according to GLP residues of carbofuran and 3-OH-carbofuran were determined separately and, except for a single trial on rice in India, the LOD was 0.01 mg/kg and LOQ 0.05 mg/kg for each. In India the LOD was 0.05 and LOQ 0.1 mg/kg for each. When residues were estimated (≥ 0.01 and <0.05 mg/kg for each compound), total residues were calculated according to the FAO Manual (2002):

carbofuran	3-OH-carbofuran	Total carbofuran
<0.01 (0.02) (0.02)	<0.01 <0.01 (0.02)	<0.05 <0.05 (0.03) <0.05 (0.04)

Horse bean. Summary details of a single trial in Poland were reported by the Government. Residues of carbofuran and 3-OH-carbofuran were below the LOD (<0.06 mg/kg) in the beans at a 132-day PHI after treatment at 3.5 g ai/kg seed.

Sweet corn. In six trials in the major growing regions of the USA no residues of carbofuran were detected (Table 2).

Table 2. Residues of carbofuran in sweet corn kernels plus cob (husks removed) in trials in the USA in 2000 after two foliar applications, 7-day PHI (Cornell, 2001c).

State	Application			Residues, mg/kg ¹		
	Form.	kg ai/ha	Water, l/ha	3-OH-carbofuran	carbofuran	Total
OH	4F	0.55	586	<0.01	<0.01	<u><0.05</u>
NB	4F	0.55	745	<0.01	<0.01	<u><0.05</u>
IL	4F	0.55	1040	<0.01	<0.01	<u><0.05</u>
WA	4F	0.55	1120	<0.01	<0.01	<u><0.05</u>
NY	4F	0.55	945	<0.01	<0.01	<u><0.05</u>
FL	4F	0.55	491	<0.01	<0.01	<u><0.05</u>

¹ in each trial, duplicate samples were harvested by two separate passes through the field, and analysed

Sugar beet. Two trials in Poland were reported in summary form by the Government. The seeds were treated at the GAP rate of 28 g ai/kg seed. Residues of carbofuran or 3-OH-carbofuran were not detected (<0.04 mg/kg) in leaf or root at PHIs of 107 to 149 days.

Maize. In three trials in the state of São Paulo, Brazil, one in-furrow application at 1.75 kg ai/ha was made at planting, and in three trials in the USA carbofuran was applied as a post-emergence broadcast spray at 1.1 kg ai/ha (Table 3). In all trials the residues in the grain were below the limit of detection.

Three trials in Poland were reported in summary form by the Government. No residues of carbofuran or 3-OH-carbofuran were detected (<0.04 mg/kg) at 117 to 152 days PHI in the grain of plants treated at 0.75 kg ai/ha with a granular formulation.

Table 3. Residues of carbofuran in field corn grain from supervised trials.

Country, year State	Application					PHI, days	Residues, mg/kg ¹			References
	Form.	kg ai/ha	Water, l/ha	No.	Method		3-OH- carbofuran	carbofuran	Total	
Brazil, 2001 SP	50G	1.75	NA	1	In-furrow	136	<0.01	<0.01	<0.05	Dow and Holihan, 2001. Report No. P3532. Study No. 078COF00R1
	50G	1.75	NA	1	In-furrow	138	<0.01	<0.01	<0.05	
	50G	1.75	NA	1	In-furrow	138	<0.01	<0.01	<0.05	
USA, 2001 Iowa	4F	1.1	12.6	1	Foliar	30	<0.01	<0.01	<0.05	Dow, 2001. Report No. P3526. Study No. 078COF00R2
USA, NB	4F	1.1	19.6	1	Foliar	30	<0.01	<0.01	<0.05	
IL	4F	1.1	15	1	Foliar	30	<0.01	<0.01	<0.05	

NA: not applicable

¹ LOD 0.01 mg/kg, LOQ 0.05 mg/kg in each trial, duplicate samples were harvested by two separate passes through the field and analysed.

Rice. Nine trials were conducted in Brazil, Colombia, India and South Korea (Table 4). In India, sampled plants were dried in the field for one day, transferred to a clean area and dried under the sun for 4-6 hours every day for 3 days. The grain was separated from the straw by being beaten on a wooden plank according to farmers' practices. Samples from South Korea were air-dried for 15 days at room temperature before analysis to obtain the right moisture content to mill the grain.

To meet the pre-harvest interval of 30 days in Brazil, application was later in the growing season than normal for early-season treatments. The plots were flooded to a depth of about 6 cm after seeding and germination, remained flooded for ≥ 100 days, and were then drained two days before single treatments at about 1.0 kg ai/ha, onto the right side of the crop row to simulate an on-furrow application.

A summary report of the field phase only of four trials in Thailand were submitted. No residues were detected at 68 days PHI in the grain from the two trials at 1 kg ai/ha and two at 2 kg ai/ha.

Table 4. Carbofuran residues in rice grain from supervised trials.

Location, year	Application				PHI, days	Sample	Residues, mg/kg			Reference
	Form.	kg ai/ha	No. (interval)	Method			3-OH-carbofuran	carbofuran	Total	
Brazil, 2000 SP	50G	0.8	1	Hand-drilled ¹	30	Grain	(0.04) ^{2,3}	0.06	<u>0.10</u>	Holihan, 2001a. Report No. P3520. Study No. 078RIC00R1
	50G	1	1	Hand-drilled	29	Grain	(0.04)	0.08	<u>0.12</u>	
	50G	1	1	Hand-drilled	30	Grain	(0.04)	0.06	<u>0.10</u>	
Colombia, 2000	3G	0.9	1	Hand-drilled ¹	95	Grain	<0.01 ^{3,4}	<0.01	<u><0.05</u>	Holihan, 2001b. Report No. P3521 Study No 078RIC00R2
	3G	0.9	1	Hand-drilled	86	Grain	<0.01	<0.01	<u><0.05</u>	
India	3G	2.0	3 ⁵	Broadcast	36	Dried grain	(0.08) ^{3,6}	(0.08)	<u>0.16</u>	Kumar and Hosmani, 2001. Study No 078RIC00R4
South Korea ⁷	3G	1.2	3 (30 and 60 d)	Hand broadcast	63	Dried grain	<0.01	<0.01	<u><0.02</u>	Lee, 2001 Report No.PC0307 Study No 078RIC00R4
	3G	1.2	3 (30 and 75 d)	Hand broadcast	45	Dried grain	0.06	0.11	<u>0.17</u>	
	3G	1.2	2 (60 d)	Hand broadcast	63	Dried grain	<0.01	<0.01	<u><0.02</u>	

¹ In ground on right side of row

² Values in parenthesis, \geq LOD (0.01 mg/kg), <LOQ (0.05 mg/kg), are estimates

³ In each plot duplicate samples were collected by two separate passes through the field and analysed, higher residue of each pair reported

⁴ LOD 0.01 mg/kg; LOQ 0.05 mg/kg

⁵ Approx. 10 days before transplant, 25 days (tillering) and 89 days (booting) after transplanting

⁶ Parentheses: estimates between the LOD (0.05 mg/kg) and LOQ (0.10 mg/kg)

⁷ Residues average of triplicate analyses of two sub-samples.

Soya bean, dry. A summary report of the field phase only of four trials in Thailand was submitted. No residues were detected at PHIs from 79 to 122 days from two trials at 1.125 kg ai/ha and two at 2.25 kg ai/ha.

Cotton seed. Four trials were conducted in Colombia in the 1999/2000 growing season and four in the state of São Paulo, Brazil (Table 5).

Table 5. Residues of carbofuran in cotton seed after single applications in supervised trials.

Country, year location	Application				PHI, days	Residues, mg/kg ¹			References
	Form.	kg ai/ha	Water, l/ha	Method		3-OH-carbofuran	carbofuran	Total	
Brazil, 2000 SP	50G	3	NA	Hand drilled	46	<0.01	<0.01	<u><0.05</u>	Cornell, 2001b. Report No. P3530 Study No 078COT00R2
	50G	3	NA	Hand-drilled	46	<0.01	<0.01	<u><0.05</u>	
	50G	3	NA	Hand-drilled	44	<0.01	<0.01	<u><0.05</u>	
	50G	3	NA	Hand-drilled	44	<0.01	<0.01	<u><0.05</u>	
Colombia, 2001	3SC	0.7	104	Foliar	26	<0.01	(0.02) ²	<u><0.05 (0.03)</u>	Cornell, 2001b. Report No. P3530 Study No 078COT00R2
	3SC	0.7	104	Foliar	25	<0.01	(0.03)	<u><0.05 (0.04)</u>	
	3SC	0.7	104	Foliar	25	<0.01	(0.03)	<u><0.05 (0.04)</u>	
	3SC	0.7	104	foliar	25	<0.01	(0.01)	<u><0.05 (0.02)</u>	

NA: not applicable

¹ In each plot, duplicate samples were collected by two separate passes through the field and analysed, higher residue of each pair reported

² Parentheses: estimates between the LOD (0.01 mg/kg) and LOQ (0.05 mg/kg)

Oilseed rape. Six trials were conducted in Poland during the 2000 growing season after seed treatment at 5.25 g/kg (Table 6). There were no detectable residues in any sample.

Table 6. Residues of carbofuran in rape seed from seed-treatment trials in Poland in 2000 (Ginzburg and Cornell, 2002, Report No.PC0314, Study FA-17-0084).

Location	Application			PHI, days	Residues, mg/kg ¹		
	Form.	g/kg seed	No.		3-OH-carbofuran	carbofuran	Total
Malysyn	35 LS	5.25	1	324	<0.01	<0.01	<u><0.05</u>
Jedrzejewo	35 LS	5.25	1	331	<0.01	<0.01	<u><0.05</u>
Przybroda	35 LS	5.25	1	330	<0.01	<0.01	<u><0.05</u>
Sosnicowice	35 LS	5.25	1	337	<0.01	<0.01	<u><0.05</u>
Winna Gora	35 LS	5.25	1	321	<0.01	<0.01	<u><0.05</u>
Trzebnica	35 LS	5.25	1	324	<0.01	<0.01	<u><0.05</u>

¹ LOD 0.01 mg/kg, LOQ 0.05 mg/kg. In each plot duplicate samples collected by two separate passes through the field and analysed.

Maize (field corn) forage and stover. Twelve trials were conducted in Brazil and the USA (Table 7). Total residues varied from <0.05 to 0.38 mg/kg in forage and 0.84 in stover. Forage was collected at late dough to early dent stage and stover at maturity.

Two trials in Poland were reported in summary by the Government. No residues of carbofuran or 3-OH-carbofuran were detected (<0.04 mg/kg) in forage at 117 and 134 days PHI from plants treated at 0.75 kg ai/ha with a granular formulation.

Table 7. Residues of carbofuran in maize (field corn) forage and stover from supervised trials. All single applications.

Location, year	Application				PHI, days	Sample	Residues, mg/kg*			References
	Form.	kg ai/ha	Water, l/ha	Method			3-OH- carbofuran	carbofuran	Total	
Brazil, 2000 SP	50G	1.75	NA	In- furrow	81	Forage ¹	<0.01	(0.01) ²	<u><0.05</u> (0.02)	Dow and Holihan, 2001 Report No. P3520 Study No 078COF00R1
	50G	1.75	NA		136	Stover	<0.01	<0.01	<u><0.05</u>	
	50G	1.75	NA	In- furrow	82	Forage ¹	<0.01	<0.01	<u><0.05</u>	
	50G	1.75	NA		138	Stover ¹	<0.01	<0.01	<u><0.05</u>	
	50G	1.75	NA	In- furrow	91	Forage ¹	<0.01	<0.01	<u><0.05</u>	
	50G	1.75	NA		135	Stover ¹	<0.01	<0.01	<u><0.05</u>	
USA, 2000 Iowa	4F	1.1	12.6	Foliar	30	Forage	0.10	<0.01	<u>0.11</u>	Dow, 2001 Report No. P3516
	4F	1.1	12.6	Foliar	30	Stover	0.13	0.38	<u>0.51</u>	
NB	4F	1.1	19.6	Foliar	30	Forage	0.32	(0.02) ²	<u>0.34</u>	Study No 078COF00 R2
	4F	1.1	12.6	Foliar	30	Stover	0.27	0.57	<u>0.84</u>	
IL	4F	1.1	15	Foliar	30	Forage	0.36	<0.01	<u>0.37</u>	
	4F	1.1	12.6	Foliar	30	Stover	0.15	0.15	<u>0.30</u>	

NA: not applicable

¹ Duplicate samples collected by two separate passes through the field and analysed, higher residue of each pair reported

² Parentheses: estimates between LOD (0.01 mg/kg) and LOQ (0.05 mg/kg)

Rice straw. Nine trials were conducted in Brazil, Colombia, India and South Korea. Total residues of carbofuran ranged from <0.05 to 0.51 mg/kg (Table 8). In Brazil and Colombia, samples consisted of dried stalks or stems with leaves attached after the grain had been harvested. In India plants were dried in the field for one day, transferred to a clean area and dried under the sun for 4-6 hours every day for 3 days, according to farmers' practices, and the grain separated from the straw by being beaten on a wooden plank. In South Korea plants were separated into rice straw and grain after harvesting. The straw samples were air-dried for 15 days at room temperature before analysis.

Table 8. Residues of carbofuran in rice straw from supervised trials.

Location, year	Application				PHI, days	Residues, mg/kg			References
	Form.	kg ai/ha	No.	Method		3-OH- carbofuran	carbofuran	Total	
Brazil, 2000 SP	50G	1	1	Hand- drilled ¹	30	(0.04) ^{2,3}	0.04	<u>0.08</u>	Holihan, 2001a Report no. P3520 Study No 078RIC00R1
	50G	1	1	Hand- drilled	29	(0.05)	0.04	<u>0.09</u>	
	50G	1	1	Hand- drilled	30	(0.04)	0.04	<u>0.08</u>	

Location, year	Application				PHI, days	Residues, mg/kg			References
	Form.	kg ai/ha	No.	Method		3-OH-carbofuran	carbofuran	Total	
Colombia, 2000	3G	0.9	1	Hand-drilled	95	<0.01 ^{3,4}	<0.01	<u><0.05</u>	Holihan, 2001b. Report No. 3521 Study No 078RIC00R2
	3G	0.9	1	Hand-drilled	86	<0.01	<0.01	<u><0.05</u>	
India	3G	2.0	3 (10, 25 and 89 d) ⁵	Broadcast	36	0.25	0.14 ^{3,6}	<u>0.39</u>	Kumar and Hosmani, 2001 Report No. 0309 Study No 078RIC00R4
South Korea ⁷	3G	1.2	3 (0, 30 and 60 d) ⁵	Hand broadcast	63	0.15	(0.03) ²	<u>0.18</u>	Lee, 2001 Report No. PC0307 Study No 078RIC00R4
	3G	1.2	3 (0, 30 and 75 d)	Hand broadcast	45	0.48	(0.03)	<u>0.51</u>	
	3G	1.2	2 (0 and 60 d)	Hand broadcast	63	<0.01	<0.01	<u><0.05</u>	

¹ In ground to right side of row

² Parenthesis: estimates between LOD (0.01 mg/kg) and LOQ (0.05 mg/kg)

³ Duplicate samples collected by two separate passes through the field and analysed, higher residue of each pair reported

⁴ LOD 0.01 mg/kg; LOQ 0.05 mg/kg

⁵ After transplanting

⁶ LOQ 0.10 mg/kg

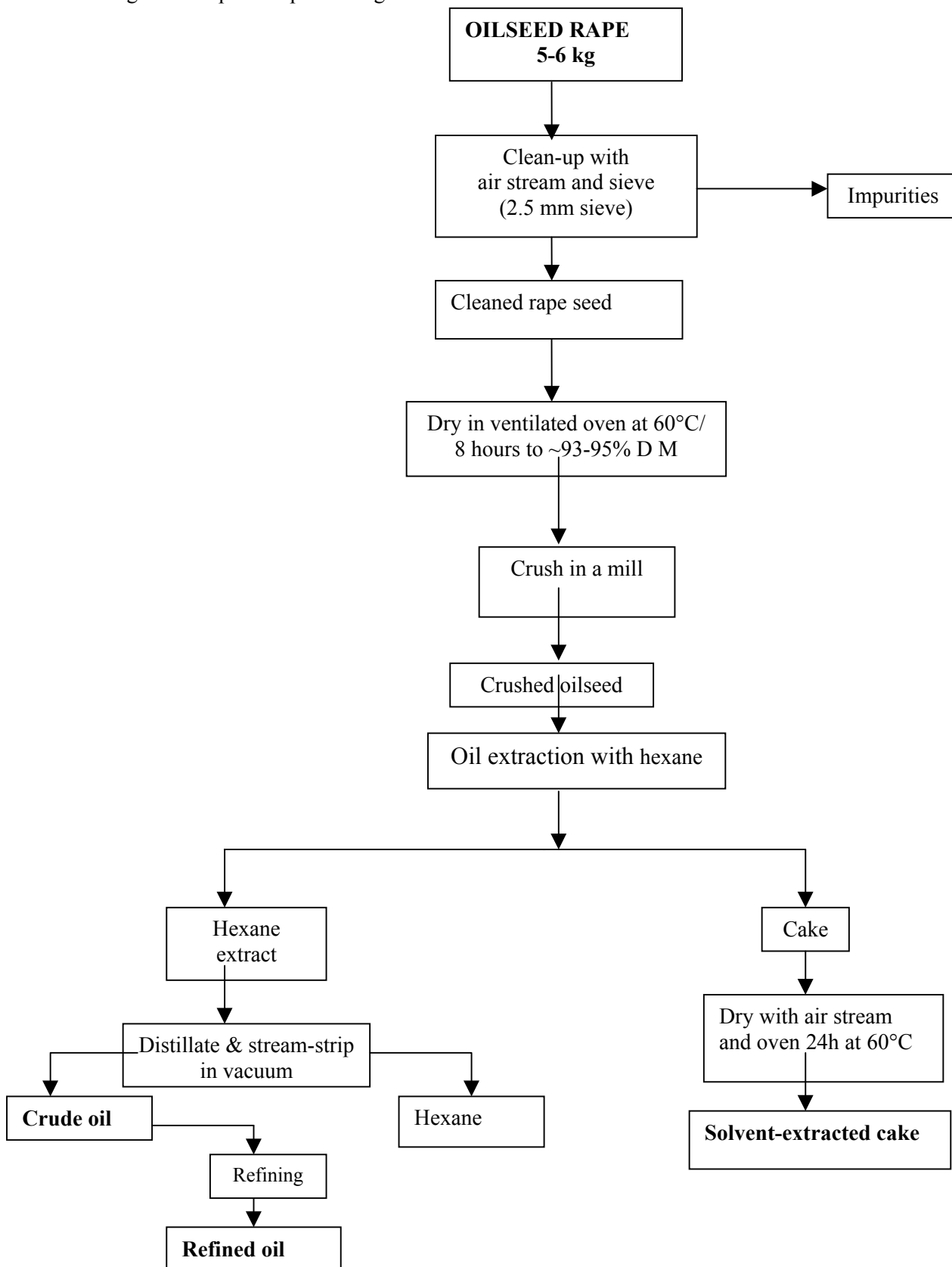
⁷ Residues average of triplicate analyses of two sub-samples.

FATE OF RESIDUES IN PROCESSING

Rice. Grain samples from the 3 rice trials in South Korea were dried for 15 days at room temperature and milled to produce hulled grain. Total carbofuran residues in the dried grain were <0.02 (LOD), 0.17 and <0.02 mg/kg (Table 4), and in hulled grain 0.02, 0.04 and <0.02 mg/kg. The values below 0.05 mg/kg (LOQ) are estimates. No detailed information on the milling process was provided (Lee, 2001). Only for the second trial is it possible to estimate a processing factor of about 0.25 for hulled rice.

Canola (oilseed rape). Rape seed was treated at 5.25 g/kg seed in six trials in Poland (Table 6). The pods plus seed were harvested at the normal stage of maturity after 321-337 days, and the seed separated in the field. Samples from five of the trials were composited for processing into meal (press-cake), crude and refined oil (Ginzburg and Cornell, 2002). The method reflects the conditions for the semi-industrial production of rape seed oil (Figure 1). There were no detectable residues of carbofuran or 3-hydroxy-carbofuran in the seed or in any of the processed samples.

Figure 1. Rape seed processing.



RESIDUES IN FOOD AT COMERCE OR AT CONSUMPTION

The USDA Pesticide Data Program (PDP) is designed to determine pesticide residues in random and targeted samples of crops and foods collected near the point of consumption with the co-operation of the individual States to represent yearly consumer exposures. In 2000, a total of 9,242 samples were analysed for carbofuran and 3-hydroxy-carbofuran. Only four samples, one cantaloupe and three sweet peppers, had any detectable residues of carbofuran, and only two (grape and sweet pepper) had detectable residues of 3-hydroxy-carbofuran (Table 9).

Table 9. Results of the USDA PDP analyses for carbofuran residues in food in 2000 (USDA, 2000).

Sample	Total samples	Samples with carbofuran	Maximum carbofuran residue (mg/kg)	Samples with 3-OH-carbofuran	Maximum 3-OH-carbofuran residue (mg/kg)
Apples	184	0		0	
Cantaloupe	406	1	~0.025	0	
Carrots	184	0		0	
Cherries	275	0		0	
Cucumbers	737	0		0	
Grapes	741	0		1	~0.017
Green beans	719	0		0	
Lettuce	740	0		0	
Nectarines	96	0		0	
Oranges	215	0		0	
Peaches (single)	536	0		0	
Peaches (composite)	534	0		0	
Peanut butter	716	0		0	
Pears (canned)	366	0		0	
Pineapples	104	0		0	
Potatoes	369	0		0	
Poultry liver	480	0		0	
Rice	178	0		0	
Strawberries (fresh)	518	0		0	
Strawberries (frozen)	37	0		0	
Sweet peppers	738	3	~0.011	1	~0.013
Tomatoes (canned)	369	0		0	

The US Food and Drug Administration (FDA) samples individual lots of domestically produced and imported foods and analyses them for pesticide residues to enforce the tolerances set by the USEPA. Domestic samples are collected close to the production site, and import samples at the ports. Emphasis is on the raw agricultural product, which is analysed as the unwashed, whole (unpeeled), raw commodity. Processed foods are also included. The FDA uses multi-residue methods (MRMs) capable of simultaneously determining approximately 400 pesticides with EPA tolerances, and many others that have no tolerances in food commodities. Most commonly used MRMs can also detect many metabolites,

impurities, and alteration products of pesticides. Residues at 0.01 mg/kg and above are usually measurable.

During the 1999 survey, a total of 9,438 samples were analysed. Of these 3,426 were domestic and 6,012 imports. As in previous surveys, fruits and vegetables accounted for the largest proportion of the commodities analysed (about 72%). Only 90 pesticides were found on the crop samples. No carbofuran was detected in any of the domestic or imported samples (US FDA, 2000).

NATIONAL MAXIMUM RESIDUE LIMITS

The following national MRLs were reported to the Meeting.

Commodity	Country	MRL (mg/kg)	Definition of the residue ¹
Cereals	Cyprus	0.1	Not specified
	European Community	0.1*	
	Poland	0.1	CF+3-OH-CF+ 3-K-CF ²
Grain	India	0.1	
Maize/Corn			
Grain	Argentina	0.1	Not specified
	European Community	0.1*	
	Kenya	0.1 T	Not specified
	Mexico	0.2	Not specified
	South Africa	0.1	
	South Korea	0.1	Not specified
	Switzerland	0.05*	Not specified
Fresh	USA	0.2	CF + 3-OH-CF
Green	South Africa	0.2	
Forage	Kenya	5.0 T	Not specified
	USA	5	CF + 3-OH-CF
Fodder	USA	5	CF + 3-OH-CF
Rice			
Husked rice	Australia	0.2	
	Brazil	0.2	Not specified
	Chile	0.2	
	Cyprus	0.02	Not specified
	European Community	0.1*T	
	Kenya	0.2	Not specified
	Mexico	0.2	Not specified
	Paraguay	0.2	Not specified
	South Korea	0.2	Not specified
	Uruguay	0.2	Not specified
Straw	USA	0.2	CF + 3-OH-CF
Oil seed			
	Chile	0.1*	
	India	0.1	
	Kenya	0.1	Not specified

Commodity	Country	MRL (mg/kg)	Definition of the residue ¹
Cotton seed	Brazil	0.1	Not specified
	European Community	0.1* T	
	Mexico	1.0	Not specified
	South Korea	0.1	Not specified
	USA	0.2	CF + 3-OH-CF
Rape seed (Canola)	European Community	0.1* T	
	Poland	0.05	CF+3-OH-CF+ 3K CF ²
Sweet corn	Argentina	0.1	Not specified
	European Community	0.1* T	
Kernel	Kenya	0.1 T	Not specified
	Mexico	1.0	
Fresh	USA	0.2	CF + 3-OH-CF
Other plant commodities	Germany	0.1*	
	Hungary	0.1	Not specified
	Netherlands	0.1*	Not specified

¹ Sum of carbofuran (CF) and 3-hydroxy carbofuran (3-OH-CF), expressed as carbofuran, unless otherwise listed

² 3-K-CF: 3-keto-carbofuran

APPRAISAL

Carbofuran (2,3-dihydro-2,2-dimethylbenzofuran-7-yl methylcarbamate) was first evaluated by the 1976 JMPR. It was last evaluated in 1996, when an ADI of 0–0.002 mg/kg bw was allocated on the basis of the NOAEL in a 4-week study in dogs. Establishment of an acute RfD was requested by the Codex Committee on Pesticide Residues, and that was the basis for the present review.

Carbofuran is a carbamate compound that exerts virtually all its effects by inhibiting cholinesterase activity in nervous tissues. Nevertheless, in one study in dogs, carbofuran also caused testicular degeneration.

A study of the reversibility of inhibition of plasma and erythrocyte cholinesterase activity, in which groups of up to nine rats of each sex per dose were given single doses of 0, 0.5 or 1 mg/kg bw of carbofuran, was reviewed. Inhibition of erythrocyte cholinesterase activity was maximal within about 15 min and was rapidly reversible within 6 h in females. Although the activity of cholinesterase was still less than 80% of the level before dosing at 8 h in males at the higher dose, the decrease at that time was only marginal. Furthermore, when compared with the activity in concurrent controls, the activity at the higher dose was not biologically significantly depressed in males after 4 h. The LOAEL was 0.5 mg/kg bw.

Three studies carried out in beagle dogs were considered relevant to establishing an acute RfD. In a 13-week study evaluated by the 1996 JMPR, which was re-evaluated at the present Meeting, the LOAEL was 10 ppm in the diet (equal to 0.43 mg/kg bw per day); a NOAEL was not identified. Significant depression of erythrocyte cholinesterase activity and clinical signs were seen on the first day of dosing at the lowest dose. A supplementary study was carried out over 4 weeks in male dogs, which was evaluated by the 1996 JMPR but not by the present Meeting. The NOAEL for cholinesterase inhibition was 5 ppm, equal to 0.22 mg/kg bw per day. An earlier 1-year feeding study in dogs, evaluated by the 1996 Meeting, was reviewed by the present Meeting. The NOAEL was 10 ppm (stated as being equal to 0.3 mg/kg bw

per day in the 1996 JMPR monograph), on the basis of concern about the potential for testicular toxicity at 20 ppm.

After considering the data available to the present Meeting as well as the 1996 evaluations, the Meeting established an acute RfD of 0.009 mg/kg bw on the basis of the NOAEL of 0.22 mg/kg bw per day in the 4-week study in dogs and a safety factor of 25, as the relevant toxic effects of carbofuran are dependent on the C_{max} (see section 2.2).

An addendum to the toxicological monograph was prepared

RESIDUE AND ANALYTICAL ASPECTS

Carbofuran has been reviewed several times initially in 1976 and more recently in 1997, when a number of commodities were recommended for withdrawals of MRLs. The 1997 JMPR considered desirable data from feeding studies with cows and processing studies on potatoes and sugar cane treated with carbofuran at exaggerated rates. At the 31st Session of the CCPR, the Committee decided to maintain the CXLs for for four years under the periodic review program for rice, maize, sweet corn, soya bean (dry) and soya bean (immature), carrot, cotton seed, eggplant, maize, maize fodder, tomato, wheat grapes, peanut, pepper sunflower seed.

The company submitted residue data for cereals and grains (field corn), rice, oil seeds (cotton seed, rape seed) and sweet corn, GAP information, fate of residue in processing, residues in food in commerce or at consumption and national residue limits. GAP information and residue data were submitted by Thailand for soya bean, rice, and sweet corn and by Poland for horse bean, maize and sugar beet. The Netherlands submitted GAP information and MRLs

Results of supervised trials

Residue definition for carbofuran is sum of carbofuran and 3-OH-carbofuran, expressed as carbofuran. For each trial under GLP, residues were determined for carbofuran and 3-OH-carbofuran separately. For all trials, except for the rice trial in India, LOD is 0.01 mg/kg and LOQ is 0.05 mg/kg for each compound. In India, LOD is 0.05 and LOQ is 0.1 mg/kg for each compound. When residues were estimated (≥ 0.01 and <0.05 mg/kg) for each compound, carbofuran residues were calculated as follows:

Carbofuran	3-OH-carbofuran	Total carbofuran
<0.01	<0.01	<0.05
(0.02)	<0.01	<0.05 (0.03)
(0.02)	(0.02)	<0.05 (0.04)

Horse bean. In one trial conducted in horse bean according to GAP and submitted by the Government of Poland, no residues of carbofuran were detected (<0.06 mg/kg). As only a summary table was provided, it was not possible to evaluate the trial.

Soya bean, dry. In four trials at GAP submitted by the Government of Thailand no residues were detected (no LOQ reported). As the analytical report was not provided, it was not possible to evaluate the trials.

Sweet corn. Six trials were conducted in sweet corn in USA according to maximum GAP for foliar application (0.56 kg a.i./ha, 7 days PHI). No residues of carbofuran (carbofuran + 3-OH-carbofuran) was detected in any sample analyzed (kernels plus the cob with the husks removed) (<0.05 mg/kg). Sixteen

trials according to GAP conducted in USA were submitted to the 1997 JMPR and the residues are <0.03 (6), 0.03 (4), 0.04 (4), 0.05 and 0.08 mg/kg. The residues from the 1997 JMPR and from the trials submitted to this Meeting are <0.03 (6), 0.03 (4), 0.04 (4), <0.05 (6), 0.05 and 0.08 mg/kg.

The Meeting confirms the previous recommendation of a maximum residue level of 0.1 mg/kg and an STMR of 0.04 mg/kg and recommends an HR of 0.08 mg/kg for carbofuran in sweet corn (corn-on-the-cob).

Sugar beet. In two trials submitted by the Government of Poland conducted in sugar beet at GAP rate residues of carbofuran were not detected (<0.04 mg/kg) in leaf and root at PHI of 107 to 149 days. As only a summary table was provided, it was not possible to evaluate the trials.

Maize. Three trials were conducted in field corn (maize) in Brazil, state of São Paulo, at the GAP in furrow at-plant application rate of 1.75 kg ai/ha with a granular formulation. For the at-plant use pattern in Brazil, the PHI is 30 days. However, with an at-plant use, crop is not mature at 30 days after application. No residues were detected (<0.02 ppm) in mature grain after 136 to 138 days after treatment, when the plants are at mature stage. These trials were considering at being at GAP and considered for estimations.

The US product label allows growers to use carbofuran as an at-plant and foliar insecticide. Three trials were conducted in the major corn-growing states of Iowa, Nebraska, and Illinois using 1 foliar application at the maximum GAP rate of 1.1 kg a.i./ha and 30 days PHI. No carbofuran residues were detected in corn grain (< 0.05 ppm). In three trials conducted at GAP in maize and submitted by the Poland Government, no residues of carbofuran (<0.04 mg/kg) were detected. As only a summary table was provided, it was not possible to evaluate these trials.

Trials conducted according to GAP are <0.05 (6) mg/kg total carbofuran. The Meeting agreed that 6 trials are not sufficient to recommend a maximum residue level in maize grain.

Rice. A total of 9 trials were conducted in rice. In Brazil, 3 trials were conducted using ground application of a granular formulation in the state of São Paulo at maximum GAP rate (0.75 to 1 kg ai/ha). Total residues of carbofuran in grain (carbofuran plus 3-OH-carbofuran, expressed as carbofuran) at 30 days PHI were 0.10 (2) and 0.12 mg/kg.

No residues were detected (<0.05 mg/kg) at 86 and 95 days PHI in two trials conducted in Colombia at maximum GAP (0.9 kg ai/ha).

In one trial in India, rice plants were treated with 3 broadcast applications at the nursery (10 days before transplant), tillering and booting (25 and 89 days after transplanting, respectively) stages at maximum GAP rate of 2 kg a.i./ha. Plant samples were harvested at 36 days PHI, dried in the field for one day and under the sun for 4-6 hours for 3 days in a clean area. The grain was then separated from the straw by beaten on a wooden plank and analyzed. Carbofuran total residues were 0.16 mg/kg.

In three trials conducted in South Korea, plants were treated 2 or 3 times at maximum GAP rate (0.9-1.2 kg a.i./ha) from transplanting to milk-ripe stage. In one trials conducted within 45 days PHI, total residues were 0.17 mg/kg and the two other trials, no residue was detected (<0.02 mg/kg) after 63 days of the last application. Grain samples were air-dried for 15 days at room temperature before analyzed (normal practice is 4 days drying).

In four trials conducted in Thailand at GAP and double GAP rates, no residues were detected at 68 days PHI in rice grain. As the analytical report was not provided, the trials could not be evaluated.

In one trial conducted in Australia according to GAP and evaluated at the 1997 JMPR gave residues of <0.05 mg/kg carbamates (carbofuran + 3-keto-carbofuran + 3-OH-carbofuran).

Trials in rice conducted according to GAP were, in rank order, <0.02 (2), <0.05, 0.10 (2), 0.12, 0.16 and 0.17 mg/kg.

The Meeting agreed to recommend a maximum residue level of 0.3 mg/kg, an STMR of 0.10 mg/kg and an HR of 0.17 mg/kg for carbofuran in rice grain

Cotton seed. Eight trials were conducted in cotton seed in South America. In four trials conducted in Brazil at maximum GAP (1.5-3 kg ai/ha and 45 days PHI) with hand drilled application of a 50G formulation, residues were <0.02 (4) mg/kg.

In four trials conducted in Colombia using 1 foliar application at maximum GAP rate of 0.7 kg a.i/ha of a SC concentration, residues of total carbofuran at 25-26 days PHI were 0.01, 0.02 and 0.03 (2) mg/kg. These values are estimates, as they are below the LOQ (0.05 mg/kg).

Residues of carbofuran in cotton seed according to GAP are 0.01, <0.02 (4), 0.02 and 0.03 and 0.04 mg/kg.

The Meeting agreed to recommend a maximum residue level of 0.1 mg/kg, an STMR of 0.02 mg/kg and an HR of 0.04 mg/kg for carbofuran in cotton seed

Rape seed. Six trials were conducted in rape seed in Poland in 2000 using one seed treatment at GAP rate of 5.25 g a.i/kg seed. Residues of total carbofuran at 321 to 324 days PHI were <0.05 (6) mg/kg. Seed treatment is the only registered use for oilseed rape in Poland.

The Meeting recommends a maximum residue level of 0.05* mg/kg and an STMR for carbofuran in rape seed

Maize forage and fodder. Twelve trials were conducted in field corn forage and stove (fodder) in Brazil and USA. Residues in forage from trials conducted in Brazil at maximum at-planting GAP rate were <0.05 mg/kg (3) at 81-91 days after treatment in soil with a granular formulation. In fodder, residues were <0.05 mg/kg (3) at 135 to 138 days after treatment.

Residues from trials conducted in USA using maximum GAP for foliar application were 0.11, 0.34 and 0.37 mg/kg in forage and 0.51, 0.84 and 0.30 mg/kg in fodder at 30 days PHI. Trials conducted using soil granular application and foliar application gave residues of different populations, which cannot be combined.

It was not possible to evaluate the two trials conducted in Poland at GAP in maize, as only a summary table was submitted.

The Meeting agreed that only 3 trials conducted at the critical foliar treatment is not sufficient to recommend maximum residue levels for carbofuran in maize forage and fodder.

Rice straw. Nine trials were conducted in rice straw in Brazil, Colombia, India and South Korea. In 3 trials conducted in Brazil with soil application at GAP rate of 0.8-1 kg ai/ha, residues within 30 days PHI were 0.10 (2) and 0.12 mg/kg of total carbofuran. In two trials conducted in Colombia at maximum GAP, no residues were detected (<0.02 mg/kg) at 86-95 days PHI. In both countries, rice straw were sampled from dried stalks or stem with leaves left after the grain had been harvested.

In one trial conducted in India, using 3 applications of the GAP rate (2 kg a.i./ha) residues in straw at 36 days PHI were 0.39 mg/kg. Sampled plants were dried in the field for one day and under the sun for 4-6 hours for 3 days in a clean area. After drying, the grain was separated from the straw by beaten on a wooden plank.

In three trials conducted in South Korea at the maximum GAP rate, the straw samples were air-dried for 15 days at room temperature before analyzed. Residues at 45 days PHI were 0.51 mg/kg. Samples harvested at 63 days had residues of <0.01 mg/kg and 0.18 mg/kg.

Trials conducted according to GAP are, in rank order, <0.1 (2), 0.10 (2), 0.12, 0.39 and 0.51 mg/kg.

The Meeting recommends a maximum residue level of 1 mg/kg and an STMR of 0.10 mg/kg for carbofuran in rice straw.

Fate of residues in processing

In the 3 trials conducted in South Korea, rice was treated with a granular formulation at 1.2 kg ai/ha and harvested at 48 or 63 days. Grain samples were dried for 15 days at room temperature and submitted to a milling process to obtain hulled rice grain (husked). Total carbofuran residues in dried grain were <0.05 (LOD), 0.18 and <0.05 mg/kg. Residues in hulled grain were (0.02), (0.02) and <0.05 mg/kg. A processing factor of 0.25 from the second trial can be derived. No detailed information on the milling process was provided.

The calculated processing factor from rice to husked rice (0.25) was applied to the recommendations for rice (maximum residue level of 0.3 mg/kg, an STMR of 0.10 mg/kg and an HR of 0.17 mg/kg). The Meeting recommends a maximum residue level of 0.1 m/kg, an STMR-P of 0.025 mg/kg and an HR-P of 0.042 mg/kg for carbofuran in rice, husked.

Rape was treated with at 5.25 g/kg seed as a seed treatment. Samples from 5 trials were collected after 321 to 337 days and composited into one sample for processing into meal (press cake), crude oil and refined oil. The method applied reflects the conditions for the semi-industrial production of rapeseed oil. There were no detectable residues of carbofuran or 3-hydroxy-carbofuran in the seed and in any of the processed samples (<0.05 ppm).

RECOMMENDATIONS

Definition of residue for compliance with MRLs and for estimation of dietary intake in plant and animal commodities: sum of carbofuran and 3-hydroxycarbofuran, expressed as carbofuran

Commodity		MRL, mg/kg		STMR or STMR-P	HR or HR-P
CCN	Name	New	Previous	mg/kg	mg/kg
SO 0691	Cotton seed	0.1		0.02	0.04

Commodity		MRL, mg/kg		STMR or STMR-P	HR or HR-P
CCN	Name	New	Previous	mg/kg	mg/kg
SO 0495	Rape seed	0.05*		0.05	
AS 0649	Rice straw and fodder, dry	1		0.10	
CM 0649	Rice, husked	0.1	W	0.025	0.042
VO 0447	Sweet corn (corn-on-the-cob)	0.1	W	0.03	0.1

DIETARY RISK ASSESSMENT

Long- term intake

Currently, the ADI for carbofuran is 0.002 mg/kg body weight/day. International estimated daily intake (IEDI) was calculated for commodities of human consumption which STMRs were estimated at the 1997 JMPR and at this Meeting. The results are shown in Annex III.

International Estimated Daily Intakes for the five GEMS/Food regional diets, based on estimated STMRs, ranged from 10 to 30% of the ADI. The Meeting concluded that the intake of residues of carbofuran resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The acute RfD for carbofuran was estimated by this Meeting as 0.009mg/kg body weight. The international estimate of short term intake (IESTI) for carbofuran was calculated for commodities for which maximum residue levels, STMR values and/or HR values were established at this Meeting (rice, husked and sweet corn (corn on the cob)). The results are shown in Annex IV.

The calculated IESTI were less than 100% of the acute RfD for children and for the general population. The Meeting concluded that short-term intake of residues of carbofuran, when used in ways that have been considered by the JMPR, is unlikely to present a public health concern.

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