

CARBOFURAN (096)

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EXPLANATION

The insecticide, nematicide and acaricide carbofuran has been evaluated a number of times by the JMPR since 1976, the most recent were in 2008 for toxicology and in 2009 for residues. The 2008 Meeting estimated an acceptable daily intake (ADI) for humans of 0–0.001 mg/kg bw and an acute reference dose (ARfD) of 0.001 mg/kg bw. The residue (for compliance with the MRL and for estimation of dietary intake) for plant and animal commodities is defined as carbofuran and 3-OH carbofuran expressed as carbofuran. The information provided in 2009 to the JMPR did not preclude that the IESTI of carbofuran in bananas would exceed the ARfD. However the 2009 Meeting also noted that the short-term dietary risk assessment for bananas could be refined, if a metabolism study on banana or residue trials employing a very sensitive analytical method were made available.

The current Meeting received new information on residue analysis, use pattern and residues resulting from supervised residue trials on bananas.

METHODS OF RESIDUE ANALYSIS

The Meeting received a residue study, containing a new more sensitive analytical method on bananas. The newly supplied method is a revision of Method P-3515 (Cornell, 2001), which has already been reviewed by the JMPR in 2002. For clarity reasons it is briefly summarized below.

Analytical methods*LC/MS/MS Method STM2327*

Carbofuran and 3-hydroxy carbofuran were extracted from homogenized whole bananas using an acidic reflux in a 0.25 M HCl solution and dilution. The sample was filtered and diluted (with HCl and acetonitrile), and the final solution was analysed using liquid chromatography with TurbolonSpray tandem mass spectrometry in positive ionization mode (LC/MS/MS). The M/Z ratio's being 238 → 163 for hydroxy carbofuran and 222 → 165 for carbofuran. The limit of quantification (LOQ) for bananas was 0.01 mg/kg for both carbofuran and 3-hydroxy carbofuran. The limit of detection (LOD) of 0.003 mg/kg for carbofuran and for 3-hydroxy carbofuran was assumed to be thirty percent of the LOQ. Method recoveries at the limit of quantification ranged from 92–111% for carbofuran (n = 8, average 99% ± 6%) and 97–144% for 3-hydroxy carbofuran (n = 8, average 110% ± 8%). This method is part of a residue trial in bananas [Gehl, 2012, FMC Report No. PC-0758] and is a revised version of method FMC P-3515 [Cornell, 2001, FMC Report P-3515]. Method validation results for bananas are presented in Table 1.

Table 1 Validation results for LC/MS/MS method STM2327

commodity	analyte	reported LOQ mg/kg	spike level mg/kg	n	% recovery		RSD _r	control samples mg/kg (n)	Reference, method
					mean	range			
banana	carbofuran	0.01	0.01	8	100	92-111	7%	ND (2)	Gehl, 2012 PC-0758, FMC Report PC0758
		0.01	0.1	5	97	91-106	5.2%		
banana	3-OH carbofuran	0.01	0.01	8	106	97-114	6.6%	ND (2)	idem
		0.01	0.1	5	117	111-126	5.1%		

ND = no peak detected < 0.3 LOQ

USE PATTERN

Carbofuran is registered as a systemic insecticide, nematicide, and acaricide on various crops. Its uses include seed treatment, soil application at-planting, and directed or foliar application to various crops. Table 2 only lists the uses for which original labels are available and for which the additional trials were submitted (banana) to the 2012 JMPR.

Table 2 Registered uses of carbofuran on bananas

Crop (code)	Country	Form	Application					PHI, days
			Method	Rate g ai/unit	Spray conc, kg ai/hl	Number	Interval	
Banana	Costa Rica	GR (100 g/kg)	ground	2.5-3	na	ns	ns	ns
Banana	Costa Rica	SC (480 g/L)	ground	2.64-3.12 ^a	ns	2	4-5 months	48 hrs
Banana	Ecuador	GR (100 g/kg) GR (50 g/kg)	ground	2-3	na	2	^d	ns
Banana	Honduras	GR (100 g/kg) GR (50 g/kg)	ground	2.5-3 ^b	na	ns	ns	ns
Banana	Honduras	SC (480 g/L)	ground	2.64-3.12 ^c	ns	2	4-5 months	≥0

na = not applicable; ns = not specified; GR = granulate; SC=soluble concentrate

^a The rate provided is against Nematodes. Rate against Banana Weevil is 1.44-1.92 g ai/unit.

^b The rate provided is against Nematodes. Rate against Banana Weevil is 1.2 g ai/unit.

^c The rate provided is against Nematodes. Rate against Banana Weevil is 1.44-1.92 g ai/unit.

^d One application before the rain period and one application after the rain period.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The Meeting received additional information on supervised residue trials applying carbofuran as ground treatments of banana.

Application rates were reported as carbofuran (parent). Unquantifiable residues are shown as below reported LOQ (< 0.01 mg/kg). Residue data are recorded unadjusted for percentage recoveries or for residues values in control samples, unless otherwise stated. Where multiple samples were taken from a single plot, individual values are reported. Where multiple analyses were conducted on a single sample, the average value is reported. Where results from separate plots with distinguishing characteristics such as different formulations, varieties or treatment schedules were reported, results are listed for each plot.

Residues from the trials conducted according to critical GAP have been used for the estimation of maximum residue levels. These results are underlined.

Banana

Supervised residue trials on bananas were conducted in Costa Rica, Honduras and Ecuador in growing season 2011/2012 [Gehl, 2012, PC-075]. Results for whole fruit are shown in Table 3. As the residue levels for whole fruit for both the parent compound as well as the acidic hydrolysable conjugates were below the LOQ of 0.01 mg/kg (LOD is assumed at 30% LOQ, being 0.003 mg/kg), the residue levels in peel and pulp were not analysed.

The Meeting noted that in some of the supervised field trials the field sample was smaller than the minimum amount of 24 units or 2 kg recommended. However taking into account the lack of detectable residues in whole fruits, the Meeting concluded that the size of the composite field sample is still sufficient to confirm the assumption of all residues being present below the LOQ.

Table 3 Residues of carbofuran in banana (whole fruit) after ground treatment

Location, year, (variety)	Form	No	Inter val (days)	g ai/ plant	date of last treatment, timing	DAT	residues (mg/kg)			reference
							carbofuran	3-OH carbofuran	total	
Zapote, Costa Rica, 2011/2012 (Gran Enano)	GR	2	124	3	Oct. 6, 2011 BBCH 46 and 71-79	0	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	Gehl, 2012, PC-0758 trial S11-02114-01
						9	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						30	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						64	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						93	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						121	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
La Maravilla, Costa Rica, 2011/2012 (Gran Enano)	GR	2	122	3	Oct. 7, 2011 BBCH 46 and 78	0	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	Gehl, 2012, PC-0758 trial S11-02114-02
						9	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						29	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						63	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						92	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						120	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
La Lima, Honduras, 2011/2012 (Giand Naine)	GR	2	122	3	Oct. 10, 2011 BBCH 51 and 65	0	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	Gehl, 2012, PC-0758 trial S11-02114-03
						10	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						30	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						60	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						91	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						120	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
Lorenzo de Garayola, Ecuador, 2011/2012 (Cavendish cultivar Williams)	GR	2	121	3	Oct. 16, 2011, BBCH 50 and 60	0	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	Gehl, 2012, PC-0758 trial S11-02114-04
						10	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						30	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						60	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						90	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	
						116	< 0.01 (ND)	< 0.01 (ND)	< 0.01 (ND)	

ND: not detected (LOD: 0.003 mg/kg)

[Gehl J, 2012, 078BAN11R1, FMC Report number PC-0758]. No unusual weather conditions. Plot size 960-2010 m², 3 months to 12 year old plants. Granules were applied homogeneously near each plant, within one meter range. Samples represented 12-18 fruits from 6 different bunches and taken from lower, middle and higher part of each bunch. Samples (whole fruit 1.5-4.1 kg; peel: 0.70-1.5 kg; pulp: 0.80-2.50 kg) were harvested at maturity (BBCH 65-91) and stored deep frozen for less than 5 months. Samples were analysed as whole fruit using a revised LC/MS/MS method STM2327. The average concurrent method recoveries were: carbofuran: 99% ± 6%; and 3-hydroxy carbofuran: 110% ± 8%.

APPRAISAL

The insecticide, nematicide and acaricide carbofuran was evaluated numerous times by the JMPR since 1976, latest 2008 for toxicology and 2009 for residues. The 2008 Meeting estimated an acceptable daily intake (ADI) for humans of 0–0.001°mg/kg bw and an acute reference dose (ARfD) of 0.001°mg/kg bw. The residue (for compliance with the MRL and for estimation of dietary intake) for plant and animal commodities is defined as carbofuran and 3-OH carbofuran expressed as carbofuran. The information provided in 2009 to the JMPR did not preclude that the IESTI of

carbofuran in bananas will be below the ARfD. However the 2009 Meeting also noted that the short-term dietary risk assessment of bananas could be refined, if a metabolism study on banana or residue trials employing a very sensitive analytical method became available.

The current Meeting received new information on residue analysis, use pattern and residues resulting from supervised residue trials on bananas.

Methods of analysis

The Meeting previously evaluated several methods of analyses for carbofuran and 3-OH carbofuran in different vegetable matrices each with varying LOQs and LODs ranging from 0.005–0.1°mg/kg for both analytes.

The method reported to the current Meeting and used in the supervised residue trials determined carbofuran and 3-OH-carbofuran. The limit of quantification (LOQ) for bananas was 0.01°mg/kg for both carbofuran and 3-OH carbofuran. The limit of detection (LOD) of 0.003°mg/kg for carbofuran and for 3- OH carbofuran was assumed to be thirty percent of the LOQ.

Results of supervised residue trial on crops

Bananas

In bananas, carbofuran residues may arise from ground treatment use against nematodes. The 2009 Meeting noted that in eight Central and South American trials, no residues of carbofuran or 3-OH carbofuran were detected in any sample (whole fruit, peel or pulp). The LOQ and LOD were 0.05°mg/kg and 0.01°mg/kg, respectively, both for carbofuran and 3-OH carbofuran. In an additional Brazilian trial (LOQ: 0.1°mg/kg) and in a Spanish trial (LOQ: 0.05°mg/kg, LOD: 0.02°mg/kg) no residues were detected in pulp or peel either.

Monitoring data from the United States Department of Agriculture (USDA) reviewed in 2009 showed that in almost 4000 banana samples no carbofuran or 3-OH carbofuran residues above the LODs (0.002–0.076°mg/kg for carbofuran and 0.004–0.076°mg/kg for 3-OH carbofuran) have been detected.

Based on the overall findings, the 2009 Meeting concluded that in the case of bananas, a zero-residue situation seemed plausible. However the Meeting decided to use the LODs for carbofuran and 3-OH carbofuran as reported in the eight Central and South American trials (0.01°mg/kg for each of them) for the estimation of an STMR and HR of 0.02°mg/kg each for carbofuran in bananas.

For the present evaluation new supervised field trials involving bananas were performed in Central America (Costa Rica, Honduras and Ecuador). The maximum GAP for carbofuran on bananas in these countries is $2 \times 3.1^\circ\text{g}^\circ\text{ai}$ per plant and year with an interval of 4–5 months and no specified PHI.

In four trials matching the GAP no carbofuran and 3-OH carbofuran residues in bananas (whole fruit) were detected following DATs ranging from 0-124 days:

- Carbofuran: $<0.01^\circ\text{mg}/\text{kg}$ (n = 4) and not detected (LOD: 0.003°mg/kg)
- 3-hydroxy-carbofuran: $<0.01^\circ\text{mg}/\text{kg}$ (n = 4) and not detected (LOD: 0.003°mg/kg).

The Meeting noted that the use of carbofuran according to the GAPs submitted leads to a very low residue situation in bananas without detectable residues in the fruits and concluded that the sum of both analytes would be unlikely to exceed 0.01°mg/kg.

The Meeting estimated a maximum residue level, an STMR and an HR of 0.01(*) mg/kg, 0.01°mg/kg and 0.01°mg/kg, respectively, for the sum of carbofuran and 3-OH carbofuran, expressed as carbofuran in bananas.

The Meeting withdraws its previous recommendation of 0.02(*) mg/kg for bananas.

RECOMMENDATIONS

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

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for plant and animal commodities: *carbofuran and 3-hydroxy carbofuran expressed as carbofuran*.

The residue is not fat-soluble.

CCN	Commodity	Recommended MRL mg/kg		STMR or STMR- P mg/kg	HR or HR-P mg/kg
		new	previous		
FI 0327	Banana	0.01*	0.02*	0.01	0.01

DIETARY RISK ASSESSMENT

Long-term intake

The Meeting of 2009 concluded that the long-term intake of residues of carbofuran from uses that have been considered by the JMPR is unlikely to present a public health concern. As the estimated STMR for bananas is lower than in 2009, no new long-term intake calculations were performed.

Short-term intake

The ARfD for carbofuran is 0.001°mg/kg bw. The International Estimated Short-term Intake (IESTI) was calculated for banana using an HR of 0.01°mg/kg for bananas. The IESTI was 90% of the ARfD for banana. The short-term intake of residues of carbofuran from uses of carbosulfan on banana is unlikely to present a public health concern.

REFERENCES

Code	Author	Year	Title, Institute & report number, Submitting manufacturer and report code, GLP/Non-GLP. Published/Unpublished
PC-0758	Gehl J	2012	Magnitude of the residue of carbofuran in/on bananas after two treatments with FURADAN 10GR in field conditions in Central America. FMC Corporation, Study No.: 078BAN11R1, Report No.: PC0578. Date: 29.02.2012. GLP, Unpublished, Provided by FMC Corporation, USA