5.6 CARBOFURAN (096)

RESIDUE AND ANALYTICAL ASPECTS

Carbofuran, 2,3-dihydro-2,2-dimethylbenzofuran-7-yl methylcarbamate, is a systemic insecticide, nematicide, and acaricide. Its uses include seed treatment, at-planting soil application, and directed or foliar applications. Carbosulfan, a pesticide in itself, produces carbofuran as a major metabolite. The main use of carbosulfan is on citrus fruits. In evaluating carbofuran, account should be taken of its residues arising from the use of carbosulfan on citrus.

A periodic review of the toxicology of carbofuran was carried out by the 1996 JMPR. An ADI of 0–0.002 mg/kg bw was established. In 2002, an ARfD of 0.009 mg/kg bw was established. The 2008 JMPR evaluated newly submitted studies on acute toxicity and re-examined relevant data which had been considered by previous Meetings. The 2008 Meeting established an ARfD of 0.001 mg/kg bw. The Meeting noted that this ARfD was lower than the current ADI of 0–0.002 mg/kg bw. The Meeting concluded that the ADI and ARfD for carbofuran should be based on the same NOAEL and revised the ADI to 0–0.001 mg/kg bw.

A periodic review of the residue and analytical aspects of both carbofuran and carbosulfan was carried out by the 1997 JMPR. The carbofuran residue is defined as carbofuran + 3-hydroxycarbofuran for compliance with MRLs. For the purposes of dietary intake, the residue definition for carbofuran arising from use of carbosulfan and carbofuran is carbofuran + free and conjugated 3-OH carbofuran, expressed as carbofuran. The analytical methods include an acid hydrolysis step to release the conjugate. The residue definition for carbosulfan for compliance with MRLs and estimation of dietary intake is carbosulfan.

When carbofuran was re-evaluated by the JMPR in 2002 and 2003, short-term risks were assessed for commodities for which recommendations had been made at those Meetings, i.e., rice, sweet corn, maize and potato. In 2003, the CCPR at its Thirty-fifth Session, taking into account concerns expressed by the Delegation of Australia and the Observer from the European Commission, requested GEMS/Food to perform a full short-term intake assessment of carbofuran, to include all the commodities for which recommendations existed, but were not evaluated previously due to a lack of an ARfD. The assessment was presented to the Thirty-sixth Session of the CCPR (CX/PR 03/4). Except for the consumption of oranges (sweet and sour) by children, none of the IESTI values exceeded the ARfD of 0.009 mg/kg bw. The assessment for oranges was conducted with the highest residue (HR) level in the edible portion of 0.5 mg/kg, as recommended by the 1997 JMPR for oranges, sweet, sour. Coming from a residue data set in whole oranges derived from 53 supervised trials conducted with carbosulfan according to GAP. A maximum residue level of 0.5 mg/kg and a STMR of 0.1 mg/kg were also recommended.

At its Thirty-sixth Session, the Committee noted (ALINORM 04/27/24) that the European Commission had established an ARfD 10 times lower than that established by the JMPR. The Committee decided to return to Step 6 the draft MRLs for cantaloupe, cucumber, mandarin, oranges, sweet and sour, summer squash; and sweet corn (corn-on-the-cob) to address short-term intake concerns.

JMPR 2004 evaluated data on residues in orange pulp in supervised trials conducted with carbosulfan previously submitted to the 1997 JMPR. The Meeting estimated an STMR and a highest residue level of 0.05 mg/kg for carbofuran in orange pulp. Using the HR of 0.05 mg/kg for citrus and the contemporary ARfD of 0.009 mg/kg bw, no acute intake concerns were noted.

However, following the re-evaluation of the toxicology which resulted in lowering the ARfD to 0.001 mg/kg bw, JMPR 2008 noted that the IESTI was higher than the ARfD for banana, cucumber, cantaloupe, milks, oranges, potato, summer squash and sweet corn on the cob (from 120 to 510% ARfD; general population). For children, the IESTI was higher than the ARfD also for mandarins (from 280 to 810% ARfD).

In 2008, the CCPR at its Fortieth Session decided to return the draft MRLs for cantaloupe, cucumber, mandarin, oranges, sweet and sour, potato, summer squash and sweet corn (corn-on-the-cob) to Step 6 due to acute intake concerns, awaiting a review of toxicology by the 2008 JMPR. A delegation indicated that they would provide carbosulfan metabolism data on citrus fruit in order to refine the acute dietary risk assessment.

In 2009, at its Forty-first Session the Committee decided to withdraw the draft MRLs for cantaloupe, cucumber, potato, summer squash, and sweet corn (corn-on-the-cob) due to the lack of new data available to resolve the dietary intake concerns, and to retain the draft MRLs for mandarin and orange, sweet and sour at Step 7 awaiting the 2009 JMPR dietary intake estimation. The Committee also decided to recommend revocation of the Codex MRLs for potato and milk because of dietary intake concerns. The Committee noted the concern form submitted by EC relating to the use of different ARfDs and agreed to reconsider the Codex MRLs for banana; edible offal; maize; meat; milks, rice husked, sugar beet, sugarcane and sunflower seed for the further discussion at its next meeting based on the JMPR response.

The Meeting received information on the metabolism of carbosulfan residues in oranges from a Delegation to the CCPR. In addition the manufacturer supplied comments on the current carbofuran dietary risk assessment for bananas and citrus fruit.

Plant metabolism/Results of supervised residue trials on crops

No new data were received for the current assessment. Both the Delegation to the CCPR and the manufacturer suggested a re-evaluation of the data, already available to JMPR 1997. The manufacturer resubmitted the relevant original study reports (metabolism of carbosulfan in/on oranges, residues in bananas and residues in oranges and mandarins).

Citrus fruits

Previously, for the citrus fruits oranges sweet, sour and mandarins, JMPR has recommended two maximum residue levels to cover carbosulfan-treated crops. One recommendation is for the parent compound carbosulfan. The other relates to the major metabolites, carbofuran + 3-hydroxy carbofuran. The maximum residue level for carbofuran gives rise to intake concerns, see above. The maximum residue level for carbosulfan does not give rise to intake concerns, but cannot go forward in the Codex step procedure because it arises from the same use as the carbofuran level.

JMPR 1997 evaluated 30 supervised field trials with carbosulfan on clementines, mandarins and oranges, conducted in 1993–4 in Brazil, Mexico and Spain. GAP on oranges was available for Brazil (2 applications of 0.93–1.69 g ai/tree, PHI 7 days) and Mexico (3–4 applications of 250 g ai/ha, PHI 7 days). Furthermore, Spanish GAP was available for oranges (2 applications of 2.83–3.14 g ai/tree or 937.5 g ai/ha, PHI 112–147 days) and mandarins and clementines (2 applications of 3.2–3.6 g ai/tree or 937.5 g ai/ha, PHI 110–115 days). The 1997 Meetings estimations were based on a dataset derived from both GAPs.

JMPR 2004 re-evaluated data on residues in orange pulp in supervised trials conducted with carbosulfan and submitted to the 1997 JMPR. The Meeting agreed that it is unlikely that residues of carbamates arising from the use of carbosulfan will be present in orange pulp at levels higher than the LOQ (0.05 mg/kg). The Meeting estimated an STMR and a highest residue level of 0.05 mg/kg for carbofuran in oranges, sweet, sour. This estimate was supported by a study on metabolism evaluated by the 1997 JMPR, in which the pulp of oranges treated with [^{14}C]carbosulfan contained no more than 0.3% of the total radioactive residues 30 days after treatment.

The present Meeting noted again that the carbosulfan metabolism study in oranges (evaluated by 1997 JMPR and resubmitted to the present Meeting both by the Belgian Delegation to the CCPR and the manufacturer) demonstrated that at day 0, 7, 15 and 30 less than 0.3% of the total radioactivity was found in the edible pulp of the fruit (as was also concluded by the 2004 JMPR). In

the 1997 JMPR evaluation, the highest residue (carbofuran + 3-hydroxycarbofuran) in whole fruit from the dataset selected for maximum residue level-setting was 0.5 mg/kg. This would equal a residue of 0.0015 mg/kg in the pulp (0.3% × 0.5 mg/kg).

In addition, the Meeting noted that in six of the Spanish trials evaluated by JMPR 1997, residues in peel and pulp were measured (JMPR Evaluation 1997, Table 22, page 228–233). All of these trials were considered to be relevant for estimating the maximum residue level. The LOQ of the method was 0.05 mg/kg. For samples where analysis resulted in residues below LOQ, but above LOD, estimated residue values were reported and marked as such in the JMPR evaluation. Not in all cases was peel/pulp data available at all sampling dates, sometimes only at days lower than the PHI (110–147 days for the various citrus varieties), see Table 5. In the pulp, estimated carbofuran residues were 0.01 mg/kg (PHI 45 days) (2); < 0.01 mg/kg (PHI 104/5 days), and 0.02 mg/kg (PHI 92 days). However, in the latter trial the control sample was also estimated to contain 0.02 mg/kg. The Meeting concluded that these data support the observation from the metabolism study that residues in pulp would be below 0.01 mg/kg.

Table 5 Estimated residues of carbofuran and 3-hydroxycarbofuran in orange and mandarin pulp resulting from supervised trials in Spain after 2 applications of a 250 EC formulation at 937.5 g ai/ha, 3000 L/ha. (Annex 5, reference *81*, Table 22, p 228–233)

Year, location, variety	PHI (days	Estimated residue [a] (furan + HO-furan) mg/kg	Reference
1993, Sueca, Newhall oranges	45	0.01	Gill, 1995d
1993, Benifay, Navel oranges	0	0.6 (c=1.1)	Gill, 1995d
	45	0.01	
1994, Catadau, Clementines	0	0.03	Gill, 1996a
	30	0.02	
	60	< 0.01	
	104	< 0.01	
1994, Sueca, Satsumas	0	0.07	Gill, 1996b
	45	0.03	
	92	0.02 (c=0.02)	
1994, Carlet, Naveline oranges	0	< 0.01	Gill, 1996c
	45	< 0.01	
	105	< 0.01	
	140	< 0.01	
1994, Sueca, Newhall oranges	0	< 0.01	Gill, 1996c
	45	< 0.01	
	105	< 0.01	
	140	< 0.01	

[a] 'estimated residue' indicates a residue below the LOQ, but above the LOD

The Meeting estimated an STMR and a highest residue level of 0.01 mg/kg for carbofuran in oranges, sweet, sour to replace the previous estimation of 0.05 mg/kg. The Meeting extrapolated these values to mandarin.

Banana

In bananas, carbofuran residues arise from the use of carbofuran directly. The 1997 JMPR concluded the following on the banana supervised field trials available.

"Field trials in Spain, Central America and South America with the application of carbofuran to banana trees were reported. No residues of carbofuran plus 3-hydroxycarbofuran (< 0.02–< 0.1 mg/kg, n=8) were found in any trial. GAP was available only for Spain, where the trial was according to GAP and undetectable residues were < 0.02 mg/kg. Because none of the trials, some of

which were at higher rates than GAP, yielded detectable residues the Meeting estimated a maximum residue level of 0.1(*) mg/kg, the same as the existing Codex MRL, and an STMR of 0.1 mg/kg."

The present Meeting noted that in the eight Central and South American trials, no residues of carbofuran or 3-hydroxy carbofuran were found in any sample. The LOQ was 0.05 mg/kg both for carbofuran and for 3-hydroxy carbofuran, so the two compounds together are quantifiable at 0.1 mg/kg. However, no residue was detected in whole fruit up to the limit of detection of 0.01 mg/kg for each of the compounds. Some peel and pulp samples were also analysed and showed the same results.

In an additional Brazilian trial no residues were found higher than the LOQ of 0.1 mg/kg (the report was much summarized; it is assumed that this level refers to the sum of carbofuran and 3-hydroxy carbofuran). In another summarized report on a Spanish trial no residues were detected in either pulp or peel below the LOQ of 0.05 mg/kg (again it is assumed that this level refers to the sum of carbofuran and 3-hydroxy carbofuran). In this trial, no residue was detected above the LOD of 0.02 mg/kg.

Monitoring data from the United States Department of Agriculture (USDA) show that in the period of 1994 to present, almost 4000 banana samples have been analysed and in all cases, no carbofuran or 3-hydroxy carbofuran residues have been detected above the LOD. The reported LOD varied depending on the year and the laboratory that performed the measurements. No information was provided on the analytical methods employed. Furthermore, no information on the percentage of crop treated during this period was available. The Meeting noted that carbofuran is not registered for use on bananas in the USA. The Meeting considered that bananas are not generally grown in the USA. Therefore, a significant part of the bananas tested presumably originate from countries where carbofuran can be used on bananas, such as countries in Central and South America. The Meeting agreed that the monitoring data provide supporting evidence that residues are not to be expected in bananas.

The Meeting also considered that in the case of bananas, a zero-residue situation seems plausible. The Meeting decided to use the LODs for carbofuran and 3-hydroxy carbofuran as reported in the eight Central and South American trials (0.01 mg/kg for each of them) for the estimation of the STMR and HR.

The Meeting estimated an STMR and a highest residue level of 0.02 mg/kg for carbofuran in bananas to replace the previous estimation of 0.1 mg/kg.

DIETARY RISK ASSESSMENT

Long-term intake

The ADI for carbofuran is 0–0.001 mg/kg bw. The International Estimated Daily Intakes (IEDI) for carbofuran was estimated by the 2008 JMPR for the 13 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by previous Meetings. The IEDI ranged from 20–70% of the maximum ADI. The Meeting 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.

Short-term intake

The ARfD for carbofuran is 0.001 mg/kg bw.

The International Estimated Short-term Intake (IESTI) was calculated for banana, oranges and mandarins using an HR of 0.01 mg/kg for oranges and mandarins and an HR of 0.02 mg/kg for bananas. The results are shown in Annex 4. For the general population, the IESTI was 80% of the ARfD for banana, 20% for mandarins, and 30% for oranges. For children, the IESTI was 150% of the ARfD for banana, 40% for mandarins, and 60% for oranges. The information provided to the 2009

JMPR precludes an estimate that the short-term intake of residues of carbofuran from the consumption of banana, will be below the ARfD. The short-term intake of residues of carbofuran from uses of carbosulfan on mandarins and oranges is unlikely to present a public health concern.

The Meeting noted that the short-term dietary risk assessment of bananas could be refined if a metabolism study on banana were available, or residue trials employing a very sensitive analytical method. The ARfD was reviewed by the present Meeting on a request by CCPR (Section 3.2). The ARfD of 0.001 mg/kg bw was confirmed and it is unlikely that it could be refined.