Final addendum to the Additional Report

- public version -

Additional risk assessment provided by the rapporteur Member State Germany for the existing active substance

CARBOFURAN

according to the Accelerated Resubmission Procedure laid down in Commission Regulation (EC) No. 33/2008

May 2009

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ANNEX B

Addendum March 2009

Carbofuran

B.8 Environmental fate and behaviour

B.8.1.2 Rate of degradation (Annex IIA 7.1.1.2.1; Annex IIIA 9.1.1.1.1)

B.8.1.2.1 Aerobic degradation

The RMS disagrees with the conclusions of the PRAPER 62 meeting on this point and would like that his argumentation is taken on board in the conclusions of carbofuran.

Study by Saxena:

- In this study two soils were used, called as acidic and alkaline soil. The alkaline soil was prepared by adding lime to the collected sandy loam soil (acidic), by this the pH was modified from 5.7 to 7.7.
- The soil indeed seems to be dry if compared with e.g. the FOCUS default values for sandy loam, but the moisture holding capacity of the soil was determined in this GLP study and the actual moisture content was set for this (75% of 1/3 bar=4.05%) in accordance with EPA guidelines (Very often, degradation determined according EPA guideline is slower).
- The microbial biomass was checked several times throughout the study and the results show that both soils were viable at the end of the study.
- According to the RMS, one soil has been tested in this study (same soil properties, except pH, same microflora). It is therefore not valid to derive 2 DT50 in order to artificially increase the mean or the median DT50.

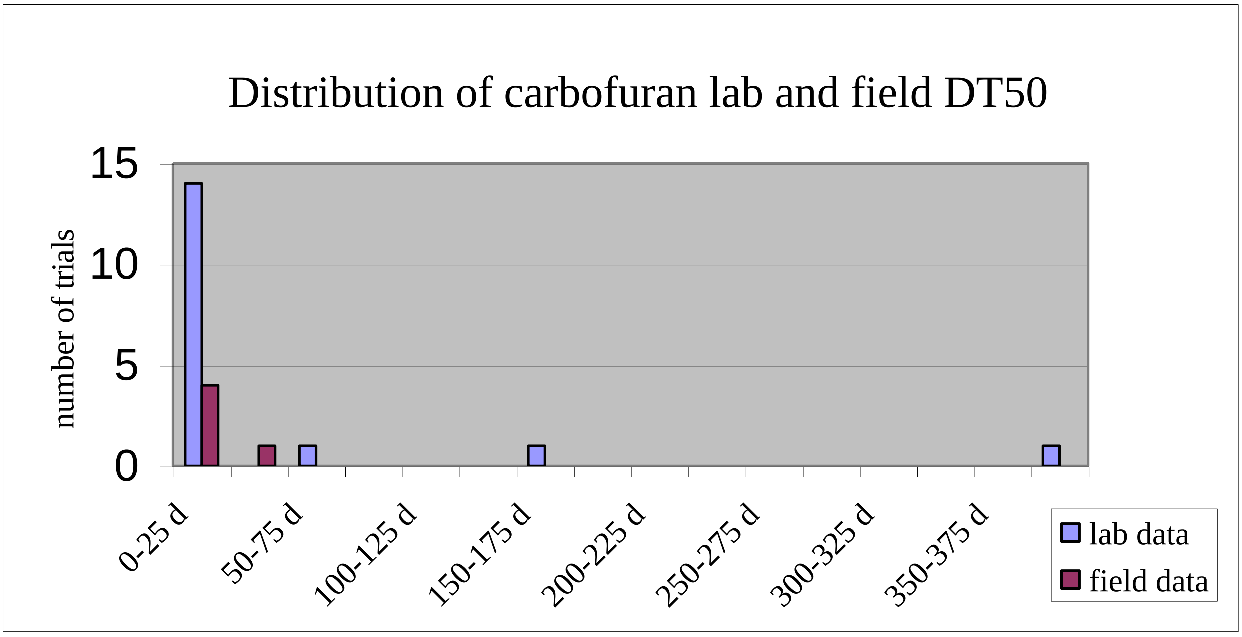
Study by Schocken:

- The pH of this sandy loam soil was also modified by lime from 5.8 to 7.1.

The microbial activity of the soil was checked by measuring the evolved $^{14}CO_2$ from ^{14}C labelled glucose up to 57 days in a parallel experiment. The evolved CO_2 was continuously increasing and reached 62.3% by the end of this term.

It was stated in the DAR that the carbofuran degradation in this study is occurring through a chemical rather than a microbial process (similar degradation rates under sterile and non-sterile conditions).
Absence of mineralization is observed in this study

The degradation of carbofuran has been determined under aerobic laboratory conditions with carbofuran, benfuracarb or carbosulfan as test substance (14 studies with DT50 ranging between 5.7 and 22.7 days) and under field conditions (5 studies with DT50 ranging between 1.3 and 27 days). Under anaerobic laboratory conditions, the DT50 in one soil is 7.6 days.



The RMS considers that there are sufficient arguments that are indicating that the DT50 of 151, 54.6 days (actually one soil tested in Saxena 1994) and 387 days (one soil in Schocken, 1989) are not valid. Considering these 3 data, the standard deviation is 94.35.

Considering the DT50 that have been recalculated by EFSA (benfuracarb endpoints list) with exclusion of the 3 outlier points, the median and geomean DT50 are respectively 12.63 days and 12.54 days. The standard deviation is then 5.61. Moreover it is clear that the distribution of DT50 population is less dissymetrical.

The field median and geomean DT50 are respectively 16 days and 8.12 days.

Relevance of the metabolites (data already available in the DAR of November 2008)

Presence in laboratory degradation studies

According to agreed guidance, PECgw calculations have to be performed for metabolites that were recovered at level >5% AR at least at two sampling points.

It has been shown in the original submission that the metabolites of carbofuran were clearly not major (never at level above 5% at 2 sampling points): 3-OH-carbofuran (max 0.8%, once in 1 out of 5 soils), 3-keto-carbofuran (once at maximum level of 6.2% AR, in 1 out of 5 soils), carbofuran-phenol (=7-phenol) (max 2.1%, once in 1 out of 5 soils) (Arysta, FMC)

However EPCO 31 agreed that 3-OH-carbofuran and 3-keto-carbofuran need to be further assessed as carbofuran metabolites containing the active carbamate moiety. Carbofuran-phenol does not contain the carbamate moeity.

PECgw calculations

The notifer has provided DT50 (the 3 metabolites are not persistent) and Koc (Koc for modelling has been chosen according to a worst case approach) for the metabolites.

The PECgw for the metabolites 7-phenol-carbofuran, 3-hydroxy- carbofuran, and 3-keto-carbofuran have been calculated assuming extreme worst case scenarios (100% formation fraction used in modelling while the observed level of the metabolites in aerobic degradation studies is <5%AR, worst case Koc derivation). In consequence, the few exceedances of the 0.1 µg/L trigger are not a concern (PEARL triennial scenarios).

The metabolites are not present in groundwater and therefore not included in the residue definition.

Toxicological relevance

5 metabolites of carbofuran were tested for their acute oral toxicity in rats. All these metabolites were detected in the rat metabolism study. While 3-hydroxy-carbofuran is of comparable toxicity as carbofuran, 3-hydroxy-7-phenol, 3-keto-carbofuran, 3-keto-7-phenol, and 7-phenol carbofuran are less toxic than the parent compound. Clinical signs of toxicity such as prostration, recumbancy, decreased locomotion, nasal, ocular and oral discharges, tremors, body staining was also observed with the parent compound. Surviving animals appeared normal when necropsied. In animals dying, most of the decedent had blood in the intestine. Acute oral toxicity of the different metabolites was summarized in the review of JMPR (1996).

The mutagenic potential of 3-OH carbofuran and carbofuran-7-phenol was investigated in a bacterial reverse mutation assay. While carbofuran phenol gave negative results, 3-OH carbofuran was mutagenic towards strain TA 1537. The biological significance of the response in the Ames test is questionable. 3-OH carbofuran is mutagenic in the TK mutation test system with and w/o metabolic activation system. The mutagenicity detected probably involves both point mutations and large genetic changes

3-OH-carbofuran LD50 oral: 8.3 mg/kg bw: Positive in Ames test strain TA1537 with S9 mix Positive in TK locus in L5178Y mouse lymphoma cells with and w/o S9 mix	 T+, R28
3-OH-7-phenol: LD50 oral: 1654 mg/kg bw	 Xn, R22
3 keto-carbofuran: LD50 oral: 107 mg/kg bw	 T , R25
3-keto-7-phenol: LD50 oral: > 800 mg/kg bw	 Xn, R22
carbofuran 7-phenol: LD50 oral: 1743 mg/kg bw negative in Ames test	 Xn, R22

Conclusions:

Despite the fact that the 3 metabolites were minor (never >5%AR at 2 sampling points), a complete PEC assessment has been performed. The metabolites are not expected to be recovered in groundwater at level >0.1 µg/L (1 occurrence of 3 keto-carbofuran in the triennal application PECgw with PEARL, worst case assumptions).

Despite the fact that the metabolites were not recovered in ground water, a complete toxicological relevance assessment has been performed.

3-OH-carbofuran has the same toxicity as carbofuran. However this metabolite is also formed in rat metabolism and has been completely investigated in the toxicological studies that have been performed with the a.s.

The two other metabolites were less toxic than the a.s.; nevertheless, they are formed in the rat metabolism and hence fully investigated in the toxicological dossier.

The RMS considers therefore that the risk of contamination of groundwater by the a.s. and metabolites has been fully assessed. As carbofuran is the most relevant indicator of groundwater contamination, it is appropriate to include carbofuran alone in the residue definition.

Evaluation of the argumentation given in the position paper by Shaaban F. Elnaggar, 2005
The argumentation points that were available in the DAR have been repeated in an addendum
Degradation studies of carbofuran and 7-phenol show that 7-phenol is a short-lived degradation product in/on soil/sediment environment.

Carbofuran-phenol does not contain the carbamate moiety.

Carbofuran-phenol is 4 orders of magnitude less toxic than carbofuran to aquatic organisms. This compound does not pose a risk to aquatic organisms.

B.8.6.1 Predicted Environmental Concentrations in ground water (PECgw) (Annex IIIA 9.21)

The notifier has proposed new PECgw calculations taking into account the endpoints that have been defined during the PRAPER meeting on benfuracarb (January 2009)

Modelling softwares:
The calculation of Predicted Environmental Concentrations (PECs) in groundwater is required as part of the registration procedure for plant protection products in the European Union (EU), using the Standard Forum for the Co-ordination of Pesticide Fate Models and their Use (FOCUS) ground water scenarios to represent a realistic worst-case (FOCUS 2000). In this case, the Dutch model Pesticide Emission Assessment at Regional and Local scales (PEARL ver. 3.3.3) (Tiktak 2003) and the Pesticide Leaching Model (PELMO ver. 3.22) (Klein 2002) were used to address the potential leaching of carbofuran and its three metabolites 1) 7-phenol-carbofuran, 2) 3-hydroxy-carbofuran, and 3) 3-keto-carbofuran to the target groundwater depth of one meter below the sugar beet field surface for nine different scenarios over a 26-year period.

Input data:
PEARL and PELMO calculations: The carbofuran PECgw after an at-plant application incorporated into the soil to 7.0 cm at a maximum rate of 0.600 kg a.s./ha annually (worst-case) and at maximum rate of 0.600 kg a.s./ha triennially (realistic worst-case) were calculated. PECgw of carbofuran at a use rate of 0.060 kg a.s./ha annually and a rate of 0.060 kg a.s./ha triennially were also calculated using the same planting and timing conditions as those used for the higher use rate.

Application occurs 14 days before crop emergence.

Table 9: The proposed sugar beet GAP for carbofuran

Application method	Application Rate	Application Timing
Applied in furrow at planting and incorporated at a depth of 7 cm	60 g/ha or 600 g/ha	Applied at the time of sugar beet planting

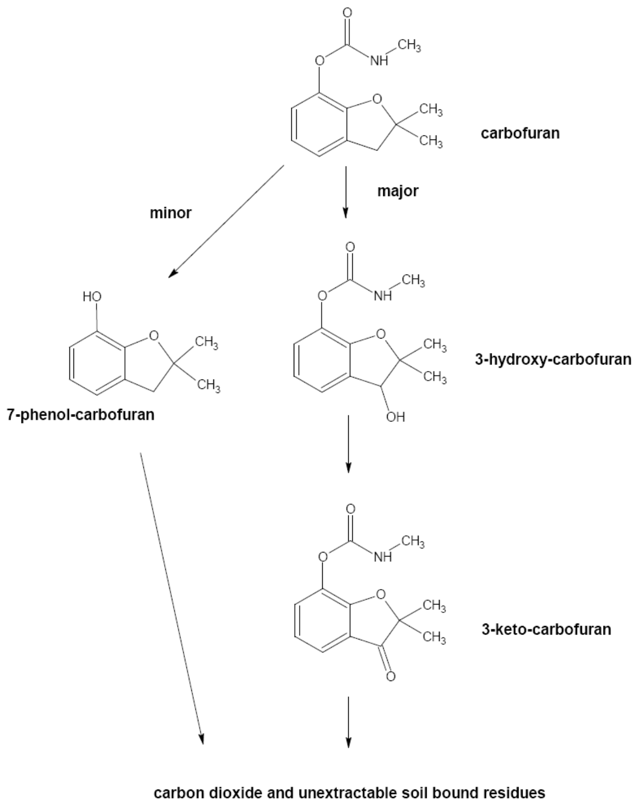
Table B.8.6.1-1: Test Substance Parameters

Parameter	**carbofuran**	**3OHCF**	**3ketoCF**	**7PCF**
Mw	221.3	237.3	235.24	164.2
Water solubility (mg/L, 20°C)	322	6207	4464	1096
Vapour pressure (Pa, 25°C)	8e-5	3.29e-3	2.6e-3	1.32
DT50 soil (days)	14	0.41	3.01	1
Kom	12.8	31.9	192	598
Koc	22	55	331	1031
1/n	0.96	1	1	0.9

Ffm		1	1	1
Q10	2.58	2.58	2.58	2.58
Plant Uptake	0	0	0	0

Proposed dissipation pathway

GW: CF to 3OHcf (ffm 1.0) to 3ketoCF (ffm 1.0) CF to 7PCF (ffm 1.0)



Findings:

Table B.8.6.1-2: 80th Percentile Annual Average Groundwater FOCUS PEARL PECs (0.600 kg a.s./ha) [runs 148-156]

Location	Application Scheme	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)
Châteaudun	Sugar beets	**1.6643**	0.0437	**0.1176**	0.0028
Hamburg	Sugar beets	**1.5890**	0.0495	**0.2085**	0.0597
Jokioinen	Sugar beets	**1.6238**	0.0391	0.0651	0.0017
Kremsmünster	Sugar beets	**1.2330**	0.0334	**0.1093**	0.0027
Okehampton	Sugar beets	**1.2805**	0.0366	**0.1185**	0.0046
Piacenza	Sugar beets	**2.3195**	0.0738	**0.4252**	**0.1055**
Porto	Sugar beets	0.0366	0.0008	0.0013	0.0000
Sevilla	Sugar beets	**7.2117**	**0.1587**	**0.2120**	0.0063
Thiva	Sugar beets	**0.1936**	0.0054	0.0171	0.0004

Table B.8.6.1-3: 80th Percentile Triennial Annual Average Groundwater FOCUS PEARL PECs (0.600 kg a.s./ha) [runs 157-165]

Location	Application Scheme	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)
Châteaudun	Sugar beets	**0.6327**	0.0165	0.0458	0.0011
Hamburg	Sugar beets	**0.5585**	0.0175	0.0733	0.0216
Jokioinen	Sugar beets	**0.5957**	0.0144	0.0224	0.0006
Kremsmünster	Sugar beets	**0.4143**	0.0111	0.0308	0.0007
Okehampton	Sugar beets	**0.3823**	0.0109	0.0371	0.0013
Piacenza	Sugar beets	**1.0945**	0.0343	**0.1782**	0.0446
Porto	Sugar beets	0.0181	0.0004	0.0006	0.0000
Sevilla	Sugar beets	**1.2633**	0.0286	0.0481	0.0013
Thiva	Sugar beets	0.0556	0.0016	0.0052	0.0001

Table B.8.6.1-4: 80th Percentile Annual Average Groundwater FOCUS PELMO PECs (0.600 kg a.s./ha)

Location	Application Scheme	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)
Châteaudun	Sugar beets	**0.639**	0.017	0.038	0.001
Hamburg	Sugar beets	**0.933**	0.029	**0.114**	0.026
Jokioinen	Sugar beets	**0.762**	0.015	0.022	0.001
Kremsmünster	Sugar beets	**0.600**	0.015	0.030	0.001
Okehampton	Sugar beets	**1.085**	0.030	0.089	0.003
Piacenza	Sugar beets	**1.205**	0.036	**0.178**	0.040
Porto	Sugar beets	0.018	0.000	0.000	0.000
Sevilla	Sugar beets	**0.480**	0.010	0.010	0.000
Thiva	Sugar beets	0.003	0.000	0.004	0.000

Table B.8.6.1-5: 80th Percentile Annual Average Groundwater FOCUS PEARL PECs (0.060 kg a.s./ha) [runs 166-174]

Location	Application Scheme	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)
Châteaudun	Sugar beets	**0.1431**	0.0039	0.0102	0.0002
Hamburg	Sugar beets	**0.1342**	0.0042	0.0178	0.0050
Jokioinen	Sugar beets	**0.1418**	0.0035	0.0054	0.0001
Kremsmünster	Sugar beets	**0.1078**	0.0030	0.0092	0.0002
Okehampton	Sugar beets	**0.1140**	0.0033	0.0101	0.0003
Piacenza	Sugar beets	**0.2044**	0.0065	0.0375	0.0093
Porto	Sugar beets	0.0027	0.0001	0.0001	0.0000
Sevilla	Sugar beets	**0.5977**	**0.0136**	**0.0187**	0.0004
Thiva	Sugar beets	**0.0170**	0.0005	0.0015	0.0000

Table B.8.6.1-6: 80th Percentile Triennial Average Groundwater FOCUS PEARL PECs (0.060 kg a.s./ha) [runs 175-183]

Location	Application Scheme	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)
Châteaudun	Sugar beets	0.0544	0.0015	0.0040	0.0001
Hamburg	Sugar beets	0.0467	0.0015	0.0062	0.0018
Jokioinen	Sugar beets	0.0496	0.0012	0.0020	0.0000
Kremsmünster	Sugar beets	0.0347	0.0009	0.0027	0.0000
Okehampton	Sugar beets	0.0330	0.0010	0.0032	0.0001
Piacenza	Sugar beets	0.0974	0.0031	0.0159	0.0039
Porto	Sugar beets	0.0013	0.0000	0.0000	0.0000
Sevilla	Sugar beets	**0.1080**	0.0025	0.0042	0.0001
Thiva	Sugar beets	0.0049	0.0001	0.0005	0.0000

Table B.8.6.1-7: 80th Percentile Annual Average Groundwater FOCUS PELMO PECs (0.060 kg a.s./ha)

Location	Application Scheme	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)
Châteaudun	Sugar beets	0.053	0.001	0.003	0.000
Hamburg	Sugar beets	0.085	0.003	0.009	0.003
Jokioinen	Sugar beets	0.054	0.001	0.002	0.000
Kremsmünster	Sugar beets	0.048	0.001	0.003	0.000
Okehampton	Sugar beets	0.096	0.003	0.008	0.000
Piacenza	Sugar beets	**0.102**	0.003	0.015	0.003
Porto	Sugar beets	0.001	0.000	0.000	0.000
Sevilla	Sugar beets	0.036	0.001	0.001	0.000
Thiva	Sugar beets	0.000	0.000	0.000	0.000

Conclusions:

The PECgw were recalculated considering the endpoints which have been defined during the PRAPeR meeting on benfuracarb (January 2009).

Application rate of 0.600 kg a.s./ha: Results of the modelling indicated that the 80th percentile annual average PECs for carbofuran and its three soil metabolites in groundwater one metre below the surface did not exceed 0.1 µg/L for 1 out of 9 PEARL scenarios and 2 out of 9 PELMO scenarios at the 0.600 kg a.s./ha use rate.

At the application rate of 0.600 kg a.s./ha, one application every 3 years, that can be considered as the representative worst case GAP (conventional sugar beet crop rotation), the 80th percentile triennial average PECgw for carbofuran and its soil metabolites did not exceed 0.1 µg/L for 2 out of 9 PEARL scenarios

The PECgw for the metabolites 7-phenol-carbofuran, 3-hydroxy- carbofuran, and 3-keto-carbofuran have been calculated assuming extreme worst case scenarios (100% formation fraction in modelling, observed level of the metabolites in aerobic degradation studies <5%AR, Koc). In consequence, the few exceedances of the 0.1 µg/L trigger are not a concern.

Application rate of 0.060 kg a.s./ha:
In his resubmission dossier, Beside the GAP at 600 g a.s./ha (as in the original dossier), FMC supports an additional use at reduced dose rate of 60 g a.s./ha. These PECgw have been included for completion.

Results of the modelling indicated that the 80th percentile annual average PECs for carbofuran and its three soil metabolites in groundwater one metre below the surface did not exceed 0.1 µg/L for 2 out of 9 PEARL scenarios and for 8out of 9 PELMO scenarios.

At the application rate of 0.060 kg a.s./ha, one application every 3 years, that can be considered as the representative worst case GAP (conventional sugar beet crop rotation), the 80th percentile triennial average PECgw for carbofuran and its soil metabolites did not exceed 0.1 µg/L for 8 out of 9 PEARL scenarios.

Based on these results, it can be expected that carbofuran would not pose a risk to groundwater in certain scenarios. These calculations also show that a minor change of the DT50 endpoint (from 12.83 d to 14 d; within the variation coefficient range) has a huge impact on the PEC outcome. It indicates that there is a large uncertainty on the modelling results. It also demonstrated that an accumulation of worst cases assumptions would lead to highly worst case outcome. In presenting the PEC conclusions to risk managers, the impact of the choice of endpoints on the PEC results should be explicitely mentioned.

It can be expect that any of the carbofuran metabolites would be expected to reach groundwater at 1 m depth in a majority of scenarios.

The RMS recommends therefore refining the groundwater risk assessment at national level.

B.8.6.2 Predicted Environmental Concentrations in surface water and sediment (PECsw) (Annex IIIA 9.2.3)

The notifier has proposed new PECsw calculations taking into account the endpoints that have been defined during the PRAPER meeting on benfuracarb (January 2009)

Modelling softwares, input parameters:
The models used to calculate PEC are SWASH (+ FOCUS drift calculator), TOXSWA, MACRO and PRZM.

The PECsw and PECsed were calculated for the following GAPs of the formulation FURADAN 5G: maximum rate of 0.600 kg a.s./ha and 0.060 kg a.s./ha (reduced application rate), once a year, at-plant application with incorporation into the soil to 7.0 cm.
The PEC were calculated for the a.s. and the metabolites 3-hydroxy-carbofuran, 3-keto-carbofuran and 7-phenol-carbofuran.

The application dates generated by SWASH were 16th March, 18th April, 17th March and 19th February respectively for the scenarios D3, D4, R1 and R3. Granular application (CAM=8, DEPI=7)

Table B.8.6.2-1: Input data

Parameter	**carbofuran**	**3OHCF**	**3ketoCF**	**7-phenolCF**
Mw	221.3	237.3 221.3 for MACRO runs*	235.24 221.3 for MACRO runs*	164.2
Water solubility (mg/L, 20°C)	322	6207	4464	1096
Vapour pressure (Pa, 25°C)	8^{e}-5	3.29e-3	2.6e-3	1.32
DT50 soil (days)	14	0.41	3.01	1
Kom	12.8	31.9	192	598
Koc	22	55	331	1031
1/n	0.96	1	1	0.9
Ffm		1	1	1
Q10	2.58	2.58	2.58	2.58
Plant Uptake	0	0	0	0
Crop washoff	0.146	0.455	0.401	0.234
Water DT50	15.3	1000	1000	9.9
Sediment DT50	1000	1000	1000	1000

*PECs adjusted for mw at end.

SW: CF to 7PhenolCF
CF to 3OHCF
CF to 3OHCF to 3KCF; non-standard MACRO runs (driver file for formation of 3KCF generated from CF to 3OHCF runs)

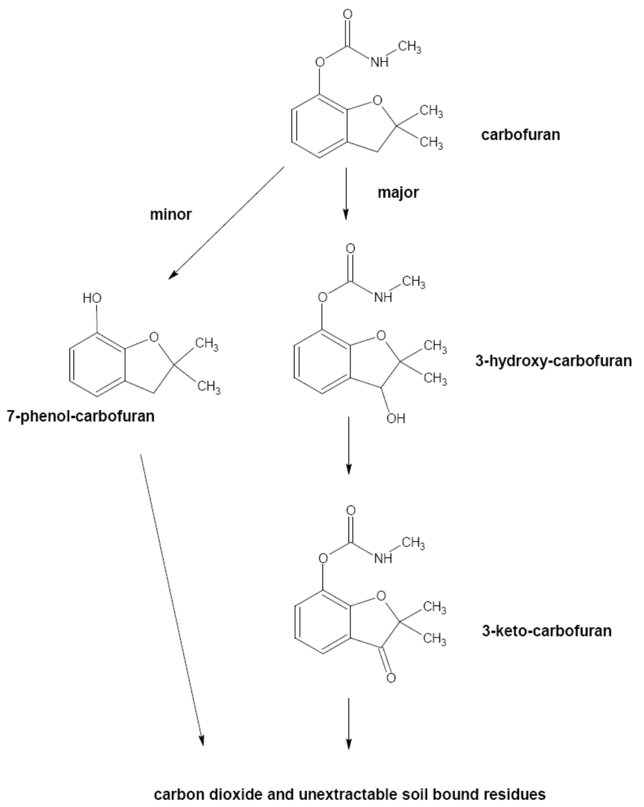


Table 9: The proposed sugar beet GAP for carbofuran

Application method	Application Rate	Application Timing
Applied in furrow at planting and incorporated at a depth of 7 cm	60 g/ha or 600 g/ha	Applied at the time of sugar beet planting

Table 25 Summary of applications for sugar beet

Scenario	Possible days of application		Application date generated by PAT
	First date	Last date	
D3	12th March	11th April	16th March
D4	21st March	20th April	18th April
R1	3rd March	2nd April	17th March
R3	4th February	6th March	19th February

PAT – Pesticide Application Timer

CAM8 depi 7 cm

Findings:

Table B.8.6.2-2: PEC SW, application of 600 g carbofuran/ha in sugar beet

File	Scenario	Compound	Max PECsw (µg/L)	Date of max PECsw	Max PECsed (µg/kg)	Date of max PECsed
00031d_pa.sum	D3 ((Ditch)	CF	0.0264	02-Feb-93	0.0461	14-Apr-93

00032p_pa.sum	D4 ((Pond)	CF	0.1030	30-Dec-85	0.1250	20-Feb-86
00032s_pa.sum	D4 ((Stream)	CF	0.0914	16-Dec-85	0.0871	31-Jan-86
00033p_pa.sum	R1 ((Pond)	CF	0.0000	01-Mar-84	0.0000	01-Mar-84
00033s_pa.sum	R1 ((Stream)	CF	0.0000	01-Mar-84	0.0000	01-Mar-84
00034s_pa.sum	R3 ((Stream)	CF	0.0000	01-Oct-80	0.0000	01-Oct-80
00031d_m1.sum	D3 ((Ditch)	7PCF	0.0000	29-Jan-93	0.0012	01-May-93
00032p_m1.sum	D4 ((Pond)	7PCF	0.0001	29-Jan-86	0.0017	23-Feb-86
00032s_m1.sum	D4 ((Stream)	7PCF	0.0002	01-Jan-85	0.0020	01-Feb-86
00033p_m1.sum	R1 ((Pond)	7PCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00033s_m1.sum	R1 ((Stream)	7PCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00034s_m1.sum	R3 ((Stream)	7PCF	0.0000	01-Oct-80	0.0000	01-Oct-80
00015d_m1.sum	D3 ((Ditch)	3OHCF	0.0008	29-Jan-93	0.0018	19-Apr-93
00016p_m1.sum	D4 ((Pond)	3OHCF	0.0041	31-Jan-86	0.0082	27-Mar-86
00016s_m1.sum	D4 ((Stream)	3OHCF	0.0024	17-Dec-85	0.0029	31-Jan-86
00009p_m1.sum	R1 ((Pond)	3OHCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00009s_m1.sum	R1 ((Stream)	3OHCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00010s_m1.sum	R3 ((Stream)	3OHCF	0.0000	01-Oct-80	0.0000	01-Oct-80
00027d_m1.sum	D3 ((Ditch)	3KCF	0.0026	30-Jan-93	0.0185	01-May-93
00028p_m1.sum	D4 ((Pond)	3KCF	0.0079	01-Feb-86	0.0476	01-May-86
00028s_m1.sum	D4 ((Stream)	3KCF	0.0044	01-Jan-85	0.0182	30-Jan-86
00045p_m2.sum	R1 ((Pond)	3KCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00045s_m2.sum	R1 ((Stream)	3KCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00046s_m2.sum	R3 ((Stream)	3KCF	0.0000	01-Oct-80	0.0000	01-Oct-80

Table B.8.6.2-3: PEC SW, application of 60 g carbofuran/ha in sugar beet

File	Scenario	Compound	Max PECsw (µg/L)	Date of max PECsw	Max PECsed (µg/kg)	Date of max PECsed
00035d_pa.sum	D3 ((Ditch)	CF	0.0020	02-Feb-93	0.0038	15-Apr-93
00036p_pa.sum	D4 ((Pond)	CF	0.0093	30-Dec-85	0.0117	21-Feb-86
00036s_pa.sum	D4 ((Stream)	CF	0.0083	16-Dec-85	0.0080	31-Jan-86
00037p_pa.sum	R1 ((Pond)	CF	0.0000	01-Mar-84	0.0000	01-Mar-84
00037s_pa.sum	R1 ((Stream)	CF	0.0000	01-Mar-84	0.0000	01-Mar-84
00038s_pa.sum	R3 ((Stream)	CF	0.0000	01-Oct-80	0.0000	01-Oct-80
00035d_m1.sum	D3 ((Ditch)	7PCF	0.0000	29-Jan-93	0.0001	01-Apr-93
00036p_m1.sum	D4 ((Pond)	7PCF	0.0000	29-Jan-86	0.0001	23-Feb-86
00036s_m1.sum	D4 ((Stream)	7PCF	0.0000	01-Jan-85	0.0002	02-Feb-86
00037p_m1.sum	R1 ((Pond)	7PCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00037s_m1.sum	R1 ((Stream)	7PCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00038s_m1.sum	R3 ((Stream)	7PCF	0.0000	01-Oct-80	0.0000	01-Oct-80
00017d_m1.sum	D3 ((Ditch)	3OHCF	0.0001	31-Jan-93	0.0001	20-Apr-93
00018p_m1.sum	D4 ((Pond)	3OHCF	0.0004	31-Jan-86	0.0007	27-Mar-86
00018s_m1.sum	D4 ((Stream)	3OHCF	0.0002	17-Dec-85	0.0003	31-Jan-86
00013p_m1.sum	R1 ((Pond)	3OHCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00013s_m1.sum	R1 ((Stream)	3OHCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00014s_m1.sum	R3 ((Stream)	3OHCF	0.0000	01-Oct-80	0.0000	01-Oct-80
00029d_m1.sum	D3 ((Ditch)	3KCF	0.0002	31-Jan-93	0.0014	01-May-93
00030p_m1.sum	D4 ((Pond)	3KCF	0.0007	31-Jan-86	0.0043	01-May-86
00030s_m1.sum	D4 ((Stream)	3KCF	0.0004	20-Dec-85	0.0016	30-Jan-86

00041p_m2.sum	R1 ((Pond)	3KCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00041s_m2.sum	R1 ((Stream)	3KCF	0.0000	01-Mar-84	0.0000	01-Mar-84
00042s_m2.sum	R3 ((Stream)	3KCF	0.0000	01-Oct-80	0.0000	01-Oct-80

Conclusions:

The PECgw were recalculated considering the endpoints which have been defined during the PRAPeR meeting on benfuracarb (January 2009).

These calculations also show that a minor change of the DT50 endpoint (from 12.83 d to 14 d; within the variation coefficient range) has a huge impact on the PEC outcome. It indicates that there is a large uncertainty on the modelling results. It also demonstrated that an accumulation of worst cases assumptions would lead to highly worst case outcome. In presenting the PEC conclusions to risk managers, the impact of the choice of endpoints on the PEC results should be explicitely mentioned.

ANNEX B

Addendum March 2009

Carbofuran

B.9 Ecotoxicology

B.9.1 Effects on birds (Annex IIA 8.1; Annex IIIA 10.1)

Comments 5(19) and 5(28) in the reporting table:

The risk for birds drinking water possibly contaminated with carbofuran is assessed by the puddle scenario.

$$PEC_{puddle} = \frac{AR / 10}{1000\ (w + Koc\ x\ s)}$$

with :
AR = application rate in g/ha; divisor of 10 to achieve rate in mg/m²
w = 0.02 (pore water term: volume)
s = 0.0015 (soil term: volume, density, organic carbon content)

The application rate for carbofuran is 0.600 kg a.s./ha. The Kfoc value for carbofuran is 23.3 mL/g.

$$PEC_{puddle} = \frac{600\ / 10}{1000\ (0.02 + 23.3\ x\ 0.0015)} = 1.09 \text{ mg a.s./L}$$

A small granivorous bird (passerines) has a drinking water rate DRW equivalent to 0.46 L/kg b.w./day.
The estimated theoretical exposure to carbofuran via drinking water is calculated as :

ETE = DRW x PEC_{puddle} = 0.46 L/kg b.w./day x 1.09 mg a.s./L = 0.50 mg a.s./kg b.w./day

The acute risk is calculated as :

TER = LD_{50} / ETE = 0.71 / 0.50 = 1.41

The acute TER is below the trigger value of 10.

However, the RMS is of the opinion that this calculation is unrealistic worst-case (birds consuming their entire drinking water demand on possibly contaminated puddles).

B.9.2 Effects on aquatic organisms (fish, aquatic invertebrates, algae) (Annex IIA 8.2; Annex IIIA 10.2)

Comment 5(52) in the reporting table:

B.9.2.15 Summary of effects to aquatic organisms (Annex IIA 8.2; Annex IIIA 10.2)

Table B. 9.2.15-1 : Summary of effects of carbofuran to aquatic organisms (FMC)

Test species	Test substance	Test system	Endpoints	References
Chironomus riparius	carbofuran	28 d static	**NOEC = 0.0032 mg a.s./L** (mean measured)	Putt E., 2008

Table B. 9.2.15-2 : Summary of effects of metabolites of carbofuran to aquatic organisms (Dianica)

Test species	Test substance	Test system	Endpoints	References
Chironomus riparius	7-phenol	25 d static	**NOEC = 5.34 mg a.s./L** (mean measured)	Memmert U., 2002

B.9.2.16 Exposure and risk assessment for aquatic organisms (Annex IIIA 10.2)

B.9.2.16.1 Risk assessment for the active substance

Table B.9.2.16.1-1 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to carbofuran in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 1 calculations

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
carbofuran	*Chironomus riparius*	0.0032	chronic	193.97	-	0.02	10

Table B.9.2.16.1-2 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to carbofuran in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 2 calculations

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	TER	Annex VI Trigger
cabofuran	N	*Chironomus riparius*	0.0032	chonic	31.26	0.10	10
	S				62.51	0.05	10

Table B.9.2.16.1-3 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to carbofuran in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Chironomus riparius*	28 d	0.0032	0.0021	1524	100
D4	Pond				0.0196	163	100
D4	Stream				0.0146	219	100
R1	Pond				0.000	-	100
R1	Stream				0.000	-	100
R3	Stream				0.000	-	100

B.9.2.16.2 Risk assessment for the metabolites

Table B.9.2.16.2-4 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to 7-phenol in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 1 calculations

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
7-phenol	*Chironomus riparius*	5.34	chronic	64.43	-	83	10

In conclusion, the risk of carbofuran and the metabolite 7-phenol to sediment dwelling organisms is acceptable based on FOCUS step 3, respectively FOCUS step 1 PECsw calculations.

B.9.3 Effects on other terrestrial vertebrates (Annex IIIA 10.3)

Comment 5(47) in the reporting table:

The risk for mammals drinking water possibly contaminated with carbofuran is assessed by the puddle scenario.

$$PEC_{puddle} = \frac{AR / 10}{1000\ (w + Koc\ x\ s)}$$

with :
AR = application rate in g/ha; divisor of 10 to achieve rate in mg/m²
w = 0.02 (pore water term: volume)
s = 0.0015 (soil term: volume, density, organic carbon content)

The application rate for carbofuran is 0.600 kg a.s./ha. The Kfoc value for carbofuran is 23.3 mL/g.

$$PEC_{puddle} = \frac{600\ /\ 10}{1000\ (0.02 + 23.3\ x\ 0.0015)} = 1.09 \text{ mg a.s./L}$$

A small granivorous mammal (non-desert species) has a drinking water rate DRW equivalent to 0.24 L/kg b.w./day.
The estimated theoretical exposure to carbofuran via drinking water is calculated as :

ETE = DRW x PEC_{puddle} = 0.24 L/kg b.w./day x 1.09 mg a.s./L = 0.26 mg a.s./kg b.w./day

The acute risk is calculated as :

TER = LD_{50} / ETE = 5.3 / 0.26 = 20

The acute TER is above the trigger value of 10, indicating that the risk is low.

ANNEX B

Carbofuran

B.7 Residue data

(Addendum April 2009)

<u>Open point 3.1 of the Evaluation tables: “</u>*The residue definition in plant commodities both for monitoring and risk assessment should be discussed in a meeting of experts”.*

1997 JMPR Report

CARBOSULFAN

-Metabolism, distribution and expression of residues of Carbosulfan in livestock

Goat metabolism study:
Guidelines*:*
US EPA GLP
Experimental design:
Goats were dosed orally once daily with either Phenyl- or Dibutylamine-labelled carbosulfan by balling gun for 7 consecutive days. The phenyl labeled dose was approximately 44.7 mg/goat/day (23 ppm in the diet). The DBA labeled dose was 40.9 mg/goat/day corresponding to 25 ppm in the diet.
Urine and feces were collected daily and milk in the afternoon and in the morning before dosing. Samples of omental and peripheral fat, liver, kidney, leg and lumbar muscle were taken for analysis.
Extraction procedure:
Organic and auqueous extracts were analysed. Some aqueous phases were subjected to enzymatic and acid hydrolysis followed by further partitioning.
The phenyl labeled milk samples were extracted with acetone/acetonitrile with further partitioning against hexane. The acetonitrile fraction was hydrolysed with β-glucosidase and sulfatase.
The DBA labeled milk samples were extracted and partitioned against different solvent mixtures. The aqueous fractions were hydrolysed with B-glucuronidase and sulfatase.
The post extraction solids were tested for association with carbohydrates (phenylhydrazone derivatization) or proteins (pepsin/pronase digestion) or characterized by size-exclusion chromatography (in order to detect highly polar residues in proteins fractions).
Characterization and identification of the metabolites were performed using normal and reverse phase TLC, HPLC, GC-MS, LC-MS and chemical derivatization in milk samples at 7 and 5 days respectively for the phenyl and DBA labeling forms, lumber muscle and omental fat for the DBA label and liver and kidney for both labels.
The residue levels in the phenyl labeled muscle and fat were too low for identification.
Findings:
Table 1: Cumulative percentages of the administered radioactivity recovered from urine, feces, milk, tissues and cage rinses of goats dosed with 14C Carbosulfan.

Sample	% of dose recovered			
	Phenyl label		Dibutylamine label	
	Goat 1	Goat 2	Goat 1	Goat 2
Urine	80.77	84.37	70.02	66.19
Feces	6.50	7.41	4.02	2.54
Cage rinse	1.40	1.30	0.35	0.31
Milk	0.16	0.17	1.97	2.66
Liver	0.02	0.02	0.37	0.31
Kidney	0.01	<0.01	0.03	0.04
Leg muscle	<0.01	<0.01	0.08	0.07
Lumbar muscle	<0.01	<0.01	0.05	0.04
Omental fat	<0.01	<0.01	0.18	0.13
Peripheral fat	<0.01	<0.01	0.06	0.05
Total	**88.86**	**93.27**	**77.13**	**72.34**

Table 2: Total radioactive residues recovered in milk and tissues of goats dosed with phenyl –and DBA- labeled Carbosulfan

TRR expressed as mg ^{14}C Carbosulfan equiv./kg						
Label	**Milk**	**Liver**	**Kidney**	**Muscle**	**Peripheral fat**	**Omental fat**
Phenyl	0.04-0.09	0.06	0.18	<0.01	0.01	0.009
DBA	0.3-0.94	1.13	0.75	0.18	0.74	1.2

Table 3: Distribution and identification of the Carbosulfan metabolites from feeding of phenyl-labelled carbosulfan to goats for 7 consecutive days (23 ppm in the diet).

Metabolites	**% of TRR**		
	Milk	**Liver**	**Kidney**
Total residue (mg/kg as Carbosulfan)	0.09	0.06	0.154
3-hydroxy carbofuran	34.20	9.50	21.50
3-OH-7-phenol	21.10	15.60	13.30
3-keto-7-phenol	29.90	3.00	8.30
7-phenol	9.20	4.60	8.90
Minor components	1.20	4.40(1)	7.60(1)
Characterised organosolubles	2.30	17.30	17.40
Protein associated metabolites	-	22.60	2.50
Polar aqueous metabolites	0.70	10.40	18.40
Unextractable residues	1.40	12.70	2.10
(1): Comprising 5-OH-carbofuran, N-hydroxy-carbofuran, 3-keto-carbofuran, Carbofuran, Carbosulfan, 3-keto-carbosulfan sulfone, 3-OH-carbosulfan and carbosulfan-sulfone.			

Table 4: Distribution and identification of the Carbosulfan metabolites from feeding of Dibutylamine-labelled carbosulfan to goats for 7 consecutive days (25 ppm in the diet).

Metabolite	**% of TRR**				
	Milk	**Fat**	**Liver**	**Kidney**	**Muscle**
Total residue (mg ^{14}Carbosulfan equi./kg)	0.680	1.286	0.986	0.823	0.193
Aminobutanols	29.7	0.8	8.1	11.9	ND
Dibutylamine(1)	6.7	0.6	13.4	10.5	9.6
Natural constituents(2)	30.2	87.3	29.1	13.8	32.0
Unconjugated amines	11.8	ND	6.3	24.3	5.9
Conjugated or bound amines	10.5	ND	18.0	12.3	14.7
Lipophilic metabolites	0.6	0.5	1.3	4.5	1.2
Polar aqueous metabolites	7.6	0.2	16.6	18.5	26.5
Post extraction solids	2.9	10.5	7.2	4.2	10.0
(1): Including related compounds of Dibutylamine: hydroxydibutylamine, butylamine. (2): In milk, fatty acids (13.4% TRR), amino acids (5.5 % TRR), carbohydrates (10.3% TRR) and triglycerides (1.1% TRR). In omental fat, fatty acids (82% TRR) and triglycerides (5.3% TRR). In lumbar muscle, 20.6 % TRR were associated with conjugated, unconjugated or bound amines and 32 %TRR with amino acids (??).					

-Metabolism, distribution and expression of residues of Carbosulfan in plants

The following study was reported both in the 1997 JMPR report and in the DAR (July, 2004): "Nature of the Residue: Metabolism of Carbosulfan in/on Oranges (Randy A., Weintraub Ph.D., 1996)".

CARBOFURAN

-Metabolism, distribution and expression of residues of Carbofuran in livestock

The following study was reported both in the 1997 JMPR report and in the Carbofuran DAR (July, 2004):
- Metabolism of ^{14}C Carbofuran in Lactating Goats (Hoffman S.L & Robinson R.A., 1994a)
- Metabolism of ^{14}C Carbofuran in Laying Hens (Hoffman S.L & Robinson R.A., 1994b)

-**Metabolism, distribution and expression of residues of Carbofuran in plants**

-Potatoes:
Experimental design:
Greenhouse grown potatoes were treated with (phenyl)14C Carbofuran in a single direct application to the soil surface at 7.4 kg a.s./ha after plant emergence. Immature vines were sampled after 56 days and mature tubers harvest after 104 days.
The samples were assayed for total radioactivity by combustion and Liquid scintillation counting.
Extraction procedure:
The extraction of immature vine and mature tubers was carried out with Methanol/water followed by partitioning against Methylene chloride to provide the organosoluble and aqueous soluble phases. The aqueous phase from the methylene chloride partitioning was sequentially incubated with B-glucosidase and hydrolysed with 0.25 N HCl and 2 N HCl in order to release organosoluble compounds from their conjugated form.
The parent compound and the metabolites were identified or characterized by reverse-phase HPLC and normal-phase TLC. Tentative identifications were confirmed by GC-MS.

Findings:

Compound	Mature tuber (104-day PHI)		Immature foliage (56-day PHI)	
	% of TRR	Mg/kg	% of TRR	Mg/kg
TRR (mg/kg)	100	0.80	100	30.5
Methanol/water extraction phase	Not given		Not given	
Methylene chloride organosoluble phase	22	0.176	6	1.83
Aqueous soluble phase	61	0.488	87	26.53
^{14}C released by enzymatic digestion (B-glucosidase)	7.9	0.063	51	15.55
^{14}C released by 0.25 N HCl	32	0.256	14	4.27
^{14}C released by 2 N HCl	9.4	0.075	13	3.96
Metabolites identification				
Carbofuran	nd	nd	3.5	1.071
3-OH-carbofuran	2.9	0.023	22.6	6.906
3-keto-carbofuran	-	-	1.1	0.324
7-phenol	45.3	0.361	6.7	2.044
3-OH-7-phenol	13.4	0.107	5.4	1.658
3-keto-7-phenol	6.6	0.052	9.4	2.858
5-OH-carbofuran	-	-	34.4	10.522
Total identified	68.2 (2.2% unconjugated)	0.543	83.1 (4.6% unconjugated)	25.383

Others	3.7	0.029	2.6	0.807
Polar residues	23.3	0.185	11.0	3.354
Unextractable residues	4.9	0.039	3.3	1.002
Total residues	100.0	0.80	100.1	30

-Soya beans:

Experimental design:

Sandy loam soil was treated with Carbofuran uniformly labeled with ^{14}C in the phenyl ring at 5.5 kg a.s./ha (USA). The test substance was applied deep furrow. Immediately after application, soya bean seeds were sown in a single row and covered with untreated soil. The soya beans were grown outdoors and samples of forage (PHI: 45 days), beans (PHI: 139 days) and hay (PHI: 139 days) were collected.

Extraction procedure:

The samples were assayed for total radioactivity by combustion and Liquid scintillation counting.

Samples were sequentially extracted with Methanol/water and with 0.25 N HCl. The extracted samples were extracted with Methylene chloride and the residual solids were sequentially hydrolysed with 0.25 N HCl, cellulose, B-glucosidase, amyloglucosidase, pectinase, protease, 6N HCl and 2N NaOH. The solid residues from the hay samples after solvent extraction were solubilized with dioxane-water to release lignin. After each hydrolysis the aqueous extracts were adjusted to pH 2 and extracted with acetonitrile to recover organosolubles.

The methanol/water and acid-reflluxed methanol/water extracts were analysed by reversed-phase HPLC. Confirmation was by normal-phase TLC and the main metabolites were identified by GC-MS. Unknown compounds separated by TLC and HPLC were investigated by HPLC-MS.

Findings:

Compound	**Total radioactive residues expressed as % of TRR and mg/kg ^{14}C Carbofuran equiv.**											
	Forage (63 mg/kg)				**Soya beans (0.32 mg/kg)**				**Hay (36 mg/kg)**			
	Methanol extract		**Acid-refluxed extract**		**Methanol extract**		**Acid-refluxed extract**		**Methanol extract**		**Acid-refluxed extract**	
	% TRR	**Mg/kg**	**% TRR**	**Mg/kg**	**% TRR**	**Mg/kg**	**% TRR**	**Mg/kg**	**% TRR**	**Mg/kg**	**% TRR**	**Mg/kg**
Carbofuran	11.6	7.3	11.4	7.2	-	-	0.42	0.001	0.30	0.11	0.62	0.22
3-keto-carbofuran	1.7	1.1	1.6	1.0	-	-	5.3	0.02	0.41	0.15	-	-
3-OH-carbofuran	10.6	6.6	28	18	0.56	0.002	1.5	0.005	3.2	0.50	7.8	2.8
7-phenol	-	-	1.4	0.90	0.38	0.001	4.0	0.013	0.67	0.24	0.72	0.26
3-keto-7-phenol	1.6	1.0	13	8.1	0.71	0.002	9.2	0.030	4.3	1.6	9.8	3.5
0-glucoside conjugate of 3-OH or 3-keto-7-phenol	16	9.9	3.4	2.1	11	0.036	-	-	3.6	1.3	-	-
2-OH-methyl-3-keto-carbofuran	-	-	3.6	2.2	-	-	0.93	0.03	-	-	0.84	0.30
Total identified.	42		62		13		21		12		20	

-Maize:

Experimental design:

Loam soil was treated with Carbofuran uniformely labelled with ^{14}C in the phenyl ring at a rate of 8.3 kg a.s./ha. The test substance was sprayed in a band on the soil and was incorporated to a depth of about 5 cm before planting maize seed.
Maize samples were taken at 3 growth stages: forage (immature stage, 47 days PHI), silage (99 days, PHI) and stover and grain (kernels without cob and husk, 158 days PHI).
Extraction procedure:
The samples were assayed for total radioactivity by combustion and Liquid scintillation counting.
Each sample was extracted with methanol/water and the extracts acidified to pH 1 and partitioned with methylene chloride/ether. The aqueous fractions from the methylene chloride/ether partitioning of the forage and silage samples were divided in 2 fractions and treated sequentially with B-glucosidase and by acid refluxing followed by partitioning against methylene chloride/ether. The aqueous layer from this extract of the silage and forage samples was acidified by acid refluxing followed by extraction with methylene chloride/ether to collect the organosoluble unconjugated metabolites.
The post extraction solids (PES) from the initial methanol/water extraction were refluxed with 0.25 N HCl. The hydrolysate from the grain was tested to determine the presence of reducing sugars with Benedict's solution and by osazone formation. Both tests indicated reducing sugars.
The residue after acid hydrolysis was treated with a surfactant.
The organosoluble fractions from the forage and silage, i.e. the methylene chloride/ether extracts of the acidified methanol/water extract and of the 0.25 N hydrolysate, were analysed by HPLC, TLC and GC-MS.
The extracts from grain and stover were not further analysed because of the very low level of recovered radioactivity.

Findings:

Fraction/Compounds	**Grain**		**Forage**		**Stover**		**Silage**	
Total radioactive residues (mg/kg)	**0.023**		**0.81**		**0.075**		**0.14**	
	% TRR	**Mg/kg**	**% TRR**	**Mg/kg**	**% TRR**	**Mg/kg**	**% TRR**	**Mg/kg**
Methylene chloride/ether (non conjugates)	5.8	0.001	42	0.34	4.4	0.003	4.6	0.006
Acid-released methylene chloride/ether (aglycones)			32	0.26	-	-	20	0.028
Glucosidase-released (aglycones)	-	-	19	0.15	-	-	23	0.032
Residual acid aqueous	-	-	8.1	0.066	22	0.016	31	0.036
Acid-released from PES	48	0.011	3.5	0.028	13	0.010	9.9	0.014
Surfactant-released from PES	-	-	1.6	0.013	4.7	0.004	5.1	0.007
Total released residue	48		87		44		71	
Identification of the metabolites in the organosoluble extracts of maize silage and forage								
Carbofuran			14	0.11			0.18	<0.001
Carbofuran aglycone			2.4	0.019			2.1	0.003
3-keto-carbofuran			1.6	0.013			-	-
3-keto-carbofuran aglycone			0.28	0.003			0.91	0.001
3-OH-carbofuran			13	0.11			1.3	0.002
3-OH-carbofuran aglycone			9.7	0.078			7.9	0.011
7-phenol			0.47	0.004			0.088	<0.001
7-phenol aglycone			7.5	0.060			2.8	<0.001
3-keto-7-phenol			4.8	0.039			1.4	0.002
3-keto-7-phenol aglycone			5.6	0.045			2.4	0.003

3-OH-7-phenol			2.4	0.020			0.88	0.001
3-OH-7-phenol aglycone			3.6	0.029			2.3	0.003
Total			65	0.53			22	0.026

The predominant compounds recovered in maize forage and silage was the carbofuran and 3-OH-carbofuran, free and conjugated. The amount of radioactivity that could not be extracted with solvent or released by acid hydrolysis increased with the PHI, suggesting incorporation of the radioactivity into plants constituents.

Residues in succeeding or rotational crops

Experimental design:
In a confined crop rotation study (Phenyl)-^{14}C-Carbofuran was applied directly to a silt loam soil at an application rate of 3.4 kg as/ha. Wheat, soya beans and sugar beet were seeded into the treated soil 4 and 12 months after treatment and grown to maturity. Wheat forage, straw and grain, soya bean silage, stems, pods and beans and sugar beet tops and roots were assayed for the determination of the total radioactive residues.
Extraction procedure:
Each sample was extracted with Methanol/water and separated into non polar and polar fractions for further metabolites identification. Conjugated metabolites were hydrolysed with 0.25 N HCl. Metabolites were identified by TLC, by co-chromatography with reference standards.

Findings:

Crop	**Sample**	**Total radioactive residues (mg/kg)**	
		4 months	**12 months**
Wheat	**Forage**	-	1.40
	Straw	54.0	0.30
	Grain	0.60	0.04
Soya bean	**Silage**	16.0	0.50
	Stem	18.0	0.70
	Pod	5.0	0.10
	Beans	1.0	0.08
Sugar beet	**Top**	0.40	0.05
	Root	0.20	0.05

The phenolic metabolites were the main degradation products recovered in the rotated crops. The carbamates (carbofuran, 3-OH-carbofuran and 3-keto-carbofuran) constituted a small proportion of the total radioactive residues (<10 % of the TRR in any crop sown at 4 and 12 months).

Open point 3.3 of the evaluation tables: "It *should be clarified whether in the data generation methods (residue trials) the efficiency of the hydrolysis step was validated?"*

The validation data package is presented here below:

-Determination of residues of carbosulfan and its metabolites carbofuran and 3-hydroxy carbofuran by HPLC-MS-MS in maize and sugar beet samples – Validation of the method. (Enriquez, 2006, Report BATTELLE A-17-05-13)

GLP :

GLP-compliance stated

Principle of the method :

Carbosulfan and Carbofuran (CS-CF) is extracted from 5 g sample with a mixture of hexane – acetone (4:1, v/v) and filtered through Celite and sodium sulphate anhydrous.

The metabolite 3-hydroxy carbofuran (3-OHCF) is extracted from the remaining filter cake by refluxing with 0.25 M hydrochloric acid. After filtration the 3-hydroxy carbofuran is cleaned-up through a C18 SPE cartridge using methanol 1% in dichloromethane.

The combined organic extract (CS-CF and 3-OHCF) is evaporated (at temperatures below 35°C and after addition of 'keeper' 1-decanol, in order to avoid losses of carbosulfan), re-constituted and kept in acetonitrile. Then the re-constituted extract is diluted with acetonitrile and water (to have the same composition of the mobile phase) and analysed by HPLC (column: Aqua C18, 50mm x 2mm ID, 5µm particles) with MS-MS detection (ESI, positive mode).

Findings:

Specificity – interferences :
- Following ion transitions were monitored (MRM): m/z 381.1 → 118.1 (carbosulfan); m/z 222.1 → 123.0 (carbofuran); m/z 237.9 → 163.0 (3-OH-carbofuran);
  LC-MS/MS is highly specific → no need for separate confirmatory method.
- No significant interferences (>30% of LOQ) were observed at the retention times of carbosulfan, carbofuran or 3-hydroxy carbofuran in any blank or control sample.

Linearity : The detector response for each compound was linear over the concentration range 1 ng/mL to 25 ng/mL (corresponding to a residue conc. range of 2 to 50 ppb). Correlation coefficients > 0.99.

Recovery – precision : see Table B.5.2.1-9b

Validation by an independent laboratory : First validation of method by Battelle; ILV described in study by Zietz (2008) was conducted by SGS Institut Fresenius.

Limit of quantification (LOQ) : 0.005 mg/kg (= 5 ppb) for each analyte in maize and sugar beet

Table B.5.2.1-9b: Lab validation of LC-MS/MS method for residues of Carbofuran and 3-OH Carbofuran in maize and sugar beet (Enriquez, 2006) (FMC)

Matrix	Analyte	Fortification level (mg/kg commodity)	Recovery			
			Number of samples	Range (%)	Mean (%)	RSD (%)
Maize grain	Carbosulfan	0.005	5	77-82	80	3
		0.050	5	70-79	75	5
		Overall	*10*	*70-82*	*78*	*5*
	Carbofuran	0.005	5	87-94	89	3
		0.050	5	96-102	99	2
		Overall	*10*	*87-102*	*94*	*6*
	3-OH carbofuran	0.005	5	94-107	97	5
		0.050	5	100-104	101	2
		Overall	*10*	*94-107*	*100*	*4*
Sugar beet	Carbosulfan	0.005	5	67-77	73	5
		0.050	5	82-91	87	4
		Overall	*10*	*67-91*	*80*	*10*
	Carbofuran	0.005	5	82-94	86	6
		0.050	5	84-104	97	8

		Overall	*10*	*82-104*	*92*	*9*
	3-OH carbofuran	0.005 0.050	5 5	102-115 75-100	107 92	5 11
		Overall	*10*	*75-115*	*100*	*11*

Conclusion:
The analytical method is suitable for the determination of carbosulfan and its metabolites carbofuran and 3-hydroxy carbofuran in maize and sugar beet samples with a LOQ of 5 ppb for each analyte.

<u>Open point 3.6 of the Evaluation tables</u>: *"Assessment of residues in animal matrices, considering information available from all animal studies, to be submitted in an addendum and reviewed by the meeting of experts"*

A) Metabolism, distribution and expression of residues of carbofuran in lactating goats

Summary of the nature of the metabolites in tissues and milk of a lactating goat orally dosed with (Phenyl ring -UL-^{14}C) –carbofuran (Feeding level: 1.35 mg/kg b.w./day) – Results expressed in % of the total radioactive residues –(mg ^{14}C carbofuran equiv/kg).

Samples	Carbofuran	3-OH-carbofuran	7-phenol	3-OH-7-phenol	3-keto-7-phenol	Aqueous residues	Polar residues	Unknown metabolites	Total identified metabolites	Bound residues	Total
Milk	0.41 (0.001)	10.01 (0.032)	15.25 (0.048)	6.83 (0.021)	31.85 (0.102)	6.34 (0.020)	21.90(1) (0.070)	4.93 (0.016)	64.38 (0.204)	2.47 (0.008)	99.9 (0.318)
Loin muscle	nd	nd	nd	nd	nd	27.57 (0.003)	nd	0.35 (<0.001)	-	72.08 (0.007)	100.1 (0.010)
Liver	nd	4.02 (0.005)	2.45 (0.003)	12.39 (0.017)	nd	31.72 (0.045)	6.87 (0.010)	35.17(2) (0.046)	18.86 (0.025)	7.37 (0.010)	99.99 (0.136)
Kidney	nd	11.00 (0.029)	nd	15.84 (0.042)	nd	28.58 (0.076)	16.64(3) (0.044)	22.96(4) (0.060)	26.84 (0.071)	4.99 (0.013)	100.01 (0.264)

Nd : not radiodetected.
(1) : sum of 3 fractions , none exceeding 19.71 % (0.063 ppm)
(2) : sum of 10 fractions , none exceeding 8.63 % (0.012 ppm)
(3) : sum of 3 fractions , none exceeding 8.34 % (0.022 ppm)
(4) : sum of 10 fractions , none exceeding 5.29 % (0.014 ppm)

Remark: Because the extraction profiles from the initial extractions of milk, liver and kidney from both the 2 treated goats were very similar, metabolite analysis was performed only on the extracts from one of the 2 goats.

B) Metabolism, distribution and expression of residues of carbofuran in laying hens

Recovery of radioactivity from hens after oral administration of (Phenyl ring -UL-^{14}C) –carbofuran (% of total administered radioactivity).

Hen group	B		C		D		Average of the % of total dose	Average of TRR (mg/kg)
	% of total dose	TRR (mg/kg)	% of total dose	TRR (mg/kg)	% of total dose	TRR (mg/kg)		
Excreta[(1)]	83.13	-	81.63	-	83.71	-	82.82	-
Egg white[(1)]	0.30	0.058	0.24	0.056	0.28	0.064	0.27	0.059
Egg yolk[(1)]	0.23	0.137	0.19	0.151	0.22	0.135	0.21	0.141
Total excretion	*83.66*		*82.06*		*84.21*		*83.33*	-
Liver	0.11	0.142	0.12	0.145	0.09	0.125	0.11	0.137
Kidney	0.01	0.034	0.01	0.035	0.01	0.033	0.01	0.034
Breast muscle	0.03	<0.010	0.02	<0.010	0.01	<0.010	0.02	<0.01
Thigh muscle	0.01	<0.010	<0.01	<0.010	<0.01	<0.010	<0.01	<0.01
Fat with skin	<0.01	0.010	0.01	<0.010	<0.01	<0.010	<0.01	0.01
Total recovery	83.82	-	82.21	-	84.32	-	83.44	-

(1): values expressed as a cumulative percentage of the total administered dose on day 7.
No justification was provided by the notifier for lacking 17 % of the total dose for the 3 hen groups.

Summary of the nature of the metabolites in tissues and eggs of laying hens orally dosed with (Phenyl ring -UL-^{14}C) –carbofuran (Feeding level : 1.92 mg/kg b.w./day) – Results expressed in (% of the total radioactive residues) –(mg ^{14}C carbofuran equiv/kg).

Samples	Carbofuran	3-OH-carbofuran	7-phenol	3-OH-7-phenol	3-keto-7-phenol	Phenolic conjugates	Aqueous residues	Polar residues	Unknown metabolites	Bound residues	Total
Egg white	nd	nd	nd	nd	nd	90.00 (0.060)	nd	nd	0.73 (<0.001)	9.27 (0.006)	100.0 (0.066)
Egg yolk	nd	12.05 (0.019)	15.66 (0.026)	39.16 (0.062)	7.41 (0.012)	nd	4.58 (0.007)	nd	12.7 (0.021)	8.45 (0.014)	100.01 (0.161)
Liver	nd	nd	5.68 (0.008)	7.36 (0.010)	nd	nd	26.09 (0.035)	11.79 (0.016)	45.84[(1)] (0.065)	3.24 (0.005)	100.0 (0.139)
Kidney	nd	nd	4.87 (0.001)	5.35 (0.002)	nd	nd	22.21 (0.008)	30.13 (0.010)	34.91[(2)] (0.011)	2.55 (0.001)	100.02 (0.033)

Nd: not radiodetected.
(1) : this value represents the sum of 9 fractions, none exceeding 9.26 % (0.013 mg/kg)
(2) : this value represents the sum of 7 fractions, none exceeding 15.44 % (0.005 mg/kg)

The residue levels recovered in the following matrices were determined in compliance with the proposed residue definition for risk assessment: 3-OH-carbofuran, free and conjugated expressed as 3-OH-carbofuran.

Ruminants (metabolism study):
-Milk: 0.0003 mg/kg (Table B.7.2.1-3 in the DAR)
-Liver: 0.00005 mg/kg (Table B.7.2.1-3 in the DAR)
-Kidney: 0.0003 mg/kg (Table B.7.2.1-3 in the DAR)
-Muscle: TRR: 0.000083 mg/kg (Table B.7.2.1-1 in the DAR)
-Fat: TRR: 0.000083 mg/kg (Table B.7.2.1-1 in the DAR)

Poultry (metabolism study):
-Eggs: 0.000008 mg/kg (Table B.7.2.2-3 in the DAR)
3-OH-carbofuran was not detected in egg white, liver, kidney, muscle and fat.

Open point: 3.9 of the Evaluation Tables: "*The consumer risk assessment should be discussed in a meeting of expert, considering all relevant sources of exposure to carbofuran residues with respect to the notified use"*

A) Dietary intake risk assessment to Carbofuran and 3-OH carbofuran residues according to EFSA PRIMo

Input values:

Sugar beet root (residue trials): 0.01 mg/kg (LoQ of the analytical method for the sum of Carbofuran and 3-OH carbofuran, free and conjugated, expressed as carbofuran)

The residue levels recovered in the following matrices were in compliance with the proposed residue definition for risk assessment: 3-OH-carbofuran, free and conjugated expressed as 3-OH-carbofuran.

Ruminants (metabolism study):
-Milk: 0.0003 mg/kg (Table B.7.2.1-3 in the DAR)
-Liver: 0.00005 mg/kg (Table B.7.2.1-3 in the DAR)
-Kidney: 0.0003 mg/kg (Table B.7.2.1-3 in the DAR)
-Muscle: TRR: 0.000083 mg/kg (Table B.7.2.1-1 in the DAR)
-Fat: TRR: 0.000083 mg/kg (Table B.7.2.1-1 in the DAR)

Poultry (metabolism study):

-Eggs: 0.000008 mg/kg (Table B.7.2.2-3 in the DAR)
3-OH-carbofuran was not detected in egg white, liver, kidney, muscle and fat.

Rotational crops (Table B.7.9.2 in the DAR)*:*
-Succeeding root crops: TRR=0.006 mg/kg
-Succeeding leafy crops: TRR=0.031 mg/kg
-Succeeding cereals crops: TRR=0.001 mg/kg

Carbofuran + 3-OH-carbofuran			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):	0,005	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0,00015**	ARfD (mg/kg bw):	**0,00015**
Source of ADI:	**DAR**	Source of ARfD:	**DAR**
Year of evaluation:	**2009**	Year of evaluation:	**2009**

Chronic risk assessment

TMDI (range) in % of ADI
minimum - maximum

10 173

No of diets exceeding ADI: 1

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
172,9	UK Toddler	152,5	Sugar beet (root)	14,0	Potatoes	3,0	CEREALS	3,1
89,4	UK Infant	67,2	Sugar beet (root)	13,0	Potatoes	5,3	Carrots	3,0
54,0	NL child	23,6	Potatoes	7,6	Spinach & similar (leaves)	6,4	Lettuce and other salad plants including Brassicacea	9,7
49,5	FR toddler	20,3	Potatoes	14,2	Spinach & similar (leaves)	9,8	Carrots	2,1
43,2	FR infant	16,5	Potatoes	10,6	Carrots	8,9	Spinach & similar (leaves)	5,8
42,8	SE general population 90th percentile	16,7	Potatoes	8,3	Lettuce and other salad plants including Brassicacea	5,2	Leafy brassica	5,8
40,8	WHO Cluster diet B	10,7	Potatoes	8,2	Lettuce and other salad plants including Brassicacea	7,9	CEREALS	8,7
37,4	UK Adult	26,6	Sugar beet (root)	5,6	Potatoes	2,4	Lettuce and other salad	1,4

							plants including Brassicacea	
37,2	UK vegetarian	25,2	Sugar beet (root)	5,5	Potatoes	2,9	Lettuce and other salad plants including Brassicacea	1,7
33,1	WHO cluster diet D	16,2	Potatoes	7,6	Leafy brassica	5,6	CEREALS	6,6
31,9	WHO regional European diet	16,1	Potatoes	8,5	Lettuce and other salad plants including Brassicacea	2,5	CEREALS	3,5
30,8	WHO Cluster diet F	13,6	Potatoes	6,2	Lettuce and other salad plants including Brassicacea	3,6	CEREALS	4,5
29,8	PT General population	21,3	Potatoes	3,6	CEREALS	2,7	Carrots	3,6
29,0	IE adult	9,2	Potatoes	4,4	CEREALS	4,1	Leafy brassica	5,0
28,4	WHO cluster diet E	15,3	Potatoes	4,1	Lettuce and other salad plants including Brassicacea	4,0	CEREALS	4,7
27,9	DE child	10,3	Potatoes	4,2	Spinach & similar (leaves)	4,1	Carrots	6,6
26,3	ES child	8,6	Lettuce and other salad plants including Brassicacea	7,4	Potatoes	3,5	CEREALS	6,1
25,7	NL general	11,0	Potatoes	5,0	Lettuce and other salad plants including Brassicacea	3,0	Spinach & similar (leaves)	3,2
25,5	DK child	9,7	Potatoes	6,9	CEREALS	5,5	Carrots	7,0
23,0	IT adult	11,5	Lettuce and other salad plants including Brassicacea	4,4	Spinach & similar (leaves)	3,4	CEREALS	3,4
22,3	IT kids/toddler	8,5	Lettuce and other salad plants including Brassicacea	5,6	CEREALS	3,6	Potatoes	5,6
21,9	ES adult	11,1	Lettuce and other salad plants including Brassicacea	3,7	Potatoes	3,3	Spinach & similar (leaves)	3,2
17,8	LT adult	12,7	Potatoes	1,8	CEREALS	1,3	Lettuce and other salad plants including Brassicacea	2,6
17,1	PL general population	13,7	Potatoes	1,2	Carrots	0,9	Beetroot	0,0
16,1	FR all population	6,6	Lettuce and other salad plants	4,5	Potatoes	2,3	CEREALS	2,9

				including Brassicacea					
	13,1	DK adult	5,8	Potatoes	2,7	Lettuce and other salad plants including Brassicacea	1,9	CEREALS	2,0
	9,8	FI adult	4,9	Potatoes	1,6	Lettuce and other salad plants including Brassicacea	1,3	CEREALS	1,3
Acute risk assessment /children					**Acute risk assessment / adults / general population**				

In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used.
In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3.

Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.

Unprocessed commodities	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		**16**	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		**16**	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		**9**	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		**8**
	IESTI 1	***)**	****)**	**IESTI 2**	***)**	****)**	**IESTI 1**	***)**	****)**	**IESTI 2**	***)**	**)
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	1806,8	Scarole (broad-leaf endive)	0,031 / 0	1806,8	Scarole (broad-leaf endive)	0,031 / 0	738,1	Chinese cabbage	0,031 / 0	738,1	Chinese cabbage	0,031 / 0
	1397,1	Kale	0,031 / 0	998,3	Kale	0,031 / 0	421,2	Kale	0,031 / 0	313,0	Kale	0,031 / 0
	767,4	Chinese cabbage	0,031 / 0	767,4	Chinese cabbage	0,031 / 0	227,1	Lettuce	0,031 / 0,01	187,9	Purslane	0,03 / 0,01
	615,0	Potatoes	0,006 / 0	452,0	Spinach	0,03 / 0	206,7	Purslane	0,03 / 0,01	183,4	Scarole (broad-leaf endive)	0,031 / 0,01
	556,0	Lettuce	0,031 / 0	439,3	Potatoes	0,006 / 0	183,4	Scarole (broad-leaf endive)	0,031 / 0,01	178,7	Spinach	0,03 / 0,01
	452,0	Spinach	0,03 / 0	425,7	Sugar beet (root)	0,01 / 0	178,7	Spinach	0,03 / 0,01	172,9	Sugar beet (root)	0,01 / 0
	425,7	Sugar beet (root)	0,01 / 0	333,6	Lettuce	0,031 / 0	172,9	Sugar beet (root)	0,01 / 0	136,3	Lettuce	0,031 / 0,02
	351,1	Beet leaves (chard)	0,03 / 0	266,4	Beet leaves (chard)	0,03 / 0,01	148,4	Beet leaves (chard)	0,03 / 0,02	125,4	Beet leaves (chard)	0,03 / 0,02
	302,2	Purslane	0,03 / 0	229,1	Purslane	0,03 / 0,01	119,4	Potatoes	0,006 / 0	95,6	Swedes	0,006 / -
	253,6	Carrots	0,006 / 0	221,2	Celeriac	0,006 / 0	95,6	Swedes	0,006 / -	93,5	Potatoes	0,006 / -

	221,2	Celeriac	0,006 / 0	206,9	Swedes	0,006 / 0
	206,9	Swedes	0,006 / 0	181,1	Carrots	0,006 / 0
	175,3	Beetroot	0,006 / 0	130,2	Beetroot	0,006 / 0
	157,1	Salsify	0,006 / 0	112,2	Salsify	0,006 / 0
	144,5	Parsnips	0,006 / 0	103,2	Parsnips	0,006 / 0
	143,7	Turnips	0,006 / 0	102,6	Turnips	0,006 / 0
	No of critical MRLs (IESTI 1)		16	**No of critical MRLs (IESTI 2)**		16
Processed commodities	**No of commodities for which ARfD/ADI is exceeded:**		**1**	**No of commodities for which ARfD/ADI is exceeded:**		**---**
			*****)**			*****)**
	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)
	171,6	Carrot, juice	0,006 / 0	3,5	Potato uree (flakes)	0,006 / -
	54,5	Potato puree (flakes)	0,006 / -	3,3	Fried potatoes	0,006 / -
	52,9	Celeriac juice	0,006 / -	2,9	Bread/pizza	0,001 / -
	7,9	Wheat flour	0,001 / -	0,2	Maize flour	0,001 / -
	5,7	Fried potatoes	0,006 / -			
	For processed commodities, the ARfD/ADI was exceeded in one or several cases.					

Conclusion:

There is a chronic and acute intake concern when the input values here above mentioned are incorporated into the EFSA PRIMo.
This calculation can be considered as overestimated for the following reasons:
-*Sugar beet root*: The maximum food intake reported at the 97.5th percentile for the UK 4-6 year old child (20.5 kg bw) and for the UK adult (76 kg bw) accounted for 1309 g/day and 1971 g/day of sugar beet root, respectively.
If we assume that the sugar beet root contains approximately 16 % of sugar, the actual sugar consumption can be estimated to raise 209 g/day for the UK 4-6 year old child and 315 g/day for the UK adult.
The recommended maximum sugar intake for an adult and a 4-6 year old child are 50 g/day and 40 g/day of sugar, respectively.

In addition, when taking into account the no-residue situation in sugar beet root characterized by an extremely low Limit of Quantification (0.005 mg/kg for each analyte), the soil DT_{90} values of Carbofuran and 3-OH-carbofuran and assuming that any residue that may be left in the roots is substantially reduced during production of sugar, the outcome of the model can be considered as clearly conservative.
-*Rotational crops*: The input values in the EFSA PRIMo corresponded to the amount of TRR found in the succeeding crops after 30 days (simulating a crop failure). This approach is rather conservative since the residue levels of Carbofuran and 3-OH-carbofuran are lower than the TRR values (see available plant metabolism studies performed with Carbosulfan and Carbofuran) considering the DT50/90 values of Carbofuran and 3-OH-carbofuran and also the metabolisation of Carbofuran into its other carbamate and phenolic metabolites that occurs in soil before planting the succeeding crops.

B) Dietary intake risk assessment to Carbofuran and 3-OH carbofuran residues according to UK Model

Same input values as for point A.

Chronic dietary intake risk assessment

Active substance: Carbofuran **ADI:** 0,00015 mg/kg bw/day **Source:** DAR 2009

	TOTAL INTAKE based on 97.5th percentile									
	ADULT	INFANT	TODDLER	4-6 YEARS	7-10 YEARS	11-14 YEARS	15-18 YEARS	VEGETARIAN	ELDERLY (OWN HOME)	ELDERLY (RESIDENTIAL)
mg/kg bw/day	0,00005	0,00014	0,00015	0,00011	0,00010	0,00007	0,00006	0,00005	0,00005	0,00005
% of ADI	32%	93%	*101%*	75%	65%	46%	42%	37%	33%	32%

Commodity	STMR (mg/kg)	P	COMMODITY INTAKES (mg/kg bw/day)									
Beetroot	0,006		0,00000	L/C	0,00001	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Carrots	0,006		0,00000	0,00002	0,00001	0,00001	0,00001	0,00001	0,00001	0,00001	0,00001	0,00000
Celeriac	0,006		0,00000	L/C	L/C	0,00000	0,00000	L/C	L/C	L/C	L/C	L/C
Horseradish	0,006		0,00000	L/C	L/C	L/C	L/C	L/C	L/C	L/C	0,00000	L/C
Jerusalem artichokes	0,006		0,00000	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Parsnips	0,006		0,00000	0,00001	0,00001	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Radishes	0,006		0,00000	L/C	0,00001	L/C	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000

Salsify	0,006		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Swedes	0,006		0,00000	0,00002	0,00001	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Turnips	0,006		0,00000	L/C	0,00001	0,00001	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Cress	0,031		0,00000	L/C	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Lettuce	0,031		0,00002	0,00001	0,00003	0,00002	0,00002	0,00001	0,00001	0,00002	0,00002	0,00001
Spinach	0,031		0,00002	0,00003	0,00005	0,00003	0,00003	0,00002	0,00001	0,00002	0,00002	0,00001
Watercress	0,031		0,00000	L/C	L/C	0,00000	0,00000	0,00001	L/C	0,00001	0,00001	L/C
Chicory	0,031		0,00000	L/C	L/C	L/C	L/C	L/C	L/C	0,00000	L/C	L/C
Parsley	0,031		0,00001	L/C	0,00000	L/C	0,00000	0,00000	0,00000	0,00001	0,00001	0,00001
Potatoes	0,006		0,00002	0,00007	0,00006	0,00005	0,00004	0,00003	0,00003	0,00002	0,00002	0,00002
Oats	0,001		0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Barley	0,001		0,00000	L/C	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Buckwheat	0,001		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Maize	0,001		0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Wheat	0,001		0,00000	0,00000	0,00001	0,00001	0,00001	0,00000	0,00000	0,00000	0,00000	0,00000
Rye	0,001		0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Poultry	0,000083		0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Meat fat	0,000083		0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Meat excl. poultry & offal	0,000083		0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
All types of kidney	0,0003		0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	L/C	0,00000	0,00000
All types of Liver	0,00005		0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	L/C	0,00000	0,00000
Eggs	0,000008		0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000	0,00000
Milk	0,0003		0,00000	0,00003	0,00002	0,00001	0,00001	0,00000	0,00000	0,00000	0,00000	0,00000
Refined sugar	0,01		0,00002	0,00005	0,00008	0,00005	0,00005	0,00003	0,00003	0,00002	0,00002	0,00002

Acute dietary intake risk assessment
Acute Intakes (97.5th percentiles)

			adult		infant		toddler		4-6 year old child		7-10 year old child	
commodity	**HR**	**P**	**NESTI**	**%ARfD**	**NESTI**	**%ARfD**	**NESTI**	**%ARfD**	**NESTI**	**%ARfD**	**NESTI**	**%ARfD**
Potatoes	0,01		0,00014	96,1	0,00092	615,0	0,00064	425,3	0,00048	320,4	0,00033	220,2
Beetroot	0,01		0,00003	17,5	0,00000	0,0	0,00010	70,0	0,00007	48,8	0,00005	35,7
Carrots	0,01		0,00005	34,7	0,00038	253,6	0,00024	157,2	0,00018	117,9	0,00011	76,5
Celeriac	0,01		0,00007	47,4	0,00000	0,0	0,00001	5,2	0,00001	6,5	0,00001	8,6
Horseradish	0,01		0,00000	1,9	0,00000	0,0	0,00000	0,0	0,00000	0,0	0,00000	0,0
Jerusalem artichoke	0,01		0,00003	16,8	0,00000	0,0	0,00000	0,0	0,00000	0,0	0,00000	0,0
Parsnips	0,01		0,00007	48,0	0,00022	144,5	0,00016	108,9	0,00018	117,3	0,00014	95,0
Radishes	0,01		0,00001	4,2	0,00000	0,0	0,00002	12,5	0,00001	5,1	0,00001	3,6
Salsify	0,01		0,00000	0,0	0,00000	0,0	0,00000	0,0	0,00000	0,0	0,00000	0,0
Swedes	0,01		0,00008	53,0	0,00031	206,9	0,00018	121,8	0,00014	95,6	0,00009	58,1
Turnips	0,01		0,00006	42,2	0,00000	0,0	0,00017	110,8	0,00022	143,7	0,00010	66,9
Cress	0,03		0,00001	3,5	0,00000	0,0	0,00001	6,0	0,00001	6,0	0,00001	3,3
Lettuce	0,03		0,00031	203,9	0,00039	261,3	0,00037	249,4	0,00055	368,0	0,00042	277,9
Spinach	0,03		0,00039	261,2	0,00082	544,0	0,00061	409,8	0,00088	586,2	0,00050	334,4
Watercress	0,03		0,00002	10,9	0,00000	0,0	0,00001	5,7	0,00001	9,5	0,00001	9,6
Chicory	0,03		0,00011	76,1	0,00000	0,0	0,00000	0,0	0,00000	0,0	0,00030	201,3
Parsley	0,03		0,00002	13,5	0,00000	0,0	0,00001	6,4	0,00001	6,0	0,00003	22,6
Oats	0,00		0,00000	0,6	0,00000	2,1	0,00000	2,1	0,00000	1,2	0,00000	1,4
Barley	0,00		0,00000	0,5	0,00000	0,0	0,00000	0,5	0,00000	1,2	0,00001	3,7
Maize	0,00		0,00000	0,3	0,00001	4,5	0,00000	2,5	0,00000	1,1	0,00000	0,5
Wheat	0,00		0,00001	4,0	0,00001	8,6	0,00001	8,8	0,00001	9,6	0,00001	7,3
Rye	0,00		0,00000	0,9	0,00001	4,2	0,00000	0,8	0,00000	1,3	0,00000	1,0
Poultry	0,00		0,00000	0,3	0,00000	0,4	0,00000	0,5	0,00000	0,5	0,00000	0,4
Meat fat	0,00		0,00000	0,0	0,00000	0,1	0,00000	0,1	0,00000	0,1	0,00000	0,1
Meat excl.poultry & offal	0,00		0,00000	0,3	0,00000	0,7	0,00000	0,6	0,00000	0,5	0,00000	0,4
All types of kidney	0,00		0,00000	0,3	0,00000	0,5	0,00000	0,8	0,00000	0,5	0,00000	0,3
All types of liver	0,00		0,00000	0,1	0,00000	0,3	0,00000	0,2	0,00000	0,1	0,00000	0,1
Eggs	0,00		0,00000	0,0	0,00000	0,1	0,00000	0,0	0,00000	0,0	0,00000	0,0

Milk	0,00		0,00000	2,6	0,00004	24,8	0,00002	14,7	0,00001	9,3	0,00001	6,0
Sugar Beet	0,01		0,00026	172,9	0,00056	370,7	0,00078	518,3	0,00064	425,7	0,00052	348,8
Refined sugar	0,01		0,00004	25,1	0,00004	25,1	0,00004	25,1	0,00004	25,1	0,00004	25,1

			11-14 year old child		**15-18 year old child**		**vegetarian**		**Elderly - own home**		**Elderly - residential**	
commodity	**HR**	**P**	**NESTI**	**%ARfD**	**NESTI**	**%ARfD**	**NESTI**	**%ARfD**	**NESTI**	**%ARfD**	**NESTI**	**%ARfD**
Potatoes	0,01		0,00023	155,8	0,00017	116,3	0,00018	119,4	0,00014	95,0	0,00016	103,9
Beetroot	0,01		0,00004	23,7	0,00003	16,8	0,00003	19,4	0,00003	19,1	0,00002	16,3
Carrots	0,01		0,00008	51,2	0,00006	42,2	0,00006	39,4	0,00005	35,6	0,00006	37,7
Celeriac	0,01		0,00001	4,8	0,00000	2,4	0,00005	34,2	0,00000	0,0	0,00000	0,0
Horseradish	0,01		0,00000	1,6	0,00000	0,5	0,00000	1,8	0,00000	1,8	0,00000	0,6
Jerusalem artichoke	0,01		0,00000	0,0	0,00000	0,0	0,00003	22,7	0,00000	0,0	0,00000	0,0
Parsnips	0,01		0,00011	70,6	0,00006	40,2	0,00008	56,3	0,00008	50,8	0,00005	31,2
Radishes	0,01		0,00000	3,2	0,00000	2,9	0,00001	4,9	0,00001	3,9	0,00000	1,0
Salsify	0,01		0,00000	0,0	0,00000	0,0	0,00006	42,8	0,00000	0,0	0,00000	0,0
Swedes	0,01		0,00011	71,2	0,00008	52,6	0,00007	48,9	0,00006	39,8	0,00005	35,6
Turnips	0,01		0,00011	70,1	0,00006	39,4	0,00004	27,2	0,00007	44,6	0,00005	33,1
Cress	0,03		0,00000	2,8	0,00000	2,7	0,00001	7,8	0,00001	5,0	0,00001	3,4
Lettuce	0,03		0,00026	172,2	0,00025	165,9	0,00034	227,1	0,00022	145,7	0,00012	81,5
Spinach	0,03		0,00048	316,9	0,00025	168,1	0,00056	370,1	0,00033	220,7	0,00022	145,8
Watercress	0,03		0,00001	8,3	0,00001	6,3	0,00003	22,2	0,00002	15,6	0,00000	0,7
Chicory	0,03		0,00000	0,0	0,00043	285,7	0,00007	43,4	0,00000	0,0	0,00000	0,0
Parsley	0,03		0,00001	6,0	0,00000	2,1	0,00004	24,8	0,00001	9,0	0,00001	8,7
Oats	0,00		0,00000	0,6	0,00000	1,0	0,00000	0,8	0,00000	0,5	0,00000	0,4
Barley	0,00		0,00000	0,3	0,00000	0,4	0,00000	0,5	0,00000	0,3	0,00000	0,2
Maize	0,00		0,00000	0,5	0,00000	0,7	0,00000	1,4	0,00000	0,3	0,00000	0,2
Wheat	0,00		0,00001	5,9	0,00001	5,6	0,00001	5,2	0,00000	3,1	0,00000	3,0
Rye	0,00		0,00000	0,5	0,00000	0,5	0,00000	1,1	0,00000	0,6	0,00000	0,2
Poultry	0,00		0,00000	0,3	0,00000	0,3	0,00000	0,6	0,00000	0,3	0,00000	0,1
Meat fat	0,00		0,00000	0,1	0,00000	0,1	0,00000	0,0	0,00000	0,0	0,00000	0,0
Meat excl.poultry & offal	0,00		0,00000	0,3	0,00000	0,3	0,00000	0,1	0,00000	0,2	0,00000	0,2

All types of kidney	0,00		0,00000	0,3	0,00000	0,4	0,00000	0,0	0,00000	0,3	0,00000	0,3
All types of liver	0,00		0,00000	0,1	0,00000	0,1	0,00000	0,0	0,00000	0,1	0,00000	0,1
Eggs	0,00		0,00000	0,0	0,00000	0,0	0,00000	0,0	0,00000	0,0	0,00000	0,0
Milk	0,00		0,00001	4,1	0,00001	3,5	0,00000	3,0	0,00000	2,2	0,00000	2,9
Sugar Beet	0,01		0,00039	260,4	0,00036	239,5	0,00021	139,0	0,00014	92,9	0,00019	126,0
Refined sugar	0,01		0,00004	25,1	0,00004	25,1	0,00004	25,1	0,00004	25,1	0,00004	25,1

Conclusion**:**
In the chronic dietary intake risk assessment, the intake of sugar beet root was not considered since it is assumed that only the processed sugar represents the main consumption data.
There is a chronic intake concern for the UK toddlers (101 % of the ADI).
Exceedances of the ARfD were observed for all the categories of UK consumers when consuming sugar beet roots and root vegetables (except for UK adults) and leafy vegetables grown as rotated crops.
There is no acute intake concern for refined sugar.

ANNEX B

Original version July 2004, revised in november 2008

Carbofuran

B.6 Toxicology and metabolism

Addendum May 2009

Introductory note

Following the expert meeting round 14 (PRAPeR 69, 04-08.2009), the proposed AOEL of 0.0003 mg/kg b.w./d was confirmed.
The level of skin absorption was also discussed, and the meeting agreed to adopt *a default* 10% rat *in-vivo* absorption rate instead of the proposed 6.19% measured in the *in-vivo* rat study after 24h, based on the uncertainty of a further absorption beyond this time-point (NL comment).
The rat/human absorption ratio of 2.08 , obtained in the *in-vitro* rat/human study remained unaltered.
Thus, a final absorption value of 10 ÷ 2.08 = 4.8%, rounded to 5% was adopted.

As a consequence, the operator exposure was recalculated, based on the revised skin absorption study.
(changed values are highlighted in green). The exposure calculations were only based upon the PHED-model, as the UK and German models were not considered appropriate for a granular application.

B.6.15 Exposure data (Annex IIIA 7.2)

B.6.15.1 Estimation of operator exposure (Annex IIIA 7.2.1.1)

Notifier (FMC) proposal:
Furadan 5G is a granular product containing 50-g/kg carbofuran and is to use in field crops of sugar beet and maize at the time of drilling. The product is applied using a tractor mounted granule applicator by placement in the open furrow directly behind each drill coulter. The product is applied using a maximum rate of 12 kg product per hectare, which is equivalent to 600 g active substance per hectare. A maximum work rate of 15 ha/day has been estimated for sugar beet and maize. The vapor pressure of technical carbofuran is $3.55x10^{-5}$ Pa at 20°C. Furadan 5 G is formulated to ensure that the end product is virtually dust-free.
Notifier proposed to apply a skin absorption value of 0.11%, and to propose the original AOEL = 0.001 mg/kg b.w./d.

RMS proposal:
A new estimation of exposure to granular formulation was performed using 10 ha/day as work rate according to the PHED model, with or without additional protection during loading and without additional protection during application.
As explained under B.6.10 and B.6.12, the AOEL was revised downwards to 0.0003 mg/kg b.w. i.o. 0.001 mg/kg b.w./d. In addition, the dermal absorption was 5% i.o. the notifier's proposal of 0.11%.

The POEM model for granules was devised by PSD after examining the American pesticides Handlers Exposure Database (PHED). The PHED is a compilation of actual field monitoring data on dermal and inhalation exposure drawn from field studies reflecting actual occupational situations. PSD looked at all of the available data in the PHED and selected data sets to determine appropriate surrogate values for the estimation of operator exposure resulting from loading and application of the granules.

The appropriate data are selected in terms of product type, method of application, and central tendency values are normally calculated for dermal and inhalation exposure. However, the PHED exposure calculation provides no information on the total levels of exposure experienced by the individuals involved in the monitoring studies.

Dermal and inhalation data from a large number of field studies are incorporated in this database and the appropriate data have been selected to estimate exposure for the relevant usage scenario. The 75th percentile exposure values from these data subsets have been used as conservative estimates of likely exposure from the proposed uses of granular formulations assuming that gloves are worn for all activities. Exposure at the 75th and 95th percentiles will therefore assume a relatively dusty formulation. In the case of Furadan 5G, which is virtually dust free, the exposure estimates are likely to be a worst case.

Applications parameters:

Table B.6.15.1-1: exposure to granular formulations: vehicle-mounted equipment

Variables:	
Work rate	10 ha/day
Application rate	0.6 kg a.s. /ha
Kg as. Loaded/day	6 kg
Dermal absorption	5%
Inhalation absorption	100%
Systemic AOEL as proposed by RMS	0.0003 mg/kg bw/d

Remark

In the PHED studies gloves and normal workwear were worn during loading .and application operations. Thus, this level of PPE is assumed in the PHED estimates.

(i) Expected operator exposure according to the PHED model:

In table B.6.15.1-2 (Annex A, estimates I, II and III), the estimated exposure of the operator handling and spreading Furadan 5G granules was tabulated. The values were calculated in the absence and in the presence of a half-mask with P2 filter possessing an assigned protection factor of 10×. The RPE was assumed during the tasks of loading and spreading of the product.

Table B.6.15.1-2: Estimated operator exposure for the use of Furadan 5G according to the PHED model

Application method	Dermal exposure (5 % dermal absorption)			Inhalation exposure (100% inhalation absorption)			Total exposure
	Load	Apply	Total	Load	Apply	Total	
without RPE	0.005249	0.001538	0.006787	0.124861	0.005996	0.130857	0,137644
with RPE §	0.005249	0.001538	0.006787	0.124861	0.005996	0.130857	0,019873

The calculations were based on 75th percentile surrogate values; values expressed in mg/person/day;
§: a half mask with a respiratory filter (EN 149, FFP2) conferring a protection of 90% is assumed with this RPE.

Predicted exposure (75th percentile values) as a proportion of the AOEL

A comparison of the systemic AOEL with the above estimates of operator exposure is presented in table B.6.15.1-3.
-The exposure of the operator (assuming a 70 kg body weight), wearing gloves both during the loading and the spreading, but in the absence of RPE amounted to 0.0001966 mg/kg b.w./d, corresponding with about 6.6× the AOEL.
-This exposure was reduced to about 0.0002839 mg/kg b.w./d, in the presence of RPE with 90% protection factor, equivalent to about 95% of the AOEL. It is thus considered that this exposure was safe under conditions of good agricultural practice, and the wearing of both PPE and RPE.

Table B.6.15.1-3: Exposure as a proportion of AOEL

Application method	Total systemic exposure		% of AOEL	
	without RPE	with RPE	without RPE	with RPE
Vehicle mounted equipment:	0.0001966	0.0002839	655%	95%

Values expressed in mg/kg b.w./d, assuming an operator weight of 70 kg; compared with AOEL = 0.0003 mg/kg bw/d

Assessment and conclusion:

The estimated exposure of the operator without RPE protection is about 7× the systemic AOEL according to the PHED model. Thus, additional protective measures are needed.
Taking into account the toxicological properties of the plant protection product Furadan 5G, reflected by the corresponding classification and labeling, personal protective equipment must be used.
Using adequate repiratory protection reduces the operator exposure to 95% of AOEL according to the PHED.

In conclusion, the operator exposure assessment shows that exposure to Furadan 5G is acceptable according to the PHED model, when both gloves and respiratory protection is used during the loading

and the spreading of the granules. Moreover, it is worthwile to stress that the application should be restricted to a granular application only.

B.6.15.2 Measurement of operator exposure (Annex IIIA 7.2.1.2)

No information available. Based on exposure modeling, these should not be required.

B.6.15.3 Estimation of bystander exposure (Annex IIIA 7.2.2)

According to the explanation of the applicant, carbofuran is not volatile, the granular formulation is applied by ground-directed equipment that is nearly dust free, the level of bystander exposure to vapor or airborne particles at the time of application is likely to be negligible. The movement of carbofuran from the point of application is likely to be further mitigated by the sub-surface application of these products. Dermal exposure is therefore not expected. The use of Furadan 5G should not pose a risk to bystanders.

B.6.15.4 Estimation of worker exposure (Annex IIIA 7.2.3.1)

Furadan 5G is incorporated by mechanical means into the soil when sowing. Therefore, worker exposure to carbofuran is unlikely to occur.

B.6.15.5 Measurement of worker exposure (Annex IIIA 7.2.3.2)

Not required.

ANNEX B

FURADAN 5G

Appendix A: Estimations of the exposure

PHED MODEL:

-ESTIMATE I: FURADAN 5G: GLOVES WHEN HANDLING THE PRODUCT AND DURING APPLICATION

-ESTIMATE II: FURADAN 5G: GLOVES AND RPE (EN 149, FFP2) WHEN HANDLING THE PRODUCT DURING LOADING BUT NOT DURING APPLICATION

-ESTIMATE III: Furadan 5G: Gloves and RPE (EN 149, FFP2) when handling the product during loading and during application.

ESTIMATE I: FURADAN 5G: GLOVES WHEN HANDLING THE PRODUCT AND DURING APPLICATION

EXPOSURE TO GRANULAR FORMULATIONS: VEHICLE-MOUNTED EQUIPMENT					
VARIABLES					
Work rate	10	ha/day	**RPE**		
Application rate	0,6	kg a.s./ha	**Loading**	no	
Dermal absorption	5	%	**Application**	no	
Inhalation absorption	100	%			1
Systemic AOEL	0,0003	mg/kg bw/day			1

	75th PERCENTILES		95th PERCENTILES	
LOADER				
Dermal exposure				
PHED surrogate - hands ADE	0,001414707	mg/kg a.s.	0,006876188	mg/kg a.s.
PHED surrogate - body ADE	0,016083379	mg/kg a.s.	0,038017233	mg/kg a.s.
kg a.s. loaded	6	kg a.s./day	6	kg a.s./day
dermal exposure	0,104988516	mg a.s./day	0,269360526	mg a.s./day
absorbed dose	0,005249426	5%	0,013468026	5%
	7,49918E-05	mg a.s./kg bw/d	0,0001924	mg a.s./kg bw/d
Inhalation exposure				
PHED surrogate	0,020810185	mg/kg a.s.	0,045293628	mg/kg a.s.
kg a.s. loaded	6	kg a.s./day	6	kg a.s./day
inhalation exposure	0,12486111	mg a.s./day	0,271761768	mg a.s./day
absorbed dose	0,12486111	100%	0,271761768	100%
	0,00178373	mg a.s./kg bw/d	0,003882311	mg a.s./kg bw/d
APPLICATOR				

Dermal exposure				
PHED surrogate - hands ADE	0,000346426	mg/kg a.s.	0,000959819	mg/kg a.s.
PHED surrogate - body ADE	0,004781305	mg/kg a.s.	0,015843348	mg/kg a.s.
kg a.s. applied	6	kg a.s./day	6	kg a.s./day
dermal exposure	0,030766386	mg a.s./day	0,100819002	mg a.s./day
absorbed dose	0,001538319	5%	0,00504095	5%
	2,1976E-05	mg a.s./kg bw/d	7,20136E-05	mg a.s./kg bw/d
Inhalation exposure				
PHED surrogate	0,000999325	mg/kg a.s.	0,004377544	mg/kg a.s.
kg a.s. applied	6	kg a.s./day	6	kg a.s./day
inhalation exposure	0,00599595	mg a.s./day	0,026265264	mg a.s./day
absorbed dose	0,00599595	100%	0,026265264	100%
	8,56564E-05	mg a.s./kg bw/d	0,000375218	mg a.s./kg bw/d
TOTAL SYSTEMIC	0,00196635	mg/kg bw/d	0,00452194	mg/kg bw/d
EXPOSURE AS % OF AOEL	655,45	%	1507,31	%

PPE: In the PHED studies gloves and normal workwear were worn during loading and application operations. This level of PPE is assumed in the above estimate.

ESTIMATE II: FURADAN 5G: GLOVES AND RPE (EN 149, FFP2) WHEN HANDLING THE PRODUCT DURING LOADING BUT NOT DURING APPLICATION.

EXPOSURE TO GRANULAR FORMULATIONS: VEHICLE-MOUNTED EQUIPMENT				
VARIABLES				
Work rate	10	ha/day	**RPE**	
Application rate	0,6	kg a.s./ha	**Loading**	yes
Dermal absorption	5	%	**Application**	no
Inhalation absorption	100	%		0,1
Systemic AOEL	0,0003	mg/kg bw/day		1

	75th PERCENTILES		**95th PERCENTILES**	
LOADER				
Dermal exposure				
PHED surrogate - hands ADE	0,001414707	mg/kg a.s.	0,006876188	mg/kg a.s.
PHED surrogate - body ADE	0,016083379	mg/kg a.s.	0,038017233	mg/kg a.s.
kg a.s. loaded	6	kg a.s./day	6	kg a.s./day
dermal exposure	0,104988516	mg a.s./day	0,269360526	mg a.s./day
absorbed dose	0,005249426	5%	0,013468026	5%
	7,49918E-05	mg a.s./kg bw/d	0,0001924	mg a.s./kg bw/d
Inhalation exposure				
PHED surrogate	0,020810185	mg/kg a.s.	0,045293628	mg/kg a.s.
kg a.s. loaded	6	kg a.s./day	6	kg a.s./day
inhalation exposure	0,012486111	mg a.s./day	0,027176177	mg a.s./day
absorbed dose	0,012486111	100%	0,027176177	100%
	0,000178373	mg a.s./kg bw/d	0,000388231	mg a.s./kg bw/d
APPLICATOR				

Dermal exposure				
PHED surrogate - hands ADE	0,000346426	mg/kg a.s.	0,000959819	mg/kg a.s.
PHED surrogate - body ADE	0,004781305	mg/kg a.s.	0,015843348	mg/kg a.s.
kg a.s. applied	6	kg a.s./day	6	kg a.s./day
dermal exposure	0,030766386	mg a.s./day	0,100819002	mg a.s./day
absorbed dose	0,001538319	5%	0,00504095	5%
	2,1976E-05	mg a.s./kg bw/d	7,20136E-05	mg a.s./kg bw/d
Inhalation exposure				
PHED surrogate	0,000999325	mg/kg a.s.	0,004377544	mg/kg a.s.
kg a.s. applied	6	kg a.s./day	6	kg a.s./day
inhalation exposure	0,00599595	mg a.s./day	0,026265264	mg a.s./day
absorbed dose	0,00599595	100%	0,026265264	100%
	8,56564E-05	mg a.s./kg bw/d	0,000375218	mg a.s./kg bw/d
TOTAL SYSTEMIC	0,00036100	mg/kg bw/d	0,00102786	mg/kg bw/d
EXPOSURE AS % OF AOEL	120,33	%	342,62	%

PPE: In the PHED studies gloves and normal workwear were worn during loading and application operations. This level of PPE is assumed in the above estimate.

ESTIMATE III: FURADAN 5G: GLOVES AND RPE (EN 149, FFP2) WHEN HANDLING THE PRODUCT DURING LOADING AND DURING APPLICATION.

EXPOSURE TO GRANULAR FORMULATIONS: VEHICLE-MOUNTED EQUIPMENT				
VARIABLES				
Work rate	10	ha/day	**RPE**	
Application rate	0,6	kg a.s./ha	**Loading**	yes
Dermal absorption	5	%	**Application**	yes
Inhalation absorption	100	%		0,1
Systemic AOEL	0,0003	mg/kg bw/day		0,1

	75th PERCENTILES		95th PERCENTILES	
LOADER				
Dermal exposure				
PHED surrogate - hands ADE	0,001414707	mg/kg a.s.	0,006876188	mg/kg a.s.
PHED surrogate - body ADE	0,016083379	mg/kg a.s.	0,038017233	mg/kg a.s.
kg a.s. loaded	6	kg a.s./day	6	kg a.s./day
dermal exposure	0,104988516	mg a.s./day	0,269360526	mg a.s./day
absorbed dose	0,005249426	5%	0,013468026	5%
	7,49918E-05	mg a.s./kg bw/d	0,0001924	mg a.s./kg bw/d
Inhalation exposure				
PHED surrogate	0,020810185	mg/kg a.s.	0,045293628	mg/kg a.s.
kg a.s. loaded	6	kg a.s./day	6	kg a.s./day
inhalation exposure	0,012486111	mg a.s./day	0,027176177	mg a.s./day
absorbed dose	0,012486111	100%	0,027176177	100%
	0,000178373	mg a.s./kg bw/d	0,000388231	mg a.s./kg bw/d
APPLICATOR				

Dermal exposure				
PHED surrogate - hands ADE	0,000346426	mg/kg a.s.	0,000959819	mg/kg a.s.
PHED surrogate - body ADE	0,004781305	mg/kg a.s.	0,015843348	mg/kg a.s.
kg a.s. applied	6	kg a.s./day	6	kg a.s./day
dermal exposure	0,030766386	mg a.s./day	0,100819002	mg a.s./day
absorbed dose	0,001538319	5%	0,00504095	5%
	2,1976E-05	mg a.s./kg bw/d	7,20136E-05	mg a.s./kg bw/d
Inhalation exposure				
PHED surrogate	0,000999325	mg/kg a.s.	0,004377544	mg/kg a.s.
kg a.s. applied	6	kg a.s./day	6	kg a.s./day
inhalation exposure	0,000599595	mg a.s./day	0,002626526	mg a.s./day
absorbed dose	0,000599595	100%	0,002626526	100%
	8,56564E-06	mg a.s./kg bw/d	3,75218E-05	mg a.s./kg bw/d
TOTAL SYSTEMIC	0,00028391	mg/kg bw/d	0,00069017	mg/kg bw/d
EXPOSURE AS % OF AOEL	94,64	%	230,06	%

PPE: In the PHED studies gloves and normal workwear were worn during loading and application operations. This level of PPE is assumed in the above estimate.

Appendix B: PHED model

GRANULE RECORDS FROM PHED AND DERIVED SURROGATE EXPOSURE VALUES

TRACTOR-MOUNTED/DRAWN EQUIPMENT: LOADER RECORDS

Record number	Data points	kg a.s. handled/applied			% a.s. in form'n	PPE	Engineering control	Acceptability
		Min.	**Max.**	**Mean**				
0422	2	90.72	90.72	90.72	15	gloves	none	yes
0425	3	10.21	12.25	10.89	10	gloves	none	yes
0427	1	2.84	2.84	2.84	10	gloves	none	yes
0448	8	182.35	444.53	287.70	10	gloves	none	yes
1003	22	314.69	935.55	744.95	15	gloves	none	yes
1004	15	3.13	5.44	4.42	5	gloves and coveralls	none	yes
1011	30	9.07	26.04	14.07	5	gloves	none	yes
1027	15	0.66	1.20	0.87	undisclosed	gloves	none	no

75th percentile actual dermal exposure (less hands): 0.016 mg/kg a.s. handled/person/day

95th percentile actual dermal exposure (less hands): 0.038 mg/kg a.s. handled/person/day

75th percentile actual hand exposure: 0.0014 mg/kg a.s. handled/person/day

95th percentile actual hand exposure: 0.0069 mg/kg a.s. handled/person/day

75th percentile inhalation exposure: 0.021 mg/kg a.s. handled/person/day

95th percentile inhalation exposure: 0.045 mg/kg a.s. handled/person/day

TRACTOR-MOUNTED/DRAWN EQUIPMENT: APPLICATOR RECORDS

Record number	Data points	Kg a.s. handled/applied			% a.s. in form'n	PPE	Engineering control	Acceptability
		Min.	Max.	Mean				
0422	2	10.61	12.25	11.43	15	gloves	cab (closed windows)	yes
0425	3	10.21	12.25	10.89	10	gloves	cab (closed windows)	yes
0427	1	2.84	2.84	2.84	10	gloves	no cab	yes
1004	15	3.13	5.44	4.42	5	gloves and coveralls (12) gloves (3)	filtered cab	yes
1011	29	8.39	22.68	12.90	5	gloves	filtered cab (25) no cab (4)	yes

75th percentile actual dermal exposure (less hands): 0.0048 mg/kg a.s. handled/person/day

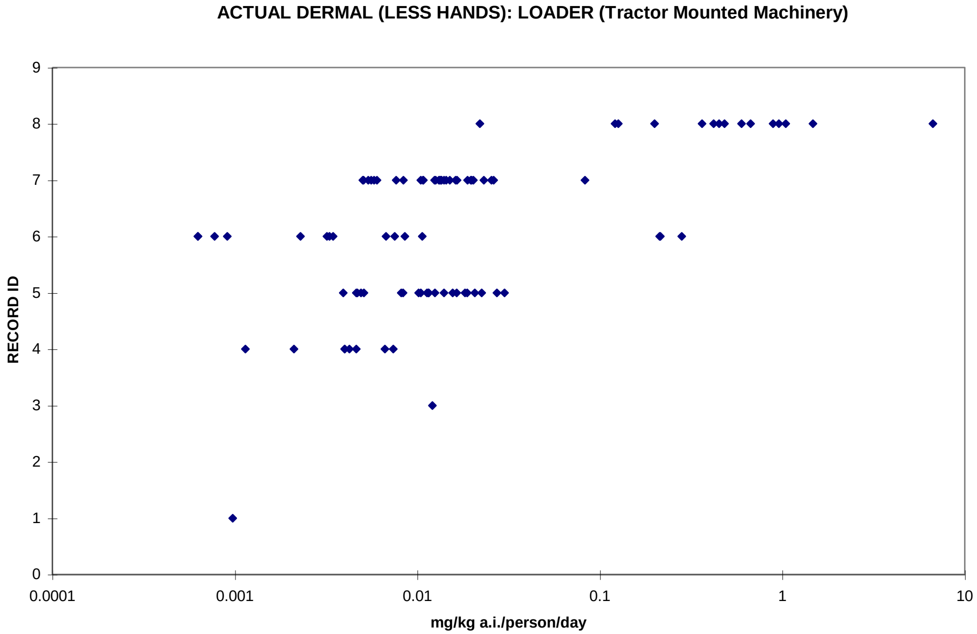
95th percentile actual dermal exposure (less hands): 0.016 mg/kg a.s. handled/person/day

75th percentile actual hand exposure: 0.00035 mg/kg a.s. handled/person/day

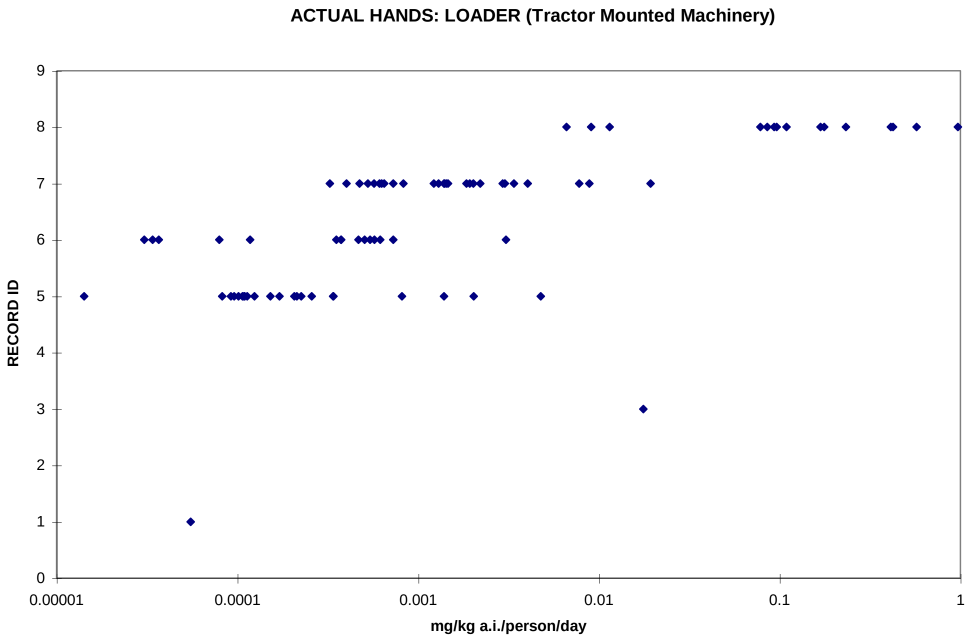
95th percentile actual hand exposure: 0.00096 mg/kg a.s. handled/person/day

75th percentile inhalation exposure: 0.0010 mg/kg a.s. handled/person/day

95th percentile inhalation exposure: 0.0044 mg/kg a.s. handled/person/day

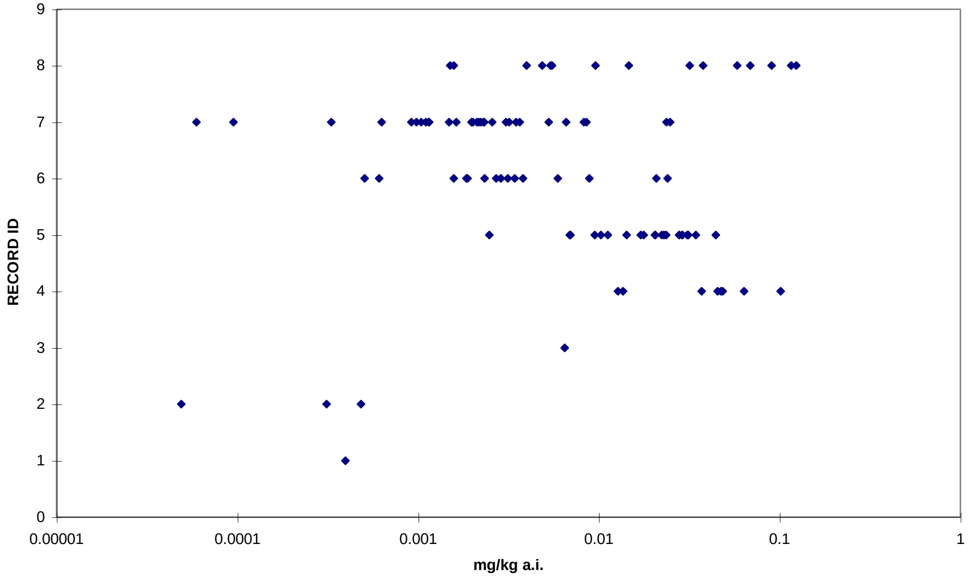


Record ID	1	2	3	4	5	6	7	8
Study Ref.	0422	0425	0427	0448	1003	1004	1011	1027

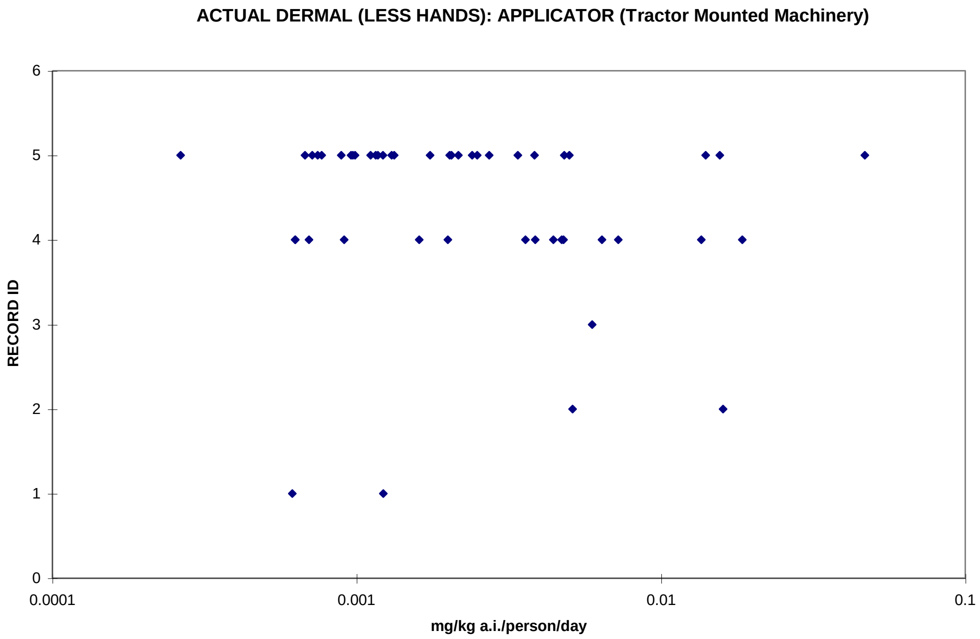


Record ID	1	2	3	4	5	6	7	8
Study Ref.	0422	0425	0427	0448	1003	1004	1011	1027

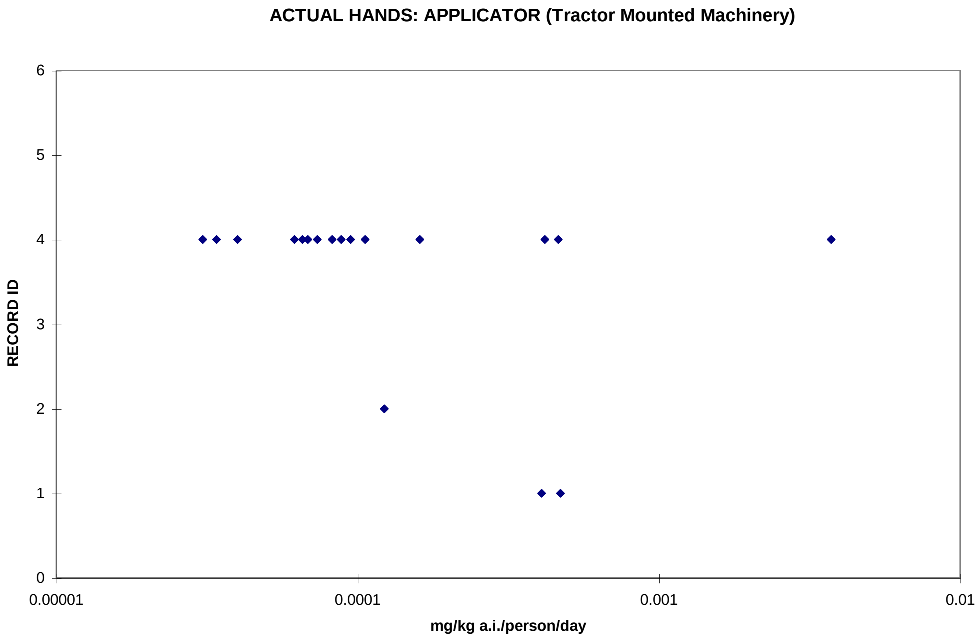
INHALATION: LOADER (Tractor Mounted Machinery)



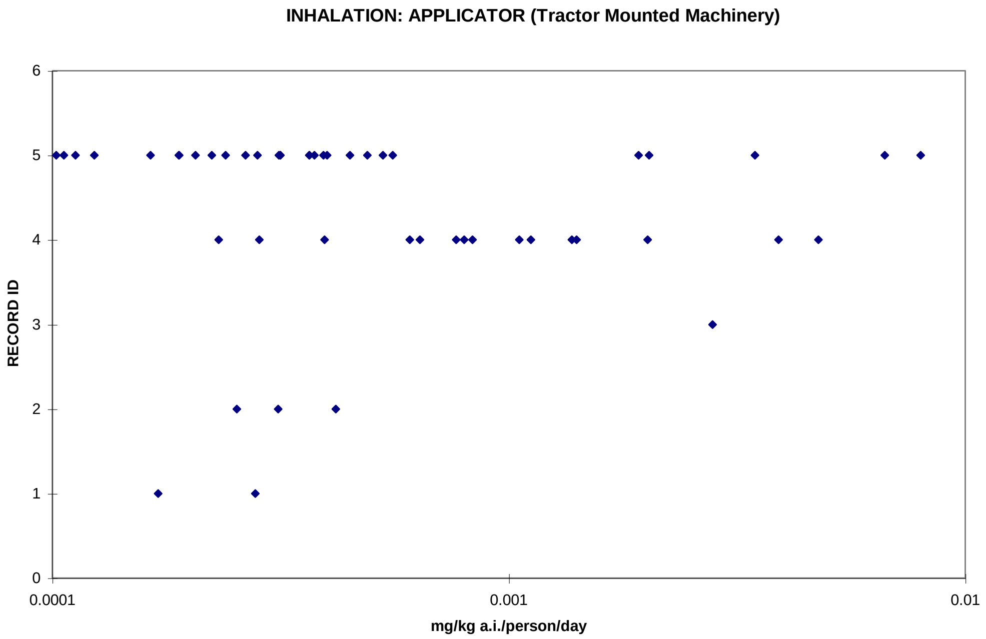
Record ID	1	2	3	4	5	6	7	8
Study Ref.	0422	0425	0427	0448	1003	1004	1011	1027



Record ID	1	2	3	4	5
Study Ref.	0422	0425	0427	1004	1011



Record ID	1	2	3	4	5
Study Ref.	0422	0425	0427	1004	1011



Record ID	1	2	3	4	5
Study Ref.	0422	0425	0427	1004	1011

ANNEX B

Addendum April 2009
Update May 2009 (after PRAPeR 68)

Carbofuran

B.9 Ecotoxicology

B.9.1 Effects on birds (Annex IIA 8.1; Annex IIIA 10.1)

Comments 5(19) and 5(28) in the reporting table:

The risk for birds drinking water possibly contaminated with carbofuran is assessed by the puddle scenario.

$$PEC_{puddle} = \frac{AR / 10}{1000\ (w + Koc\ x\ s)}$$

with :
AR = application rate in g/ha; divisor of 10 to achieve rate in mg/m²
w = 0.02 (pore water term: volume)
s = 0.0015 (soil term: volume, density, organic carbon content)

The application rate for carbofuran is 0.600 kg a.s./ha. The Kfoc value for carbofuran is 23.3 mL/g.

$$PEC_{puddle} = \frac{600\ / 10}{1000\ (0.02 + 23.3\ x\ 0.0015)} = 1.09 \text{ mg a.s./L}$$

A small granivorous bird (passerines) has a drinking water rate DRW equivalent to 0.46 L/kg b.w./day.
The estimated theoretical exposure to carbofuran via drinking water is calculated as :

ETE = DRW x PEC_{puddle} = 0.46 L/kg b.w./day x 1.09 mg a.s./L = 0.50 mg a.s./kg b.w./day

The acute risk is calculated as :

TER = LD_{50} / ETE = 0.71 / 0.50 = 1.41

The acute TER is below the trigger value of 10.

However, the RMS is of the opinion that this calculation is unrealistic worst-case (birds consuming their entire drinking water demand on possibly contaminated puddles).

B.9.2 Effects on aquatic organisms (fish, aquatic invertebrates, algae) (Annex IIA 8.2; Annex IIIA 10.2)

Comment 5(52) in the reporting table:

B.9.2.15 Summary of effects to aquatic organisms (Annex IIA 8.2; Annex IIIA 10.2)

Table B. 9.2.15-1 : Summary of effects of carbofuran to aquatic organisms (FMC)

Test species	Test substance	Test system	Endpoints	References
Chironomus riparius	carbofuran	28 d static	**NOEC = 0.0032 mg a.s./L** (mean measured)	Putt E., 2008

Table B. 9.2.15-2 : Summary of effects of metabolites of carbofuran to aquatic organisms (Dianica)

Test species	Test substance	Test system	Endpoints	References
Chironomus riparius	7-phenol	25 d static	**NOEC = 5.34 mg a.s./L** (mean measured)	Memmert U., 2002

B.9.2.16 Exposure and risk assessment for aquatic organisms (Annex IIIA 10.2)

B.9.2.16.1 Risk assessment for the active substance

Table B.9.2.16.1-1 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to carbofuran in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 1 calculations

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
carbofuran	*Chironomus riparius*	0.0032	chronic	193.97	-	0.02	10

Table B.9.2.16.1-2 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to carbofuran in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 2 calculations

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	TER	Annex VI Trigger
cabofuran	N	*Chironomus riparius*	0.0032	chonic	31.26	0.10	10
	S				62.51	0.05	10

B.9.2.16.2 Risk assessment for the metabolites

Table B.9.2.16.2-4 : Toxicity Exposure Ratio’s (TER’s) for aquatic organisms exposed to 7-phenol in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 1 calculations

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
7-phenol	*Chironomus riparius*	5.34	chronic	64.43	-	83	10

In conclusion, the risk of carbofuran and the metabolite 7-phenol to sediment dwelling organisms is acceptable based on FOCUS step 3, respectively FOCUS step 1 PECsw calculations.

B.9.3 Effects on other terrestrial vertebrates (Annex IIIA 10.3)

Comment 5(47) in the reporting table:

The risk for mammals drinking water possibly contaminated with carbofuran is assessed by the puddle scenario.

$$PEC_{puddle} = \frac{AR / 10}{1000\ (w + Koc\ x\ s)}$$

with :
AR = application rate in g/ha; divisor of 10 to achieve rate in mg/m²
w = 0.02 (pore water term: volume)
s = 0.0015 (soil term: volume, density, organic carbon content)

The application rate for carbofuran is 0.600 kg a.s./ha. The Kfoc value for carbofuran is 23.3 mL/g.

$$PEC_{puddle} = \frac{600\ / 10}{1000\ (0.02 + 23.3\ x\ 0.0015)} = 1.09 \text{ mg a.s./L}$$

A small granivorous mammal (non-desert species) has a drinking water rate DRW equivalent to 0.24 L/kg b.w./day.
The estimated theoretical exposure to carbofuran via drinking water is calculated as :

ETE = DRW x PEC_{puddle} = 0.24 L/kg b.w./day x 1.09 mg a.s./L = 0.26 mg a.s./kg b.w./day

The acute risk is calculated as :

TER = LD_{50} / ETE = 5.3 / 0.26 = 20

The acute TER is above the trigger value of 10, indicating that the risk is low.

In the discussion table of PRAPeR 68, open point 5.12, a concern was raised on the determination of the relevant long-term endpoint for mammals.

In agreement with the mam tox experts, the RMS has following opinion on the ecotoxicologically relevant NOAEL :

"For human health risk assessment, all reference doses were established on the toxicologically relevant decrease of AChE levels in the brain. This was a conservative approach, as at the LOAEL for a 20% AChE decrease, overt cholinergic clinical signs were not observed.

In the recent acute neurotoxicity studies in rat, it appeared that after gavage administration of Carbofuran, tremors appeared at 0.3 mg/kg b.w. in PND11 pups (Tyl, 2005a, c; Hoberman, 2007a). In adults, the clinical signs appeared slightly later (at 12h post-treatment Tyl, 2005c) at 0.3 mg/kg b.w. and above. 53% decreases of motor activity were observed at 0.3-0.5 mg/kg b.w., and more severe cholinergic signs increasing in a dose-dependent way appeared at 0.75 mg/kg b.w. and above (Mc Daniel et al, 2007).
Further support for this dose was found in the short-term studies; in a 1 year dog capsule feeding study (Spicer, 1990) clinical signs appeared at 1 mg/kg b.w./d, and a NOAEL at 0.1 mg/kg b.w./d. In a 1 year dietary dog study, testicular degeneration was observed at 0.5 mg/kg b.w./d, with a NOAEL of 0.25 mg/kg b.w./d. Finally, in a rat developmental study (gavage), clinical signs were observed at 0.3 mg/kg b.w./d, with a NOAEL of 0.1 mg/kg b.w./d (Roa, 1978). In a more recent 60d gavage study, tremor, hypoactivity and salivation occurred at 0.8 mg/kg b.w./d, with a NOAEL of 0.2 mg/kg b.w./d.
Finally, in the rabbit developmental studies, increased mortality and clinical signs were obvious at 2 mg/kg b.w./d, with a NOAEL of 0.5-0.6 mg/kg b.w./d. Although these effects were not always replicated in similar studies, the findings were not ignored.
The most relevant reprotoxicity NOAEL was established at 1.2 mg/kg b.w./d, for severe effects (decreased pup survival) at 2.9 mg/kg b.w./d (Goldenthal, 1979).

Generally speaking, the appearance of clinical signs are considered relevant in the risk assessment of mammals from the ecotoxicological point of view. Especially for NMC's, it is felt that the impact of these signs should not be neglected, also knowing that pups are more sensitive and the onset may be earlier, when compared with adults. A relevant NOAEL of 0.1 mg/kg b.w. may be a point of departure, knowing that the effects increase in severity in the dose-range of 0.3-1 mg/kg b.w..
In the pragmatic approach of taking an 'average' NOAEL of 0.71 mg/kg b.w., it would appear that the margin of safety (MOS) to the doses where overt clinical signs (and mortality in rabbits) appear, is quite small.

As a conclusion, the conservative adoption of a NOAEL of 0.1 mg/kg b.w., based upon clinical signs and neurotoxicity, at doses showing significant drops of 30-60% of brain AChE activity, may be defendable. This leaves a MOS of about 30x to the doses where severe pup toxicity was observed in a multigeneration study."

During the Peer Review of Carbofuran the notifier submitted following statement in April 2009.

Updated and Comparative Risk Assessment of the carbofuran use on sugar beet at 60 g ai/ha versus 600 g ai/ha. (2009).

INTRODUCTION :

FMC re-applied for Annex I inclusion of the active ingredient carbofuran under the rules laid down in Regulation 33/2008/EC – Chapter 3 (accelerated procedure). Article 15(1b) of this Regulation states that:

> "*The supported uses are the same as those that were the subject of the non-inclusion Decision. They may only be changed insofar as this is necessary, in the light of the reasons which gave rise to the non-inclusion Decision, to permit inclusion of that substance in Annex I to Directive 91/414/EEC*".

Whilst we still support the use of carbofuran on sugar beet at 600 g ai/ha[1] – and welcome the efforts to evaluate the risk assessment at this dose rate - we also appreciate that interpretation of endpoints and acceptability of refinement route may differ from the notifier to the evaluator's view. Therefore, we introduced additional risk assessments at lower dose rates, in particular at 60 g ai/ha, in order to increase the chances to identify a safe use scenario.

The RA conducted by the RMS shows that while the risk to granular intake at 600 g ai/ha is acceptable according to the EPPO scheme, the risk to secondary poisoning via ingestion of treated seedlings, earthworms and/or arthropods needs further refinement. Furthermore, the evaluation table highlights that field study conducted on non target arthropods and soil macro-organisms may only cover use of carbofuran up to 375 g ai/ha. This suggests that a lower application rate should be considered for the risk assessments, as wisely foreseen by Article 15b of the Regulation.

Should the EC decide that registration of carbofuran is possible only with limitation on its maximum applied dose rate, this issue would be dealt by FMC at national level. Indeed, we are confident that certain technologies are efficient at dose rate equal or lower to 60 g carbofuran/ha.

The aim of the present document is to compare the critical outcome of the risk assessment for application of 60 g carbofuran/ha versus 600 g carbofuran/ha. It will shortly investigate Operator exposure, consumer exposure, PEC calculation, Risk to non target organisms and eventually focus on the risk to birds and mammals via secondary poisoning.

[1] At planting – in furrow – granule buried at 7 cm from the surface.

Risk to birds and mammals :

Granule intake

The RA conducted by the RMS shows that the risk to granular intake at 600 g ai/ha is acceptable according to the EPPO scheme. A similar conclusion can be drawn from the Probabilistic Risk assessment submitted by FMC (Bastiansen F. and Wang M., 2008). Reducing the dose rate to 60 g ai/ha can only further increase the confidence that the risk to birds via granule intake is acceptable.

Secondary poisoning risk assessment for birds and mammals

Residue of carbofuran in seedlings

Several residue trials and metabolism studies are evaluated in the carbofuran DAR in order to investigate the residue in seedling. The most valuable information comes from the decline curve residue trails (Waalkens and Baltussen, 2005 - France N&S), but its results must be corrected with a conversion factor in order to translate the measured carbofuran residue in carbofuran + 3-OH-carbofuran residue. Taking into consideration the evaluation of benfuracarb and the seedling metabolism studies provided in the carbofuran DAR, a conversion factor of 2.5 should be applied to short term and long term residue.

Indeed, the sugar beet seedling metabolism (Mamouni A., 2006b) provides the following residue values in cotyledons, as documented under table B7.1.4-3 in carbofuran DAR:

Day	**Carbofuran (mg/kg)**	**3-OH-Carbofuran (mg/kg)**	**Total (mg/kg)**	**Ratio**
3 (acute)	43.825	11.62	55.445	**1.27**
7 (short term)	16.516	9.571	26.087	**1.58**
14	7.534	8.958	16.492	2.19
28	0.313	5.153	5.466	17.46
TWA 3-28 days (long term)	14.45		29.32	**2.03**

This demonstrates that a conversion factor of 2.5 is protective to correcting the residue 7 days (short term) and TWA (long term). For the acute risk, residue after 3 days remains mainly carbofuran. No correction factor needs therefore to be applied to the residue value at that time point.

We propose to use the following residue endpoints for a risk assessment at 600 g ai/ha, on the basis of the residue trial results documented in table B.9.1.8-5 in the DAR.
Acute toxicity: use 10.4 mg/kg. At this time point, no significant 3-OH-carbofuran metabolisation has started.
Short term toxicity: use 6.6 x 2.5 = **16.5 mg/kg** (carbofuran + 3-OH-carbofuran)
Long term toxicity: use TWA of 2.4 x 2.5 = **6 mg/kg** (carbofuran + 3-OH-carbofuran).

Residue values will be 10 times lower when conducting the risk assessment at 60 g ai/ha. Indeed, the validity of applying the RUD rule is confirmed by some trials undertaken by Zietz (2008) where residue in seedling of carbofuran + 3-OH-carbofuran was compared after application of 600 g ai/ha and 60 g ai/ha in the same climatic and soil condition. The results show a response linear with the dose rate. Results of the trails by Zietz (2008) are documented in table B9.1.8-2, which is copied here after for easier reference.

Carbofuran and 3-OH-carbofuran in sugar beet seedlings – trials performed in Southern France and Italy

Trial No.	**Specimen material**	**Appl. Rate kg a.s./ha**	**Row interval (m)**	**g a.s./m row**	**Timing (BBCH)**	**DALA**	**Carbofuran (mg kg^{-1})**	**3-hydroxy carbofuran (mg kg^{-1})**	**Ratio (3OH + a.s.)/a.s.**	**Carbofuran + 3OH carbofuran**
07-SF-013	Fodder beet seedling	Control	0.65	-	12	20	< 0.005 nd	< 0.005 nd	-	-
07-SF-013		600	0.65	0.039	12	20	0.022	0.083	4.5	0.099
07-SF-014	Fodder beet seedling	Control	0.5	-	12	24	< 0.005 nd	< 0.005 nd	-	-
07-SF-014		600	0.5	0.030	12	24	< 0.005	0.033	7.1	0.036
07-IT-019	Fodder beet seedling	Control	0.6	-	11 – 12	36	< 0.005 nd	< 0.005 nd	-	-
07-IT-019		**600**	0.6	0.036	11 – 12	36	1.1	3.4	3.9	**4.271**
07-IT-019		**60**	0.6	0.0036	11 – 12	36	0.066	0.29	5.1	**0.336**
07-IT-020	Sugar beet seedling	Control	0.6	-	11 – 12	36	< 0.005 nd	< 0.005 nd	-	-
07-IT-020		**600**	0.6	0.036	11 – 12	36	0.20	2.4	12.2	**2.438**
07-IT-020		**60**	0.6	0.0036	11 – 12	36	< 0.005	0.13	25.2	**0.126**
								Mean	9.67	
								Median	6.10	

DALA = days after last treatment
< 0.005 nd = no peak was detected

The results from trials 07-IT-019 and 07-IT-020 (highlighted in bold) confirm that – in the same conditions - the expected residue at 60 g carbofuran/ha is 10 times lower than at 600 g ai/ha.

Therefore, the proposed Residue values (normalized from the measured residue obtained from Waalkens and Baltussen, 2005) and corrected for 3-OH-carbofuran content will be

Seedlings residue to be used in the birds and mammals Risk assessment

App rate [g as/ha]	Acute [DAT 1]	Short-term [DAT 5]	Long-term [twa]
600	10.4	16.5	6
60	1.04	1.65	0.6

Residue of carbofuran in earthworms and insects

Residue in earthworms and beetles should only consider carbofuran. Indeed, 3-OH-carbofuran is a minor metabolite in soil (<5%: see B.8.1.1.1 of original DAR) and will therefore not contaminate insect and soil dwelling arthropods in any significant concentrations. This is confirmed in the DAR of benfuracarb were the notifier Otsuka analysed both carbofuran and 3-OH-carbofuran in earthworm. These data confirm the modest contribution of 3-OH-carbofuran to the carbofuran residue.

Proposed Residue values are derived by normalizing measured residue obtained from Brown et al (2007) at an app rate of 375 g as/ha. The RUD rules apply well to these values since residue in earthworms and arthropods is driven by the PEC soil, which is a linear function of the applied dose rate.

Earthworm residue to be used in the birds and mammals Risk assessment

App rate [g as/ha]	Acute [DAT 1]	Short-term [DAT 5]	Long-term [twa]
600	0.128	0.224	0.128
60	0.0128	0.0224	0.0128

Arthropods residue to be used in the birds and mammals Risk assessment

App rate [g as/ha]	Acute [DAT 1]	Short-term [DAT 5]	Long-term [twa]
600	5.84	0.512	2
60	0.584	0.05	0.2

Birds and mammals TER summaries

The TERs were re-calculated on the focal species using the FIR and PD values determined by RMS in the DAR. The residue values as described here above were entered to assess the acute, short term and long term risk of birds and mammals at 60 and 600 g ai/ha, in order to offer a revised deterministic evaluation of the secondary poisoning.

Birds and mammals Risk assessment – summary table

Species	App rate [g as/ha]		App rate [g as/ha]		App rate [g as/ha]	
	600	60	600	60	600	60
	TERacute		TERst		TERlt	
Woodpigeon	0.33	3.3	0.5	4.68	0.5	5.15
Yellow wagtail	0.2	2	5	51	0.53	5
Blackbird	5	51	7	66	5	46
Skylark	0.13	1.25	0.2	2.1	0.2	2.1
Hare	4.9	49	nd	nd	1.1	11.4
Shrew	2.9	28.8	nd	nd	1.0	9.7

These TER values show that reducing the dose rate to 60 g ai/ha allows finding an acceptable risk to mammals and significantly improves the risk assessment to birds. Some TER values for birds still range from 1.25 to 4.68, but they could be further refined if taking into account:

- The use of a PT value on top of a PD value;

- Consideration of the reversibility of the AChE inhibition and rapid metabolisation/excretion of carbofuran;
- Or any other refinement step the evaluator judges appropriate in order to reflect the risk to birds and mammals in a more realistic manner.

Detailed birds and mammals TER calculation are provided in the document of the notifier.

Conclusion of the RMS :
The RMS maintains its position that the proposal of the notifier for an additional risk assessment at a reduced granular dose rate of 60 g a.s./ha, corresponding to the doses used for seed treatment is not acceptable. It is indeed very questionable whether such use can be considered as a representative use :

- it is not representative for the use of a granular formulation as the dosage of 60 g carbofuran/ha is much lower than the authorized dosages. The GAPs for granule formulations that were authorized in 2002 in EU MS consisted in applications at sowing or transplant time, with incorporation in the furrow at maximum rate of 600-750 g a.s./ha. (Broadcast applications were performed at even higher dosages)
- it is not representative for the use of a seed treatment formulation at similar rates of 60 g a.s./ha because the exposure routes and risk assessments are not equivalent; for example, it is obvious that the exposures of the consumer, of the operator, of the birds and mammals will be significantly different if we compare a granular application to a seed treatment
- the resubmitted dossier does not contain trials performed at 60 g a.s./ha in order to determine the residue levels in bird and mammal feed items (sugar beet seedlings, earthworms, arthropods).

The RMS concluded on the granule intake by birds, in addition to the notifiers statement :
The first tier risk assessment shows that birds in a body weight range of 15 to 50 g reach the LD_{50}, LC_{50} and the long-term NOEC with 0.2 – 1.8 granules.
The calculations according to the EPPO scheme show ETR values of 0.0062 to 0.7438 for realistic worst case scenarios. However, no safety factor is taken on board in these calculations.
According to the RMS, there are numerous shortcomings in the probabilistic risk assessment (granules) and therefore no sound conclusions can be drawn.
In conclusion, the risk of Furadan 5G granules to birds is not acceptable for the intended use.

The RMS cannot agree with the proposed conversion factor carbofuran / 3-OH-carbofuran of 2.5 from the benfuracarb dossier. Also, the notifiers statement that residues in earthworms and beetles should only consider carbofuran (3-OH-carbofuran residues are negligible) is based on the benfuracarb dossier. If data from benfuracarb dossier are used, this should be accompanied by a letter of access.

The RMS disagrees with the statement of the notifier that the residue values at 60 g a.s./ha will be 10 times lower compared to 600 g a.s./ha. The results showing a linear response with the dose rate are based on only 2 residue trials. RMS also raises questions about the reduced dose rate :
- If carbofuran is applied at 60 g a.s./ha, the product will be applied in the plant hole, closer to the plant, to be as effective as the higher dose rate. No extrapolation of the residues is possible from a residue trial conducted at 600 g a.s./ha in the furrow. Only a residue trial conducted at 60 g a.s./ha in the plant hole will give the residue level in the field situation.
- If 60 g a.s./ha is efficient, why is the use at 600 g a.s./ha supported ?

Moreover, the RMS disagrees with the extrapolation factor of 2.5 from the benfuracarb dossier (cabbage) to the carbofuran dossier (sugar beet). Only a residue trial conducted in the relevant crop (sugar beet) can be used to calculate the conversion factor carbofuran / 3-OH-carbofuran.

The RMS concluded that the risk of carbofuran to birds and mammals consuming sugar beet seedlings, earthworms and arthropods is not acceptable for the intended use based on insufficient information on the actual residue level in feed items. In order to refine the risk to birds and mammals, more information is needed on the actual residue levels in feed items (sugar beet seedlings, earthworms, arthropods). The information should allow to perform statistical evaluations (enough residue trials, N and S European conditions, sampling over time, enough sampling material, …). Also, the residue trials should be relevant for the intended use (crop, application rate, granular or seed treatment use).

Risk to aquatic organisms :

Risk assessment for aquatic organisms was re-calculated using the PEC surface water recently re-calculated and the ecotoxicological endpoints agreed in the DAR. TERs are provided in the tables in the document of the notifier.

Conclusion of the notifier :

Whilst all run off scenarios show acceptable risk to the aquatic organisms for applications at 600 or 60 g carbofuran/ha, the low dose rate application at 60 g carbofuran/ha also presents acceptable risk to *Dapnia magna* and *Cerodapnia dubia* in the drainage scenarios.

Calculations of the RMS :

Risk assessment for the active substance (0.600 kg a.s./ha)

Table B.9.2.16.1-3 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to carbofuran in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	**Water body type**	**Test organism**	**Time scale**	**Toxicity end point (mg/L)**	**PECsw (µg/L)**	**TER**	**Annex VI trigger**
D3	Ditch	*Lepomis macrochirus*	96 h	0.18	0.0264	6818	100
D4	Pond				0.1030	1748	100
D4	Stream				0.0914	1969	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100
D3	Ditch	*Cyprinodon variegatus*	35 d	0.006	0.0264	227	10
D4	Pond				0.1030	58	10
D4	Stream				0.0914	66	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10
D3	Ditch	*Daphnia magna*	48 h	0.00205	0.0264	**78**	100
D4	Pond				0.1030	**20**	100
D4	Stream				0.0914	**22**	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100
D3	Ditch	*Ceriodaphnia dubia*	7 d	0.00016	0.0264	**6.1**	10
D4	Pond				0.1030	**1.6**	10

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D4	Stream				0.0914	**1.8**	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10
D3	Ditch	*Pseudokirchneriella subcapitata*	72 h	6.5	0.0264	246212	10
D4	Pond				0.1030	63107	10
D4	Stream				0.0914	71116	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10
D3	Ditch	*Chironomus riparius*	28 d	0.0032	0.0264	121	10
D4	Pond				0.1030	31	10
D4	Stream				0.0914	35	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

Table B.9.2.16.1-6 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to carbofuran in sediment for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/kg)	PEC_{sed} (µg/kg)	TER	Annex VI trigger
D3	Ditch	*Chironomus riparius*	28 d	0.0022	0.0461	69	10
D4	Pond				0.1250	26	10
D4	Stream				0.0871	37	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

Risk assessment for the metabolites (0.600 kg a.s./ha)

Table B.9.2.16.2-3 : Toxicity Exposure Ratio’s (TER’s) for aquatic organisms exposed to 3-keto-carbofuran in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Ceriodaphnia dubia*	48 h	0.049	0.0026	18846	100
D4	Pond				0.0079	6203	100
D4	Stream				0.0044	11136	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100

Table B.9.2.16.2-5bis : Toxicity Exposure Ratio’s (TER’s) for aquatic organisms exposed to 3-OH-carbofuran in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Ceriodaphnia dubia*	48 h	0.023	0.0008	28750	100
D4	Pond				0.0041	5610	100
D4	Stream				0.0024	9583	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100

Table B.9.2.16.2-6bis : Toxicity Exposure Ratio’s (TER’s) for aquatic organisms exposed to 7-phenol in surface water for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Chironomus riparius*	25 d	5.34	0.0000	-	10
D4	Pond				0.0001	53400000	10
D4	Stream				0.0002	26700000	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
R3	Stream				0.0000	-	10

Table B.9.2.16.2-7bis : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to 7-phenol in sediment for the intended use in sugar beet (1 x 0.600 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/kg)	PEC_{sed} (µg/kg)	TER	Annex VI trigger
D3	Ditch	*Chironomus riparius*	25 d	1.36	0.0012	1133333	10
D4	Pond				0.0017	800000	10
D4	Stream				0.0020	680000	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

Risk assessment for the active substance (0.060 kg a.s./ha)

Table B.9.2.16.1-3 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to carbofuran in surface water for the intended use in sugar beet (1 x 0.060 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Lepomis macrochirus*	96 h	0.18	0.0020	90000	100
D4	Pond				0.0093	19355	100
D4	Stream				0.0083	21687	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100
D3	Ditch	*Cyprinodon variegatus*	35 d	0.006	0.0020	3000	10
D4	Pond				0.0093	645	10
D4	Stream				0.0083	723	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10
D3	Ditch	*Daphnia magna*	48 h	0.00205	0.0020	1025	100
D4	Pond				0.0093	220	100
D4	Stream				0.0083	247	100

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100
D3	Ditch	*Ceriodaphnia dubia*	7 d	0.00016	0.0020	80	10
D4	Pond				0.0093	17	10
D4	Stream				0.0083	19	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10
D3	Ditch	*Pseudokirchneriella subcapitata*	72 h	6.5	0.0020	3250000	10
D4	Pond				0.0093	698925	10
D4	Stream				0.0083	783133	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10
D3	Ditch	*Chironomus riparius*	28 d	0.0032	0.0020	1600	10
D4	Pond				0.0093	344	10
D4	Stream				0.0083	386	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

Table B.9.2.16.1-6 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to carbofuran in sediment for the intended use in sugar beet (1 x 0.060 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/kg)	PEC_{sed} (µg/kg)	TER	Annex VI trigger
D3	Ditch	*Chironomus riparius*	28 d	0.0022	0.0038	842	10
D4	Pond				0.0117	274	10
D4	Stream				0.0080	400	10

Scenario	**Water body type**	**Test organism**	**Time scale**	**Toxicity end point (mg/kg)**	**PEC_{sed} (µg/kg)**	**TER**	**Annex VI trigger**
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

Risk assessment for the metabolites (0.060 kg a.s./ha)

Table B.9.2.16.2-3 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to 3-keto-carbofuran in surface water for the intended use in sugar beet (1 x 0.060 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Ceriodaphnia dubia*	48 h	0.049	0.0002	245000	100
D4	Pond				0.0007	70000	100
D4	Stream				0.0004	122500	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100

Table B.9.2.16.2-5bis : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to 3-OH-carbofuran in surface water for the intended use in sugar beet (1 x 0.060 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Ceriodaphnia dubia*	48 h	0.023	0.0001	230000	100
D4	Pond				0.0004	57500	100
D4	Stream				0.0002	115000	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100

Table B.9.2.16.2-6bis : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to 7-phenol in surface water for the intended use in sugar beet (1 x 0.060 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Chironomus riparius*	25 d	5.34	0.0000	-	10
D4	Pond				0.0000	-	10
D4	Stream				0.0000	-	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
R3	Stream				0.0000	-	10

Table B.9.2.16.2-7bis : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to 7-phenol in sediment for the intended use in sugar beet (1 x 0.060 kg a.s./ha) based on FOCUS Step 3 calculations

Scenario	**Water body type**	**Test organism**	**Time scale**	**Toxicity end point (mg/kg)**	**PEC$_{sed}$ (µg/kg)**	**TER**	**Annex VI trigger**
D3	Ditch	*Chironomus riparius*	25 d	1.36	0.0001	13600000	10
D4	Pond				0.0001	13600000	10
D4	Stream				0.0002	6800000	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

Conclusion of the RMS :
The calculations of the notifier and RMS are in close agreement.
The risk of carbofuran and its relevant metabolites (3-keto-carbofuran, 3-OH-carbofuran and 7-phenol) at the application rate of 0.600 kg a.s./ha to aquatic organisms is acceptable for all run-off scenarios and for all drainage scenarios except for *Daphnia magna* and *Ceriodaphnia dubia*.
The risk of carbofuran and its relevant metabolites (3-keto-carbofuran, 3-OH-carbofuran and 7-phenol) at the application rate of 0.060 kg a.s./ha to aquatic organisms is acceptable for all run-off scenarios and for all drainage scenarios.

Risk to Non target arthropods and macro soil organisms :

The risk to these organisms is addressed by a field study (Brown K.C., Forster A., Davies N.A., 2007) which show acceptable risk at a dose rate of 375 g carbofuran/ha. Therefore, this study fully covers the risk at the low dose rate (60 g carbofuran/ha). However, FMC observes from the evaluation tables that it is open for discussion rather the same study also covers the risk at application rate of 600 g carbofuran/ha.

Conclusion of the RMS :

The risk of carbofuran at the application rate of 600 g a.s./ha is not acceptable for non-target arthropods, including *Folsomia candida*.

Risk to earthworms, bees, micro-organisms and non target plants :

The use of 600 g carbofuran/ha to these organisms is acceptable. Reducing the dose rate can only offer more level of confidence.

Conclusion of the RMS :

RMS agrees with the notifier.