

Conclusion regarding the peer review of the pesticide risk assessment of the active substance

carbaryl

finalised: 12 May 2006

(revised version of 10 July with minor editorial changes marked yellow)

SUMMARY

Carbaryl is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000¹, as amended by Commission Regulation (EC) No 1490/2002². This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

Spain being the designated rapporteur Member State submitted the DAR on carbaryl in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 29 April 2004. Following a quality check on the DAR, the peer review was initiated on 3 September 2004 by dispatching the DAR for consultation of the Member States and the sole applicant Bayer CropScience S.A. (notification and submission made by Aventis CropScience prior to merger to form Bayer CropScience). Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 7 March 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in September 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 7 April 2006 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative use as a plant growth regulator as proposed by the applicant. The application method is by tractor mounted orchard sprayer with application to apple trees for the purpose of fruit thinning. The application rate is up to 0.9 kg of carbaryl per hectare. It should be noted that only the use as a plant growth regulator will be supported in the EU review programme. However, carbaryl is also an insecticide and acaracide.

¹ OJ No L 53, 29.02.2000, p. 25

² OJ No L 224, 21.08.2002, p. 25

The representative formulated product for the evaluation was Sevin XLR plus, a suspension concentrate (SC) containing 480 g/L carbaryl, formulations are also registered under different trade names in Europe.

In the main adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined by HPLC with fluorescence detection. Carbaryl can not be analysed by any currently available published monitoring methods due to the nature of the residues. For the other matrices only single methods are available for the same reasons as given above. For water and soil the method is HPLC with fluorescence detection and air is by HPLC-MS/MS. The method of analysis does not analyse for all components of the residue definition in surface water and therefore further data will be required to validate it for the compound 1-Naphthol.

Methods to determine residues of carbaryl in products of animal origin or for body fluids and tissues are not required because no MRLs will be set for products of animal origin and carbaryl is not classified as toxic or very toxic.

Sufficient methods of analysis for carbaryl and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. However, methods of analysis are not available for the relevant impurities in the formulation and the current storage data are not acceptable as the relevant impurities were not analysed for before and after storage.

Carbaryl is harmful if swallowed (oral LD₅₀ 614 mg/kg bw) and by inhalation (LC₅₀ 2.43 mg/L); it has a low acute dermal toxicity (dermal LD₅₀ higher than 5000mg/kg bw). Carbaryl is not irritant to skin and eyes and it is not a skin sensitiser. The following classification was proposed: Harmful, R20 'Harmful by inhalation' and R22 'Harmful if swallowed'. The critical effect in short and long term studies was the inhibition of cholinesterase activity. The weight of evidence indicates that carbaryl is not an *in vivo* genotoxic agent. In mice and rats, carbaryl was found to be carcinogenic; classification with R40 'Limited evidence of a carcinogenic effect' or R45? 'May cause cancer' was discussed and agreed on to be forwarded to ECB. Carbaryl did not show any potential for reproductive and developmental toxicity. The ADI is 0.0075 mg/kg bw/day (safety factor of 2000 because of the carcinogenicity issue); the AOEL and ARfD are 0.01 mg/kg bw/day (safety factor 100). Operator exposure is below the AOEL when estimated with German model and considering the use of PPE like gloves during mixing/loading and hood, visor, coverall and sturdy footwear during application.

The metabolism of carbaryl has been investigated in four crop groups, allowing the elucidation of the degradation pathway of the compound, which includes methyl and ring hydroxylation, carbamate ester hydrolysis and N-demethylation. Most of the metabolites formed may be further conjugated to form water-soluble glycosides. The metabolic pattern of carbaryl is evolving with time. For long PHIs the available data suggest that relevant metabolites can be present at levels representing a possible significant contribution to the toxicological burden. For the use of carbaryl for apple thinning, with a PHI of 80 days, 2 metabolites, 4- and 5-hydroxy carbaryl, which are cholinesterase inhibitors, are

expected to be present in amounts of the same order of magnitude as the parent compound. Therefore these metabolites were included in the residue definition for risk assessment. Supervised residue trials were carried out with analysis of parent compound only. This allows proposing the MRL for apple to be set below the Limit of Quantification of 0.05 mg/kg, but a robust risk assessment is not possible to be conducted as information on the actual level at harvest of the 2 hydroxy metabolites is lacking. Considering that the exposure to the parent compound only is close to 50% of the ARfD for some specific population sub-groups, it cannot be excluded that the contribution of the metabolites leads to a global exceedence of the ARfD for those sub-groups.

Residues in succeeding crops, in processed commodities and in animal products are not expected.

In soil carbaryl exhibited low to medium persistence. The most significant sink for the 1-naphthyl-¹⁴C- radiolabel position used in the aerobic laboratory studies was residue not extracted by methanol/water and acidified acetone water (20-39% of applied radioactivity (AR) after 100 days). Mineralisation to CO₂ accounted for 15-58%AR at 100 days. In 4 of the 5 soils investigated no major (>10%AR) metabolites were identified in soil extracts. In the fifth soil 1-naphthol was a major breakdown product accounting for a maximum of 35%AR at 2 days. 1-Naphthol however exhibited very low persistence in this soil. Under anaerobic soil conditions 1-naphthol was also a major soil breakdown product. Carbaryl exhibited medium soil mobility based on the results of guideline batch laboratory adsorption experiments. 1-Naphthol was characterised as also exhibiting medium soil mobility on the basis of the estimation provided by a guideline HPLC method.

In aerobic laboratory natural sediment water system experiments, carbaryl exhibited low persistence (dissipation DT₅₀ in water 1.2-5 days) as a consequence of a combination of partitioning to sediment (accounting for up to 24%AR at 0-60 days) and biodegradation. In the water phase the metabolite 1-naphthol accounted for a maximum of 35%AR 2 days after application, levels subsequently declined. 1-naphthol was also present in sediment but at low levels (maximum 9.5%AR). Residues not extracted from sediment by acidified methanol:water and acidified acetone:water represented 36-64%AR at study end (30-101 days). Mineralisation to CO₂ of the 1-naphthol-¹⁴C-radiolabel used accounted for 10.6-18 % AR by 101 days. The available surface water exposure assessment just considered the spray drift route of entry to surface water. The potential exposure of surface water with parent carbaryl via the drainage and runoff routes of entry has not been assessed in the available EU level exposure assessment. Member states should therefore carry out a surface water exposure and consequent aquatic risk assessment for carbaryl from the runoff and drainage routes of exposure at the national level, should carbaryl be included in annex 1.

Appropriate FOCUS groundwater modelling indicated that for the applied for intended use on apples leaching to groundwater above the parametric drinking water limit (0.1µg/L) would not be expected for either carbaryl or 1-naphthol.

A high long-term risk to insectivorous birds and a high acute and long-term risk to herbivorous mammals were identified in a first tier risk assessment. The submitted information was not sufficient to address the potential high risk to insectivorous birds in orchards and a data gap was identified in the EPCO expert meeting. A refined risk assessment based on residue decline was not accepted to

refine the acute risk to herbivorous mammals. For the long-term risk assessment more information was requested on how the DT_{50} value for the residue decline was calculated. This information was included in addendum 2 of February 2006. The EFSA considers the information as sufficient and considers the long-term risk to herbivorous mammals as low. However, the potential high acute risk to herbivorous mammals still needs to be addressed.

Carbaryl is very toxic to aquatic arthropods. The submitted microcosm study was assessed by the RMS as not being of use in deriving an EAC value since the exposure regime was representative only for aquatic habitats with very basic pH conditions where carbaryl degrades very rapidly. The proposed probabilistic approach was discussed by the EPCO experts' meeting. Uncertainty remained on which endpoints were used to construct the SSD. The splitting of data as suggested by the applicant would only be accepted if data fall into discrete groups based on sensitivity. The meeting considered the proposed trigger of 1 based on acute LC_{50} values as not acceptable. The meeting proposed to take the awaited opinion of the PPR panel on the possibility of lowering the uncertainty factor into account. Based on the PPR opinion on the possibility of lowering the uncertainty factor (see main text) the EFSA calculated the TER values for insects and crustaceans. The TERs are still below the trigger of 100 even if a no-spray buffer zone of 50 m is taken into account for the PEC_{sw} calculation. Overall it is concluded that the representative use of carbaryl poses a high acute and long-term risk to crustaceans and aquatic insects.

The HQ values for bees indicated a high risk from oral and dermal exposure. A field study was submitted to address the potential high risk. Although the EPCO experts had some reservations regarding the submitted field study, the meeting was content that the particular use does not pose a high risk to bees because the product is applied only once per year after flowering.

The in-field and off-field HQ values indicated a high risk to *Aphidius rhopalosiphi*. Extended laboratory studies showed that residue decline within 14 days is sufficient to allow recolonisation of treated fields. However a high off-field risk remains. The HQ trigger of 2 is not met even at a distance of 250 m from the treated field. No field data were submitted to show recovery/recolonisation of non-target insects in the treated area. Therefore it is concluded that recolonisation of the treated in-field area from unaffected off-field populations is not sufficiently demonstrated and needs to be further addressed.

Since the DT_{90} of carbaryl was in the range of 100 to 365 days and the standard HQ for non-target arthropods was exceeded a study with other soil non-target macro organisms is triggered. A data gap was identified by the EFSA to submit a study with collembola to assess the effects on other soil-macro organisms.

The risk to earthworms, soil non-target micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.



Key words: carbaryl, peer review, risk assessment, pesticide, insecticide, acaricide and plant growth regulator.

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BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Carbaryl is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Spain as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Spain submitted the report of its initial evaluation of the dossier on carbaryl, hereafter referred to as the draft assessment report, to the EFSA on 29 April 2004. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 3 September 2004 to the Member States and the main applicant Bayer CropScience S.A. (notification and submission made by Aventis CropScience prior to merger to form Bayer CropScience) as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 7 March 2005 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier attended this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team of the Pesticide Safety Directorate (PSD) in York, United Kingdom in September 2005. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 7 April 2006 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR).

In accordance with Article 8(7) of the amended Regulation (EC) No 451/2000, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received
- the resulting reporting table (rev. 1-1 of 16 March 2005)
- the consultation report

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation
- the evaluation table (rev. 2-1 of 12 May 2006)

Given the importance of the draft assessment report including its addendum (compiled version of March 2006 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the draft assessment report which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can basically be found in the original draft assessment report together with the peer review report which both is publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Carbaryl is the ISO common name for 1-naphthyl N-methylcarbamate (IUPAC).

Carbaryl, belonging to the class of carbamate insecticides and acaracides such as aldicarb, it is a weak cholinesterase inhibitor and it works by stomach and contact action it is also slightly systemic.

The representative formulated product for the evaluation was Sevin XLR plus, which is a suspension concentrate its registration status is unknown.

The evaluated representative use is as a plant growth regulator. The application method is by tractor mounted orchard sprayer with application to apple trees for the purpose of fruit thinning. The application rate is up to 0.9 kg of carbaryl per hectare.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of carbaryl as manufactured should not be less than 990 g/kg, which is higher than the minimum purity given in the FAO specification 26/TC/S (1989) of 960 g/kg. The higher value relates to the submitted results of current batch analysis and not to any toxicological concern to increase the minimum purity.

The technical material contains 2-naphthol and 2-naphthyl methylcarbamate which have to be regarded as relevant impurities. The maximum content in the technical material should not be higher than 0.5 g/kg for each compound (FAO specification 26/TC/S (1989)). However, it should be pointed out that no data were supplied by the applicant to either confirm or refute the relevance of these impurities.

As there is only one applicant with a single source a check for equivalence of technical material is not required.

The content of carbaryl in the representative formulation is 480 g/L (pure).

The assessment of the data package revealed no critical areas of concern with respect to the identity, physical, chemical and technical properties of carbaryl or the respective formulation.

The main data regarding the identity of carbaryl and its physical and chemical properties are given in appendix 1.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of carbaryl in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material. However, methods of analysis are not available for the relevant impurities in the formulation and the current storage data are not acceptable as the relevant impurities were not analysed for before and after storage.

Therefore, there are limited data available to ensure that quality control measurements of the plant protection product are possible.

In the main adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined by HPLC with fluorescence detection. Carbaryl can not be analysed by any currently available published monitoring methods due to the nature of the residues. For the other matrices only single methods are available for the same reasons as given above. For water and soil the method is HPLC with fluorescence detection and air is by HPLC/MS/MS. The method of analysis does not analyse for all components of the residue definition

in surface water and therefore further data will be required to validate it for the compound 1-naphthol.

Methods to determine residues of carbaryl in products of animal origin or for body foods and tissues are not required because no MRL's will be set for products of animal origin and carbaryl is not classified as toxic or very toxic.

The discussion in the experts' meeting (EPCO 35, 26 September 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material and the possibly relevant impurities in the technical material.

2. Mammalian toxicology

Carbaryl mammalian toxicology was discussed during the EPCO experts' meeting (EPCO 33) in September 2005.

2.1. ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Carbaryl is rapidly absorbed, about 91.5% within 24 hours based on urinary excretion. It is widely distributed, with the highest levels found in the kidney at 7 days. Carbaryl does not show any evidence of accumulation. It is extensively metabolised (only 2.9% of unchanged compound can be found in urine) through three main metabolic pathways:

Arene oxide formation with hydrolysis to dihydrodihydroxycarbaryl and glucuronide conjugation; hydrolysis to form 1-naphthol and conjugation; oxidation of N-methyl moiety (alkyl oxidation).

2.2. ACUTE TOXICITY

Carbaryl is harmful if swallowed (oral LD₅₀ 614 mg/kg bw) and by inhalation (LC₅₀ 2.43 mg/L); it has a low acute dermal toxicity (dermal LD₅₀ higher than 5000 mg/kg bw). Carbaryl is not irritant to skin and eyes and it is not a skin sensitiser. The following classification was proposed: Harmful, R20 'Harmful by inhalation' and R22 'Harmful if swallowed'.

2.3. SHORT TERM TOXICITY

Carbaryl short term toxicity was assessed in studies in rats, mice and dogs.

The critical effect was the inhibition of cholinesterase activity, while the target organ was the liver (increase of weight and histopathology changes). The relevant oral NOAEL was lower than 3.37 mg/kg/day in the 1-year dog study, due to RBC cholinesterase inhibition at all tested doses. The relevant dermal NOAEL was 20 mg/kg/day (4-week rat study).

2.4. GENOTOXICITY

The genotoxicity of carbaryl has been investigated in a number of *in vitro* and *in vivo* assays, including gene mutation, chromosomal aberration, DNA damage and DNA binding as endpoints, with purity levels ranging from 99.0% to 99.7%.

Carbaryl gave negative results in bacterial systems in the presence or absence of S9 from rat liver and in the culture mammalian cells in the absence of S9. Although there were equivocal results in the *in vitro* mammalian assay with S9, negative results were obtained in the *in vitro* UDS assay.

Positive results were obtained for *in vitro* chromosome aberrations with metabolic activation in mammalian (CHO) cells. The clastogenicity was not confirmed *in vivo*, for somatic cells in mouse bone marrow micronucleus and rat bone marrow chromosome aberrations assay. In relation to DNA damage, negative results were obtained for *in vivo* DNA binding.

In conclusion, the weight of evidence indicates that carbaryl is not an *in vivo* genotoxic agent.

2.5. LONG TERM TOXICITY

A rat combined chronic toxicity/carcinogenicity and a mouse carcinogenicity studies were conducted. Data from mechanistic studies, using induction of hepatic enzyme and cellular proliferation as endpoints, and from a test using heterozygous p53-deficient mice (proposed model for detection tumours caused by genotoxic carcinogens) were also supplied.

During the meeting, the RMS was asked to prepare a brief summary of a recent publication by Jacobson-Kram et al, Toxicologic Pathology, 32, (suppl.1):49-52, 2004 in an addendum, which was made available in February 2006.

When the test substance was administered to rats via the diet for 2 years, the main toxic effect observed was a decrease in erythrocyte and brain cholinesterase activity at 1500 ppm. Based on this effect, the chronic NOAEL was set at 250 ppm (10 mg/kg bw/day). Carbaryl was found to be carcinogenic at 349 mg/kg bw/day (a concentration exceeding the Maximum Tolerated Dose). In rats thyroid follicular adenomas and carcinomas (males), hepatocellular adenoma (females), carcinomas and adenomas in the urinary bladder (both sexes), a carcinoma in kidney (male) were recorded.

In mice the dietary administration of carbaryl for 2 years resulted in both neoplastic and non neoplastic findings. Based on the inhibition of erythrocyte and brain acetylcholinesterase activity and histopathological changes in the bladder, the relevant NOAEL for non-neoplastic lesion was 15 mg/kg/day. As for neoplastic findings, vascular tumors (located predominantly in the liver and spleen) at 15 mg/kg bw/day in males renal tubular cell adenoma and carcinoma, hepatocellular carcinoma and adenoma at 1248 mg/kg bw/day were recorded. Based on these observations, the NOAEL for carcinogenicity was not established.

Mechanistic studies suggested that the tumorigenic response was due to cell proliferation associated with a mitogenic effect of carbaryl or one of its metabolites. The results identified carbaryl as a weak barbiturate-type inducer of cytochrome P450 in the mouse liver.

Classification with R40 'Limited evidence of a carcinogenic effect' or R45? 'May cause cancer' was discussed and agreed on to be forwarded to ECB and indicated in the list of end points. Furthermore, during the meeting the experts discussed the toxicological significance of Non Hodgkin Lymphomas (NHL) and concluded that no particular concerns were identified in the available studies.

2.6. REPRODUCTIVE TOXICITY

One two-generation study in rats and one developmental studies in both rat and rabbit were performed.

The relevant parental, offspring and reproductive NOAEL was 4.67 mg/kg bw/day, based on the decreased body weight in the parents and on the significant reduction of the F2 n° pups/Litter and of the F2 pup survival at 21.04 mg/kg bw/day. Based on the studies available, the experts concluded that carbaryl did not have effects on sperm morphology.

The teratogenicity study performed in rats revealed that at the dose of 30 mg/kg bw/day, dams showed some clinic signs typical of anticholinesterase agents (increase of salivation), and affected the body weight of the dams and foetuses that decreased significantly; in addition, a delayed ossification in foetuses was observed, therefore the NOAEL for maternal and developmental toxicity was set at 4 mg/kg bw/day in rats.

2.7. NEUROTOXICITY

The main sensitive endpoints in acute and subacute studies were the observations in the functional observational battery (FOB) and the reduction in the cholinesterase activity and motor activity. The severity and frequency of clinical signs and reduction of cholinesterase activity were related to dose and decreased with time. The lowest oral NOAEL in neurotoxicity studies was 1 mg/kg bw per day based on a 13-week study. No signs of developmental neurotoxicity were recorded.

2.8. FURTHER STUDIES

Metabolites

Two metabolites were identified: 4-hydroxycarbaryl and 5-hydroxycarbaryl. They are both structurally similar to carbaryl, and therefore likely to be ChE inhibitors. They were of particular concern as it is not known whether the parent or metabolites are responsible for the carcinogenic effects. In the recently submitted addendum, 4-hydroxycarbaryl and 5-hydroxycarbaryl were discussed. They are found in plants and animals. According to the FAO monograph (1969) toxicological data show that the acute oral toxicity of 5-hydroxycarbaryl (LD₅₀ 297 mg/kg bw) is comparable to carbaryl (LD₅₀ 614 mg/kg bw) while LD₅₀ values for 4-hydroxycarbaryl and 1-naphthol are higher than the LD₅₀ value established for carbaryl (1190 mg/kg bw and 2590 mg/kg bw, respectively). The short-term toxicity of these metabolites was lower when compared to the parent compound carbaryl. *In vitro* cholinesterase inhibition studies showed that 1-naphthol, 4- and 5-hydroxycarbaryl are also inhibitors of cholinesterase activity, with similar or higher IC₅₀ values. The experts agreed they should be considered in the consumers' risk assessment. The RMS concludes that the toxicological information indicates that 4-hydroxycarbaryl and 5-hydroxycarbaryl should not be considered of toxicological relevance. This assessment was neither discussed nor agreed.

EFSA notes that, according to the data submitted, both metabolites are cholinesterase inhibitors, with inhibition activity comparable to carbaryl; further, 5-hydroxycarbaryl LD₅₀ is even lower than carbaryl's.

Metabolites - impurities

1-naphthol is a metabolite found in plants and animals, and it is also an impurity. According to European Chemical Information System 1-naphthol is classified as R21/22, harmful in contact with skin and if swallowed, R37/38 Irritating to respiratory system and skin and R41, risk of serious damage to eyes.

Impurities

1-naphthyl 2,4-dimethyl allophanate is an impurity. No experimental data are available but a position paper with a DEREK analysis has been submitted by the applicant and summarised in the addendum (Feb 06). The RMS states that according to the toxicological characteristics, this impurity does not pose any concerns. These assessments provided by the RMS were not peer reviewed.

A new data gap was identified during the meeting for the applicant to provide information on the levels of impurities (1-naphthol and 1-naphthyl 2,4-dimethyl allophanate) in batches used in toxicity studies as well as information on their toxicological properties.

For the two impurities 2-naphthol and 2-naphthyl methylcarbamate no toxicological data was provided.

2.9. MEDICAL DATA

Among the medical effects on manufacturing personnel, only one of the available studies showed that carbaryl increased the rate of sperm shape abnormalities. The clinical cases and poisoning incidents revealed only one fatal case of death due to ingestion of Sevin (carbaryl), whose results are nevertheless controversial.

One epidemiological study made on exposed farmers showed the evidence of occurrence of Non-Hodgkin Lymphoma (NHL) in men handling carbaryl for more than 20 years and epidemiological studies on mortality ratio revealed an association with NHL, liver cancer (not specified) and kidney cancer.

The experts noted that the manufacturer had provided no information relating to the routine, monitoring of workers other than that they monitored. A new data requirement was set for further information relating to this. So far, no new data was submitted by the notifier.

2.10. ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

ADI

The meeting discussed the carcinogenic effects observed with carbaryl in relation to the derivation of the ADI. It was noted that tumours were observed in multiple organs in rats and mice, and that mechanistic studies indicated a non-genotoxic effect. It was additionally noted that a non-carcinogenic effect had not been demonstrated in humans. As a result it was concluded that while the LOAEL in the mouse carcinogenicity study was high compared to NOAELs from other studies, the use of the LOAEL from the mouse carcinogenicity study (with additional safety factors due to the use of LOAEL) highlighted the concern relating to this effect. Application of a safety factor of 2000 derived an ADI of 0.0075 mg/kg bw/day.

AOEL

From all the available data, it was considered appropriate to use the NOAEL of 1 mg/kg/day from the 13-week neurotoxicity study, where an inhibition of all types of ChE measured was observed. A safety factor of 100 was considered appropriate as LOAEL irreversible effect/AOEL > 1000. The AOEL was as follows:

$$\text{AOEL} = (1 \text{ mg/kg/day})/100 = 0.01 \text{ mg/kg/day}$$

ARfD

The studies available for the derivation of the ARfD were considered. Acute neurotoxicity studies were conducted at doses of ≥ 10 mg/kg bw, and a LOAEL of 10 mg/kg bw obtained, at which marked inhibition (40-50%) occurred. In the subchronic neurotoxicity a NOAEL of 1 mg/kg bw/day was obtained. Therefore it was considered appropriate to derive the ARfD from this study; applying a safety factor of 100, an ARfD of 0.01 mg/kg bw was derived.

2.11. DERMAL ABSORPTION

In vivo and *in vitro* studies lead to the conclusion that dermal absorption for Sevin XRL Plus was 9.54-15.3% within 10-24 h, respectively, for the dilution and 0.37-0.59% within 10-24 h, respectively, for the concentrate. During the EPCO dermal absorption values after 10h were considered and rounded up from 0.37% to 0.5% for concentrate and 9.54% to 10% for dilution.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

DAR

Operators

Estimations of the potential operator exposure have been undertaken using the UK POEM and the German model. Estimated values ranged from 443.12-667.4% AOEL for UKPOEM at 10-24 hr and between 188.6-290.9 %AOEL at 10-24 hr for BBA Model.

Workers

Worker exposure was evaluated taking into account a new transfer coefficient extrapolated from a field study using iprodione. Estimated exposure levels ranged from 100-350.25 % of AOEL using 10hr to 24 hr dermal penetration data.

Bystanders

Bystanders exposure was estimated to be 7.43 or 10.27 % of AOEL using 10hr or 24 hr dermal absorption data.

Field studies reported in the DAR and conducted with in scenarios similar to the one under discussion but with different a.s., confirmed that exposure exceeded the AOEL.

Refinement after EPCO

According to the EPCO outcomes, the RMS was asked to recalculate operator and bystander exposure; worker exposure has to be recalculated also considering EUROPOEM transfer coefficients. In the feb 06 submitted addendum, not peer reviewed, recalculations are provided.

Operators

	UK POEM		BBA	
	Exposure	% of AOEL	Exposure	% of AOEL
	(mg/kg bw/day)		(mg/kg bw/day)	
Without PPE	0.18	1800	0.12	1200
PPE: Gloves ML & Applic.	0.13	1300		
PPE: Gloves ML & Applic. Hood and visor, Coverall and sturdy footwear in application			0.0075	75

Operator exposure is below the AOEL when estimated with German model and considering the use of PPE like gloves during mixing/loading and hood, visor, coverall and sturdy footwear during application.

Workers

The assessment has been performed considering data in the EUROPOEM database for hand harvesting suggest a transfer coefficient of 4500 cm²/person/hr for worker harvesting fruits from trees. The DFR is predicted from conservative assumptions which assume a DFR of 3 µg/cm² per kg a.s./ha applied. Estimated exposure corresponds to 81% of the AOEL.

Bystanders

Direct measurements of simulated bystander exposure for applications made to orchards in the UK by broadcast air assisted sprayers reported in a study by Lloyd and Cross (1987) were used as surrogate values. Estimated exposure corresponds to 60% of the AOEL.

3. Residues

Carbaryl was discussed during the EPCO experts' meeting for residues (EPCO 34) in September 2005.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of carbaryl after foliar application in plants has been investigated in lettuce, soybean, radish and apple. The metabolic pattern observed was rather similar between these crops. Carbaryl is

stable when present on the surface of the plant and undergoes biotransformation when it enters into the plant tissues. The metabolic pathway includes methyl and ring hydroxylation, carbamate ester hydrolysis and N-demethylation. Most of the metabolites formed may be further conjugated to form water-soluble glycosides. These studies were conducted with rather short PHIs (8 days for lettuce, 45 days for soybean, 7 days for radish and 28 and 53 days for apples) in comparison with the PHI proposed for the use of carbaryl for apple thinning. Under these conditions, carbaryl was in all plant parts, except in soybean seeds, the dominant compound. Some metabolites present under conjugated form were found in the range of 10% of the TRR: hydroxymethyl carbaryl in soybean as well as 4- and 5-hydroxycarbaryl (both resulting of ring hydroxylation) in apples.

In apples, the ratio of the sum of these later two metabolites to parent compound appears to be dependant on the precocity of the application of carbaryl: this ratio is about 1/10 for application made 28 days before harvest and increases to 1/1 when the application occurs 53 days before harvest. Therefore, their expected contribution to the global toxicological burden for a PHI of 80 days can be considered as significant. The expert meeting (EPCO 34) discussed the residue definition applicable to apples. It was agreed that the parent compound is a valid indicator for monitoring. For risk assessment it was concluded that the necessity to include the 4- and 5-hydroxycarbaryl metabolites in the definition was depending on their toxicological relevance. As indicated under point 2.8, the available toxicological information suggests that they may have a similar level of toxicity as the parent compound and therefore they are included in the residue definition for risk assessment. The available data are not sufficient to fix a conversion factor between the residue definitions for monitoring and risk assessment. It must be noted that for other crops, beyond the scope of this peer-review, the residue definition for risk assessment may be different, depending of the specific metabolic pattern.

Nine valid supervised residue trials were submitted by the notifier according to the representative use supported by the applicant with 1 treatment at growth stage 71-73. Seven trials were carried out in Northern Europe and 2 were carried out in Southern Europe. In these trials only carbaryl was analysed. Results for PHIs varying from 76 to 83 days were 5 times < 0.05 mg/kg and 4 times < 0.01 mg/kg, depending on the method of analysis used and related Limit of Quantification (LOQ). These results are supported by storage stability studies demonstrating that residues of carbaryl are stable up to 24 months of storage at -20°C .

Additional data should be submitted concerning the residues of 4- and 5-hydroxy carbaryl in apples at harvest in order to have all the needed information to conduct a robust risk assessment for the safety of the consumer.

As carbaryl residues in raw apples are below the LOQ, the effect of processing on the nature and the level of residues were not investigated.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Apple being a perennial crop, it is not relevant to investigate the potential of transfer of residues from the soil to succeeding and rotational crops.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

The use of carbaryl for apple thinning does not lead to significant animal exposure. Even if residue data are not available for 4- and 5-hydroxy carbaryl in apples it is expected given the early stage of application of the product that the amount of carbaryl and its metabolites present in apple pomace is low and at least not such that the animal exposure could be higher than 0.1 mg/kg total feed (fruit pomace is a processed feed item resulting from the mixing of products of different origins and enters for a maximum of 30% of the dry matter in animal diet). For this reason it is considered that livestock metabolism and feeding studies as well as residue definitions and MRLs for animal products are not necessary.

3.3. CONSUMER RISK ASSESSMENT

Assessments of the chronic and acute exposures of consumers could not be conducted on the basis of the residue definition proposed for risk assessment as data on the actual level of the metabolites 4- and 5-hydroxy carbaryl in plant commodities are lacking.

Only exposure assessments to carbaryl are at this stage possible and were performed by the RMS.

Chronic exposure.

The chronic dietary exposure assessment has been carried out according to the WHO guidelines for calculating Theoretical Maximum Daily Intakes (TMDI). Four consumption patterns were considered: the WHO European typical diet for adult consumers, the diets of UK for infants, toddlers, children and adults populations, which take into consideration high individual consumption levels (at the 97.5th percentile of the distribution of consumptions in the respective populations), the Spanish diet for adult consumers and the German diet for the 4-6 years old girl.

For TMDI calculations, residues in apples were assumed to be at the level of LOQ proposed as MRL on the basis of the supervised residue trials. No exposure resulting from the consumption of animal commodities was considered as the exposure of animals and the resulting transfer to edible animal commodities is considered not significant. These calculations indicated that the chronic exposure of all the here above mentioned populations was well below the ADI of carbaryl. The highest exposure was calculated for toddlers in UK (6% of the ADI).

Acute exposure.

The acute exposure to residues of carbaryl in apples has been assessed according to the WHO model for estimates of short term intakes. Large portion consumption data for various population groups (infants, toddlers, children, adults) in UK, France and Netherlands were used. Calculations were carried out considering residues in composite samples of treated apples at the level of the LOQ as well as high unit to unit variability (variability factor of 7). The highest predicted short term intakes were found for infants and toddlers in UK and were amounting to 36 and 49% respectively of the ARfD.

It must be kept in mind that the exposure assessments summarised here above represent an underestimation of the actual toxicological burden as the 4- and 5- hydroxyl metabolites of carbaryl

were not included in the calculations. Considering that the exposure to the parent compound only is close to 50% of the ARfD for some specific population sub-groups, it cannot be excluded that the contribution of the metabolites leads to a global exceedence of the ARfD for those sub-groups.

3.4. PROPOSED MRLs

The results of supervised residue trials suggest setting the MRL for carbaryl in apples below the LOQ of 0.05 mg/kg, supporting the representative use in Northern Europe.

4. Environmental fate and behaviour

The fate and behaviour in the environment of carbaryl was discussed in the experts' meeting (EPCO 31) of September 2005 on basis of the addendum to the DAR dated June 2005. After the meeting the RMS clarified the key open points identified by that meeting in the Corrigendum B-8, dated February 2006.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

In soil experiments (5 different soils) carried out under aerobic conditions in the laboratory (20-25°C 75% field capacity (FC) or 40-52% maximum water holding capacity (MWHC) in the dark, the formation of residues not extracted by methanol:water followed by acidified acetone:water was a significant sink for the applied 1-naphthyl-¹⁴C-radiolabel (20-39% of the applied radiolabel (AR) after 100 days). Mineralisation to carbon dioxide of the radiolabel accounted for 15-58 % AR after 100 days). The most significant extractable breakdown product identified was 1-naphthol where maximum measured concentrations in 4 of the soils accounted for: not detected (2 soils) to 1.27% AR. In the fifth sandy loam soil, 1-naphthol accounted for 35% AR 1 day after treatment. In the sample taken on the second day after treatment, it accounted for only 2.8% AR. Other extracted unidentified resolved breakdown products accounted for a maximum of 1.6% AR.

Under anaerobic conditions in soil, the degradate pattern was essentially the same as described above for aerobic conditions, except the 1-naphthol formed would give a longer exposure duration, it accounted for a maximum of 21.7% AR at 94 days declining to 13.2% AR at the study end (126 days). In a laboratory soil photolysis study, the rate of degradation on light exposed 75% FC soil moisture soil was comparable to that observed in the dark control. No novel photodegradation products were identified, the degradation of parent carbaryl in the experiment was limited (6% AR over the 12 days experimental duration).

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The rate of degradation of carbaryl was estimated from the results of the studies described in 4.1.1 above and was also investigated under aerobic conditions at a range of temperatures in an additional 2

soils. On the basis of the nine available study results where seven different soils were investigated, the single first order DT_{50} were: 80.9 days (10°C and 50% MWHC), 11.9 days (15°C, at 75% FC), 4-25.2 days (25°C at 75% FC) and 7.08-99 days (20°C and 40-52% MWHC). After normalisation to FOCUS reference conditions³ (20°C and -10kPa soil moisture content) this range becomes 2.3-98.7 days (arithmetic mean 25.8 days geometric mean that is appropriate for use in FOCUS modelling 15.8 days).

The major degradation product (> 10 %AR), formed in major amounts in just 1 soil 1-naphthol also degraded rapidly in soil with an estimated single first-order DT_{50} in this single soil of 0.9 days (normalised to FOCUS reference conditions 0.53 days).

The potential for the degradation of carbaryl to be pH dependant was considered by the RMS, but there was no correlation of first order DT_{50} with this soil property⁴.

No field soil dissipation studies were provided. As in 1 soil at 20°C and pF2 (-10kPa), the single first order DT_{50} was > 60 days (DT_{50} 98.7 days, extrapolated DT_{90} 328 days) field dissipation studies are triggered. On the basis of the remaining 8 single first order DT_{50} results field dissipation studies would not be triggered (the next longest 20°C and pF2 value was 31.9 days). In this case, for this active substance, with this laboratory soil study database, as it is not possible to attribute any single or combination of soil properties as being the cause of the longer DT_{50} , it is unlikely that any field trial database generated would add significant new information to improve our understanding of the fate and behaviour of carbaryl in soil. The EFSA considers having field data would not significantly increase the reliability of the environmental exposure assessment in this case. Therefore the EFSA considers the environmental exposure assessment at the EU level can be concluded without field soil dissipation studies on the basis of the available laboratory studies, as this is likely to result in a precautionary exposure and subsequent risk assessment.

The longest available laboratory single first order soil DT_{50} of 99 days was selected for use in PEC soil calculations with a crop interception of 70% agreed by the experts from member states as being appropriate for the growth stage after flowering in apples⁵.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The adsorption / desorption of carbaryl was investigated in four soils in guideline batch adsorptions studies. Calculated adsorption K_{oc} values varied from 177 to 249 mL/g, (mean 211 mL/g) indicating that carbaryl is moderately mobile in soil (1/n 0.78 – 0.84, mean 0.81). There was no evidence of a correlation of adsorption with pH.

³ Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

⁴ Corrigendum B-8 dated February 2006.

⁵ in line interception tables in generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002..

The adsorption of 1-naphthol was investigated in four soils using the batch adsorption screening experiments prescribed by OECD 106. The compound was unstable in the test soils and even under the non equilibrium conditions of 30 minutes shaking the mass balance of the test substance was low accounting for only 7-27% of that applied. As a result the definitive adsorption / desorption test could not be completed. Consequently the OECD screening test OECD 121 that estimates adsorption using an HPLC column (and not measurements with soil) was employed. This gave an estimated 1-naphthol K_{doc} value of 245mL/g. The experts from the member states agreed this estimate was an acceptable value to use in FOCUS modelling.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

The aqueous hydrolysis of carbaryl under sterile conditions was faster under basic conditions than acidic ones. At pH 7, (the value tested closest to natural conditions), carbaryl was more stable than when microorganisms are present (the 25°C single first order DT_{50} was 12 days). The main hydrolysis product in these sterile conditions was 1-naphthol.

The aqueous photolysis of carbaryl investigated under sterile pH 5 conditions, where hydrolysis was slow, indicated the rate of degradation was slower than under dark microbially active conditions (single first order laboratory DT_{50} equated to summer sublight at 30-50°N was 11-14 days. No major (>10%AR) metabolites were formed in the study. Photolysis is not expected to be a significant route of dissipation of carbaryl in the environment as biodegradation is more rapid.

A ready biodegradability test (OECD 301D) indicated that carbaryl is 'readily biodegradable' using the criteria defined by the test.

In water-sediment studies (3 systems studied at 20-25°C in the laboratory, sediment pH 5 -7.6, water pH 6.5-9) carbaryl demonstrated low persistence in both the water phase (single first order DT_{50} 1.2-5 days) and in the total system (single first order DT_{50} 1.62-9.9 days). The metabolite 1-naphthol (max. 34.7 % AR at 2 days after treatment) was detected in the water phase but accounted for <1%AR in the water phase by 7-30 days. The terminal metabolite, CO_2 , accounted for 10.6-18 % AR by 101 days. Residues not extracted from sediment by acidified methanol:water and acidified acetone:water were a significant sink representing 36-64%AR at study end (30-101 days). The only major (>10%AR) residue in sediment extracts was parent carbaryl (max. 24%AR at 0-60 days) for which a single first order DT_{50} in sediment of 4.3 days was estimated. The experts from the member states discussed which water DT_{50} values should be used in the calculation of PEC surface water, which were presented based on late season spray drift values⁶ to a static 30cm deep water body. They confirmed the longest first order dissipation DT_{50} value for parent carbaryl of 5 days from the available dark water sediment studies should be used.

⁶ Appendix 1 Guidance document on aquatic ecotoxicology Sanco/3268/2001 date 1 October 2001.

The available surface water exposure assessment just considered the spray drift route of entry to surface water. The potential exposure of surface water with parent carbaryl via the drainage and runoff routes of entry has not been assessed in the available EU level exposure assessment. Member states should therefore carry out a surface water exposure and consequent aquatic risk assessment for carbaryl from the runoff and drainage routes of exposure at the national level, should carbaryl be included in annex 1. A drainage and runoff entry surface water exposure assessment is considered unnecessary for the major soil metabolite 1-naphthol in situations (such as the applied for intended use on apples) where prolonged anaerobic soil conditions can be excluded, due to its impersistence in soil under aerobic conditions.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

FOCUS PELMO 3.3.2 simulations were carried out for the good agricultural practice (GAP) of 1 application of 0.9 kg/ha (0.27 kg/ha accounting for 70% crop interception) being made to apples, with applications being made in March to May. Appropriate (though more conservative than guidance requires) substance properties of: carbaryl single first order DT_{50} 25.7 days K_{foc} 211.53 mL/g $1/n=0.81$ and 1-naphthol single first order DT_{50} 0.6 days K_{doc} 245mL/g or 0, $1/n=1.0$, formation fraction from carbaryl 100% were used as input. In these simulations annual average concentrations in leachate leaving the top 1m soil column were estimated to be $<0.001 \mu\text{g/L}$ for both compounds at all 9 FOCUS groundwater scenarios.

Based on this modelling, leaching to groundwater from the applied for intended uses on Apples above the parametric drinking water limit ($0.1 \mu\text{g/L}$) would not be expected for either carbaryl or 1-naphthol.

4.3. FATE AND BEHAVIOUR IN AIR

The vapour pressure of carbaryl (4.16×10^{-5} Pa at 25°C) means that carbaryl would be classified under the national scheme of The Netherlands as very slightly volatile, indicating limited losses due to volatilisation would be expected. Therefore the PEC_{air} is considered to be negligible. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half life estimated at 0.377 days (assuming an atmospheric hydroxyl radical concentration of 1.5×10^6 radicals cm^{-3} and a 12 hour photoperiod) indicating the small proportion of applied carbaryl that did volatilise would be unlikely to be subject to long range atmospheric transport.

5. Ecotoxicology

Carbaryl was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 32) in September 2005.

5.1. RISK TO TERRESTRIAL VERTEBRATE

A risk assessment for birds and mammals was conducted according to SANCO/4145/2000 for insectivorous and earthworm-eating birds. A high long-term risk was indicated in a first tier risk assessment for insectivorous birds. Two published articles on effects of carbaryl on killdeer (*Charadrius vociferous*) and tree swallow (*Tachycineta bicolor*) were submitted by the applicant. The meeting was concerned about some lack of detail in the study reports (e.g. it was not certain if low effects were due to low exposure if the birds were foraging elsewhere rather than in the treated orchard). The relevance of tree swallow as a focal species was questioned due to its mode of feeding i.e. taking insects from the air rather than from the treated crop. The meeting agreed that the submitted information is not sufficient to address the potential high long-term risk to insectivorous birds and identified a data gap.

The RMS presented a TER calculation for herbivorous birds. The first tier TER values indicated a potential long-term risk. In addendum 1 (June 2005) a new TER calculation was presented taking into account 70% interception because the product is applied at a stage when the foliage of the trees is fully developed. It was noted that the RUD value for leafy crops was used for the TER calculation for medium herbivorous birds. Using the correct value of 76 for residues in short grass in orchards and 70% interception the resulting long-term TER would be 3.63. However, the meeting agreed that the risk assessment for herbivorous birds in orchards is not standard and that the risk to herbivorous birds is sufficiently addressed.

From the observed endpoints from studies with the formulation Sevin XLR and mammals the RMS suggested that the formulated carbaryl is about a factor 2 more toxic than technical carbaryl. The meeting considered that the observed difference is not very pronounced and that the difference might also be explained by natural variation. It was concluded that it is not necessary to request a formulation study with birds taking into account that exposure via residues on food items will be primarily from the active substance.

The first tier risk assessment for herbivorous and earthworm-eating mammals indicated a potential high acute and long-term risk. A new risk assessment based on refinement of PD and f(twa) and taking into account 70% interception was presented in addendum 1 (June 2005). This resulted in an acute TER of 7.9 and long-term TER of 6.1 indicating a high acute risk. The suggested PD refinement was accepted for the long-term risk but rejected for the acute risk assessment. The meeting considered that it cannot be excluded that the animals feed solely on one food type in a short period of time relevant for the acute risk assessment. The information provided in the addendum was insufficient to assess the derivation of the f(twa) value of 0.28. It was agreed that clarification is required regarding the relevance of the crop, situation (i.e. northern Member States vs. southern Member States) and how the DT₅₀ was calculated. It was agreed by the meeting that the endpoint from the F1 generation should be used for the long-term risk assessment instead of the lower endpoint observed in F2 because the duration of exposure in the test is much longer than expected in the field. The use of the acute endpoint from the formulation or technical carbaryl was discussed. The meeting agreed that the lowest observed endpoint should be used. It was noted that the LD50 was the mean of the LD50s for male and female rats. The meeting concluded that the lower endpoint of the two sexes should be used and confirmed the data requirement for a refined acute risk assessment. The acute TER was

recalculated as 4.6 based on the lowest observed endpoint for female rats from a test with the formulation.

Further details were provided in addendum 2 from February 2006 on how the DT_{50} for the residue decline was calculated. The EFSA is of the opinion that the information is sufficient to conclude that the DT_{50} of 4.21 is acceptable and can be used to adjust the $f(twa)$. Hence, the long-term risk to herbivorous mammals is considered to be low.

The risk from uptake of contaminated drinking water was assessed as low based on PEC_{sw} water values. A new calculation according to SANCO/4145/2000 for a medium sized bird was presented in addendum 2. A mistake in the exposure concentration was noticed (it should read 180 mg a.s./L instead of 0.018 mg/L). Therefore the EFSA recalculated the TER values in an addendum. The acute and short-term TER values exceeded the Annex VI trigger in a first tier risk assessment except the acute TER for mammals (9.5) at the higher recommended concentration of the spray solution. The long-term TERs are below the trigger. However since the product is applied only once per growing season it is considered unlikely that contaminated drinking water would be available for a period of time long enough to cause long-term effects. Overall it is concluded that the risk from uptake of contaminated drinking water is assumed to be low for the representative use if sprayed at the lowest recommended concentration. A refined risk assessment is required to address the potential high acute risk to mammals for the highest recommended concentration of the spray solution.

Overall it is concluded that a high long-term risk to insectivorous birds and a high acute risk to herbivorous mammals cannot be excluded for the representative use.

5.2. RISK TO AQUATIC ORGANISMS

The lowest endpoints for carbaryl were observed in studies with aquatic invertebrates. The TER values in the DAR calculated with PEC_{sw} from spray drift indicated a high acute and chronic risk to aquatic invertebrates from exposure to carbaryl and a high chronic risk to fish from exposure to the metabolite 1-naphtol. One microcosm study and published articles on the effects of carbaryl on aquatic habitats were submitted. The published articles were assessed to be of use as additional information but cannot be used directly to derive an EAC value since the tests did not comply to accepted guidelines (e.g. test substance was not measured during the test). The exposure regime in the microcosm study was assessed by the RMS as being representative only for habitats with basic water conditions ($pH > 9$) where carbaryl degrades significantly more rapidly than under neutral or acidic conditions. The meeting wished to have a more detailed summary of the study e.g. a graphical presentation of the results (e.g. PRCs). A probabilistic risk assessment was suggested by the RMS to refine the risk to aquatic organisms.

A new aquatic risk assessment was presented in addendum 1 of June 2005 to address the comments received by Member States. The probabilistic approach suggested by the RMS and the new probabilistic assessment submitted by the applicant were discussed in the experts' meeting. The meeting did not reach a final judgement on the proposed use of the SSD. Uncertainty remained regarding the quality of data which were used to construct the SSD. The meeting requested a short

summary indicating the studies used and the endpoints selected in order to aid transparency and understanding. It was agreed that HC5 values should be read-off the experimental data and from the fitted curve. The applicant suggested splitting the data set. The proposed splitting was not agreed by the meeting but it was noted that it might be acceptable to split data into groups provided that data fall into discrete groups based on sensitivity. Once these issues had been addressed the HC5 could be used in the risk assessment. The proposed trigger value of 1 based on acute LC50s was not accepted by the meeting.

With regard to the long-term risk assessment the meeting agreed that time weighted PECs can be used only if the time to onset of effects is known. Hence the long-term risk assessment should be based on initial PECs. The RMS presented a new long-term TER calculation based on initial PEC_{sw} for Daphnids in addendum 2 (February 2006). The results suggest a high long-term risk to aquatic invertebrates even if a no-spray buffer zone of 50 m is applied.

The metabolite 1-naphtol is of similar toxicity to fish but is significantly less toxic to crustaceans compared to carbaryl. The long-term TERs for fish are 8.54 and 123 for a PEC_{sw} of 11.7 µg 1-naphtol/L (initial at 3 m) and 0.81 µg 1-naphtol/L (initial at 20 m). The risk from 1-naphtol to fish is significantly lower than the risk from carbaryl to aquatic arthropods. Hence the risk from 1-naphtol to fish is covered by risk mitigation measures for aquatic arthropods, e.g. large buffer zones. The meeting accepted the argumentation that 1-naphtol was formed in the test with *Lemna gibba* and that the endpoint from the Lemna study covers also potential effects of 1-naphtol.

The use of a long-term endpoint for fish from a published article was discussed and considered acceptable because fish toxicity is not driving the risk assessment. Hence a new study is dispensable.

The meeting proposed to take the awaited opinion of the PPR panel on the possibility of lowering the uncertainty factor into account. Based on the opinion⁷ the EFSA calculated geometric mean values⁸ for crustaceans and insects as 28.2 µg carbaryl/L and 40.76 µg carbaryl/L. The resulting TERs for a PEC_{sw} of 0.66 µg carbaryl/L (entry via spray drift, 50 m no spray buffer zone) for crustaceans and insects are 42.77 and 53.97. The TERs are below the Annex VI trigger value of 100 indicating a high acute risk to crustaceans and aquatic insects from the representative use of carbaryl.

Overall it is concluded that the representative use of carbaryl poses a high acute and long-term risk to crustaceans and aquatic insects.

⁷ Opinion of the Scientific Panel on Plant health, Plant protection products and their Residues on a request from EFSA related to the assessment of the acute and chronic risk to aquatic organisms with regard to the possibility of lowering the uncertainty factor if additional species were tested. (Question N° EFSA-Q-2005-042). *The EFSA Journal*(2005) 301, 1-45

http://www.efsa.eu.int/science/ppr/ppr_opinions/1332/ppr_op_ej301_aquatic_ecotox_en1.pdf

⁸ All endpoints from studies which were assessed as acceptable by the RMS and listed in Table 9.2.10.2-1b in addendum 2 of February 2006 were included. Only the lowest endpoint observed in three studies with *Mysidopsis bahia* was included in the geometric mean for crustaceans to avoid giving more weight to the endpoints observed for *Mysidopsis bahia* compared to the other tested species.

5.3. RISK TO BEES

The HQ values for bees were calculated as 4285 and 6429 for the risk from oral and contact exposure to carbaryl indicating a potential high risk to bees. The experts' meeting was concerned that the submitted field study was too short to address potential effects on the bee brood and the study design was such that it was not certain that bees had actually foraged in the treated crop. The meeting was content that the particular use poses no high risk to bees because the product is applied only once per year after flowering. For other uses reservations remained about the adequacy of the field study.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The risk assessment according to ESCORT 2 resulted in HQ values of 36437 and 5730 indicating a high in and off-field risk for *Aphidius rhopalosiphi*. The risk for *Typhlodromus pyri* was assessed as low. The tested insects were more sensitive than the tested mites and spiders. No mortality or sublethal effects were observed in extended laboratory studies with *T. pyri*, *Chrysoperla carnea* and *A. rhopalosiphi* after exposure to residues on foliage after 14 days of ageing showing the potential of recolonisation. However the off-crop HQ for *A. rhopalosiphi* indicated a high off-field risk. No spray buffer zones of more than 250 m would be required to protect non-target arthropods in the off-field area. No field studies were submitted. It is questionable if recolonisation of in-field areas from unaffected off-field areas is possible within one year taking the high off-field risk into account.

Overall it is concluded that a high risk to non-target arthropods cannot be excluded for the representative use. Further data (e.g. field studies) are required to address the potential high risk to non-target arthropods.

5.5. RISK TO EARTHWORMS

Several acute toxicity studies were conducted with *Eisenia foetida*. The TER values for this species were markedly above the trigger of 10. However, the first tier risk assessment indicated a high acute risk to *Allobophora caliginosa*. Two field studies were submitted to address the potential high risk to earthworms. Transient effects on earthworm populations were observed in two field studies. The meeting agreed to the assessment of the RMS presented in addendum 1 of June 2005 that no long-term effects on earthworms are expected from the representative use. The risk from 1-naphtol to earthworms was assessed as low.

The risk from the representative use posed to earthworms is considered to be low.

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

The field DT₉₀ for carbaryl was not determined. The DT₉₀ derived from laboratory studies was 328 days. The effects to soil micro-organisms were < 25% and the long-term risk to earthworms were assessed as low. However, the standard HQ for non-target arthropods of 2 was exceeded. Therefore a study with collembola or mites is triggered. The test should be conducted with collembola since mites were less sensitive compared to insects (see 5.4.). The EFSA proposes a data gap for a study with collembola to address the potential high risk to other soil non-target organism.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects of $> \pm 25\%$ on soil respiration and nitrification were observed in tests with technical and formulated carbaryl at dose rates equivalent to 5 times and 3.9 times the suggested application rate. Therefore the risk to soil non-target micro-organisms is considered to be low for the representative use of carbaryl.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

Only very slight effects for some plant species were observed in screening tests with the formulated product on seedling emergence and vegetative vigour of 12 monocotyl and 12 dicotyl plant species at a dose of about 4 times the suggested field rate. Effects of up to 14% reduction in dry weight of cucumber, soybean and tomato were observed in a second study with six different crops at the proposed application rate of 900 g carbaryl/ha. However, the observed effects were less than 50 % and considering non-target plants in the off-field area which are exposed via spray drift and thus exposed to lower amounts of carbaryl the risk to non-target plants is considered to be low for the representative use.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

No consistent inhibitory effects on respiration of activated sewage sludge were observed at concentrations of 10 and 32 mg carbaryl/L. Inhibitory effects increased from 29 % to 45 % with the amount of applied carbaryl of 100 to 1000 mg carbaryl/L. The EC_{50} for inhibition of respiration of activated sewage sludge was extrapolated to 1232 mg carbaryl/L. Therefore no risk to biological methods of sewage treatment is anticipated from the representative use.

6. Residue definitions

Soil

Definitions for risk assessment: carbaryl and 1-naphthol

Definitions for monitoring: carbaryl

Water

Ground water

Definitions for exposure assessment: carbaryl and 1-naphthol

Definitions for monitoring: carbaryl

Surface water

Definitions for risk assessment: surface water carbaryl and 1-naphthol
sediment carbaryl

Definitions for monitoring: water carbaryl and 1-naphthol
sediment carbaryl

Air

Definitions for risk assessment: carbaryl

Definitions for monitoring: carbaryl

Food of plant origin

Definitions for risk assessment: sum of carbaryl, 4-hydroxycarbaryl and 5-hydroxycarbaryl expressed as carbaryl

Definitions for monitoring: carbaryl

Food of animal origin

Definitions for risk assessment: no residue definition needed due to low exposure of livestock

Definitions for monitoring: no residue definition needed due to low exposure of livestock

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
carbaryl	Low to medium persistence Single first order DT ₅₀ 2.3-98.7 days (20°C -10kPa soil moisture)	A potential acute risk was observed for one of the tested earthworm species. No long-term effects were detected in two field studies with earthworms. A potential high risk to other non-target macro-organisms (in particular with regard to soil dwelling insects) cannot be excluded. A data gap for a study with collembola was identified.
1-naphthol	Very low persistence Single first order DT ₅₀ 0.53 days (20°C -10kPa soil moisture)	The risk of 1-naphthol to earthworms was assessed as low.

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
carbaryl	Medium mobility K_{foc} 177-249 mL/g	No	Yes	Yes	Carbaryl is very toxic to aquatic arthropods. The risk to aquatic arthropods dwelling in surface water was assessed as high
1-naphthol	Medium mobility K_{doc} 245 mL/g	No	1-naphthol acts as a growth regulator for plants	R21/22: harmful in contact with skin and if swallowed R37/38 Irritating to respiratory system and skin R41, risk of serious damage to eyes.	The first tier risk assessment indicated a potential long-term risk to fish

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
carbaryl	Carbaryl is very toxic to aquatic arthropods. The acute and long-term risk to aquatic arthropods is high.
1-naphthol	The first tier risk assessment indicated a potential long-term risk to fish.



Air

Compound (name and/or code)	Toxicology
carbaryl	Harmful by inhalation (LC ₅₀ 2.43 mg/L)

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- Validated method of analysis for the relevant impurities in the formulation (data gap identified by RMS in DAR and confirmed by EPCO 35, September 2005; date of submission unknown; refer to chapter 1).
- Storage stability study where the relevant impurities are analysed before and after storage (date of submission unknown, data gap identified by EPCO 35 September 2005 see evaluation table; refer to chapter 1).
- Validated method of analysis for 1-naphthol in surface water with an appropriate limit of quantification (data gap identified by EFSA; date of submission unknown; refer to chapter 1).
- Supervised residue trials with analysis of 4- and 5-hydroxy carbaryl (data gap identified as a result of the inclusion of 4- and 5- hydroxyl carbaryl in the residue definition for risk assessment by the EPCO expert meeting; no submission date proposed by the notifier; refer to point 3.1.1).
- The long-term risk to insectivorous birds needs to be addressed (data gap identified at the EPCO experts' meeting in September 2005; date of submission unknown; refer to point 5.1).
- A refined risk assessment is required to address the acute risk to mammals from uptake of contaminated drinking water if the product is sprayed at the highest recommended concentration (data gap identified by EFSA; date of submission unknown; refer to point 5.1).
- The risk to aquatic invertebrates needs to be further addressed (data gap identified in the EPCO expert meeting; date of submission unknown; refer to point 5.2).
- Further data (e.g. field studies) are required to address the potential high in-field and off-field risk to non-target arthropods (data gap identified by EFSA; date of submission unknown; refer to point 5.4).
- A study with collembola is required to address the potential high risk to other soil non-target organism (data gap identified by EFSA; date of submission unknown; refer to point 5.6).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative use as a plant growth regulator as proposed by the applicant. The application method is by tractor mounted orchard sprayer with application to apple trees for the purpose of fruit thinning. The application rate is up to 0.9 kg of carbaryl per hectare. It should be noted that only the use as a plant growth regulator will be supported in the EU review programme. However, carbaryl is also an insecticide and acaricide.

The representative formulated product for the evaluation was Sevin XLR plus, a suspension concentrate (SC) containing 480 g/L carbaryl, formulations are also registered under different trade names in Europe.

In the main adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined by HPLC with fluorescence detection.

Carbaryl can not be analysed by any currently available published monitoring methods due to the nature of the residues. For the other matrices only single methods are available for the same reasons as given above. For water and soil the method is HPLC with fluorescence detection and air is by HPLC-MS/MS. The method of analysis does not analyse for all components of the residue definition in surface water and therefore further data will be required to validate it for the compound 1-naphthol. Methods to determine residues of carbaryl in products of animal origin or for body foods and tissues are not required because no MRLs will be set for products of animal origin and carbaryl is not classified as toxic or very toxic.

Sufficient methods of analysis for carbaryl and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. However, methods of analysis are not available for the relevant impurities in the formulation and the current storage data are not acceptable as the relevant impurities were not analysed for before and after storage.

Carbaryl is harmful if swallowed (oral LD₅₀ 614 mg/kg bw) and by inhalation (LC₅₀ 2.43 mg/L); it has a low acute dermal toxicity (dermal LD₅₀ higher than 5000mg/kg bw). Carbaryl is not irritant to skin and eyes and it is not a skin sensitiser. The following classification was proposed: Harmful, R20 'Harmful by inhalation' and R22 'Harmful if swallowed'. The critical effect in short and long term studies was the inhibition of cholinesterase activity. The weight of evidence indicates that carbaryl is not an *in vivo* genotoxic agent. In mice and rats, carbaryl was found to be carcinogenic; classification with R40 'Limited evidence of a carcinogenic effect' or R45? 'May cause cancer' was discussed and agreed on to be forwarded to ECB. Carbaryl did not show any potential for reproductive and developmental toxicity. The ADI is 0.0075 mg/kg bw/day (safety factor of 2000 because of the carcinogenicity issue); the AOEL and ARfD are 0.01 mg/kg bw/day (safety factor 100). Operator exposure is below the AOEL when estimated with German model and considering the use of PPE like gloves during mixing/loading and hood, visor, coverall and sturdy footwear during application.

The metabolism of carbaryl has been investigated in four crop groups, allowing the elucidation of the degradation pathway of the compound, which includes methyl and ring hydroxylation, carbamate ester hydrolysis and N-demethylation. Most of the metabolites formed may be further conjugated to form water-soluble glycosides. The metabolic pattern of carbaryl is evolving with time. For long PHIs the available data suggest that relevant metabolites can be present at levels representing a possible significant contribution to the toxicological burden. For the use of carbaryl for apple thinning, with a PHI of 80 days, 2 metabolites, 4- and 5-hydroxy carbaryl, which are cholinesterase inhibitors, are expected to be present in amounts of the same order of magnitude as the parent compound. Therefore these metabolites were included in the residue definition for risk assessment. Supervised residue trials were carried out with analysis of parent compound only. This allows proposing the MRL for apple to be set below the Limit of Quantification of 0.05 mg/kg, but a robust risk assessment is not possible to be conducted as information on the actual level at harvest of the 2 hydroxy metabolites is lacking. Considering that the exposure to the parent compound only is close to 50% of the ARfD for some

specific population sub-groups, it cannot be excluded that the contribution of the metabolites leads to a global exceedence of the ARfD for those sub-groups.

Residues in succeeding crops, in processed commodities and in animal products are not expected.

The available information on the fate and behaviour of carbaryl in the environment is considered sufficient to complete an appropriate EU level environmental exposure assessment. Whilst based on annex II data requirements, one of the laboratory degradation results would trigger field soil dissipation studies and these are not available, it is considered that having field data would not significantly increase the reliability of the environmental exposure assessment in this particular case. The available surface water exposure assessment just considered the spray drift route of entry to surface water. The potential exposure of surface water with parent carbaryl via the drainage and runoff routes of entry has not been assessed in the available EU level exposure assessment. Member states should therefore carry out a surface water exposure and consequent aquatic risk assessment for carbaryl from the runoff and drainage routes of exposure to surface water at the national level, should carbaryl be included in annex 1.

Appropriate FOCUS groundwater modelling indicated that for the applied for intended use on apples leaching to groundwater above the parametric drinking water limit (0.1µg/L) would not be expected for either carbaryl or its potential major soil metabolite 1-naphthol.

A high long-term risk to insectivorous birds and a high acute and long-term risk to herbivorous mammals were identified in a first tier risk assessment. The submitted information was not sufficient to address the potential high risk to insectivorous birds in orchards. A refined risk assessment based on residue decline was not accepted to refine the acute risk to herbivorous mammals. For the long-term risk assessment more information was requested on how the DT₅₀ value for the residue decline was calculated. This information was included in addendum 2 of February 2006. The EFSA considers the information as sufficient and considers the long-term risk to herbivorous mammals as low. However, the potential high acute risk to herbivorous mammals needs to be addressed.

Carbaryl is very toxic to aquatic arthropods. The submitted microcosm study was assessed by the RMS as not being of use in deriving an EAC value since the exposure regime was representative only for aquatic habitats with very basic pH conditions where carbaryl degrades very rapidly. The proposed probabilistic approach was discussed by the EPCO experts' meeting. Uncertainty remained on which endpoints were used to construct the SSD. The splitting of data as suggested by the applicant would only be accepted if data fall into discrete groups based on sensitivity. The meeting considered the proposed trigger of 1 based on acute LC₅₀ values as not acceptable. Based on the PPR opinion the EFSA calculated the TER values for insects and crustaceans. The TERs are still below the trigger of 100 even if a no-spray buffer zone of 50 m is taken into account for the PEC_{sw} calculation indicating a high acute risk. Overall it is concluded that the representative use of carbaryl poses a high acute and long-term risk to crustaceans and aquatic insects.

Although carbaryl is very toxic to bees, the meeting was content that the representative use does not pose a high risk to bees because it is applied only once a year after flowering. A high in-field and off-

field risk to non-target arthropods (particularly with regard to insects) was indicated. Further data e.g. field studies are needed to show recovery of non-target insects in fields. Since the DT₉₀ of carbaryl was in the range of 100 to 365 days and the standard HQ for non-target arthropods was exceeded a study with other soil non-target macro organisms is needed.

Particular conditions proposed to be taken into account to manage the risk(s) identified

- Estimated operator exposure is below the AOEL considering the use of PPE like gloves during mixing/loading and hood, visor, coverall and sturdy footwear during application.

Critical areas of concern

- A threshold for vascular tumours in the liver and spleen in mouse was not identified. Classification of R40 or R45 was discussed in the expert meeting.
- A robust risk assessment for the safety of the consumer is not possible due to the lack of information on the actual levels of 4- and 5-hydroxy carbaryl in apples. Considering that the exposure to the parent compound only is close to 50% of the ARfD for some specific population sub-groups, it cannot be excluded that the contribution of the metabolites leads to a global exceedence of the ARfD for those sub-groups.
- A high long-term risk to insectivorous birds and a high acute risk to herbivorous mammals.
- A high acute and chronic risk to aquatic invertebrates which require considerable risk mitigation measures (with 50 m no-spray bufferzone, the TER is still below the trigger).
- A high risk to non-target arthropods (particularly with regard to insects) which require considerable risk mitigation measures, e.g. no-spray buffer zones of more than 250 m would be required to protect non-target arthropods in the off-field area.

APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

(Abbreviations used in this list are explained in appendix 2)

Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡

Carbaryl

Function (e.g. fungicide)

Insecticide, acaricide and plant growth regulator.

Rapporteur Member State

Spain

Co-rapporteur Member State

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Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡

1-Naphthyl *N* - methylcarbamate

Chemical name (CA) ‡

1-Naphthalenyl- methylcarbamate

CIPAC No ‡

26

CAS No ‡

63-25-2

EEC No (EINECS or ELINCS) ‡

200-555-0

FAO Specification ‡ (including year of publication)

Specifications comply with FAO specification 26/TC/S (year 1989):

Carbaryl: 980 g/kg ± 20 g/kg

2-naphthol: 0.5 g/kg

2-naphthyl methylcarbamate: 0.5 g/kg

Lose on vacuum drying: 10 g/kg

Minimum purity of the active substance as manufactured ‡ (g/kg)

990 g/kg

Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)

2-Naphthol, maximum content 0.5 g/kg,
2-naphthyl methylcarbamate, maximum content 0.5 g/kg

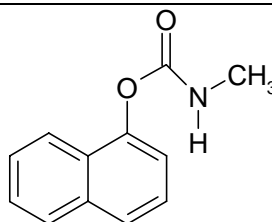
Molecular formula ‡

C₁₂H₁₁NO₂

Molecular mass ‡

201.2

Structural formula ‡



‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	138.0 ± 0.2°C (purity: 99.1%)
Boiling point (state purity) ‡	210°C (mean boiling point by Differential Scanning Calorimetry), 212.0 ± 0.2°C (boiling point by photocell detection method) (purity: 99.1%)
Temperature of decomposition	254°C: start of the exothermal decomposition (purity: 99.1%)
Appearance (state purity) ‡	White powder (purity: 99.1%)
Relative density (state purity) ‡	1.21 ± 0.01 at 20°C (purity: 99.1%)
Surface tension	65.5 mN/m (90% water saturated solution at 20°C) (purity: 99.1%)
Vapour pressure (in Pa, state temperature) ‡	4.16 x 10 ⁻⁵ ± 4.51 x 10 ⁻⁶ Pa at 23.5°C (purity: 99.1%)
Henry's law constant (Pa m ³ mol ⁻¹) ‡	9.2 x 10 ⁻⁵ Pa m ³ mol ⁻¹ @ 20°C
Solubility in water ‡ (g/L or mg/L, state temperature)	pH 4: 9.4 ± 0.2 mg/L
	pH 7: 9.1 ± 0.3 mg/L
	pH 9: 7.2 ± 0.3 mg/L at 20±0.5°C (purity: 99.1%)
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	n-Heptane: 0.25g/L
	Xylene: 9.86 g/L
	1,2-Dichloroethane 100-120 g/L
	Methanol: 75-100 g/L
	Acetone: 150-200 g/L
	Ethylacetate: 75-100 g/L
	Acetonitrile: 100-120 g/L
	Dimethylsulfoxide: > 600 g/L at 20 ± 0.5 °C (purity: 99.1%)
Partition co-efficient (log POW) ‡ (state pH and temperature)	Carbaryl: 2.36 ± 0.012 (RSD = 0.51%) at 23 °C ± 2°C in Milli-Q purified water (neutral pH) (purity: 99.8%)
	1-naphtol: 2.995 ± 0.02 (RSD = 0.7%) at 23 °C. (purity: 99.8%)
Hydrolytic stability (DT ₅₀) ‡ (state pH and temperature)	pH 5: Stable
	pH 7: Degraded with half-life values of 12.5 and 11.6 days in both pH7 buffers.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

	pH 9: Degraded with half-life of 3.2 hours. (radiochemical purity >98%)																				
Dissociation constant ‡	$pK_a = 10.4 \pm 0.4$ (s), n=7. In solution in water, there is no dissociated species but carbaryl itself. Temperature: $24.3 \pm 0.1^\circ\text{C}$. (purity: 99.7%)																				
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ϵ at wavelength)	All findings are consistent with the compound structure. <table> <tr> <th>λ_{max}[nm]</th><th>ϵ[L·mol⁻¹·cm⁻¹]</th></tr> <tr> <td colspan="2"><u>neutral water</u></td></tr> <tr> <td>220</td><td>82696</td></tr> <tr> <td>270</td><td>5743</td></tr> <tr> <td>279</td><td>6434</td></tr> <tr> <td>291</td><td>4211</td></tr> <tr> <td colspan="2"><u>acidic MeOH:</u></td></tr> <tr> <td>221.5</td><td>18362</td></tr> <tr> <td>280.0</td><td>6703</td></tr> <tr> <td>295</td><td><2743.</td></tr> </table> <p><u>Modifications of the spectrum were observed in basic medium, due to the hydrolysis of carbaryl in 1-naphthol.</u></p>	λ_{max} [nm]	ϵ [L·mol ⁻¹ ·cm ⁻¹]	<u>neutral water</u>		220	82696	270	5743	279	6434	291	4211	<u>acidic MeOH:</u>		221.5	18362	280.0	6703	295	<2743.
λ_{max} [nm]	ϵ [L·mol ⁻¹ ·cm ⁻¹]																				
<u>neutral water</u>																					
220	82696																				
270	5743																				
279	6434																				
291	4211																				
<u>acidic MeOH:</u>																					
221.5	18362																				
280.0	6703																				
295	<2743.																				
Photostability (DT ₅₀) ‡ (aqueous, sunlight, state pH)	pH = 5: 25 °C DT ₅₀ : 9.9 days ($r^2 = 0.98$), assuming first order kinetic and based on experimental conditions of 12 hour light/dark cycles. 1-Naphthol is a minor degradation product ¹⁴ CO ₂ representing an average of 30.2% AR (radiochemical purity >98%)																				
Quantum yield of direct phototransformation in water at $\lambda > 290$ nm ‡	2.67×10^{-3} .																				
Flammability ‡	Not a readily combustible solid (purity: 99.1%)																				
Explosive properties ‡	No explosive (purity: 99.1%)																				

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



Appendix 1 – list of endpoints

List of representative uses evaluated*

Crop and/or situation	Member State or Country	Product name	F G or	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
					Type	Conc. of a.s.	method kind	growth stage & season	number min max	interval between applications (min)	kg a.s./hl	water l/ha	kg a.s./ha	(l)	(m)
(a)			(b)	(c)	(d-f)	(i)	(f-h)	(j)	(k)		min max	min max	min max		
Apple	North and South Europe	Sevin XLR plus	F	Apple thinning after flowering	SC	480 g/L	High volume spray	End of flowering BBCH 71-72	1	-	0.06-0.09	1000-1500	0.9	80	[1] [2]

[1] The risk assessment has revealed a risk (exceedance of relevant threshold) in section 5.

[2] A robust risk assessment for the safety of the consumer is not possible due to the lack of information on the actual levels of 4- and 5-hydroxy carbaryl in apples. Considering that the exposure to the parent compound only is close to 50% of the ARfD for some specific population sub-groups, it cannot be excluded that the contribution of the metabolites leads to a global exceedance of the ARfD for those sub-groups

Remarks:	*	Uses for which risk assessment could not been concluded due to lack of essential data are marked grey	(h)	Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
	(a)	For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)	(i)	g/kg or g/L
	(b)	Outdoor or field use (F), glasshouse application (G) or indoor application (I)	(j)	Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
	(c)	e.g. biting and suckling insects, soil born insects, foliar fungi, weeds		
	(d)	e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989		
	(f)	Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench	(l)	PHI - minimum pre-harvest interval
	(g)	All abbreviations used must be explained	(m)	Remarks may include: Extent of use/economic importance/restrictions

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.2: Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (principle of method)	<p>CIPAC Method: Liquid Chromatography method using an UV detector (CIPAC Method)</p> <p>AL042/01-1. Reversed phase isocratic HPLC with UV detection. Quantification external standard of certified reference substance of AE F054158</p>
Impurities in technical as (principle of method)	<p>Gradient profile HPLC method</p> <p>AL040/01-1 employing a reversed stationary phase and UV detection. Quantification external standard of certified substances.</p> <p>Confirmatory method by HPLC/DAD</p>
Plant protection product (principle of method)	<p>C-989-02-99. Standard and sample solutions (5 µL) are injected twice in the HPLC-UV system (Column: Nucleosil C18, 12.5 cm, Eluent: Acetonitrile/Water (55:45), Tcolumn = 40 °C, UV 1 = 280 nm). Amount of active ingredient is calculated by comparison of peak areas of Carbaryl peak in standard and samples.</p> <p><i>Data gap: method for the determination of impurities in the formulated product.</i></p>

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	<p>Method: AR 269-01: apples, apple juice and olives. extraction of carbaryl residues with dichloromethane. HPLC equipped with post-column hydrolysis/derivatisation system and fluorescence detection on an octadecyl column. Quantification is done by external standardisation. The qualitative confirmatory test was performed for apples and apple juice by HPLC equipped with post-column hydrolysis / derivatisation system and fluorescence detection on a phenyl column (column of different polarity). LOQ is 0.01 mg/kg</p> <p>An independent laboratory validation of Method No AR-269-01 was performed.</p>
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Soil (principle of method and LOQ)	Method AR 287-01 : extraction of the soil sample with a 50:50 acetone:water solution and determination of carbaryl residues by HPLC (Isocratic: water 50 % - methanol 50 %; Column: Puresil C18, Waters; 40 °C) with a post-column hydrolysis and fluorescence detection system. LOQ = 0.005 mg/kg.
Water (principle of method and LOQ)	Method AR 281-01 : hydrolysis and determination of carbaryl residues by liquid chromatography on an octadecyl column using fluorescence detection system. Quantification is made through external standardisation. LOQ = 0.10 µg/L for surface and drinking water. <i>Data gap: method required for 1-naphthol in surface water.</i>
Air (principle of method and LOQ)	Method AR 270-01 : Air was sucked through XAD [®] adsorption tubes at about 1.4 L/min for 6 hours for a total air sampling volume of 0.5 m ³ . The adsorption Tmaterial was extracted with acetonitrile and the extract analysed by liquid chromatography with mass spectrometric detection (LC/MS/MS). A limit of quantification (LOQ) of 0.3 µg/m ³ was achieved for carbaryl residues in air.
Body fluids and tissues (principle of method and LOQ)	Not required

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None
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‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.3: Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism in mammals (Annex IIA, point 5.1)

Rate and extent of absorption ‡	Rapidly absorbed, about 91.5% within 24 hours based on urine (rat, 1 or 50 mg/kg bw)
Distribution ‡	Widely distributed, highest levels in the kidney at 7 days
Potential for accumulation ‡	No evidence of accumulation
Rate and extent of excretion ‡	Mainly via urine: about 91.5% within 24 hours.
Metabolism in animals ‡	Extensively metabolised. 2.9% of unchanged Carbaryl in urine. Three main metabolic pathways: Arene oxide formation with hydrolysis to dihydrodihydroxycarbaryl and glucuronide conjugation; Hydrolysis to form 1-naphthol and conjugation; Oxidation of N-methyl moiety (alkyl oxidation)
Toxicologically significant compounds ‡ (animals, plants and environment)	Carbaryl

Acute toxicity (Annex IIA, point 5.2)

Rat LD ₅₀ oral ‡	614 mg/kg bw, R22
Rat LD ₅₀ dermal ‡	>5000mg/kg bw
Rat LC ₅₀ inhalation ‡	2.4 mg/L for females, R20
Skin irritation ‡	Non-irritant
Eye irritation ‡	Non-irritant
Skin sensitization ‡ (test method used and result)	Non-sensitising (Maximisation test)

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Inhibition of brain and red blood cell cholinesterase activity
Lowest relevant oral NOAEL / NOEL ‡	<3.73 mg/kg bw/day, female dogs (1year, diet)
Lowest relevant dermal NOAEL / NOEL ‡	20 mg/kg bw/day, rats (5 days/week, 4 weeks)
Lowest relevant inhalation NOAEL / NOEL ‡	No data

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Genotoxicity ‡ (Annex IIA, point 5.4)

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No genotoxic potential

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡

Erythrocyte and brain cholinesterase inhibitions in rats and mice

Mice: Urinary bladder (intracytoplasmic droplets).

Lowest relevant NOAEL / NOEL ‡

10 mg/kg bw/day (2-year dietary study in rats)

LOAEL: 15 mg/kg bw/day (2-year dietary study in mice)

Carcinogenicity ‡

Rats: thyroid follicular adenomas and carcinomas (males), hepatocellular adenoma (females), carcinomas and adenomas in the urinary bladder (both sexes), a carcinoma in kidney (male) at 349 mg/kg bw/day.

Mice: vascular tumors at 15 mg/kg bw/day (males) (lowest dose tested). Renal tubular cell adenoma and carcinoma (males) and hepatocellular carcinoma and adenoma (female) and vascular tumors (females) at 1248 mg/kg bw/day.

R40, R45?

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡

Parental: reduced bodyweight and food consumption

Reproductive: reduction in pup numbers

Offspring: reduced pup survival

Lowest relevant reproductive NOAEL / NOEL ‡

Reproductive, parental and offspring NOAEL of 4.7 mg/kg bw/day

Two-generation study in rats

Developmental target / critical effect ‡

Reduction in maternal and foetal body weight, delayed ossification

Lowest relevant developmental NOAEL / NOEL ‡

NOAEL for maternal/development of 4 mg/kg bw/day (developmental study in rat)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Neurotoxicity / Delayed neurotoxicity ‡ (Annex IIA, point 5.7)

.....

Tremors, autonomic signs, inhibition of all types of cholinesterase activity.
Oral neurotoxicity NOAEL = 1 mg/kg bw/day (13-weeks; by gavage; rat)
No adverse effects on development neurotoxicity identified following exposure by the oral route
LOAEL = 10 mg/kg bw in acute neurotoxicity study
NOAEL = 10 mg/kg bw/day in developmental neurotoxicity study

Other toxicological studies ‡ (Annex IIA, point 5.8)

Mechanistic studies

Rats: a significant increase in the number of PCNA positive urothelial cells was seen in the urinary bladder of males, a slight increase in the number of cycling cells was observed in the thyroid glands of males and in the liver of females. Carbaryl did not modify the total liver cytochrome P-450 content, a small increase in CYP1A activity was observed at 40 mg/kg/day in males only. Carbaryl increased significantly T4 and T3-UGT in males (40 mg/kg/day) and females (10 and 40 mg/kg/day) (Phenobarbital like inducer profile). An increase in cells in G1 and S was observed at 10 (females) and 40 mg/kg/day (males and females). In conclusion, tumors in rats were compatible with a non-genotoxic potential of carbaryl, associated with prolonged cellular proliferation leading tumor formation after long-term exposure at high dose levels.

Mice: when carbaryl was administered to p53 knockout mice for 6 months at concentration ranged 0 to 4000 ppm) no neoplastic or preneoplastic changes were observed in the vascular tissue in any organ. Studies conducted with PCNA staining in liver and kidney showed an increased PCNA-positive cortical tubular cells in males and females at 8000 ppm, no increase in PCNA positive cells were observed in the liver. Carbaryl administration to mice for 2 weeks induced an increase in hepatic microsomal protein content, an elevated microsomal cytochrome P450 content, an increased EROD activity, and PORD activity as well as a slight increase in microsomal testosterone hydroxylation. These results identify carbaryl as a weak barbiturate type inducer in

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

mouse liver.

Metabolites 4-hydroxycarbaryl and 5-hydroxycarbaryl are likely to be ChE inhibitors; acute oral toxicity of 5-hydroxycarbaryl (LD50 297 mg/kg bw); LD50 values for 4-hydroxycarbaryl and 1-naphthol are 1190 mg/kg bw and 2590 mg/kg bw, respectively. The short-term toxicity of these metabolites was lower when compared to the parent compound carbaryl.

In vitro cholinesterase inhibition studies showed that 1-naphthol, 4- and 5-hydroxycarbaryl are also inhibitors of cholinesterase activity, with similar or higher IC50 values.

1-naphthol is a metabolite found in plants and animals, and it is also an impurity. According to European Chemical Information System 1-naphthol is classified as R21/22, harmful in contact with skin and if swallowed, R37/38 Irritating to respiratory system and skin and R41, risk of serious damage to eyes.

1-naphthyl 2,4-dimethyl allophanate is an impurity. A DEREK analysis indicates that it does not pose any concerns.

Medical data ‡ (Annex IIA, point 5.9)

.....

Epidemiological studies of exposed populations were inconclusive. Scarce fatal cases of poisoning. Treatment with oximes is contraindicated when carbaryl poisoning

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.0075mg/kg bw/day	2 year study mouse study (based on LOAEL for tumours)	2000*
AOEL ‡	0.01mg/kg bw/day	13-week rat neurotoxicity study	100
ARfD ‡ (acute reference dose)	0.01mg/kg bw/day	13-week rat neurotoxicity study	100

* an additional safety factor was considered due to the use of LOAEL to derive the reference value

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



Dermal absorption (Annex IIIA, point 7.3)

Sevin XLR Plus

0.5% for concentrate and 10% for dilution, based on in vivo rat and in vitro rat/human

Acceptable exposure scenarios (including method of calculation)

Operator

Tractor-mounted/trailed broadcast air-assisted sprayer

Citrus, pome fruit, olive tree

Workers

Bystanders

75% AOEL (PPE) BBA Model
1300% AOEL (PPE) UK-POEM
PPE: Gloves ML & applic. hood and visor,
Coverall and sturdy footwear in application

81% AOEL
pre-harvest interval recommended:
-Apple: 80 days
-Citrus, Olive: 7-14 days

60% AOEL

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data

Xn;	Harmful
R20/R22	Harmful if swallowed and by inhalation
R40	Limited evidence of a carcinogenic effect
R45?	May cause cancer

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



Appendix 1.4: Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Lettuce (leafy crops), radish (root and tuber), soybean (oilseeds) and apples (fruits)
Rotational crops	Not required (supported use apple thinning)
Plant residue definition for monitoring	Carbaryl
Plant residue definition for risk assessment	Sum of carbaryl, 4-hydroxy carbaryl and 5-hydroxy carbaryl, expressed as carbaryl (valid for apples only)
Conversion factor (monitoring to risk assessment)	Cannot be determined on the basis of the available information

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Not required (supported use apple thinning)
Animal residue definition for monitoring	
Animal residue definition for risk assessment	
Conversion factor (monitoring to risk assessment)	
Metabolism in rat and ruminant similar (yes/no)	
Fat soluble residue: (yes/no)	

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

.....	Not required (supported use apple thinning)
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Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 introduction)

.....	Stable on apples, olives, olive oil for 2 years at -20 °C.
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Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: no	Poultry: no	Pig: no
Muscle	Not required (supported use apple thinning)		
Liver			
Kidney			

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



Fat

Milk

Eggs



Note: Based on current information, only a realistic expectation can be made that the intake by animal of all toxicologically relevant residual compounds is < 0.1 mg/kg diet. A final and fully reliable exposure assessment of livestock will only be possible when quantitative data on the amount of 4- and 5-OH carbaryl in apple pomace will be available.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



Appendix 1 – list of endpoints

Summary of critical residues data (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a) mg carbaryl/kg	Recommendation/comments	MRL	STMR (b)
Apple	N	5 X < 0.01; 2 X < 0.05	This table reports residue levels of carbaryl only as only the parent compound was analysed in the reported residue trials. A full package of supervised residue trials with analysis of carbaryl and its 2 hydroxy metabolites should be submitted.	0.05* mg/kg	0.01
	S	2 X < 0.05		0.05* mg/kg	0.05

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17

(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.0075 mg/kg bw/d
TMDI (% ADI) according to WHO European diet	0.4% (European adult)
TMDI (% ADI) according to national (to be specified) diets	6% (UK diet for toddlers), 2% (German diet for the 4-6 years old girl), 0.8% (Spanish diet for adults)
ARfD	0.01 mg/kg bw/d
NESTI (% ARfD) according to national (to be specified) large portion consumption data	United Kingdom: Infants: 36% Toddlers: 49%

Note: all these exposure assessments (acute and chronic) were made considering the contribution of the parent compound only). They may therefore underestimate the actual toxicological burden.

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Not required. Supervised residue trials showed no residue situation			

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Apple	0.05* mg/kg
-------	-------------

*: LOQ

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.5: Fate and Behaviour in the Environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡	15-58.4% after 100 d, [1-naphthyl-methylcarbamate]-label (n= 4) 59.7 % after 14 d, [1-naphthyl- methylcarbamate]-label (n= 1) Sterile conditions: no data
Non-extractable residues after 100 days ‡	20-39% after 100 d, [1-naphthyl-methylcarbamate]-label (n= 4) max .64% at 21 days (n=1) 17.7 % after 14 d, [1-naphthyl- methylcarbamate]-label (n= 1) Sterile conditions: No data
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	1-Naphthol- 34.6 % at 2d (n= 1) <2% in the other 4 soils tested

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡	Mineralisation – 12.4 % after 126d Non-extractable residues 23.6 % after 126 d [1-naphthyl- methylcarbamate]-label (n= 1) carbaryl 21.7% at 126 d Metabolites 1-naphthol –max 26.3% at 94 d [1-naphthyl- methylcarbamate]-label (n= 1)
Soil photolysis ‡	Soil: well structured at 20°C and 75% of 1/3 bar water holding capacity No significant photodegradation was observed at the end of the study: CO ₂ : 0.6 % AR at the end of the study Unextracted residues: 6.9% at the end of the study Carbaryl: 93.6% at the end of the study 1-naphthol: 1.1% at the end of the study

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies

DT₅₀ values

Carbaryl

Study	Soil code	Soil type	pH	GWC @ pF2	Incub T ^a (°C)	Incub Moist % v/v	Model	Exp DT ₅₀ (d)	R ²	Norm. DT ₅₀ @ pF2 and 20°C (d)
7.1.1.1.1/01	N Carolina	Sandy loam	6.7	19 ¹	25	5.08	SFO ²	4.0	0.7	2.3
7.1.1.2.1.1/01	Texas	Sandy loam	7.8	19 ¹	25	18.53	SFO	9.1	0.97	13.0
7.1.1.2.1.1/01	Texas	Sandy loam	7.8	19 ¹	15	18.53	SFO	11.9	0.95	8.0
7.1.1.2.1.1/01	California	Silty clay loam	8.1	3	25	24.75	SFO	25.2	0.98	31.9
7.1.1.1.1/02	02/02	Sandy loam	5.8 ³	14.5	20	16.2	SFO	22.4	0.934	22.4
7.1.1.1.1/02	02/03	Sandy loam	4.1 ³	22.7	20	22.6	SFO	99	0.93	98.7
7.1.1.1.1/02	02/05	Loam	6.9 ³	36.4	10	24.2	SFO	80.9	0.961	27.8
7.1.1.1.1/02	02/05	Loam	6.9 ³	36.4	20	24.2	SFO	30.4	0.937	22.8
7.1.1.1.1/02	02/06	Clay loam	7.6 ³	41.6	20	29.7	SFO	7.08	0.83	5.6
Arithmetic mean									25.8	
Geometric mean									15.8	

1 Wosten et al 1998; PETE as presented in FOCUS (2000)

2 The DT₅₀ calculated by the applicant using TopFit was 1.8 d (r² 0.802) that normalized at 20°C and FC gave a value of 1.7 d However this small difference in 1 value is not considered to have an impact on the arithmetic mean result that was used in FOCUS GW modelling.

3 pH measured in CaCl² solution

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

1-Naphthol

Study	Soil code	Soil type	pH	GWC @ pF2	Incub T ^a (°C)	Incub Moist % v/v	Model	Exp DT ₅₀ (d)	R ²	Norm. DT ₅₀ @ pF2 and 20°C (d)
7.1.1.1.1/01	N Carolina	Sandy loam	6.7	19 ¹	25	5.08	SFO ²	0.9	0.76	0.53

1 Wosten et al 1998; PETE as presented in FOCUS (2000)

2 The applicant calculated a DT₅₀ using TopFit of 0.6 d ($r^2=0.802$) that normalized at 20°C and FC gave a value of 0.35 d However these small differences were not considered to have an impact on the result of FOCUS GW modelling where 0.6 days was used.

DT₉₀ values

Carbaryl

Study	Soil code	Soil type	pH	Incub T ^a (°C)	Incub Moist % v/v	Model	Exp DT ₉₀ (d)	R ²
7.1.1.1.1/01	N Carolina	Sandy loam	6.7	25	5.08	SFO	13.29	0.7
7.1.1.2.1.1/01	Texas	Sandy loam	7.8	25	18.53	SFO	30.23	0.97
7.1.1.2.1.1/01	Texas	Sandy loam	7.8	15	18.53	SFO	39.53	0.95
7.1.1.2.1.1/01	California	Silty clay loam	8.1	25	24.75	SFO	83.71	0.98
7.1.1.1.1/02	02/02	Sandy loam	5.8 ³	20	16.2	SFO	74.41	0.934
7.1.1.1.1/02	02/03	Sandy loam	4.1 ³	20	22.6	SFO	328.57	0.93
7.1.1.1.1/02	02/05	Loam	6.9 ³	10	24.2	SFO	268.74	0.961
7.1.1.1.1/02	02/05	Loam	6.9 ³	20	24.2	SFO	100.99	0.937
7.1.1.1.1/02	02/06	Clay loam	7.6 ³	20	29.7	SFO	23.52	0.83

1 Wosten et al 1998; PETE as presented in FOCUS (2000)

3 pH measured in CaCl₂ solution

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

1-Naphthol

Study	Soil code	Soil type	pH	Incub T ^a (°C)	Incub Moist % v/v	Model	Exp DT ₉₀ (d)	R ²
7.1.1.1.1/01	N Carolina	Sandy loam	6.7	25	5.08	SFO	2.99	0.76

Anaerobic conditions

DT_{50lab} (25°C, anaerobic): 72.2 d (n= 1, r²= 0.93).Linear. 1st order kinetics.

degradation in the saturated zone ‡: No data submitted, no data required

Field studies ‡ (state location, range or median with n value)

Data not available, formally data triggered. However considered not required to complete the EU level environmental exposure assessment.

Soil accumulation and plateau concentration ‡

No data

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Carbaryl

Kf/Koc (mL/g)

	Soil proprieties		Adsorption				Desorption			
	pH	%OC	K _f	K _{oc}	1/n	r ²	K	K _{oc}	1/n	r ²
Sandy Loam	5.3	0.84	1.74	207	0.84	0.997	6.72	800	1.016	0.999
Silty Clay Loam	6.7	1.99	3.52	177	0.797	0.999	7.66	385	0.858	0.997
Silt Loam	6.7	1.42	3.00	211	0.784	1.000	6.89	485	0.861	0.998
Sediment	7.5	0.82	2.04	249	0.835	0.999	6.78	827	0.949	1.000
Mean			2.58	211	0.813	1.000	7.01	624	0.920	1.000

Kd ‡

pH dependence ‡ (yes / no) (if yes type of dependence)

Not required

No

Kf was positively correlated with the percent of organic matter (r²=0.97).

1-naphthol

Koc:

245 mL/g (HPLC method)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡	No data
Aged residues leaching ‡	<p>Guideline: Pesticide Assessment Guidelines, Subdiv. N, Section 163-1</p> <p>Aged for (d): Time period (d): 7-13 d Precipitation (mm): 50.8 mm Leachate: 2-4 % total residues/radioactivity in leachate</p> <p>>74.8-89.0% total residues/radioactivity retained in top 6 cm</p>
Lysimeter/ field leaching studies ‡	No data

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	<p>DT₅₀ (d): 99 days Kinetics: 1st order Field or Lab: representative worst case from laboratory studies.</p>
Application rate	<p>Crop: apples % plant interception: 70 Number of applications: 1 Interval (d): <i>n.a</i> Application rate(s): 900 g a.s./ha</p>

PEC _(s) (mg/kg)	70% crop interception	
	Single application Actual	Single application Time weighted average
Initial	0.360	0.360
Short term 24 h	0.357	0.359
2 d	0.355	0.357
4 d	0.350	0.355

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

PEC _(s) (mg/kg)	70% crop interception	
	Single application Actual	Single application Time weighted average
Long term 7 d	0.343	0.351
14 d	0.326	0.343
21 d	0.311	0.335
28 d	0.296	0.327
50 d	0.254	0.304
100 d	0.179	0.259

1-naphthol

Method of calculation

Application rate

Kinetics: first order kinetics.

Crop: apples

% plant interception: 70%

Number of applications: 1

Interval (d): *n.a*

Application rate(s): 900 g a.s./ha (assumed 1-naphthol is formed at a maximum of 34.6% the applied dose)

PEC _(s) (mg/kg)	70% crop interception	
	Single application Actual	Single application Time weighted average
Initial	0.089	

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolysis of active substance and relevant metabolites (DT₅₀) ‡

(state pH and temperature)

pH5: 25 °C DT₅₀ negligible at 30 d

pH7: 25 °C DT₅₀ 12 d (1st order, r²=0.99)

1-naphthol: 76.02% AR (30 d)

pH9: 25 °C DT₅₀ 3 h (1st order, r²=0.99)

1-naphthol: 94.66% AR (2 d)

Photolytic degradation of active substance and relevant metabolites ‡

Study 1

Experimental conditions: buffer solution at pH 5 at 25 °C

Irradiation apparatus: Heraeus Suntest CPS+ with

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

a xenon arc lamp. With UV glass filter.

Sunlight intensity: 455 W/m² (for the 300-800nm region)

Exposure time and intensity in the sunset unit: The average solar energy at 40 °N lastitude is 4560 W/m².

Thus 10 h of artificial light irradiation is equivalent to one day of sunlight exposure.

Experimental DT₅₀: 9.9 d (r²= 0.98) for 12 h light/dark cycles.

Quantum yield: 2.67 x 10⁻³

Environmental half lives:

Theoretical Lifetime (days) at the Water Surface	Spring	Summer	Autumn	Winter
Latitude 30° N	13.2	11.0	19.8	32.1
Latitude 40° N	16.4	12.0	30.2	66.2
Latitude 50° N	22.2	13.9	113.8	193.7

Study 2

Identification of metabolites

Experimental conditions: buffer solution at pH 5

Irradiation apparatus: Suntest XLS+ unit containing a Heraeus xenon-arc lamp. Eliminated wavelengths < 290 nm.

Sunset Light intensity: 680 W/m² (290-800 nm)

Exposure time and intensity in the Sunset unit: Approximate natural solar radiation found in Phoenix, Arizona. Meteorological data obtained from the weather station (DSET Laboratories) in New River, AZ (June 23, 1988; Tilt angle: 5% South; Total radiant exposure:9.5MJ/m2)

7.0 h represents 1 environmental day, 216 h of continuous irradiation at 680 W/m2 is equivalent to 30.8 environmental days

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



	<p>Experimental DT₅₀: 16.2 d</p> <p>Environmental DT₅₀:</p> <p>55 of solar summer days at Phoenix (New River Arizona, USA)</p> <p>81.8 of solar summer days in Athens, Greece).</p> <p>Incubation conditions: 25° C</p> <p>No metabolites > 10% were identified at the end of the study:</p> <p>Phthalic acid: 6.4 % AR</p> <p>Phthalic acid hydrated: 6.3% AR</p> <p>Metabolite A: 6.2 % AR</p> <p>Metabolite G 3.9% AR</p> <p>Metabolite H: 4.6% AR</p>
Readily biodegradable (yes/no)	Yes
Degradation in water/sediment	
- DT ₅₀ water ‡	1.21- 5.0 days dissipation from the water column
- DT ₉₀ water ‡	4 –18.23 days (1st order, r2= 0.99-0.97, n= 2)
- DT ₅₀ whole system ‡	1.62-9.9 days
- DT ₉₀ whole system ‡	5.4-32.8 days (1st order, r2= 0.98-0.9, n= 2)
Mineralization	0.88% (at 30 d, study end, n= 1) 18.53-10.58 %AR (at 101 d, study end, n= 2)
Non-extractable residues	63.8% (at 30 d, study end, n= 1) 42.37-36.13% AR (at 101 d, study end, n= 2)
Distribution in water / sediment systems (active substance) ‡	Maximum of 23.66-23.57 %AR in sediment after 0-60 days. DT ₅₀ in sediment 4.3 days (DT90 13.8 days, 1st order, r2= 0.95, n= 1)
Distribution in water / sediment systems (metabolites) ‡	1-Naphthol: water: 34.73% (at -2 days, n= 2) sediment: 9.46 % (at 2 days, n=1)
PEC (surface water) (Annex IIIA, point 9.2.3)	
Parent	
Method of calculation	<p>DT₅₀ (d) in water phase: 5.0 days</p> <p>Kinetics: 1st order</p> <p>Lab: representative worst case from sediment water studies</p>

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Application rate

Crop: apples
 Number of applications: 1
 Interval (d): *n.a*
 Application rate(s): 900 g a.s./ha
 Depth of water body: 30 cm

Main routes of entry

Late season drift in line with GAP
 15.73% at 3 m
 1.09% at 20 m
 0.22% at 50 m

PEC(sw) (µg / L DAT)	3 m		20 m		50 m	
	Single application Actual	Single application TWA	Single application Actual	Single application TWA	Single application Actual	Single application TWA
0	47.19		3.27	3.27	0.660	0.660
24h	41.08	44.07	2.85	3.05	0.616	0.575
2	35.76	41.21	2.48	2.86	0.577	0.501
3	31.13	38.61	2.16	2.68		
4	27.1	36.22	1.88	2.51	0.507	0.380
7	17.88	30.2	1.24	2.09	0.423	0.251
10	11.8	25.53	0.82	1.77	0.358	0.166
14					0.292	0.096
15	5.9	19.86	0.41	1.38	x	x

PEC(sw) (µg / L DAT)	3 m		20 m		50 m	
	Single application Actual	Single application TWA	Single application Actual	Single application TWA	Single application Actual	Single application TWA
21	2.602	15.39	0.18	1.066	0.215	0.036
28					0.167	0.014
29	0.85	11.53	0.06	0.8		
30	0.74	11.17	0.00	0.77		
50						
60	0.01	5.67	0.00	0.39	0.096	0.000
90	0.00	3.78	0.00	0.26		
100	0.00	3.4	0.00	0.24	0.048	0.000

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



1-naphthol

Method of calculation	DT ₅₀ (d): not required to calculate an initial PEC when there is only 1 application per year. Kinetics: Lab: representative worst case from sediment water studies)
Application rate	Crop: apples Number of applications: 1 Interval (d): n.a Application rate(s): 900 g a.s./ha (assumed 1-naphthol is formed at a maximum of 34.73% of the applied dose in water) Depth of water body: 30 cm
Main routes of entry	15.73% drift from 3 metres 1.09 % from 20 m 0.22 % from 50 m
PEC _(sw) (µg / l)	Single application Actual
Initial at 3 m	11.7
Initial at 20 m	0.81
Initial at 50 m	0.16

PEC (sediment)

Parent

Method of calculation	(see below)	
Application rate	Crop: apples Number of applications: <i>1</i> Interval (d): <i>n.a</i> Application rate(s): <i>900</i> g a.s./ha	
PEC_(sed) (µg / L)	Single application Actual	Method of calculation
Initial at 3 m	11.13 µg/L	Taking into account an initial PEC _{sw} 47.19 ug/L with a buffer zone of 3 m and a maximum observed in the sediment 23.6% AR:

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

PEC _(sed) (µg / L)	Single application Actual	Method of calculation
Initial at 20 m	0.77 µg/L	Taking into account an initial PEC _{sw} 3.27 ug/L with a buffer zone of 20 m and a maximum observed in the sediment 23.6% AR:
Initial at 50 m	0.16 µg/L	taking into account an initial PEC _{sw} 0.66ug/L with a buffer zone of 50 m and a maximum observed in the sediment 23.6% AR:

PEC _(sed) (µg / kg)	Single application Actual	Method of calculation
Initial at 3 m	51.4 µg/kg	Considering a depth layer of 5 cm; bulk density =1.3 g/cc and an rate of entry in the water layer = 900x 15.73/100= 141.6 g/ha (buffer zone of 3 m) and considering a max amount of 23.6% AR:in the sediment
Initial at 20 m	2.31 µg/kg	Considering a depth layer of 5 cm; bulk density =1.3 g/cc and an rate of entry in the water layer = 900x 0.54/100= 4.9 g/ha (buffer zone of 20 m) and considering a max amount of 23.6% AR:in the sediment
Initial at 50 m	0.72 µg/kg	Considering a depth layer of 5 cm; bulk density =1.3 g/cc and an rate of entry in the water layer = 900x 0.22/100= 1.98 g/ha (buffer zone of 50 m) and considering a max amount of 23.6% AR:in the sediment

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (e.g. modelling, monitoring, lysimeter)

Inputs

For FOCUS gw modelling, values used –
PELMO 3.0 (Apples scenarios; BBCH growth stage 71-79; interception 70%)

Application rate: 900 g/ha (effective application rate 270 g/Ha)
No. of applications:1
Time of application (month or season):10 days after emergence
parent K_{foc}: 211 ml/g; 1/n exponenet: 0.81
parent DT₅₀: 25.7 days (mean of normalized data at FC and 20 °C)
1-naphthol K_{oc}: 245 ml/g (by HPLC method). 1/n=

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



	1.0 1-naphthol DT ₅₀ : 0.6 d (TopFit 2.0, 5 compartments, normalized at FC and 20°C).
PEC_(gw)	
Maximum concentration	< 0.001 µg/L
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	< 0.001 µg/L

PEC(gw) - FOCUS modelling results

	Scenario	Parent (µg/L)	Metabolite (µg/L)		
			1-naphthol	2	3
PELMO 3.0/Apples	Châteaudun ⁽¹⁾	< 0.001	< 0.001		
	Hamburg	< 0.001	< 0.001		
	Jokioinen	< 0.001	< 0.001		
	Kremsmünster	< 0.001	< 0.001		
	Okehampton	< 0.001	< 0.001		
	Piacenza ⁽¹⁾	< 0.001	< 0.001		
	Porto	< 0.001	< 0.001		
	Sevilla ⁽¹⁾	< 0.001	< 0.001		
	Thiva ⁽¹⁾	< 0.001	< 0.001		

(1) irrigation option

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡	Not studied
Quantum yield of direct phototransformation	Active substance: f 2.67 10 ⁻³ based on a concurrently irradiated (PNAP/PYR) actinometer
Photochemical oxidative degradation in air ‡	Half life 0.277 days assuming an atmospheric OH concentration of 1.5 x 10 ⁶ radicals cm ⁻³
Volatilization ‡	No data

PEC (air)

Method of calculation	No data
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‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



PEC_(a)

Maximum concentration

No data

Provisional Definition of the Residue (Annex IIA, point 7.3)

Residue definition for risk assessment

Soil and groundwater: carbaryl and 1-naphtol
Surface water carbaryl and, 1-naphtol

Sediment: carbaryl

Air: carbaryl

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)

No data

Surface water
(indicate
location and
type of study)

Location	µg/L	Number of samples	log µg/L	Sampling period
Spain (León)	< LOQ-0.2	2/40	0.03	Autumn
Italy	0.05	1	0.01	A year. Sampling were taken at 15 days intervals from March 1995
Spain (Valencia)	1231-6484	6/40	1.49- 0.482	once a month between April 1997 and September 1998
Spain (Huelva)	River: 0.7-0.4 (naphthol) wells: 1.2-0.2 (carbaryl) 4.8-0.6 (naphthol)		0.1-1	
Ioannina	0.001-0.038	23/97	-	1984 to Oct. 1985.

Ground water (indicate location and type of
study)

No data

Air (indicate location and type of study)

No data

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data

N; Dangerous for the environment

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.6: Effects on non-target Species

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Acute toxicity to mammals	<p><u>Oral</u> technical: LD₅₀: 614 mg/kg_{bw}/d (rat, male/female rats combined).</p> <p>Formulation*: LD₅₀: 300 mg a.s./kg_{bw}/d, rat, sex combined)</p> <p><u>Inhalation</u> LD₅₀ 2.43 mg/L (rat, female)</p>
Long term toxicity to mammals	<p>Oral NOAEL: 10.8 mg a.s./kg_{bw}/d (dog)</p> <p>Reproduction NOEL: 4.67 mg a.s./kg_{bw}/d (rat, 2nd generat.)</p> <p>NOEL: 31.34 mg a.s./kg_{bw}/d (rat, 1st generat.)</p>
Acute toxicity to birds	<p>Technical: LD₅₀ > 2000 mg a.s./kg_{bw} (Mallard duck)</p> <p>Formulation: Not required since it is considered that birds will be exposed primarily from the active residue substance not the spray formulation.</p> <p>Metabolites: No data</p>
Dietary toxicity to birds (short term)	<p>Technical: Bobwhite quail</p> <p>LC₅₀ > 1000 mg a.s./kg_{bw}/d (5000 mg a.s./kg_{food})</p> <p>Metabolites: No data</p>
Long term toxicity to birds	<p>Technical: Mallard duck</p> <p>NOEC 30 mg a.s./kg_{bw}/d (300 mg/kg diet)</p> <p>Metabolites: No data</p>
Reproductive toxicity to birds	<p>Technical: Mallard duck</p> <p>NOEC 30 mg a.s./kg_{bw}/d (300 mg/kg diet)</p>

* The acute risk assessment to mammals will be done with LD₅₀ 246 mg a.s./kg_{bw} for female (from LD₅₀ 575 mg formul/kg_{bw} female)

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Application rate (kg a.s./ha)	Crop	Category (e.g. insectivorous bird)	Time-scale	TER	Annex VI Trigger
Ground-feeding birds					
0.9	apple orchard	Large herbivorous	acute	118	10
0.9	apple orchard	Small insectivorous birds	acute	41	10
0.9	apple orchard	Earthworms feeding	acute	4360	10
0.9	apple orchard	Large herbivorous	Short term	110	10
0.9	apple orchard	Small insectivorous birds	short-term	36	10

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Application rate (kg a.s./ha)	Crop	Category (e.g. insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.9	apple orchard	Earthworm-feeding	short-term	2183	10
0.9	apple orchard	Large herbivorous	long-term and (reproduction)	6.2	5
0.9	apple orchard	Small insectivorous birds	long-term and (reproduction)	1.1	5
0.9	apple orchard	Earthworms feeding	long-term (reproduction)	65	5
Ground-feeding mammals					
0.9	apple orchard	Herbivorous mammals	acute	4.6	10
0.9	apple orchard	Earthworms-feeding mammals	acute	514	10
0.9	apple orchard	Herbivorous mammals	long-term	6.1	5
0.9	apple orchard	Earthworms-feeding mammals	long-term	8	5

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Laboratory tests ‡				
Fish				
Sheepshead minnow <i>Cyprinodon variegates</i>	Technical	Acute dynamic	96h LD ₅₀	2.60
Rainbow trout <i>Oncorhynchus mykiss</i>	Sevin (81.5 % a.s.)	Acute dynamic	96h LD ₅₀	0.61
Fathead minnow <i>Pimephales promelas</i>	Sevin (80% a.s.)	Chronic dynamic	34d NOEC	0.21
Bluegill sunfish	1-naphtol	Acute semistatic	96h LD ₅₀	0.75
Fathead minnow <i>Pimephales promelas</i>	1-naphtol	Chronic dynamic (early life stage)	34d NOEC	0.10
Invertebrates				
<i>Daphnia pulex</i>	Technical	Acute	48h EC ₅₀	0.0064
<i>Mysidopsis bahia</i> (marine)	Technical	Acute	LC ₅₀	0.0057

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
<i>Daphnia longispina</i> (with sediment)	Technical	Acute	48h EC ₅₀	0.0078
<i>Daphnia magna</i>	Technical	Chronic flow through	48h NOEC	0.0033
<i>Mysidopsis bahia</i> (marine)	1-naphtol	Acute	48h EC ₅₀	0.2
<i>Daphnia magna</i>	1-naphtol	Chronic	21d NOEC	0.25
Algae				
<i>Skeletonema sp.</i> (marine)	Technical	Acute	120 h EC ₅₀	0.70
<i>Skeletonema sp.</i>	Technical	Chronic	NOEC	0.36
Plant <i>Lemna gibba</i>	Technical	Acute static	7 d IrC50	13.70
<i>Lemna gibba</i>	Technical	Acute static	7 d-NOErC	5.0

Microcosm or mesocosm tests

An outdoor microcosm study provided evidence that exposure levels up to and including 20 µg/L carbaryl did not result in effects upon phytoplankton, macrophytes, fish and benthic macroinvertebrates. Unfortunately, it can't be employed to assess the risk due to the pH of water is very high (pH 9.2) and the DT₅₀ at this pH is too short comparing with the DT₅₀ at neutral pH.

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

Application rate (kg a.s./ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
0.9	apple orchard	Rainbow trout	96 hours	15	129	100
0.9	apple orchard	<i>Fathead minnow</i>	34 days	3	19	10
0.9	apple orchard	<i>Mysidopsis bahia</i>	48 h	20	1.7	100
0.9	apple orchard	<i>Daphnia magna</i>	21 days	20	1	10
				50	5	
0.9	apple orchard	Algae	72 hours	3	17	10
0.9	apple orchard	Higher aquatic plants	7 days	3	290	10

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Bioconcentration

Bioconcentration factor (BCF) ‡

BCF (whole fish)= 44

Not required log Pow = 2.36 and DT₉₀<100 days

Annex VI Trigger:for the bioconcentration factor

Not applicable

Clearance time (CT₅₀)
(CT₉₀)

Not required

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Acute oral toxicity ‡

Technical 72 h-LD₅₀ ≥ 0.21 µg a.s./bee

Formulation 72h-LD₅₀ > 1.08µg form./bee
(>0.69µg a.s./bee)

Acute contact toxicity ‡

Technical 72 h-LD₅₀ 0.14 µg a.s./bee

Formulation 72h-LD₅₀ > 3.84µg form./bee
(>1.69µg a.s./bee)

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Application rate (kg a.s./ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.9	apple orchard	oral	4285	50
0.9	apple orchard	contact	6429	50

Field or semi-field tests

The EPCO experts' meeting considered the risk to bees as low because the product is applied only once a year after flowering. For other uses reservations remain on the adequacy of the submitted field study.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Species	Stage	Test Substance	Dose (kg a.s./ha)	Endpoint	LR50* (g a.s./ha)	HQ	Annex VI Trigger
Laboratory tests							
<i>Aphidius rhopalosiphi</i>	adults	Sevin® XLR Plus	0.00213 - 0.05	Mortality	0.0247	3637 in field 5730 off field	2
<i>Typhlodromus pyri</i>	proto-nymphs	Sevin® XLR Plus	8.5 - 850	Mortality	457	0.31	2
<i>Pardosa sp.</i>	adults	Sevin® XLR Plus	850 and 28.9	Mortality	> 28.9	Not applicable	Not applicable
<i>Chrysoperla carnea</i>	larvae	Sevin® XLR Plus	1.1 - 22.83	Mortality	< 1.1	Not applicable	Not applicable
Extended laboratory tests							
<i>Chrysoperla carnea</i>	larvae	Sevin® XLR Plus	1.875 L product/ha	Mortality	0 DAA: lethal 14 DAA: NOEC	98% 16%	50%
<i>Typhlodromus pyri</i>	proto-nymphs	Sevin® XLR Plus	1.875 L product/ha	Mortality	0 DAA: lethal 14 DAA: NOEC	38% 6%	50%
<i>Aphidius rhopalosiphi</i>	adult	Sevin® XLR Plus	1.875 L product/ha	Mortality	0 DAA: lethal 14 DAA: NOEC	100% 0%	50%
				Reproduction	14 DAA: NOEC	3.5%	50%

*DAA: days after application.

Tier 2 off-crop HQ values for *Aphidius rhopalosiphi*

Specie	Substance	Distance from crop	Drift factor (%)	Drift rate (g a.s/ha)	LR50 (g a.s/ha)	HQ	Annex VI Trigger
<i>Aphidius rhopalosiphi</i>	adults	3 m	15.73	141.5	0.0247	5730	2
		50 m	0.22	1.98		80	
		150 m	0.03	0.27		10	
		250 m	0.006	0.171		2.1	

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



Field or semi-field tests
No data available

Effects on earthworms (Annex IIA, point 8.4, Annex IIIA, point 10.6)

Acute toxicity ‡

Technical:

A. caliginosa 14 days-LC₅₀ < 4 mg a.s./kg soil
(corrected <2 mg a.s./kg)

1-Naphtol:

E. fetida 14 days-LC₅₀ = 472mg /kg soil
(corrected <236 mg a.s./kg)

Reproductive toxicity ‡

NOEC: no submitted study but field study
provided.

Toxicity/exposure ratios for earthworms (Annex IIIA, point 10.6)

Application rate (kg a.s./ha)	Crop	Time-scale	TER	Annex VI Trigger
0.9	apple orchard	14 days	< 3.3	10

Field study

The canopy application of the plant protection product in apples for fruit thinning at a dose of 1.875L/ha resulted in a slight transient effect on the earthworms community due to the partial impact on *A. caliginosa* population. However, this effect was completely recovered after 4 months.

Effects on soil micro-organisms (Annex IIA, point 8.5, Annex IIIA, point 10.7)

Nitrogen mineralization ‡

< ±25% at a concentration of 6.5 mg a.s./kg soil

Carbon mineralization ‡

< ±25% at a concentration of 6.5 mg a.s./kg soil

Effects on non-target plants

.....

Under green house conditions Sevin (formulation) did not cause any significant impact on seedling Emergence and Vegetative Vigour of a great amount of different plants from different taxonomic groups at spray concentrations up to 13.89 g a.s./L (equivalent to 4.4 time the recommended application rate) when it is applied pre and post emergence.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles



Effects on biological methods for sewage treatment

.....

The EC50 was 1232 mg/L. Carbaryl has low toxicity to the respiration of activated sludge.

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data

N	Dangerous for the environment
R50	Very toxic to aquatic organisms

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT ₅₀	period required for 50 percent dissipation (define method of estimation)
DT ₉₀	period required for 90 percent dissipation (define method of estimation)
ϵ	decadic molar extinction coefficient
EC ₅₀	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K _{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC ₅₀	lethal concentration, median

LD ₅₀	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC _A	predicted environmental concentration in air
PEC _S	predicted environmental concentration in soil
PEC _{SW}	predicted environmental concentration in surface water
PEC _{GW}	predicted environmental concentration in ground water
PHI	pre-harvest interval
pK _a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10 ⁻⁶)
ppp	plant protection product
r ²	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year