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

# propamocarb

## finalised: 12 May 2006

(version of 3 July 2006 with minor editorial changes marked yellow)

## SUMMARY

Propamocarb is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. 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.

Ireland being the designated rapporteur Member State submitted the DAR on propamocarb in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 5 October 2004. Following a quality check on the DAR, the peer review was initiated on 14 October 2004 by dispatching the DAR for consultation of the Member States and the two applicants Bayer CropScience and Chimac Agriphar. 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 18 May 2005. The two notifiers informed the meeting that they had now formed a task force for the purpose of the active substance review. 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 6 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 uses as fungicide, which comprise foliar spraying, drenching or drip irrigation to control a broad spectrum of plant diseases in lettuce, potatoes, tomato (grown in soil and rock wool).
The application rates are:

[1] OJ No L 53, 29.02.2000, p. 25
[2] OJ No L 224, 21.08.2002, p. 25

- in lettuce 2 applications resulting in a maximum total dose of 144.4 kg propamocarb hydrochloride per hectare (drenching) and 2 applications resulting in a maximum total dose 3.32 kg per hectare (spraying)
- in potatoes up to 6 applications resulting in a maximum total dose of 6.498 kg per hectare (spraying)
- in tomatoes (soil grown) 2 applications resulting in a maximum total dose of 144.4 kg per hectare (drenching) and 2 applications resulting in a maximum total dose of 4.332 kg per hectare (drip irrigation)
- in tomatoes (rock wool grown) 1 application 28.9 kg per hectare (drenching) and 4 applications resulting in a maximum total dose of 8.664 kg per hectare (drip irrigation).

Only the use of propamocarb as a fungicide was evaluated.
The representative formulated products for the evaluation were "Previcur N" and "Proplant", both are soluble concentrate (SL), registered in most of the Member State of the EU.

Adequate methods are available to monitor all compounds given in the respective residue definition. Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues. It should be noted that the analytical methods are not able to differentiate between residue of propamocarb and its salts.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Propamocarb hydrochloride is of low acute oral, dermal and inhalation toxicity; it is not a skin or an eye irritant, but it is a skin sensitiser, as confirmed during the meeting on the basis of the positive results in the Magnusson & Kligman test and the recently submitted LLNA (R43 “May cause sensitisation by skin contact” is proposed). There is no evidence of genotoxicity or carcinogenic potential associated with propamocarb hydrochloride. In the reproductive toxicity studies, the parental ~~NOAEL was 15 mg a.s./kg bw/day, while the~~ and reproductive NOAELs were 37.5. mg a.s /kg bw/day based on decreased sperm concentration and count in the epididymis; the parental and developmental NOAELs were 31 mg a.s./kg bw/day based on decreased individual foetal body weight and increased number of small foetuses at 123 mg a.s/kg bw/day in the rat. The NOAEL for acute neurotoxicity was set at 1321 mg /kg bw/day propamocarb hydrochloride; the NOAEL for subchronic neurotoxicity in rat was 72 mg/kg bw /day propamocarb hydrochloride, based on the occurrence of intra-epithelial vacuolation of the choroids plexus in cerebrum and cerebellum at higher doses. The ADI and AOEL are 0.29 mg propamocarb hydrochloride/kg bw/day, while the ARfD is 1 mg propamocarb hydrochloride/kg bw/day. The operator, worker and bystander risk assessment is inconclusive.

The metabolism of propamocarb hydrochloride in plants has been fully elucidated. Applied by foliar treatment of plants, the compound is degraded through hydroxylation, oxidation, N-demethylation and cyclisation, but however remains the major compound of the residue pattern. Applied by soil treatment or hydroponically with nutritive solution, its levels, as well as those of its structurally related metabolites, resulting from uptake and translocation into edible parts of the plants are low. In this case the major part of the radioactivity present in plants is due to the incorporation in the plant of the $CO_2$ produced by complete degradation of the compound. Similar residue pattern is found in potato tubers after foliar treatment of the aerial parts of the plant. The residue definition proposed consists therefore in the sum of propamocarb and its salts.

Supervised residue trials adequately supporting all the representative uses have been submitted. In lettuce it has been identified that the use of propamocarb hydrochloride in winter under glasshouse condition leads to the highest residue levels. In tomatoes, hydroponical application on rockwool may lead to low measurable residue levels, while this type of application on soil-grown tomatoes leads consistently to residue levels below the LOQ of the employed method of analysis (0.01 mg/kg). In potatoes, residues were always below the LOQ of the method of analysis (0.1 mg/kg). On the basis of these residue trials, MRLs can be proposed at 30 mg/kg for lettuce and at 0.1 mg/kg for both tomatoes and potatoes.

In succeeding and rotational crops, residues of propamocarb may be present for short plant back intervals. Based on the available information, a delay of 120 days should be observed between the last application of propamocarb hydrochloride and the sowing or planting of the following crop to avoid any significant transfer of soil residues.

Residues in animal commodities or in processed commodities resulting from the representative uses are not expected.

The conducted acute and chronic exposure assessments do not suggest any risk for the health of the consumer.

Laboratory soil metabolism and field dissipation data showed that propamocarb hydrochloride degrades readily in viable agricultural soils. The aerobic and anaerobic soil metabolism and soil photolysis studies indicated that no metabolites or degradation products were observed to form at levels greater than 10%, with the exception of $CO_2$ (accounting for 56-66.2% AR after 120 days). Propamocarb hydrochloride was either converted to non-extractable residues in the humic acid, fulvic acid, or humin fractions, or into transient non-accumulating metabolites. Under anaerobic conditions only limited $CO_2$ levels were observed, indicating no significant mineralisation. The rates of degradation of propamocarb hydrochloride observed in laboratory studies triggered the need for a field dissipation study ($DT_{50lab,\ 20\ °C}$ = 10.9 – 136 days). Results of field dissipation studies performed in USA suggested that propamocarb hydrochloride dissipates rapidly under field conditions with a $DT_{50}$ ranging from 17.4 and 23.7 days.

Batch equilibrium sorption data suggested that the active ingredient has a limited potential for mobility in soil and should not adversely impact groundwater under normal use conditions. This conclusion was supported by FOCUS groundwater modelling, showing 80$^{th}$ percentile $PEC_{GW}$ values at 1 m depth for propamocarb hydrochloride less than 0.1 µg/L for all modelled scenarios. However, recalculations for the use on tomatoes taking into account the drip irrigation method in the field application should be performed.

Propamocarb hydrochloride is stable to hydrolysis and photodegradation is not a relevant degradation pathway for propamocarb hydrochloride in the aquatic environment. In natural surface water systems [$^{14}$C]-propamocarb hydrochloride partitioned readily from the water phase and shifted partly to the sediment. There were no major metabolites in water or sediment.

The environmental exposure assessments available were sufficient to complete appropriate EU level estimates of $PEC_{sw/sed}$ for the intended use on potatoes, lettuce and tomatoes. However, new modelling is required for the use on tomatoes taking into account the drip irrigation method for the application in the field.

Volatilization is not considered a probable route of dissipation of propamocarb hydrochloride, and the half-life in air indicated that long range transport is not likely.

The first tier risk assessment indicated a potential acute, short-term and long term risk to herbivorous birds and a long-term risk to insectivorous birds. It was agreed by the Experts´ meeting on ecotoxicology that the risk from the uses in tomatoes and potatoes is low because tomato and potato leaves are not attractive as a food source. For the use in lettuce it is questionable if the risk is sufficiently addressed on the basis of the submitted residue data in lettuce. Further information to support the PT assumption is required. The risk to mammals and to insectivorous birds is considered to be low for all representative uses. The risk to aquatic organisms was assessed as low for all representative uses assuming that the potato use is the critical gap in terms of exposure of aquatic organisms. It is not certain if this is true for the use in tomatoes in southern Europe and an aquatic risk assessment has to be conducted for this use. A high in-field risk was indicated for non-target arthropods. The experts´ meeting agreed that the submitted higher tier studies (extended laboratory studies) provided sufficient information to conclude on a low off-field and in-field risk to non-target arthropods for all representative uses. No effects were observed in tests with Previcur N at a concentration of more than 2 times the initial PEC soil for the critical GAP (potatoes). Effects of >±25% on soil nitrification were observed in a test with Proplant. However, the tested dose was 100 times the proposed field rate and the observed effect decreased with time. Therefore the risk to soil non-target micro organisms risk is considered to be low for all representative uses.

The risk to aquatic organisms, bees, earthworms, other non target organisms and biological methods of sewage treatment was assessed as low for all representative uses.

**Key words: propamocarb, propamocarb hydrochloride, peer review, risk assessment, pesticide, fungicide**

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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. Propamocarb is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Ireland as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Ireland submitted the report of its initial evaluation of the dossiers on propamocarb, hereafter referred to as the draft assessment report, to the EFSA on 5 October 2004. For this report it should be noted that Ireland did not differentiate in the list of data requirements (level 4 of Volume 1) between data requirements for the different dossiers but listed only those data requirements which were not sufficiently addressed by any of the available dossiers. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the draft assessment report was distributed on 14 October 2004 for consultation to the Member States and the main applicants Bayer CropScience and Chimac Agriphar 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 18 May 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. The two notifiers informed the meeting that they had now formed a task force for the purpose of the active substance review.

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 at 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 6 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 7 June 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 9 May 2006)

Given the importance of the draft assessment report including its addendum (compiled version of April 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.

## THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Propamocarb is the ISO common name for propyl 3-(dimethylamino)propylcarbamate (IUPAC). Due to the fact that the hydrochloride, a variant of propamocarb, is used in the formulated product, it should be noted that the evaluated data belong to the variant hydrochloride, unless otherwise specified.

Propamocarb and propamocarb hydrochloride, respectively, belong to the class of carbamate fungicides such as benthiavalicarb and thiophanate-methyl. It is taken up via leaves or roots and acts as a multi-site inhibitor with protective action which specifically controls phycomycetous diseases.

The representative formulated products for the evaluation were "Previcur N" and "Proplant", both are soluble concentrate (SL), registered in most of the Member State of the EU.

The evaluated representative uses as fungicide, which comprise foliar spraying, drenching or drip irrigation to control a broad spectrum of plant diseases in lettuce, potatoes, tomato (grown in soil and rock wool).

The application rates are:

- in lettuce 2 applications resulting in a maximum total dose of 144.4 kg propamocarb hydrochloride per hectare (drenching) and 2 applications resulting in a maximum total dose 3.32 kg per hectare (spraying)
- in potatoes up to 6 applications resulting in a maximum total dose of 6.498 kg per hectare (spraying)
- in tomatoes (soil grown) 2 applications resulting in a maximum total dose of 144.4 kg per hectare (drenching) and 2 applications resulting in a maximum total dose of 4.332 kg per hectare (drip irrigation)
- in tomatoes (rock wool grown) 1 application 28.9 kg per hectare (drenching) and 4 applications resulting in a maximum total dose of 8.664 kg per hectare (drip irrigation).

Only the use of propamocarb as a fungicide was evaluated.

## Specific Conclusions of the Evaluation

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

The minimum purity of propamocarb hydrochloride on dry weight basis as manufactured should not be less than 920 g/kg (in the case of the Bayer CropScience source) and not less than 970 g/kg (in the case of the Chimac Agriphar source), respectively. At the moment no FAO specification exists.

It should be noted that from an analytical point of view the two technical materials cannot be regarded as equivalent. The toxicological assessment given by the rapporteur Member State in the addendum to Volume 4 (July 2005) concludes that the materials are comparable. This assessment was neither peer reviewed nor discussed in a meeting of toxicologists.
However, due to the fact that two complete data packages were provided and always the relevant end point was used for the assessment, the EFSA is of the opinion that potential differences in the toxicity of the technical material are covered by the toxicological risk assessment.

No information with respect to ecotoxicology is provided. However, studies on ecotoxicological effects were provided for all groups of organisms by both applicants. The observed end points suggest a similar toxicity of both technical materials. The lowest observed end points from the submitted studies were used in the risk assessment. Therefore, the EFSA is of the opinion that potential differences in the ecotoxicity of the technical material are covered by the ecotoxicological risk assessment.
Furthermore, it should be noted that if the applicants want a common specification (which was unclear at the meeting of experts), the applicants will have to analyse new batch data for all the impurities in the common specification in the respective technical materials.

The technical materials contain no relevant impurities.

The content of propamocarb hydrochloride in the representative formulations is 722 g/L (pure).

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of propamocarb and propamocarb hydrochloride, respectively, or the representative formulation. However, the following data gap was identified:

– data or a justification on the effects of pH on the water solubility.

The main data regarding the identity of propamocarb and propamocarb hydrochloride, respectively, as well as physical and chemical properties of propamocarb hydrochloride are given in appendix 1.

Sufficient analytical methods are available for the determination of propamocarb in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.
However, the following data gap was identified:
Data on the derivatisation step used in the analytical method for the determination of one impurity in the technical material are missing and required from Chimac Agriphar.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. propamocarb and its salts in food of plant origin, soil, water and air.

The methodology used is HPLC with MS/MS detection. A multi-residue method like the Dutch MM1 or the German S19 is not applicable due to the nature of the residues. An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2).

The discussion in the meeting of experts (EPCO 35, September 2005) on identity, physical and chemical properties and analytical methods was limited to the specification and the equivalence of the technical materials, some physical, chemical and technical properties of propamocarb hydrochloride and the representative formulations. Furthermore, some issues on the analytical methods were discussed.
Required clarification with respect to the vapour pressure, the surface tension and the absorbance above 290 nm are given only in the evaluation table.

## 2. Mammalian toxicology

In September 2005 propamocarb was discussed in the EPCO expert meeting on toxicology (EPCO 33).

The notifier was asked to provide information for the definitive studies as used in the endpoints table. Issues were identified in determining the test material used in the toxicity studies (i.e. propamocarb or propamocarb hydrochloride). Information has been submitted to the rapporteur Member State in March 2006 but not peer reviewed (see section 1).

## 2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Propamocarb hydrochloride was extensively and rapidly absorbed (78 – 96% within 72 h); there is no evidence of accumulation of the active substance or its metabolites in animal tissues. Residue levels were generally an order of magnitude greater in the high-dosed rats compared with the low-dosed animals. In the rat, excretion was rapid, primarily via the urinary route. Propamocarb hydrochloride is extensively metabolised, with only 1.1 – 11% of the low doses being excreted as unchanged in the urine and the 20% for the high doses.

## 2.2. Acute toxicity

Propamocarb hydrochloride is of low acute oral, dermal and inhalation toxicity ($LD_{50}$ > 2000 mg/kg bw, $LC_{50}$ > 5.01 mg/L); it is not a skin or an eye irritant, but it is a skin sensitiser, as confirmed during the meeting on the basis of the positive results in the Magnusson & Kligman test and the recently submitted LLNA (**R43 "May cause sensitisation by skin contact"** is proposed).

## 2.3. Short term toxicity

The critical toxicological endpoint in rats and dogs was represented by vacuolar alterations/vacuolation of secretory epithelial tissues (the choroid plexus in the rat and, in some cases, also the lacrimal glands; in the dog vacuolar changes were much more widespread, occurring within a range of secretory tissues and organs (the trachea, oesophagus, stomach (fundus), salivary glands (sublingual and parotid), lacrimal glands, mandibular lymph nodes and in the lungs (bronchi/submucosal glands). In rats the vacuolar alterations were apparent only after 28 days of propamocarb hydrochloride administration. The overall lowest relevant NOAELs were considered to be <39 mg/kg/day propamocarb hydrochloride, based on the vacuolar alterations observed in the 52-week dog study, 45 mg/kg bw/day in 90 day dog study and 100 mg/kg bw/day in 28 day rat study

## 2.4. Genotoxicity

The potential genotoxicity of propamocarb hydrochloride has been extensively investigated both *in vitro* and *in vivo*. There is no evidence of genotoxicity associated with propamocarb hydrochloride.

## 2.5. Long term toxicity

Based on the incidence of intracytoplasmic vacuolation in the choroid plexus of the brain and vacuolation of the lacrimal gland ducts, the relevant NOAEL for long term toxicity in rats (1 year-study) is 29 mg/kg bw/day (propamocarb hydrochloride).
Propamocarb hydrochloride did not show any evidence for carcinogenic potential.

## 2.6. REPRODUCTIVE TOXICITY

In the reproductive toxicity studies, based on a decrease in female body weight, food consumption and an increase in gestation length, the parental ~~NOAEL was 15 mg a.s./kg bw/day, while the~~ and reproductive NOAELs were 37.5 mg a.s /kg bw/day based on decreased sperm concentration and count in the epipdidymis at 200 mg Proplant/kg bw/day. The meeting noted that in the rat multigeneration study, reduced sperm count was recorded in the F1 generation at maternally toxic doses. This was flagged to ISPRA for consideration of classification.

The parental and developmental NOAELs were 31 mg a.s./kg bw/day based on decreased individual foetal body weight and increased trend in the number of small foetuses, still within the range of biological variation, at 123 mg a.s./kg bw/day in the rat. A higher number of small foetuses was observed in the control group.

## 2.7. NEUROTOXICITY

Acute neurotoxicity

There were no adverse clinical signs, effects on body weight or neuropathological effects of treatment observed at any dose. Some generalized toxicity was observed around the time of dosing. The NOAEL for acute neurotoxicity was set at 1321 mg /kg bw/day propamocarb hydrochloride.

Subchronic neurotoxicity

Propamocarb hydrochloride was administered in the diet to rats at doses for up to 104 days. No mortalities occurred during the study and there were no adverse clinical or neurobehavioural signs observed at any dose level. Decreased body weight effects and, in some cases, coinciding lower food consumption were associated with generalized toxicity. The NOAEL for subchronic neurotoxicity in rat was 72 mg/kg bw /day propamocarb hydrochloride, based on the occurrence of intra-epithelial vacuolation of the choroids plexus in cerebrum and cerebellum at higher doses.

## 2.8. FURTHER STUDIES

Impurities:

Acute oral toxicity studies in rats and *in vitro* bacterial reverse mutation assays were conducted on the following 4 impurities of propamocarb hydrochloride: HOE 131392, HOE 131394, AE B108563, AE F132339. They showed low acute toxicity; none of them any mutagenic potential in the bacterial reverse mutation assays, when tested up to doses of 5000 µg/plate.

The experts concluded that these impurities were not toxicologically significant.

## 2.9. MEDICAL DATA

Propamocarb hydrochloride has been produced, formulated and packaged in Germany since 1976. Since 1991, the compound has been synthesised in closed systems. Periodic annual examinations of the workers are carried out: results of the monitoring programme did not reveal any effects on cholinesterase activities, or any other significant effects which could be clearly related to propamocarb hydrochloride exposure. None of the medical examinations carried out since 1976 have indicated any hazard to workers following exposure to propamocarb hydrochloride.

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

ADI

The meeting considered the studies available for the derivation of the ADI. It was noted that the parental NOAEL in the reproductive toxicity was lower than in the 52 week rat study. However, the NOAEL in the reproductive study was based on bodyweight and food consumption effects, which were not the critical effect. It was agreed that the dog was the most sensitive species, but that vacuolation of the choroid plexus was not seen. Additionally, the 1 year dog study derived a LOAEL, and thus an additional safety factor would be required, and no effects were seen in the two year dog study. The meeting therefore considered that the proposed ADI of 0.29 mg propamocarb hydrochloride/kg bw/day, derived from the NOAEL of 29 mg/kg bw/day in the 52 week rat study, was appropriate with a safety factor of 100.

ARfD

An ARfD of 1 mg propamocarb hydrochloride/kg bw/day was derived, based on the 28-day gavage study in rats, applying a safety factor of 100.

AOEL

The experts noted that, based on the proposed pattern of use (e.g. greenhouses) a long term study was appropriate for the derivation of the AOEL, instead of the 90-day study in dogs, leading to an AOEL of 0.45 mg/kg bw/day. Therefore an AOEL of 0.29 mg propamocarb hydrochloride/kg bw/day was derived, based on the NOAEL of 29 mg/kg bw/day in the 52 week rat study was agreed with a safety factor of 100.

## 2.11. DERMAL ABSORPTION

In the DAR, dermal absorption values from two *in vivo* rat studies were used (12% for the concentrated formulation and 10% for the spray strength dilution).

During the meeting, a new *in vitro* rat/human skin study was considered, indicating a dermal absorption for the dilution of 9.68% in human skin and 23% in rat skin. Taken together with the studies originally in the DAR a provisional dermal absorption study of 10% was derived for concentrate and dilution based on rat *in vivo* and rat/human *in vitro* (Previcur N). During the EPCO, the rapporteur Member State was asked to evaluate the new *in vitro* study and circulate to Member States for comments and confirmation of the dermal absorption values.

As the study had been submitted just before the EPCO expert meeting and was briefly presented during the meeting, an addendum with the evaluation of the study was produced by the rapporteur which has not been peer reviewed. The rapporteur Member State proposes new, lower, dermal absorption values.

**EFSA *proposes*** to remain with the provisional dermal absorption value of 10% and that the new study and evaluation by the rapporteur Member State is to be considered by MS at national level.

## 2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Propamocarb hydrochloride, formulated as Previcur N and Proplant is intended to be used on lettuce (in field and greenhouses, drenching, 72.2 kg/ha and foliar spraying, 1.66 kg/ha) and on tomatoes (only greenhouses, drenching, 28.88 kg/ha, and soil nutrition, 3.61 kg/ha).

**EFSA note**: the rapporteur Member State has been asked to refine the calculations based on the EPCO outcomes with regard to the new agreed AOEL and dermal absorption value of 10%, together with an assessment of the *in vitro* study submitted by the notifier and received just before the experts' meeting.
During the meeting, the weaknesses of the (submitted) risk assessment presented in the DAR were highlighted. In particular, only the hand held application was considered for field treatment, with a reduced treated area (0.5 ha/day). The rapporteur Member State considered this scenario, together with drenching, as being representative of the worst cases with respect to operator exposure, although no clarification has been provided for the foliar spraying use with tractor. A refinement of the operator, worker and bystander risk assessment has been provided with an addendum in January 2006, considering dermal absorption values lower than the ones agreed during the meeting, obtained from the newly/recently submitted dermal absorption study. In this addendum no explanation is given about the values and the study is not summarised.
At the moment, therefore, a risk assessment with the agreed input parameters is not available. Below, for transparency the risk assessment reported in the DAR is described. It considered the dermal absorption values of 12% for the concentrated formulation and 10% for the spray strength dilution, and an AOEL of 0.45 mg/kg bw/day.

In conclusion, the operator, worker and bystander risk assessment is inconclusive.

In the **DAR**, the assessment of the operator exposure was based on some assumptions:
the area treated in one day is: 0.3 ha/day for drenching
0.5 ha/day for foliar spraying
the application rate is:
Drenching for lettuce: 100 L/ha of PREVICUR N resulting in 72.2 kg propamocarb hydrochloride /ha for each single treatment.
Foliar application on lettuce: 2.3 L/ha of PREVICUR N resulting in 1.66 kg propamocarb hydrochloride /ha for each single treatment.

Calculations were made based on:
- Drenching: calculated on the basis of contamination obtained only during mixing loading in a tank as for tractor application
- Foliar spraying:

- Using knapsack scenario from POEM and BBA model
- Using tank + lance scenario from POEM and BBA model

- Using POEM and BBA model and IVA[3] data in greenhouse: contamination during mixing loading calculated with POEM and German model and contamination during application extrapolated with the IVA model.

The dermal absorption values of 12% for the concentrated formulation and 10% for the spray strength dilution were used. The AOEL considered was 0.45 mg/kg bw/day.

According to the UK POEM, four uses have been identified for propamocarb hydrochloride giving exposure levels below the AOEL (<76%):

1. Drench application to lettuce, 5L narrow aperture – gloves at mixing and loading.
2. Drench application to lettuce, 5L 45/63mm aperture – no requirement for PPE.
3. Foliar application to lettuce, 5L narrow aperture – gloves at mixing and loading and gloves and impermeable coveralls at application.
4. Foliar application to lettuce, 5L 45/63mm aperture – gloves at mixing and loading and gloves and impermeable coveralls at application.

**EFSA note**: on the basis of the reduction of the AOEL, it can be argued that some of the uses considered may exceed the threshold. Further, based on the refinement provided by the rapporteur Member State, only the hand held application could be in principle considered. Nevertheless, some uncertainties are still present due to the very narrow range of uses leading to exposure levels possibly below the AOEL.

<u>Worker exposure</u>

In the DAR, the worker exposure assessment is not fully transparent, since no calculations are shown and a clear rationale for the model selected is not presented. Furthermore, the re-entry activities considered are related to crops not included in the intended uses.

The revised assessment in the addendum considers the 'drenching of lettuce before transplanting' scenario as the worst case (72.2 kg as/ha) and is based on the default value from the EUROPOEM II, 2002). Assuming dermal absorption values lower than the one agreed during the meeting, the estimated exposure exceeds the AOEL.

**EFSA notes** that this last assessment shows some weaknesses, either because of the model characteristics or from a scientific point of view.

<u>Bystander exposure</u>

In the DAR, the rapporteur Member State agrees with the applicant's position in that the bystander exposure could be kept at minimum since access in greenhouses can be completely regulated.

**EFSA notes** that in the addendum provided by the rapporteur Member State, new calculations are not shown. The approach cannot be considered transparent.

[3] IVA, 1996: Industrieverband Agrar e.V. (German Agrochemical Association). "Operator Exposure in Greenhouses during practical use of plant protection products" – Final Report/June 6, 1996

# 3. Residues

Propamocarb was discussed at 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 propamocarb hydrochloride in plants has been investigated in spinach, potatoes, cucumbers, lettuce and tomatoes. Studies were submitted by both notifiers and as they agreed in conducting a task-force, the entire information was used independently of its source to understand the behaviour in plants of the compound when applied according to the representative uses supported by both notifiers. The information provided is sufficient with regard to all representative uses.

The metabolic pattern found in plants is strongly influenced by the mode of application of the product.

In lettuce, after foliar applications, residues are highly extractable (90% of the Total Radioactive Residues – TRR) and consist essentially in propamocarb. Two minor metabolites, accounting for less than 5% of the TRR were also identified, hydroxypropyl-propamocarb and propamocarb-N-oxyde, indicating that the degradation of propamocarb hydrochloride proceeds through hydroxylation and oxidation. Similar pattern was observed in spinach after foliar treatment, with 2 further metabolites identified, resulting from N-demethylation and cyclization of the hydroxy metabolite identified in lettuce. Foliar treatment of tomato plants also resulted in propamocarb being the major constituent in tomato fruits (75% of the TRR).

Propamocarb hydrochloride applied hydroponically or as soil treatment in tomatoes or lettuce results in a quite different metabolic pattern in harvested lettuce and tomatoes. The amounts of unchanged parent and of its structurally related metabolites are low when present, but the TRR are essentially constituted of polar material rather similar for the 2 plants and indicating the reincorporation in endogenous material of $CO_2$ resulting from the degradation of propamocarb hydrochloride by the plant or in the soil. In contrast to the observations made in lettuce and tomatoes, cucumbers grown hydroponically and treated with propamocarb hydrochloride applied in the nutrient solution showed an important level of parent propamocarb (50% of the TRR).

Two metabolism studies on potatoes were submitted. Unchanged propamocarb-anion was present in tubers at 15% of the TRR in one study and at 2% of the TRR in the second study. In both cases the vast majority of the radioactivity present could be allocated to natural plant constituents (mainly starch), demonstrating the incorporation in plant material of $CO_2$ produced by the degradation of propamocarb hydrochloride.

The residue definition in plant commodities for monitoring and risk assessment is proposed to be restricted to propamocarb and its salts, the sum being expressed as propamocarb, as no metabolite structurally related to propamocarb is present at level suggesting a significant contribution to the toxicological burden, whatever the plant or the type of treatment. In addition to this no metabolite has been identified in plant which was not present in rat metabolism.

A large amount of residue trials were submitted by both notifiers in support of representative uses. For uses on lettuce many trials were conducted before the implementation of GLP rules and individually many trials do not meet the current standards of acceptability. Nevertheless as many trials as possible were considered to understand correctly the residue situation in lettuce. Lettuce produced under glass clearly present higher residue levels than field lettuce. Nevertheless, when protected and field lettuces are separately considered, the dispersion of the residue levels is very wide. This is clearly related to the season of production of lettuce. In winter, the 21 days PHI allow treatment of lettuce at later growth stages than in other seasons, due to the relatively slower growth rate in winter conditions. A set of recent glasshouse trials on lettuce grown in winter clearly demonstrate this with a STMR calculated at 12 mg/kg while the STMR for data base covering other seasons of production is 4.35 mg/kg. The HR found on winter lettuce was 26.2 mg/kg. These typical winter conditions leading to particularly high residue levels need to be taken into account in MRL setting.

In tomatoes low levels of measurable residues (up to 0.09 mg/kg) were found in case of cultivation on rockwool (9 trials), while residues are consistently below the Limit of Quantification (LOQ of 0.01 mg/kg) for cultivation on soil (10 trials) under field or glasshouse conditions.

Twelve residue trials were submitted in support of the use in potatoes, 8 were carried out in Northern Europe and 4 in Southern Europe. All results were below the LOQ of 0.1 mg/kg.

These results are supported by storage stability studies of propamocarb residues on tomatoes, cucumbers, lettuce and Brussels sprouts indicating that the compound is stable under deep freeze conditions (-18 °C) for periods ranging from 12 to 24 months.

Both notifiers indicated that of the representative crops used in the peer-review, lettuce is not processed and residues of propamocarb will not exceed 0.1 mg/kg in either potatoes or tomatoes. Consequently processing studies are not required for these crops.

### 3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Confined rotational crop studies conducted after soil treatment with a dose rate similar to the total amount of propamocarb hydrochloride applied for protecting crops selected as representative uses indicated potential residues of propamocarb clearly above the LOQ in crops (wheat, lettuce, radish) sowed or planted 30 days after this treatment (up to 1 mg/kg in radish tops). The metabolic pattern in following crops was similar to that observed in primary crops and no specific residue definition is needed for rotational crops. Residues in crops planted at least 120 days after the treatment were 1 to 2 orders of magnitude lower.

Field studies were conducted in the US, and resulted in propamocarb residues being present in wheat only (hay, straw and forage). However in these trials the selected crops (wheat, soybean, sugar beet, table beet and dry beans) were less critical, due to their mass and long growing period, than those used in the confined study. Therefore, the information provided does not demonstrate that the presence of residues in rotational or succeeding crops planted shortly after harvest of the treated crop are excluded. A label restriction should indicate that crops should not be grown on soil treated with propamocarb hydrochloride for at least 120 days after the last application of the product. Further field trials should be conducted to refine this restriction and/or to set MRLs in following crops.

## 3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Based on the representative uses supported by the notifiers, potatoes is the only feed item which may contain residues of propamocarb. Given the residue levels to expect in practice, the actual exposure of animals is however very low (less than 0.02 and 0.007 mg/kg bw/d for beef and diary cattle respectively) and no transfer of residues resulting in measurable amounts in animal commodities is expected. However a metabolism study in lactating cow has been submitted. This study was conducted with an exposure rate of animals 2 orders of magnitude higher than the expected level of exposure of animals and showed limited transfer of residues to animal commodities. Liver contained the highest levels of TRR (0.4 mg/kg). The metabolic pattern was similar to that observed in rats and plants, and no sign of potential accumulation was identified.

Therefore, taking into account the practical low level of exposure of livestock, there is no need to establish any residue definition nor MRLs for animal commodities.

## 3.3. CONSUMER RISK ASSESSMENT

Chronic exposure.

The chronic dietary exposure assessment has been carried out according to the WHO guidelines for calculating Theoretical Maximum Daily Intakes (TMDI). Two consumption patterns were considered: the WHO European typical diet for adult consumers and the national German diet for a 4-6 year old girl. These TMDI calculations were conducted, considering that commodities contained residues at the level of the respective proposed MRLs. This resulted in theoretical intakes amounting to less than 5% of the ADI for both considered diets.

Acute exposure.

The acute exposure to residues of propamocarb has been assessed according to the WHO model for estimates of short term intakes (NESTI, National Estimated Short Term Intakes). Large portion consumption data for adults, toddlers and infants in UK were used. Calculations were carried out considering residues in treated commodities at the level of the respective MRLs as well as high unit to unit variability (7 for tomatoes and potatoes, 5 for lettuce). This resulted in NESTI values below 2% of the ARfD for potatoes and tomatoes in all population subgroups, and amounting to 50% of the ARfD for lettuce in the most exposed population subgroup (children of 4-6 years old). These calculations demonstrate that no risk for the safety of consumers is expected resulting from the use of propamocarb hydrochloride according to the representative uses in tomatoes, lettuce and potatoes.

Note : The acute and chronic exposure assessments were carried out without converting the proposed MRLs as propamocarb to propamocarb hydrochloride. However this does not affect their outcomes significantly.

## 3.4. PROPOSED MRLS

Based on the results of supervised residue trials on glasshouse lettuce produced under winter conditions and their analysis according to statistical tools recommended by current guidelines a MRL of 30 mg/kg is proposed. For tomatoes, the highest residue found in the residue trials was considered and this leads to a proposal for an MRL of 0.1 mg/kg.

For potatoes, it was discussed during the expert meeting whether the MRL could be set at a lower LOQ (0.05 mg/kg) than that used in the residue trials (0.1 mg/kg). It was observed that from metabolism studies, it was not possible to firmly conclude on a no-residue situation. In addition, some MS stated having set at national level MRLs up to 0.5 mg/kg. Therefore, based on the available data for the peer review, it was decided to establish the MRL at 0.1 mg/kg.

# 4. Environmental fate and behaviour

Propamocarb (propamocarb as its hydrochloride salt) was discussed at the EPCO experts' meeting for the environmental fate and behaviour (EPCO 31) in September 2005.

## 4.1. Fate and behaviour in soil

### 4.1.1. Route of degradation in soil

The metabolism of propamocarb hydrochloride was studied in a range of soil types under aerobic conditions at 20 ºC and 40-45% maximum water holding capacity. Two different radiolabelled versions of propamocarb hydrochloride were used: aminopropyl-1-[$^{14}$C] position and aminopropyl-2-[$^{14}$C] position (specific information on the radiolabelled versions of propamocarb hydrochloride used in the environmental fate studies was provided in the addendum to the DAR dated July 2005). The primary degradation pathway is considered to be the ready breakdown of propamocarb hydrochloride by microbial attack to transient non-accumulating degradation products (the sum of the components never exceeded values >8.1% AR), non extractable residues (up to 56% AR at 14d) and $CO_2$ (up to 66.2% AR after 120 days, study end). No metabolites were observed accounting in amounts greater than 10% AR. Further work to identify the nature of non-extractable residues indicated that more than 50% of the NER was located in the fulvic acid fraction of the soils. The position of the radiolabelling was not observed to have an effect on the soil degradation pathway.

Additional supplementary information on soil metabolism of propamocarb hydrochloride was derived from non-GLP aerobic soil metabolism investigations performed at 15 ºC and 25 ºC. Results confirmed the microbial degradation of propamocarb hydrochloride leading to carbon dioxide as the main degradation product.

Similarly to the incubation of test soils applied with propamocarb hydrochloride at 20 ºC, propamocarb hydrochloride at the lower test temperature of 10ºC showed rapid and near complete degradation in two soils. Likewise, the major route of degradation resulted in the conversion to and release of $^{14}CO_2$ (maximum 57.9% AR after 120 days, study end) and the significant formation of non extractable residues (maximum 47.5% after 120 days). No single metabolite formed that exceeded 10% AR, indicating that at low temperature the metabolites formed still remain transient in nature.

In an additional laboratory study, the metabolism of propamocarb hydrochloride at 10ºC was investigated in soil sub-horizons at depths of 20, 40, 60, and 90 cm. Results indicated that the degree of degradation was partially a function of soil depth. Carbon dioxide and NER were the principal degradation products formed. However, with increasing soil depth the formation of $^{14}CO_2$ decreased to amounts that were almost negligible and a greater portion of the active substance was bound as

NER (at the study end 26.9% AR and 36.8% AR at 20cm and 90cm, respectively). Nevertheless, during the incubation period the maximum value for a single component never exceeded 10% AR.

In laboratory investigations under anaerobic conditions in two soils, propamocarb hydrochloride was degraded slowly, in comparison with aerobic investigations. Observed $CO_2$ levels were negligible throughout the study indicating no significant mineralisation of the carbon in both the labelled position (maximum 7.7% AR after 90d). No metabolites were observed accounting for levels greater than 10% AR.

The photodegradation of propamocarb hydrochloride on two soils by simulated sunlight ($\lambda > 290$ nm, in the same order of magnitude as moderate northern latitudes during the summer months) was also investigated. In the first study, photodegradation was limited. In both irradiated and dark control samples propamocarb hydrochloride was the principal constituent found in soil extracts. Propamocarb hydrochloride was observed to degrade at a slower rate under irradiated conditions (non linear simple first order $DT_{50}$ = 199.2 d) than in the dark control (non linear simple first order $DT_{50}$ = 103.1 d). However, in the second study, irradiation appeared to increase degradation of the active substance ($DT_{50}$ = 35.4 d) when compared to the dark control ($DT_{50}$ value not calculated).

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

The degradation rates for propamocarb hydrochloride were determined in the same laboratory aerobic and anaerobic top soil metabolism studies described in section 4.1.1. Using the data from each study, $DT_{50}$ and $DT_{90}$ values for propamocarb hydrochloride were calculated assuming non-linear simple first order degradation of the active substance. Further details on the method used to fit decline curves to residue data and the goodness-of-fit values obtained for some of the studies, were provided by the rapporteur Member State in the addendum to the DAR (July 2005).

In the aerobic soil metabolism studies at 20 ºC, single first order $DT_{50lab}$ were in the range of 10.9 to 136 days (n= 9, two separate studies from the two applicants). Under the experimental conditions at various temperatures (between 15 ºC and 25 ºC) of the non-GLP studies, a short lag phase was assumed during which nearly no degradation occurred. After this lag phase, the degradation was described again by first-order, mono-phasic kinetics. The estimated $DT_{50}$ values were in the range of 10.0 – 28.0 days (n = 5).

The $DT_{50lab}$ mean values, normalised to 20 ºC and field capacity (-10kPa) as defined by FOCUS for use as modelling input, were estimated to be 17.08 days and 10.20 days, depending on the dataset provided by each applicant. Whereas, if the datasets from both the studies are considered as whole, the more appropriate geometric mean $DT_{50lab}$ value of aerobic topsoil values normalised to 20ºC and pF2 moisture content, should be 13.91 days (n= 16).

Propamocarb hydrochloride degraded at 10ºC with an estimated half-life of 25.3 days, 47.2 days and 73.7 days. The laboratory investigation using the soil sub-horizons at depths of 20, 40, 60 and 90 cm at temperature of 10ºC indicated that the rate of degradation slowed with depth, with first order $DT_{50}$ values of 73.7, 136, 239, and 267 days respectively.

In the anaerobic soil degradation study, the breakdown of propamocarb hydrochloride was limited, resulting in first order $DT_{50}$ values of 65.7 and 308.2 days (at 20 ºC) and 459 days (at 25 ºC).

The rates of degradation of propamocarb hydrochloride observed in laboratory studies triggered the need for a field dissipation study, as $DT_{50lab}$ results ranged over the limit of 60 days as outlined in the Directive 95/36/EC. Two field dissipation trials were conducted in the USA (Georgia and California) to investigate the dissipation rate of propamocarb hydrochloride in a typical range of soils under different climatic conditions over a period of 1 year. The trials were carried out under field use conditions on turf and bare soil following four foliar applications. The largest propamocarb residues were observed in bare soil in both trials. Dissipation in the environment was fairly rapid with non-linear simple first order $DT_{50}$ values ranging from 17.4 to 23.7 days. $DT_{50}$ values determined for grass (between 13.2 and 18.1 days) indicate that propamocarb hydrochloride is readily dissipated when intercepted by a grass layer.

For PECsoil calculations, the foliar spray application of propamocarb hydrochloride in the environment to potatoes was considered the worst-case scenario, based on the information appearing in the GAPs and after estimation of equivalent field application rates for glasshouse applications to tomatoes and lettuce. In order to generate worst-case PECsoil values for potatoes, all of the 6 applications (maximum application rate of 1.083 kg a.s./ha each) were lumped into a single field application of 6.498 kg a.s./ha. Crop interception was assumed to be zero percent and the longest $DT_{50}$ value of 136.0 days for propamocarb hydrochloride obtained under laboratory aerobic conditions (20 ºC and 40% MWHC) was used.

### 4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

The adsorption/desorption behaviour of [$^{14}$C]-propamocarb hydrochloride was investigated on 12 different soils, covering a broad range of properties (organic carbon 0.48 – 3.48; pH 5.2 – 7.4; clay content 4 – 48.5%). The Freundlich adsorption coefficients ranged widely between 0.671 and 77.20 mL/g (mean 10.5 mL/g). Overall, propamocarb hydrochloride showed a very high to slight mobility ($K_{foc}$ = 41 – 2451 mL/g; mean = 535.6 mL/g). Since propamocarb will be applied as propamocarb hydrochloride ~~protonated in soil~~, factors such as the amount and type of clay minerals present in the soil, the cation exchange capacity and pH all have a potential to influence the sorption of the compound to soil.

The adsorption/desorption behaviour of [$^{14}$C]-propamocarb hydrochloride was also investigated on four different subsoil horizons at soil depths of 20, 40, 60 and 90 cm. The $K_{foc}$ values ranged from 171 mL/g in the 20 cm subsoil horizon to 3600 mL/g in the 90 cm subsoil horizon.

The use of adsorption values related to clay content at different soil depths was discussed at the meeting of experts. It was agreed that for MS authorization the approach could be used if sufficient statistical analysis support that the clay content relationship was predominant over the relationship with organic carbon.

The mobility of propamocarb hydrochloride was further investigated in soil column leaching studies. The comparative leaching of [$^{14}$C]-propamocarb hydrochloride in acidic (pH 5.6) and alkali (pH 8.1) soils was investigated in two loamy sand soils. Results indicated that whilst the active ingredient is slightly more mobile in alkali soils (more than 80% AR remaining in the top 15 cm of the soil column and less than 0.3% AR in the leachate) than in acidic soils (more than 90% AR remaining in the top 5

cm of the soil column and less than 0.05% AR in the leachate), it is not readily leached in either soil type.
Aged (23 and 12 days) residues of [$^{14}$C]-propamocarb were relatively immobile (< 1% AR in leachates) in 30-cm columns of two sandy loam soils. Most of the soil associated activity (27.9 to 44.5% AR) was recovered in the top 6 cm of the column. Some downward movement of activity was observed down to 18 cm in both soils (< 6.1%AR and <10.9% AR in the section 12-18 cm of the column).

## 4.2. FATE AND BEHAVIOUR IN WATER

### 4.2.1. SURFACE WATER AND SEDIMENT

The hydrolytic stability of propamocarb hydrochloride was investigated in three studies conducted under dark and sterile conditions over 5 days at pH values of 4, 5, 7 and 9 and at temperatures up to 50 ºC. Results indicated that the active ingredient is stable to abiotic hydrolytic degradation at these pH values. Investigations were also carried out under extremely alkaline conditions (pH 12, 13, and 14) at 90 ºC. Even at a pH of 14, the half life was measured to be approximately 5 days, confirming the hydrolytic stability of propamocarb hydrochloride.
Three photochemical degradation studies are available. A study carried out to determine the UV-VIS absorption spectrum of propamocarb hydrochloride determined the maximum absorption wavelengths to be 217 nm, with a maximum molecular extinction coefficient of 261.0 $dm^3\ mol^{-1}\ cm^{-1}$. Therefore irradiation of propamocarb hydrochloride in the spectrum of wavelengths greater than 290 nm is not expected to induce any photochemical transformation. This was further supported by the two other studies showing no difference in degradation between the irradiated samples and the dark controls. Therefore, it can be concluded that photodegradation is not a relevant degradation pathway for propamocarb hydrochloride in the aquatic environment.
Ready biodegradability tests were performed according to the OECD guidelines. For some inoculations under the conditions of the modified Sturm tests, findings were ambivalent, with highly variable $CO_2$ evolution levels being obtained from replicate incubations. No explanation was offered for this variability. However, because 5 out of the 6 tests did not match the required pass levels for biodegradation (60% $ThCO_2$ to be reached in a 10-day window within the 28-day period of the test) propamocarb hydrochloride can be considered as not readily biodegradable.
The route and rate of degradation of propamocarb hydrochloride was investigated in two water/sediment studies conducted under aerobic conditions at 20ºC. Propamocarb hydrochloride partitioned readily from the water phase and shifted partly to the sediment (max. 36.9% AR after 14 days). Propamocarb hydrochloride was mineralised principally to carbon dioxide (max. 67.5-94.7% AR at 104-105 days, study end) and non-extractable residues (max. 10.3-16.0% AR at 42-63 days). No accumulation of intermediate degradation products was observed in both studies. In total a maximum amount of three or eight minor metabolite peaks were observed during the incubation periods, never exceeding the 4% of the applied radioactivity. The first order $DT_{50}$ values of propamocarb hydrochloride in the water phase and in the whole system were calculated to be $DT_{50water}$ = 11.6 – 15 days and $DT_{50whole\_system}$ = 15.5 – 21 days. Investigations of the water/sediment

systems under sterile conditions suggested that propamocarb hydrochloride degradation in natural water and associated sediment occurs principally through the action of micro-organisms.

In addition, the degradation of propamocarb hydrochloride was investigated under anaerobic aquatic conditions in one water/sediment system. As with aerobic conditions, the proportion of radioactivity in the surface water declined throughout the incubation period, which matched rates of partitioning to sediment observed under aerobic conditions. Rate of degradation in the total system was lower than under aerobic conditions ($DT_{50whole\_system}$ = 100.0 days), whereas in the water phase the estimated first order $DT_{50}$ was in the same range ($DT_{50water}$ = 12.1).

No negative impact on water treatment procedures is expected.

In the original DAR, $PEC_{sw}$ calculations were performed combining a lumped spray drift and runoff contribution (2.77% and 0.5%, respectively) to the adjacent water body. However, during the peer review it was challenged that $PEC_{sw}$ values could be underestimated in some instances, since the assumed value of 0.5% for input via runoff is considerably lower than the combined runoff/drainage input utilised in the FOCUS surface water modelling process (10% for Step 1 and 2-5% for Step 2). Therefore, new $PEC_{sw}$ and $PEC_{sed}$ calculations using the FOCUS Steps 1-2 calculator were provided by the applicant and presented in an addendum (July 2005). Degradation and adsorption input parameters used in FOCUS calculator were selected from only one of the two available datasets. However, the choice of values represented a worst-case selection, appropriate for modelling, if both datasets are considered as a whole. Calculations were performed for use on lettuce, use on potatoes and use on tomatoes. The modelled GAPs for lettuce and tomatoes both involved two spray applications in the field, with a treatment rate per application of 1660 g a.s./ha and a spray interval of 12 days for lettuce, and a treatment rate per application of 2166 g a.s./ha and a spray interval of 7 days for tomatoes. However, during the EPCO meeting experts doubted on the suitability of the spray application for tomatoes use in the GAPs table. Following the clarification provided by the experts of the physical/chemical section (refer to the new open point 1.22 of the reporting table) specifying that for tomatoes a nutrient drip application should be used in the field, the $PEC_{sw/sed}$ values calculated with spray drift application for tomatoes can not be considered valid. Because a 50% crop interception was used, the expected aquatic concentrations calculated with the correct application (i.e. no drift, incorporation or seed treatment) will result in higher values due to a higher loading to the water body via runoff/drainage. As a consequence, it is not assured that calculations performed with potatoes, involving up to six broadcast spray foliar applications with a treatment rate of 1083 g a.s./ha and a crop interception of 15% of the application rate, can be considered to be the critical (worst case) GAP, as it is stated in the addendum. Therefore, Member States in southern Europe should require that predicted environmental concentrations for the use on tomatoes be revised to take into account of the drip irrigation method being used for field applications to tomatoes. It should be noted that, only in case that new aquatic exposure will result in $PEC_{sw}$ values 6 times higher than $PEC_{sw}$ values calculated for potatoes use, the ecotoxicological trigger for aquatic organisms will not be met (refer to section 5.2).

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

The FOCUS PELMO model was used in two studies to investigate the potential for propamocarb hydrochloride to leach to groundwater, one considering the potatoes application, and the second the tomatoes and lettuce applications. Two different datasets, derived from separate studies provided by the two applicants, were used in the modelling. The suitability of using different soil adsorption values related to the clay content at different soil depths in the calculations for tomatoes and lettuce applications was discussed by the experts (EPCO 31). The meeting agreed that no impact on the risk assessment for propamocarb hydrochloride whether using the clay content/soil adsorption relationship or the organic carbon content/soil adsorption relationship in $FOCUS_{gw}$ modelling is expected. It was also agreed that the use of combined values from the two data sets will not adversely affect the groundwater contamination assessment for propamocarb hydrochloride. For reason of transparency the appropriate mean $K_{foc}$, 1/n and $DT_{50}$ values derived from the combined data set are indicated in the list of end points.

In accordance with the defined GAP, the applications for tomatoes and lettuce in the greenhouse were accounted for groundwater leaching by calculating the amount of propamocarb residue (corresponding to effective outdoor application rates) transferred to the field with the transplanting soil of each plant, after the seeds drench application in the nursery. Similarly to the surface water potential contamination assessment, $PEC_{gw}$ calculations for tomatoes were performed based on the erroneous spray drift application in the field in place of the drip irrigation (see section 4.2.1). Therefore, Member States in southern Europe should recalculate the predicted environmental concentrations for the use on tomatoes taking into account the drip irrigation method being used for field applications. Nevertheless, due to the fact that the predicted 80$^{th}$ percentile concentrations of all scenarios calculated for potatoes were at least 2 orders of magnitude below the groundwater limit, the EFSA is of the opinion that the results of the appropriate calculations for tomatoes with drip irrigation application would not affect the overall risk assessment. Results of the FOCUS-PELMO simulations for lettuce indicated that all scenarios yielded < 0.1µg/L of propamocarb hydrochloride in the leachate.

## 4.3. FATE AND BEHAVIOUR IN AIR

Based on its vapour pressure (3.1 – 4.7 * $10^{-5}$ Pa at 20 ºC and <1.7 * $10^{-3}$ Pa at 25 ºC) and its Henry's Law constant (<1.7 * $10^{-8}$ Pa $m^3$ $mol^{-1}$ at 20 ºC and 3.54 * $10^{-7}$ Pa $m^3$ $mol^{-1}$at 25 ºC), the volatility of propamocarb hydrochloride can be considered low. This suggestion was further supported following investigation of the volatility of propamocarb hydrochloride from soil (loss <0.001% of the applied amount, calculated with the Dow method) and leaf surfaces. Bimolecular rate constants for atmospheric reactions with photo-generated hydroxyl radicals were calculated to be 9.54 * $10^{-11}$ $cm^3$ $molecule^{-1}$ $s^{-1}$ and 2.878322 * $10^{-11}$ $cm^3$ $molecule^{-1}$ $s^{-1}$ in two oxidative studies, corresponding to atmospheric $DT_{50}$ values estimated to be 4.03 hours and 13.4 hours, respectively. All these factors suggested that levels of propamocarb hydrochloride in air following normal agricultural use of the formulated product will be low.

# 5. Ecotoxicology

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

Studies on toxicological effects were provided for all groups of organisms by both applicants. The observed endpoints suggest a similar toxicity of both technical materials. The lowest observed endpoints from the submitted studies were used in the risk assessment. Therefore potential differences in the toxicity of the technical materials are covered by the ecotoxicological risk assessment.

The need for clarification whether the use in tomatoes in southern Europe includes soil drench application in the field was identified as a data requirement in the Evaluation meeting of May 2005. A statement of the applicant was summarised in the addendum of July 2005. The experts´ meeting concluded that further clarification is needed regarding the method of application to tomatoes. The presented risk assessment is based on the assumption that the drench use occurs only indoors. The risk assessment needs to be revised for the use in tomatoes in southern Europe if the drench use is outdoors.

## 5.1. Risk to terrestrial vertebrates

A risk assessment for birds and mammals was conducted according to SANCO/4145/2000. The rapporteur Member State suggested the uses in tomato (Previcur N) and potato (Proplant) as being the critical GAPs for the avian risk assessment. The first tier risk assessment indicated a high acute, short-term and long-term risk to herbivorous birds and a long-term risk to insectivorous birds from the use of Previcur N in tomatoes. A high long-term risk was indicated for herbivorous and insectivorous birds from the use of Proplant in potatoes. The refined risk assessment was based on measured residues of propamocarb in lettuce and a PT refinement for insectivorous birds. An addendum was prepared in July 2005 to address the comments on the refinement of the long-term risk assessment for herbivorous and insectivorous birds. In addition a risk assessment for fruit-eating birds for the use of Previcur N in tomatoes and a risk assessment for herbivorous birds for the use of Previcur N in lettuce was included in the addendum.

The long-term risk to fruit-eating birds was assessed as low for the use in tomatoes (Previcur N). The long-term risk to herbivorous birds form consumption of tomato and potato foliage was considered to be low due to its very low attractiveness as a food source (relevant for Previcur N and Proplant). The risk from consumption of contaminated weed-seedlings growing in tomato fields was assessed as low. The expert meeting noted that it is not appropriate to use an interception factor for seedlings since the product is applied by drip irrigation. However the meeting agreed that the scenario of exposure of birds by consumption of contaminated weeds is not realistic and hence this route of exposure was regarded to be of no concern. The long-term risk to herbivorous birds from consumption of lettuce leaves was refined based on data from residue trials. The experts´ meeting noted that the $DT_{50}$ value was derived from pooled residue data. The meeting agreed that the rapporteur Member State should reconsider the $DT_{50}$ calculation and produce separate $DT_{50}$ values for the separate trials and carry out, in the first instance, the risk assessment for the longest $DT_{50}$. A new calculation of the average $DT_{50}$

value was included in the addendum of January 2006. The $DT_{50}$s ranged from 46.44 to 1.87 days and the average was calculated as 4.69 days. The long-term TER was calculated to be 8.8 taking a PT value of 0.5 into account. The EFSA is of the opinion that a refinement of PT needs to be supported by data. The risk assessment is based on the standard RUD value of 40 instead of measured residues and a MAF for two applications was applied. The EFSA is of the opinion that it would be more appropriate to use measured residues instead of a standard RUD value in the refined risk assessment. Comments were received from Member States on the calculation of the average $DT_{50}$ value. The correctness of the calculation presented in the addendum of January 2006 was questioned (e.g. $DT_{50}$ calculated from average residue data instead of calculating the mean of the $DT_{50}$s from each individual trial, geometric mean vs. arithmetic mean).

No risk assessment was conducted by the rapporteur Member State for the use of Proplant in lettuce. The first tier TER values calculated by EFSA indicated a potential long-term risk for herbivorous birds (TERlt = 3.34). The refined long-term risk assessment for herbivorous birds for the use of Proplant in potato presented in the DAR was based on pooled residue data in lettuce. No comments were received and no discussion on the acceptability of the $DT_{50}$ value took place at the EPCO meeting. However it is noted that the approximate $DT_{50}$ given in the DAR was based on pooled data which was not accepted by the EPCO meeting for Previcur N. A refined risk assessment is required for the use of Proplant in lettuce to address the potential high long-term risk to herbivorous birds.

The expert meeting agreed to the choice of yellow wagtail (*Motacilla flava*) as a focal species to refine the risk to insectivorous birds. The meeting decided that a FIR/bw of 0.91 should be used in the risk assessment and that the PT value should remain as 1 in the absence of supporting data. The PD values of 0.2 and 0.8 were suggested for the proportion of small and large insects in the diet. The proposal to use an interception factor was rejected by the meeting because interception is already taken into account in the RUD value for insects. The revised risk assessment based on the suggestions of the expert meeting resulted in a long-term TER value of 7 for the use in lettuce indicating a low long-term risk to insectivorous birds. The risk from the use in potato is considered to be covered by the risk assessment for lettuce since the application rate in potato is lower.

Risk to insectivorous birds from uptake of contaminated insects in tomato crops was assessed as low. As regards the risk to insectivorous birds from the use in tomatoes the meeting considered that the risk would be primarily from the consumption of soil dwelling invertebrates, e.g. earthworms and asked the rapporteur Member State to revise the risk assessment accordingly. A new risk assessment was presented in the addendum of January 2006. Since the log Pow of propamocarb hydrochloride is less than 1 it is unlikely that propamocarb hydrochloride accumulates in earthworms. Therefore the risk assessment was not based on the formulation suggested in SANCO/4145/2000. Instead it was assumed that the PECworm is similar to the PEC soil. The PECsoil 7d twa of 8.511 mg/kg was used for the TER calculation. The TERlt of 11.22 gives an indication that the risk to earthworm eating birds is low. The addendum is not peer reviewed.

The applicant suggested using a higher NOEC value for the long-term risk assessment. The meeting agreed with the assessment of the rapporteur Member State and concluded that 105 mg/kg bw/d is appropriate for the risk assessment.

The acute and long-term risk to the indicator species for leafy crops (medium sized herbivorous mammal) was assessed as low for all representative uses.

No risk assessment for the uptake of contaminated drinking water was available. It is not clear whether exposure to contaminated drinking water can be excluded for the representative uses of propamocarb hydrochloride in lettuce and potato. Therefore EFSA calculated in an addendum the TER values according to SANCO/4145/2000. The acute risk to birds and mammals was assessed as low for all representative uses except for Previcur N at the highest recommended concentration of the spray solution. However the TER of > 8.23 is based on a $LC_{50}$ value greater than the highest tested dose. Therefore the actual risk might be lower than indicated by the TER value. The first tier risk assessment indicated a potential short-term risk to birds for the use of Previcur N at the highest recommended concentration of the spray solution and for the use of Proplant in potatoes. The trigger for the long-term risk was breached for all representative uses indicating a potential long-term risk to birds and mammals.

A refined risk assessment for the uptake of contaminated drinking water is required for the intended uses of Previcur N in lettuce to address the potential acute, short-term and long-term risk to birds and the long-term risk to mammals if the product is applied at the highest recommended concentration. A refined risk assessment is required for the use of Previcur N and Propalant in lettuce to address the potential long-term risk to birds and mammals if a spray solution of 720 mg propamocarb hydrochloride /L is applied. The potential short-term and long-term risk to birds and the long-term risk to mammals need to be addressed with a refined risk assessment for the use of Proplant in potato.

A high risk from contaminated drinking water was shown from a first tier risk assessment based on worst case assumptions (e.g. the total daily water demand is taken from leaf axils or puddles which are contaminated by the sprayed solutions). Some Member States are of the opinion that long-term exposure to contaminated drinking water can be excluded and hence regard the long-term risk from uptake of contaminated drinking water as low. However, no common agreement among Member States exists yet on the potential long-term risk from contaminated drinking water. It is planned to discuss the risk to birds and mammals from uptake of contaminated drinking water as a general point in an EPCO expert meeting.

Overall it is concluded that the risk to herbivorous birds is low for the representative uses in tomato and potato. For the use of Previcur N in lettuce it is questionable if the risk is sufficiently addressed on the basis of the submitted residue data in lettuce. The risk to mammals and to insectivorous birds is considered to be low for all representative uses.

## 5.2. RISK TO AQUATIC ORGANISMS

A revised risk assessment was presented in the addendum of July 2005. The risk assessment was accepted by the expert meeting. The TER values were calculated with the peak PECsw of 147.8 µg/L for the use in potatoes. No risk assessment was conducted for sediment dwelling organisms since the toxicity of propamocarb hydrochloride to daphnids is low. The TER values indicated a low acute and chronic risk to aquatic organisms. It is not certain if the PECsw calculated for potatoes are higher than the $PEC_{sw}$ from the tomato use in southern Europe (see point 4.2.1). Therefore a PECsw calculation and an aquatic risk assessment are required for the use in tomatoes in southern Europe. However, only in case that the PECsw is 6 times higher than for the potato use the Annex VI TER trigger of 100 would not be met.

## 5.3. RISK TO BEES

The HQ values for the acute oral and contact exposure of bees for application rates of 2166 g propamocarb hydrochloride/ha and 1083 g propamocarb hydrochloride/ha were lower than the Annex VI trigger of 50. Therefore the risk to bees is considered to be low for all representative uses.

## 5.4. RISK TO OTHER ARTHROPOD SPECIES

A new risk assessment was presented in the addendum of July 2005. The in- and off-field risk was evaluated for the use of Previcur N in tomatoes and for Proplant in potatoes. The risk from the representative uses of both formulations in lettuce were considered to be covered since the suggested application rates in lettuce are lower. The in-field HQ value exceeded the trigger of 2 for both uses. The higher tier risk assessment was based on extended laboratory studies. The meeting agreed that the risk had been correctly assessed as low although it was not expressed entirely correctly in the addendum.

No effects of >50% were observed in a higher tier study with Proplant and *Aphidius rhopalosiphi* at a concentration of 3450 g propamocarb hydrochloride/ha. No effects of > 30% were observed in tests with *Coccinella septempunctata* and *Chrysoperla carnea* larvae on glassplates following exposure to Proplant at a dose equivalent to one application. No effects of > 30% were observed in tests with two additional ground dwelling species (*Poecilus curpreus*, *Pardosa sp.*) after exposure to a dose equivalent 100 times higher than a single application rate. The meeting agreed that the information is sufficient to conclude that the risk to non target arthropods is low for all representative uses.

## 5.5. RISK TO EARTHWORMS

Acute endpoints were available for Previcur N and Proplant. A study on the chronic toxicity to earthworms was conducted with Previcur N. The highest PECsoil was calculated for the use in potatoes. The risk assessment was based on the maximum PECsoil for the potato use which was identified as the use leading to the highest PECsoil values. The acute and long-term TERs were above the trigger of 10 and 5 indicating a low risk to earthworms for all representative uses.

### 5.6. Risk to other soil non-target macro-organisms

A risk assessment is not triggered since the $DT_{90}$(field) is < 100 days.

### 5.7. Risk to soil non-target micro-organisms

Previcur N did not affect soil respiration at concentrations of 2.89 and 28.9 mg propamocarb hydrochloride/kg soil. Effects of > ± 25% on soil nitrification were observed after 14 days but reached control levels after 28 days. Effects of on soil nitrification exceeding the trigger of 25% were observed in studies with Proplant at an application rate of 108.3 kg/ha (= 100 times the field rate). In the clayey sand soil the effect were less than 25 % at the end of the study on day 90 but the effect of + 31.36 % was still above the trigger in the sandy loam soil after 90 days. Since the tested dose was 100 times the proposed field rate and the observed effect decreased with time (which could have resulted in levels below 25 % after 100 days) the risk is considered to be low for soil non-target micro organisms.

The experts´ meeting discussed whether the effects observed in the ammonium concentrations should be considered in the risk assessment. The meeting concluded that ammonium is a variable interim product and hence not relevant as an endpoint. The meeting agreed that there are no concerns about the nitrogen metabolism.

The risk to soil non-target micro-organisms is considered to be low for all representative uses.

### 5.8. Risk to other non-target-organisms (flora and fauna)

The effects of Previcur N on emergence of seedlings and on vegetative vigor were tested with 4 monocotyledonous and 6 dicotyledonous plant species at a dose rate of 9.18 kg propamocarb hydrochloride/ha. No significant effects were observed except for oat, wheat, cucumber and soybean. The effects were less than 50%. A dose response test with cucumber and wheat was conducted at dose rates ranging from 1.02 to 82.62 kg propamocarb hydrochloride/ha. No effects of >16% were observed on seedling emergence and vegetative vigor up to the highest tested dose and the NOEC was determined as 9.18 mg propamocarb hydrochloride/ha.

The risk to other non-target plants is considered to be low for all representative uses.

### 5.9. Risk to biological methods of sewage treatment

No significant inhibitory effects on the respiration of activated sewage sludge were observed after 30 minutes and 3 hours of exposure to a dose of 666 mg propamocarb hydrochloride/L (Previcur N) and 100 mg propamocarb hydrochloride/L (Proplant). The observed endpoints are three orders of magnitude higher than the peak PECsw values. Therefore it is concluded that the risk to biological methods of sewage treatment is low for all representative uses.

## 6. Residue definitions

**Soil**

Definitions for risk assessment: propamocarb hydrochloride

Definitions for monitoring in the case of accident or misuse: propamocarb and its salts, expressed as propamocarb

**Water**

**Ground water**

Definitions for exposure assessment: propamocarb hydrochloride

Definitions for monitoring in the case of accident or misuse: propamocarb and its salts, expressed as propamocarb

**Surface water**

Definitions for risk assessment: propamocarb hydrochloride

Definitions for monitoring in the case of accident or misuse: propamocarb and its salts, expressed as propamocarb

**Air**

Definitions for risk assessment: propamocarb hydrochloride

Definitions for monitoring in the case of accident or misuse: propamocarb and its salts, expressed as propamocarb

**Food of plant origin**

Definitions for risk assessment: sum of propamocarb and its salts, expressed as propamocarb ~~(hydrochloride)~~

Definitions for monitoring: sum of propamocarb and its salts, expressed as propamocarb ~~(hydrochloride)~~

**Food of animal origin**

Definitions for risk assessment: no residue definition is needed as livestock exposure is not significant.

Definitions for monitoring: no residue definition is needed as livestock exposure is not significant.

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

**Soil**

| **Compound (name and/or code)** | **Persistence** | **Ecotoxicology** |
|---|---|---|
| Propamocarb hydrochloride | Moderate to high persistent<br>$DT_{50lab,\ 20^{\circ}C}$ 10.9 – 136.0 days | The risk to earthworms and soil non-target micro-organisms was assessed as low. |

**Ground water**

| **Compound (name and/or code)** | **Mobility in soil** | **> 0.1 µg / L 1m depth for the representative uses**<br>**(at least one FOCUS scenario or relevant lysimeter)** | **Pesticidal activity** | **Toxicological relevance** | **Ecotoxicological relevance** |
|---|---|---|---|---|---|
| Propamocarb hydrochloride | Slight to very high mobile<br>$K_{foc}$ = 41.0 – 2451.0 mL/g | FOCUS PELMO for lettuce and potatoes use: <0.1 µg/L for all scenarios<br>Modelling for tomatoes use is needed but it is unlikely to have an impact on the assessment | Yes | Yes | |

**Surface water and sediment**

| **Compound (name and/or code)** | **Ecotoxicology** |
|---|---|
| Propamocarb hydrochloride | The risk to aquatic organisms was assessed as low for all representative uses based on the assumption that the use in potatoes is the critical GAP in terms of exposure of aquatic organisms. This assumption is not certain for the use in tomatoes in southern Europe and a PECsw calculation and a risk assessment for aquatic organisms is required. |

**Air**

| **Compound (name and/or code)** | **Toxicology** |
|---|---|
| Propamocarb hydrochloride | Low acute toxicity via inhalation |

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

- Data or a justification on the effects of pH on the water solubility (relevant for Bayer CropScience, the rapporteur Member State has received a study but not evaluate it, March 2006, data gap identified by EFSA after the meeting of experts and the needed clarification from the rapporteur Member State; refer to chapter 1).
- Data on the derivatisation step used in the analytical method for the determination of one impurity in the technical material (relevant for Chimac Agriphar , the rapporteur Member State has received a study but not evaluate it, March 2006, data gap identified during the meeting of experts, refer to chapter 1).
- Depending on whether or not the applicants want a common specification, the applicants will have to analyse new batch data for all the impurities in the common specification in the respective technical materials (refer to chapter 1).
- A new *in vitro* dermal absorption study is available but not peer reviewed.(relevant for Bayer CropScience; the rapporteur Member State has received the study in September 2005 and summarised it in March 2006)
- Potential surface water contamination for use on tomatoes in Southern Europe applied in the field (T3 & T4) with drip irrigation (data gap identified by EFSA after the meeting of experts, date of submission unknown; refer to point 4.2).
- Potential ground water contamination for use on tomatoes in Southern Europe applied in the field (T3 & T4) with drip irrigation (data gap identified by EFSA after the meeting of experts, date of submission unknown; refer to point 4.2)[4].
- Information to support the PT assumption for herbivorous birds (relevant for the use of Previcur N in lettuce; data gap identified by EFSA; date of submission unknown; refer to point 5.1).
- Data to support the PT refinement and a new calculation of residue decline is required to address the long-term risk to herbivorous birds (relevant for the use of Proplant in lettuce; data gap identified by EFSA; date of submission unknown; refer to point 5.1.)
- A refined risk assessment for birds and mammals for the uptake of contaminated drinking water (relevant for all representative uses; data gap identified by EFSA; date of submission unknown; refer to point 5.1).
- Clarification is needed whether the use in tomatoes in southern Europe includes a soil drench application in the field. (relevant for the use in tomatoes in southern Europe; data requirement identified in the Evaluation meeting of May 2005, the experts' meeting confirmed the need of further clarification whether the use in tomatoes in Southern Europe includes a drench use outdoors; further information submitted by BCS in March 2006; refer to point 5).
- An aquatic risk assessment has to be conducted for the use in tomatoes in southern Europe. (relevant for the use in tomatoes in southern Europe; data gap identified by EFSA; date of submission unknown; refer to point 5.2).

[4] Modelling results are not expected to have an impact on the risk assessment.

## CONCLUSIONS AND RECOMMENDATIONS

**Overall conclusions**

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide, which comprise foliar spraying, drenching or drip irrigation to control a broad spectrum of plant diseases in lettuce, potatoes, tomato (grown in soil and rock wool).

The application rates are:

- in lettuce 2 applications resulting in a maximum total dose of 144.4 kg propamocarb hydrochloride per hectare (drenching) and 2 applications resulting in a maximum total dose 3.32 kg per hectare (spraying)
- in potatoes up to 6 applications resulting in a maximum total dose of 6.498 kg per hectare (spraying)
- in tomatoes (soil grown) 2 applications resulting in a maximum total dose of 144.4 kg per hectare (drenching) and 2 applications resulting in a maximum total dose of 4.332 kg per hectare (drip irrigation)
- in tomatoes (rock wool grown) 1 application 28.9 kg per hectare (drenching) and 4 applications resulting in a maximum total dose of 8.664 kg per hectare (drip irrigation).

Propamocarb can only be used as fungicide.

The representative formulated products for the evaluation were "Previcur N" and "Proplant", both are soluble concentrate (SL), registered in most of the Member State of the EU.

Adequate methods are available to monitor all compounds given in the respective residue definition. Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues. It should be noted that the analytical methods are not able to differentiate between residue of propamocarb and its salts.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Propamocarb hydrochloride is of low acute oral, dermal and inhalation toxicity; it is not a skin or an eye irritant, but it is a skin sensitiser, as confirmed during the meeting on the basis of the positive results in the Magnusson & Kligman test and the recently submitted LLNA (**R43 "May cause sensitisation by skin contact"** is proposed). There is no evidence of genotoxicity or carcinogenic potential associated with propamocarb hydrochloride. In the reproductive toxicity studies, the parental ~~NOAEL was 15 mg a.s./kg bw/day, while the~~ and reproductive NOAELs were 37.5. mg a.s /kg bw/day based on decreased sperm concentration and count in the epipdidymis; the parental and developmental NOAELs were 31 mg a.s./kg bw/day based on decreased individual foetal body weight and increased number of small foetuses at 123 mg a.s/kg bw/day in the rat. The NOAEL for acute neurotoxicity was set at 1321 mg /kg bw/day propamocarb hydrochloride; the NOAEL for subchronic neurotoxicity in rat was 72mg/kg bw /day propamocarb hydrochloride, based on the occurrence of intra-epithelial vacuolation of the choroids plexus in cerebrum and cerebellum at higher doses. The ADI and AOEL are 0.29 mg/kg bw/day, while the ARfD is 1 mg/kg bw/day. The operator, worker and bystander risk assessment is inconclusive.

The metabolism of propamocarb hydrochloride in plants has been fully elucidated. Applied by foliar treatment of plants, the compound is degraded through hydroxylation, oxidation, N-demethylation and cyclisation, but however remains the major compound of the residue pattern. Applied by soil treatment or hydroponically with nutritive solution, its levels, as well as those of its structurally related metabolites, resulting from uptake and translocation into edible parts of the plants are low. In this case the major part of the radioactivity present in plants is due to the incorporation in the plant of the $CO_2$ produced by complete degradation of the compound. Similar residue pattern is found in potato tubers after foliar treatment of the aerial parts of the plant. The residue definition proposed consists therefore in the sum of propamocarb and its salts.

Supervised residue trials adequately supporting all the representative uses have been submitted. In lettuce it has been identified that the use of propamocarb hydrochloride in winter under glasshouse condition leads to the highest residue levels. In tomatoes, hydroponical application on rockwool may lead to low measurable residue levels, while this type of application on soil-grown tomatoes leads consistently to residue levels below the LOQ of the employed method of analysis (0.01 mg/kg). In potatoes, residues were always below the LOQ of the method of analysis (0.1 mg/kg). On the basis of these residue trials, MRLs can be proposed at 30 mg/kg for lettuce and at 0.1 mg/kg for both tomatoes and potatoes.

In succeeding and rotational crops, residues of propamocarb may be present for short plant back intervals. Based on the available information, a delay of 120 days should be observed between the last application of propamocarb hydrochloride and the sowing or planting of the following crop to avoid any significant transfer of soil residues.

Residues in animal commodities or in processed commodities resulting from the representative uses are not expected.

The conducted acute and chronic exposure assessments do not suggest any risk for the health of the consumer.

Sufficient data are available to assess the route and rate of degradation of propamocarb hydrochloride in soil, surface water and associated sediment, and air. The studies available indicated that propamocarb hydrochloride is relatively non-persistent, with degradation primarily through biotic processes such as microbial mediated metabolism. The active ingredient does not leach and is not expected to contaminate the groundwater. Member States may require that predicted environmental concentrations in surface water and in groundwater for the use on tomatoes should be revised to take into account the drip irrigation method being used for field applications. Furthermore, Member States should consider the possibility of a relationship between the extent of adsorption of propamocarb hydrochloride to soil and the clay content of soil, if supported by sufficient statistical analysis.

For the use in lettuce it is questionable if the risk to herbivorous birds is sufficiently addressed on the basis of the submitted residue data in lettuce. Further information to support the PT assumption is required. The risk to mammals and to insectivorous birds is considered to be sufficiently addressed for all representative uses. The risk to aquatic organisms was assessed as low for all representative uses assuming that the potato use is the critical gap in terms of exposure of aquatic organisms. It is not certain if this is true for the use in tomatoes in southern Europe and an aquatic risk assessment has to be conducted for this use. A high in-field risk was indicated for non-target arthropods. The experts´ meeting agreed that the submitted higher tier studies (extended laboratory studies) provided sufficient information to conclude on a low off-field and in-field risk to non-target arthropods for all representative uses. No effects were observed in tests with Previcur N at a concentration of more than 2 times the initial PEC soil for the critical GAP (potatoes). Effects of > ± 25% on soil nitrification were observed in a test with Proplant. However, the tested dose was 100 times the proposed field rate and the observed effect decreased with time. Therefore the risk to soil non-target micro organisms risk is considered to be low for all representative uses.
The risk to bees, earthworms, other non target organisms and biological methods of sewage treatment was assessed as low for all representative uses.

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

- None

## Critical areas of concern

- The operator, worker and bystander risk assessment is inconclusive.

# 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) ‡ | Propamocarb<br>(unless otherwise stated, the following data relate to the variant propamocarb hydrochloride) |
| Function (e.g. fungicide) | Fungicide |

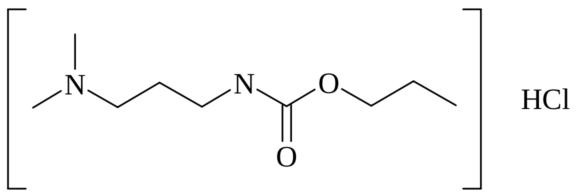
| | |
|---|---|
| Rapporteur Member State | Ireland |
| Co-rapporteur Member State | -- |

**Identity (Annex IIA, point 1)**

| | |
|---|---|
| Chemical name (IUPAC) ‡ | Propyl 3-(dimethylamino)propylcarbamate (propamocarb)<br>Propyl 3-(dimethylamino) propylcarbamate hydrochloride |
| Chemical name (CA) ‡ | Propyl [3-(dimethylamino)propyl]carbamate (propamocarb)<br>carbamic acid, [3-dimethylaminopropyl]-, propyl ester, monochloride |
| CIPAC No ‡ | 399 (Propamocarb)<br>399.601 (Propamocarb HCl) |
| CAS No ‡ | 24579-73-5 (Propamocarb)<br>25606-41-1 (Propamocarb HCl) |
| EEC No (EINECS or ELINCS) ‡ | 247-125-9 (Propamocarb HCl) |
| FAO Specification ‡ (including year of publication) | No FAO specification |
| Minimum purity of the active substance as manufactured ‡ (g/kg) | TC: 92% w/w, 920g/kg **(Bayer CropScience)**<br>97% w/w, 970 g/kg **(Chimac Agriphar)**<br>TK: 69% w/w, 749 g/L **(Bayer CropScience)** |
| Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg) | None identified |
| Molecular formula ‡ | $C_9H_{21}ClN_2O_2$ |
| Molecular mass ‡ | 224.7 |

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

Structural formula ‡



**Physical-chemical properties (Annex IIA, point 2)**

| | |
|---|---|
| Melting point (state purity) ‡ | 64.2 ºC (100.3% purity) |
| Boiling point (state purity) ‡ | Product decomposed at 150 ºC (99.1% purity) |
| Temperature of decomposition | 150 ºC (99.1% purity) |
| Appearance (state purity) ‡ | White/cream soft solid (97.2% purity) |
| Relative density (state purity) ‡ | 1.16 at 20.5 ºC (97.2% purity) |
| Surface tension | 71.98 mN/m at 20 ºC (97.2% purity)<br>Concentration of test substance = 1g/L |
| Vapour pressure (Pa at 25°C) ‡ | Two values have been submitted<br>8.1 x 10-5 Pa at 25 ºC [97.7% purity]<br>1.66 x 10-3 Pa at 25 ºC [99.1% purity]<br>Test substance is slightly volatile |
| Henry's law constant (Pa $m^3$ $mol^{-1}$) ‡ | K = 8.5 x 10 –9 Pa m3 mol-1 . |
| Solubility in water ‡ (g/L , at 20°C) | Between 89.2 and 93.5%w/w at pH 4<br>Between 89.1 and 93.8%w/w at pH 7<br>Between 89.6 and 94.6%w/w at pH 10 (20 ºC)<br>Purity of test substance 99.1% |
| | 1005 g/kg (pH unknown, ***data required***) (Bayer CropScience)<br>Purity of test substance 100.0% |
| Solubility in organic solvents ‡ (g/L, at 20°C) | Hexane <0.01<br>Toluene 0.04<br>Methanol >656<br>Dichloromethane >626<br>Ethyl acetate 4.8<br>Acetone 560<br>Xylene $1.6x10^{-2}$<br>Heptane $<1x10^{-4}$<br>Purity of test substance 100.0% |

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

| | |
|---|---|
| Partition co-efficient (log POW) ‡ (state pH and temperature) | Two values have been submitted<br>log $P_{OW}$ = -2.9, -1.2 & 0.67 at pH 2, 7 & 9, respectively<br>log $P_{OW}$ = -0.98, -1.4 & 0.32 at pH 2, 7 & 9, respectively |
| Hydrolytic stability ($DT_{50}$) ‡ (state pH and temperature) | <10% hydrolysis at PH 4, 7 & 9 at 50ºC over a five day period |
| Dissociation constant ‡ | pKa = 9.6 at 20 ºC |
| UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength) | Absorption observed at λ 203 and 217nm at pH 7, in 0.1M HCl and in 0.1M NaOH. No absorbance >290nm. |
| Photostability in water ($DT_{50}$) ‡ | No degradation of a.s. in aqueous solution when irradiated for 92 hr. at 20 ºC with a wavelength of λ >290nm. |
| Quantum yield of direct phototransformation in water at λ > 290 nm ‡ | N.A. No photodegradation. |
| Flammability ‡ | Not flammable (TK) |
| Explosive properties ‡ | Not explosive |

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

## Summary of representative uses evaluated (propamocarb hydrochloride – Bayer CropScience)*

| **Crop and/or situation** | **Country** | **Product name** | **F G or I** | **Pests or Group of pests controlled** | **Preparation** | | **Application** | | | | **Application rate per treatment** | | | **PHI (days)** | **Remarks:** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | (l) | (m) |
| (a) | | | (b) | (c) | Type (d-f) | Conc. of a.s. (i) | method kind (f-h) | growth stage & season (j) | number min max (k) | interval between applications (min) | kg as/hl min max | water L/ha min max | kg as/ha min max | | |
| Bayer CropScience | | | | | | | | | | | | | | | |
| Lettuce | North and South | Previcur N | F/ G | *Bremia lactucae* | SL | 0.72 kg/L | Drench | - | 2 | T1: after seeding<br>T2: before transplanting | T1: 0.360<br>T2: 0.18 | 20000 | T1: 72.2 (10ml/m$^2$)<br>T2: 36.1 (5ml/m$^2$) | 21 | [1] [3] |
| | | | | | | | Foliar spray | - | 2 | T3: just after transplanting<br>T4: 12-16d after transplanting | T3 & T4: 0.072 - 0.415 | 400 - 2000 | T3 & T4: 1.44 - 1.66 | | |
| Tomato rockwool | North and South | Previcur N | G | *Phytophtora spp.*<br>*Pythium spp.* | SL | 0.72 kg/L | Drench | -- | 1 | T1: 0-10d after seeding | T1: 0.058-0.144 | 20000 - 50000 | T1: 28.9 (4ml/m$^2$) | 3 | [1] |
| | | | | | | | Nutrient solution | - | 4 | T2: just after transplanting<br>T3: T2 + 7 d<br>T4: maturing<br>T5: T5 + 7-10 d | T2, T3, T4 & T5: 0.024 - 0.12 | 3000 | T2, T3, T4 & T5: 0.722-2.166 | | |

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

| Crop and/or situation | Country | Product name | F G or I | Pests or Group of pests controlled | Preparation | | Application | | | | Application rate per treatment | | | PHI (days) (l) | Remarks: (m) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (a) | | | (b) | (c) | Type (d-f) | Conc. of a.s. (i) | method kind (f-h) | growth stage & season (j) | number min max (k) | interval between applications (min) | kg as/hl min max | water L/ha min max | kg as/ha min max | | |
| Tomato<br>(soil grown crop) | Indoor & outdoor in South | Previcur N | G & F | *Phytophora spp.*<br>*Pythium spp.* | SL | 722 g/L | Drench | - | 2 | T1: 0 –10 d after seeding<br>T2: 7-10d before transplanting | T1: 0.36<br>T2: 0.18 | 20,000 – 40,000 | T1 & T2: 72.2 (10ml/m$^2$) | 3 | Protected in field (Plastic tunnel) |
| | | | | | | | Nutrient solution | - | 2 | T3: maturing<br>T4: T3 + 7-10d | T3 &T4: 0.0722 | 3,000 | T3 &T4: 2.166 | | Outdoor only in Southern Europe<br>[1] [2] [3] |
| Chimac Agriphar | | | | | | | | | | | | | | | |
| Lettuce | N & S | Proplant | G | *Damping off: Phytophtora spp. / Pythium spp.* | SL | 722 g/L | Drench in nurserie s | - | 2 max | T1: at sowing<br>T2: before transplanting | T1 & T2: 0.06 - 0.24 | 30,000 – 60,000<br>(3-6 L/m2) | T1 & T2: 36.1-72.2<br>(5-10ml/m$^2$) | n.a. | 5-10 ml Proplant/m$^2$ : 3-6 L of 0.15% solution (15ml Proplant in 10L water) / m$^2$<br>USED IN NURSERIES |
| | | | F & G | *Bremia lactucae* | | | Foliar spray | - | 3 max | T3: after transplanting<br>T4/T5 :repeat after 10 days | T3-T5: 0.072 | 1500 L | T3-T5 : 1.083 | 21 | 1.5 L Proplant/ha<br>[1] [2] [3] |

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

| Crop and/or situation | Country | Product name | F G or I | Pests or Group of pests controlled | Preparation | | Application | | | | Application rate per treatment | | | PHI (days) | Remarks: |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | (l) | (m) |
| (a) | | | (b) | (c) | Type (d-f) | Conc. of a.s. (i) | method kind (f-h) | growth stage & season (j) | number min max (k) | interval between applications (min) | kg as/hl min max | water L/ha min max | kg as/ha min max | | |
| Potatoes | N & S | Proplant | F | Mildew: Phytophthora infestans | SL | 722 g/L | Foliar spray | As 1$^{st}$ symptoms occur | 6 max | Repeat each 7 days | T1-T6 : 0.216 | 500 L | T1-T6 : 1.083 | 14 | 1.5 L Proplant/ha in association with half rate of applic. of any contact fungicide e.g. 1.6 kg/ha mancozeb or 1.0 kg/ha chlorothalonil [1] |

[1] The risk assessment for operators, workers and bystanders is inconclusive
[2] The risk assessment has revealed data gaps in section 4.
[3] The risk assessment has revealed data gaps in section 5.

| 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 |

North of Europe (N) or South of Europe (S)

‡ 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) | Test substance dissolved in methanol/water (80:20, v/v) and analysed using HPLC with UV detection. |
| Impurities in technical as (principle of method) | The following methods were used for analysis of the various impurities.<br>1. Test substance dissolved in dichloromethane, analysed using GC with FID detection.<br>2. Test substance dissolved in DMSO, equilibrated at 75 °C prior to head space injection and analysis using GC/FID.<br>3. Test material was dissolved in water, to which aqueous sodium hydroxide was added. Following extraction with dichloromethane, the aqueous solution was derivatized using benzoyl chloride and the resultant derivative extracted into dichloromethane and analysed using GC/FID.<br>4. Test material diluted in methanol/water was analysed using HPLC, with UV detection.<br>5. Test material was dissolved in water, diluted to 50ml with 1,4-dioxane and filtered. The sample was then analysed using GC/FID. |
| Plant protection product (principle of method) | Test substance dissolved in methanol/water (80:20, v/v) and analysed using HPLC with UV detection at 210 nm.<br>(CIPAC method 399, 1993). |

### Analytical methods for residues (Annex IIA, point 4.2)

| | |
|---|---|
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) | 1. Propamocarb residues were extracted with acetic acid (1% aqueous solution), eluted from C18 SPE with acetonitrile/water/acetic acid (20:80:1, v/v). Residues were determined by HPLC with MS/MS detection.<br>Detection was at *m/z* = 189 (parent ion) –>102 + 144 (daughter ion).<br>LOQ = 0.01 mg/kg.<br>The method was independently validated for tomatoes and lettuce.<br>The method is acceptable for analysis of residues of propamocarb and its salts in food/feed |

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

| | |
|---|---|
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) | An analytical method is not required due to fact that no MRL is proposed. |
| Soil (principle of method and LOQ) | 1. 1 N Hydrochloric acid was added to soil and the samples were shaken on a horizontal flatbed shaker for approx. 60 min., then centrifuged and the supernatant removed. The extracts were collected and brought to pH 6-7 with an ammonia solution (~25%). The extract was cleaned up on a C18 column and analysed using HPLC-MS/MS. Atmospheric pressure chemical ionisation (APCI) mode was used. The parent ion *m/z* 189 and two fragment ions *m/z* 102.1 and 144 were used for quantitation<br>LOQ = 0.02 mg/kg<br>Soil samples were shaken in methanol/saturated NaCl (5:1, v/v) and the methanol fraction was evaporated. The aqueous fraction was adjusted to pH 3-4 using a 0.1 N HCl solution. This was then washed with dichloromethane and the pH of the aqueous phase was adjusted to >11.5. Combined dichloromethane fractions were evaporated to dryness, reconstituted in methanol/water (80:20, v/v) and analysed using HPLC-MS/MS in the positive ion mode. The ions monitored were *m/z* 189.3 (parent ion) and *m/z* 102.3 (fragment ion).<br>LOQ = 0.02 mg/kg<br>The method is acceptable for analysis of residues of propamocarb and its salts in soil |
| Water (principle of method and LOQ) | Alkaline treated water was extracted with dichloromethane. Dichloromethane was evaporated off and the extract reconstituted in a suitable solvent prior to analysis using HPLC-MS/MS in the positive ion mode. The ions monitored were *m/z* 189 (parent ion) and *m/z* 102 (fragment ion). The samples tested represented both drinking and surface water<br>LOQ = 0.05 µg/L<br>The method is acceptable for analysis of residues of propamocarb and its salts in drinking and surface water |
| Air (principle of method and LOQ) | Two methods were considered suitable for analysis of residues of propamocarb in air.<br>1. Samples of air were drawn through silica gel adsorption tubes at a flow rate of ~0.3 L/min. for a period of 6 hr. (total air sampling volume = 0.1 $m^3$). The silica gel was extracted three times with a mixture of acetonitrile/water/acetic acid/ammonia |

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

| | |
|---|---|
| | (200:800:10:2, v/v/v/v). The total combined extract was analysed using LC-MS/MS with atmospheric pressure chemical ionisation (APCI) source. Quantification was based on MS of the daughter ion peak 144 *m/z*, resulting from the protonated molecular propamocarb ion observed at 189 *m/z*. For further confirmation a second transition resulting in a daughter ion at 102 *m/z* was included in the method.<br>LOQ = 9 µg/$m^3$.<br><br>2. Tenax TA was spiked with a methanol solution of propamocarb. The efficiency of the extraction procedure with methanol/water (80:20) was assessed by recovery after 7.5 hr. with an air flow of 3 L/min. The degree of trapping was assessed by 2 hr. and 7.5 hr. recovery tests of samples, with an air flow of 3 L/min at 35 ºC and >80% relative humidity.<br>The stability of propamocarb adsorbed on Tenax TA was demonstrated for a period of 14 days at ambient temperature and at -20 ºC. Residues were determined by GC-MS/MS.<br>LOQ = 0.4 µg/$m^3$ |
| 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 | No classification required. |

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

## Appendix 1.3: Impact on Human and Animal Health

The notifiers were asked to provide information for the test material used in the toxicity studies (i.e. propamocarb or propamocarb hydrochloride). Information has been submitted to the RMS in March 2006 but not peer reviewed, therefore it's still missing from the below reported table.

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

| | |
|---|---|
| Rate and extent of absorption ‡ | Rapid (78 – 96%) within 72h |
| Distribution ‡ | Mainly in organs associated with biotransformation (liver, lung, kidney). These were the only ones which had quantifiable amounts recorded (<0.17 mg equivalents/kg tissue). The highest transitory concentrations of radiolabel were detected in liver and kidneys between 0.75 and 3 hours post-dosing. Terminal half-life for all tissues was 11 – 26h |
| Potential for accumulation ‡ | No evidence of accumulation |
| Rate and extent of excretion ‡ | Rapid excretion - 91 to 94% within 72h for LD and HD respectively. Majority via urine (88 – 92% in 72h). Gender independent |
| Metabolism in animals ‡ | Extensively metabolised with only between 1.1 and 11% excreted as unchanged propamocarb-anion in the low dose animals and up to 20% in high dose. Four major metabolites identified:<br>2-hydroxypropyl 3-(dimethylamino)propylcarbamate, propyl [3-(methylamino)propyl]carbamate, propyl-3-(dimethylamino)propylcarbamate-N-oxide and 3-(3-dimethylaminopropyl)-4-hydroxy-4-methyloxazolidin-2-one |
| Toxicologically significant compounds ‡ (animals, plants and environment) | Propamocarb hydrochloride, 2-hydroxypropyl 3-(dimethylamino)propylcarbamate, propyl [3-(methylamino)propyl]carbamate, propyl-3-(dimethylamino)propylcarbamate-N-oxide and 3-(3-dimethylaminopropyl)-4-hydroxy-4-methyloxazolidin-2-one |

### Acute toxicity (Annex IIA, point 5.2)

| | |
|---|---|
| $LD_{50}$ oral | $LD_{50}$ > 2000 mg/kg bw |
| $LD_{50}$ dermal | $LD_{50}$> 2000 mg/kg bw |
| $LC_{50}$ inhalation | $LC_{50}$ > 5.01 mg/L |
| Skin irritation | Non-irritant |
| Eye irritation | Non-irritant |

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

| | |
|---|---|
| Skin sensitization (result and test method used) | Sensitiser (9/20 animals sensitised) (Magnusson and Kligman) **R43** |

**Short term toxicity (Annex IIA, point 5.3)**

| | |
|---|---|
| Target / critical effect ‡ | Vacuolar alterations of secretory epithelial cells in rat and dog. In the **rat** vacuolation occurred in the choroid plexus and lacrimal glands; in the **dog** vacuolation was evident in salivary glands, tracheal glands, lungs (bronchial glands), oesophagus, stomach (pyloric glands), duodenum (brunners glands), lacrimal glands and mandibular lymph nodes. |
| Lowest relevant oral NOAEL / NOEL ‡ | < 39 mg/kg /day Propamocarb (lowest dose tested), in a 1-year dog feeding study.<br>45 mg/kg bw/day in 90 day dog study<br>100 mg/kg bw/day in 28 day rat study |
| Lowest relevant dermal NOAEL / NOEL ‡ | 300 mg/kg propamocarb, based on vacuolation of the choroid plexus in a 28-day rat study. Dermal irritation was observed at 71.7 mg/kg a.s. in a 21-day rat study. |
| Lowest relevant inhalation NOAEL / NOEL ‡ | No data, not required |

**Genotoxicity ‡ (Annex IIA, point 5.4)**

| | |
|---|---|
| ...................................................................... | No genotoxic potential |

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

| | |
|---|---|
| Target/critical effect ‡ | Vacuolar change, choroid plexus |
| Lowest relevant NOAEL / NOEL ‡ | 29 mg/kg bw/day (female rat; 52-week dietary study) |
| Carcinogenicity ‡ | No evidence of carcinogenic potential |

**Reproductive toxicity (Annex IIA, point 5.6)**

| | |
|---|---|
| Parental/maternal critical effect ‡ | Bodyweight, food consumption and vacuolar changes ($F_o$ females) |
| Lowest relevant parental/maternal NOAEL / NOEL ‡ | 37 mg/kg bw/day as (rat, gavage) |
| Reproduction target / critical effect | Sperm concentration and count (F1 males) |
| Lowest relevant reproductive NOAEL / NOEL | 37.5 mg/kg bw/day as (rat, gavage) |

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

| | |
|---|---|
| Developmental target / critical effect ‡ | Increased number of small foetuses and ↓ weight of live foetuses |
| Lowest relevant developmental NOAEL / NOEL ‡ | 31 mg/kg bw/day (rat, dietary) |

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

| | |
|---|---|
| Target / critical effects | Vacuolation of choroids plexus in ventricles of cerebrum and cerebellum |
| Lowest relevant NOAEL / NOEL | 72(♂); 86(♀) (1500 ppm) from rat 90-day study<br>Acute neurotoxicity – no neurotoxicity at 1321 mg/kg bw (highest dose tested), NOAEL 134 mg/kg bw (reduced bodyweight) |

**Other toxicological studies ‡ (Annex IIA, point 5.8)**

| | |
|---|---|
| | None available. |

**Medical data ‡ (Annex IIA, point 5.9)**

| | |
|---|---|
| | No actual cases of human intoxication with propamocarb (hydrochloride) documented. The low animal toxicity of the active substance suggests accidental or occupational poisoning to be unlikely. No known cases of general ill health in production plant workers. |

| **Summary (Annex IIA, point 5.10)** | Value | Study | Safety factor |
|---|---|---|---|
| ADI ‡ | 0.29 mg propamocarb hydrochloride/ kg bw/day | 52-week dietary study in rats | 100 |
| $AOEL_{Systemic}$ ‡ | 0.29 mg propamocarb hydrochloride/ kg bw/day | 52-week dietary study in rats | 100 |
| ARfD ‡ (acute reference dose) | 1 mg propamocarb hydrochloride/ kg bw/day | 28-day rat study (gavage) | 100 |

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

**Dermal absorption (Annex IIIA, point 7.3)**

| | |
|---|---|
| *In vivo* dermal absorption, human | Provisional value of 10% for concentrate and dilution based on rat *in vivo* and rat/human *in vitro* (Previcur N). |

**Acceptable exposure scenarios (including method of calculation)**

| | |
|---|---|
| Operator | Inconclusive |
| Workers | Inconclusive |
| Bystanders | Inconclusive |

**Classification and proposed labelling (Annex IIA, point 10)**

| | | |
|---|---|---|
| with regard to toxicological data | $X_i$; R43 | May cause sensitisation by skin contact |
| | Safety phrases | |
| | S2 | Keep out of the reach of children |
| | S24 | Avoid contact with skin |
| | S37 | Wear suitable gloves |
| | S46 | If swallowed, seek medical advice immediately and show this container or label. |

‡ 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 | Leafy crops (spinach and lettuce), fruits (tomatoes and cucumbers) and root vegetables (potatoes). |
| Rotational crops | Lettuce, radish and wheat. |
| Plant residue definition for monitoring | Sum of propamocarb and its salts, expressed as propamocarb ~~(hydrochloride)~~. |
| Plant residue definition for risk assessment | Same definition as above. |
| Conversion factor (monitoring to risk assessment) | Not applicable. |

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

| | |
|---|---|
| Animals covered | A metabolism study was not required. A metabolism study in the cow was however submitted. |
| Animal residue definition for monitoring | None required or proposed. |
| Animal residue definition for risk assessment | None required or proposed. |
| Conversion factor (monitoring to risk assessment) | Not applicable |
| Metabolism in rat and ruminant similar (yes/no) | Yes |
| Fat soluble residue: (yes/no) | Non fat soluble. |

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

| | |
|---|---|
| Information was provided | The studies indicate that residues may be present in crops planted within 30 after the application of propamocarb. The residue pattern in rotational crops is similar to that in primary crops. A recommendation on propamocarb products should indicate that crops should not be sowed or planted on soil within 120 days of the application of propamocarb. |

### Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 introduction)

| | |
|---|---|
| Stability studies were presented. | Propamocarb was found to be stable in lettuce, cucumber, tomato and in Brussels sprouts when stored in a freezer for the duration of the test periods which ranged from 1 to 2 years. |

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

**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 |
| | No feeding studies required | | |

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

**Summary of uses supported by available residue data (Annex IIA, point 6.3, Annex IIIA, point 8.2)**

| Crop | Northern or Mediterranean Region | Trials results relevant to the critical GAP (mg propamocarb/kg)[1] (a) | Recommendation/comments | MRL | STMR (b) |
|---|---|---|---|---|---|
| Protected lettuce | North and South | 1.48; 3.34; 9.1; 9.7; 12; 15; 15; 15.6; 26.2 (*values related to winter production*)<br>1.8; 1.9; 0.4; 0.6; 1.7; 7.8; 2.0; 5.9; 1.0; 0.2; 2.2; 4.7; 3.7; 15.7; 6.3; 5.6; 9.0; 21.2; 2.5; 4.0; 2.5; 5.38; 4.8; 14.0; 8.2; 10.4; 3.0; 7.0 (values for other seasons of production) | 2-3 foliar applications amounting to a total of 2.88 to 4.2 kg/ha, combined or not with drench application on seed bed<br><br>Note: Many trials were carried out before implementation of GLP and their individual reliability may be questionable for different reasons. However in their entirety they allow tendencies and conclusions to be drawn. That's the reason why a large selection of available results is reported here, rather than a narrow selection of trials which fully meet the current standards of acceptability. | 30 mg/kg | 12 mg/kg (winter production)<br><br>4.35 mg/kg (other seasons of production) |

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

| Crop | Northern or Mediterranean Region | Trials results relevant to the critical GAP (mg propamocarb/kg)[1] (a) | Recommendation/comments | MRL | STMR (b) |
|---|---|---|---|---|---|
| Field lettuce | North and South | 0.3; 0.2; 0.3; 1.64; 0.37; 0.4; 0.4; 11.2; 1.3; 7.2; 8.7; 0.04; (11); (31); (6.0); 0.1; 0.3; 2.5; 0.04; 0.3; 0.1; 1.0; 0.1; 0.3; <0.1; 0.3; 0.1; 0.2; 1.7; 1.0<br><br>Results in brackets winter cultivation (not representative for field lettuce) | 2-3 foliar applications amounting to a total of 3.15 to 4.2 kg/ha, combined or not with drench application on seed bed.<br><br>Note: Many trials were carried out before implementation of GLP and their individual reliability may be questionable for different reasons. However in their entirety they allow tendencies and conclusions to be drawn. That's the reason why a large selection of available results is reported here, rather than a narrow selection of trials which fully meet the current standards of acceptability. | 10 mg/kg | 0.34 mg/kg |
| Tomato | Cultivation on rockwool (Glasshouse). | 6 x < 0.01; 0.01; 0.02; 0.09. | | 0.1 mg/kg | 0.01 mg/kg |
| Tomato | Cultivation on soil (Field or glasshouse) | 10 x < 0.01 | | 0.01* mg/kg | 0.01 mg/kg |
| Potato. | N & S | 12 x < 0.1 mg/kg. | | 0.1 mg/kg | 0.1 mg/kg |

[1] In some trials the results was given as mg propamocarb hydrochloride. However this has no influence on the MRL proposals.
* Indicates that the MRL is set at the level of the LOQ

(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 | 0.29 mg propamocarb hydrochloride/kg/bw/day |
| TMDI (European Diet) (% ADI) | < 5% of the ADI for WHO European diet (adults) and for the national German diet (4-6 year old girl) |
| ARfD | 1 mg/kg propamocarb hydrochloride/kg bw/day |
| NESTI (% ARfD) | According to UK large portion size consumption data:<br>Tomatoes and potatoes: < 2 % of the ARfD<br>Lettuce: 50 % of the ARfD for 4-6 years old children (most exposed population sub-group). |

Note : The acute and chronic exposure assessments were carried out without converting the proposed MRLs as propamocarb to propamocarb hydrochloride. However this does not affect their outcomes significantly.

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

| Crop/processed crop | Number of studies | Transfer factor | % Transference * |
|---|---|---|---|
| Not applicable | Not applicable | | |

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

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

| | |
|---|---|
| For food of plant origin with the exception of lettuce, potatoes and tomatoes | 0.05* mg/kg. |
| Lettuce | 30 mg/kg |
| Tomatoes | 0.1 mg/kg |
| Potatoes | 0.1 mg/kg. |
| Food of animal origin | No MRL is proposed for food of animal origin as livestock exposure is not significant. |

*) Indicates that the MRL is set at the level of 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 ‡ | At 20 °C:<br>11.7-52.5% AR after 90d (n = 9)<br><br>At 25 °C<br>82.2-83.6% AR after 90d (n = 2)<br><br>Two different radiolabelled versions (aminopropyl-1-[$^{14}$C] and aminopropyl-2-[$^{14}$C]) of propamocarb hydrochloride were used in the fate studies. The position of radiolabelling was not observed to have an effect on any fate endpoint. |
| Non-extractable residues after 100 days ‡ | NER maximum levels<br>17.8-49.0% AR after 90d at 20 °C- (n=9)<br>11.8-12.6% AR after 90d at 25 °C- (n=2) |
| Relevant metabolites - name and/or code, % of applied ‡ (range and maximum) | Transient unidentified metabolites reached maximum individual levels ranging from 1.0-8.7% of applied radioactivity (time of maximum occurrence = 0-90 days) (n = 22 incubations; 15 soils tested – 9 soils incubated at 20 °C, 3 soils incubated at 10 °C, 1 soil incubated at 15 °C, 1 soil incubated at 22 °C, 5 soils incubated at 25 °C) |

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

| | |
|---|---|
| Anaerobic degradation ‡ | n = 2 soils (>30 days conditioning under anaerobic conditions followed by 121-365 days anaerobic incubation)<br>Mineralisation: $CO_2$ = 1.9, 3.5, and 7.7% after 365, 121, and 90 days, respectively<br>Non-extractable residues: 8.1, 33.5, and 40.64% after 14, 269, and 121 days, respectively<br><br>Metabolites:<br>Transient unidentified metabolites reached maximum individual levels of <2.0% and 6.65% after 180 and 365 days, respectively |
| Soil photolysis ‡ | n = 2 soils<br>Mineralisation: $CO_2$ = 1.9-2.7% after 31 days (irradiated samples), $CO_2$ = 0.0-8.8% after 31 days (non-irradiated samples)<br>Non-extractable residues: 9.5-21.0% after 31 days (irradiated samples), 6.6-15.6% after 31 days (non- |

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

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|---|---|
| | irradiated samples)<br><br>Metabolites:<br>Transient unidentified metabolites reached maximum individual levels of 1.0% and 8.7% after 14 and 30 days, respectively |

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

| | |
|---|---|
| Method of calculation | Laboratory:<br>Aerobic studies on propamocarb hydrochloride – non-linear simple first order, mono-exponential regression of parent (using Microsoft Excel tools Solver and RATEFIT). Where a short lag phase was observed the lag time data was fitted using zero-order degradation.<br>Aerobic studies on metabolites – not applicable<br><br>Anaerobic study – non-linear simple first order, mono-exponential and simple linear first order regression of parent, was used for the total system. A bi-exponential equation was used for the water phase.<br><br>Soil photolysis study – non-linear simple first order, mono-exponential and simple linear first order regression, accounting for the effect of non-photolytic degradation<br>Saturated zone degradation studies – not applicable<br><br>Field studies:<br>Non-linear simple first order regression of parent. |
| Laboratory studies ‡ (range or median, with n value, with $r^2$ value) | Aerobic studies (HCl: hydrochloride):<br>Propamocarb HCl $DT_{50lab}$ (20 °C, aerobic): 10.9, 11.7, 14.1, 17.8, 22.4, 23.4, 29.7, 87.7, 137 days (n = 9 soils, $r^2$ = 0.91-0.98), mean = 39.3 days<br>Propamocarb HCl $DT_{50lab}$ (25 °C, aerobic): 10.0, 13.0, 14.0, 28.0 days, (n = 3 soils) mean = 16.25 days<br>Propamocarb HCl $DT_{50lab}$ (22 °C, aerobic): 17.7 days (n = 1 soil)<br>Metabolites: Not applicable<br><br>For FOCUSgw modeling (two studies):<br>Propamocarb HCl $DT_{50lab}$ (aerobic, 1st order |

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

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|---|---|
| | kinetics): mean = 17.08 days and 10.20 days (normalised to 10kPa, 20 °C with Q10 of 2.2)<br>If the datasets of both notifiers are considered as a whole, the geometric mean $DT_{50}$ value of laboratory aerobic topsoil values normalised to 20 °C and pF2 moisture content from both datasets is 13.91 days (n = 17 values).<br><br>Metabolites: Not applicable |
| | Propamocarb HCl $DT_{90lab}$ (20 °C, aerobic): 36.1-452.0 days (n = 8 soils, $r^2$ = 0.91-0.98), mean = 130.6 days<br>Propamocarb HCl $DT_{90lab}$ (25 °C, aerobic): 17.0-72.4 days (n = 3 soils), mean = 35.5 days<br>Propamocarb HCl $DT_{90lab}$ (22 °C, aerobic): 27.8 days (n = 1 soil)<br>Metabolites: Not applicable |
| | (10 °C, aerobic): laboratory values<br>Propamocarb HCl $DT_{50lab}$ (10 °C, aerobic): 25.3, 47.2, 73.7 days (n = 3 soils, $r^2$ = 0.93), mean = 48.7<br>Propamocarb HCl $DT_{50lab}$ (15 °C, aerobic): 22.0, 24.0 days (n = 2 soils), mean = 23.0 days<br>Metabolites: Not applicable<br><br>Propamocarb HCl $DT_{90lab}$ (10 °C, aerobic): 84.1, 156.9, 245.0 days (n = 3 soils, $r^2$ = 0.93), mean = 162.0<br>Propamocarb HCl $DT_{90lab}$ (15 °C, aerobic): 73.1, 79.7 days (n = 2 soils), mean = 76.4 days<br>Metabolites: Not applicable |

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

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|---|---|
| | Anaerobic soil:<br>Propamocarb HCl $DT_{50lab}$ (20 °C, anaerobic): 65.68-308.16 days (n = 1 soil type, 2 incubations, $r^2$ = 0.9815-9838)<br>Propamocarb HCl $DT_{50lab}$ (25 °C, anaerobic): 459.0 days (n = 1 soil, $r^2$ = 0.76)<br>Metabolites: Not applicable<br>[Rates are whole-system values (soil and flood water combined)]<br><br>Anaerobic water phase:<br>Propamocarb HCl $DT_{50lab}$ (20 °C, anaerobic): 7.03-14.70 days (n = 1 water system type, 2 incubations, $r^2$ = 0.9797-0.9873)<br>Metabolites: Not applicable |
| | Soil photolysis:<br>Propamocarb HCl $DT_{50lab}$ (irradiated samples): 35.4, 199.2 days (8 h light, 16 h dark, and 12 h light and dark photoperiods) (n = 2 soils, $r^2$ = 0.812-0.819) mean = 117.3 days<br>Propamocarb $DT_{50lab}$ (dark control samples): 103.1 days (n = 1 soil, $r^2$ = 0.86)<br>Metabolites: Not applicable |
| | Aerobic subsoil degradation (n = 1 soil, 10 °C):<br>Propamocarb HCl $DT_{50lab}$ (aerobic): 73.7, 136.0, 239.0, 267.0 days (n = 4 subsoil horizons 20-90cm) mean = 178.9 days<br>Metabolites: Not applicable |

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

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|---|---|
| Field studies ‡ (state location, range or median with n value) | $DT_{50f}$:<br>USA, Georgia, loamy sand (bare soil):<br>Propamocarb HCl $DT_{50field}$: 17.6 days (n = 1, $r^2$ = 0.76)<br>USA, Georgia, loamy sand (thatch):<br>Propamocarb HCl $DT_{50field}$: 17.4 days (n = 1, $r^2$ = 0.78)<br>Metabolites: Not applicable<br><br>USA, California, sandy loam (bare soil):<br>Propamocarb HCl $DT_{50field}$: 22.1 days (n = 1, $r^2$ = 0.99)<br>USA, California, sandy loam (thatch):<br>Propamocarb HCl $DT_{50field}$: 23.7 days (n = 1, $r^2$ = 0.92)<br>Metabolites: Not applicable |
| | $DT_{90f}$:<br>USA, Georgia, loamy sand (bare soil):<br>Propamocarb HCl $DT_{90field}$: 58.6 days (n = 1, $r^2$ = 0.76)<br>USA, Georgia, loamy sand (thatch):<br>Propamocarb HCl $DT_{90field}$: 57.7 days (n = 1, $r^2$ = 0.78)<br>Metabolites: Not applicable<br><br>USA, California, sandy loam (bare soil):<br>Propamocarb HCl $DT_{90field}$: 73.3 days (n = 1, $r^2$ = 0.99)<br>USA, California, sandy loam (thatch):<br>Propamocarb HCl $DT_{90field}$: 78.6 days (n = 1, $r^2$ = 0.92)<br>Metabolites: Not applicable |
| Soil accumulation and plateau concentration ‡ | Not applicable |

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

**Soil adsorption/desorption (Annex IIA, point 7.1.2)**

| | |
|---|---|
| $K_f$ /$K_{oc}$ ‡<br>$K_d$ ‡<br>pH dependence ‡ (yes / no) (if yes type of dependence) | Propamocarb HCl (topsoil):<br>$K_f$: 0.671-77.20 mL/g (mean = 10.50 mL/g, 12 soils)<br>$K_{foc}$: 41.0-2451.0 mL/g (mean = 535.56 mL/g, 12 soils)<br>1/n: 0.822-0.926 (mean = 0.867, 12 soils)<br>$K_d$: 1.34-17.6 mL/g (mean = 7.77 mL/g, 4 soils)<br>$K_{oc}$: 59.14-1680.79 mL/g (mean = 718.81 mL/g, 4 soils)<br><br>Propamocarb HCl (subsoil horizons):<br>$K_f$: 0.72-1.04 mL/g (mean = 0.93 mL/g, 1 soil)<br>$K_{foc}$: 171.0-3600.0 mL/g (mean = 1190.0 mL/g, 1 soil)<br>1/n: 0.86-0.91 (mean = 0.872, 1 soil)<br><br>[$K_{foc}$ = $K_f$ normalized to organic carbon content, $K_{oc}$ = $K_d$ normalized to organic carbon content]<br><br>Metabolites: not applicable<br><br>No obvious pH dependence for Propamocarb. However, there is a possibility that adsorption to soil may depend on the clay content of the soil. |

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

| | |
|---|---|
| Column leaching ‡ | Guideline: BBA Part IV, Section 4-2 (1986)<br>Precipitation: 200 mm<br>Time period: 5 days<br>Leachate: 0.043-0.260% total residues in leachate, 37.0-92.8% radioactivity retained in top 5 cm, 0.5-41.62% radioactivity retained in 5-10 cm column segment, 0.5-13.1% radioactivity retained in 10-15 cm column segment, <0.1-0.2% radioactivity retained in 15-20 cm column segment, <0.1% radioactivity retained in the remaining segments 20-25 cm and 25-30 cm |

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

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|---|---|
| Aged residues leaching ‡ | Guideline: SETAC (1995), Part 1, Section 6<br>Aged for: 12 days (Midwest 3), 23 days (Speyer 2.3)<br>Time period: 2 days<br>Precipitation: 200 mm<br>Leachate: 0.67-0.90% radioactivity in leachate, 27.88-44.49% radioactivity retained in top 6 cm, 6.21-14.86% radioactivity retained in 6-12 cm column segment, 1.60-10.90% radioactivity retained in 12-18 cm column segment, 0.28-3.90% radioactivity retained in 18-24 cm column segment, 0.07-1.06% radioactivity retained in 24-30 cm column segment |
| Lysimeter/ field leaching studie ‡ | Not required |

**PEC (soil) (Annex IIIA, point 9.1.3)**

**Propamocarb hydrochloride**

| | |
|---|---|
| Method of calculation | Kinetics: first order<br>$DT_{50}$ – calculations performed with lab values:<br>136.0 days (worst case first order laboratory value, undertaken at 40-50% MWHC and a temperature of 20 °C)<br>Soil depth: 5 cm |
| Application rate | Crops: potatoes (critical GAP) [$PEC_s$ calculations for tomatoes and lettuce may be found in Vol. 3, Annex B, Section B.8.3]<br>% plant interception: none (worst case application to bare soil assumed)<br>Number of applications: 1 (lumped)<br>Application rate: 6.498 kg propamocarb hydrochloride/ha (1.083 kg propamocarb hydrochloride /ha x 6) |

| **$PEC_{(s)}$** (mg/kg) | | Annual total dose Actual | Annual total dose Time weighted average | Multiple application Actual | Multiple application Time weighted average |
|---|---|---|---|---|---|
| Initial | | 8.664 | - | Not applicable | Not applicable |
| Short term | 24h | 8.620 | 8.642 | Not applicable | Not applicable |
| | 2d | 8.576 | 8.620 | Not applicable | Not applicable |
| | 4d | 8.489 | 8.576 | Not applicable | Not applicable |

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

| **PEC$_{(s)}$** (mg/kg) | | Annual total dose Actual | Annual total dose Time weighted average | Multiple application Actual | Multiple application Time weighted average |
|---|---|---|---|---|---|
| Long term | 7d | 8.360 | 8.511 | Not applicable | Not applicable |
| | 28d | 7.512 | 8.074 | Not applicable | Not applicable |
| | 50d | 6.715 | 7.648 | Not applicable | Not applicable |
| | 100d | 5.204 | 6.788 | Not applicable | Not applicable |

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

| | |
|---|---|
| Hydrolysis of active substance and relevant metabolites ($DT_{50}$) ‡<br>(state pH and temperature) | pH 4 and pH 5 (HCl: hydrochloride)<br>Propamocarb HCl $DT_{50}$ (pH 4 & 5, 50 °C): stable ($DT_{50}$ >365 days)<br>Propamocarb HCl $DT_{50}$ (pH 4 & 5, 25 °C): stable ($DT_{50}$ >365 days)<br><br>Metabolites: not applicable |
| | pH 7<br>Propamocarb HCl $DT_{50}$ (50 °C): stable ($DT_{50}$ >365 days)<br>Propamocarb HCl $DT_{50}$ (25 °C): stable ($DT_{50}$ >365 days)<br><br>Metabolites: not applicable |
| | pH 9<br>Propamocarb HCl $DT_{50}$ (50 °C): stable ($DT_{50}$ >365 days)<br>Propamocarb HCl $DT_{50}$ (25 °C): stable ($DT_{50}$ >365 days)<br><br>Metabolites: not applicable |
| Photolytic degradation of active substance and relevant metabolites ‡ | Propamocarb HCl: (pH 4-5, 24 °C) stable<br>[Irradiation with artificial light, stated to be equivalent to 4× light intensity seen in summer at Les Borges, Switzerland.]<br>UV-VIS study indicates that wavelength of maximum absorption is <250 nm. Irradiation at wavelengths ≥290 nm are not expected to induce any photochemical transformation.<br><br>Metabolites: not applicable |

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

| | |
|---|---|
| Readily biodegradable (yes/no) | [Mean cumulative CO2 production data obtained from Propamocarb HCl test mixtures are ambivalent. Results from a study indicate highly variable CO2 evolution from test replicates. However, Propamocarb HCl route and rate of degradation has been extensively investigated in soil metabolism and water/sediment studies.] |
| Degradation in water/sediment<br>$DT_{50}$ water ‡<br>$DT_{90}$ water ‡<br><br><br><br><br><br><br><br><br><br>$DT_{50}$ whole system ‡<br>$DT_{90}$ whole system ‡ | [Two aerobic studies provided and one anaerobic study for Propamocarb HCl]<br>Water phase:<br>Propamocarb HCl (aerobic) $DT_{50}$ = 11.6-12.0 days, $DT_{90}$ = 38.4-39.9 days (1st order, n = 2, $r^2$ = 0.894-0.967)<br>Propamocarb HCl (aerobic) $DT_{50}$ = 10.0-15.0 days, $DT_{90}$ = 34.0-49.0 days (non-linear 1st order using KIM B1.0 model, n = 2)<br>Metabolites: not applicable<br><br>Propamocarb HCl (anaerobic) $DT_{50}$ = 12.1 days, $DT_{90}$ = 40.1 days (linear 1st order regression, n = 1)<br>Metabolites: not applicable<br><br>Whole system:<br>Propamocarb HCl (aerobic) $DT_{50}$ = 15.5-15.9 days, $DT_{90}$ = 51.5-52.7 days (1st order, n = 2, $r^2$ = 0.905-0.913)<br>Propamocarb HCl (aerobic) $DT_{50}$ = 16.0-21.0 days, $DT_{90}$ = 53.0-69.0 days (non-linear 1st order using KIM B1.0, n = 2)<br>Metabolites: not applicable<br><br>Propamocarb HCl (anaerobic) $DT_{50}$ = 100.0 days, $DT_{90}$ = 332.3 days (linear 1st order regression, n = 1)<br>Metabolites: not applicable |
| Mineralization | $CO_2$ maximum (aerobic) = 67.5-94.7% (at 104-105 days, study end, n = 4)<br>$CO_2$ maximum (anaerobic) = 69.0 % (at 370 days, study end, n = 1) |
| Non-extractable residues | Non-extractable maximum residues (aerobic) = 10.3-16.0% (at 42-63 days, n = 4)<br>Non-extractable maximum residues (anaerobic) = 20.1% (at 110 days, n = 1) |

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

| | |
|---|---|
| Distribution in water / sediment systems (active substance) ‡ | Water phase:<br>Propamocarb HCl (aerobic) = 87.0-102.3% (day 0), 82.7-86.9% (day 1) and not detected by day 104/105 (n = 4 systems)<br>Propamocarb HCl (anaerobic) = 100.9% (day 0), 53.3% (day 13), 0.3% (day 370) (n = 1 system)<br><br>Sediment phase:<br>Propamocarb HCl (aerobic) = 12.4-21.5% (day 1), 15.8-36.9% (7-28 days), 0.0-5.6% (104/105 days) (n = 4 systems)<br>Maximum of 36.9% applied radioactivity in sediment after 14 days.<br>$DT_{50}$ in sediment (aerobic) 23-26 days (1$^{st}$ order, n = 2)<br>Propamocarb HCl (anaerobic) = 2.0% (day 0), 80.1% (day 54), 14.0% (day 370) (n = 1 system)<br>Maximum of 80.1% applied radioactivity in sediment after 54 days.<br>$DT_{50}$ in sediment (anaerobic) 93 days (1$^{st}$ order, n = 1)<br>[Dosing method – application to water, no mixing] |
| Distribution in water / sediment systems (metabolites) ‡ | Transient unidentified metabolites reached maximum individual levels in aerobic water and sediment phases combined of 1.7-5.6% of applied radioactivity (time of maximum occurrence = 7-28 days) (n = 4 systems, incubated at 20 °C)<br>Transient unidentified metabolites reached maximum individual levels in anaerobic water and sediment phases of 3.9% and 0.9%, respectively (time of maximum occurrence = 13 days) (n = 1 system, incubated at 25 °C) |

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

**PEC (surface water) (Annex IIIA, point 9.2.3)**

**Propamocarb hydrochloride**

| | |
|---|---|
| Method of calculation | FOCUS Steps 1-2 calculator, version 1.1<br>Propamocarb hydrochloride only, no metabolites<br>Water solubility (mg/L): 1005000<br>$K_{oc}$ (L/kg): 516.7 (average $K_{foc}$ value from 8 topsoils)<br>$DT_{50}$ soil (d): 10.19 (median first order value of 13 lab values from 8 aerobic topsoils, corresponding to first order degradation rate constants that had been normalised to 20 °C and pF2 moisture content)<br>$DT_{50}$ water/sediment system (d): 18.3 (used in Step 1 – geometric mean of 2 values)<br>$DT_{50}$ water (d): 12.2 (used in Step 2 – geometric mean of 2 values)<br>$DT_{50}$ sediment (d): 24.5 (used in Step 2 – geometric mean of 2 values)<br><br>Degradation and adsorption input parameters used in FOCUS Steps 1-2 calculator were selected from only one of the available datasets.  However, the choice of values represents a worst-case selection, appropriate for modelling, if both datasets are considered as a whole. |
| Application rate | Crop: lettuce, potatoes<br>Crop interception (%) 25 for lettuce (vegetables, leafy), 15 for potatoes<br>Number of applications: 2 for lettuce, 6 for potatoes<br>Interval (d): 12 for lettuce, 7 for potatoes<br>Application rate (g a.s./ha): 1660 for lettuce, 1083 for potatoes<br><br>Crop: tomatoes, data not available. Modelling required based on the drip irrigation method being used for field applications to tomatoes in Southern Europe. |

**Step 2 $PEC_{SW}$ values for propamocarb hydrochloride**

| **Modelled GAP** | **Time after max. conc. (days)** | **$PEC_{SW}$ (µg/L)** | **TWA $PEC_{SW}$ (µg/L)** |
|---|---|---|---|
| **Lettuce**<br>2 x 1660 g/ha<br>12 day interval<br>25% crop interception<br>South Europe, March-May | 0 | 119.8 | - |
| | 1 | 111.7 | 115.8 |
| | 2 | 106.8 | 112.5 |
| | 4 | 97.6 | 107.3 |
| | 7 | 85.3 | 100.5 |
| | 14 | 62.2 | 86.8 |
| | 21 | 45.4 | 75.6 |
| | 28 | 33.1 | 66.5 |
| | 42 | 17.6 | 52.5 |
| | 50 | 12.3 | 46.5 |
| | 100 | 1.3 | 25.7 |
| **Potatoes**<br>6 x 1083 g/ha<br>7 day interval<br>15% crop interception<br>South Europe, March-May | 0 | 147.8 | - |
| | 1 | 138.4 | 143.1 |
| | 2 | 132.3 | 139.2 |
| | 4 | 120.9 | 132.9 |
| | 7 | 105.6 | 124.4 |
| | 14 | 77.0 | 107.5 |
| | 21 | 56.2 | 93.7 |
| | 28 | 41.0 | 82.3 |
| | 42 | 21.8 | 65.0 |
| | 50 | 15.2 | 57.5 |
| | 100 | 1.6 | 31.8 |

**PEC (sediment)**

**Propamocarb hydrochloride**

| | |
|---|---|
| Method of calculation | FOCUS Steps 1-2 calculator, version 1.1<br>Propamocarb HCl only, no metabolites<br>Water solubility (mg/L): 1005000<br>Koc (L/kg): 516.7 (average Kfoc value from 8 topsoils)<br>$DT_{50}$ soil (d): 10.19 (median first order value of 13 lab values from 8 aerobic topsoils, corresponding to |

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

| | |
|---|---|
| | first order degradation rate constants that had been normalised to 20 °C and pF2 moisture content)<br>$DT_{50}$ water/sediment system (d): 18.3 (used in Step 1 – geometric mean of 2 values)<br>$DT_{50}$ water (d): 12.2 (used in Step 2 – geometric mean of 2 values)<br>$DT_{50}$ sediment (d): 24.5 (used in Step 2 – geometric mean of 2 values)<br><br>Degradation and adsorption input parameters used in FOCUS Steps 1-2 calculator were selected from only one of the available datasets. However, the choice of values represents a worst-case selection, appropriate for modelling, if both datasets are considered as a whole. |
| Application rate | Crop: lettuce, potatoes<br>Crop interception (%) 25 for lettuce (vegetables, leafy), 15 for potatoes<br>Number of applications: 2 for lettuce, 6 for potatoes<br>Interval (d): 12 for lettuce, 7 for potatoes<br>Application rate (g a.s./ha): 1660 for lettuce, 1083 for potatoes<br><br>Crop: tomatoes, data not available. Modelling required based on the drip irrigation method being used for field applications to tomatoes in Southern Europe. |

**Step 2 $PEC_{SED}$ values for propamocarb hydrochloride**

| Modelled GAP | Time after max. conc. (days) | $PEC_{SED}$ (µg/kg) | TWA $PEC_{SED}$ (µg/kg) |
|---|---|---|---|
| **Lettuce**<br>2 x 1660 g/ha<br>12 day interval<br>25% crop interception<br>South Europe, March-May | 0 | 599.9 | - |
| | 1 | 594.1 | 597.0 |
| | 2 | 567.9 | 589.0 |
| | 4 | 519.0 | 566.1 |
| | 7 | 453.3 | 531.5 |
| | 14 | 330.6 | 460.2 |
| | 21 | 241.2 | 401.3 |
| | 28 | 175.9 | 352.7 |
| | 42 | 93.6 | 278.6 |

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

| Modelled GAP | Time after max. conc. (days) | $PEC_{SED}$ (µg/kg) | TWA $PEC_{SED}$ (µg/kg) |
|---|---|---|---|
| | 50 | 65.2 | 246.6 |
| | 100 | 6.8 | 136.3 |
| **Potatoes**<br>6 x 1083 g/ha<br>7 day interval<br>15% crop interception<br>South Europe, March-May | 0 | 747.4 | - |
| | 1 | 735.9 | 741.7 |
| | 2 | 703.4 | 730.7 |
| | 4 | 642.8 | 701.7 |
| | 7 | 561.5 | 658.7 |
| | 14 | 409.5 | 570.1 |
| | 21 | 298.7 | 497.2 |
| | 28 | 217.9 | 436.9 |
| | 42 | 115.9 | 345.1 |
| | 50 | 80.8 | 305.5 |
| | 100 | 8.5 | 168.8 |

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

**Propamocarb hydrochloride**

| | |
|---|---|
| Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter ) | Modelling using FOCUS groundwater scenarios<br><br>Two studies evaluated – 1 for potatoes, 1 for lettuce and tomatoes<br>Model used: FOCUS PELMO 1.1.1 including the FOCUS shell and simulation model PELMO 3.2.<br>Scenarios (list of names): Chateaudun, Hamburg, Okehampton, Jokioinen, Kremsmünster, Porto, Sevilla, Piacenza, Thiva<br>Crop: potatoes (all 9 FOCUS scenarios are relevant), tomato (5 FOCUS scenarios are relevant), lettuce (7 FOCUS scenarios are relevant)<br><br>Calculations based on average first order $DT_{50}$ values for soil (determined from the aerobic laboratory studies with viable soil, corrected to pF2 moisture and 20 °C where appropriate) and averaged Freundlich sorption data ($K_{oc}$ or $K_{f, ads}$, 1/n) for potatoes and (1/n) for lettuce and tomatoes; regression data were used for lettuce and tomatoes in order to determine $K_{f, ads}$. |

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

| | |
|---|---|
| | [$DT_{50}$ = 17.08 days (potatoes), 10.20 days (tomato and lettuce) for Propamocarb hydrochloride; $K_{oc}$ = 718.81 $cm^3$/g (potatoes), $K_{f,\ ads}$ = 0.07-6.70 l/kg over 7 horizons at 9 scenario locations (tomato, lettuce). $K_{f,\ ads}$ with depth were calculated using regression equation established from the relationship between $K_{f,\ ads}$ and clay content (= 0.2015*Cclay (in %) + 0.0665) for Propamocarb hydrochloride; 1/n = 0.87 (potatoes), 0.871 (tomato, lettuce) for Propamocarb hydrochloride]<br><br>If the datasets of both notifiers are considered as a whole, the arithmetic mean $K_{foc}$ value is 535.56 mL/g (n = 12 soils) and the arithmetic mean 1/n value is 0.867 (n = 12 soils). The geometric mean $DT_{50}$ value of laboratory aerobic topsoil values normalised to 20 °C and pF2 moisture content from both datasets is 13.91 days (n = 17 values).<br><br>Metabolites: not applicable |
| Application rate | Time of application: planting dates for <u>potatoes</u> in FOCUS scenarios [15 May (Chateaudun, Okehampton, and Piacenza), 1 June (Hamburg and Kremsmünster), 15 April (Porto), 20 February (Sevilla), 20 March (Thiva), and 20 June (Jokioinen)]<br><br>Application regime: six applications each year for 20 consecutive years<br>Application rate: T1 = 0.92055 kg a.s./ha, T2-T6 = 0.5415 kg propamocarb hydrochloride/ha<br>Simulated time period: 26 years<br><br>Time of application: planting dates for <u>tomatoes</u> in FOCUS scenarios [10 May (Chateaudun, and Piacenza), 15 March (Porto), 15 April (Sevilla), 10 April (Thiva)]<br><br>Application regime: four applications each year for 20 consecutive years<br>Application rate: T1and T2 = 0.08 kg a.s./ha, T3/T4 = 2.166 kg propamocarb hydrochloride/ha per treatment<br>Simulated time period: 26 years<br><br>Time of application: planting dates for <u>lettuce</u> (as per scenarios with cabbage) in FOCUS scenarios |

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

| | |
|---|---|
| | [20 April (Chateaudun, Hamburg, and Kremsmünster), 20 May (Jokioinen), 28 February (Porto), 1 March (Sevilla), 15 August (Thiva)]<br><br>Application regime: four applications each year for 20 consecutive years<br>Application rate: T1and T2 = 0.359 kg a.s./ha, T3/T4 = 1.66 kg propamocarb hydrochloride /ha per treatment<br>Simulated time period: 26 years |
| **PEC$_{(gw)}$** | |
| Maximum concentration | Maximum 80$^{th}$ percentile annual average concentrations at 1 m depth<br><br>FOCUS PELMO 1.1.1 (potatoes):<br>Propamocarb = 0.00 µg/L (all relevant scenarios)<br>FOCUS PELMO 1.1.1 (tomatoes):<br>Data not valid. Modelling required based on the drip irrigation method being used for field applications to tomatoes in Southern Europe<br>FOCUS PELMO 1.1.1 (lettuce):<br>Propamocarb hydrochloride = <0.001 µg/L (all relevant scenarios) |
| Average annual concentration<br>(Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance) | Average 80$^{th}$ percentile annual average concentrations at 1 m depth (n = 9 scenarios)<br><br>FOCUS PELMO 1.1.1 (potatoes):<br>Propamocarb hydrochloride = 0.00 µg/L (all relevant scenarios)<br>FOCUS PELMO 1.1.1 (tomatoes):<br>Data not valid. Modelling required based on the drip irrigation method being used for field applications to tomatoes in Southern Europe.<br>FOCUS PELMO 1.1.1 (lettuce):<br>Propamocarb hydrochloride = <0.001 µg/L (all relevant scenarios) |

**80$^{th}$ percentile PEC$_{GW}$ values at 1 m depth for Propamocarb hydrochloride**

| FOCUS scenario | FOCUS PELMO 1.1.1 (µg/L) | |
|---|---|---|
| | Potatoes | Lettuce |
| Châteaudun | 0.000 | <0.001 |
| Hamburg | 0.000 | <0.001 |

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

| FOCUS scenario | FOCUS PELMO 1.1.1 (µg/L) | |
|---|---|---|
| | Potatoes | Lettuce |
| Jokioinen | 0.000 | <0.001 |
| Kremsmünster | 0.000 | <0.001 |
| Okehampton | 0.000 | - |
| Piacenza | 0.000 | - |
| Porto | 0.000 | <0.001 |
| Sevilla | 0.000 | <0.001 |
| Thiva | 0.000 | <0.001 |

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

| | |
|---|---|
| Direct photolysis in air ‡ | Not determined – no data requested |
| Quantum yield of direct phototransformation | Not determined in air |
| Photochemical oxidative degradation in air ‡ | $DT_{50}$ = 4.03 and 13.4 hours (Atkinson method) |
| Volatilization ‡ | From plant surfaces: Propamocarb hydrochloride was found to volatilise from plant surfaces (French beans) <10.0%, this value is less than the BBA trigger value of 20.0% in volatilisation studies conducted over a 24 hour period.<br><br>from soil: volatilisation loss of Propamocarb hydrochloride is estimated to be <0.0001% of the applied amount within 24 hours after treatment (Dow method) and was found to evaporate <15.0% in volatilisation studies conducted over a 24 hour period, which is less than the BBA trigger value of 20.0%. |

**PEC (air)**

| | |
|---|---|
| Method of calculation | Expert judgment based on vapour pressure, Henry's Law Constant, method of application, photochemical oxidative $DT_{50}$ in air and "Dow method" estimation of volatilisation loss from soil. |

**PEC$_{(a)}$**

| | |
|---|---|
| Maximum concentration | Negligible |

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

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

| | |
|---|---|
| Relevant to the environment | Soil:<br>Propamocarb and its salts, expressed as propamocarb<br><br>Water (surface and ground water):<br>Propamocarb and its salts, expressed as propamocarb<br><br>Air:<br>Propamocarb and its salts, expressed as propamocarb |

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

| | |
|---|---|
| Soil (indicate location and type of study) | Relevant European data not available |
| Surface water (indicate location and type of study) | Relevant European data not available |
| Ground water (indicate location and type of study) | Relevant European data not available |
| Air (indicate location and type of study) | Relevant European data not available |

**Classification and proposed labelling (Annex IIA, point 10)**

| | |
|---|---|
| with regard to fate and behaviour data | Candidate for<br>R53 May cause long-term adverse effect in the aquatic environment |

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

## Appendix 1.6: Effects on non-target Species

It should be noted that **all** the values given in this section belong to propamocarb hydrochloride, a variant of propamocarb.

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

| | |
|---|---|
| Acute toxicity to mammals ‡ | >1330 mg a.s./kg b.w./day |
| Long-term toxicity to mammals | 104 mg a.s./kg b.w./day |
| Acute toxicity to birds ‡ | >1842 mg a.s./kg b.w./day |
| Dietary toxicity to birds ‡ | >962 mg a.s./kg b.w./day |
| Reproductive toxicity to birds ‡ | 105 mg a.s./kg b.w./day |

**Critical toxicity/exposure ratios for terrestrial vertebrates** (Annex IIIA, points 10.1 and 10.3)

| Application rate* (kg a.s./ha) | ETE (mg a.s./ kg bw/day) | Critical endpoint Crop | Category | Time-scale | TER | Annex VI trigger |
|---|---|---|---|---|---|---|
| **Previcur N** | | | | | | |
| 2.166 x 2 | 117.1 | Tomatoes | Insectivorous bird | Acute | 15.7 | 10 |
| 2.166 x 2 | 65.3 | Tomatoes | Insectivorous bird | Short-term | 14.7 | 10 |
| 2.166 x 2 | 65.3 | Tomatoes | Insectivorous bird | Long-term | 1.5 | 5 |
| 2.166 x 2 | 200.5 | Tomatoes | Herbivorous bird | Acute | 9.2 | 10 |
| 2.166 x 2 | 105.4 | Tomatoes | Herbivorous bird | Short-term | 9.1 | 10 |
| 2.166 x 2 | 55.8 | Tomatoes | Herbivorous bird | Long-term | 1.8 | 5 |
| 2.166 x 2 | 73.9 | Tomatoes | Herbivorous mammal | Acute | 18 | 10 |
| 2.166 x 2 | 20.6 | Tomatoes | Herbivorous mammal | Long-term | 5.04 | 5 |
| **Proplant** | | | | | | |
| 1.083 x 6 | 58.5 | Potatoes | Insectivorous bird | Acute | 31.4 | 10 |
| 1.083 x 6 | 32.7 | Potatoes | Insectivorous bird | Short-term | 29.4 | 10 |
| 1.083 x 6 | 32.7 | Potatoes | Insectivorous bird | Long-term | 3.1 | 5 |
| 1.083 x 6 | 136.1 | Potatoes | Herbivorous bird | Acute | 13.5 | 10 |
| 1.083 x 6 | 82.3 | Potatoes | Herbivorous bird | Short-term | 11.7 | 10 |
| 1.083 x 6 | 43.6 | Potatoes | Herbivorous bird | Long-term | 2.3 | 5 |
| 1.083 x 6 | 50.1 | Potatoes | Herbivorous mammal | Acute | 26.6 | 10 |
| 1.083 x 6 | 16.1 | Potatoes | Herbivorous mammal | Long-term | 6.45 | 5 |

* Corresponding to each critical ETE

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

No first tier risk assessment was conducted for herbivorous birds and mammals for the uses in lettuce. The higher tier risk assessment to address the potential long term risk to herbivorous birds from the use of Previcur N was questioned in the EPCO meeting. No risk assessment was conducted by the RMS for the use of Proplant in lettuce.

**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) |
|---|---|---|---|---|
| Acute | | | | |
| Rainbow trout *(Onchoryhynchus mykiss)* | Propamocarb-HCl | 96 hours | Mortality, LC50 | >99 |
| Bluegill Sunfish *(Lepomis macrochirus)* | Propamocarb-HCl | 96 hours | Mortality, LC50 | >92 |
| *Daphnia magna* | Propamocarb-HCl | 48 hours | Mortalities, EC50 | >100 |
| *Pseudokirchneriella subcapitata* | Propamocarb-HCl | 72 hours | Growth Rate, EC50 | >85 |
| *Lemna gibba* | Propamocarb-HCl | 14 days | Frond No., EC50 | >18 |
| Chronic | | | | |
| Bluegill sunfish *(Lepomis macrochirus)* | Propamocarb-HCl | 32 days | NOEC | >6.3 |
| *Daphnia magna* | Propamocarb-HCl | 21 days | NOEC | 12.3 |

| Microcosm or mesocosm tests |
|---|
| Not required |

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

| Application Rate (kg as/ha) | Crop | Initial $PEC_{SW}$ (µg/L) | Organisms | Time-scale | Distance (m) | TER | Annex VI Trigger |
|---|---|---|---|---|---|---|---|
| Acute | | | | | | | |
| 1.083 x 6 | Potatoes | 147.8 | Bluegill Sunfish *(Lepomis macrochirus)* | 96 hours | 1 | 622 | 100 |

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

| Application Rate (kg as/ha) | Crop | Initial $PEC_{SW}$ (µg/L) | Organisms | Time-scale | Distance (m) | TER | Annex VI Trigger |
|---|---|---|---|---|---|---|---|
| 1.083 x 6 | Potatoes | 147.8 | *Daphnia magna* | 48 hours | 1 | 677 | 100 |
| 1.083 x 6 | Potatoes | 147.8 | *Pseudokirchneriella subcapitata* | 72 hours | 1 | 575 | 10 |
| 1.083 x 6 | Potatoes | 147.8 | *Lemna gibba* | 14 days | 1 | 122 | 10 |
| Chronic | | | | | | | |
| 1.083 x 6 | Potatoes | 147.8 | Bluegill Sunfish *(Lepomis macrochirus)* | 32 days | 1 | 43 | 10 |
| 1.083 x 6 | Potatoes | 147.8 | *Daphnia magna* | 21 days | 1 | 83 | 10 |

**Bioconcentration**

| | |
|---|---|
| Bioconcentration factor (BCF) ‡ | Not required as Log $P_{ow}$<3 |
| Annex VI Trigger:for the bioconcentration factor | >3 |
| Clearance time ($CT_{50}$) ($CT_{90}$) | Not relevant |
| Level of residues (%) in organisms after the 14 day depuration phase | Not relevant |

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

| | |
|---|---|
| Acute oral toxicity ‡ | $LD_{50}$ >84 µg a.s./bee |
| Acute contact toxicity ‡ | $LD_{50}$ >100 µg a.s./bee |

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

| Application rate (kg as/ha) | Crop | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|---|
| 2166 | Tomato | Oral | <26 | 50 |
| 1083 | Potato | Oral | <13 | 50 |
| 2166 | Tomato | Contact | <22 | 50 |
| 1083 | Potato | Contact | <11 | 50 |

* Risk assessment for lettuce is covered by the application rates for tomato and potato.

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

| |
|---|
| Field or semi-field tests |
| Not required |

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

**Previcur N**

| Species | Stage | Study type | Toxicity Endpoints (g a.s./ha) | | |
|---|---|---|---|---|---|
| | | | $LD/EC_{50}$ | LOEL | NOEL |
| *Aphidius rhopalosiphi* | Adults | Lab (glass) | 500 | 500 | 170 |
| *Aphidius rhopalosiphi* | Adults | Ext. Lab (barley) | >4315 | >4315 | 4315 |
| *Diaeretiella rapae* | Adults | Lab (glass) | >2190 | >2190 | <2190 |
| *Trichogramma caoeciae* | Adults | Lab (glass) | 790 | 790 | - |
| *Typhlodromus pyri* | Adults | Lab (glass) | >360 | >360 | 360 |
| *Typhlodromus pyri* | Protonymphs/ Adults | Ext. Lab (lettuce) | >3 x 1450 | >3 x 1450 | 3 x 1450 |
| *Aleochara bilineata* | Adults | Lab (sand) | >9690 | >9690 | 9690 |
| *Poecilus cupreus* | Adults | Lab (sand) | >9690 | >9690 | 9690 |
| *Chrysoperla carnea* | 2-3 day old larvae 2-3 day old larvae | Lab (glass) | >1080 | >1080 | <1080 |
| *Chrysoperla carnea* | 2-3 day old larvae | Ext. Lab (lettuce) | >3 x 1453 | >3 x 1453 | 3 x 1453 |
| *Coccinella septempunctata* | 2-3 day old larvae | Lab (glass) | >1920 | >1920 | 1920 |

| |
|---|
| Field or semi-field tests |
| Not required |

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

**Proplant**

| Species | Stage | Test Substance | Dose (kg as/ha) | Endpoint | Effect | ESCORT 2 Trigger |
|---|---|---|---|---|---|---|
| *Aphidius rhopalosiphi* | Adults | Proplant | 1.083* | Mortality / Fertility | 32.6% -72.4% | 50% |
| *Aphidius rhopalosiphi* | Adults | | 3.450 | Mortality / Fertility | 9.1% -23.9% | 50% |
| *Typhlodromus pyri* | Protonymph/ Adult | | 1.083* | Mortality / Fertility | -1.1% 21.1% | 50% |
| *Coccinella septempunctata* | Larvae | | 1.083* | Mortality / Fertility | -3.5% 19.0% | 50% |
| *Chrysoperla carnea* | Larvae | | 1.083* | Mortality / Fertility | -7.2% 10.04% | 50% |
| *Poecilus cupreus* | Adults | | 108.3 | Mortality / Food consumption | 3.6% -4.4% | 50% |
| *Pardosa sp.* | Adults | | 108.3 | Mortality / Food consumption | 0.0% -7.5% | 50% |

* no MAF is taken into account, the dose in the test is equivalent to a single application only.

| |
|---|
| Field or semi-field tests |
| Not required |

**Risk to Non-target Arthropods**

**Tier I for Previcur N and Proplant**

| Material | Species | Study type | Endpoint value | Applic. rate | MAF | DF | VDF | CF | In-field HQ | Off-field HQ | ESCORT 2 Trigger HQ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | g a.s./ha | | | | | | | | |
| Previcur N | *A. rhopalosiphi* | Lab (glass) | 580 | 2166 | 1.1 | 0.0238 | 10 | 10 | 4.1 | 0.09 | 2 |
| | *T. pyri* | Lab (glass) | >360 | 2166 | 1.1 | 0.0238 | 10 | 10 | 2.2 | 0.05 | 2 |
| Proplant | *A. rhopalosiphi* | Lab (glass) | >1083 | 1083 | 1.1 | 0.0164 | 10 | 10 | 1.1 | 0.02 | 2 |
| | *T. pyri* | Lab (glass) | >1083 | 1083 | 1.1 | 0.0164 | 10 | 10 | 1.1 | 0.02 | 2 |

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

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

| | |
|---|---|
| Acute toxicity ‡ | $LC_{50}$ > 660 mg a.s./kg dry soil |
| Reproductive toxicity ‡ | NOEC 362 mg a.s./kg dry soil |

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

| Critical $PEC_s$ * | Time-scale | TER | Annex VI Trigger |
|---|---|---|---|
| 8.664 | 14-day | >76 | 10 |
| 8.664 | 56 days | 42 | 10 |

* Worst-case scenario immediately following a lumped application to potatoes. The critical $PEC_s$ was derived from the GAP for potatoes (6 x 1.083 kg a.s. /ha) and was used in the risk assessment

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

| | |
|---|---|
| Nitrogen mineralization ‡ | No adverse effects up to 28.9 kg a.s./ha |
| Carbon mineralization ‡ | No adverse effects up to 28.9 kg a.s./ha |

**Effects on non target plants (**Annex IIA, point 8.6, Annex IIIA, point 10.8)

Preliminary screening data (Tier 1):

Previcur N had no phytotoxic effect on seed germination or vegetative vigour over a range of monocotyledons and dicotyledons that were exposed to a concentration of 9.18 kg Propamocarb HCl/ha.

Emergence of cucumber and wheat was adversely effected in a Tier I study at an exposure rate of 9.18 kg Propamocarb HCl/ha.

Dose Response Studies (Tier II):

Seedling emergence: Cucumber seedling emergence was significantly lowere than the control at 27.54 and 82.62 kg a.s./ha (% effect ranged from –16% to +2%). There was no effect on this parameter in wheat.

Mean Length: In cucumber, mean length was significantly different in the highest treatment group. No effects were observed in wheat.

Dry weight: There was no significant different in the dry weight of either cucumber or wheat exposed to up to 82.62 kg a.s./ha.

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

**Effects on biological methods for sewage treatment** (Annex IIA 8.7)

| Test type | Endpoint |
|---|---|
| Activated sludge | $EC_{50}$ (3h) >100 mg propamocarb HCl/L |

**Classification and proposed labelling (Annex IIA, point 10)**

| | | |
|---|---|---|
| with regard to ecotoxicological data | R52 | Harmful to aquatic organisms |
| | S61 | Avoid release to the environment. Refer to special instructions/Safety data sheets. |

‡ 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) |
| $\varepsilon$ | 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<br>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 |
| TC | technical material |
| TER | toxicity exposure ratio |
| TK | technical concentrate |
| TMDI | theoretical maximum daily intake |
| UV | ultraviolet |
| WHO | World Health Organisation |
| WG | water dispersible granule |
| yr | year |