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

ethoprophos

finalised: 3 March 2006

SUMMARY

Ethoprophos 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.

The United Kingdom being the designated rapporteur Member State submitted the DAR on ethoprophos in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 19 January 2004. Following a quality check on the DAR, the peer review was initiated on 18 May 2004 by dispatching the DAR for consultation of the Member States and the sole notifier Bayer CropScience (the original notification was made by Aventis CropScience which merged with Bayer AG in 2002 to form Bayer CropScience).. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 8 November 2004. 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 April and May 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 7 February 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 insecticide and nematicide, as proposed by the applicant. This comprises direct overall or band/row application followed by soil incorporation to control a broad spectrum of insects and nematodes in potatoes at application rate up 11 kg ethoprophos per hectare. Ethoprophos can be used as insecticide and nematicide.
The representative formulated product for the evaluation was "Mocap 10G" ("AE F034142 00 FG10 A1" or "EXP05806A"), a granule formulation (GR), registered in the South and the North of the EU.

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

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. ethoprophos in food of plant origin (potatoes, only) in soil, water and air.
A validated analytical method for the determination of ethoprophos in blood and animal tissues is also available.
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.
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.

Ethoprophos has a high acute toxicity and is a skin sensitizer. The proposal for classification is T+, R26/27 "Very toxic by inhalation and in contact with skin"; T, R25 "Toxic if swallowed"; Xi, R43 "May cause sensitisation by skin contact".
The most sensitive endpoint during short term exposure was cholinesterase inhibition in all species. Considering available evidence, there is no genotoxic or carcinogenic potential. The classification Xn, R48/22 "Harmful: danger of serious damage to health by prolonged exposure if swallowed", based on the high mortality in the first weeks of the long term rat study, is proposed. There is no evidence of reproductive toxicity, and ethoprophos was not shown to be teratogenic. Delayed neurotoxicity in acute studies with hens has not been demonstrated.
The Acceptable Daily Intake (ADI) is 0.0004 mg/kg bw/day, the Acceptable Operator Exposure Level (AOEL) 0.001 mg/kg bw/day, and the Acute Reference Dose (ARfD) 0.01 mg/kg bw/day. All reference values were set using a safety factor of 100. The agreed dermal absorption value of 10% represents a worst case assumption.
The measurements of operator exposure in a field study are above the AOEL, even assuming the use of personal protective equipment and respiratory protective equipment. Only the use of Surefill containers might reduce the extent of exposure below the AOEL. Based on an air monitoring study, worker and bystander exposure are clearly below the AOEL.

The metabolism of ethoprophos in plants after soil application has been investigated in potatoes, cabbage and sweet corn. The degradation involves the hydrolysis of the S-propyl and 0-ethyl ester links and further degradation to compounds later integrated in the structure of natural plant components. The major metabolite observed in plants is ethyl phosphate. This compound has no toxicological relevance. Other compounds were identified at lower levels: EPPA (O-ethyl-S-propyl-phosphorothioate), OME (O-ethyl-O-methyl-S-propyl-phosphorothioate) and SME (O-Ethyl-S-methyl-S-propyl-phosphorothioate). These metabolites have a level of toxicity similar to that of ethoprophos. In rotational crops metabolism data suggest a similar degradation pathway. A residue definition for risk assessment is proposed as the sum of ethoprophos, EPPA, OME and SME expressed as ethoprophos. This definition is proposed taking the available information on all crops into consideration because the data on potato tubers are not conclusive enough for a reliable residue definition for that crop. The residue definition for monitoring purposes is ethoprophos only.

Supervised residue trials on potatoes were conducted in accordance with the representative uses supported by the notifier. They lead to a proposal for a MRL of 0.02 mg/kg for potatoes, covering potatoes harvested in an early stage of their growth to be specifically marketed as small size potatoes. These trials were carried out with analysis of ethoprophos only and therefore are not appropriate to be used for risk assessment for the health of the consumer. Additional supervised residue trials in potatoes are necessary with analysis of residues according to the residue definition for risk assessment. Such studies are currently ongoing and a first set of results has already been submitted to the RMS. Before finalising acute and chronic risk assessments, further information on the nature of extractable residues in rotational crops and, depending on that information, field trials on rotational crops are also necessary.
Due to the very low exposure of livestock to residues of ethoprophos, residues in animal commodities are expected to be extremely low and do not need to be monitored and taken into consideration for assessment of the risk for the health of the consumer.

The route of degradation in soil of ethoprophos was studied under aerobic and anaerobic conditions using ethyl- or propyl-labelled compound. Ethoprophos was degraded to the minor metabolite O-ethyl-S-propylphosphorothioic acid (AE 0592496) with final degradation products CO_2 and unextracted residues. The route of degradation of ethoprophos under anaerobic conditions was comparable to that under aerobic conditions. The rate of degradation under laboratory conditions indicate that ethoprophos is moderately to highly persistent in soil. There is some indication (1 laboratory and two field soils) that at the low end of the soil pH range (pH 5.3 and 4.5) ethoprophos may degrade more slowly. Adsorption studies have shown that ethoprophos has very high to medium potential for mobility in soil. These data combined with groundwater modelling, indicate under European conditions there is generally a negligible risk that ethoprophos will reach ground water when applied in accordance with usual Good Agricultural Practice for potatoes, except when grown in vulnerable scenarios (i.e. FOCUS groundwater scenarios of Piacenza and Hamburg). Chemical hydrolysis and photodegradation are not considered to be relevant degradation pathways under natural environmental conditions. The metabolic pattern in water/sediment system under aerobic conditions was similar to that observed in soil. In sediment with high organic carbon content, up to 44% of ethoprophos partitioning to sediment can be observed. Estimated concentrations of ethoprophos in surface water, arising from sub surface flow, indicate that except in very vulnerable situations, there is no cause for concern. Concentrations of ethoprophos in the air compartment will be negligible, due to the method of application (soil incorporation) and short persistence in the atmosphere. There were no major metabolites identified in any of the fate and behaviour studies.

The consumption of contaminated soil organisms (earthworms) and systemic residues in volunteer plants growing in potato fields were assumed as the main routes of exposure for birds and mammals. Uptake of granules as grit was identified to be a main route of exposure for birds. The acute risk, short-term risk and long term-risk to small granivorous birds from intentional uptake of granules is high. Further risk refinement steps and risk mitigation measures to ensure high incorporation efficiency are required. The refined acute risk assessment for herbivorous birds is low but needs

further support by data. The short term risk and the long-term risk to herbivorous birds were considered to be low. A high acute, short-term and long-term risk to earthworm eating birds was indicated and further data are required to support the suggested risk refinement steps. The acute and long-term risk to herbivorous mammals such as the hare was assessed as low. The long-term risk to earthworm eating mammals is high. Further risk refinement steps are required. The chronic risk to aquatic invertebrates and the potential risk of bioaccumulation is high under vulnerable conditions where contamination of surface water arises. The study with *Chironomus riparius* needs to be evaluated in order to draw a final conclusion on the risk to sediment dwelling organisms. A potential risk of bioaccumulation in aquatic organisms was identified if contamination of aquatic habitats arises. For conditions where contamination of surface water arises the risk of biomagnification in aquatic food chains and the risk of secondary poisoning of fish eating birds and mammals needs to be addressed. Severe acute and sublethal effects were observed in tests with non-target arthropods and a high risk was indicated. The higher tier risk assessment for non-target arthropods was discussed in the EPCO expert meeting. It was concluded that the potential of recovery was sufficiently demonstrated taking into account that the field margins remain unaffected and thus providing a reservoir for recolonisation. A high acute and long-term risk was indicated for earthworms in the first tier risk assessment. In a field study severe acute effects were observed. However the effects full recovery was observed within 5 months after the application and it is concluded that the risk to earthworms is sufficiently addressed. The risk to bees, soil non-target micro-organisms, non-target flora and biological methods of sewage treatment is considered to be low.

Key words: ethoprophos, peer review, risk assessment, pesticide, insecticide, nematicide

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

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, the United Kingdom submitted the report of its initial evaluation of the dossier on ethoprophos, hereafter referred to as the draft assessment report, which was received by the EFSA on 19 January 2004. Following a quality check, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 18 May 2004 to the Member States and the main notifier as identified by the rapporteur Member State: Bayer CropScience (the original notification was made by Aventis CropScience which merged with Bayer AG in 2002 to form Bayer CropScience).

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 8 November 2004 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier attended this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team at the Federal Office for Consumer Protection and Food Safety in Braunschweig, Germany, in April and May 2005. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 7 February 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 10 December 2004)
- 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 1 March 2006)

Given the importance of the draft assessment report including its addendum (compiled version of October 2005 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

Ethoprophos is the ISO common name for *O*-ethyl *S*,*S*-dipropyl phosphorodithioate (IUPAC).

Ethoprophos belongs to the class of aliphatic organothiophosphate insecticides such as cadusafos and malathion and to the class of organothiophosphate nematicides such as cadusafos, dimethoate and fosthiazate. Ethoprophos is acting by inhibiting the cholinesterase enzyme system.

The representative formulated product for the evaluation was "Mocap 10G" ("AE F034142 00 FG10 A1" or "EXP05806A"), a granule formulation (GR), registered in the South and the North of the EU.

The evaluated representative uses as insecticide and nematicide, as proposed by the applicant, comprises direct overall or band/row application followed by soil incorporation to control a broad spectrum of insects and nematodes in potatoes at application rate up 11 kg ethoprophos per hectare. Ethoprophos can be used as insecticide and nematicide.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of ethoprophos as manufactured should not be less than 940 g/kg. At the moment no FAO specification exists.

The technical material contains no relevant impurities.
However, since clarification is required with respect to certain impurities to confirm the identity of the impurities, the specification for the impurities should be regarded as provisional at the moment.

Besides this, the assessment of the data package revealed no particular area of concern with respect of the identity, physical, chemical and technical properties of ethoprophos or the respective formulation. However, it should be noted that for the refillable containers no shelf-life study is available.

During the risk assessment process the applicant submitted data to support a new manufacturing site (March 2005). These data were evaluated by the RMS and presented in Addendum 3 to Volume 4 (October 2005). The evaluation has not been peer reviewed or agreed in the assessment process. However, it should be noted that in these batches a new impurity was determined. MS will need to consider the equivalence of this new source, if necessary during the re-registration process.

The content of ethoprophos in the representative formulation is 100 g/kg (pure).

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

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of ethoprophos 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.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. ethoprophos in food of plant origin (potatoes, only) in soil, water and air.
A validated analytical method for the determination of ethoprophos in blood and animal tissues to address Annex point 4.2.5 of Directive 96/46/EC is also available.
The methodology used is GC with FP detection or HPLC with MS/MS detection. None of them is enantio selective. A multi-residue method like the Dutch MM1 or the German S19 is not applicable to due 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 expert meeting (EPCO 25, May 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material(s) and to some clarifications with respect to physical and chemical properties of ethoprophos as well as to the analytical methods.

2. Mammalian toxicology

Ethoprophos was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 23) in May 2005.

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

Ethoprophos was rapidly and extensively (>80%) absorbed following oral administration to the rat. The maximum blood concentration (Cmax) was attained within one hour of dosing. Excretion was rapid, mainly in urine (~40-60%), but also in exhaled air (~15%) and faeces (~10-30%) (within 48h). Biliary excretion may occur to a limited extent (~8%). Low residual tissue levels (up to 3.5%) were mainly detected in the liver, kidney, lung, fat, adrenals, thyroid and intestines.
Ethoprophos was completely metabolised by dealkylation, followed by hydroxylation and conjugation. Findings suggest that ethoprophos may also be metabolised by hydrolysis to ethanol and CO_2. N-propyl mercaptan is also predicted to be a metabolite of ethoprophos following dealkylation.

2.2. Acute toxicity

Ethoprophos is of high acute oral toxicity in the rat (LD_{50} 47 mg/kg bw), showing toxicological signs of cholinesterase inhibition. The mouse is comparatively more sensitive by this route (LD_{50} 31 mg/kg bw). By dermal exposure, ethoprophos is harmful to the rat (LD_{50} 226 mg/kg bw), but very toxic for the rabbit (LD_{50} 7.9 mg/kg bw in males). The toxicity is also high by inhalation in the rat (LC_{50} 0.123 mg/L). Dermal and ocular irritation have not been assessed due to the high dermal toxicity, however it is a skin sensitiser (Magnusson & Kligman test).
The proposed classification for acute toxicity is: **T+ R26/27 "Very toxic by inhalation and in contact with skin", T R25 "Toxic if swallowed", and Xi R43 "May cause sensitisation by skin contact"**.

2.3. Short term toxicity

Ethoprophos was administered orally to rats (two 28-day and one 90-day studies), mice (6-week and 6-month), and dogs (90-day, 20-week and 1-year). Effects after dermal application were studied in rats (two 21-day studies), and rabbits (two 21-day studies).
Cholinesterase inhibition is the most sensitive endpoint in all species. Based on the newly submitted 90-day dog study, an overall NOAEL of 0.1 mg/kg bw/day in the dog was agreed by the experts,

instead of 0.025 mg/kg bw/day as previously proposed in the DAR. Thus, the relevant oral NOAEL is 0.1 mg/kg bw/day from the rat and dog studies, based on erythrocyte and brain cholinesterase inhibition.
The relevant dermal NOAEL is 0.1 mg/kg bw/day from the rabbit studies.
No studies were submitted on repeated inhalation, nor required.

2.4. GENOTOXICITY

The genotoxicity of ethoprophos has been investigated in a battery of 7 studies *in vitro* and 4 studies *in vivo*.
Results *in vitro* suggest that ethoprophos may be weakly genotoxic in the presence of metabolic activation, generally at cytotoxic concentrations (mouse lymphoma assay, HPRT assay, sister chromatid exchange, and chromosomal aberration test in CHO cells).
Two recent *in vivo* studies have not reproduced the clastogenicity (in rat bone marrow) and germ cell mutagenicity (rat dominant lethal assay), as shown in older studies. The experts have not considered ethoprophos to be genotoxic *in vivo* on the balance of the available evidence.

2.5. LONG TERM TOXICITY

Three long term studies in the rat and one in the mouse were submitted in the dossier.
The NOAELs for both species are based on the inhibition of the cholinesterase activity, i.e. 0.04 mg/kg bw/day for the rat, and 0.3 mg/kg bw/day for the mouse.
There was no evidence of carcinogenicity in the mouse.
The relevance of the findings in the rat was discussed by the experts. Slightly increased incidences above historical control data of thyroid C-cell tumours in male rats at higher dose levels, and uterine polyps and tumours in female rats have been observed. However, they were observed in combination with general toxicity and increased survival in this study. As in other long term studies they were not confirmed or within the range of historical control data, the experts considered the increased incidence of tumours in rats of limited relevance to man.
Based on the high mortality in the recent rat study (Williams, 1992), the classification **Xn, R48/22 "Harmful: danger of serious damage to health by prolonged exposure if swallowed"** has been proposed by the experts. However, after the meeting, the RMS stated that the effective intake is just above the threshold of 50 mg/kg bw/day. The final decision of classification and labelling is taken by ECB.

2.6. REPRODUCTIVE TOXICITY

The reproductive toxicity of ethoprophos was investigated in two multi-generation studies in the rat. Some evidence of reproductive toxicity was observed in a three-generation study, but associated with general toxicity and not reproduced in a second two-generation study. Thus the relevant parental and offspring NOAEL is 7.3 mg/kg bw/day, based on decreased weight gain and reduced pup survival. Based on a lower fertility index, the relevant reproductive NOAEL is 15.7 mg/kg bw/day.

The teratogenic effects of ethoprophos were studied in the rat, rabbit and mouse. No evidence of teratogenicity was seen, even at dose levels producing significant maternal toxicity. In the rat, the maternal NOAEL is 1.6 mg/kg bw/day, based on mortality (or abortions) and reduced bodyweights, whereas the foetal NOAEL is 16 mg/kg bw/day. In the rabbit, the maternal NOAEL is 0.125 mg/kg bw/day, based on reduced bodyweight gain, and the foetal NOAEL is 2.0 mg/kg bw/day.

2.7. NEUROTOXICITY

Three studies were performed in the rat (acute and subchronic) but no evidence of treatment-related neuropathology was seen.

Delayed neurotoxicity was investigated in two acute studies in hens, which were discussed by the experts. As there is no indication of irreversible effects, no classification is proposed. But as the NTE inhibition is up to 60% the experts agreed that a repeat dose study is needed, regardless of the pathological findings in the acute study. Thus, a data requirement was set.

2.8. FURTHER STUDIES

Studies on metabolites

Acute oral studies were performed in rats with

- EPPA (O-ethyl-S-propyl phosphorothioate/M1) : LD_{50} 246 mg/kg bw
- O-ethylphosphoric acid: LD_{50} > 2000 mg/kg bw
- SME (O-ethyl-S-methyl-S-phosphorodithioate) : LD_{50} 41.0 mg/kg bw
- OME (O-ethyl-O-methyl-S-phosphorothioate) : LD_{50} 19.2 mg/kg bw

Cholinesterase inhibition in rats was investigated more extensively in three further studies.

Single exposure showed that cholinesterase activity in all brain areas was more affected than erythrocyte cholinesterase activity. Full recovery was not seen over the 15-day recovery period. Exposure during gestation showed no evidence of developmental neurotoxicity or neuropathology in neonates. The extent of cholinesterase inhibition in neonates was lower than in dams, which resulted in a NOAEL of 30 mg/kg bw/day for the offspring. Acute exposure of young rats and neonates showed that brain cholinesterase activity in neonates was relatively more sensitive than in adults; however the overall NOAEL based on cholinesterase inhibition is 1.0 mg/kg bw.

Two antidote studies with mice indicate that a combination of atropine and 2-PAM would be the most effective antidote in cases of ethoprophos poisoning.

2.9. MEDICAL DATA

Monitoring for the past 30 years with monthly cholinesterase analysis in blood samples didn't reveal any incidence of poisoning at the plant.

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

ADI

Initially the RMS proposed an ADI of 0.0003 mg/kg bw/day, based on the dog studies. Finally the experts decided to use the NOAEL of the rat 2-year toxicity study, which gives an ADI of 0.0004 mg/kg bw/day using a safety factor of 100.

AOEL

The systemic AOEL of 0.001 mg/kg bw/day is based on the 28-day rat, and 90-day dog and rat studies, with a safety factor of 100.

ARfD

The initial proposal from the RMS was derived from the rabbit developmental toxicity study where the maternal NOAEL was 0.125 mg/kg bw/day.

Based on a new study of cholinesterase inhibition adult and neonates rats, presented in the addendum, the experts agreed an ARfD of 0.01 mg/kg bw, with a safety factor of 100.

EFSA notes: To be highlighted with respect to setting of MRL. WHO (1999) based the ARfD of 0.05 mg/kg bw/day on an old neurotoxicity study in rat and a NOAEL of 5 mg/kg bw/day. The WHO has now presented a paper for setting an ARfD.

2.11. DERMAL ABSORPTION

One *in vitro* study on human, rabbit, mouse and rat skin was realised with an emulsified concentrate (70%) formulation and a dilution (1:19) in distilled water. Results showed that dermal penetration through human skin is 0.1% for the concentrate and 5% for the dilution, whereas through rat skin it is 5% for the concentrate and 23% for the dilution. In a first approach, the default value of 10% for *in vivo* dermal absorption through human skin was considered to be appropriate for Mocap 10 and similar granular formulations.

A second *in vitro* study on human and rat skin, presented in an addendum, was performed with the formulation Mocap 10G (granular) undiluted but moistened with distilled water. The dermal absorption value was 1.7% for human skin and 3% for rat skin.

This was discussed by the experts who finally agreed to keep the default value of 10% for prudency. The reason was first of all, the dose used did not represent the real situation, and secondly uncertainties remained on the level of intactness of the granular, so the absorption might be higher. As this is a worst case assumption, further refinements at MS level might be considered.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Mocap 10G is a granular formulation (GR) containing 10% w/w ethoprophos, for tractor-mounted overall or band/row application on potato crops, followed by soil incorporation.

Operator exposure

According to the intended uses submitted by the notifier the maximum applied dose is 110 kg of product /ha (11 kg ethoprophos /ha).

The RMS's assessment of the risk to operators is based on operator monitoring studies, performed in 1999 and GLP compliant:

i) a dosimetry study

ii) a biomonitoring study carried out concurrently

i) Dosimetry study

General description of the study:

The product was loaded and applied by 11 farmers, each operator was monitored using two types of packaging (15 kg boxes and 20 kg 'Surefill' containers). In total 21 measurements of daily exposure were performed. The used equipment was tractor-mounted boom (for the representative application rate of 11 kg as/ha) or stone separator/planter (for the representative use of 6 kg/ha, in band row application).

Results

Measured exposure (75th percentile values) from the dosimetry study, presented as % of AOEL (0.001 mg/kg bw/day), assuming a dermal absorption of 10% for the formulation, applied doses 5-12 kg as/ha and use of PPE

Supply	No RPE	With RPE (APF 10)	With RPE (APF 20)
15 kg boxes	442%	165%	150%
20 kg 'Surefill' containers	222%	79%	71%

RPE (respiratory protective equipment) with APF 10 or 20 (assigned protection factor)

In the DAR, the following conclusion was drawn by the RMS:

On the basis of the 75th percentile values for systemic exposure summarised above, the use of 'Mocap 10G' on potatoes results in an operator exposure below the AOEL (79%) when the product is supplied in 'Surefill' containers and the following operator protection requirements are observed:

- vehicles with a closed cab must be used both when making applications and when incorporating the product
- suitable protective clothing (coveralls), suitable protective gloves and suitable respiratory protective equipment (disposable filtering facepiece respirator to at least EN149 FFP3, or equivalent) when handling the product and when handling contaminated surfaces
- suitable protective clothing (coveralls) during granule placement by tractor-drawn/mounted apparatus
- do not apply by hand or hand-held equipment

However, EFSA notes: the use of 75th percentile might be questioned. The number of individual exposures above the AOEL should also be given. Furthermore, despite all mitigation measures (closed cab, PPE, RPE, Surefill), the level of exposure is close to the AOEL.

The RMS has estimated exposures predicted to result from application at the maximum dose supported for the representative product (11kg as/ha for the overall application, and 6 kg as/ha for the band/row application). Unfortunately, due to the very small numbers of operators within each group, the levels of exposure cannot be confidently characterised for each type of application and for each packaging type (regular boxes or 'Surefill' containers).
As a very high level of operator protective equipment is required (see conclusions of the field study above), the use of 'Surefill' containers might even not be sufficient to reduce the exposure below the AOEL.

ii) Biomonitoring study

During this part of the study, 17 farmers were performing loading and application with granule applicators mounted on the bed-former, stone separator or planter, or a tractor/vehicle-mounted boom applicator. Among them, 11 subjects were also involved in the concurrent dosimetry study.
Given that the biomonitoring results show no significant depression in cholinesterase activity, details of PPE/RPE worn by each operator are not described and it can be argued as a worst case assumption without these details that the results reflect exposures of operators wearing PPE and RPE.

Worker exposure

Dermal exposure of the workers is expected to be low as the product is soil incorporated and there will be no dislodgeable foliar residues.
From an air monitoring study performed in California (US EPA), assuming 24 hours exposure at the highest level observed at about 20 metres from the treatment site, the exposure is 5% of the AOEL.

Bystander exposure

Based on an air monitoring study published by the US EPA, the estimates of exposure are 14% and 5% of the AOEL for the child and adult, respectively.

3. Residues

Ethoprophos was discussed at EPCO experts' meeting for residues (EPCO 24) in May 2005.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of ethoprophos has been investigated in potatoes under conditions close to but not identical to the representative use supported by the notifier (the compound was applied formulated as an EC (emulsion concentrate) instead of under granular form). Under these conditions about 50% of the total radioactivity present in potato leaves and tubers could be extracted. In tubers, the level of total residues were comparable before and after washing as well as between peel and pulp, indicating that the residues present are not contact residues but result from translocation of the radioactivity through the plant. One major component of the residue forming 13 and 38 % of the TRR (Total Radioactive Residues) in leaves and tubers respectively was identified as ethyl phosphate. In tubers

no other compound was identified nor was present at a level above 0.01 mg/kg. In leaves ethoprophos and 2 further metabolites were identified: EPPA (O-ethyl-S-propyl-phosphorothioate) and OME (O-ethyl-O-methyl-S-propyl-phosphorothioate). Further experimentations under specific extraction conditions of tubers and leaves indicated that degradation products were incorporated in natural plant components. Further metabolism studies on cabbage and sweetcorn confirmed ethyl phosphate as the major residual product in plant after soil treatment with ethoprophos, EPPA, OME and SME (O-Ethyl-S-methyl-S-propyl-phosphorothioate) being identified at low levels.

The metabolites identified in potato leaves, cabbage and sweet corn (EPPA, OME and SME) have been considered by the expert meeting on toxicology (EPCO 23) and it was concluded that they were toxicologically relevant as their level of toxicity is similar to that of the parent compound. Ethyl phosphate is not toxicologically relevant.

It was postulated during the review process that OME and SME could be an artefact resulting from their formation under the experimental conditions of extraction but this hypothesis was rejected on the basis of further specific investigations.

The need for including EPPA, OME and SME in the residue definition was widely discussed in the expert meeting (EPCO 24). It was considered that the metabolism study on potatoes could not be fully conclusive in this respect as the amount of each compound of toxicological relevance eventually present in tubers was under the level allowing its identification and that it was therefore impossible to have useful information on their ratios. Therefore it was decided to include the 3 metabolites in the residue definition for risk assessment which is therefore established as the sum of ethoprophos, OME, SME and EPPA expressed as ethoprophos. The residue definition for monitoring is currently limited to ethoprophos only and is valid for potatoes only. No conversion factor can be fixed on the basis of the current data due to the lack of relevant information in the metabolism study as explained here above.

In addition the expert meeting estimated that new residue trials with analysis of the residues according to the residue definition for risk assessment should be conducted in order to allow a robust risk assessment for the health of the consumer to be carried out. Such studies are currently ongoing and a first set of results has been submitted to the RMS, but due this late submission could not be taken into account.

The supervised residue trials (12 for the Northern region of EU and 6 for the Southern region of EU) available during the peer review were carried out with analysis of the parent compound only.

These trials were conducted according to the Good Agricultural Practice supported as representative use by the notifier, with pre-planting application and a PHI of 80 days. All these trials were made with overall application of the full dose rate of ethoprophos. No trial was conducted according to the band application at lower dose. The expert meeting (EPCO 24) considered that trials with local application where not necessary on the basis of the fact that the treated surface, either by bandwidth or by in-furrow application, receives the same amount of ethoprophos as in the case of an overall application. The expert meeting also discussed the relevance of a PHI of 80 days taking into account the normally longer needed time for full maturity of potatoes. The RMS stated that residue data at 80 days PHI allow conclusion on the residue level for early growth stages and early varieties as there is, in the United Kingdom, a market for small tubers. These small potatoes are harvested earlier than

other potatoes. The expert meeting agreed therefore on the relevance of the residue levels at 80 days PHI for setting MRL. In these conditions most of the results were below of the LOQ (Limit of Quantification) of the method used in the trials (0.005 or 0.01 mg/kg) while the highest measurable residues found in potatoes were 0.011 mg/kg for the Northern region and 0.019 mg/kg for the Southern region. In one trial 100 tubers were individually analysed in order to obtain information on the unit to unit variability of residues. The average residue of the 100 tubers was 0.014 mg/kg and the highest individual value found was 0.076 mg/kg.

In 2 trials separate analyses were carried out on peel and pulp of potatoes. The results suggest that the major part of ethoprophos residues is located on the peel. Given the very low residue levels in potatoes, it is not necessary to further investigate the effects of processing on the nature and the level of residues.

These results can be considered as reliable on the basis of storage stability studies indicating that residues of ethoprophos are stable in potatoes under storage conditions at < 18°C for 9 months.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

A confined rotational crop study was conducted with radish, spinach and wheat sowed 30, 120 and 365 days after soil treatment with ethoprophos. Total radioactive residues in the tested plants were high at harvest, ranging from 1 to 50 mg/kg, depending on the crop and crop part, for the post-application intervals of 30 and 120 days. With the exception of straw for each post-application interval and radish sowed after 365 days after application, the extractability of residues was above 50 %.

Ethyl phosphate was present as major residual compound in all samples. Ethoprophos was present in radish at 0.33 and 0.07 mg/kg for post-application interval of 30 and 120 days respectively, in spinach at 0.07 mg/kg for post-application interval of 30 days and in straw at 0.60 mg/kg for post-application interval of 30 days. EPPA was also found in radish at 0.91 and 0.55 mg/kg for post-application-intervals of 30 and 120 days respectively as well as in wheat grains for the 30 days post-application interval. This suggests that the metabolite pattern in rotational crop is similar to that in primary crops.

However, the amount of unidentified radioactivity in extracts was high (1.42, 7.28 and 0.19 mg/kg in radish, spinach and wheat grains respectively for the shortest post-application interval). This was considered by the expert meeting (EPCO 24) as a major deficiency of the study and it was concluded that further identification of metabolites in succeeding crops, with particular investigation on the presence of OME, SME and EPPA should be submitted. Once this information will be submitted, all the information concerning the possible occurrence of residues in rotational crops should be reconsidered to evaluate the need for further field succeeding crop studies and/or the need for fixing an interval between the use of ethoprophos and the installation of a rotational crop.

Therefore the residue definitions for monitoring and risk assessment in rotational crops should be the same as for primary crops.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Although not required as the theoretical maximum daily intakes by domestic animals from the consumption of potatoes does not exceed 0.1 mg/kg diet, a metabolism study in goats was submitted

by the notifier. This study was carried out with an exposure level about 3 orders of magnitude above the expected actual level of exposure. In these conditions the total residue level in tissues was less than 0.1 mg/kg in muscle and fat, around 0.5 mg/kg in milk, 0.8 mg/kg in kidneys and 8 mg/kg in liver. The extractability of the residues was low. The metabolic pattern was similar to that observed in rats with EPPA and ethyl phosphate (tentatively) identified as intermediary metabolites before further degradation and incorporation in endogenous material. Due to the low level of residues observed in this study, their poor extractability and the very low exposure of livestock in practical conditions, no residue definition needs to be established. For the same reasons, no feeding study was conducted.

3.3. CONSUMER RISK ASSESSMENT

A robust consumer risk assessment cannot be conducted at this stage given the lack of residue data for both primary and rotational crops according to the residue definition for risk assessment.
However chronic and acute dietary risk assessment has been carried out by the RMS on the basis of the available data, restricted to the levels of ethoprophos only on potatoes only, and using the WHO European typical diet for adult consumers and of UK national diets for several populations of consumers. The calculation models were those recommended by the WHO and the calculated acute and chronic exposures of consumers were below the trigger toxicological end points (ADI and ARfD).
For the reason mentioned here above, a final conclusion on the actual risk for the consumer will only be possible after submission of data in compliance with the residue definition established for risk assessment.

3.4. PROPOSED MRLS

Based on the results of supervised residue trials a MRL of 0.02 mg/kg can be proposed for potatoes.
No MRL is proposed for animal commodities, given that no residue is expected due to the very low exposure of domestic animals.

4. Environmental fate and behaviour

Ethoprophos was discussed at the EPCO experts' meeting on environmental fate and behaviour (EPCO 21) in April 2005.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Laboratory metabolism of ethoprophos was investigated under dark aerobic conditions with the active substance either ^{14}C-labelled in the propyl or in the ethyl moiety in three different soils. The three soils covered a range of pH (5.3-7.0), clay contents (7.6%-28%) and organic carbon content (0.99%-3.7%). Additionally one of the soils was tested at 10ºC with the propyl-labelled compound. The major degradation product was CO_2 which accounted for 56-60% AR after 90d (propyl-label) and 30% AR after 112 d (ethyl labelled). The fractions of non-extractable radioactivity were 11.3/14.1%

AR (90 d, propyl-labelled) and 9.7% AR (112 d, ethyl label). In all extracts examined from the three soils, the majority of radioactivity was associated with unchanged ethoprophos and accounted to 97.5/99.2% AR (day 0) and 24.2/24.8% AR (day 252) in the study with the ethyl-labelled ethoprophos, and 7.2/9.0% AR (day 90) in the study with the propyl-labelled ethoprophos. One main metabolite was identified as O-ethyl-S-propylphosphorothioic acid AE 0592496 (max. 3.6/7.9% AR).
Under anaerobic conditions, the route of degradation of ethoprophos was comparable to that under aerobic conditions showing O-ethyl-S-propylphosphorothioic acid (AE 0592496) as the major metabolite but at much lower concentrations (max. 0.6% AR).
The soil photolysis study demonstrated that ethoprophos was not degraded during 30 days of irradiation and can be considered stable to photolytic breakdown.

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

Additional to the metabolism studies, degradation of ethoprophos was investigated with non-labelled compound in other 3 soils (pH 5.5-6.8; clay content 5.1-16.9%; OC 1.34-2.29%) at 20ºC and 40% of the maximum water holding capacity. The studies indicate that ethoprophos is moderately (DT_{50} = 10 d, 23 d, 25 d, 27 d) to highly (DT_{50} = 113 d) persistent in soil under aerobic conditions under environmental relevant conditions (t = 20–25 ºC, MWHC = 40-50% MWHC). The median DT_{50} = 22.8 d (normalised to -10kPa, 20ºC with Q10 of 2.2) was used in FOCUSgw modelling. Because the anaerobic degradation rate was calculated with only three data points (DT_{50} = 110.5 d) the need of a new anaerobic soil degradation study was discussed at the experts' meeting (EPCO 21). The meeting agreed that only at Member State level may be the necessity for requirement of new study depending on conditions in agriculture. Degradation of ethoprophos is slower at lower temperatures (DT_{50} = 36 & 54 days at 10 ºC vs 27 & 23 days at 22 ºC in the same soils and conditions).
Soil dissipation studies conducted in the United States (10 field trials) and in The Netherlands (2 trials) showed ethoprophos to have primary first order DT_{50}'s in the ranges from 4 to 87 days and DT_{90}'s from 13 and 290 days. The longest field degradation rates were observed in lower pH soils (2 Dutch trials with pH ca. 4.5). Excluding results from these very low pH soils, the mean DT_{50f} is 16.5 days. There is some indication (1 laboratory incubation and two filed soils) that at the low end of the soil pH range (pH 5.3 and 4.5) ethoprophos may degrade more slowly. During the evaluation process the U.S. field degradation data were discussed. The DAR contains information on the soil type, OC, CEC, pH and air temperature ranges over the DT_{90} period, indicating these properties were comparable to conditions that occur in central and southern Europe. However, it was agreed by the experts (EPCO 21) that an explanation regarding how representative the US field trial sites were to European conditions was required as information on precipitation / soil moisture was not summarized in the DAR.
There is no potential for an accumulation of residues of ethoprophos and its minor metabolite AE 0592496 in soil following years.
PECsoil used in the ecotoxicological risk assessment is based on soil concentrations calculated with a first order kinetics longest field DT_{50} from top soil with pH > 4.7 (DT_{50} = 42 d).

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

Batch adsorption/desorption studies in 11 soils (pH 5.3-7.4, 0.6-3.8% OC) are available for ethoprophos with propyl- and ethyl-labelled compound. The data indicate that ethoprophos has very high to medium potential for mobility in soil (K_{foc}= 38 – 186 ml/g, mean 111 ml/g). Freundlich slope 1/n were 0.82-0.96 (mean 0.89). K_{oc} values for the different desorption cycles of the same soil type increased with each succeeding desorption cycle indicating that the influence of organic matter and organic carbon on the strength of soil retention of ethoprophos also was increasing. There was no evidence of a relationship between K_{oc} and clay/cation exchange capacity content of the soil and also no direct relationship with pH value of the soil.

Column leaching was studied in two soils (sandy clay loam and clay loam) with propyl-labelled ethoprophos. Small amounts of radioactivity were detected in leachate (2.2 and 1.9% AR) that was collected over 4 days. The results of soil analysis demonstrated that the downward movement of the compound was essentially limited to the depth of 15 to 20 cm. The aged residues column leaching study demonstrated the same results i.e. downward movement to 15 to 20 cm.

The leaching behaviour of ethyl-labelled ethoprophos was examined in two lysimeters over two-year period under outdoor conditions in the UK where ethoprophos granules were incorporated to a depth of 10 cm. In the leachate, the fraction of applied radioactivity was 0.14% and 0.28% in the two lysimeters respectively over the two year period. Maximum annual average concentrations of ethoprophos accounted for 0.143 µg/L and 4.02 µg/L during the first year, and 0.024 µg/L and 0.037 µg/L during the second year. Soil analysis indicated that essentially all of the ethoprophos present at the end of the study was located in the upper 30 cm of the soil.

Also in field leaching studies conducted in the Netherlands with an application rate of 3.35 kg/ha, almost all the ethoprophos estimated was in the upper 15 cm layer. Leachate was collected and measured only in one study, resulting in concentrations < 0.1 µg/L, with the exception of the day after spraying when the concentrations reached 0.8 µg/L.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Ethoprophos was stable to hydrolysis under sterile conditions at temperatures up to 35 ºC and pH in the range of 3 to 7 using ethyl- or propyl-labelling (DT_{50} > 365 d). At pH 9 and the same temperature range hydrolysis, was observed with assumed products ethyl alcohol and S,S-dipropyl phosphorodithioic acid (DT_{50} = 39-83 at 20-25 ºC). In an aqueous photolysis study with ethyl- or propyl-labelled ethoprophos at 25 ºC and pH 7 during 30 days, the compound was found to be photolytically stable.

A ready biodegradability test indicated that ethoprophos should be classified as a non readily biodegradable substance.

Two water/sediment studies were conducted in a stream pond (7.8% OC in sediment) and in a pool run-off (0.4% OC in sediment) system at 20 ºC. The metabolic pattern in water/sediment under aerobic conditions was similar to that observed in soil. Concentration of ^{14}C-ethoprophos in water

decreased from 83% AR (day 0) to 20% AR (study end, 100 days) for pool system and from 90 % AR (day 0) to 12% AR (study end, 100 days) in the pond system. Partitioning of applied radioactivity to sediment was seen during the 100 days period of study (maximum 28%AR/44% AR at 14 and 59 days for low/high OC respectively). Unextracted residues in the sediment increased up to 11% AR in both systems. The metabolite O-ethyl-S-propylphosphorothioic acid (AE 0592496) accounted for maximum of 1.1% AR in the sediment extract. Degradation of ethoprophos in the entire system followed first order kinetics and half-lives determined by linear regression analysis were 71 and 95 days in the two systems. In the water phase, graphically estimated DT_{50} values were 40 and 20 days and square root first order DT_{50} using linear regression were 25 and 14 days.

In the original DAR, PEC_{sw} were calculated on the basis of a potential for "sub surface flow" in typically well draining potato growing soils as the main entry route to surface water. FOCUS PELMO groundwater modelling (see section 4.2.2) was used by considering the daily flux concentrations passing 1 m depth, for the most vulnerable chromatographic leaching scenarios Piacenza, Hamburg and Okehampton. These concentrations, representing lateral sub surface flow concentrations, were then divided by 10 as upon reaching a surface water body. RMS repeated the calculations using the independently assessed input parameters (DT_{50} = 22.8 d; K_{oc} = 111 mL/g and 1/n = 0.89) providing higher concentrations. These values were used in the risk assessment. PEC_{sed} were calculated assuming 39% partitioning to sediment at 14 days, in place of the worst case of 44% at 59 days. No sediment-dwelling toxicity data are available. Following the evaluation meeting (November, 2004) the assessment of potential surface water contamination through run-off and drainage for the representative uses was required. The applicant submitted new PEC_{sw} calculations according to the provisions of FOCUS surface water (FOCUS step 3 estimation and FOCUS step 4 estimation with buffer zones). However, due to late submission of the documents (end of March 2005), the study[3] was not peer reviewed. Member States will have to consider the appropriate risk management measures at the national level.

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

FOCUS PELMO calculations presented by the applicant and summarised in the DAR, were recalculated by RMS using an updated version of the model (ver. 3.3.2), longer DT_{50} (22.8 days vs. 14.7 days) and slightly higher K_{oc} value (111 mL/g vs. 100.68 mL/g). The assessment of the leaching risk of ethoprophos included the nine European scenarios, with one application per season (pre-planting) to potatoes at a maximum application rate of 11 kg/ha in Northern Europe and 10 kg/ha in Southern Europe. A 15 cm incorporation depth in soil was taken into account. Results showed that the 80th percentiles of the predicted annual ethoprophos leachate concentrations at the evaluation depth of 1 m did not exceed the ground water limit of 0.1 µg/L in seven of the nine scenarios. In the Piacenza and Hamburg scenarios the predicted concentrations were 1.84 µg/L and 0.16 µg/L, respectively. In a four years monitoring program in the Netherlands, ethoprophos was occasionally detected at

[3] BCS Report: C047608: Schaefer, D., 2005a.

concentrations slightly above 0.1 µg/L in three out of thirteen shallow groundwater wells (maximum 1.5 µg/L).

4.3. FATE AND BEHAVIOUR IN AIR

Ethoprophos was slowly photochemically degraded in the vapour phase with DT_{50} of 129 days (at 30 ºC) indicating direct atmospheric photodegradation is not a significant degradation pathway for this compound in the environment. The estimation of the degradation of ethoprophos by photo-oxidation in air was calculated according to Atkinson. The theoretical calculated rate constant for the reaction of ethoprophos with OH radicals in the atmosphere was 69.048 × 10^{-12} cm^3 × $molecule^{-1}$ × s^{-1}. The calculations resulted in very short atmospheric half-life of ethoprophos of 0.155 days, indicating that the substance should be removed from the atmosphere by reaction with photochemically produced OH-radicals that are present during day light hours. Volatilisation from soil is expected to be minimal particularly in the case of the granular formulation incorporated into soil after application.
Air concentrations would be expected to be negligible, due to low volatility.

5. Ecotoxicology

Ethoprophos was discussed at the EPCO experts' meeting on ecotoxicology (EPCO 22) in April 2005.

5.1. RISK TO TERRESTRIAL VERTEBRATES

Risk to birds

Tests were conducted with the technical a.s. and the formulation. Comparative results of toxicity tests conducted with ethoprophos technical and granular formulations show that the toxicity of ethoprophos is not enhanced when formulated as granules. The lowest endpoint for the acute toxicity was observed in a test with house-sparrow (*Passer domesticus*) LD_{50} = 4.21 mg/kg bw. The study was not GLP and another acute toxicity study with bobwhite quail (*Colinus virginianus*) was available. The endpoint for bobwhite quail was close to the most sensitive tested species (*Passer domesticus*). Since the toxicity value for bobwhite quail was obtained from a regulatory study conducted to current standards, the bobwhite quail value was considered as the most suitable for risk assessment by the RMS (LD_{50} = 6.04 mg a.s./kg bw). The lowest endpoint for short-term dietary toxicity was observed in a test with the technical a.s. and bobwhite quail (LC_{50} = 29 ppm).

The carrier for Mocap 10G is sepiolite. It has no nutritional value and therefore unlikely to be actively selected as a food source by birds. Possible routes of exposure identified by the RMS:

1) Uptake of granules as grit.
2) Consumption of contaminated soil organisms (earthworms).
3) Systemic residues in volunteer plants growing in potato fields.

The risk assessment presented by the applicant was based on the EPPO scheme. For the worst case scenario a daily grit intake of 20 granules per day was assumed resulting in acute TER values below the standard Annex VI trigger of 10.

The RMS calculated the theoretical number of granules containing an acute LD_{50} dose for a range of granivorous birds. The calculation was based on an average granule weight of 0.079 mg and a concentration of ethoprophos in Mocap 10G (10 % w/w). The number of granules needed for a LD_{50} was 12.1, 19.1, 61.2 for granivorous birds with a bodyweight of 15, 25 and 80 g, respectively. By applying a safety factor of 10 the number of granules needed for a LD_{50} dose would be 1.21, 1.91, 6.12. This indicates a high acute risk to birds.

Higher tier studies were conducted with *Colinus virginianus*, *Phasanus colchicus* and *Lanchura punctuate* and a number of field surveys were reported. The studies and field surveys were assessed by the RMS. Overall it was concluded that the provided information is insufficient to demonstrate that the risk, particularly to small granivorous bird species is low.

Studies on the incorporation efficiency, characterization of particle size of arable soils and of Mocap 10G granules, dissipation of ethoprophos from Mocap 10G granules and residue levels in potential food items were submitted to refine estimations of exposure for terrestrial vertebrates. Furthermore a new acute oral toxicity study with technical ethoprophos and canary bird (*Serinus canaria*) and acceptance studies with granules and canary birds (*Serinus canaria*) and wild caught house sparrows (*Passer domesticus*) were submitted by the applicant and evaluated by the RMS in an addendum.

The risk assessment provided in the addendum followed the approach proposed in Luttik, 2003[4] which introduces the concept of daily grit ingestion and relative granule exposure. The following formula was used to calculate the estimated theoretical exposure:

$$ETE = \frac{DGI \times \frac{G_{surface}}{SP_{surface} + G_{surface}} \times G_{loading}}{kg \quad bw}$$

$G_{surface}$ = No. of granules in relevant size classes for birds at the soil surface after incorporation.

$SP_{surface}$ = No. of available grit particles on the soil surface in relevant size classes for birds.

$G_{loading}$ = mg a.s./granule

DGI = Daily grit intake (particles/bird/day)

The relative granule exposure was calculated for three different soil types in UK.

The TER calculation based on 97.5 % incorporation rate of the granules resulted in acute TER values of 0.39, 0.65 and 0.69.

The refined risk assessment included the following refinement steps:

1. A probabilistic approach was used to define the acute toxicity value for birds. The HD_5 of 3.477 mg a.s./kg bw based on LD_{50} data of 9 species. The HD_5 did not differ markedly from the LD_{50} for bobwhite quail (LD_{50} = 6.04 mg/kg bw) which was used in the deterministic risk assessment. For the

[4] Luttik R. (2003): Risk assessment scheme fort he impact of plant protection products on birds and mammals. Thesis, Leiden University.

risk assessment the applicant proposed to use a lower safety factor of 5 instead of the standard value of 10 due to the use of the HD_5 value.
2. The daily grit intake was calculated to be 386 particles/bird/day instead of the default value of 651 particles/bird/day.
3. An incorporation efficiency of 99%, based on the results of a new study on the incorporation efficiency.
4. The proportion of grit taken up from treated fields was reduced from 1 to 0.15. The reduction was based on observations on habitat preferences of granivorous birds.

The above listed refinement steps resulted in acute TER values of 5.9, 9.8 and 10.7 for three different soil types. RMS recalculated the TER values because the relative granule exposure (RGE) values presented by the applicant were slightly incorrect and the daily grit intake (DGI) was reset to 651 because considerable uncertainty exists on the robustness of the turnover factor for grit and the proposal to reduce the default value was poorly supported. The resulting acute TER values are 3.7, 6.35 and 6.35.
The PT value of 0.15 was considered by the RMS to need further verification under practical use conditions. The applicant proposed to conduct further field research to support the reduction in the PT value.

The avoidance study with canary birds (*Serinus canaria*) failed to justify that the acute risk to birds is low. The birds were exposed to a number of 3595 granules/m2 corresponding to an incorporation efficiency of 97.5 %. In one of six aviaries 3 of 5 birds died while in the other aviaries no effects were observed. The applicant explained the pattern of mortality in an uneven scattering of granules. No evidence was provided to substantiate this explanation and therefore it was concluded by the RMS that the study results provide an indication of the potential hazard to small granivorous birds at an incorporation efficiency of 97.5 %. The second study with wild caught house sparrows (*Passer domesticus*) was conducted with a different formulation Mocap 20G and natural grit was added to the surface of the organic test soil. Therefore it was difficult to establish the direct relevance of the study.

The RMS concluded that the acute risk from deliberate ingestion of Mocap 10G granules has not been fully quantified and the RMS is of the opinion that some mortalities could occur.

The new study on the incorporation efficiency was discussed in the expert meeting. It was agreed that the 10^{th} centile incorporation efficiency would be more appropriate because the 90^{th} centile represents rather a best case than a worst case scenario. The 10^{th} centile incorporation efficiency is 98.76 %. It is assumed that the use of the 10^{th} centile would not change the outcome of the risk assessment. The incorporation of granules at the row ends was questioned to be a common practice in all MS of the EU. The meeting agreed that a high level of incorporation of granules in headlands is required and end of the row incorporation has to be set as a risk mitigation measure.
The use of the median HD_5 value for risk assessment was accepted in the expert meeting. No agreement was reached on the safety factor which should be applied in the risk assessment. RMS

pointed out during the meeting that using the HD_5 value with an uncertainty factor of 5 results in this case in the same regulatory toxicity endpoint as using the bobwhite quail LD_{50} value and an uncertainty value of 10.
A risk assessment for unintentional ingestion of ethoprophos residues in soil was conducted. The amount of soil which is required to reach the HQ_5 dose was calculated as 14% of the birds' bodyweight if a safety factor of 5 is applied. It was concluded by the RMS that the risk from unintentional uptake of contaminated soil will be much lower than that posed by deliberate ingestion of Mocap 10G granules remaining on the soil surface.

Overall it is concluded that the acute risk to small granivorous birds from intentional uptake of granules is high. Further risk refinement steps and risk mitigation measures to ensure high incorporation efficiency are required.

A new risk assessment for herbivorous and earthworm eating birds was presented in the addendum of the RMS. The maximum recorded residue level of 2.7 mg a.s./kg from 3 residue studies with young cereal plants was used in the risk assessment. The acute first tier TER value for herbivorous birds was calculated to be 5.1. For risk refinement wood pigeon (*Columba palumbus*) and skylark (*Alauda arvensis*) were chosen as focal species. PT values of 0.33 (wood pigeon) and 0.15 (skylark) and a reduced safety factor of 5 in relation with using the HD_5 value were proposed by the applicant.
The choice of focal species was questioned by the RMS because evidence was lacking that these species prefers open habitat of newly planted potato fields, although the applicant provided some references to indicate that these species are found in arable landscapes. The suggested PT values were not supported by any detailed observation of the feeding activity in such habitats. However the RMS agreed that the proposed values for PT are likely to be conservative and that the use of HQ values should allow some reduction in the safety factor. Hence, the RMS concluded that the risk to herbivorous birds is low. The expert meeting discussed the use of the residue data from the three field trials. It was agreed that the maximum value should be used for the acute risk, geometric mean of maxima for the short-term risk and 21 d twa values for long-term risk assessment. In order to address the risk to herbivorous birds the applicant proposed to conduct field monitoring studies to quantify the presence of herbage in potato fields and usage of newly planted potato fields by herbivorous birds. EFSA is of the opinion that the studies on the presence of herbage in the potato fields and usage by herbivorous birds are required to support the assumptions made in the refined risk assessment and thus allowing a final conclusion on the risk to herbivorous birds.

The risk assessment from uptake of contaminated earthworms was based on measured residues in earthworms. The first tier acute TER value of 2.1 was below the acute Annex VI trigger of 10. Acute TER values of 6.1, 6.9 and 6.2 were calculated for blackbird (*Turdus merula*), rook (*Corvus frugilagus*) and black headed gull (*Larus ridibundus*) in a refined risk assessment. The refinements were based on PT values of 0.2 and 0.33. Furthermore the applicant proposed to use an acute trigger of 5 instead of 10 because of the use of the HD_5 value (3.477 mg a.s./kg bw). The refinement of PT values was not supported by data on the feeding activity in such habitats. The applicant proposed to

conduct further work to verify the proposed refinements of PT. The outcome of the studies on the use of potato fields by earthworm eating birds is required to draw a final conclusion on the acute risk to earthworm eating birds. A refinement of PT in the context of acute risk assessment is problematic. Scientific based evidence must be delivered that birds cannot feed enough contaminated earthworms in a short time in the treated field to reach a level of exposure exceeding the $LD_{50}/10$.
The short term risk assessment for herbivorous birds and earthworm eating birds was assessed on the basis of measured residues (see above). The first tier short-term TER value exceeded the Annex VI trigger value for herbivorous birds but not for earthworm eating birds. Based on a refined PT of 0.2 for blackbird and 0.33 for rook and black headed gull the acute short-term TERs were calculated to be 11.42, 13.02 and 11.6. The PT refinement was not supported by data. The notifier proposed to conduct further field research to verify the proposed PT values (see above acute risk assessment).
The short term risk to granivorous birds from deliberate uptake of granules as grit was assessed as high for all three soil types for which the relative granule exposure was determined. Hence a refined risk assessment is required to address the short-term risk to granivorous birds. The RMS is of the opinion that ethoprophos acts primarily as an acute toxin and in case that the acute risk is sufficiently addressed the RMS does not consider it necessary to provide any further information to address the short-term risk to birds. In case that the applicant wishes to address the short term risk with the acute risk assessment a detailed explanation should be given why the acute risk assessment covers also the short-term risk.

Reproduction studies were available with technical ethoprophos and mallard duck (*Anas platyrhynchus*) and bobwhite quail (*Colinus virginianus*). Because of substantial mortality in the lowest tested dose of 40 ppm no NOEC could be derived from the study with mallard duck. Mortality rates of 88 %, 44 % and 0% were observed at dose rates of 30 ppm, 15 ppm an 7.5 ppm in the study with bobwhite quail. A reduction in egg production of 22 % was observed in the 7.5 ppm dose group. However no statistical significant effect on reproduction parameters (including egg production) was seen at a dose of 7.5 ppm. The effects seen in the study was primarily related to parental toxicity including mortality. The dose of 7.5 ppm is considered as being close to the lethal threshold and reduction in reproductive parameters is likely to result from parental intoxication. For the risk assessment the applicant proposed to use the endpoint of 7.5 ppm as a NOEAEL. The expert meeting agreed that the NOEC from the reproduction study with bobwhite quail is not reliable because a 22 % reduction in egg production was observed at this dose level and it was not possible for the applicant to submit historical control data supporting the setting of the NOEC. It was concluded at the meeting that a more robust justification of the proposed NOEAEL is needed before it can be used as a regulatory endpoint. Further toxicity studies may be required in which the applicant is advised to discuss the protocol with the RMS before conducting a new study. The applicant has meanwhile initiated a new avian reproduction study. The proposed submission date is February/March 2006.

The first tier long-term risk assessment based on the NOEC of 7.5 ppm (= 0.6 mg a.s./kg bw d) resulted in a high long term risk to herbivorous and earthworm eating birds. The refined risk assessment was based on 21 d twa concentrations of measured residues in cereals and earthworms.

The refined TERs were calculated for herbivorous birds, wood pigeon and skylark to be 18.75 and 8.45 based on PT values of 0.33 and 0.15, respectively. The refined long-term TERs for earthworm eating birds were 6.5, 6.12 and 5.45 for blackbird, rook and black headed gull by applying a PT value of 0.10 and 0.20. The refinement of PT was not supported by data. The use of 21d twa concentrations for the long-term risk assessment was agreed by the expert meeting. The RMS considers the risk to herbivorous birds as low based on the assumption that it is unlikely that herbivorous birds obtain a significant amount of their food from potato fields and taking into account that the first tier TER value of 4.6 is close to the Annex VI trigger of 5. The risk to earthworm eating birds is considered as high because the PT reduction is not sufficiently supported by data and the first tier TERlt is well below the trigger of 5.
The long-term risk to granivorous birds from uptake of granules was assessed as low based on dissipation of ethoprophos from the granules with a DT_{50} of 8.5 h at a moisture content of the soil of 70 % of its water holding capacity and on a daily grit intake of 386. The RMS assessed the recalculation of the daily grit intake to 386 particles/bird d as not acceptable (see above the acute risk assessment). Some uncertainty is also related to the assumption that the soil moisture will be as high as 70 %. Therefore it is concluded that the long-term risk from uptake of granules is not sufficiently addressed.

Before drawing a final conclusion on the long-term risk to birds a reliable NOEC has to be established taking into account the new avian reproduction study which is proposed to be submitted in February/March 2006.
In October 2005, to address acute and short term risk, the notifier submitted an avian field monitoring study together with a supporting study evaluating bird carcasses found during monitoring. In November 2005, revised acute and short term risk assessments for granivorous and earthworm-eating birds were submitted. To aid consideration of avian risk a study further exploring the results of the Mocap field incorporation study was also submitted in October 2005. These studies should be taken into account for the risk assessment at Member State level.

Risk to mammals

Two main routes of exposure for wild mammals were identified:
1) via contaminated earthworms
2) via consumption of contaminated plants (systemic uptake of ethoprophos)

The uptake of granules is not considered to be a major route of exposure since mammals are not known to actively seek grit, the granules have no nutritional value and because of the low size of the granules it is unlikely that they are mistaken for food items.

For the first tier risk assessment a small herbivorous mammal, (common vole, *Microtus arvalis*) and a small insectivorous mammal (common shrew, *Sorex araneus*) were chosen as indicator species according to SANCO/4145/2000.

Measured residues in cereals and earthworms were used for the risk assessment (see above risk assessment for birds). The first tier TER values for herbivorous and earthworm eating mammals were 8.8 and 9.4. For the refined risk assessment a medium herbivorous mammal (hare) was chosen and the PT values were set to 0.33 for hare and 0.25 for common shrew. The refined acute TER values were 132 and 37 for hare and common shrew. The RMS accepted the hare as indicator species but the reduction in PT was assessed as not sufficiently supported. Without applying a reduced PT the acute TER for hare would still be above the Annex VI trigger of 10 and hence the risk to herbivorous mammals is considered to be low. The RMS agreed to the common shrew as an appropriate species for the risk assessment for earthworm eating mammals but the PT of 0.25 was not sufficiently supported by data. RMS considered it as unlikely that the focal species spends sufficient time in the treated field to take up a lethal dose. Taking into account that a hypothetical PT value of 0.8 would still result in a TER >10 the RMS is of the opinion that the acute risk to earthworm eating mammals is low. EFSA is not convinced that a refinement of PT in the context of acute risk assessment is appropriate. However, some information was provided that the treated potato fields in springtime are not a preferred habitat because they don't offer sufficient protection from predators. Taking these arguments into account it was agreed in the evaluation meeting of February 2006 that it is likely that the acute risk to small insectivorous mammals is low.

The applicant considered the long-term risk to herbivorous and earthworm eating mammals as low. The risk assessment was based on an endpoint at which reduced offspring survival and weight gain were reported. Since no scientific argument has been provided to support the use of this endpoint the RMS suggested to use the next lower dose of 30 ppm (equivalent to 1.3 mg a.s./kg bw d). The risk assessment based on the NOEC of 1.3 mg a.s./kg bw d resulted in TERlt values of 15.8 and 1.14 for hare and common shrew, respectively. The risk assessment was based on measured residues and ftwa values which were agreed in the expert meeting and also used in the long-term risk assessment for birds (see above). It is concluded that the long-term risk to herbivorous mammals such as hare is low but a high risk to earthworm eating mammals is indicated. Further risk refinement steps are necessary to address the long-term risk to mammals.
In October 2005 the notifier submitted a revised long term risk assessment for earthworm eating mammals. In support of the refined risk assessment the applicant submitted, in September 2005, a comparison of available multi-generation reproduction studies of ethoprophos to determine a relevant NOEL for the chronic wild mammal risk assessment and a literature survey and expert statement: "Bare soil fields as food habitats for shrews". These studies and the revised higher tier risk assessment have not been evaluated but should be taken into account at Member State level.

5.2. RISK TO AQUATIC ORGANISMS

The lowest endpoints from studies with the technical a.s. assessed by the RMS as valid and acceptable for the risk assessment were observed for daphnids (acute 48 h EC_{50} = 0.2 mg a.s./L, chronic 21 d NOEC = 0.002 mg/L). Studies with the formulation were not considered necessary since the main routes of entry into surface water are run-off and drainage. The PECsw was calculated by the RMS using FOCUS groundwater models. The three worst case scenarios resulted in maximum

PEC values of 0.87 – 0.0064 µg a.s./L. The acute TER values for fish, daphnids and algae were markedly above the Annex VI trigger of 100. However, the chronic TER value for daphnids of 2.6 did not meet the Annex VI trigger value of 10 indicating a high chronic risk to aquatic invertebrates.

The active substance partitions to a high extend to the sediment phase. 39 % of applied radioactivity was found in the sediment phase after 14 d and a maximum of 44 % of applied radioactivity was reached in the sediment phase after 65 days. No studies were available for sediment dwelling organisms. A study with chironomus was submitted by the applicant in March 2005 but not assessed by the RMS because the submission was made after the finalisation of documentation for consideration at the expert meetings for ecotoxicology. A final conclusion on the risk to sediment dwelling organisms can be drawn after evaluation of the study with chironomus.

A new PECsw calculation was submitted by the applicant according to the provisions of FOCUS surface water as well as an aquatic risk assessment in compliance with the FOCUSsw calculations but these were not assessed by the RMS because the submissions were made after the finalisation of documentation for consideration at the expert meetings for ecotoxicology and environmental fate and behaviour. Therefore the new PECsw calculations and aquatic risk assessment will have to be taken into consideration at Member State level.

The log Pow for ethoprophos is 2.99 (95 % confidence interval of 2.9 – 3.1). Two bioconcentration studies were conducted with bluegill sunfish (*Lepomis macrochirus*). The BCFss values were calculated with BIOFAC to be 180 and 210. The RMS raised concerns whether the calculated BCF values reflect the measured uptake/depuration kinetics but accepted the values because of the absence of a more accurate way of determining the BCFss and suggests to use the BCF of 210 for the risk assessment. Ethoprophos is not ready biodegradable. Therefore it is concluded that there is a potential risk of bioaccumulation in aquatic organisms if contamination of aquatic habitats arises. For conditions where contamination of surface water arises the risk of biomagnification in aquatic food chains and the risk of secondary poisoning of fish eating birds and mammals needs to be addressed.

5.3. RISK TO BEES

Data on the contact toxicity of technical ethoprophos indicate an acute contact LD_{50} of 5.56 µg/bee. The risk to bees was assessed by the RMS as low because of low systemicity in a range of plants and the low likelihood that residues will be found in nectar or pollen. The assessment of the RMS was discussed in the expert meeting. The meeting agreed that the risk to bees from the representative use in potatoes is low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Taking into account that the product is applied as granules which are incorporated in soil and its low systemicity only ground dwelling species are expected to be exposed to ethoprophos. Toxicity testing was therefore limited to ground dwelling species and no studies were conducted with the two standard sensitive species (*Aphidius rhopalosiphi* and *Typhlodromus pyri*). Severe acute effects (100

% mortality) were observed for the *Aleochara bilineata* and *Poecilus cupreus* in laboratory studies at nominal concentrations of (21 mg a.s./kg soil and 28 mg a.s./kg soil). The tested concentrations exceeded clearly the estimated PEC in soil (4.89 mg a.s./kg soil). In aged residue test simulating an initial PEC soil of about 1.5 times the initial PEC resulted in 57 % mortality of adult *P. cupreus* after aging for 1 month. After a period of 2 months of ageing no effects were observed on adult *P. cupreus*. Negative effects on reproduction of *A. bilineata* was observed even after ageing for 3 months. A new extended laboratory study was conducted with four bioassays carried out over a whole year. Severe effects were observed if the beetles were exposed to residues aged in the field for 7 days and 13 weeks, respectively. Sublethal effects were observed in the 3rd bioassay (70% reduction in reproduction if exposed to residues aged for 23 weeks). No significant effect on reproduction was observed in bioassay 4 (residues aged for 10.5 months). The RMS concluded that the potential for recolonisation was shown within a year of the treatment. In addition a field study was conducted. No effects on ground dwelling beetles were found. The number of individuals recorded in the study was low and no toxic reference substance was applied. Therefore it was concluded that the study provides only limited evidence of the absence of adverse effects in the field.

The risk to non-target arthropods was discussed in the expert meeting. The meeting agreed that the potential of recovery within 1 year is sufficiently demonstrated taking into account that the field margins remain unaffected (granular application) hence providing a reservoir for recolonisation.

5.5. RISK TO EARTHWORMS

The acute and chronic toxicity of the formulation Mocap 10G was tested. Based on initial PECsoil values (4.89 µg/kg soil) the first tier risk assessment indicated a high acute and long-term risk to earthworms (acute TER = 4.05, long-term TER < 0.17). A field study was submitted. The results confirmed that ethoprophos can cause severe acute effects (significant reductions in abundance and biomass of earthworms were observed in the field study one month after the treatment). These effects were short-lived as full recovery occurred within the same growing season of the treatment. 5 months after the application no significant differences compared to the control plots were observed. Overall it is concluded that the risk to earthworms is low from the representative use in potatoes.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

Since the DT_{90} field exceeded 100 days in some field trials and severe adverse acute and long-term effects on ground dwelling arthropods and earthworms were observed a requirement for a litter-bag study is triggered. The applicant submitted a litterbag study on 21. September 2005 together with a final risk assessment for soil non-target organisms. The study was not evaluated and therefore a final conclusion on the risk from the representative use in potatoes posed to soil non-target organisms cannot be drawn.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of technical ethoprophos on soil respiration and nitrification were tested. No significant effects of > 25% were observed at a dose rate of 33.33 mg a.s./kg soil indicating a low risk to soil micro-organisms from the representative use in potatoes.

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

The results of screening studies on the herbicidal activity suggest that ethoprophos is phytotoxic to some plant species if exposure takes place before emergence. However since spray drift does not occur because the product is a granule, plants in the off-crop area are not exposed to ethoprophos and therefore the risk to non-target plants in the off-crop area is considered to be low.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The inhibitory effect of technical ethoprophos on respiration of sewage sludge was tested. The EC_{50} after 3 h was calculated as 780 mg a.s./L. Since the product is applied as a granule no significant contamination of biological sewage treatment plants is expected and the risk to biological sewage treatment plants is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: ethoprophos
Definitions for monitoring: ethoprophos

Water

Ground water

Definitions for exposure assessment: ethoprophos
Definitions for monitoring: ethoprophos

Surface water

Definitions for risk assessment: ethoprophos
Definitions for monitoring: ethoprophos

Air

Definitions for risk assessment: ethoprophos
Definitions for monitoring: ethoprophos

Food of plant origin

Definitions for risk assessment: sum of ethoprophos, OME, SME and EPPA expressed as ethoprophos

Definitions for monitoring: ethoprophos

Food of animal origin

Definitions for risk assessment: no residue definition needed due to low exposure of livestock to residues present in feedingstuffs.

Definitions for monitoring: no residue definition needed due to low exposure of livestock to residues present in feedingstuffs.

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
ethoprophos	Moderate to high persistence ($DT_{50\ lab}$ = 10-113 d, 20-25°C, different soil moisture conditions, see section 4.1.2);	High acute and chronic toxicity and risk to soil dwelling arthropods and earthworms. Higher tier studies showed the potential of recovery and recolonisation.

Ground water

Compound (name and/or code)	**Mobility in soil**	**> 0.1 µg / L 1m depth for the representative uses** **(at least one FOCUS scenario or relevant lysimeter)**	**Pesticidal activity**	**Toxicological activity**	**Ecotoxicological activity**
ethoprophos	Very high to medium mobility (Koc = 38-186 mL/g)	FOCUS modelling: yes 2 out of 9 FOCUS groundwater scenarios (concentrations: 0.16 µg/L for Hamburg and 1.84 µg/L for Piacenza). Annual average concentrations in leachate: yes in the first of 2 years (0.143 µg/L and 4.02 µg/L)	Yes	Yes	High chronic risk to aquatic invertebrates in vulnerable conditions, not readily biodegradable, risk of bioaccumulation

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
ethoprophos	See point 5.2.

Air

Compound (name and/or code)	Toxicology
ethoprophos	Very toxic by acute inhalation: rat LC_{50} 0.123 mg/L, no repeated dose studies submitted.

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

- Data to confirm on how the initial identity of the impurities has been performed must be provided to address the requirement of the Directive on the specificity of the method(s) (date of submission indicated by the applicant for February 2006, refer to chapter 1).
- A repeat-dose neurotoxicity study in hens is required (submission date proposed by the notifier: autumn 2006; refer to point 2.7).
- Supervised residue trials with analysis of the residues according to the residue definition for risk assessment (relevant for all representative uses; studies submitted to the RMS in November 2005 for the 1st year of trials – but have not been evaluated; refer to point 3.1.1).
- Further identification of extractable metabolites in rotational crops, with particular investigation on the presence of OME, SME and EPPA (relevant for all representative uses; the notifier states that a confined rotational crop study is ongoing with preliminary data available in April 2006; refer to point 3.1.2).
- Depending on the information to be provided on the nature of residues in rotational crops, field rotational crops studies may be required (relevant for all representative uses; no submission date proposed; refer to point 3.1.2).
- PT refinement for uptake of grit needs further verification (the applicant has submitted a revised acute and short term risk assessment for birds based on the results of field monitoring and supported by other information – this was submitted to the RMS in November 2005 but has not been evaluated, refer to point 5.1).
- Refined acute, short-term and long-term risk assessment for granivorous birds for the uptake of grit (the applicant has submitted a revised acute and short term risk assessment for birds based on the results of field monitoring and supported by other information – this was submitted to the RMS in November 2005 but has not been evaluated, refer to point 5.1).
- Studies on the presence of herbage in potato fields and usage of newly planted potato fields by herbivorous birds to refine the acute risk to herbivorous birds (the applicant has submitted a revised acute and short term risk assessment for birds based on the results of field monitoring and supported by other information – this was submitted to the RMS in November 2005 but has not been evaluated, refer to point 5.1).
- Further refinement of the risk to earthworm eating birds (the applicant has submitted a revised acute and short term risk assessment, and also a revised long-term risk assessment, for earthworm eating birds – these assessments were submitted to the RMS in November 2005 but have not been evaluated, refer to point 5.1).
- A new avian reproduction study to establish a reliable NOEC for birds (submission date proposed by the applicant: February/March 2006, refer to point 5.1.)
- An avian monitoring study to address the risk to risk to birds was conducted in 2005 (relevant for all representative uses, this was submitted to the RMS in October 2005 but not evaluated, refer to point 5.1).

- A revised higher-tier risk assessment for birds based on the findings of the avian monitoring study (including an evaluation of bird carcass found during the avian field study) (relevant for all representative uses, this was submitted to the RMS in November 2005 but has not been evaluated, refer to point 5.1).
- A revised higher-tier long-term risk assessment for earthworm eating mammals. (relevant for all representative uses, submitted by the applicant in October 2005, refer to point 5.1).
- In support of the above intended submission the applicant submitted a comparison of available multi-generation reproduction studies with ethoprophos to determine a relevant NOEL for the chronic risk assessment and a literature survey and expert statement: Bare soil fields as food habitats for shrews. (relevant for all representative uses, submission date: 21. September 2005, refer to point 5.1).
- A study with *Chironomus riparius* (relevant for all representative uses) was submitted but not evaluated. (refer to point 5.2).
- For conditions where contamination of surface water arises the risk of biomagnification in aquatic food chains and the risk of secondary poisoning of fish eating birds and mammals needs to be addressed (relevant for all representative uses, no submission date proposed, refer to point 5.2).
- PEC calculations according to FOCUS surface water (relevant for all representative uses) were submitted to the RMS in March 2005 together with a revised aquatic risk assessment but not evaluated. (refer to points 4.2. and 5.2).
- A litterbag study (relevant for all representative uses) was submitted to the RMS in September 2005 but has not been evaluated. (refer to point 5.6).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide and nematicide, as proposed by the applicant. This comprises direct overall or band/row application followed by soil incorporation to control a broad spectrum of insects and nematodes in potatoes at application rate up 11 kg ethoprophos per hectare. Ethoprophos can be used as insecticide and nematicide.

The representative formulated product for the evaluation was "Mocap 10G" ("AE F034142 00 FG10 A1" or "EXP05806A"), a granule formulation (GR), registered in the South and the North of the EU.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. ethoprophos in food of plant origin (potatoes, only) in soil, water and air.

A validated analytical method for the determination of ethoprophos in blood and animal tissues is also available.

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.

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.

Ethoprophos was rapidly and extensively absorbed, completely metabolised, and rapidly excreted, with low potential for bioaccumulation. The acute toxicity is high and it is a skin sensitizer.
The proposal for classification is T+, R26/27 "Very toxic by inhalation and in contact with skin"; T, R25 "Toxic if swallowed"; Xi, R43 "May cause sensitisation by skin contact".
The most sensitive endpoint during short term exposure was cholinesterase inhibition in all species. Considering available evidence, there is no genotoxic or carcinogenic potential. The classification Xn, R48/22 "Harmful: danger of serious damage to health by prolonged exposure if swallowed", based on the high mortality in the first weeks of the long term rat study, is proposed. There is no clear evidence of reproductive toxicity, and ethoprophos was not shown teratogenic. Delayed neurotoxicity in acute studies with hens has not been demonstrated.
The Acceptable Daily Intake (ADI) is 0.0004 mg/kg bw/day, the Acceptable Operator Exposure Level (AOEL) 0.001 mg/kg bw/day, and the Acute Reference Dose (ARfD) 0.01 mg/kg bw/day. All reference values were set using a safety factor of 100. The agreed dermal absorption value of 10% represents a worst case assumption.
The measurements of operator exposure in a field study are above the AOEL, even assuming the use of personal protective equipment and respiratory protective equipment. Only the use of Surefill containers might reduce the extent of exposure below the AOEL. Based on an air monitoring study, worker and bystander exposure are clearly below the AOEL.

The metabolism of ethoprophos in plants after soil application has been investigated in potatoes, cabbage and sweet corn. The degradation involves the hydrolysis of the S-propyl and 0-ethyl ester links and further degradation to compounds later integrated in the structure of natural plant components. The major metabolite observed in plants is ethyl phosphate. This compound has no toxicological relevance. Other compounds were identified at lower levels: EPPA (O-ethyl-S-propyl-phosphorothioate), OME (O-ethyl-O-methyl-S-propyl-phosphorothioate) and SME (O-Ethyl-S-methyl-S-propyl-phosphorothioate). These metabolites have a level of toxicity similar to that of ethoprophos. In rotational crops metabolism data suggest a similar degradation pathway. A residue definition for risk assessment is proposed as the sum of ethoprophos, EPPA, OME and SME expressed as ethoprophos. This definition is proposed taking the available information on all crops into consideration because the data on potato tubers are not conclusive enough for a reliable residue definition for that crop. The residue definition for monitoring purposes is ethoprophos only.
Supervised residue trials on potatoes were conducted in accordance with the representative uses supported by the notifier. They lead to a proposal for a MRL of 0.02 mg/kg for potatoes, covering potatoes harvested in an early stage of their growth to be specifically marketed as small size potatoes. These trials were carried out with analysis of ethoprophos only and therefore are not appropriate to be used for risk assessment for the health of the consumer. Additional supervised residue trials in potatoes are necessary with analysis of residues according to the residue definition for risk

assessment. Such studies are currently ongoing and a first set of results has already been submitted to the RMS. Before finalising acute and chronic risk assessments, further information on the nature of extractable residues in rotational crops and, depending on that information, field trials on rotational crops are also necessary.
Due to the very low exposure of livestock to residues of ethoprophos, residues in animal commodities are expected to be extremely low and do not need to be monitored and taken into consideration for assessment of the risk for the health of the consumer.

The environmental fate and behaviour data presented for ethoprophos indicate that when released to soil and water, ethoprophos will degrade primarily through biodegradation. Available studies have indicated that biodegradation is the major degradation process in soil (DT_{50lab}= 10-113 days; DT_{50f}= 4-42 days, excluding very low pH soils). At Member State level may be the necessity for requirement of new anaerobic soil degradation study depending on conditions in agriculture. Adsorption studies have shown that ethoprophos has very high to medium potential for mobility in soil (K_{foc}= 38 – 186 ml/g, mean 111 ml/g). These data, combined with those on mobility in soil, indicate that for most situations the risk for contamination of groundwater is acceptable. However, in vulnerable scenarios (very large leachate, low clay content, low OC content and shallow groundwater) ethoprophos may have the potential to exceed the drinking water limit (0.1 µg/L) in groundwater from the intended supported use on potatoes. Aqueous hydrolysis may become an important process only in alkaline water (DT_{50} = 83 days at pH 9 and 25ºC). The dissipation DT_{50} values of ethoprophos from the water phase were 14-25 days (square root first order) at 20ºC in the laboratory and 71-95 days for the whole system. Estimated concentrations of ethoprophos in surface water, arising from sub surface flow, indicate that except in very vulnerable situations, there is no cause for concern. Information on potential surface water contamination trough run-off and drainage for the representative uses is available, but was not peer reviewed. Concentrations of ethoprophos in the air compartment will be negligible, due to the method of application (soil incorporation) and short persistence in the atmosphere (DT_{50} = 0.15 days).

The acute risk, short-term risk and long term-risk to small granivorous birds from intentional uptake of granules is high. Further risk refinement steps and risk mitigation measures to ensure high incorporation efficiency are required. The refined acute risk assessment for herbivorous birds is low but needs further support by data. A high acute, short-term and long-term risk to earthworm eating birds was indicated and further data are required to support the suggested risk refinement steps. The acute and long-term risk to earthworm eating mammals is high. Further risk refinement steps are required. The chronic risk to aquatic invertebrates and the potential risk of bioaccumulation is high under vulnerable conditions where contamination of surface water arises. The study with *Chironomus riparius* needs to be evaluated in order to draw a final conclusion on the risk to sediment dwelling organisms. There is a risk of bioaccumulation in aquatic organisms if contamination of aquatic habitats arises. For conditions where contamination of surface water arises the risk of biomagnification in aquatic food chains and the risk of secondary poisoning of fish eating birds and mammals needs to be addressed. The PECsw calculations based on the provisions of FOCUS surface

water should be taken into account for the risk assessment at Member State level. Severe acute and sublethal effects were observed in tests with non-target arthropods and a high risk was indicated. The higher tier risk assessment for non-target arthropods was discussed in the EPCO expert meeting. It was concluded that the potential of recovery was sufficiently demonstrated taking into account that the field margins remain unaffected and thus providing a reservoir for recolonisation. A high acute and long-term risk was indicated for earthworms in the first tier risk assessment. In a field study severe acute effects were observed. However full recovery was observed within 5 months after the application and it is concluded that the risk to earthworms is sufficiently addressed.

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

- MS will need to consider the equivalence of the new source (addendum 3 to volume 4, October 2005), if necessary during the re-registration process.
- As the operator exposure is high, the use of PPE, RPE as well as 'Surefill' containers is needed.
- A high incorporation efficiency, including end of the row incorporation, is required to mitigate the risk to granivorous birds.
- Further risk assessment is needed for vulnerable conditions under which contamination of surface water arises to address the long-term risk to aquatic invertebrates and the risk of bioaccumulation.

Critical areas of concern

- At the moment no final specification can be set, because some clarification is needed with respect to certain impurities (refer to chapter 1).
- Very high acute toxicity by dermal and inhalation exposure, high acute toxicity by oral exposure.
- Operator exposure during tractor-mounted overall application as well as band row application exceeds the AOEL, even with PPE and RPE used. The use of surefill containers might reduce the exposure.
- Potential for groundwater contamination under vulnerable conditions.
- High risk to birds and mammals
- High chronic risk to aquatic invertebrates and risk of bioaccumulation under vulnerable conditions where contamination of surface water potentially occurs.

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

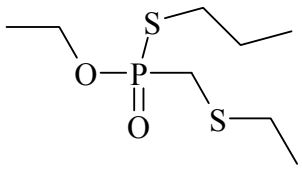
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	Ethoprophos
Function (e.g. fungicide)	Nematicide and soil insecticide

Rapporteur Member State	United Kingdom
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	*O*-ethyl *S*,*S*-dipropyl phosphorodithioate
Chemical name (CA) ‡	Phosphorodithioic acid, *O*-ethyl *S*,*S*-dipropyl ester
CIPAC No ‡	218
CAS No ‡	13194-48-4
EEC No (EINECS or ELINCS) ‡	236-152-1
FAO Specification ‡ (including year of publication)	There is no FAO specification.
Minimum purity of the active substance as manufactured ‡ (g/kg)	940 g/kg (see confidential information).
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula ‡	$C_8H_{19}O_2PS_2$
Molecular mass ‡	242.3
Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	<-70 °C (99.1%)
Boiling point (state purity) ‡	244.3 °C (99.1%) with decomposition
Temperature of decomposition	Starts at 244.3 °C

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

Appearance (state purity) ‡	Clear colourless liquid for both pure and technical (99.1% and 94.4%)
Relative density (state purity) ‡	1.096 (99.1%)
Surface tension	at 20 °C: 45.1 mN/m (90% solution in water – pure 99.1%) 45.9 mN/m (90% saturated solution in water (94.4%)
Vapour pressure (in Pa, state temperature) ‡	7.8×10^{-2} Pa at 20 °C (99.1%) 12.3×10^{-2} Pa at 25 °C (99.1%)
Henry's law constant (Pa m^3 mol^{-1}) ‡	1.35×10^{-2} Pa m^3 mol^{-1} at 25 °C
Solubility in water ‡ (g/L or mg/L, state temperature)	pH 4: 1.3 g/L at 30 °C pH unadjusted: 1.4 g/L at 30 °C pH 9: 1.3 g/L at 30 °C (all 99.1%)
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	acetone; acetonitrile; dichloromethane; ethyl acetate; *n*-hexane; methanol; *n*-octanol and toluene: all >500 g/L at room temperature
Partition co-efficient (log POW) ‡ (state pH and temperature)	log P_{OW} 2.99 determined experimentally, however ethoprophos is surface active (effect of pH not investigated) log Pow > 3.1 to 3.6 (two separate models)
Hydrolytic stability (DT_{50}) ‡ (state pH and temperature)	pH: 3 & 6 and 20 °C stable. At pH 9, DT_{50} was 39-44 days – metabolite formed was *O*-ethyl-*S*-propyl phosphorothioic acid (^{14}C-propyl)
	pH: 5 & 7 stable. At pH 9 DT_{50} was 83 days with 2 metabolites: ethanol and *S*,*S*-dipropyl phosphorodithioic acid (^{14}C-ethyl)
	pH: 4% 20ºC, DT_{50} >36 days (^{14}C-propyl)
Dissociation constant ‡	No ionisable groups. No dissociation
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	No absorbance >290nm
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	Stable in pH7 at 25 °C light intensity = 40 °N equinox.
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	Estimated to be 0 due to photostability
Flammability ‡	Flash point = 141 °C – Not flammable. (94.4%)
Explosive properties ‡	No sensitivity to flame or mechanical shock. (94.4%)

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

List of representative uses evaluated*

Crop and/or situation	Member State or Country	Product Name	F G or I	Pest or group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
					Type	Conc. of a.s.	method, kind	growth stage & season	number (range)	interval between applications (minimum)	kg a.s./hl min-max	water l/ha min-max	kg a.s./ha min-max		
(a)			(b)	(c)	(d-f)	(i)	(f-h)	(j)	(k)		(l)			(m)	
Potato	Northern Europe	Mocap, Sanimul	F	Soil nematodes and insects	GR	100 g/kg	Overall application followed by soil incorporation	Pre planting	1	-		-	7 - 11	80	Representative use Northern Europe Early and late potatoes [1]
Potato	Northern Europe		F	Soil nematodes and insects	GR	100 g/kg	Band / row application followed by soil incorporation[#]	Pre planting	1	-		-	4 - 6	80	Representative use Northern Europe Early and late potatoes [1]
Potato	Southern Europe	Mocap, Sanimul	F	Soil nematodes and insects	GR	100 g/kg	Overall application followed by soil incorporation	Pre planting	1	-		-	7 - 10	80	Representative use Southern Europe [1]

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

Crop and/or situation	Member State or Country	Product Name	F G or I	Pest or group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
					Type	Conc. of a.s.	method, kind	growth stage & season	number (range)	interval between applications (minimum)	kg a.s./hl min-max	water l/ha min-max	kg a.s./ha min-max		
(a)			(b)	(c)	(d-f)	(i)	(f-h)	(j)	(k)		(l)			(m)	
Potato	Southern Europe		F	Soil nematodes and insects	GR	100 g/kg	Band / row application followed by soil incorporation[#]	Pre planting	1	-		-	4 - 6	80	Representative use Southern Europe Early and late potatoes [1]

[#] Includes application of Mocap 10G as an 'in furrow application' at planting (full details on application methods for Mocap 10G are given in the DAR).
[1] The risk assessment has revealed a risk (exceedance of relevant threshold) in section 5.

Remarks:	*	For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).	(i)	g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).
	(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)		
	(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)		
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989	(k)	Indicate the minimum and maximum number of application possible under practical conditions of use
	(f)	All abbreviations used must be explained		
	(g)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(l)	The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
	(h)	Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated	(m)	PHI - minimum pre-harvest interval

‡ 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)	Samples dissolved in dichloromethane and ethoprophos determined by GC-FID
Impurities in technical as (principle of method)	Samples dissolved in dichloromethane and impurities determined by GC-FID
Plant protection product (principle of method)	Sample dissolved in acetone and filtered. Ethoprophos was determined by GC-FID

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Method AR 52-87 (Potato): Extraction with methanol, partitioned into hexane and filtered. Analysis of ethoprophos is by GC-FPD. LOQ = 0.01 mg/kg
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required as no MRLs have been set for products of animal origin.
Soil (principle of method and LOQ)	RP Method 172 (monitoring): Extraction with methanol, concentrated and partitioned into hexane. Analysis of ethoprophos is by GC-FPD. LOQ = 0.01 mg/kg. Method 00897 (revised confirmatory). Extraction with water/acetonitrile/acetic acid (500/500/1, v/v/v), filtered. Analysis of ethoprophos is by LC-MS/MS (quantitation *m/z* Q1 = 243.3, *m/z* Q3 = 131.1). LOQ =1.0 µg/kg.
Water (principle of method and LOQ)	Method RP 176 (monitoring surface, ground and drinking water). Extraction using C18 SPE, eluted with ethyl acetate, concentrated and partitioned into hexane. Analysis of ethoprophos is by GC-FPD. LOQ = 0.02µg/L. Method RP 176 (updated) Extraction by hexane. Analysis of ethoprophos is by GC-MS/MS (SIM with *m/z* 200, 158 & 139). LOQ = 0.1 µg/L.
Air (principle of method and LOQ)	Method AR-273-01. Extraction of XAD tubes with ethyl acetate. Analysis of ethoprophos is by GC-FPD. LOQ = 0.8µg/m^3 air without breakthrough.
Body fluids and tissues (principle of method and LOQ)	Method AR-272-01 (blood and urine). Extraction with methanol, concentrated and partitioned into hexane. Analysis of ethoprophos is by GC-FPD. LOQ = 0.01 mg/kg. Method AR-273-01 (muscle, fat, liver, eggs and

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

	milk). Extraction with methanol, concentrated and partitioned into hexane. Analysis of ethoprophos is by GC-MS/MS (quantitation *m/z* = 114, precursor *m/z* = 158). LOQ = 0.01 mg/kg.

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapidly and extensively absorbed: >80% based on comparison of excretion following oral and intravenous dosing. Maximum blood concentration within 1 hour.
Distribution ‡	Widely distributed: highest values in organs of excretion, fat, adrenals and thyroid
Potential for accumulation ‡	No evidence for accumulation.
Rate and extent of excretion ‡	Rapidly excreted: ~60% in urine, ~10% in faeces and ~15% in expired air within 48 hours. Biliary excretion estimated to be ~8%.
Metabolism in animals ‡	Complete metabolism. Dealkylation followed by hydroxylation and conjugation. Hydrolysis to CO_2.
Toxicologically significant compounds ‡ (animals, plants and environment)	O-ethyl-S-methyl-S-propyl-phosphorodithioate (SME) O-ethyl-O-methyl-S-propyl-phosphorothioate (OME) O-ethyl-S-propyl-phosphorothioate (EPPA / M1)

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	47 mg/kg bw	**T, R25**
Rat LD_{50} dermal ‡	226 mg/kg bw rabbit LD_{50} 7.9 mg/kg bw (males)	 **T^+, R27**
Rat LC_{50} inhalation ‡	0.123 mg/L (4 hour, nose-only)	**T^+, R26**
Skin irritation ‡	Not assessed due to high toxicity	
Eye irritation ‡	Not assessed due to high toxicity	
Skin sensitization ‡ (test method used and result)	Positive (M&K Maximisation)	**Xi, R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Inhibition of erythrocyte and brain cholinesterase activity.
Lowest relevant oral NOAEL / NOEL ‡	0.1 mg/kg bw/d: rat 28-day, rat 90-day Overall NOAEL 0.1 mg/kg bw/d in the dog
Lowest relevant dermal NOAEL / NOEL ‡	0.1 mg/kg bw/d: rabbit 21-day
Lowest relevant inhalation NOAEL / NOEL ‡	No data available

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

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	Evidence of mutagenicity and clastogenicity in vitro in the presence of metabolic activation at high concentrations associated with cytotoxicity. Non-reproducible evidence for clastogenicity (bone marrow) and germ cell mutagenicity (dominant lethal) in vivo. Not considered to be genotoxic in vivo on the balance of evidence.

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

Target/critical effect ‡	Inhibition of erythrocyte and brain cholinesterase activity.
Lowest relevant NOAEL / NOEL ‡	0.04 mg/kg bw/d; rat chronic study **Xn, R48/22**
Carcinogenicity ‡	Increased incidences of thyroid 'C' cell tumours in male rats at high dose levels, uterine polyps and tumours in female rats. Clear threshold and association with general toxicity. Limited relevance to man.

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Some evidence for reduced fertility and litter size in one study.
Lowest relevant reproductive NOAEL / NOEL ‡	Reproductive : 15.7 mg/kg bw/d; parental and offspring : 7.3 mg/kg bw/d
Developmental target / critical effect ‡	No evidence of teratogenicity or developmental toxicity at maternally toxic dose levels.
Lowest relevant developmental NOAEL / NOEL ‡	Rat, maternal: 1.6 mg/kg bw/d; rat, developmental: 16 mg/kg bw/d; rabbit, maternal: 0.125 mg/kg bw/d; rabbit, developmental: 2.0 mg/kg bw/d

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

.....	Behavioural effects consistent with cholinesterase inhibition; no evidence of neuropathology in the rat. Inhibition of NTE (up to 60%) but no behavioural or histopathological evidence of delayed neurotoxicity in the hen.

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

Other toxicological studies ‡ (Annex IIA, point 5.8)

Mechanistic study	Peak effect on cholinesterase inhibition seen at 2-6 hours following a single dose. Cholinesterase inhibition may not be rapidly reversible. NOAEL for adult rats and neonates 1.0 mg/kg bw.
Acute toxicity of metabolites	O-ethyl-S-propyl-phosphorothioate (EPPA / M1): LD_{50} 246 mg/kg bw (females) O-ethylphosphoric acid: LD_{50} > 2000 mg/kg bw SME (O-ethyl-S-methyl-S-phosphorodithioate): LD_{50} 41.0 mg/kg bw OME (O-ethyl-O-methyl-S-phosphorothioate): LD_{50} 19.2 mg/kg bw

Medical data ‡ (Annex IIA, point 5.9)

.....	No evidence of effects in manufacturing personnel.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.0004 mg/kg bw/d	2 year rat	100
AOEL ‡	0.001 mg/kg bw/d	Rat 28-day Dog studies	100
ARfD ‡ (acute reference dose)	0.01 mg/kg bw/d	Rat cholinesterase inhibition study	100

Dermal absorption (Annex IIIA, point 7.3)

Mocap 10G	10% default value

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

Acceptable exposure scenarios (including method of calculation)

Operator	The operator exposure (% AOEL) has been estimated on the basis of field studies: dosimetry study and biomonitoring.

Supply	PPE No RPE	PPE + RPE (APF 10)	PPE + RPE (APF 20)
15 kg boxes	442%	165%	150%
20 kg 'Surefill' containers	222%	79%	71%

Despite all mitigation measures required (closed cab, coverall, gloves, RPE, no hand-held equipment), the level of exposure is close to the AOEL. So the use of 'Surefill' containers might even not be sufficient to reduce the operator exposure below the AOEL.

Workers	Estimated exposure is 5% of the AOEL at about 20 meters from the treatment site.
Bystanders	Estimates of exposure are 14% and 5% of the AOEL for the child and adult, respectively

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T+; Very toxic
	R26 Very toxic by inhalation
	R27 Very toxic in contact with skin
	R25 Toxic if swallowed
	R43 May cause sensitisation by skin contact
	R48/22 Danger of serious damage to health by prolonged exposure if swallowed

‡ 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	Potato (R) Cabbage (L): supporting information Sweet corn (C): supporting information (soil application in all crops)
Rotational crops	Radish (R), spinach (L) and wheat (C)
Plant residue definition for monitoring	Ethoprophos
Plant residue definition for risk assessment	Sum of ethoprophos, OME, SME and EPPA expressed as ethoprophos
Conversion factor (monitoring to risk assessment)	Cannot be established on the basis of the current data

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

Animals covered	Not applicable (N/A)
Animal residue definition for monitoring	Not applicable (N/A)
Animal residue definition for risk assessment	Not applicable (N/A)
Conversion factor (monitoring to risk assessment)	Not applicable (N/A)
Metabolism in rat and ruminant similar (yes/no)	Not applicable (N/A)
Fat soluble residue: (yes/no)	Not applicable (N/A)

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

.....	The metabolism in succeeding crops was investigated using 1-ethyl-14C-ethoprophos on radish, spinach and wheat planted 30, 120 and 365 days after application at approximately N rate. TRR were up to 47.39 mg/kg in wheat straw with major metabolites being ethyl phosphate and O-ethyl-S-propyl phosphorothioate. Parent accounted for up to 0.33 mg/kg in radish, 0.07 mg/kg in spinach, <0.05 mg/kg in grain and 0.6 mg/kg in straw. Overall, these studies suggest that metabolism in succeeding crops is similar to that seen in primary crops. Further information is however needed on the nature of the extractable residues in rotational crops.

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

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

.....	Residues of ethoprophos in frozen samples of sweet potato, tobacco, broccoli and cabbage are stable for up to 9 months, with stability extended to 18 months for green tobacco. The stability shown for 9 months is sufficient to cover the storage of harvested samples in the residue trials.

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: no	Poultry: no	Pig: no
Muscle	No study required		
Liver			
Kidney			
Fat			
Milk			
Eggs			

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

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

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP mg ethoprophos/kg (a)	Recommendation/comments	MRL	STMR (b)
Potato	N S	8 x < 0.005, 0.005, 0.0085, 0.01,0.011 4 x < 0.01, 0.011, 0.019	All trials with overall application. Highest residue is 0.019 from Southern trials	0.02	0.01

(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	0.0004 mg/kg bw/day
TMDI (European Diet) (% ADI)	0.00007625 mg/kg bw/day (19.1%) Assessment based on currently available trials with only ethoprophos analysed. New trials and consumer risk assessments are required according to residue definition for risk assessment.
NEDI (% ADI)	Total UK NEDIs for all consumers are within the ADI of 0.0004 mg/kg bw/day. The critical consumers are infants with intakes of 0.000111 mg/kg bw/day (28% of the ADI). Assessment based on currently available trials with only ethoprophos analysed. New trials and consumer risk assessments are required according to residue definition for risk assessment.
Factors included in NEDI	STMR
ARfD	0.01 mg/kg bw/day
Acute exposure (% ARfD)	The NESTIs for all 10 UK consumer groups were below the ARfD. The critical consumers for the short term exposure estimates are infants with intakes up to 29.2% of the ARfD for potatoes (all). Assessment based on currently available trials with only ethoprophos analysed. New trials and consumer risk assessments are required according to residue definition for risk assessment.

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Potato/potato products	No information provided due to the very low residue levels in raw potatoes		

* 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)

Potato	0.02 mg/kg

‡ 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 ‡	Propyl label 56 – 60 %AR (90 d) Ethyl label 30 % AR (112 d)
Non-extractable residues after 100 days ‡	Propyl label 11 – 14 % AR (90 d) Ethyl label 10 % AR (112 d)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	None major (> 10%AR)

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

Anaerobic degradation ‡	Mineralisation 3% after 28 days (study end) Non-extractable residues 8% after 28 days (study end) No major metabolites (> 10%AR)
Soil photolysis ‡	Ethoprophos is stable to photolysis in soil

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

Method of calculation	Simple first order kinetics, linear regression or non linear curve fitting minimising least squares, some field studies manual plotting on log graph paper.
Laboratory studies ‡ (range or median, with n value, with r^2 value)	DT_{50lab} ‡ (20°C, aerobic): 10-25 days (n=3, r^2=0.91-0.99) (22°C, aerobic): ‡23&27 days (n=2, r^2=0.99&1.0) (25°C, aerobic): ‡113 days (n=1, r^2=0.96) For FOCUS gw modelling – (aerobic, first order kinetics):median of DT_{50lab} 22.8days (normalised to –10kPa, 20°C with Q10 of 2.2)
	DT_{90lab} ‡ (20°C, aerobic): 34-85 days (n=3, r^2=0.91-0.99) (22°C, aerobic): 78&89 days (n=2, r^2=0.99-1.0) (25°C, aerobic): 367 days (n=1, r^2=0.96 extrapolated beyond end of study)
	DT_{50lab} (10°C, aerobic): Measured 36&54 days (n=2, r^2=0.98&0.81)‡
	DT_{50lab} (25°C, anaerobic): ‡ 110.5 days (n=1, r^2=1 but based on only 3 data points)
	degradation in the saturated zone ‡: no data none required

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

Field studies ‡ (state location, range or median with n value)	**US studies** (Columbus, New Jersey; York, Nebraska; Geneseo, Illinois; Fortescue, Missouri; Lucama, North Carolina; Ashville, Florida; Ephrata, Washington; Clayton, North Carolina; San Juan Bautista, California) high temperatures, only representative of southern and central Europe DT_{50f}: 4 – 25 days (n = 5, graphical plotting) DT_{50f}: 12 – 42 days (n = 5, linear regression, r^2 = 0.71 – 0.97) **NL studies** (soil columns taken from fields in Renkum) Linear regression only 4 sampling times statistical fit not reported. $DT_{50}f$: 28 &28 days (n = 2, pH7.2&7.3) $DT_{50}f$: 87 &87 days (n = 2, pH4.5&4.6) All sites excluding very low pH soils (4.5 and 4.6) $DT_{50}f$: 4-42 days (n=12, mean=16.5days) **US studies** (Columbus, New Jersey; York, Nebraska; Geneseo, Illinois; Fortescue, Missouri; Lucama, North Carolina; Ashville, Florida; Ephrata, Washington; Clayton, North Carolina; San Juan Bautista, California) DT_{90f}: 13 – 83 days (n = 5, graphical plotting) DT_{90f}: 40 – 140 days (n = 5, linear regression, r^2 = 0.71 – 0.97) **NL studies** (soil columns taken from fields in Renkum) Linear regression only 4 sampling times statistical fit not reported. $DT_{90}f$: 93 &93 days (n = 2, pH7.2&7.3) $DT_{90}f$: 290 &290 days (n = 2, pH4.5&4.6) All sites excluding very low pH soils (4.5 and 4.6) $DT_{90}f$: 13-140 days (n=12)
Soil accumulation and plateau concentration ‡	No accumulation anticipated due to the rapid degradation

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡	K_f 0.56 – 5.60mL/g / K_{foc} 38 – 186 mL/g (mean K_{foc} 111mL/g, 1/n=0.82-0.96, n = 11)
K_d ‡	not calculated, K_f taken from Freundlich Isotherms
pH dependence ‡ (yes / no) (if yes type of dependence)	no For FOCUS gw modelling- Kfoc: mean 111mL/g, 1/n=0.89.

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

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

Column leaching ‡	Dutch guideline section G.1.2 Precipitation 200mm over 4 days 1.9 – 2.2 % AR in the leachates, n=2. Leachate radioactivity not characterised.
Aged residues leaching ‡	Dutch guideline section G.1.2 Aged for 1 half life. Precipitation 200mm over 4 days 1.0 – 5.5 % AR in the leachates, n=2. Leachate radioactivity not characterised.
Lysimeter/ field leaching studies ‡	<u>BBA guideline Part IV 4-3 (1989) Lysimeter study</u> UK Ongar Essex, loamy sand monoliths 1.08m depth 1 granular applic. 9.44kg a.s./ha (0.86N) incorporated to 10cm per year before planting potatoes (May) in the first year only, cereals subsequently planted. Over 2 years total precipitation +irrigation was 1882mm Leachate volume was 645mm Annual average concentrations ethoprophos in leachate: 0.143 µg/L 4.02 µg/L (first year) 0.024 µg/L 0.037 µg/L (second year) <u>Confined field leaching</u> The Netherlands Vredepeel, humic sand soil 800mm rainfall over ca. 18 month study duration. 1 spray application 3.35kg a.s./ha (0.3N) on 22 November w wheat and then mustard grown. No ethoprophos was found in ground water samples at any level and any sampling time > LOQ 0.1µg/L shallowest samples of aquifer water taken at 1.0-1.2m.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	DT_{50} (d): 42 days, 1st order kinetics longest field DT_{50} from topsoil with pH>4.7.

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

Application rate	11 kg a.s./ha in single application onto bare soil soil incorporation depth 15 cm

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	4.89	4.89	not relevant	not relevant
Short term 24h	4.81	4.85	not relevant	not relevant
2d	4.73	4.81		
4d	4.58	4.73		
Long term 7d	4.36	4.62	not relevant	not relevant
14d	3.88	4.36		
28d	3.08	3.91		
50d	2.14	3.33		
100d	0.94	2.39		

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡ (state pH and temperature)	pH 4: > 365 days (25°C) pH 7: > 365 days (25°C) pH 9: 83 days (25°C)
Photolytic degradation of active substance and relevant metabolites ‡	The active substance is stable to photolysis
Readily biodegradable (yes/no)	No
Degradation in water/sediment - DT_{50} water ‡	40 / 20 days (graphical estimation) (n = 2) 25 / 14 days (linear regression, √1st order r^2=0.97/0.98)
- DT_{90} water ‡	280/150 days (√1st order extrapolated beyond study end)
- DT_{50} whole system ‡	71 / 95 days (linear regression, first order, r2=1/0.98)
- DT_{90} whole system ‡	236/316 days (extrapolated beyond study end)
Mineralization	21.6/22.0 %AR at study end 100 days
Non-extractable residues	10.2/11.6 %AR at study end 100 days
Distribution in water / sediment systems (active substance) ‡	Mainly in water In sediment: maximum of 28 % AR / 44% AR (low/high organic carbon) at 14 and 59 days, respectively
Distribution in water / sediment systems (metabolites) ‡	No major (>10%AR) metabolites present in either phase.

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

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

Parent

Method of calculation	Daily concentrations at 1m depth predicted by FOCUSPELMO3.3.2 ÷ 10 at the Hamburg, Okehampton and Piacenza groundwater scenarios
Application rate	11 kg a.s./ha Hamburg & Okehampton, 10 kg a.s./ha Piacenza
Main routes of entry	Subsurface flow (product is an incorporated granule) from soil water at 1m depth.

Note in many potato growing situations there will be no surface water exposure.

PEC$_{(sw)}$ (µg/L)	Single application Actual	Single application 21 d Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	Hamburg 0.078 Okehampton 0.0064 Piacenza 0.87		Not relevant	Not relevant
21d		Hamburg 0.076 Okehampton 0.0061 Piacenza 0.86		

PEC (sediment)

Parent

Method of calculation	As above for PECsurface water assuming worst case 39% partitioning to sediment at 14 days observed in sediment water study, 30cm overlying water depth, even distribution in 5cm sediment and sediment bulk density 1.3g/cm^3
Application rate	As above for PECsurface water

PEC$_{(sed)}$ (µg / kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	Hamburg 0.14 Okehampton 0.0.01 Piacenza 1.56		Not relevant	Not relevant

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

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Modelling using FOCUSPELMO 3.3.2 with pertinent FOCUSgw scenarios, according to FOCUS Guidance. Crop potatoes therefore all scenarios. Median parent DT_{50} 22.8 days (normalised 10kPa and 20°C with Q10 2.2). Mean K_{foc} 111mL/g 1/n 0.89
Application rate	10 kg a.s /ha S Europe, 11 kg a.s./ha N Europe scenarios incorporated to 15cm. Pre planting of tubers

$PEC_{(gw)}$

Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Annual average concentrations or triannual average concentrations (80th percentile period) according to FOCUS guidance <0.001-1.84 µg/L See detailed results in table below

PEC(gw) - FOCUS modelling results

Model /Crop	Scenario	Parent annual applications (µg/L)	Parent applications 1 year in 3 (µg/L)
PELMO 3.3.2 / Potatoes	Chateaudun	0.002	0.001
	Hamburg	0.16	0.025
	Jokionen	<0.001	<0.001
	Kremsmunster	0.006	0.002
	Okehampton	0.046	0.012
	Piacenza	1.84	0.733
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	<0.001

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

Direct photolysis in air ‡	Negligible degradation of ethoprophos measured in EPA study 30°C
Quantum yield of direct phototransformation	The quantum yield of direct phototransformation is zero

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

Photochemical oxidative degradation in air ‡	Standard Atkinson calculation: DT_{50} = 0.155 days (scenario with 1.5×10^6 OH radicals per cm^3 and a time frame of 12 hours/day)
Volatilization ‡	From plant surfaces: ‡ not applicable for soil incorporated granule; from soil: ‡ not measured by soil incorporation will reduce the potential to volatilise.

PEC (air)

Method of calculation	Expert judgement based on vapour pressure, Henrys law constant and the method of application (soil incorporation)

$PEC_{(a)}$

Maximum concentration	negligible

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	No major (> 10%AR) metabolites were formed in any environmental compartment. Parent ethoprophos should therefore be the only component of the residue definition.

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

Soil (indicate location and type of study)	No data available
Surface water (indicate location and type of study)	Greece (surface and ground water monitoring) Bracciano lake basin, ITA (surface and ground water monitoring)
Ground water (indicate location and type of study)	Ter Apel, fen district, NL (ground water monitoring)
Air (indicate location and type of study)	No data available

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Possibly a candidate for R53: May cause long-term adverse effects 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

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

Acute toxicity to mammals ‡	LD_{50} 32.9 mg a.s./kg bw (based on combined male/female rat formulation study) LD_{50} 47 mg a.s.kg bw (based on active substance study with rat (combined sexes) LD_50 31 mg a.s.kg (active substance study mouse)
Long-term toxicity to mammals	2 generation repro. NOEC 30 ppm (equivalent to NOEL of 1.3 mg/kg bw/day rat)
Acute toxicity to birds ‡	LD_{50} 6.04 mg a.s./kg bw (*Colinus. virginianus*) based on a.s. study HD_{05} 3.47 mg a.s./kg (calculated using LD_{50} values for 9 species)
Dietary toxicity to birds ‡	LC_{50} 6.51 mg a.s./kg bw/d (29 ppm) *(C. virginianus*)
Reproductive toxicity to birds ‡	NOEC <0.6 mg a.s./kg bw/d (<7.5 ppm) (*C. virginianus*) (22% reduction in egg laying recorded at 7.5 ppm (lowest concentration tested) in 21 week study)

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

The risk posed by the use of soil incorporated granules represents a non-standard scenario for which there are no agreed assessment procedures under EC Dir 91/414. Birds are known to ingest grit particles from soil. To address the deliberate ingestion of 'Mocap 10G' granules by birds the Notifier has proposed a novel approach based on the scheme of Luttik (2003). This relies upon the view that birds are unlikely to deliberately ingest particles of a size less than 0.5 mm. The size distribution overlap of 'Mocap 10G' granules and soil particles has been used to assess Relative Granule Exposure. This has been compared with estimates of Daily Grit Intake for birds. Field efficiency incorporation studies have been conducted with the same soil types to support the opinion that high levels of incorporation are achievable. The Estimated Theoretical Exposure has been compared to the lowest available LD_{50} value for a standard test species (bobwhite quail) and, in a refined assessment to a calculated HD05 value. A standard uncertainty factor of 10 has been applied to the LD_{50} value, the Notifier proposes that a factor of 5 should be applied to the HD05 value.

Mammals are not known to have any specific requirements for grit but may take surface granules indirectly with other food items.

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

Key factors in the risk assessment for deliberate ingestion of surface granules of 'Mocap 10G'

Factor	Comment
Granule size	'Mocap 10 G' is a 'fine' granule: 7.7% >0.425 mm, 90.3% ≥ 0.425 to <0.710 mm, 1.8% ≥ 0.71mm (by weight Uceda *et al* 2000) % of 'Mocap 10G' carrier 'Sepiolite 30/60' in size classes: 0.25– 0.50 mm 59.9%, 0.50 -0.75 mm 40.1% (by size Van der Poll & de Snoo, 2004)
Particle size taken deliberately by birds	>0.5 – 2.5 mm (de Leuuw *et al* 1995) Based on gizzard analysis of 9 small granivorous species this data set is the most comprehensive published data available.
Average weight of single 'Mocap 10G' granule	0.076mg
Amount of ethoprophos on single granule	0.0076 mg
Incorporation efficiencies of 'Mocap 10G' in 3 UK soil types under field conditions	Overall 10 centile incorporation across 3 soil types and 4 application methods 98.99% efficiency (Rea 2004)
Predicted number of 'Mocap 10G' granules required for median LD_{50} and HD_{05}dose (birds only)	1.26 granules/small bird (based on 15 g linnet, *C virginianus* LD_{50} value 6.04 mg a.s./kg, max proposed dose/ha and including a standard tier 1 uncertainty factor (10). 1.36 granules (based on 15 g linnet, HD_{05} value of 3.47 mg a.s./kg bw and including the Notifiers proposed uncertainty factor of 5) . 4.1 granules/small mammal (based on 10 g shrew, LD_{50} value of 32.9 mg a.s./kg bw, max proposed dose/ha and including a standard tier 1 uncertainty factor (10).
Predicted number of 'Mocap 10G' granules remaining on surface assuming 99% incorporation efficiency	1438 per m2 (based on max application rate 110 kg product/ha and mean granule weight of 0.0765 mg). Based on the size distribution overlap study of Van der Poll & De Snoo (2004), 40.1 % of these granules will be of a size >0.5 mm and hence potentially deliberately taken as grit. Adjusted for proportion of 'Mocap 10G' granules between 0.5 and 2.5 mm, this is equivalent to 577 granules/m2.
Estimated TERs	Birds: Acute TER values range from 3.7 to 6.3 based on an HD05 value of 3.477 mg/kg bw, 99% incorporation, PT 0.15 (poorly supported)

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

Higher tier avian effects studies	33% mortality (*C virginianus*) when broadcast at 6.72 kg a.s./ha without incorporation in pen study. No mortalities in adult *C virginianus* following exposure at surface density equivalent to 1.6 LD_{50}'s/bird in a palatability study. 3/16 birds poisoned (1 fatally) following exposure at a surface density equivalent to 11.5 LD_{50}'s/bird where no additional grit was provided. Relevance to smaller granivorous species not established 10% mortality of Canary birds exposed to 'Mocap 10G' at a surface density representing a 97.5% incorporation efficiency in a pen study (Barfknecht, 2004) No mortality in house sparrows exposed to 'Mocap 20G' at a surface density representing 99% incorporation efficiency in a pen study (Brewer & Miller, 2002) Field surveys indicate absence of impacts but all lack any validation of the efficiency of the carcass searching methodologies.
Higher tier mammalian exposure studies	A single UK field survey indicated absence of impacts but lacked validation of the efficiency of the carcass searching methodology.
Recommendation	Birds; High acute risk to from surface granules. Short term risk via this route of exposure will be covered by demonstration of acceptable acute risk. Long term exposure via this route highly unlikely since dissipation from granule expected to be rapid. Notifier proposes to conduct further field monitoring to demonstrate an acceptable risk. Mammals. Risk considered to be acceptable, no requirement for grit and granule of no nutritive value (ingestion of residues on contaminated food items more important route of exposure).

Risk from consumption of ethoprophos residues in contaminated soil.

'Mocap 10G' is 'fine' granule with approximately 60% of granules being <0.5 mm. Assessment of the risk from these granules which may be accidentally ingested with soil has been provided.

Birds: Based on PECmax (4.89 mg a.s./kg) and an HD_{05} value of 3.477 mg a.s./kg bw/d the amount of soil required as proportion of bodyweight for TERs of 5, 3 and 1 respectively are calculated to be 14%, 24% and 71% respectively. Relative to the gizzard size and expressed as volumes such quantities of soil are considered unlikely to be consumed.

Mammals: LD_{50} value higher than for birds therefore risk no greater than for birds

Risk from consumption of contaminated earthworms

Birds and mammals are both at risk from consumption of contaminated earthworms, a SANCO 4145 TER based approach has been presented for this:

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

Risk to birds and mammals from the ingestion of earthworms contaminated with ethoprophos

Species (FIR/bw)	Residues in earthworm (mg a.s./kg)	ETE Daily intake (mg a.s./kg bw)	Acute toxicity (mg a.s./kg bw)	Short-term toxicity LC_{50} (DDD mg a.s./kg bw/d)	Long-term toxicity NOEL (mg a.s./kg bw/d)	TERa	TERst	TERlt
medium sized bird[1] (1.13)	2.51[2]	0.57[4] (acute and short term) 0.092[5,6] (long term)	HD_{05} 3.477[3]	6.51	Could not be determined [7]	6.1	11.4	6.5
Small mammal[8] (1.40)	2.51[2]	0.88[9] (acute) 1.14[10] (long term)	LD_{50} 32.9[11]	NA	1.3	37	NA	1.14

[1] 100 g blackbird (*Turdus merula*)
[2] maximum residue recorded in field study (used for acute, short term and long term ETE values)
[3] calculated using multi-species LD_{50} values
[4] assuming a PT value of 0.2. This value is poorly supported.
[5] assuming a PT value of 0.1. This value is poorly supported
[6] based on a 21-day ftwa of 0.325 calculated from measured residues in field study
[7] NOEL could not be determined due to reduction in egg production in *C virginianus* study at 7.5 ppm (lowest concentration tested) which is equivalent to DDD of 0.6 mg a.s./kg bw/d
[8] 10 g common shrew (*Sorex araneus*)
[9] assuming a PT value of 0.25. This value is poorly supported
[10] based on a 21-day 0.325 calculated from measured declines in residues studies, but with PTreset to 1.
[11] based on rat formulation study

Long term risk to birds and mammals from consumption of contaminated earthworms requires further consideration..

Risk from consumption of contaminated vegetation

Vegetation germinating in potato fields treated with 'Mocap 10G' represents a possible route of exposure. Given the likelihood that the density of any such vegetative cover will be low this route of exposure is considered to be less important than the other routes. The following section is therefore presented primarily for illustrative purposes only.

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

Risk to birds and mammals from the ingestion of herbivorous material contaminated with ethoprophos

Species (FIR/bw)	Residues in young cereals (mg a.s./kg) ‡	ETE Daily intake (mg a.s./kg bw)	Acute toxicity (mg a.s./kg bw)	Short-term toxicity LC_{50} (DDD mg a.s./kg bw/d)	Long-term toxicity NOEL (mg a.s./kg bw/d)	TERa	TERst	TERlt
medium sized bird[1] (0.33)	2.70[2] (acute) 1.13[5] (short term and long term)	0.29[4] (acute) 1.19[6] (short term) 0.032[7] (long term)	HD_{05} 3.477[3]	6.51	Could not be determined [7]	12	13.1	18.7
large herbivorous mammal[8] (0.28)	2.70[2] (acute) 1.13[5] (short term)	0.25[9] (acute) 0.08[10] (long term)	LD_{50} 32.9[b]	NA	1.3	132	NA	15.8

[1] wood pigeon (*Columba palumbus*) 480g
[2] maximum residue recorded in field study
[3] calculated using multi-species LD_{50} values
[4] assuming a PT value of 0.33. This value is poorly supported.
[5] geometric mean of the maximum recorded concentrations from 3 plant residue trials
[6] assumes a FIR/bw of 0.44 (generic SANCO bird).
[7] based on a 21-day ftwa 0.262 calculated from measured declines in residues studies
[8] European hare (*Lepus europaeus*) 3000 g
[9] assumes PT of 0.33. This is poorly supported.
[10] based on a 21-day ftwa of 0.262 but with PT reset to 1

It is considered that risk management (use of direct placement machinery and high levels of granular incorporation) is essential to reduce potential risk to birds and mammals.

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Laboratory tests ‡				
Fish (*Lepomis macrochirus*) #	Active substance	96 h	OECD 203 LC_{50}	0.32
Fish (*Oncorhynchus mykiss*) #	Active substance	21 d	OECD 204 NOEC	0.064
Aquatic invertebrates (*Daphnia magna*) #	Active substance	48 h	OECD 202 EC_{50}	0.20

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Aquatic algae (*Pseudokirchneriella subcapitatum*) #	Active substance	5 days	OECD 201 EbC50	2.4
Aquatic invertebrates (*Daphnia magna*) #	Active substance	21 day	OECD 202 NOEC	0.002
Sediment dwellers (*Chironomus riparius*) #	Active substance			No data presented

based on measured concentrations. All test conducted in accordance with GLP

No reliable formulation toxicity studies were presented for 'Mocap 10G'. ECCO 69 (fosthiazate) has previously agreed that inert carriers are unlikely to increase toxicity above that of the active substance. As direct exposure to granules is expected to be minimal from the proposed application machinery, no risk assessment is necessary. In the absence of any significant direct exposure formulation studies are also not considered necessary.

Metabolites

No toxicity data presented. Sediment/water and soil metabolism studies indicate that no metabolites >10% AR are likely to be produced.

Microcosm or mesocosm tests
None submitted

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

In line with the decision taken for fosthiazate, it is considered that application restricted to direct placement machinery will result in minimal risk of contamination of surface water by "drift" of granules. Application via other granule applicators may result in contamination of surface water via "drift". There are no reliable data to estimate the extent of "drift" from such machinery. Therefore, Member States should consider the potential risk to aquatic life if direct placement machinery is not used.

A potential route of exposure via sub-surface flow has been identified. The risk to aquatic life from this route of exposure for ethoprophos is given in the following table:

Acute TERs resulting from sub-surface flow exposure in the three worst case FOCUS chromatographic leaching scenarios.

Species (LC/EC_{50})/FOCUS scenario (PECmax sub-surface flow	Hamburg (0.078 µg a.s./L)	Okehampton (0.0064 µg.a.s./L)	Piacenza (0.87 µg.a.s./L)
Fish (320 µg a.s./L)	4102	50000	368
Daphnia (200 µg a.s./L)	2564	31250	230
Algae (2400 µg a.s./L)	30769	375000	2758

Thus, the acute risk to fish, aquatic invertebrates and aquatic plants from this potential route of exposure is acceptable (TERs > respective Annex VI triggers) for the three worst case exposure scenarios. No sediment-dwelling toxicity data available. Sediment/water studies indicate potential for partitioning of ethoprophos to

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

sediment (max. 39% AR). Those MS where sub-surface flow is considered to represent a significant route of exposure should ensure that the risk to sediment-dwelling aquatic organisms is satisfactorily addressed.

Potential chronic TERs resulting from sub-surface flow exposure in the three worst case FOCUS chromatographic leaching scenarios.

Species (NOEC)/FOCUS scenario (PECmax sub-surface flow	Hamburg (0.078 µg a.s./L)	Okehampton (0.0064 µg.a.s./L)	Piacenza (0.87 µg.a.s./L)
Fish (64 µg a.s./L)	820	10000	73.5
Daphnia (2.3 µg a.s./L)	29.5	359	**2.6**

Those MS where sub-surface flow is considered to represent a significant route of exposure should ensure that the chronic risk to aquatic invertebrates is satisfactorily addressed.

Bioconcentration

log Pow 2.99 (pH not reported)

Bioconcentration factor (BCF) ‡	Exposure concentration 1.5 µg a.s./L used in studies 210x, whole fish
Annex VI Trigger: for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	50% depuration 8-12 days 90% not given
Level of residues (%) in organisms after the 14 day depuration phase	63%

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

Acute oral toxicity ‡	No data presented
Acute contact toxicity ‡	LD_{50} 5.56 µg a.s./bee*

* Methodology not described

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
11000 g a.s./ha		Contact	QHC 1978*	50
11000 g a.s./ha		Oral	NA	50

* For illustrative purposes only.

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

Field or semi-field tests None submitted.

Exposure of bees expected to be low due to formulation type, pre-planting timing, method of application and low systemicity.

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

Species	Stage	Test Substance	Dose (kg a.s./ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests – inert substrate						
Poecilus cupreus	Adult	Mocap 20G[A]	7 kg a.s./ha	Mortality	100%	30%
Aleochara bileneata	Adult	Mocap 20G[A]	10 kg a.s./ha	Mortality	100%	30%
Laboratory tests – extended (natural substrate)						
Aleochara bileneata	Adult	Mocap 10G[B]	11 kg a.s./ha (calculated PEC 7.4 mg a.s./kg equivalent to 1.5 times max PEC)	Parasitisation	99.9% reduction compared to untreated control after exposure to 28-day old aged residues. 100% reduction compared to untreated control after exposure to 86 day old aged residues.	30%

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

Species	Stage	Test Substance	Dose (kg a.s./ha)	Endpoint	Effect	Annex VI Trigger
Poecilus cupreus	Adult	Mocap 10G[B]	11 kg a.s./ha (calculated soil PEC 7.3 mg a.s./kg equivalent to 1.5 times max. PEC)	Mortality, food intake	56.7% mortality after exposure to 30 day old aged residues, 0% mortalilty after exposure to 59 day old aged residues. 53.8% reduction in food consumption after exposure to 30 day old aged residues. No reduction in food consumption after exposure to 59 days old aged residues.	30%

[A] Test substance mixed into sand
[B] Test substance mixed into natural soil

Field or semi-field tests

Mocap 10G broadcast at 11 kg a.s./ha onto bare soil in arable field, incorporation to 10-15 cm. Adult *Aleochara bileneata* beetles exposed to a range of aged residues in lab. (Drexler 2002)

Mortality after 7 days:

6 days old residues: Control: 0%

'Mocap 10G': 100%

Reference: 26.7%.

Reduction in reproduction compared to control:

13 weeks old residues:

Control: 640 adults emerged

'Mocap 10G': 1 emerged (99.9% compared to control);

23 weeks old residues:

Control: 619 adults emerged

'Mocap 10G': 189 emerged (69.5% compared to control);

10.5 months old residues:

Control: 635 adults emerged

'Mocap 10G': 586 emerged (7.7% compared to control)

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

Extended lab studies using aged residues indicate potential for recolonisation of sensitive species. Infrequent use pattern arising from normal potatoes crop rotation combined with DT_{90} (max 140 days) indicate that there should not be any significant accumulation of ethoprophos residues. No long term impact on relevant species is expected.

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

Acute toxicity ethoprophos‡	No a.s. studies presented
Acute toxicity formulated product [1]	LC_{50} 14 day - 39.6 mg/kg dry soil (based on Mocap 10G)* LC_{50} 14 day – 46.4 mg/kg dry soil (based on Mocap 20G)*
Reproductive toxicity [2]	56-day NOEC < 8.3 mg Mocap 20G/kg (equivalent to <1.67 mg a.s./kg)
Field tests [3]	Mocap 20G applied at 55 kg/ha (equivalent to 11 kg a.s./ha) 2 days before potatoes were planted. Short term reduction (1 month after treatment) in abundance and biomass in Mocap treated plots. Recovery apparent by autumn and following spring.

[1] OECD 207 and GLP
[2] BBA Guideline VI 2-2 and to GLP
[3] BBA Guideline VI 2-3 and to GLP

* estimated value below the lowest concentration tested (57.9 mg a.s./kg soil).

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

Application rate (kg as/ha)	Time-scale	TER[1]	Annex VI Trigger
11 kg a.s./ha	short term (acute)	**4.05**[A]	10
11 kg a.s./ha	long term (chronic)	**<0.17**[B]	5

[1] Adjusted to take into account the log pow > 2.
[A] Using 14-day LC_{50} 39.6 mg a.s./kg and the initial worst case soil PEC of 4.89 mg a.s./kg soil (max. application rate 11.0 kg a.s./ha incorporated to a depth of 15 cm)
[B] Using NOEC from 56-day study (<1.67 mg a.s./kg) and initial worst case soil PEC of 4.89 mg a.s./kg soil (max. application rate 11.0 kg a.s./ha incorporated to a depth of 15 cm)
Field study (Luhrs 2001) demonstrated absence of lasting impacts on a range of epilobus and tanylobus species as a rate equivalent to the max. recommended dose.

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

Nitrogen mineralization ‡	<25% effect after 44 days at up to 33.33 mg a.s./kg [A]
Carbon mineralization ‡	<25% effect after 44 days at up to 33.33 mg a.s./kg [A]

[A] Initial worst case soil PEC 4.89 mg a.s./kg soil

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N; Dangerous for the environment R50: Very toxic to aquatic organisms. R53: May cause long-term adverse effects in the aquatic environment S60: This material and its container must be disposed of as hazardous waste S61: Avoid release to the environment

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

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

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

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