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

phosalone

finalised: 13 January 2006

(version of 24 July 2007 with a corrected structural formula)

SUMMARY

Phosalone 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.

Austria being the designated rapporteur Member State submitted the DAR on phosalone in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 7 May 2004. Following a quality check on the DAR, the peer review was initiated on 6 July 2004 by dispatching the DAR for consultation of the Member States and the sole applicant Cheminova A/S. 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 in December 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 – May 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 29 November 2005 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 as proposed by the applicant which comprises foliar spraying to control chewing and sucking insects in pome fruit (apples, pears) at application rate up to 900 g per hectare. Phosalone can be used as insecticide and acaricide. It should be noted that only the use as insecticide was supported for the EU review programme.
The representative formulated product for the evaluation was "Zolone" (Rubitox; "AE F016629 00 EC A1xx"), an emulsifiable concentrate (EC), registered under different trade names in Europe.

[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. Residues in food of plant origin can be determined with a multi-method (the German S19 method has been validated). For the other matrices only single methods are available to determine residues of phosalone.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least limited quality control measurements of the plant protection product are possible.

Phosalone was found to have a very high acute toxicity when tested by the oral route, and is harmful after acute dermal and inhalative application. It is minimally irritating to skin and eyes and has sensitising properties. The classification proposed is: T, R 25 "Toxic if swallowed"; Xn, R 20/21 "Harmful by inhalation and in contact with skin"; Xi, R 43 "May cause sensitization by skin contact".
In subchronic and chronic toxicity tests, the main effect identified was cholinesterase inhibition. Data for phosalone do not support evidence of genotoxic, carcinogenic and teratogenic effects.
The Acceptable Daily Intake (ADI) and Acceptable Operator Exposure Level (AOEL) are 0.01 mg/kg bw/day and the Acute Reference Dose (ARfD) is 0.1 mg/kg bw/day, with a safety factor of 100. The estimated operator exposure according to the German model is below the AOEL if personal protective equipment is used.

The metabolism of phosalone has been investigated in fruits. The metabolism is rather limited and all metabolites formed were found at low levels. Phosalone is the dominant compound of the residue and the residue definition for monitoring is proposed to be phosalone only. One metabolite, oxophosalone, anticipated to be at least as toxic as the parent compound, is included in the residue definition for risk assessment. This metabolite should be toxicologically characterized.
Supervised residue trials in apples and pears were submitted, allowing a MRL proposal of 2 mg/kg for pome fruits. The effects of processing on the nature and the level of residues were investigated. Although studies in buffer solution demonstrated an extensive degradation under conditions simulating baking/brewing/boiling and sterilisation, phosalone seems to be stable under practical conditions of production of apple juice and puree. The reasons for this have not been fully elucidated. The transfer factors to apple juice and puree are very low, with residues essentially left in the pomace and peel fractions. One degradation product observed after processing in buffer solution needs to be investigated for its toxicological relevance as it was not identified in the rat metabolism (2-amino-7-chloro-3H-phenoxazin-3-one).
As the intended uses are restricted to pome fruits, studies on succeeding or rotational crops are not required.
Livestock can be exposed to residues of phosalone through consumption of pomace. Metabolism studies in lactating goat indicated that phosalone is not found in animal tissues. Only metabolites could be identified. The information obtained from the metabolism study in livestock is not sufficient to propose a residue definition and further information is needed on the identification of major residues in animal matrices. From the data submitted it may be expected that some metabolites may be present at measurable levels in animal tissues.

The consumer risk assessment was carried out taking into account chronic and acute exposures to phosalone only. The potential contribution of oxophosalone to the toxicological burden as well as of residues present in animal commodities is not known at this stage. Therefore, no robust conclusions can be drawn. Considering phosalone only, the acute and chronic exposure assessments, made according to current guidelines, give results below the ADI but may exceed in some cases the ARfD. However, the level of the proposed MRL in pome fruits, which is significantly lower than the level considered in exposure assessments, causes concern in terms of consumer safety. The acute exposure of toddlers may lead to higher exceedance of the ARfD for samples in compliance with the proposed MRL but with high unit to unit variability of residues.

Under aerobic conditions phosalone is rapidly metabolised in soil, initially to many minor metabolites, and ultimately to CO_2 and soil bound residues. The extensive formation of soil bound residues is rapid and is due in part to the formation of metabolites containing functional groups which are rapidly and tightly bound to organic matter in soil. Under anaerobic conditions the major metabolite AE F114970 (2-amino-5-chlorophenol) was found in the water phase. Phosalone can be classified as very low to low persistent and low to slight mobile in soil. Modelling for the representative uses evaluated indicated that phosalone is unlikely to contaminate groundwater when used as recommended.

If released in water, phosalone would adsorb to sediment and particulate matter in the water column and photolysed in the surface layers. Phosalone is relatively stable to transformation by hydrolysis at pH 4 and pH 7, but it is hydrolyzed at pH 9 to metabolites AE0941954 (S-6-chloro-2,3-dihydro-2-oxo-benzoxazol-3-ylmethyl and AE F054014 (6-chloro-2(3H)-benzoxazolone). Another major metabolite, AE 0651017 (=RP18726, phenoxazone) was found in the water phase of the sediment/water study.

PECsw were recalculated based on a safety factor for DT_{50} value derived from experimental data in order to take into account the pH dependency for hydrolysis of phosalone. PECsw and PECsed calculations for phosalone and metabolite AE 0651017 were based on the critical GAP from the table of representative uses and spray drift loadings. As additional information, contribution to surface water contamination via runoff and drainage was assessed with Exposit model and included in an addendum.

Concentration of phosalone in the air compartment and transport through it is not expected to be significant.

A high long-term risk was identified for insectivorous birds, considering the blue tit as a focal species. A high acute risk was also identified for small herbivorous mammals and a long-term risk to small and medium sized herbivorous mammals, insectivorous mammals and earthworm-eating mammals. Additionally a high risk was identified for the aquatic environment. Even with a buffer zone of 50 m the TER values are below the agreed trigger value for an available microcosm study. The risk to honey bees is high and risk mitigation measures should be set at Member State level also for flowering weeds below trees in orchards. The available studies indicate a high potential risk to non-target arthropods, both in-field and off-field. Even if phosalone residues on vegetation can be

assumed to degrade relatively rapidly allowing for recolonisation, the off-field risk has to be addressed and further data e.g. a field study with predatory mites under the intended conditions is required. Risk mitigation measures at Member State level to protect off-field non-target parasitoids are proposed. Furthermore a new study on one additional arthropod species is required. The acute risk to earthworms is considered low. However, sublethal effects were observed in the acute studies and therefore a long-term reproduction study is required to make sure that phosalone does not cause unacceptable effects on earthworm reproduction. The risk to soil micro organisms, non-target flora and fauna and biological methods of sewage treatment plants is considered low.

Key words: phosalone, peer review, risk assessment, pesticide, insecticide, acaricide

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

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Austria submitted the report of its initial evaluation of the dossier on phosalone, hereafter referred to as the draft assessment report, to the EFSA on 7 May 2004. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 6 July 2004 to the Member States and the main applicant Cheminova A/S as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 14 December 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 (BVL) in Braunschweig in April – 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 29 November 2005 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 22 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.1-2 of 2 December 2005)

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

Phosalone is the ISO common name for *S*-6-chloro-2,3-dihydro-2-oxobenzoxazol-3-ylmethyl *O,O*-diethyl phosphorodithioate (IUPAC).

Phosalone belongs to the class of heterocyclic organothiophosphate insecticides such as pyraclofos and to the class of organothiophosphate acaricides such as diazinon, malathion and phosmet. Phosalone is active by contact and ingestion on larval and adult stage of many lepidopterous and coleopterous pests. Acting as an acetyl-cholinesterase inhibitor it provokes the accumulation of acetylcholine in the synapsis leading to paralysis and death.

The representative formulated product for the evaluation was "Zolone" (Rubitox; "AE F016629 00 EC A1xx"), an emulsifiable concentrate (EC), registered under different trade names in Europe.

The evaluated representative uses as insecticide as proposed by the applicant which comprises foliar spraying to control chewing and sucking insects in pome fruit (apples, pears) at application rate up 900 g per hectare. Phosalone can be used as insecticide and acaricide. It should be noted that only the use as insecticide was supported for the EU review programme.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of phosalone as manufactured should not be less than 940 g/kg (which is higher than the minimum purity given in the FAO specification 109/TC/S (1988) of 910 g/kg. The higher value relates to the submitted results of current batch analysis and not to any toxicological concern to increase the minimum purity.

The technical material contains one relevant impurity of toxicological concern, which is not mentioned in the FAO specification. For the moment it is not possible to set a maximum level for *S*-chloromethyl *O*,*O*-diethyl phosphorodithioate (AE F073749) due to the fact that no information is available about the levels of this impurity in the respective toxicological studies (refer to 2). Therefore, the specification as a whole should be regarded as provisional at the moment.

Beside this, the assessment of the data package revealed no particular area of concern.

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

The content of phosalone in the representative formulation is 350 g/L (pure). The data package for the EC formulation is in compliance with the criteria mentioned in the FAO specification for emulsifiable concentrates (109/EC/S, 1983).

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of phosalone in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material. It should be noted that concerning the relevant impurity neither spectra nor information about the content of AE F073749 in the formulation during the shelf-life test or an analytical method for the determination in the formulation is available.

However, being aware that the content of the relevant impurity cannot be measured, enough data are available to ensure that at least limited 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. phosalone in food of plant origin, soil, water and air.

In case 2-amino-/-chloro-3Hphenoxazin-3-one (AE0651017, RP18726, phenoxazone) will be included in the residue definition for ground water, the submitted method should be reconsidered.

Residues in food of plant origin can be determine with a multi-method (the German S19 method has been validated). For the other matrices only single methods are available to determine residues of phosalone. The methodology used is GC with PN, FP, EC or MS/MS detection.

An analytical method for food of animal origin is not required due to the fact that currently no residue definition can be proposed (see 3.2 and 3.4). Therefore the submitted analytical method should be reconsidered, if a residue definition is set.

The discussion in the expert meeting (EPCO 25, May 2005) on identity, physical and chemical properties and analytical methods was limited to the specified max levels of the impurities in the technical material and the acceptability of the enforcement method for surface water. For the latter, the applicability was confirmed after the expert meeting due to the fact that the value to be monitored of 2.5 µg/L was confirmed by EFSA.

2. Mammalian toxicology

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

The impurity AE F073749 is more acutely toxic than phosalone (LD_{50} 18 mg/kg bw as compared to 120 mg/kg bw for phosalone) and is mutagenic towards one strain of bacteria in an Ames test. No other tests have been performed with this impurity (see 2.8.).

The specification of AE F073749 in phosalone technical is maximum 1.5% w/w. However, in the toxicological studies, where at least 15 different batches were used, no information is available about the concentration of the impurity in the batches. Thus, a threshold level cannot be confirmed for this impurity in the technical material.

In order to confirm the threshold level, the need of further tests with the current technical material should be considered. In a first step, the genotoxic activity should be investigated in an Ames test, a gene mutation test with mammalian cells, and a chromosome aberration test. Equivocal results in *in vitro* studies should be substantiated by *in vivo* experiments. In a second step, it should also be tested for the carcinogenicity in a long term study. This might have an impact on the long term NOAEL and thus the reference values agreed until now should be regarded as provisional.

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

Phosalone is rapidly absorbed from the rat gastrointestinal tract (80-90 %) after single or repeated exposure. Bioaccumulation is low (almost non-detectable levels by 72 hours). The metabolism of the compound was extensive and rapid, with only low amounts (<5%) of the parent material found in faecal samples within 24 hours. The excreted metabolites were obtained by four different routes (sulphate/glucuronide conjugation, oxidative desulfation, oxidative dealkylation and hydrolysis).

2.2. Acute toxicity

Phosalone is of high acute oral toxicity (LD_{50} 120 mg/kg bw). By acute dermal or inhalative application, the compound is harmful with a LD_{50} of 1530 mg/kg bw, and a LC_{50} of 1.26 mg/L. Phosalone is mildly irritating to skin and eyes but no classification proposed, and has sensitizing properties (M&K test). **Classification for acute toxicity is needed and the proposed risk phrases**

are: T, R 25 "Toxic if swallowed"; Xn, R 20/21 "Harmful by inhalation and in contact with skin"; Xi, R 43 "May cause sensitization by skin contact".

2.3. SHORT TERM TOXICITY

The short-term toxicity of phosalone has been investigated in rats in one 8-week study and in dogs in one 1-year study.

In the 8-week dietary study in rats, the main effect identified was cholinesterase inhibition. Based on that, the NOAEL was 0.9 mg/kg bw/day.

With the results of the 1-year dog study, the experts considered primarily the inhibition of brain acetylcholinesterase and clinical signs, and agreed on a NOAEL of 0.9 mg/kg bw/day.

No short term dermal or inhalation toxicity studies have been submitted.

2.4. GENOTOXICITY

The genotoxic properties of phosalone were studied in a battery consisting of six *in vitro* studies and two *in vivo* studies. One DNA repair test *in vitro* was weakly positive at a cytotoxic level, but this was not confirmed in a second test with lower levels. The experts concluded that phosalone did not possess any genotoxic potential. However, due to the limitations of the *in vivo* micronucleus test, a new data requirement was set, and an acceptable *in vivo* test in somatic cells should be submitted at Member State level for confirmatory reasons.

As the level of the impurity AE F073749 (10 times more toxic than phosalone and mutagenic) is not confirmed in the toxicological batches used for phosalone, further data are required with the current technical material. In a first step, the genotoxic activity should be investigated in an Ames test, a gene mutation test with mammalian cells, and a chromosome aberration test. Equivocal results in *in vitro* studies should be substantiated by *in vivo* experiments.

2.5. LONG TERM TOXICITY

One long-term study in the rat and one in the mouse have been submitted.

In the 2-year rat study, the main findings were a decrease in erythrocyte, plasma and brain cholinesterase levels, in addition to adverse effects on body weight gain and food consumption. Treatment-related changes were also observed in the adrenals and in the testes. There was no evidence of a tumorigenic potential. The experts have taken into consideration the inhibition of brain acetylcholinesterase and clinical signs to determine a NOAEL of 1.8 mg/kg bw/d.

In the 2-year mouse study, reductions of erythrocyte cholinesterase and plasma cholinesterase were observed in the high dose groups, but these activities were not evaluated at the lower dose levels. Consequently, the experts decided that a NOAEL could not be determined for this study. There was no evidence of a carcinogenic effect.

The overall NOAEL for the long term toxicity, taken from the 2-year rat study, is 1.8 mg/kg bw/d.

As the level of the impurity AE F073749 (10 times more toxic than phosalone and mutagenic) is not confirmed in the toxicological batches used for phosalone, a new carcinogenicity study with the

current technical material should be performed. This might have an impact on the long term NOAEL and thus the reference values agreed until now should be regarded as provisional.

2.6. REPRODUCTIVE TOXICITY

One rat multigeneration study has been submitted in order to determine the reproductive effects of phosalone. Taking into account the inhibition of brain acetylcholinesterase and clinical signs (decreased maternal and pup weights, increased pup mortality at the high dose), the experts established the NOAEL for systemic toxicity (parental and offspring) and reproductive parameters at 3.5 mg/kg bw/day. No direct effect on reproductive performance or fertility was observed.

In the rat teratogenicity study, no developmental effect was shown to be related to the test compound. The NOAEL for maternal and developmental toxicity was 10 mg/kg bw/day, based on clinical signs, decreased body weight, and increased incidence of embryonic resorptions at 20 mg/kg bw/day.

In the rabbit teratogenicity study, no adverse effects on foetal parameters were observed up to the highest dosage examined, where maternal and foetal toxicity were evident (clinical signs, reduced food consumption and body weight, increased incidence of embryonic resorptions). Taking into account the historical control data range for post-implantation losses, the experts have applied the same NOAEL for maternal and developmental toxicity, which is 10 mg/kg bw/day.

2.7. NEUROTOXICITY

Acute delayed neurotoxicity in hens was investigated with phosalone. Acute toxicity was observed (deaths), but there was no behavioural or histopathological evidence of acute delayed neurotoxicity.

In an acute neurotoxicity study with rats, the NOAEL was 25 mg/kg bw, based on neurological clinical signs, brain and erythrocyte cholinesterase inhibition.

In a 13-week neurotoxicity in rats, there was no clinical sign of neurotoxicity, but lower plasma-, erythrocyte- and brain cholinesterase levels were observed at all concentrations, so it was not possible to establish a NOAEL (< 4 mg/kg bw/day).

2.8. FURTHER STUDIES

Toxicity studies on metabolites.

The metabolite **oxophosalone** (RP 12244) was found to be more toxic than phosalone after dermal administration to the rat (LD_{50} 380 mg/kg bw).

The acute oral LD_{50} value of the **sulphone** metabolite (19 888 R.P.) in mice was greater than 5000 mg/kg bw. The acute oral LD_{50} of the **sulphoxide** metabolite was about 350 mg/kg bw. The **sulphide** metabolite (19 914 R.P.) had an acute oral LD_{50} of 590 mg/kg bw in males and 837 mg/kg bw in females.

All these four metabolites have been identified in the ADME-studies in rats.

Phenoxazone (AE 0651017) is a soil metabolite which has not been identified in rat metabolism studies. In a rat acute oral test, the LD_{50} was greater than 2000 mg/kg bw. Two bacterial *in vitro* tests and one *in vivo* test with mammalian cells were submitted. In the two *in vitro* tests, phenoxazone was shown mutagenic to the same bacterial strain (Salmonella typhimurium TA 1537) in the presence of

metabolic activation; however there was no evidence of induced unscheduled DNA synthesis in rat hepatocytes in the *in vivo* test.
If the metabolite phenoxazone would exceed the threshold of 0.1 µg/L in the groundwater, at least an *in vitro* gene mutation test with mammalian cells could be required at Member State level for confirmatory reason, according to the experts.

Toxicity studies on impurities.
The acute oral LD_{50} of AE F073749 in rats is 18 mg/kg bw, and a mutagenic activity was induced in the Ames test with Salmonella typhimurium strain TA 100 both with and without metabolic activation. Thus the impurity is 10 times more toxic than phosalone as well as mutagenic.
However, in the toxicological studies for phosalone, where at least 15 different batches were used, no information is available about the concentration of the impurity in the batches. In order to determine the threshold level of the impurity in the current technical material, the need of further tests should be considered. In a first step, the genotoxic activity should be investigated in an Ames test, a gene mutation test with mammalian cells, and a chromosome aberration test. Equivocal results in *in vitro* studies should be substantiated by *in vivo* experiments. In a second step, it should also be tested for the carcinogenicity in a long term study. This might have an impact on the long term NOAEL and thus the reference values agreed until now should be regarded as provisional.

2.9. MEDICAL DATA

During a biological monitoring of personnel exposed to phosalone from 1985 to 1986 and from 1987 to 1988, no blood abnormalities or clinical signs were detected which could be attributed to phosalone.
No clinical cases and poisoning incidents are known.

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

All the references values were calculated using a safety factor of 100.

ADI
Initially the RMS proposed an ADI of 0.002 mg/kg bw/day, based on the NOAEL of 0.2 mg/kg bw/day in the 2-year rat study. The experts agreed for a revised ADI of 0.01 mg/kg bw/day, based on the revised NOAEL of 0.9 mg/kg bw/day in the 1-year dog study.
Due to the data requirement in **2.8.**, this reference value should be regarded as provisional.

AOEL
Initially the RMS proposed an AOEL of 0.002 mg/kg bw/day, based on the NOAEL of 0.2 mg/kg bw/day in the 1-year dog study. The experts agreed for a revised AOEL of 0.01 mg/kg bw/day, based on the revised NOAEL of 0.9 mg/kg bw/day in 1-year dog study.

ARfD

Initially the RMS proposed an ARfD of 0.01 mg/kg bw, based on the NOAEL of 1 mg/kg bw/day in the rabbit teratology study. The experts agreed for a revised ARfD of 0.1 mg/kg bw, derived from the revised NOAEL of 10 mg/kg bw/day in the rabbit teratology study.

2.11. DERMAL ABSORPTION

The dermal absorption of phosalone was studied with the concentrate formulation (350 g phosalone/L) and the spray dilution (1:880) of the formulation.

For the rat *in vivo* study, the experts agreed that the amount of phosalone remaining at the sampling time of 192h in the stratum corneum was not bioavailable, as there was no decrease in skin strips and stripped skin with time. The same was applied in the *in vitro* study comparing absorption through human and rat skin membranes, and the resulting dermal absorption was 3.6% for the field dilution and 0.7% for the concentrate.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Zolone is an EC-formulation containing 350 g /L of phosalone, for foliar application on pome fruit.

Operator exposure

According to the intended uses submitted by the applicant, the maximum applied dose is 900 g phosalone/ha and the minimum volume 1000 L/ha, using tractor airblast sprayers or hand held equipment (knapsack). As the AOEL was agreed to be changed to 0.01 instead of 0.002 mg/kg bw/day, it was expected that the operator exposure would probably be below the AOEL if personal protective equipment was worn. New calculations are presented in the addendum.

Estimated exposure presented as % of AOEL (0.01 mg/kg bw/day), according to calculations with the German and UK POEM model. The default for body weight of operator is 70 kg in the German model and 60 kg in the UK-POEM model.

Model	Use	No PPE	With PPE*:
German	tractor sprayer	462 %	40 %
	knapsack	416 %	54 %
UK POEM	tractor sprayer	1100 %	400 %
	knapsack	4460 %	600 %

*PPE (personal protective equipment):

- for UK POEM: gloves during mixing/loading and application;
- for German model: gloves during mixing/loading; gloves, coverall, hat and faceshield during application.

In a field study, the measurement of operator exposure was estimated to be 50% of AOEL, but the application rate was only 570 g phosalone/ha whereas the intended use is 900 g phosalone/ha.

Worker exposure

New calculations were provided based on the experts' conclusion that the exposure estimate would be below the AOEL. A German re-entry model[3] was used for the calculations, but a revised transfer factor was applied according to the US EPA recommendations for re-entry risk assessment. According to the revised AOEL, the estimated worker exposure would be approximately 72 % of the AOEL without personal protective equipment, and 3.6 % of the AOEL with the use of gloves.

Bystander exposure

After revision of the AOEL, the experts agreed that new calculations would provide an estimated exposure for bystanders below the AOEL. New calculations are presented in the addendum, and the estimated exposure is 33% of the AOEL.

3. Residues

Phosalone 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 phosalone has been investigated in apples, grapes and sorghum. On fruits the conditions of the studies were representative of the use supported by the applicant on apples. In apples and grapes, the metabolic pattern was quite similar. Phosalone was the main component of the extractable radioactivity (more than 80% of the extracted material). The identified metabolites were always present at low levels and indicated that the metabolic pathway of phosalone in fruits involves processes as dechlorination leading to RP 11690[4], oxidation to RP 12244[5], hydrolysis to RP 11881[6] and possible formation of glycosides. Considering the known high toxicity of analogue chemical compounds, the RMS set a requirement for investigating further the toxicological relevance of RP 12244, but it was considered by the expert meeting (EPCO 24) that this requirement was not really justified as this metabolite is found at very low level (at least one order of magnitude lower than the levels of the parent compound). It is the opinion of EFSA that it cannot be excluded that this compound, although present at low levels, has a significant contribution to the toxicological burden, depending on its own toxicity, which seems to be higher than that of the parent compound as mentioned under point 2.8. The potential presence of this compound in the plant metabolism should also be considered at Member State level if the use of phosalone on other crop groups should be considered for authorisation. The proposed residue definition for monitoring is phosalone. In the

[3] Hoenicke *et al*., 1998. Hinweise in der Gebrauchsanleitung zum Schutz von Personen bei Nachfolgearbeiten in mit Pflanzenschutzmitteln behandelten Kulturen. Nachrichtenbl. Deut. Pflanzenschutzd. 50 (10), p 267.
[4] RP 11690: deschlorophosalone
[5] RP 12244: oxophosalone
[6] RP 11881: 6-chlorobenzoxazolone

residue definition for risk assessment it is proposed to include RP 12244, as it has not been demonstrated that its contribution to the toxicological burden is not significant.

A sufficient amount of acceptable residue trials were carried out in accordance with the representative uses of phosalone (13 trials on apples and pears for the Northern region of EU and 12 trials on apples and pears for the Southern region of EU). The highest residues found in both regions were 1.2 mg/kg, while the STMRs (Supervised Trials Median Residue) were 0.55 and 0.81 mg/kg for the Northern and Southern regions respectively. These residue trials can be considered as reliable on the basis of storage stability studies indicating that residues of phosalone are stable in fruits matrices under storage conditions at < 20°C for 24 months. The information provided is sufficient to propose MLRs. RP 12244 was not analysed in these trials and this is a deficiency for performing a robust risk assessment for the safety of the consumer.

Studies on the effect of processing on the nature and levels of residues present in raw commodities were submitted by the applicant.

In standard buffer solutions and under conditions simulating pasteurisation, baking/brewing/boiling and sterilisation, ^{14}C-phosalone undergoes a degradation into a compound M1[7], RP 18709[8], AE 0651017[9] and other unidentified degradation products present at low levels. The main degradation product is metabolite M1, representing 60-70% of the total of residues present in condition simulating baking/brewing/boiling and sterilisation. In contrast with these results, almost no degradation occurs under practical conditions of production of apple juice and compote fortified with ^{14}C-phosalone. The differences in test conditions were considered by the RMS to find explanations to the differences observed in the results. The pH seems to be the only parameter which could have had an influence on the results, with a lower pH in apple juice and compote due to the presence of vegetal acids than in the standard buffer solutions used in classical hydrolysis studies.

The toxicological relevance of the identified degradation products was examined and while metabolites M1 and RP 18709 can be considered as covered by the toxicological dossier as they are found in the rat metabolism, no conclusion can be drawn at this stage concerning AE 0651017 which was not found in the rat metabolism.

The effects of processing on the level of residues were investigated in 4 studies. Transfer factors were established for apple juice and apple puree, indicating that residues are transferred to a very limited extent to apple juice and apple puree. In these studies only phosalone was analysed and no direct analysis was made of the degradation products formed in buffer solutions under hydrolysis conditions. The expert meeting (EPCO 24) considered the available balance sheets established from these studies, to have indirect information on the extent of degradation of the parent compound. However this approach was not conclusive given the dispersion of the results and/or the fact that certain fractions (peels) were not analysed in 2 processing studies.

[7] M1: desethyl phosalone
[8] RP 18709: 2-hydroxy-p-chloroaniline
[9] AE 0651017: 2-amino-7-chloro-3H-phenoxazin-3-one

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

As the intended uses are restricted to pome fruits, studies on succeeding or rotational crops are not required.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

The metabolism of phosalone has been investigated in lactating ruminants. After administration of the compound to lactating goats, only degradation products could be identified in milk, liver and kidneys. Radioactivity present in muscle and fat was too low to allow identification of the compounds present in these matrices. Based on the nature on the degradation products, the route of metabolism of phosalone was found to be primarily via hydrolytic cleavage of the S-P bond to form an unstable mercapto compound followed by methylation (metabolite RP 19914[10], major in liver) and further oxidation (metabolite RP 19889[11], major in liver). More extensive metabolism leads to RP 18709 (major in milk). Another metabolite, major in milk and kidneys, unstable and degrading to RP 19889, could not be fully identified. For this reason, it was concluded by the expert meeting that the study provided did not give all the needed details for proposing a residue definition and that further information on the metabolism of phosalone in lactating ruminants should be provided to allow the identification of major residues in the animal tissues.

A poultry metabolism study is not considered necessary based on the representative uses, apple pomace not being fed to poultry.

No feeding study in lactating cow is available. However, taking into account the nutrition practices of ruminants and in particular the possible incorporation rate of apple pomace in the diet, it is not possible to exclude the occurrence of individual metabolites at measurable levels in animal commodities, in particular in liver and kidneys. Therefore it was considered by the expert meeting (EPCO 24) that a feeding study in cattle should be carried out, depending on the outcome of the evaluation of the required data on metabolism and the resulting decision on the residue definition.

3.3. CONSUMER RISK ASSESSMENT

Exposure assessments presented here below were not made on the basis of the proposed residue definition for risk assessment, as only phosalone can be taken under consideration at this stage. The contribution to the risk of RP 12244 is not possible to determine due to the lack of data on its toxicological properties and its actual level in commodities.

A chronic dietary exposure assessment has been carried out following the Theoretical Maximum Daily Intake (TMDI) calculation model of WHO using the WHO European typical diet for adult consumers (60 kg bodyweight) as well as the national diet of Germany for the 4-6 year old girl (13.5 kg bodyweight). Residues in apples and pears were considered to be at the level of the proposed MRL (2 mg/kg). The contribution of possible residues in animal commodities was not considered given that information is lacking for proposing a residue definition and MRLs for those commodities. The calculations made for both diets indicated TMDI values below the ADI of phosalone (17 and 72 % of

[10] RP 19914: 6-chloro-2,3-dihydro-3-methylthiomethyl-1,3-benzoxazol-2-one
[11] RP 19889: 6-chloro-2,3-dihydro-3-methylsulfinylmethyl-1,3-benzoxazol-2-one

the ADI for the WHO European diet and for the German diet respectively). More refined calculations (I(N)EDI – International (National) Estimated Daily Intake) were also carried out using the STMR in pome fruits for the Southern EU and the processing factors for apple juice, demonstrating that the actual exposure of the consumers is below 10 % of the ADI.

The acute exposure to residues of phosalone has been estimated according to the WHO model for estimates of short term intakes. Large portion consumption data for adults and toddlers in UK were used by the RMS. Calculations showed potential exposures below the ARfD for adults (17 and 20 % of the ARfD for apples and pears respectively) and close to the ARfD for toddlers (72 and 98 % of the ARfD for apples and pears respectively). Similar results were obtained by EFSA (no addendum available) with recent consumption data for German toddlers (99% and 110% of the ARfD for apples and pears respectively). It must be pointed out that the calculations were carried out in line with relevant guidance documents using the highest residue found in supervised trials (1.2 mg/kg) and not the proposed MRL (2 mg/kg). This means that residues present at the level of the proposed MRL would represent an exposure clearly above the ARfD for toddlers in case of high unit to unit variability in the analysed sample.

In addition to that, it is reiterated that RP12244 was not taken into account and therefore the actual toxicological burden for the consumer may be significantly underestimated, depending on the toxicological potency of this metabolite. Therefore it is expected that the ARfD will be exceeded in practice by the global toxicological burden of phosalone and its metabolite RP 12244 for apples and pears.

A final conclusion on the risk for the consumer is not possible to be drawn at this stage as information on the toxicological properties and the contribution to the toxicological burden of RP 12244 (metabolite in plants) and AE 0651017 (degradation product under processing) as well as on metabolism in livestock is missing.

3.4. PROPOSED MRLS

Based on the results of supervised residue trials on apples and pears and their analysis according to statistical tools recommended by current guidelines a MRLs of 2 mg/kg would be necessary for pome fruits. However as mentioned here above under point 3.3 this MRL is questionable in terms of consumer safety.

No MRL is proposed for animal commodities, given that data are lacking for establishing a residue definition. The information available from the metabolism in goat does not suggest a no-residue situation for animal commodities as far as metabolites are concerned.

4. Environmental fate and behaviour

Phosalone was discussed in the EPCO experts' meeting on fate and behaviour in the environment (EPCO 21) in April 2005.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Phosalone metabolism in soil was investigated under aerobic conditions (dark, 20 ± 2 ºC and 40-45% of the maximum water holding capacity (MWHC)) in 4 soils, which varied in texture (clay contents: 2.2 – 24.3%), organic carbon content (0.5 – 2.3 %) and pH values (5.5 – 7.7). Additionally, one of the soils was also incubated at 10 ± 2 ºC as well as under sterile conditions. After 120 days at 20 ± 2 ºC, 14.9-29.7 % AR of UL-^{14}C-chlorophenyl-labelled phosalone was converted to CO_2. At lower temperatures the rate of mineralization is lower. The amounts of bound residues increased rapidly reaching a maximum of 89.9% AR at day 85 in one of the soils, and 67-80% AR at the end of the study (120 days). The major amount of bound residues was associated with the humin fractions (53% AR) followed by humic acids and fulvic acids. The parent compound represented the main extractable radioactive fraction and up to 12 metabolites, including benzoxazole (AE F054014) and the trycyclic compound phenoxazone (AE 0651017), were found, none accounted for more than 5.8% AR at any sampling time.

Based on products identified in soil, a metabolic pathway was proposed in which (^{14}C)-phosalone undergoes to hydrolysis (probably via oxophosalone, AE 0591540) to form 6-chlorobenzoxazolone (AE F054014), and opening of the heterocyclic ring followed by condensation to form phenoxazone (AE 0651017) and ultimately metabolised to CO_2 and soil bound residues.

Under sterile conditions virtually no degradation of phosalone was observed, meaning that degradation is microbially mediated.

Under anaerobic conditions (1 soil) the degradation of phosalone follows the same pathway as observed under aerobic conditions with the exception that under anaerobic conditions metabolite phenoxazone (AE 0651017) was not observed. On the other hand, the metabolite AE F114970 (2-amino-5-chlorophenol) was found up to 20% AR in the water phase (day 3) and a maximum of 8.1% AR (day 14) in soil extracts.

Phototransformation on soil is not an important route of transformation of phosalone in the environment.

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

The rate of degradation in soil of phosalone under aerobic conditions in laboratory studies (20 ºC and 10 ºC) was investigated as part of the metabolism studies described at 4.1.1 above, and in 3 additional soils. The RMS recalculated the degradation rates for three soils on the basis of simple 1st order kinetics and included the results in an addendum (March 2005). DT_{50} values range between 0.8 and 4.9 days at 20 ºC, with a mean of 2.1 days. Phosalone can be classified as low persistent. Applying simple 1st order kinetics DT_{90} values are between 2.8 and 16.3 days with a mean of 7.2 days. Degradation was reduced at lower temperature (10 ºC): the calculated DT_{50} and DT_{90} values are 8.5 and 28.1 days respectively. The half-life of phosalone under anaerobic conditions was comparable to that under aerobic conditions (= 4.3 days using the KIM compartment model). Since the parent compound was rapidly degraded in soil laboratory experiments (< 5 days), no filed dissipation studies are requested.

PECs soil were calculated based on the worst case laboratory DT_{50} (= 4.9 d), and on the maximum seasonal rate (= 900 g ai/ha) for 2 applications at growth stages BBCH 50 and BBCH 85.

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

Data on batch adsorption of phosalone were available for 4 soils. The derived Freundlich adsorption coefficients K_f (6.2 – 35.1 dm^3/kg) and K_{oc} values (870 – 2680 dm^3/kg) indicate medium adsorption and slight to low mobility. The desorption K_{oc} values were substantially higher than the adsorption K_{oc} values, indicating that once adsorbed to soil, phosalone is even less likely to be removed with water.

A non reliable study (not done under GLP and material balance not established) with fresh and aged phenyl ring labelled phosalone gave some indications that phosalone has low potential to leach into deeper soil layer.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Hydrolysis of phosalone is pH dependant. Phosalone is relatively stable to transformation by hydrolysis at pH 4 and pH 7, but is hydrolyzed at pH 9. The calculated DT_{50} values at 20 ºC were > 365 d (pH 4), 321 d (pH 7) and 17.8 d (pH 9). MS requested the characterisation of unidentified degradation products occurring at levels > 10% AR. The study on the identification of the hydrolysis products (Maurer T., 2002d) was presented in an addendum (March 2005) and discussed at the experts' meeting (EPCO 21). The meeting considered valid the identification of metabolites as **AE0941954**[12] and **AE F054014**[13] found up to 21% AR at pH 9 in the hydrolysis study. Another major metabolite, AE 0651017[14] (=RP18726) was found in the water phase of the sediment/water study and further assessed for hydrolytic degradation. AE 065107 is considered to be hydrolytic degradable at ambient temperature (DT_{50} values at 20ºC were 3.35 d, 21 d and 40 d at pH 9, pH 7 and pH 4 respectively).

In aqueous photolysis studies where phosalone was dosed, a single first order half life was calculated to be 1.8 days midsummer sunlight at 40ºN at the surface of pure water. Six major (> 10% AR) photodegradates of phosalone were found and further investigated for characterisation. The metabolites M2, M4 and M6 were identified, whilst M10, M12 and M13 were not sufficiently identified due to methodical restrictions. RMS considered that further identification of these photolysis metabolites is not necessary and provided his/her comments in an addendum (March 2005). The water/sediment study metabolite AE0651017 (=RP18726) degraded fast with a DT_{50} value of 1.1 d calculated for a latitude of 40ºN, pH 7 and 20ºC.

[12] AE 0941954: S-6-chloro-2,3-dihydro-2-oxo-benzoxazol-3-ylmethyl
[13] AE F054014: 6-chloro-2(3H)-benzoxazolone
[14] AE 0651017: (=RP18726) 2-amino-7-chloro-3H-phenoxazin-3-one; phenoxazone

The results of a study on biological degradation indicated that phosalone should be classified as "not readily biodegradable" according to the OECD criteria.

In the water/sediment system (2 systems studied in the laboratory at 20ºC in the dark) phosalone dissipates rapidly. The DT_{50} values of phosalone for the water phase and the whole system were 2.8-4.7 d and 3.7 and 6.8 d respectively. A high percentage of bound residues up to 65.9% and 67.3% AR at 30 and 60 days was measured, and the observed rapid dissipation may have occurred due to partitioning form the water phase into sediment. The majority of non-extractable residues were associated with humin and humic acid fractions of the sediment. Mineralization to CO_2 was minimal, reaching a maximum of about 10% AR at the end of the study (60 days). The major metabolite was **AE 0651017** (=RP18726, phenoxazone) with maximum levels in the water phase of 13.1% and 22.4% AR at 14 d and 8 d. Concerns raised on the fate of phosalone and of metabolite AE651017 in acidic water/sediment systems because both systems investigated were alkaline. This issue was discussed at the experts meeting (EPCO 21). It was concluded that microbiological degradation will be the main degradation pathway in the aquatic environment. However contribution of hydrolysis can not be fully excluded. It was not deemed necessary to require an additional water/sediment study but, since, the DT_{50} value is a critical input parameter for PEC surface water calculation for multiple applications, the meeting agreed to use a reasonable worst case approach. A safety factor of 3, derived from experimental data, was set for PEC_{sw} calculations as a consequence of a slower degradation in the sediment phases at acidic pH (DT_{50} of 4 days at pH 6.2 and DT_{50} of 1.6 days at pH 8.1).

PEC_{sw} and PEC_{sed} were recalculated for phosalone and the major metabolite AE0651017 taking into account the safety parameter data (DT_{50} water = 3 x 4.7 d). Results are reported in an addendum (September 2005) that has not been peer reviewed. Modelling was based on worst case application schemes according to GAP and spray drift loadings to a static 30cm deep water body. The contribution from runoff and drainage was not taken into account in the EU risk assessment. However, potential contamination via drainage and run-off was calculated by RMS with EXPOSIT model (a German national model) and included in the addendum (September 2005). Results were not peer reviewed. For information, the Netherlands representative at the evaluation meeting (November 2005) stated they had performed FOCUSsw calculations which showed higher PEC values than the EXPOSIT model). Member States should therefore carry out a surface water exposure and consequent aquatic risk assessment for phosalone and metabolite AE0651017 (phenoxazone) from the runoff and drainage routes of exposure at the national level.

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

Residues of phosalone in groundwater were modelled using FOCUS PELMO 2.2.2. The concentration in the leachate at one metre soil depth was estimated for all nine defined FOCUS groundwater scenarios considering the maximum number and highest rates of application (2 x 0.9 kg ai/ha) to pome fruits (apples) with 50 days interval. In PEC_{gw} calculations the normalised DT_{50} value

of 2.1 days was used. This value was derived from 4 out of 7 degradation rates in soil. The arithmetic mean of all laboratory degradation half-lives including the recalculated values from the one of the degradation study (see 4.1.2) is 2.15 days (addendum March 2005). The experts' meeting (EPCO 21) agreed that the use of the reliable DT_{50} value will not affect the results of PEC_{gw} calculations. All relevant scenarios resulted in predicted groundwater concentrations of phosalone below the trigger value of 0.1 µg/L.

The evaluation meeting pointed out the potential relevance of soil metabolite AE0651017 (phenoxazone) for groundwater contamination. The need for the outcome of the genotoxicological assessment by the mammalian toxicology section (EPCO 23) was seen at the experts' meeting. Following the result of the discussion of the toxicology experts meeting, a genotoxic potential of the metabolite AE0651017 has not been proven but cannot be excluded based on limitations on the available data. Therefore, a data gap for the groundwater contamination assessment for phenoxazone can be identified. If the threshold of 0.1 µg/L is exceeded, a new in vivo study (gene mutation) should be performed in order to assess the relevance of this metabolite (see section 2.8).

4.3. FATE AND BEHAVIOUR IN AIR

When phosalone is applied as formulated product "ZOLONE PM", it did not volatilise form plant surface or soil in the course of a 24-hour period. Its reactivity with OH radicals in the troposphere is predicted to be very rapid. Calculations according to the model by Atkinson showed that assuming a concentration of 1.5×10^6 OH radicals/cm^3, the half life calculated would be 4 minutes.

5. Ecotoxicology

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

5.1. RISK TO TERRESTRIAL VERTEBRATES

Plant protection products containing phosalone are to be applied to pome fruits, therefore birds and mammals feeding on vegetation, seeds and fruits, earthworms and/or insects may be at risk of exposure. The first tier risk to birds and mammals was calculated according to the Guidance Document on Birds and Mammals (SANCO/4145/2000) based on toxicity data for the active substance. No toxicity data are available for the formulated product. Maximum application rate according to the proposed GAP as a single application was used.

To assess the risk to birds a small insectivorous bird was considered. The calculated acute TER value is 10.3 which are slightly above the Annex VI trigger of 10 and hence no further consideration is required. The short-term and long-term TER values are 8.6 and 0.44 respectively, indicating a high potential risk.

The long-term assessment was refined by choosing the blue tit as focal species. Proposals for refinements of "portion of diet obtained in the treated area" (PT), "proportion of different food types in the diet" (PD), residues and dissipation time were discussed at the experts' meeting. Extrapolation

of residue decline from vegetation to insects was not considered appropriate, but the experts' opinion was that it could possibly be taken into account in a weight of evidence approach. It was however agreed that a PD factor of 0.67 can be used, meaning that two thirds of the diet of blue tits in orchards consists of over sprayed arthropods. It was also agreed that a PT value of 0.61 was appropriate, based on supporting literature data. The refinements lead to a long-term TER of 1.1. Since this value is still below the Annex VI trigger a high risk for insectivorous birds is concluded and the risk needs to be further addressed.

To assess the risk to mammals a 10 g insectivorous mammal, a 25 g herbivorous mammal and a 3000 g brown hare was considered. A deposition factor of 0.4 was used. The first tier TER values for acute risk are above the Annex VI trigger for medium herbivorous mammals and insectivorous mammals, indicating a low acute risk. The acute TER for small herbivorous mammals is 1.7 and the long-term TER values are all below the trigger (3.09, 0.17 and 1.15 respectively) indicating a potential high risk to wild mammals. A data requirement for the applicant to further address the acute risk to small herbivorous mammals was therefore set at the experts' meeting.

Proposals for refinements of the risk assessment were discussed at the experts' meeting. The meeting agreed with the RMS that extrapolation of residue data from chicory leaves to short grass or from studies with another organophosphate substance is not acceptable. An assumption of a worst case DT_{50} for vegetation of 5 days was however agreed on. The use of bank vole (*Clethrinomys glareolus*) as proposed by the applicant was questioned by the experts and therefore the refinements of PD and PT was not discussed in detail. Even if the assumptions for the bank vole would have been accepted, the TER values remain below the trigger and needs to be further addressed.

The risks to earthworm- and fish-eating birds and mammals were calculated according to the Guidance Document on Birds and Mammals (SANCO/4145/2000). TER values obtained for birds are above the Annex VI trigger indicating a low risk from bioaccumulation via the food chain. The TER value for earthworm-eating mammals is 2.2, based on the agreed NOEL of 3.5 mg a.s./kg bw day, indicating a potential risk. For fish-eating mammals the risk is considered low.

In conclusion a high long-term risk has been identified for insectivorous birds. A high acute risk has also been identified for small herbivorous mammals and a long-term risk to small and medium sized herbivorous mammals, insectivorous mammals and earthworm-eating mammals.

5.2. RISK TO AQUATIC ORGANISMS

Phosalone is very toxic to aquatic organisms. The most sensitive aquatic organism tested with phosalone was *Daphnia magna* with an acute EC_{50} of 0.74 µg/L for the active substance and 0.40 µg/L for the formulation. The NOEC for *Daphnia* based on reproduction effects is 0.14 µg/L. Fish and algae are less sensitive.

The first tier risk assessment is based on predicted environmental concentration in surface water due to spray drift at different distances from an early application of 900 g a.s./ha (see 4.2.1). The resulting acute TER values are 203 (30 m), 0.44 (50 m, based on toxicity of the formulation) and 13 (30 m) for fish, *Daphnia* and algae respectively, thus indicating the need for risk mitigation measures and a high acute risk for Cladocerans even with a buffer zone of 50 m. Also the long-term TER values indicate a high risk. For fish and Chironomids buffer zones of 20 and 40 m respectively are required to meet the Annex VI trigger. For *Daphnia* the long-term TER is 0.24 for the formulation even with a buffer zone of 50 m.

A higher tier microcosm study is available. This study was discussed at the experts' meeting and it was agreed to use a NOEAC of 2.5 µg a.s./L based on no significant effects on the community level. A safety factor of 10 was decided. The high safety factor was agreed since the study had some shortcomings leading to higher uncertainty when extrapolating to natural ecosystems. In particular the high pH in the study was regarded of concern since hydrolysation of phosalone occurs at alkaline conditions. Special attention to the risk for the aquatic environment should therefore be given by Member States were more acidic conditions occur. Furthermore, indirect effects on fish populations and the phytoplankton community composition were not investigated in the microcosm. Based on the NOEAC from the microcosm study a TER value of 2.78 was obtained with a buffer zone of 50 m, which doesn't meet the agreed trigger of 10, and hence a high risk to the aquatic environment is concluded.

One major metabolite, AE0651017, (13-22% of applied radioactivity) was detected in the water phase in the water/sediment study. This metabolite is of lower acute toxicity and of no concern compared to the active substance.

Since the $logP_{ow}$ for phosalone is >3 the potential for bioaccumulation was investigated. The results indicate that although phosalone is readily taken up it is also rapidly eliminated (CT_{90}=2.4 d). The risk for bioaccumulation is therefore considered to be low. No data on the bioaccumulation potential for the metabolite AE0651017 are available.

5.3. RISK TO BEES

Honey bees foraging on flowers and weeds in or adjacent to treated crops may be exposed to phosalone by direct spraying, through contact with fresh or dry residues, or by oral uptake of contaminated pollen, nectar and honey dew. For the representative use in pome fruit orchards, with application at an early growth stage before flowering and a second application at ripening of fruits, no significant exposure of foraging bees is expected.

The available studies with phosalone and the formulated product indicate a high oral and contact toxicity to honeybees. The results also indicate that the formulation is more toxic than the active substance alone. The calculated HQ values were above the Annex VI trigger indicating a high risk. Several higher tier studies are available but since these studies used other formulations or unrealistic

exposure duration they do not allow a definite conclusion. The risk to bees was discussed at the experts' meeting and it was concluded that the risk is high and risk mitigation measures have to be set at Member State level also for flowering weeds below the trees.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Non-target arthropods may be exposed to products containing phosalone by direct spraying, contact with fresh or dry residues, oral uptake of contaminated prey, nectar or pollen or via host organisms. Laboratory studies on inert substrates are available for the two standard species *Aphidius rhopalosiphi* and *Typhlodromus pyri*, for the foliar dwelling *Crysoperla carnea* and the ground dwelling *Poecilus cupreus* with an SC formulation containing 500 g a.s./L. Extended laboratory studies are available for *A. rhopalosiphi, T. pyri* and *C. carnea* with the lead formulation. An additional extended study with *T. pyri*, but with another formulation is also available. The results indicate that the lead formulation is more toxic and therefore studies using other formulations than the lead formulation were disregarded for the risk assessment.

The LR_{50} (45.8 g a.s./ha) derived from the laboratory study was used for the risk assessment for *T. pyri*. The in-field HQ value based on a single application of 900 g a.s./ha and calculated according to the ESCORT II procedure is 19.7 and the off-field HQ values are 5.7 (early application) and 3.1 (late application). These values are above the trigger of 2 and thus indicate a potential high risk both in-field and off-field. Even if phosalone residues on vegetation can be assumed to degrade relatively rapidly allowing for recolonisation, the off-field risk has to be addressed and further data e.g. a field study with predatory mites under the intended conditions is required.

For the parasitoid *A. rhopalosiphi* first tier studies resulted in complete mortality. Also residues on a natural surface caused harmful effects at an in-crop rate. With 35 days aged residues effects were below 50%, hence indicating a potential for recolonisation from off-field populations. However, a rate of 316 g a.s./ha caused 40% mortality and 74% reduction of fecundity. This rate is slightly higher than the estimated off-field rate at 3 m distance (263 g a.s./ha) but it cannot be excluded that off-field populations are affected. The EFSA therefore proposes risk mitigation measures at Member State level to protect off-field non-target parasitoids.

The extended laboratory study on *C. carnea* showed effects on mortality below 50% and no effect on reproduction at in-field rates and hence the risk to this species is considered low. Since the first tier study with *P. cupreus* was disregarded a new study on the toxicity to one additional species is required.

5.5. RISK TO EARTHWORMS

Studies on the acute toxicity to earthworms from phosalone and two formulations, EXP 60308 (a WP formulation containing 313 g phosalone/kg) and AE F016629 00 EC34 A1 (an EC formulation containing 350 g phosalone/L) are available. The calculated TER values are well above the trigger of 10. It can be concluded that the acute risk of phosalone to earthworms is low from the proposed use.

Sublethal effects were however observed in the studies and it was agreed in the experts' meeting to set a data requirement for a long-term reproduction study with earthworms to make sure that the use of phosalone does not cause unacceptable effects on earthworm reproduction.

No major soil metabolites of phosalone were detected in the soil degradation studies.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

No data on other soil non-target macro-organisms are available since DT_{90} <100 days in soil, only two applications are proposed and the acute risk for earthworms was considered low. However sublethal effects were observed in the acute studies with earthworms and therefore a data requirement for a long-term study with earthworms was agreed in the experts' meeting (see 5.5). The conclusion for risk to non-target soil macro-organisms is therefore pending the evaluation of this study.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of phosalone on soil microflora respiration and nitrogen turnover were tested. No deviations of more than 25% were observed. Hence the Annex VI trigger was met indicating a low risk. No major soil metabolites of phosalone were detected in the soil degradation studies.

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

Results from a standard screening test using 5 different crops and 9 monocotyledonae and 10 dicotyledonae weed species with the product Zolone 34 EC are available. At the intended representative use rates, the risk to non-target plants is expected to be low.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Data from a test with activated sludge are available and indicate that the risk to biological methods of sewage treatment plants is low.

6. Residue definitions

Soil

Definitions for risk assessment: phosalone

Definitions for monitoring: phosalone

Water

Ground water

Definitions for exposure assessment: phosalone, AE0651017[15] (pending on PECgw calculations)

Definitions for monitoring: phosalone, AE0651017 (pending on PECgw calculations)

[15] AE 0651017: (=RP18726) 2-amino-7-chloro-3H-phenoxazin-3-one; phenoxazone

Surface water

Definitions for risk assessment: phosalone, AE0651017

Definitions for monitoring: phosalone

Air

Definitions for risk assessment: phosalone

Definitions for monitoring: phosalone

Food of plant origin

Definitions for risk assessment: phosalone, RP 12244[16]

Definitions for monitoring: phosalone

Food of animal origin

Definitions for risk assessment: data not sufficient

Definitions for monitoring: data not sufficient

[16] RP 12244: oxophosalone

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Phosalone	Very low to low persistent (DT_{50lab} = 0.8 – 4.9 d)	Acute risk low but sublethal effects observed. Long-term reproduction study required

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
Phosalone	Low to slight mobility (870 – 2680 dm^3/kg)	FOCUS modelling: no Lysimeter: no reliable data	Yes	Yes	Very toxic EC_{50} = 0.74 µg/L for *Daphnia*
AE0651017 (phenoxazone)	No data	FOCUS modelling: no data Lysimeter: no reliable data	No information available	LD_{50} >2000 mg/kg bw Ames test positive In vivo UDS negative	EC_{50} >0.83 mg/L for *Daphnia* (highest dose tested)

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Phosalone	Very toxic EC_{50} = 0.74 µg/L for *Daphnia*
AE0651017 (phenoxazone)	EC_{50} >0.83 mg/L for *Daphnia* (highest dose tested)

Air

Compound (name and/or code)	Toxicology
Phosalone	Harmful, LC_{50} 1.26 mg/L

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

- Spectra for the relevant impurity *S*-chloromethyl *O*,*O*-diethyl phosphorodithioate (AE F073749) according to Directive 94/37/EC (no submission date proposed, data gap identified by EFSA after the expert meetings, refer to chapter 1).
- A shelf-life study (incl. a validated analytical method) to ensure that levels of *S*-chloromethyl *O*,*O*-diethyl phosphorodithioate (AE F073749) do not increase upon storage (no submission date proposed, data gap identified by EFSA after the expert meetings, refer to point to chapter 1).
- An acceptable micronucleus or chromosome aberration test *in vivo* with phosalone should be submitted at Member State level (refer to point 2.4).
- In order to determine the threshold level of the impurity AE F073749 in the technical material, additional genotoxicity tests with the current technical material are required (Ames test, gene mutation test with mammalian cells, and chromosome aberration test). Equivocal results in vitro should be substantiated by in vivo experiments (no submission date proposed, data gap identified by EFSA after the expert meetings, refer to point 2.8).
- In order to determine the threshold level of the impurity AE F073749 in the technical material and to confirm the reference values for phosalone, a new carcinogenicity study with the current technical material is required (no submission date proposed, data gap identified by EFSA after the expert meetings, refer to point 2.8).
- Further information on the metabolism of phosalone in lactating ruminants to allow the identification of the major compounds of the residue in animal tissues (relevant for the representative uses evaluated; no submission date proposed; refer to point 3.2).
- Depending on the outcome of the evaluation of the required data on metabolism in lactating ruminants and depending on the resulting decision on the residue definition, a feeding study in lactating ruminants should be conducted (relevant for the representative uses evaluated; no submission date proposed; refer to point 3.2).
- Potential groundwater contamination assessment for the soil metabolite AE0651017 (phenoxazone) (relevant for the representative uses evaluated; no submission date proposed; data gap identified by EFSA after the expert meetings; refer to point 4.2.2).
- The long-term risk to insectivorous birds must be addressed (relevant for the representative use evaluated; no submission date proposed; refer to point 5.1).
- The acute risk to small herbivorous mammals and the long-term risk to small and medium sized herbivorous mammals, insectivorous mammals and earthworm-eating mammals must be addressed (relevant for the representative use evaluated; no submission date proposed; refer to point 5.1).
- Data on log P_{ow} and bioaccumulation potential for the metabolite AE0651017 (relevant for the representative use evaluated; no submission date proposed; refer to point 5.2).
- A field study with predatory mites (relevant for the representative use evaluated; no submission date proposed; refer to point 5.4).

- A laboratory study with one additional crop relevant arthropod species (relevant for the representative use evaluated; no submission date proposed; refer to point 5.4)
- A long-term reproduction study with earthworms (relevant for the representative use evaluated; no submission date proposed; refer to point 5.5)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide as proposed by the applicant which comprises foliar spraying to control chewing and sucking insects in pome fruit (apples, pears) at application rate up 900 g per hectare. Phosalone can be used as insecticide and acaricide. It should be noted that only the use as insecticide was supported for the EU review programme.

The representative formulated product for the evaluation was "Zolone" (Rubitox; "AE F016629 00 EC A1xx"), an emulsifiable concentrate (EC), registered under different trade names in Europe.

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a multi-method (the German S19 method has been validated). For the other matrices only single methods are available to determine residues of phosalone.

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

The absorption of phosalone is high (80-90 %) and rapid. Bioaccumulation is low, it is rapidly and extensively metabolised and excreted mainly via urine. Phosalone has a high acute oral toxicity (LD_{50} 120 mg/kg bw), and a moderate acute toxicity by inhalation (LC_{50} 1.26 mg/L) or dermal exposure (LD_{50} 1530 mg/kg bw). The skin and eye irritating effects are minimal but the compound is a skin sensitizer. Proposal for classification is **T, R 25 "Toxic if swallowed"; Xn, R 20/21 "Harmful by inhalation and in contact with skin"; Xi, R 43 "May cause sensitization by skin contact"**.

Cholinesterase inhibition was observed in short term toxicity studies (8-week rat and 52-week dog), and the relevant NOAEL was 0.9 mg/kg bw/d in both studies.

Phosalone was tested in six *in vitro* and two *in vivo* mutagenicity assays. Due to weakly positive results *in vitro*, and an unconclusive *in vivo* test, further *in vivo* test should be submitted at Member State level.

In the long-term studies (rat and mouse) there was no evidence of a tumorigenic potential, and the inhibition of brain acetylcholinesterase activity lead to a NOAEL of 1.8 mg/kg bw/day in the rat. No direct effect on reproductive performance, fertility or foetal parameters was demonstrated. The rat parental, pup and reproductive NOAEL is 3.5 mg/kg bw/day, and the rat/rabbit maternal and developmental NOAEL is 10 mg/kg bw/day.

The metabolite **oxophosalone** was found to be more toxic than phosalone after dermal administration, whereas the sulphone, sulphoxide and sulphide metabolites are less toxic. All these four metabolites have been identified in the ADME-studies in rats.
The soil metabolite **phenoxazone** has a low acute oral toxicity in rats, but is mutagenic towards one bacterial strain, in the presence of metabolic activation. However in an *in vivo/in vitro* UDS assay in rat hepatocytes, phenoxazone was proved to be non-genotoxic.
The **ADI** and **AOEL** are 0.01 mg/kg bw/day based on the NOAEL of the 1-year dog study, with the use of a safety factor of 100. The **ARfD** is 0.1 mg/kg bw/day based on the NOAEL of the teratology study in rabbits, applying the safety factor of 100.
The dermal absorption values are 3.6 % for the field dilution and 0.7 % for the concentrate.
With the use of the German model, the operator exposure estimates are below the AOEL if personal protective equipment is worn during mixing/loading and application, whereas this is always exceeded with the UK POEM.
The impurity **AE F073749** has been shown 10 times more toxic than phosalone as well as mutagenic, but its level has not been confirmed in the toxicological batches used for phosalone. Further genotoxicity and carcinogenicity data are required with the current technical material in order to establish a threshold level for the impurity in the technical material, and to confirm the reference values for phosalone.

The metabolism of phosalone has been investigated in fruits. The metabolism is rather limited and all metabolites formed were found at low levels. Phosalone is the dominant compound of the residue and the residue definition for monitoring is proposed to be phosalone only. One metabolite, oxophosalone, anticipated to be at least as toxic as the parent compound, is included in the residue definition for risk assessment. This metabolite should be toxicologically characterized.
Supervised residue trials in apples and pears were submitted, allowing a MRL proposal of 2 mg/kg for pome fruits. The effects of processing on the nature and the level of residues were investigated. Although studies in buffer solution demonstrated an extensive degradation under conditions simulating baking/brewing/boiling and sterilisation, phosalone seems to be stable under practical conditions of production of apple juice and puree. The reasons for this have not been fully elucidated. The transfer factors to apple juice and puree are very low, with residues essentially left in the pomace and peel fractions. One degradation product observed after processing in buffer solution needs to be investigated for its toxicological relevance as it was not identified in the rat metabolism (2-amino-7-chloro-3H-phenoxazin-3-one).
As the intended uses are restricted to pome fruits, studies on succeeding or rotational crops are not required.
Livestock can be exposed to residues of phosalone through consumption of pomace. Metabolism studies in lactating goat indicated that phosalone is not found in animal tissues. Only metabolites could be identified. The information obtained from the metabolism study in livestock is not sufficient to propose a residue definition and further information is needed on the identification of major residues in animal matrices. From the data submitted it may be expected that some metabolites may be present at measurable levels in animal tissues.

The consumer risk assessment was carried out taking into account chronic and acute exposures to phosalone only. The potential contribution of oxophosalone to the toxicological burden as well as of residues present in animal commodities is not known at this stage. Therefore no robust conclusions can be drawn. Considering phosalone only, the acute and chronic exposure assessments, made according to current guidelines, give results below the ADI but may exceed in some cases the ARfD. However, the level of the proposed MRL in pome fruits, which is significantly lower than the level considered in exposure assessments, causes concern in terms of consumer safety. The acute exposure of toddlers may lead to higher exceedance of the ARfD for samples in compliance with the proposed MRL but with high unit to unit variability of residues.

Under aerobic conditions phosalone is rapidly metabolised in soil, initially to many minor metabolites, and ultimately to CO_2 and soil bound residues. The extensive formation of soil bound residues is rapid and is due in part to the formation of metabolites containing functional groups which are rapidly and tightly bound to organic matter in soil. Under anaerobic conditions the degradation of phosalone follows the same pathway as observed under aerobic conditions with the exception that under anaerobic conditions metabolite phenoxazone (AE 0651017) was not observed while the metabolite AE F114970 (2-amino-5-chlorophenol) was found up to 20% AR in the water phase (day 3) and a maximum of 8.1% AR (day 14) in soil extracts.

Phototransformation on soil is not an important route of transformation of phosalone in the environment. Available information on laboratory aerobic degradation of phosalone resulted in dissipation time to 50% (DT_{50}) ranging from 0.8 to 4.9 days, classifying phosalone as very low to low persistent. The batch soil adsorption/desorption studies indicate that phosalone is low to slight mobile in soil (Koc = 870 – 2680 dm^3/kg).

Hydrolysis of phosalone is pH dependant. Phosalone is relatively stable to transformation by hydrolysis at pH 4 and pH 7, but is hydrolyzed at pH 9. The calculated DT_{50} values at 20 ºC were > 365 d (pH 4), 321 d (pH 7) and 17.8 d (pH 9). Two metabolites AE0941954 and AE F054014 were found up to 21% AR at pH 9. Another major metabolite, AE 0651017 (=RP18726, phenoxazone) was found in the water phase of the sediment/water study and further assessed for hydrolytic degradation (DT_{50} at pH 7 and 20ºC = 21 days). Phosalone was rapidly degraded by photolysis.

The active substance dissipates rapidly in the water/sediment system (DT_{50} water = 2.8-4.7 d and DT_{50} whole system = 3.7 - 6.8 d). The rapid disappearance of phosalone from the water phase was due to a shift towards the non-extractable residues fraction. The major metabolite was AE0651017 (=RP18726, phenoxazone) with maximum levels in the water phase of 13.1% AR and 22.4% AR at 14 and 8 days. Mineralization to CO_2 was low and reached levels of about 10% at 60 days.

PEC_{sw} and PEC_{sed} were recalculated for phosalone and the major metabolite AE0651017.

Residues of phosalone in groundwater were modelled using FOCUS PELMO 2.2.2. All relevant scenarios resulted in predicted groundwater concentrations of phosalone below the trigger value of 0.1 µg/L. As the genotoxic potential for the soil metabolite AE0651017 (phenoxazone) has not been proven but cannot be excluded, groundwater contamination assessment for this metabolite is required.

Concentration of phosalone in the air compartment and transport through it is not expected to be significant.

A high long-term risk was identified for insectivorous bird, considering the blue tit as a focal species. A high acute risk was also identified for small herbivorous mammals and a long-term risk to small and medium sized herbivorous mammals, insectivorous mammals and earthworm-eating mammals. Additionally a high risk was identified for the aquatic environment. Even with a buffer zone of 50 m the TER values are below the agreed trigger value for an available microcosm study. The risk to honey bees is high and risk mitigation measures should be set at Member State level also for flowering weeds below trees in orchards. The available studies indicate a high potential risk to non-target arthropods, both in-field and off-field. Even if phosalone residues on vegetation can be assumed to degrade relatively rapidly allowing for recolonisation, the off-field risk has to be addressed and further data e.g. a field study with predatory mites under the intended conditions is required. Risk mitigation measures at Member State level to protect off-field non-target parasitoids are proposed. Furthermore, a new study on one additional arthropod species is required. The acute risk to earthworms is considered low. However, sublethal effects were observed in the acute studies and therefore a long-term reproduction study is required to make sure that phosalone does not cause unacceptable effects on earthworm reproduction. The risk to soil micro organisms, non-target flora and fauna and biological methods of sewage treatment plants is considered low.

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

- The AOEL was exceeded for operators exposed to phosalone. Therefore, the use of PPE is needed both during mixing/loading (gloves) as well as during applications (gloves, standard protective garment, hat and face-shield) in order to have estimated exposure level below the AOEL (refer to point 2.12).
- Risk mitigation measures should be considered at Member State level to reduce the risk to honey bees. Application when bees are present must be avoided. Risk mitigation measures at Member State level should also be considered for flowering weeds below the trees (refer to point 5.3).
- Risk mitigation measures should be considered to reduce the risk to off-field parasitoids (refer to point 5.4).

Critical areas of concern

- At the moment the specification of the technical material should be regarded as provisional, due to the fact that a maximum level for the relevant impurity AE F073749 cannot be set.
- The impurity AE F073749 has been shown 10 times more toxic than phosalone and mutagenic, but its level has not been confirmed in the toxicological batches used for phosalone. Further genotoxicity and carcinogenicity data are required with the current technical material in order to establish a threshold level for the impurity in the technical material, and to confirm the reference values for phosalone.

- An acute dietary risk for toddlers consuming apples and pears is expected as the ARfD will be very likely exceeded by the global toxicological burden of phosalone and its metabolite RP 12244. Even for phosalone only, the ARfD has been shown to be exceeded for some consumption patterns.
- The level of the proposed MRL in pome fruits, which almost 2 times higher the highest residue level in field trials in critical conditions, causes concern in terms of consumer safety. The acute exposure of toddlers may exceed the ARfD for samples in compliance with the proposed MRL but with high unit to unit variability of residues.
- A high long-term risk to insectivorous birds.
- A high acute risk for small herbivorous mammals, high long-term risk to small and medium sized herbivorous mammals, insectivorous mammals and earthworm-eating mammals.
- A high risk to the aquatic environment even with buffer zones of 50 m.
- A high risk to honey bees. Application when bees are present must be avoided.
- A high risk to non-target arthropods. Risk mitigation measures should be considered.

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

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

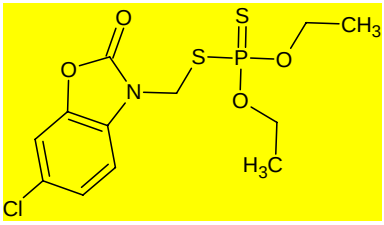
Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Phosalone
Function (e.g. fungicide)	Insecticide, acaricide
Rapporteur Member State	Austria
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	*S*-(6-chloro-2,3-dihydro-2-oxo-1,3-benzoxazol-3-ylmethyl *O*,*O*-diethyl phosphorodithioate or *S*-6-chloro-2,3-dihydro-2-oxobenzoxazol-3-ylmethyl *O*,*O*-diethyl phosphorodithioate
Chemical name (CA) ‡	*S*-[(6-chloro-2-oxo-3(*2H*)-benzoxazolyl)-methyl] *O*,*O*-diethyl phosphorodithioate
CIPAC No ‡	109
CAS No ‡	2310-17-0
EEC No (EINECS or ELINCS) ‡	218-996-2
FAO Specification ‡ (including year of publication)	The phosalone content shall be declared not less than 930 g/kg and when determined, the content obtained shall not differ from the declared by more than +/- 20 g (1988) Impurities: Water and volatile impurities: max.: 10 g/kg
Minimum purity of the active substance as manufactured ‡ (g/kg)	940 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	*S*-chloromethyl *O*,*O*-diethyl phosphorodithioate (AE F073749) A max value cannot be set at the moment
Molecular formula ‡	$C_{12}H_{15}ClNO_4PS_2$
Molecular mass ‡	367.82

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

Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	46.9 °C	purity: 995 g/kg
Boiling point (state purity) ‡	Not relevant	
Temperature of decomposition	174.6 °C	purity: 995 g/kg
Appearance (state purity) ‡	White crystalline powder	purity: 995 g/kg
Relative density (state purity) ‡	d^{20}_{20} = 1.49	purity: 995 g/kg
Surface tension	71.78 mN.m^{-1}	purity: 937 g/kg
Vapour pressure (in Pa, state temperature) ‡	1.56 x 10^{-5} Pa (25 °C)	purity: 995 g/kg
Henry's law constant (Pa m^3 mol $^{-1}$) ‡	2.04 x 10^{-3} Pa·m^3·mol^{-1}	
Solubility in water ‡ (g/l or mg/l, state temperature)	pH 5.9: 1.4 mg/L at 20 °C	purity: 995 g/kg
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	Solubility at 20 °C: acetone dichloromethane ethyl acetate *n*-heptane toluene methanol *n*-octanol	purity: 949 g/kg > 1000 g/L > 1000 g/L > 1000 g/L 26.3 g/L > 1000 g/L > 1000 g/L 266.8 g/L
Partition co-efficient (log POW) ‡ (state pH and temperature)	log P_{OW} = 4.01 at 20 °C	purity: 995 g/kg
Hydrolytic stability (DT50) ‡ (state pH and temperature)	DT_{50} (20) pH 4: > 365 d pH 7: 321 d pH 9: 17.8 d	DT_{50} (25 °C) > 365 d 157 d 7.6 d
Dissociation constant ‡	Not relevant due to chemical structure of phosalone.	
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	Neutral conditions (methanol): wavelength [nm] / ε (molar absorption coefficient) [L*mol^{-1}*cm^{-1}] 203 46918 236 14820 284 4602 291 3575	purity: 995 g/kg

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

Photostability (DT50) ‡ (aqueous, sunlight, state pH)	"Suntest"*) Sunlight**) 50 °N 40 °N 30 °N DT_{50} 0.4 d 1.3 d 1.2 d 1.2 d *) continuous irradiation **) correlation of the half-life to natural summer sunlight days
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	$\Phi = 3.93 * 10^{-3}$ molecules degraded photon^{-1}
Flammability ‡	Not highly flammable.
Explosive properties ‡	Not explosive.

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

List of representative uses evaluated*

CROP and /or situation (a)	Member State or Country	Product name	F G or I (b)	Pest or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Pome fruit Apples Pears	Northern and Southern Europe	Zolone	F	Chewing and sucking insects	EC	350 g/L	Medium/ high volume foliar spraying	BBCH 51-59 (T1) BBCH 85 (T2)	2	T1-T2: > 50 d	0.04 – 0.09	1000 - 1500	0.6 – 0.9	28	[1] [2] [3]

[1] The risk assessment has revealed data gaps in section 2 and 5.
[2] The risk assessment has revealed a risk (exceedance of relevant threshold) in section 5.
[3] The risk assessment has revealed that a risk is likely to be present in section 3 (Acute dietary risk for the consumer)

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

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

Appendix 1.2: Methods of Analysis

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

Technical as (principle of method)	Reversed phase HPLC with water/perchloric acid/ acetonitrile as mobile phase and UV detection at 210 nm; external standard evaluation.
	CIPAC method: Gas chromatography with thermal conductivity or flame ionisation detector.
Impurities in technical as (principle of method)	1) HPLC using a reversed phase column and UV detection 2) GC-FID on fused silica capillary column
Plant protection product (principle of method)	Reversed phase HPLC with UV detection at 280 nm.
	CIPAC method: Gas chromatography with thermal conductivity or flame ionisation detector.

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Extraction by acetone/water; liquid-liquid partition; quantification by GC-NPD or GC-FPD; confirmation by GC-MS. LOQ = 0.01 - 0.05 mg/kg for apples LOQ = 0.05 mg/kg for rape seed and barley grain
	Multi-residue enforcement method (DFG S19): Extraction with acetone, liquid-liquid partition; gel permeation chromatography; quantification by GC-NPD; confirmation by GC/MS/MS. LOQ = 0.05 mg/kg for apples
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	At the moment no residue definition can be proposed Extraction by acetone/methanol or just acetone; solvent partition; solid phase extraction using a florisil cartridge; quantification by GC-MS or GC-NPD. LOQ = 0.05 mg/kg for meat, fat, kidney, liver and eggs LOQ = 0.01 mg/kg for milk
Soil (principle of method and LOQ)	Extraction with acetone/water; solid phase extraction using a diol cartridge; quantification by GC-ECD or GC-MS. Analytes: phosalone and RP018726 LOQ = 0.02 mg/kg

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

Water (principle of method and LOQ)	Extraction with *n*-hexane; quantification by GC-ECD or NPD. LOQ = 0.1 µg/L for mineral and tap water LOQ = 0.1 - 1.0 µg/L for surface water (river)
	Extraction with dichloromethane; quantification by GC-ECD or NPD. LOQ = 0.1 µg/L for mineral and tap water LOQ = 1.0 µg/L for surface water (river)
Air (principle of method and LOQ)	Adsorbed on cartridges filled with porous styrene/divenylbenzene copolymer; desorption with toluene; quantification by GC-ECD. LOQ = 0.033 µg/m^3
Body fluids and tissues (principle of method and LOQ)	Extraction by water, aqueous saturated sodium chloride solution and methylene chloride; solvent partition; quantification by GC-MS LOQ = 0.05 mg/kg for blood and urine
	Tissues: see method for the determination of residues in food of animal origin

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 ‡	Rapid, 80 – 90 % after single and repeated oral dose (rat studies)
Distribution ‡	Highest levels found in liver and kidneys and intestine + contents
Potential for accumulation ‡	No potential for accumulation
Rate and extent of excretion ‡	Rapid, 90 % within 24 - 48 hours, mainly via urine
Metabolism in animals ‡	Extensively metabolized; four different metabolic pathways: sulphate conjugation, oxidative desulfation, oxidative dealkylation and hydrolysis
Toxicologically significant compounds ‡ (animals, plants and environment)	Phosalone, metabolite oxophosalone, impurity AE F073749

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	120 mg/kg bw	**T, R 25**
Rat LD_{50} dermal ‡	1530 mg/kg bw	**Xn, R 21**
Rat LC_{50} inhalation ‡	1.26 mg/L aerosol, nose-only exposure	**Xn, R 20**
Skin irritation ‡	Mildly irritating, no classification proposed	
Eye irritation ‡	Slightly irritating, no classification proposed	
Skin sensitization ‡ (test method used and result)	Sensitizing (Magnusson and Kligman)	**Xi, R 43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Reduced body weight and body weight gain; cholinesterase inhibition
Lowest relevant oral NOAEL / NOEL ‡	52-weeks dog, 0.9 mg/kg bw
Lowest relevant dermal NOAEL / NOEL ‡	No data – not required
Lowest relevant inhalation NOAEL / NOEL ‡	No data – not required

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	No genotoxic potential of relevance to human risk assessment

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

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

Target/critical effect ‡	Reduced body weight gain; cholinesterase inhibition; histological changes in adrenals (degeneration); testicular tubular atrophy (degeneration)
Lowest relevant NOAEL / NOEL ‡	104-weeks rat, 1.8 mg/kg bw
Carcinogenicity ‡	No evidence of a carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Increased pup mortality; decreased growth rate and decreased litter and pup weight at parental toxic dose
Lowest relevant reproductive NOAEL / NOEL ‡	Rat: 3.5 mg/kg bw/d for parental and reproductive toxicity
Developmental target / critical effect ‡	Increased embryonic resorptions and postimplantation loss
Lowest relevant developmental NOAEL / NOEL ‡	Rabbit: 10 mg/kg bw/d (maternal, developmental, and offspring)

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

Target/critical effect	Tremor, low locomotor activity, cholinesterase inhibition
Lowest relevant NOAEL / NOEL	Single oral rat 25 mg/kg bw 13-weeks rat establishment of NOAEL not possible (plasma-, erythrocyte- and brain cholinesterase inhibition at all dose levels)

Other toxicological studies ‡ (Annex IIA, point 5.8)

Metabolites:	Oxophosalone (RP 12244, AE 0591540 resp.): LD_{50} oral rat 12 mg/kg bw LD_{50} dermal rat 380 mg/kg bw; 19888 R.P.(sulphone): LD_{50} oral mouse > 5000 mg/kg bw 19889 R.P.(sulphoxid): LD_{50} oral mouse 350 mg/kg bw

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

Impurities:	19914 R.P.(sulphide): LD_{50} oral mouse 590 mg/kg bw Phenoxazone (soil metabolite): LD_{50} oral rat > 2000 mg/kg bw Ames test positive in vivo/in vitro UDS negative AE C500659/RPA 13515: LD_{50} 100-200 rat oral Ames test negative AE F073749/RPA 590184: LD_{50} oral rat 18 mg/kg bw Ames test positive

Medical data ‡ (Annex IIA, point 5.9)

.....	Available data indicate no detrimental effects on health of plant personnel in manufacturing of phosalone; studies on worker exposure indicate inhibition of cholinesterase activity

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/d	52-week dog study	100
AOEL ‡	0.01 mg/kg bw/d	52-week dog study	100
ARfD ‡ (acute reference dose)	0.1 mg/kg bw/d	rabbit: teratology study	100

Dermal absorption (Annex IIIA, point 7.3)

Zolone	0.7 % for the concentrate and 3.6 % for the spray dilution based on in vivo and in vitro dermal absorption studies

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

Acceptable exposure scenarios (including method of calculation)

Operator	Application rate 900 g/ha German model: without PPE — with PPE - tractor appl.: 462% — 40% of the AOEL - hand held ap.: 416% — 54% of the AOEL UK model: without PPE — with PPE - tractor appl.: 1100% — 400% of the AOEL - hand held ap.: 4460% — 600% of the AOEL
Workers	The estimated worker exposure is below the AOEL (without PPE 72 %, with PPE 3.6 % of AOEL)
Bystanders	The estimated exposure of a bystander is 33 % of AOEL

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T,	Toxic;
	R 20,	Harmful by inhalation
	R 21,	Harmful in contact with skin
	R 25,	Toxic if swallowed
	R 43	May cause sensitisation by skin contact

‡ 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	Fruits (grapes, apples)
Rotational crops	Not required
Plant residue definition for monitoring	phosalone
Plant residue definition for risk assessment	Phosalone and oxophosalone
Conversion factor (monitoring to risk assessment)	Data not sufficient to propose a conversion factor

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

Animals covered	Lactating ruminants (goat)
Animal residue definition for monitoring	Data not sufficient to propose a residue definition
Animal residue definition for risk assessment	Data not sufficient to propose a residue definition
Conversion factor (monitoring to risk assessment)	Data not sufficient
Metabolism in rat and ruminant similar (yes/no)	Data not sufficient
Fat soluble residue: (yes/no)	Data not sufficient

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

.....	Not required

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

.....	Stable at – 18 ° C for 24 months (peaches, almonds)

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

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: Yes (2.59 mg/kg feed item)	Poultry: no	Pig: no
Muscle	Feeding study in lactating ruminant 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 phosalone/kg] (a)	Recommendation/comments	MRL [mg phosalone/kg]	STMR [mg phosalone/kg] (b)
Apples	North	PHI = 27 – 31: 1 x 0.28, 1 x 0.36, 1 x 0.46, 1 x 0.55, 1 x 0.60, 1 x 0.65, 1 x 0.67, 1 x 0.75, 1 x 1.1, 1 x 1.2	According to the working document 7525/VI/95-rev.7 (draft) extrapolation from the results of residue trials on apples or pears (with a minimum of 4 apple trials) to the whole group "pome fruit" is possible	2	0.55
Pears	North	PHI = 27 – 29: 1 x 0.45, 1 x 0.49, 1 x 0.51			
Apples	South	PHI = 27 - 29 1 x 0.12, 1 x 0.19, 1 x 0.53, 1 x 0.77, 1 x 0.84, 1 x 0.87, 1 x 0.91, 1 x 0.93, 1 x 0.95, 1 x 1.2		2	0.81
Pears	South	PHI = 28 - 30 1 x 0.23, 1 x 0.26			

(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	0.01 mg/kg bw/day		
TMDI (European Diet) (% ADI)	TMDI (European diet; adult of 60 kg): 17% of ADI TMDI (German diet; girl of 13.5 kg body weight): 72% of ADI		
IEDI (% ADI)	IEDI (European diet; adult of 60 kg): 7% of ADI IEDI (German diet; girl of 13.5 kg body weight): 8% of ADI		
Factors included in IEDI	STMR = 0.81 mg/kg Transfer factor (juice) = (<) 0.02 (only used for the assessment on basis of the German diet)		
ARfD	0.1 mg/kg bw/day		
Acute exposure (% ARfD)		adult aged 16 – 64 years	toddlers aged 1 ½ - 4 ½ years
	apples – fruit	17 %	72 %[17]
	apples – juice	0.1 %	0.6 %
	pears - fruit	20 %	98 %[18]
Factors included in acute exposure calculations	Highest residue of 1.2 mg/kg (not MRL), variability factor of 7		

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
apples / apple juice	4	<0.02	-
apples / apple juice	4	0.05	-
apples / apple juice	4	3.2	-

* 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)

Apples	2 mg/kg [1])
Pears	2 mg/kg [1])

[1]) Residue definition: phosalone

[17] Calculations by EFSA with recent consumption data for German toddlers indicated acute exposure estimates of 99% ARfD

[18] Calculations by EFSA with recent consumption data for German toddlers indicated acute exposure estimates of 110% ARfD

‡ 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 ‡	After 120 days: 15-30 %AR ^{14}C-chlorophenyl-labelled (n= 4)
Non-extractable residues after 100 days ‡	After 120 days: 67-80 %AR ^{14}C-chlorophenyl-labelled (n= 4)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	No major soil metabolites under aerobic conditions

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

Anaerobic degradation ‡	Major metabolite AE F114970: max. 20 %AR in the water phase (day 3) and max. 8.1 %AR in the sediment phase (day 14)
Soil photolysis ‡	No significant degradation by photolytic processes on soil surface.

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

Method of calculation	1st order reaction kinetics; r^2 = 0.876-0.997; n = 7
Laboratory studies ‡ (range or median, with n value, with r^2 value)	DT_{50lab} (20°C, aerobic): 0.8 - 4.9 days; mean = 2.0 days DT_{90lab} (20°C, aerobic): 2.8 - 16.3 days; mean = 7.2 days DT_{50lab} (10°C, aerobic): 8.5 days, n = 1 KIM model; r^2 = 0.99; n = 1 DT_{50lab} (20°C, anaerobic): Phosalone: 0.1 days (water phase) 4.3 days (soil) AE F114970: 10.2 days (water phase) 29.1 days (entire system)
	Degradation in the saturated zone: not provided, not requested. Phosalone is not expected to leach into deep soil layers.
Field studies ‡ (state location, range or median with n value)	No data provided, not requested
Soil accumulation and plateau concentration ‡	No data provided, not requested

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡	Sandy loam: K_{OC} = 2680, K_f = 22.5, 1/n = 0.87 Silty clay loam: K_{OC} = 870, K_f = 6.2, 1/n = 0.71 Loam: K_{OC} = 2640, K_f = 35.1, 1/n = 0.96 Clay: not generated due to fast degradation of phosalone
K_d	Sandy loam: $K_{F,DES}$: 40.0 Silty clay loam: not generated, fast degradation Loam: $K_{F,DES}$: 53.8 Clay: not generated, fast degradation
pH dependence (yes/no) (if yes type of dependence)	No

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

Column leaching ‡	Study available, but not acceptable.
Aged residues leaching ‡	Study available, but not acceptable.
Lysimeter/ field leaching studie ‡	Not provided, not requested

PEC (soil) (Annex IIIA, point 9.1.3)

Method of calculation	$PEC_s(t) = \sum_{i=1}^{n} PEC_{s,\ init,\ i} \bullet e^{-k(t-t_i)}$ $TWAC_{1\ day}(T_j) = \frac{PEC(T_{j-1}) + PEC(T_j)}{2} \bullet (T_j - T_{j-1})$ $TWAC_{m\ days}(T_j) = \frac{1}{m} \bullet \sum_{k=1}^{m} TWA_{1\ day}(T_{j+1-k})$
Application rate	2 x 900 g a.s./ha to apples (BBCH 50 and 85). The interval between the two applications is at least 50 days. Due to the short half life of Phosalone only single application was calculated. Interception: 50% (1st application), 80% (2nd application) DT_{50}: 4.9 days Soil depth: 5 cm Soil density: 1.5 g/cm^3

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

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
	1st application		2nd application	
Initial	0.600	0.600	0.241	0.241
Short term 24h	0.521	0.559	0.209	0.224
2d	0.452	0.523	0.181	0.209
4d	0.341	0.458	0.137	0.184
Long term 7d	0.223	0.381	0.089	0.153
28d	0.011	0.149	0.005	0.060
50d	0.001	0.085	0.000	0.034
100d	0.000	0.042	0.000	0.017

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: Phosalone: 20°C DT_{50} > 365 d pH 7: Phosalone: 20°C DT_{50} = 321 d pH 9: Phosalone: 20°C DT_{50} = 17.8 d AE F054014 and AE F0941954, up to 21 % AR each; three minor unidentified metabolites and a polar fraction (single peaks <10% AR).
	In water/sediment study: Metabolite AE065107, at 20°C DT_{50} = 40 d (pH 4), 21 d (pH 7), 17.8 d (pH 9).
Photolytic degradation of active substance and relevant metabolites ‡	Phosalone: artificial light, latitude 40°N: summer/winter: 1.8/5.8 d Metabolite AE065107: artificial light, latitude 40°N: summer: 1.1 d
Readily biodegradable (yes/no)	No
Degradation in water/sediment	
- DT_{50} water ‡ 20°C	4.7 d (pH 8) and 2.8 d (pH 7.7)
- DT_{90} water ‡	15.7 d and 9.4 d
- DT_{50} sediment ‡	TopFit calculations: 3.98 d (pH 6.2) and 1.56 d (pH 8.1)

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

- DT_{50} whole system ‡	6.8 d (pH of sediment 6.2) and 3.7 d (pH of sediment 8.1)
- DT_{90} whole system ‡	16.1 d and 8 d
Mineralization	Max. 10.2 % and 10 % CO_2 at 60 d, end of study
Non-extractable residues	Max. 65.9 % (30 d) and 67.3 % (59 d), end of study after 60 d
Distribution in water / sediment systems (active substance) ‡	The a.s. partitioned rapidly between water and sediment phase. One hour after application 21.5 – 21.1 % a.s. was found in the sediment phase. Phosalone was eliminated fast from the water phase and declined to 0.1 % - 0 % at day 30 (S1) and at day 14 (S2). DT_{50} in sediment = 3.98 and 1.56 (determined by TopFit calculation)
Distribution in water / sediment systems (metabolites) ‡	Metabolite RP 18726 (=AE 0651017): Water: Max. 13.1 % - 22.4 % after 14 and 8 days DT_{50} = 4.15 and 1.5 d (TopFit calculation) Sediment: Max. 3.4 % - 7.3 % after 14 days DT_{50} = 1.63 and 2.42 d (TopFit calculation)

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

Parent

Method of calculation	The calculation was based on a single application since the DT_{50} of phosalone and the major metabolite AE0651017 were less than 3 x the interval between the applications. The calculation was based on 90th percentile worst case spray drift values from German (BBA) spray drift tables. DT_{50} (water phase) = 3 x 4.7 d
Application rate	Orchards, early and late stage: 2 x 0.9 kg/ha
Main routes of entry	Spray drift RMS calculations with a German national model (Exposit 1.0) for possible entry via drainage and run off available in an addendum (September 2005)

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

Early application:

PEC$_{(sw)}$ (µg / l) Distance / % drift	Single application 3 m / 29.2 % Actual	Single application 3 m / 29.2 % Time weighted average	Single application 50 m / 0.3 % Actual	Single application 50 m / 0.3 % Time weighted average
Initial	87.6	87.6	0.9	0.9
Short term 24h	83.398	85.482	0.857	0.878
2d	79.397	83.431	0.816	0.857
4d	71.962	79.525	0.739	0.817
Long term 7d	62.095	74.118	0.638	0.761
21d	31.201	54.632	0.321	0.561
28d	22.116	47.574	0.227	0.489
50d	7.499	32.588	0.077	0.335
100d	0.642	17.689	0.007	0.182

Late application:

PEC$_{(sw)}$ (µg / l) Distance / % drift	Single application 3 m / 15.73 % Actual	Single application 3 m / 15.73 % Time weighted average	Single application 50 m / 0.22 % Actual	Single application 50 m / 0.22 % Time weighted average
Initial	47.19	47.19	0.66	0.66
Short term 24h	44.926	46.049	0.628	0.644
2d	42.771	44.944	0.598	0.629
4d	38.766	42.840	0.542	0.599
Long term 7d	33.450	39.927	0.468	0.558
21d	16.808	29.430	0.235	0.412
28d	11.914	25.628	0.167	0.358
50d	4.040	17.555	0.057	0.246
100d	0.346	9.529	0.005	0.133

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

Metabolite AE0651017 (=RP 18726)

Method of calculation	The calculation was based on a single application since the DT_{50} of the metabolite AE0651017 was less than 3 x the interval between the applications. The calculation was based on 90th percentile worst case spray drift values from German (BBA) spray drift tables. DT_{50} (water phase) = 4.15 d Max. percentage of metabolite: 22.4% AR Molar fraction: 0.67 relative to phosalone
Application rate	Orchards, early and late stage: 2 x 0.9 kg/ha
Main routes of entry	Spray drift

Early application:

PEC$_{(sw)}$ (µg / l) Distance / % drift	Single application 3 m / 29.2 % Actual	Single application 3 m / 29.2 % Time weighted average	Single application 50 m / 0.3 % Actual	Single application 50 m / 0.3 % Time weighted average
Initial	13.123	13.123	0.135	0.135
Short term 24h	11.105	12.086	0.114	0.124
2d	9.397	11.157	0.097	0.115
4d	6.728	9.572	0.069	0.098
Long term 7d	4.076	7.738	0.042	0.079
28d	0.122	2.780	0.001	0.029
50d	0.003	1.571	0.000	0.016
100d	0.000	0.786	0.000	0.008

Late application:

PEC$_{(sw)}$ (µg / l) Distance / % drift	Single application 3 m / 15.73 % Actual	Single application 3 m / 15.73 % Time weighted average	Single application 50 m / 0.22 % Actual	Single application 50 m / 0.22 % Time weighted average
Initial	7.07	7.07	0.099	0.099
Short term 24h	5.98	6.5	0.084	0.091
2d	5.06	6.01	0.071	0.084
4d	3.62	5.16	0.051	0.072

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

PEC$_{(sw)}$ (µg / l) Distance / % drift	Single application 3 m / 15.73 % Actual	Single application 3 m / 15.73 % Time weighted average	Single application 50 m / 0.22 % Actual	Single application 50 m / 0.22 % Time weighted average
Long term 7d	2.2	4.17	0.031	0.058
28d	0.066	1.5	0.00092	0.021
50d	0.0017	0.85	2.3E-05	0.012
100d	3.9E-07	0.423	5.5E-09	0.0059

PEC (sediment)

Parent

Method of calculation	A PECsw value was used in the ecotoxicological risk assessment for sediment-dwelling organisms. The study with *Chironomus riparius* was conducted with spiked water. Therefore, the PECsediment values, presented below for completeness, have not been relied upon in the ecotoxicology risk assessment. The calculation was based on a single application since the DT_{50} of phosalone and the metabolite AE0651017 were less than 3 x the interval between the applications. The calculation was based on 90th percentile worst case spray drift values from German (BBA) spray drift tables. Phosalone: max. 21.5 % after 1 h, DT_{50} (sediment) = 3.98 d (worst case DT_{50} from Top fit calculation Metabolite AE0651017: max. 7.3 % after 14 d, DT_{50} (sediment) = 2.42 d (worst case DT_{50} from Top fit calculation.)
Application rate	Orchards, late stage: 2 x 0.9 kg/ha

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

PEC$_{(sed)}$ (µg / l) Distance / % drift	Single application 3m / 15.73 % Actual	Single application 3m / 15.73 % Time weighted average	Single application 50 m / 15.73 % Actual	Single application 3 m / 15.73 % Time weighted average
	Phosalone		AE0651017	
Initial	234.14	234.14	53.17	53.17
Short term 24h	196.71	214.88	39.9	46.23
2d	165.27	197.7	29.98	40.48
4d	116.66	168.63	16.9	31.65
Long term 7d	69.19	135.3	7.16	22.95
28d	1.79	47.65	0.017	6.63
50d	0.039	26.88	3.2E-05	3.71
100d	6.4E-06	13.44	1.9E-11	1.86

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUS PELMO 2.2.2
Application rate	2 x 900 g a.s./ha to apples. Interval: 50 days. Interception: 50% (1st application), 80% (2nd application) DT_{50}: 2.1 days (mean of laboratory studies) K_{OC}: 870 (worst case of 3 soils)

PEC$_{(gw)}$

Maximum concentration	not an output of the FOCUS shell; not required
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	80th percentile, in 1 m depth: 0.000 µg/L for all FOCUS scenarios

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

Direct photolysis in air ‡	Not studied, no data requested
Quantum yield of direct phototransformation	3.93 x 10^{-3} molecules/degraded photon
Photochemical oxidative degradation in air ‡	Model of Atkinson: DT_{50}:4 minutes

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

Volatilization ‡	Phosalone formulated as "ZOLONE PM" (EXP 60308): from plant surfaces: no volatilisation after 24 hours Phosalone formulated as "ZOLONE PM" (EXP 60308): from soil: <1 % after 24 hours

PEC (air)

Method of calculation	Not required due to limited volatilisation and rapid photochemical oxidative degradation

$PEC_{(a)}$

Maximum concentration	Negligible

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil: Phosalone Surface water: Phosalone and AE0651017 Ground water: Phosalone and AE0651017 (pending on groundwater assessment) Sediment: Phosalone Air: Phosalone

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

Soil (indicate location and type of study)	No data provided, none requested
Surface water (indicate location and type of study)	No data provided, none requested
Ground water (indicate location and type of study)	No data provided, none requested
Air (indicate location and type of study)	No data provided, none requested

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	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} 120 mg/kg bw (rat)
Acute toxicity to birds ‡	LD_{50} 503 mg/kg bw (domestic chicken)
Dietary toxicity to birds ‡	LC_{50} 1659 ppm (mallard duck) LC_{50} 2033 ppm ≅ LD_{50} 233 mg/kg bw (bobwhite quail)
Reproductive toxicity to birds ‡	NOEC 90 ppm ≅ NOEL 11.9 mg/kg bw (mallard duck)
Reproductive toxicity to mammals ‡	NOAEC 50 ppm ≅ NOAEL 3.5 mg/kg bw (ecologically relevant endpoint, 2-generations rat)

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
Tier 1 (for herbivores interception considered, RUD estimated)					
0.9	apples / pears	insectivorous bird	acute	10.3	10
		insectivorous bird	short-term	8.6	10
		insectivorous bird	long-term	0.44	5
		earthworm-eating bird		9.5	5
		fish-eating bird		36	5
0.9	apples / pears	small herbivorous mammal	acute	1.7	10
		medium herbivorous mammal		11	10
		insectivorous mammal		38	10
		small herbivorous mammal	long-term	0.17	5
		medium herbivorous mammal		1.15	5
		insectivorous mammal		3.09	5
		earthworm-eating mammal		2.2	5
		fish-eating mammal		17.5	5

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
Birds, refinement 1 (refinement of PT)					
0.9	apples / pears	insectivorous bird	short-term	14.1	10
		insectivorous bird	long-term	0.72	5
Birds, refinement 2 (refinement of PT and PD)					
0.9	apples / pears	insectivorous bird	long-term	1.1	5
Mammals (refinement based on measured degradation time in plants, DT_{50} = 5 d))					
		small herbivorous mammal	long-term	0.29	5
		medium herbivorous mammal		1.9	5

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg a.s./l)
Laboratory tests ‡				
Oncorhynchus mykiss	Phosalone	96 h	Mortality, LC_{50}	0.63
Daphnia magna	Phosalone	48 h	Mortality, EC_{50}	0.00074
Scenedesmus subspicatus	Phosalone	72 h	Growth, EbC_{50}	1.1
Daphnia magna	AE0651017	48 h	Mortality, EC_{50}	> 0.83
Oncorhynchus mykiss	Zolone 30WP (= EXP 60308)	96 h	Mortality, LC_{50}	1.06
Daphnia magna	AEF 016629 00 EC34 (= Zolone 35 EC)	48 h	Mortality, EC_{50}	0.000396
Scenedesmus subspicatus	Zolone 30WP (= EXP 60308)	72 h	Biomass, EbC_{50}	0.41
Oncorhynchus mykiss	Phosalone	21 d	Growth NOEC	0.056
Daphnia magna	Phosalone	21 d	Reproduction, NOEC	0.000136
Chrionomus riparius	Phosalone	25 d	Emergence, NOEC	0.0191
Daphnia magna	Rubitox flow (= EXP 05531A)	21 d	Reproduction, NOEC	0.000018

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

Microcosm or mesocosm tests				
Zooplancton community microcosm	AEF 016629 00 EC34 (= Zolone 35 EC)	115 d	community	0.0025

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
Phosalone						
2 x 0.9	Apples	*Oncorhynchus mykiss*	96 h	30	203	100
2 x 0.9	Apples	*Daphnia magna*	48 h	50	**0.822**	100
2 x 0.9	Apples	*Scenedesmus subspicatus*	72 h	3	13	10
2 x 0.9	Apples	*Oncorhynchus mykiss*	21 d	20	10.8	10
2 x 0.9	Apples	*Daphnia magna*	21 d	50	**0.24**	10
2 x 0.9	Apples	*Chironomus riparius*	25 d	40	12	10
Metabolite AE0651017						
2 x 0.9	Apples	*Daphnia magna*	48 h	10	> 156	100
Formulation Zolone 30WP (= EXP 60308)						
2 x 0.9	Apples	*Oncorhynchus mykiss*	96 h	30	109	100
2 x 0.9	Apples	*Scenedesmus subspicatus*	72 h	10	12	10
Formulation Rubitox flow (= EXP 05531A)						
2 x 0.9	Apples	*Daphnia magna*	21 d	50	**0.032**	10
Formulation AEF 016629 00 EC34 (= Zolone 35 EC)						
2 x 0.9	Apples	*Daphnia magna*	48 h	50	**0.44**	10
2 x 0.9	Apples	*Zooplancton community (microcosm)*	115 d	50	**2.78**	10

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

Bioconcentration

Bioconcentration factor (BCF) ‡	180
Annex VI Trigger:for the bioconcentration factor	100 (for substances which are not ready biodegradable)
Clearance time (CT_{50}) (CT_{90})	0.71 d 2.4 d
Level of residues (%) in organisms after the 14 day depuration phase	3 %, whole fish

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

Acute oral toxicity ‡	Phosalone: LD_{50} = 103 µg a.s./bee 30 % WP: LD_{50} = 12.4 µg a.s./bee Zolone liquid (35 % phosalone): LD_{50} = 2.6 µg a.s./bee
Acute contact toxicity ‡	Phosalone: LD_{50} = 4.4 µg a.s./bee 30 % WP: LD_{50} = 10.4 µg a.s./bee Zolone liquid (35 % phosalone): LD_{50} = 4.5 µg a.s./bee

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

Hazard quotient T1: based on field rate;
Hazard quotient ref. (refined): based on PIEC rates for foliage / ground, interception considered

Application rate (kg a.s./ha)	Crop	Route	Hazard quotient T1	Hazard quotient T2	Annex VI Trigger
Phosalone					
0.9	apples / pears	oral	8.7	3.5 / 4.4	50
		contact	204.5	81.8 / 102.3	
30 % WP					
0.9	apples / pears	oral	72.6	29 / 36.3	50
		contact	84.1	33.6 / 42.1	
Zolone liquid (35 % phosalone)					
0.9	apples / pears	oral	346	138.5 / 173.1	50
		contact	200	80 / 100	

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Field or semi-field tests ext lab study: Zolone on apple leaves at 900 g a.s./ha; bioassays with 12, 24 and 48 hours, 4 and 7 days old residues. Results: harmful effects after exposition for a duration of 72 h under lab conditions up to an residue age of 4 days. Residues aged for 7 days after application caused only a slight increase in mortality (21.7 %). semi-field study ("additional info"): EC formulation of phosalone (unknown composition) applied at a rate of 1200 g a.s./ha to flowering *Phacelia* plants in pots. Results: no significant impact on honeybees. tunnel test: Zolone Flo (500 g phosalone/L SC) applied on blooming *Phacelia* at a rate of 600 g a.s./ha. Results: no clear impact, bee populations stayed stable. field study: Zolone Flo mixed with a fungicide was applied by air to oilseed rape in full flower at 1000 g a.s./ha. Results: disorientation occurred in a few bees after Zolone treatment; no significant differences regarding the number of dead bees; no effect on the brood. Study of limited validity.

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

Species	Stage	Test Substance	Dose (g a.s./ha)	Endpoint	Effect	Annex VI Trigger
Laboratory studies						
Typhlodromus pyri	protonymphs + adults	Phosalone 350 g/L EC (Zolone)	5 11.5 26.5 60.8 139.9	mortality / fecundity	15.8 / 2.6 10.5 / -3.9 36.8 / 10.4 47.4 / 51.9 96.5 / - LR50 =45.8g a.s./ha	30 %
Typhlodromus pyri	protonymphs	EXP06027B (500 g/L SC formulation)	360	mortality fecundity comb.effect	14 22 32.9	30 %
Aphidius rhopalosiphi	adults		360 720	mortality	100 100	30 %
Poecilus cupreus	adults		360, 900	mortality, feeding capacity	No effect	30 %
Chrysoperla carnea	larvae until adult		360	mortality fecundity	13 no effect	30 %
			720	mortality fecundity	21 no effect	30 %

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

Species	Stage	Test Substance	Dose (g a.s./ha)	Endpoint	Effect	Annex VI Trigger
Extended laboratory studies						
Typhlodromus pyri	protonymphs + adults	Zolone 35 EC	contact with dried residues	mortality / fecundity	0 / -4.1 19 / 5.2 32.8 / 44.3 53.5 / 49.5 87.9 / - LR50 =201.4 g a.s./ha	30 %
Aphidius rhopalosiphi	adults		315.9 568.6 1032.5 1842.8 3316.2	mortality fecundity mortality	39.5 74.5 86.8 100 100 100	30 %
Aphidius rhopalosiphi	adults		900, cont. with dried 0-21 d aged residues	mortality	95 - 100	30 %
			900, cont. with dried 28 d aged residues	mortality fecundity	62.5 44	30 %
			900, cont. with dried 35 d aged residues		42.1 47.7	30 %
			900, cont. with dried min. 42 d aged residues		≤ 12.8 ≤ 6.3	30 %
Chrysoperla carnea	larvae until adult		contact with dried residues	mortality fecundity	2.5 5 17.5 37.5 50 no effect on reproduction LR_{50} =2415 g a.s./ha	30 %

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

Field or semi-field tests none provided

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

Acute toxicity ‡	14 days LC_{50}: 22.5 mg/kg
Reproductive toxicity ‡	Not provided

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

Application rate (kg as/ha)	Crop	PECi (mg/kg)	Time-scale	TER	Annex VI Trigger
1st application: 0.9 kg a.s./ha 50 % interception	apples	0.60	Acute 14 days	159	10
2nd application: 0.9 kg a.s./ha 80 % interception	apples	0.24	Acute 14 days	396	10

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

Nitrogen mineralization ‡	No unacceptable effects at concentrations up to 12.7 mg a.s./kg soil (dw)
Carbon mineralization ‡	No unacceptable effects at concentrations up to 12.7 mg a.s./kg soil (dw)

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N, R 50/53	Harmful Very toxic to aquatic organisms, 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 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
mg	milligram
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
pH	pH-value
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