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

metrafenone

finalised: 13 January 2006

SUMMARY

Metrafenone is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[1] United Kingdom received an application from BASF for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2003/105/EC[2].

Following the agreement between the EU-Commission and the EFSA for the EFSA to organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after June 2002, the designated rapporteur Member State United Kingdom made the report of its initial evaluation of the dossier on metrafenone, hereafter referred to as the draft assessment report (DAR), available on 31 October 2003. This draft assessment report was distributed for consultation to the Member States and the notifier on 24 November 2003.

The peer review was initiated on 24 November 2003 by dispatching the draft assessment report for consultation of the Member States and the notifier. 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 July 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 January – March 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 fungicide which comprises broadcast spraying to control powdery mildew in cereals (wheat and barley) and grapevines at application rates up 150 g metrafenone per hectare (cereals)[3] and 100 g per hectare (grapevines), respectively. Metrafenone can be used only as fungicide.

[1] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 279, 22.10.2005, p.63
[2] OJ No L 43, 18.2.2003, p. 45
[3] It should be noted that the efficacy evaluation made by the RMS concluded that useful reduction of eyespot (*Pseudocersporella herpotrichioides)* was achieved in winter and spring wheat only

The representative formulated products for the evaluation were "BAS 560 00 F" (cereal use) and "BAS 560 02 F" (grapevine use), both are suspension concentrates (SC).

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

Metrafenone is rapidly absorbed and excreted and widely distributed. The acute toxicity is low. It is not a skin or an eye irritant, nor a skin sensitiser. The target organ in all species was the liver (increased weight and histopathological findings). Metrafenone did not show any genotoxic potential. It is carcinogenic in rodents at very high doses of limited relevance for humans. Metrafenone did not affect reproductive and developmental parameters at not maternally toxic doses. Metrafenone does not show any neurotoxic potential. No reports are available on medical surveillance and acute poisonings because industrial production of metrafenone has not yet commenced.
The Acceptable Daily Intake (ADI) for metrafenone is 0.25 mg/kg bw/day and the Acceptable Operator Exposure Level (AOEL) is 0.43 mg/kg bw/day with a safety factor (SF) of 100. Based on the toxicological characteristics of metrafenone setting an ARfD is not needed.
The exposure for the operators applying metrafenone has been assessed with UK and German models (not exceeding the 53% of the AOEL). Exposure is below the AOEL for re-entry workers or bystanders.

Applied to wheat plants and vines by foliar application metrafenone itself was the major component identified at harvest in the analysed plant parts. Few metabolites of metrafenone were identified in vine leaves and wheat straw, and, basically, there was no evidence that molecular cleavage occurred. In grain the majority of the radioactivity got incorporated into plant material. In rotational crop studies metrafenone was not present at significant levels in the succeeding crops. Decline of metrafenone residues under processing conditions does not occur.
Fed to ruminants and poultry, metrafenone was extensively metabolised in the liver and kidney. The metabolites identified in the goat metabolism study are structurally similar to those found in the rat metabolism study. Even though metrafenone is classified as fat-soluble (logPow 4) there was no evidence for accumulation of residues in adipose tissue.
The chronic dietary exposure assessment for consumers based on the representative GAP indicated that for all consumer subgroup the intake was less then 1% of the proposed ADI.

Metrafenone exhibited high persistence in soil under aerobic conditions. Very low levels of extractable metabolites were found and identified. Mineralization was low and unextractable radioactivity accounted for 24.8 % AR after 120 d.

Under anaerobic conditions metrafenone degrades much faster than under aerobic conditions and a large number of metabolite fractions are formed. A high amount of the radioactivity corresponded to unresolved areas on TLC plates and procedural losses (up to 30 % AR). Since extraction procedures included some harsh treatments the applicant considered that the majority of the residue in soil would not be bioavailable. In a second anaerobic study, the main metabolites identified were CL 377160 (max. 5.3 % at 7d) and CL 4084564 (7.3 % at 28 d).

Photolysis also contributes to the degradation of metraphenone. Compound CL 377160 (max. 18.9 % AR) was formed as a major soil photolysis product.

Under dark aerobic conditions, the photolysis metabolite CL 377160 is rapidly degraded (DT_{90} < 7 d). Most of the degradation will contribute the formation of unextractable residue (63.1 – 74.2 % AR at 120 d, end of the study). The major fraction of the unextractable residue is associated with the humin soil fraction (22.2 – 35.9 % AR).

Field dissipation studies were conducted in four sites in Europe located in Germany, United Kingdom, Denmark and Northern France. Under field conditions metrafenone is medium to high persistent in soil ($DT_{50\ field}$ = 70 – 144 d). Since the field studies were performed on bare soils (with a potentially high contribution of photolysis) and the representative uses proposed are for developed crops were the foliage will shadow the field, RMS proposed to use the worst case laboratory half life for the EU risk assessment.

Four field accumulation studies were initiated in 1999 and planned to finalise in 2004. Three trials were performed in grapevines in Germany, Italy and Spain and a trial in cereals in Germany. Interim reports of these studies were submitted to the RMS. The main concern raised by these studies was that after 5 years the plateau was still not reached. A modelling exercise based on PEARL leaching model with worst case degradation input parameters show that the plateau is reached after 10 years of continuous application. The results of this model have been used as PEC soil for the EU risk assessment.

Metrafenone may be classified as low mobile to immobile (K_{foc} = 1592 – 5556 mL / g) and metabolite CL 377160 as slightly mobile to immobile (K_{foc} = 2199 – 21649 mL / g) in soil. Metrafenone is expected to be stable to hydrolysis under environmental conditions of pH and temperature. Photolysis may contribute to the degradation of metrafenone in water.

Metrafenone is not readily biodegradable.

Two aerobic water sediment systems at 20 °C under dark conditions were investigated. Metrafenone was found to dissipate relatively rapidly from water. Metrafenone is also low persistent in the total systems ($DT_{50\ total\ systems}$ = 8.5 – 9.2 d). Unextractable residues were formed up to 15.7 – 26.4 % AR at the study end. Mineralization was 2.6 – 12.4 % at the study end. Only minor metabolites were identified in the water / sediment systems.

PEC_{SW} were calculated for the buffer distances of 3 m, 5m and 10m assuming spray drift from single and multiple applications (2 x 150 g/ha with 21 d interval in cereals and 8 x 100 g/ha with 12 d interval in vines) taking as basis the worst case dissipation half life observed in the water phase of the dark water sediment study ($DT_{50\ water}$ = 4.6 d). Same premises were used to calculate initial PEC_{SED}.

The RMS also provided PEC_{SW} of metrafenone and its soil photolysis metabolite CL 377160 derived from drainage on cereal crops based on their national scheme. For the active substance the calculation

also considered the drainflow of the accumulated substance in soil. The drainflow concentration obtained was of 0.97 µg/ L (70 % of what would be expected form spray drift at 1m). Potential surface water contamination through run-off was not assessed in the DAR. Experts' meeting agreed that due to the high K_{oc} of the active substance runoff and drainage will be of limited significance and that for the purposes of the EU risk assessment no further information was necessary. However, Member States may need to pay special attention to runoff and drain flow in their national risk assessment taking into considerations the particular conditions of their crops.
The 80th percentile PEC_{GW} concentrations of metrafenone and metabolite CL 377160 at 1m depth were less than 0.001 µg / L for the spring and winter cereals and vines in all the relevant FOCUS Groundwater Scenarios (FOCUS PEARL, v. 1.1.1.).
Metrafenone may be prone to some volatilization from soil or water surfaces. However, it is strongly adsorbed in soil matrices and its atmospheric photochemical oxidative half life was calculated to be 0.63 h and it is not expected to be subject to long-range transport.

The risk to birds and mammals was calculated using the nomogram of Hoerger and Kenaga (EPPO 1992) and according to the Guidance Document on Risk Assessment for Birds and mammals Under Council Directive 91/414/EEC (SANCO/4145/2000). The risk to herbivorous and insectivorous birds in cereals and to insectivorous birds in grapevines can be regarded as low according to both risk assessments. Also the risk to herbivorous and insectivorous mammals in cereals and herbivorous mammals in grapevines can be regarded as low according to both risk assessments. The risk to birds and mammals from secondary poisoning is regarded to be low for the representative uses evaluated. It was noted by EFSA that no risk assessment for birds and mammals from consumption of contaminated drinking water was performed. This risk assessment is presented in the addendum by EFSA. The risk to birds and mammals from consumption of contaminated drinking water is considered to be low except for the long term risk to birds in cereals for which the TER value is below the trigger value indicating a high long term risk to birds in cereals from drinking contaminated drinking water. Therefore EFSA proposes a data requirement for the notifier to refine the long term risk to birds in cereals from exposure to contaminated drinking water. This assessment was neither discussed at the EPCO expert's meeting nor peer reviewed.
The risk to aquatic organisms is regarded to be low without the need for risk mitigation measures.
The risk to bees and other arthropod species can be regarded as low based on the available studies.
The risk to earthworms, other soil non-target macro-organisms and soil micro-organisms can be regarded as low.
The risk to non-target plants and biological methods for sewage treatment is considered to be low.

Key words: metrafenone, peer review, risk assessment, pesticide, fungicide

TABLE OF CONTENTS

BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC United Kingdom received an application from BASF for inclusion of the active substance metrafenone in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2003/105/EC.

Following the agreement between the EU-Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State United Kingdom submitted the report of its initial evaluation of the dossier on metrafenone, hereafter referred to as the draft assessment report (DAR), to the ECCO team at the Federal Biological Research Center for Agriculture and Forestry (BBA) in Braunschweig on 31 October 2003. This draft assessment report was distributed for consultation to the Member States and the notifier on 24 November 2003.

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 13 July 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 was attending 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 January – March 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 14 July 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 8 December 2005)

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

Metrafenone is the ISO common name for 3′-bromo-2,3,4,6′-tetramethoxy-2′,6-dimethylbenzophenone (IUPAC).

Metrafenone is an unclassified fungicide. The biochemical mode of action is not known yet, but morphological observations show in cereal powdery mildew that metrafenone inhibits growth of mycelium on the leaf surface, leaf penetration, formation of haustoria and sporulation.

The representative formulated products for the evaluation were "BAS 560 00 F" (cereal use) and "BAS 560 02 F" (grapevine use), both are suspension concentrates (SC).

The evaluated representative uses as fungicide comprises broadcast spraying to control powdery mildew in wheat and grapevines at application rate up 150 g metrafenone per hectare (cereals)[4] and 100 g per hectare (grapevines), respectively. Metrafenone can be used only as fungicide.

[4] It should be noted that the efficacy evaluation made by the RMS concluded that useful reduction of eyespot (*Pseudocersporella herpotrichioides)* was achieved in winter and spring wheat only

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of metrafenone as manufactured should not be less than 940 g/kg. It should be noted that this purity is based on results from a pilot plant. At the moment no FAO specification exists.
The technical material contains no relevant impurities.

The content of metrafenone (pure) in the representative formulations are 300 g/L in "BAS 560 00 F" (cereal use) and 500 g/L in "BAS 560 02 F" (grapevine use), respectively.

The assessment of the data package revealed no particular area of concern. The main data regarding the identity of metrafenone and its physical and chemical properties are given in appendix 1.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of metrafenone in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. metrafenone in food of plant origin, soil, water and air.
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 metrafenone.
The methodology used is GC with EC or MS detection and HPLC with MS or MS/MS detection, respectively.
An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2).

The discussion in the expert meeting (EPCO 20, March, 2005) on identity, physical and chemical properties and analytical methods was limited to the need of confirmatory methods for the determination of metrafenone in soil, water and air, some clarification with respect to the viscosity of the formulation and the list of end points.
With respect to the confirmatory method for soil, water and air, RMS gave further details at the expert meeting and in the evaluation table (rev. 1-1, 28.07.2005). It was agreed that sufficient data are available for water and air (these data are part of the original submitted studies but were not presented in the DAR). In case of soil further clarification was needed. RMS has addressed this in the evaluation table. The RMS does not see a need for further data, because the information supplied and

the specifity shown by the MS/MS total ion chromatogram give sufficient assurance that confirmation can be achieved. This assessment was neither peer reviewed nor discussed in an expert meeting. However, EFSA confirms the assessment of the RMS.

2. Mammalian toxicology

Metrafenone was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 18) in February 2005.

2.1 Absorption, distribution, excretion and metabolism (Toxicokinetics)

Metrafenone is rapidly (72 hours) and extensively absorbed (>88%). After absorption it is widely distributed, with highest concentrations in gastrointestinal tract and liver. The potential for accumulation is low. Excretion is quite rapid: within 24 hours from administration 67-79% is excreted mainly with faeces (via bile). Metabolism is extensive, mainly occurring through substitution of the methoxy groups with hydroxyl groups, leading then to the formation of glucuronic conjugates. Several metabolites are formed in rat metabolism *in vivo*.

2.2 Acute toxicity

The acute toxicity of metrafenone is low: the oral and dermal LD_{50} in rat are >5000 mg/kg bw, the inhalatory LD_{50} is >5 mg/L. Metrafenone is not a skin or an eye irritant, nor a skin sensitiser. Therefore, no classification is needed.

2.3 Short term toxicity

Toxicity of metrafenone after short term repeated exposures have been tested in a number of studies in rats (one 4-week and two 13-week oral studies), in mice (two 13-week oral studies) and in dogs (4-week, 13-week and 52 week oral studies).
Target effect in all species was the liver (increased weight and histopathological findings).
The relevant NOAEL is 43 mg/kg bw/day from the 13-week study in rat.

2.4 Genotoxicity

Metrafenone did not show any genotoxic potential in a battery of *in vivo* (micronucleus assay in mouse) and *in vitro* (bacterial point mutation assay, mammalian cell gene mutation assay, clastogenicity in CHO cells,) genotoxicity assays.

2.5 Long term toxicity

Chronic toxicity and carcinogenicity of metrafenone were investigated in a 2-year oral study in rats and in a 18-month oral study in mice. Liver and kidney were identified as target organ (increased liver weights, histopathological changes). The issue of liver tumours in rodents was discussed at the meeting. The tumours were statistically significant only in the high dose groups and over a long period of exposure. Some chemicals, showing no evidence of mutagenicity, produce tumours

exclusively in the rodent liver following chronic administration, acting as liver tumour promoter, stimulating liver cell proliferation and also inducing cytochrome P_{450}. Over an extended period of time, the hepatocellular proliferation and enzyme induction alone is sufficient to lead to the induction of liver tumours. Based on this the proposal made by some MS of R40 ("possible risk of irreversible effects") labelling was not agreed on by the experts, due to the non-relevance to humans, since they are never likely to be exposed to these extreme doses for such a prolonged period of time.

2.6 REPRODUCTIVE TOXICITY

In a two-generation reproductive study in rats, reproductive performances were not affected by metrafenone, except for an increased proportion of abnormal sperm morphology in F1 males at high doses. Due to parental toxicity, pups showed lower weights and delay in vaginal openings in weanlings. The NOAEL for maternal toxicity is 39 mg/kg bw/day, and the NOAEL for reproductive effects is 79 mg/kg bw/day.

Rats did not show any developmental effect; in rabbits the NOAEL for maternal and developmental toxicity was found to be 50 mg/kg bw/day (reduced body weight, food consumption, increased liver weight and a single incidence of premature delivery, respectively). This effect was discussed at the meeting and it was concluded that no classification is needed.

2.7 NEUROTOXICITY

No data have been submitted investigating potential neurotoxicity of metrafenone. Based on the available data, no concern exixts.

2.8 FURTHER STUDIES

Metabolites

No toxicological data have been submitted on metabolites.

Impurities

An Ames test performed with an impurity in technical metrafenone (impurity reference number 4087263) showed no genotoxic potential.

2.9 MEDICAL DATA

No reports are available on medical surveillance because industrial production of metrafenone has not yet commenced. No data on acute poisonings are available for the same reason.

2.10 ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) and ACUTE REFERENCE DOSE (ARfD)

ADI

The proposed ADI for metrafenone is 0.25 mg/kg bw/day, based on the NOAEL of 25 mg/kg bw/day from the 2-year study in rat, with a safety factor of 100. There is a 1000-fold margin between the ADI and the LOAEL for induction of liver tumours.

AOEL

The proposed AOEL is 0.43 mg/kg bw/day on the NOAEL of the13-week oral study in rats with a SF 100.

ARfD

Based on the toxicological characteristics of metrafenone setting an ARfD is not needed.

2.11 DERMAL ABSORPTION

Dermal absorption of metrafenone (SC formulation) was determined with an *in vivo* dermal study in rat, showing a penetration of 2% for the concentrate and 20% for the diluted formulation.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Operator exposure

Metrafenone representative products are BAS 560 00F and BAS 560 02F, SC formulations containing 300 and 500 g metrafenone/L, respectively. The plant protection product BAS 560 00F is classified R43.

They are intended to be used on cereals and grapevines with application rates ranging from 0.1 to 0.15 kg metrafenone/ha.

Estimates of operator exposure were made according to the German model and the UK POEM.

BAS 560 00F

Estimated exposure presented as % of AOEL (0.43 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	No PPE	With PPE:
German	5	4
UK POEM	53	49

BAS 560 02F

Estimated exposure presented as % of AOEL (0.43 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	No PPE	With PPE:
German	6	-
UK POEM	30	-

The estimated exposure of the operators applying BAS 560 00F and BAS 560 02F is below the AOEL even when no PPE is worn.

Worker exposure

The estimated worker exposure in treated cereal crops or in grapevines is below the AOEL (0.2% and 15% of the AOEL, respectively).

Bystander exposure

Bystander exposure is well below the AOEL either for cereal application (0.14%) or for grapevine application (<3%).

3. Residues

Metrafenone was discussed at EPCO experts' meeting for residues (EPCO 19) in February 2005.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism and distribution of metrafenone in plants was investigated by applying metrafenone labelled in two positions to grapes and wheat. In the respective studies grapevines were treated at 1.25 N rate and wheat at a rate of 2.7 N maximum total dose.

In grapes sampled at harvest, the total radioactive residue (TRR) was up to 0.44 mg/kg. Metrafenone was the major component found and accounted for up to 25% TRR (0.11 mg/kg). In the grape leaves metrafenone was metabolised into several compounds of which three were identified as CL 3000402[5], CL 379395[6] and CL 1500836[7] formed by oxidation of methyl groups on the ring systems. There was no evidence that molecular cleavage occurred.

In straw and grain 35 days following the final treatment, the TRR were *ca* 8 and 0.3 mg/kg respectively. In wheat grain and straw, again, metrafenone was the major component identified accounting for ca 5% TRR and 10% TRR, respectively. In straw other metabolites were present but individually did not account for more than 10% TRR. In grain, however, up to 50% TRR were not extracted. Further attempts were made to release and identify the non-extractable residue in grain, showing that the majority of released radioactivity consisted of a fraction containing multiple minor components. As no significant components were found in the extractable material it was considered unlikely that there will be significant components in the post-extraction solids. The un-extracted radioactive residue is considered likely to consist of incorporated radioactivity.

Based on the metabolism data submitted for grapes and wheat, the residue of concern should be defined as metrafenone for risk assessment and monitoring purposes. Since the assessed metabolism data are limited to two crop categories a final residue definition for plants in general cannot be proposed.

[5] CL 3000402: see Appendix 3
[6] CL 379395: see Appendix 3
[7] CL 1500836: see Appendix 3

Residues trials were performed conforming to critical GAP on grapevine, wheat and barley in the field. The submitted trials covered use in both Northern and Southern regions of Europe. All trials were reported in sufficient detail and were supported by acceptable analytical information. Thus, based on the data MRLs can be proposed for grapes, wheat and barley grain.

Decline of metrafenone residues under processing conditions does not occur. Studies undertaken in processed grape and barley indicated that the majority of derived processing factors for commodities for human consumption were less than 1.0. However, production of bran from barley grain gives rise to a processing factor of 2.9.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

The metabolism and distribution of radioactive labelled metrafenone was studied in rotational crops of lettuce, radish and canola grown in soil treated at a rate of *ca* 2N. TRR found in the rotational crops were low and neither metrafenone nor metabolites were found at significant levels (>0.01 mg/kg). Hence it is unlikely that residues of significance will occur if metrafenone is used according to the representative GAP.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Since the intake of metrafenone residues by livestock animals is significant (>0.1 mg/kg feed), metabolism studies with goats and poultry have been carried out.

The metabolism and distribution of residues were investigated in lactating goats dosed with metrafenone labelled in two positions at dose rates of *ca* 10 and 70 mg/kg, presenting a *ca* 5N and 35N exaggerated rate, respectively, based on the highest estimated maximum daily intake by ruminants. The majority (76-86%) of the dose was excreted, mainly in the faeces. Plateau levels in milk were reached on day 3.

With regard to its logPow metrafenone is characterised as fat soluble (log Pow 4). Metrafenone was the major component found in milk and adipose tissue. However, TRR were considerably higher in liver and kidney, indicating that there might be no accumulation of residues in adipose tissue. Metrafenone was extensively metabolised in the liver and kidney with the major metabolites found identified as CL 1500698[8] and CL 1023363[9]. The metabolites identified in the goat metabolism study are structurally similar to those found in the rat metabolism study.

Laying hens were dosed orally with metrafenone labelled in two positions at dose rates of *ca* 14 mg/kg diet (*ca* 50N based on highest estimated maximum daily intake). The majority of the dose administered was excreted (86 - 95%). Plateau levels in eggs were reached by day 9. TRR for both labels were similar, with the highest levels found in the liver. No characterisation or identification of metabolites was performed. The metabolism study was carried out at an exaggerated dose rate and it is unlikely that residues in animal products will be of significance when feed produced according to the proposed GAP is fed to poultry.

[8] CL 1500698: see Appendix 3
[9] CL 1023363: see Appendix 3

RMS didn't propose a residue definition in animals with the justification that the representative uses on potential feed crops according to the proposed GAP do not give rise to significant residue levels (>0.01 mg/kg) in animal products, and hence MRLs in animal products do not need to be proposed either. EFSA notes that due to the predicted exposure of livestock from the representative uses conducting metabolism studies with livestock animals was triggered and the studies are available and have been evaluated. Metrafenone and major metabolites have been identified in edible animal matrices. Even though extrapolation from higher dose rates always includes uncertainty it is agreed that at N dose rate significant (>0.01 mg/kg) total residues (TRR) in milk, eggs, poultry products, goat fat and muscle would not be expected. This is however not the case for goat liver and kidney. Therefore further consideration is still required, and for risk assessment purposes a residue should be defined for ruminant liver and kidney.

No feeding studies were submitted. According to RMS significant residues (identity not specified by RMS) >0.01 mg/kg would not be expected in milk, eggs and ruminant and poultry animal products when metrafenone is used on potential feed crops according to the proposed GAP.

3.3. CONSUMER RISK ASSESSMENT

The total intake for an adult based on the WHO model (GEMS/Food European diet) was less than 1% of the proposed ADI. National Estimates of Daily Intake (NEDI) were calculated for UK consumers with the UK Rees/Day model (Two highest 97.5th percentile intakes plus mean intakes from other food). Total intakes for all considered consumer groups were all significantly below the ADI of 0.25 mg/kg bw/day, accounting for less than 1% of the proposed ADI.
Based on the toxicological characteristics of metrafenone setting an ARfD is not needed, and consequently no assessment of the acute risk to consumers.

3.4. PROPOSED MRLS

Grapes	0.5 mg/kg
Wheat grain	0.05 mg/kg
Barley grain	0.5 mg/kg

Currently there are no Codex MRLs for metrafenone that need to be considered.

4. Environmental fate and behaviour

Metrafenone was discussed in the experts' meeting on Fate and Behaviour in the Environment (EPCO 16) in January / February 2005.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Metrafenone metabolism in soil under dark aerobic conditions at 20 °C was investigated in one study with one soil using the [trimethoxyphenyl-U-] ^{14}C and the [bromophenyl-6-] ^{14}C labelled compounds. Degradation of metrafenone in this study was very slow with up to 69 % AR still present after 120 d. Very low levels of extractable metabolites were found and identified. Unidentified radioactivity comprising a number of compounds in various extracts reached a maximum level 8.7 % AR at 60 d. Mineralization was low 1.5 - 1.8 % AR at 120 d (2.7 – 5.3 % AR in the rate study) and unextractable radioactivity reached up to 24.8 % AR after 120 d.

The anaerobic degradation in soil at 20 °C was investigated in a study with one silt loam soil (pH = 7.1, organic C = 2.2 % AR) using the [trimethoxyphenyl-U-] ^{14}C and the [bromophenyl-6-] ^{14}C labelled compounds. Degradation was much faster than under aerobic conditions and a large number of metabolites fractions were observed during the study. Only metabolite fractions M6 (maximum 45.1 % AR at 15 d) and M 5.2 (maximum 19.4 % AR at 88 d) exceeded the 10 % AR. In the case of M6 the levels remained relatively high for a long period of time (from day 15 to the end of the study at day 120) while M5.2 only exceeds 10 % AR at a single sampling date. Metabolites CL 434223[10], CL 375816[11] and M4 (unidentified chromatographic fraction) attained levels of 8.2 % AR, 6.5 % AR and 5.3 % AR. A high amount of the radioactivity corresponds to unresolved TLC spots and procedural losses (up to 30 % AR). Since extraction procedures include some treatments considered harsh (accelerated solvent extraction ACS with acetone and methanol/5 % acetic acid followed by 0.5 N NaOH and 2N NaOH or directly with 0.5 N NaOH and 2N NaOH) applicant claimed that the majority of the residue in soil would not be bioavailable. However, actual bioavailability of the residue has not been tested. Under the mildest extraction conditions (water, acetone, and methanol-water without using acid or basic solvents) only a maximum of 5.7 % AR was extracted as metabolite fraction M6. In writing the conclusion, EFSA realized by the examination of the original reports that the most efficient extraction step is the one performed by ACS using methanol / 5 % acetic acid. This method has not necessarily to be regarded as very harsh. Therefore, the non bioavailability of this residue at in particular of M6 may not be considered fully demonstrated. However, this metabolite fraction was observed close of the origin of the TLC plate and seems to consist in multiple minor polar components and no further investigation of its nature was deemed necessary during the peer review.

A further anaerobic study in soil at 20 °C with one silty clay loam soil (pH = 7.1, organic C = 1.28 % AR) using the [trimethoxyphenyl-U-] ^{14}C and the [bromophenyl-6-] ^{14}C labelled compounds is available. The main metabolites identified in this study were CL 377160[12] (max. 5.3 % at 7d) and CL 4084564[13] (7.3 % at 28 d). Two unidentified metabolite fractions exceed 10 % AR (Met 2, Met 3). These fractions were resolved in multiple components with a maximum of 8.3 % AR in a single individual component.

[10] CL 434223: see Appendix 3
[11] CL 375816: see Appendix 3
[12] CL 377160: see Appendix 3
[13] CL 4084564: see Appendix 3

A soil photolysis study at 20 °C in one soil irradiated with a xenon arc lamp (filtered for λ < 290 nm) for 30 d is available. Compound **CL 377160** (max. 18.9 % AR) was formed as a major soil photolysis product.

The route and rate of degradation of the photolysis metabolite CL 377160 was also investigated under dark aerobic conditions at 20 °C in three soils with the compound labelled at the bromophenyl moiety. The soils cover a range of pH (7.2 – 8.7), organic carbon (1.1 – 2.0 %) and soil textures and the water was adjusted to the 50 % MWHC. Several unidentified metabolite were observed none of them attaining the 5 % AR. Mineralization was very low (0.52 – 1.22 %) and unextractable residue attained between 63.1 – 74.2 % AR at 120 d (end of the study). It is noted that mass balance at the end of the study was low with total recoveries between 79 – 83 % AR. The major fraction of the unextractable residue is associated with the humin fraction of the soil (22.2 – 35.9 % AR).

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

Rate of degradation metrafenone in soil under dark aerobic conditions at 20 °C was investigated in the route study and in one additional study with three soils employing the [bromophenyl-6-] ^{14}C labelled compound. Metrafenone is highly persistent in soil under aerobic conditions ($DT_{50\ lab\ 20\ °C}$ = 182 d – 365 d). An additional study was performed with the [bromophenyl-6-] ^{14}C labelled compound to investigate the route and rate of degradation at 10 ºC. Degradation proceed at a slower rate with 82 % AR remaining as parent after 120 d (extrapolated DT_{50} = 693 d).

Under anaerobic conditions metrafenone degrades much faster than under aerobic conditions ($DT_{50\_lab\_20°C\_anaerobic}$ = 8 d – 15 d). Photolysis also contribute to the degradation of metraphenone ($DT_{50\_photolysis}$ = 15.5 d continuous irradiation). Photolytic half life of the major photolysis product CL 377160 was also calculated by a multicompartmental model assuming first order kinetic ($DT_{50\_photolysis\_CL377160}$ = 6 d continuous irradiation).

In the aerobic degradation in soil study performed with the metabolite CL 377160 a fast degradation was observed indicating that this metabolite when formed will be rapidly degraded under these conditions (DT_{90} < 7 d). Most of the degradation will contribute the formation of unextractable residue.

Field dissipation studies were conducted in four sites in Europe located in Germany, United Kingdom, Denmark and Northern France. A SC formulation of metrafenone was applied to bare soil at rates of a.s. about 0.4 kg / ha. Under field conditions metrafenone is medium to highly persistent in soil ($DT_{50\ field\ 1st\ order}$ = 70 – 144 d). RMS considered in the DAR that the shorter half lives with respect to the laboratory studies may be due to the contribution of photolysis. Since the field studies were performed on bare soils and the representative uses proposed are for developed crops were the foliage will shadow the field, RMS proposed to use the worst case laboratory half life for the EU risk assessment.

Four field accumulation studies were initiated in 1999 and planned to finalise in 2004. Three trials were performed in grapevines in Germany, Italy and Spain and a trial in cereals in Germany. Interim reports of these studies were submitted to the RMS. During the Evaluation meeting (July 2004) applicant informed that the final report for this study would become available by August 2004. A data

requirement was set for this study. RMS received an updated interim report which results were summarized in an addendum that was discussed in the experts meeting. The main concern raised by these studies was that after 5 years the plateau was still not reached.

A modelling exercise based on PEARL leaching model with worst case degradation input parameters ($DT_{50\_norm\_worst\ case}$ = 354 d; K_{OM} = 3223 mL/g) is available in the dossier and summarized in the DAR. In the model the plateau is reached after 10 years of continuous application. The results of this model have been used as PEC soil for the EU risk assessment.

During the experts' meeting it was discussed if the applicant should continue the field accumulation studies for more seasons in order to reach the plateau in soil. The meeting agreed that the EU risk assessment relays on the PECs calculated by the accumulation model which results are confirmed by the modelling available. Therefore, the continuation of the studies is not required to finalise the EU risk assessment. However, the meeting was not conclusive on the continuation of the studies, since some experts were of the opinion that the field accumulation studies should be continued until the plateau is reached and that this information may be useful to refine risk assessment at MS level. Irrespective to the applicants' decision to continue or stop the study the final report of the study should be provided when available.

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

Batch equilibrium adsorption / desorption studies are available for metrafenone and metabolite CL 377160 with five different soils. According these studies metrafenone may be classified as low mobile to immobile (K_{foc} = 1592 – 5556 mL / g) and metabolite CL 377160 as slightly mobile to immobile (K_{foc} = 2199 – 21649 mL / g). No dependence on pH was deduced. No column leaching or lysimeters studies are available and are not deemed necessary to finalize the EU risk assessment.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

The hydrolytic stability of metrafenone was studied in sterile aqueous buffer solutions (pH 4, 7 and 9) at 50 °C. According the results of this study, metrafenone is expected to be stable to hydrolysis under environmental conditions of pH and temperature. Aqueous photolysis of metrafenone was studied at 22 °C in sterile aqueous buffer at pH 7 using the [trimethoxyphenyl-U-] ^{14}C and the [bromophenyl-6-] ^{14}C labelled compounds. Light source (filtered xenon arc lamp) was considered comparable to early autumn sunlight at aprox. 40 °N. Photolysis contributes to the degradation of metrafenone in water yielding a number of minor metabolites none of them above 10 % AR. The main aqueous photolysis metabolites identified were CL 1023424 [14](max. 4.9 % AR) and CL 4084564 (max. 7.8 % AR). The half life was calculated assuming first order kinetics ($DT_{50\_photolysis\_buffer\_pH\_7}$ = 3.1 d continuous irradiation). Using the EPA programme GC SOLAR, the applicant calculated a half life of 12.3 days in summer and 53.3 days in winter at 40 °N. In a separated study aqueous photolysis in natural water was investigated ($DT_{50\_photolysis\_natural\_water}$ = 2.6 d continuous irradiation).

Metrafenone is not readily biodegradable according to the test available.

[14] CL 1023424: see Appendix 3

Two aerobic water sediment systems at 20 °C under dark conditions were investigated using the [trimethoxyphenyl-U-] ^{14}C and the [bromophenyl-6-] ^{14}C labelled metrafenone. A number of metabolites were identified in water and sediment of both systems, but none of them above 10 % AR. Multicompartmental models based on first order kinetics were used to analyze the results of the two water sediment systems. Metrafenone was found to dissipate relatively rapidly from water (dissipation $DT_{50\ water}$ = 3.2 – 4.6 d) mainly due to rapid partition to the sediment (metrafenone in sed; max. 56.9 % AR at 3 d). Metrafenone is also degraded in the sediment (dissipation $DT_{50\ sed}$ = 4.0 – 4.1 d). Metrafenone is also low persistent in the total systems ($DT_{50\ total\ systems}$ = 8.5 – 9.2 d). Unextractable residues were formed up to 15.7 – 26.4 % AR at the study end. Mineralization was 2.6 – 12.4 % at the study end.

PEC_{SW} were calculated assuming spray drift from single and multiple applications (2 x 150 g/ha with 21 days interval in cereals and 8 100 g/ha with 12 days interval in vines) taking as basis the worst case dissipation half life observed in the water phase of the dark water sediment study ($DT_{50\ water}$ = 4.6 d). PEC_{SW} provided in DAR for the buffer distances of 3 m, 5m and 10m. Same premises were used to calculate initial PEC into the sediment. PEC_{SW} and PEC_{SED} were also calculated for the main metabolites found in the water / sediment study.

The rapporteur Member State also provided PEC_{SW} of metrafenone and its soil photolysis metabolite CL 377160 derived from drainage based on their national scheme,[15] for the UK risk assessment. This assessment was made for cereals only. For the active substance the calculation also considered the drainflow of the accumulated substance in soil. The drainflow concentration obtained was of 0.97 µg/ L (70 % of what would be expected form spray drift at 1m). Potential surface water contamination through run-off was not assessed in the DAR.

Experts' meeting discussed the need to further address potential contamination through drainflow and run-off to finalise the EU risk assessment. The concern was motivated by the high persistence of this substance in soil. Based on experts' judgment the meeting agreed that in this case runoff and drainage will be of limited significance, due to the high K_{oc} of the active substance. To support this judgement the UK national approach was used as indicative. Calculation provided by the RMS confirmed the assumptions since levels in surface water by drainage were calculated to be below the ones arising from spray drift. Therefore, the meeting decided that for the purposes of the EU risk assessment no further information was necessary. However, MS may still need to pay special attention to runoff and drain flow in their national risk assessment taking into considerations the particular situations of their crops.

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

Potential contamination of ground water by metrafenone and its soil photolysis metabolite was addressed by calculation of PEC_{GW} for the FOCUS Groundwater Scenarios using the FOCUS

[15] PSD Data requirements handbook, Chapter 6.5, pp 32-35. PSD, Mallard House, Kings Pool, 3 Peasholme Green, York, YO107OX.
http://www.pesticides.gov.uk/psd_pdfs/registration_guides/data_reqs_handbook/datareqhandbook.pdf

groundwater shell FOCUS PEARL, v. 1.1.1. The predicted 80th percentile concentrations of metrafenone and metabolite CL 377160 at 1m depth were less than 0.001 µg / L for the spring and winter cereals and vines in all the relevant scenarios. RMS performed the calculation with the MACRO modelling of the Châteaudun scenario for winter cereals to address macropore flow and specific UK situations. Also in this case predicted 80th percentile concentrations of metrafenone and metabolite CL 377160 at 1m depth were less than 0.001 µg / L.

4.3. FATE AND BEHAVIOUR IN AIR

Metrafenone may be prone to some volatilization from soil or water surfaces (vapour pressure = 1.53 x 10^{-4} Pa at 20 ºC; Henry's Law constant = 0.132 Pa m^3/mol. However, in radiolabelled studies no significant radioactivity was found in volatile traps, presumably due to strong adsorption of the active substance. In addition photochemical oxidative half life in the atmosphere was calculated to be 0.63 h. Therefore, it is not expected that metrafenone would be subject to long-range transport in the atmosphere.

5. Ecotoxicology

Metrafenone was discussed in the experts' meeting on ecotoxicology (EPCO 17) in January / February 2005.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk to birds and mammals was calculated using the nomogram of Hoerger and Kenaga (EPPO 1992) and according to the Guidance Document on Risk Assessment for Birds and mammals Under Council Directive 91/414/EEC (SANCO/4145/2000).

The risk was calculated for an herbivorous and insectivorous bird for the representative use in cereals and for an insectivorous bird for the representative use in grapevines. The resulting acute, short term and long term TER-values, from both risk assessments (see above), are all above the corresponding Annex VI trigger value indicating a low risk to herbivorous and insectivorous birds in cereals and to insectivorous birds in grapevines.

Furthermore the risk was calculated for an herbivorous and insectivorous mammal in cereals and an herbivorous mammal in grapevines. The resulting acute and long term TER-values, from both risk assessments (see above), are all above the corresponding Annex VI trigger value indicating a low risk to herbivorous and insectivorous mammals in cereals and herbivorous mammals in grapevines.

The risk to birds and mammals from secondary poisoning needs to be assessed as the logPow is above 3. The RMS was asked to revise the risk for earthworm eating birds and mammals by the EPCO expert's meeting. The RMS considers that this risk assessment, which is only available in the evaluation table, does not need to be revised. EFSA does not agree with this and considers that a wrong Kow and PEC_{soil} value has been used as already indicated by the EPCO Expert's meeting. Therefore EFSA presents the revised calculations in an addendum. Furthermore a risk assessment for

fish eating birds and mammals according to SANCO/4145/2000 is presented in the addendum by EFSA. The resulting TER values are all above the Annex VI trigger value indicating a low risk to birds and mammals from secondary poisoning for the representative uses of metrafenone evaluated.

As it is noted by EFSA that no risk assessment for birds and mammals from consumption of contaminated drinking water was performed this risk assessment is also presented in the addendum by EFSA. The risk to birds and mammals from consumption of contaminated drinking water is considered to be low except for the long term risk to birds in cereals for which the TER value is below the trigger value indicating a high long term risk to birds in cereals from drinking contaminated drinking water. Therefore EFSA proposes a data requirement for the notifier to refine the long term risk to birds in cereals from exposure to contaminated drinking water. This assessment was neither discussed at the EPCO Expert's meeting nor peer reviewed. Some MSs are of the opinion that long-term exposure to contaminated drinking water can be excluded and hence regard the long-term risk from uptake of contaminated drinking water as low. However, no common agreement among MSs exists yet on the potential long-term risk from contaminated drinking water. It is planned to discuss the risk to birds and mammals from uptake of contaminated drinking water as a general point in an EPCO expert meeting.

5.2. RISK TO AQUATIC ORGANISMS

Selenastrum capricornutum was the most sensitive species from all aquatic species tested with metrafenone on an acute time scale and *Daphnia magna* and *Pimephales promelas* were the most sensitive species tested with metrafenone on a long term time scale. *Oncorhynchus mykiss, Daphnia magna* and *Selenastrum capricornutum* were tested with both the lead formulations BAS 560 00F and BAS 560 02F. *Selenastrum capricornutum* was the most sensitive organism to BAS 560 00F. All endpoints for BAS 560 02F are higher than values from which the value for *D. magna* is the lowest.
PECsw-values were calculated assuming spray drift. Based on experts' judgment the EPCO 16 Expert meeting on Fate and behaviour agreed that in this case runoff and drainage will be of limited significance, due to the high K_{oc} of the active substance. The EPCO 16 Expert meeting on Fate and behaviour decided that for the purposes of the EU risk assessment no further information was necessary. However, MS may still need to pay special attention to runoff and drain flow in their national risk assessment taking into consideration the particular situations of their crops (see point 4.2.1).
All resulting TER-values are above the corresponding Annex VI trigger values indicating a low acute and long term risk to aquatic organisms from the representative uses of metrafenone evaluated without the need for risk mitigation measures.

As in the water sediment study the content of active substance was above 10% of the AR at or after 14 days, studies with the active substance on sediment dwelling organisms are considered necessary. A study with the active substance on *Chironomus riparius* is available indicating a low risk to sediment dwelling organisms without the need for risk mitigation measures.

No major or relevant metabolites in surface water, ground water or sediment were identified by the section on Fate and behaviour. Nevertheless the metabolites CL 375816 and CL 4084564 were tested on *Oncorhynchus mykiss*, *Daphnia magna* and *Pseudokircherniella subcapitata*. A risk assessment for these metabolites is available in the DAR indicating a low risk to aquatic organisms from these metabolites.

Metrafenone is not an herbicide so studies on aquatic plants are not considered necessary.

A study on bioconcentration in fish is made available as the LogPow exceeds 3. The resulting BCF of 530 exceeds the Annex VI trigger value of 100 for not readily biodegradable compounds. This risk is considered to be addressed as 95% depuration occurs within 2.3 days, as the risk to fish eating birds and mammals is low and as also the long term risk to fish is considered to be low.

5.3. RISK TO BEES

Acute contact and oral toxicity studies, both with metrafenone and the lead formulations BAS 560 00F and BAS 560 02F, are available. The resulting HQ values do not breach the appropriate Annex VI trigger value indicating a low risk to bees for the representative uses of metrafenone in cereals and grapevines.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory studies with *Aphidius rhopalosiphi*, *Typhlodromus pyri*, *Poecilus cupreus*, and *Chrysoperla carnea* with both the lead formulations BAS 560 00F and BAS 560 02F are available. Furthermore 4 field studies with *T. pyri* and 1 field study with *Kampinodromus aberrans* are available.

A risk assessment according to Escort I and to Escort II is available in the DAR. Effects above 30% on reproduction in *A. rhopalosiphi* were observed. These effects were not dose related and were also not statistically different from the control. Therefore these effects were considered to be not treatment related. Also during the laboratory studies with *T. pyri* effects above 30% on reproduction were observed which were statistically different from the control. Based on the available field studies, the risk to *T. pyri* can be considered as low. Effects on mortality were below 30% for the indicator species *T. pyri* and *A. rhopalosiphi*. The corresponding HQ values, according to the Escort II risk assessment, are below 2 for both representative uses indicating a low risk to non-target arthropods.

5.5. RISK TO EARTHWORMS

Studies on the acute toxicity to earthworms from metrafenone, the lead formulations BAS 560 00F and BAS 560 02F and the metabolite CL 377160 are available. Furthermore studies on the chronic toxicity to earthworms of both the lead formulations are available. The endpoints for metrafenone and the lead formulations were corrected for the organic content of the test soil as the LogPow exceeds 2. Also the endpoint for the metabolite CL 377160 was corrected for the organic content of the test soil as CL 377160 is strongly absorbed to organic matter. No chronic study with the metabolite CL

377160 is considered necessary as it is considered to have been present during the studies with the lead formulations and due to its low persistency.

The chronic risk assessment is based on the corrected NOEC of 10.44 mg as/kg soil from the study with the formulation BAS 560 02F. The two formulations "BAS 560 00F" and "BAS 560 02F" used in cereals and grapevine, respectively, differ mainly in the content of metrafenone (300 g/L and 500 g/L) and in the content of the wetting agents. "BAS 560 00F" contains significantly more wetting agents than "BAS 560 02F". The other differences are negligible. The two formulations are considered sufficiently similar for all of them to be used in support of either use.

The risk was calculated with the maximum PEC_{soil} taking into account the accumulation of metrafenone in soil (see point 4.1.2).

The resulting acute and long term TER values are all above the appropriate Annex VI trigger values indicating a low risk to earthworms from the representative uses of metrafenone evaluated.

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

As the $DT_{90field}$ exceeds 1 year, a litterbag study is considered necessary. Two litterbag studies are discussed in the DAR. Both studies were performed at dose rates below the maximum PEC_{soil} which includes accumulation of metrafenone in the soil. Therefore a new litterbag study was performed at higher dose rates. The RMS evaluated this study in the addendum of November 2004. In this study the soil concentrations were calculated to be 95% of the maximum PEC_{soil} in grapevines and 97% of the maximum PEC_{soil} in cereals. Deviations from control value in loss of mass were small, not statistically significant and the risk posed to soil degradation processes is considered to be low. This study was discussed in the EPCO Expert's meeting. The meeting agreed that this point is addressed.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of the lead formulations BAS 560 00F and BAS 560 02F and the metabolite CL 377160 were tested on soil microbial respiration and nitrogen transformation. The risk assessment is based on the study with BAS 560 00F during which a dose of 2 mg as/kg soil was tested which exceeds the maximum PEC_{soil} for both representative uses. The two formulations "BAS 560 00F" and "BAS 560 02F" used in cereals and grapevine, respectively, differ mainly in the content of metrafenone (300 g/L and 500 g/L) and in the content of the wetting agents. "BAS 560 00F" contains significantly more wetting agents than "BAS 560 02F". The other differences are negligible. The two formulations are considered sufficiently similar for all of them to be used in support of either use. No deviations of more than 25 % after 42 days were observed (i.e. no breaching of the Annex VI trigger value) at a dose rate exceeding the maximum PEC and hence the risk to soil non-target micro-organisms from metrafenone and the metabolite CL 377160 is considered to be low for the representative uses of metrafenone evaluated.

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

In 2 studies using the lead formulation BAS 560 02F there were no effects on seedling emergence or growth of young plants of 4 species of monocotyledon and 6 species of dicotyledon treated with the

equivalent of 100 and 300 g a.s./ha in glasshouse studies. Furthermore one study is available with the lead formulation BAS 560 00F during which no effects on growth of young plants of 2 species of monocotyledon and 4 species of dicotyledon treated with the equivalent of 150 and 300 g a.s./ha in glasshouse studies. All test species were crop species. The risk to non-target plants is considered to be low as no effects were seen at the highest nominal application rate.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The respiration rate EC_{50} for metrafenone exceeds 600 mg a.s./L. Based on this study the risk to biological methods of sewage treatment is considered to be low for the representative uses of metrafenone evaluated.

6. Residue definitions

Soil

Definitions for risk assessment: metrafenone and CL 377160[16]

Definitions for monitoring: metrafenone

Water

Ground water

Definitions for exposure assessment: metrafenone and CL 377160

Definitions for monitoring: metrafenone

Surface water

Definitions for risk assessment: metrafenone

Definitions for monitoring: metrafenone

Air

Definitions for risk assessment: metrafenone

Definitions for monitoring: metrafenone

Food of plant origin

Definitions for risk assessment: metrafenone

Definitions for monitoring: metrafenone

Food of animal origin

Definitions for risk assessment: not proposed by RMS[17]

Definitions for monitoring: not proposed by RMS

[16] CL 377160: see Appendix 3

[17] should be defined for ruminant liver and kidney (refer to chapter 3.2)

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
metrafenone	Highly persistent (DT_{50lab} (20 ºC) = 182 – 365 d)	See 5.5, 5.6 and 5.7
CL 377160 (photolysis metabolite)	Low persistent (DT_{50lab} (20 ºC) < 7 d)	The risk to earthworms and soil micro-organisms can be regarded as low and is lower than the parent. Regarded as not relevant by the EPCO 17 Expert's meeting.

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**
Metrafenone	Low mobile to immobile	FOCUS modelling: No	Yes	Yes	See 5.2
CL 377160	Slightly mobile to immobile	FOCUS modelling: No	No assessment required. No data available.	No assessment required. No data available	No assessment required. No data available.

Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Metrafenone (water and sediment phases)	See 5.2

Air

Compound (name and/or code)	**Toxicology**
Metrafenone	Not acutely toxic via inhalation.

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

- Final report of the field soil accumulation study should be provided when available (formal data requirement relevant for all representative uses evaluated; no submission date still proposed by the notifier; refer to point 4.1.2).
- Refinement of the long term risk to birds from exposure to contaminated drinking water. (proposed by EFSA, not peer reviewed; relevant for cereals, no submission date proposed by the notifier; refer to point 5.1)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide which comprises broadcast spraying to control powdery mildew in wheat and grapevines at application rates up 150 g metrafenone per hectare (cereals)[18] and 100 g per hectare (grapevines), respectively. Metrafenone can be used only as fungicide.

The representative formulated products for the evaluation were "BAS 560 00 F" (cereal use) and "BAS 560 02 F" (grapevine use), both are suspension concentrates (SC).

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

The acute toxicity of metrafenone is low. It is not a skin or an eye irritant, nor a skin sensitiser. The NOAEL for short term repeated exposure is 43 mg/kg bw/day and for chronic exposure is 25 mg/kg bw/day. Metrafenone did not show any genotoxic potential in a battery of genotoxicity assays. It is carcinogenic in rodents at very high doses but with no relevance to humans. The NOAEL for maternal toxicity is 39 mg/kg bw/day, and the NOAEL for reproductive effects is 79 mg/kg bw/day. In rabbits the NOAEL for maternal and developmental toxicity was 50 mg/kg bw/day. Metrafenone does not show any neurotoxic potential. The ADI for metrafenone is 0.25 mg/kg bw/day, based on the NOAEL of 25 mg/kg bw/day from the 2-year study in rat, with a safety factor of 100. The AOEL is 0.43 mg/kg bw/day on the NOAEL of the13-week oral study in rats with a SF 100. Based on the toxicological characteristics of metrafenone setting an ARfD is not needed. The exposure for the

[18] It should be noted that the efficacy evaluation made by the RMS concluded that useful reduction of eyespot (*Pseudocersporella herpotrichioides)* was achieved in winter and spring wheat only

operators is below the AOEL even without PPE. No exceedence of the AOEL is expected for re-entry workers or bystanders.

Applied to wheat plants and vines by foliar application metrafenone itself was the major component identified at harvest in the analysed plant parts. Few metabolites of metrafenone were identified in vine leaves and wheat straw, and, basically, there was no evidence that molecular cleavage occurred. In grain the majority of the radioactivity got incorporated into plant material. In rotational crop studies metrafenone was not present at significant levels in the succeeding crops. Decline of metrafenone residues under processing conditions does not occur.
Fed to ruminants and poultry, metrafenone was extensively metabolised in the liver and kidney. The metabolites identified in the goat metabolism study are structurally similar to those found in the rat metabolism study. Even though metrafenone is classified as fat-soluble (logPow 4) there was no evidence for accumulation of residues in adipose tissue.
The chronic dietary exposure assessment for consumers based on the representative GAP indicated that for all consumer subgroup the intake was less then 1% of the proposed ADI.

Metrafenone is high persistent in soil under aerobic conditions ($DT_{50\ lab\ 20\ °C}$ = 182 d – 365 d). Very low levels of extractable metabolites were found and identified. Mineralization is low and unextractable radioactivity reached up to 24.8 % AR after 120 d.
Under anaerobic conditions metrafenone degrades much faster than under aerobic conditions ($DT_{50\_lab\_20°C\_anaerobic}$ = 8 d – 15 d) and a large number of metabolite fractions are formed. A high amount of the radioactivity corresponds to unresolved TLC spots and procedural losses (up to 30 % AR). Only two major metabolite fractions M6 (maximum 45.1 % AR at 15 d) and M 5.2 (maximum 19.4 % AR at 88 d) were identified. In the case of M6 the levels remained relatively high for a long period of time (from day 15 to the end of the study at day 120). Since extraction procedures include some treatments considered harsh applicant claimed that the majority of the residue in soil would not be bioavailable. Under the mildest extraction conditions (water, acetone, and methanol-water without using acid or basic solvents) only a maximum of 5.7 % AR was extracted as metabolite fraction M6. This metabolite fraction was observed close of the origin of the TLC plate and seems to consist in multiple minor polar components. In a second anaerobic study, the main metabolites identified were CL 377160 (max. 5.3 % at 7d) and CL 4084564 (7.3 % at 28 d).
Photolysis also contribute to the degradation of metrafenone ($DT_{50\_photolysis}$ = 15.5 d continuous irradiation). Compound **CL 377160** (max. 18.9 % AR) was formed as a major soil photolysis product. Under dark aerobic conditions, the photolysis metabolite CL 377160 is rapidly degraded (DT_{90} < 7 d). Most of the degradation will contribute the formation of unextractable residue (63.1 – 74.2 % AR at 120 d, end of the study). The major fraction of the unextractable residue is associated with the humin soil fraction (22.2 – 35.9 % AR).
Field dissipation studies were conducted in four sites in Europe located in Germany, United Kingdom, Denmark and Northern France. Under field conditions metrafenone is medium to high persistent in soil ($DT_{50\ field}$ = 70 – 144 d). Since the field studies were performed on bare soils (with a potentially high contribution of photolysis) and the representative uses proposed are for developed

crops were the foliage will shadow the field, RMS proposed to use the worst case laboratory half life for the EU risk assessment.

Four field accumulation studies were initiated in 1999 and planned to finalise in 2004. Three trials were performed in grapevines in Germany, Italy and Spain and a trial in cereals in Germany. Interim reports of these studies were submitted to the RMS. The main concern raised by these studies was that after 5 years the plateau was still not reached. A modelling exercise based on PEARL leaching model with worst case degradation input parameters show that the plateau is reached after 10 years of continuous application. The results of this model have been used as PEC soil for the EU risk assessment.

Metrafenone may be classified as low mobile to immobile (K_{foc} = 1592 – 5556 mL / g) and metabolite CL 377160 as slightly mobile to immobile (K_{foc} = 2199 – 21649 mL / g) in soil. Metrafenone is expected to be stable to hydrolysis under environmental conditions of pH and temperature.

Photolysis may contribute to the degradation of metrafenone in water ($DT_{50\ summer\ 40\ °N}$ = 12.3 d; $DT_{50\ winter\ 40\ °N}$ = 53.3 d).

Metrafenone is not readily biodegradable.

Two aerobic water sediment systems at 20 °C under dark conditions were investigated. Metrafenone was found to dissipate relatively rapidly from water. Metrafenone is also low persistent in the total systems ($DT_{50\ total\ systems}$ = 8.5 – 9.2 d). Unextractable residues were formed up to 15.7 – 26.4 % AR at the study end. Mineralization was 2.6 – 12.4 % at the study end. Only minor metabolites were identified in the water / sediment systems.

PEC_{SW} were calculated for the buffer distances of 3 m, 5m and 10m assuming spray drift from single and multiple applications (2 x 150 g/ha with 21 d interval in cereals and 8 x 100 g/ha with 12 d interval in vines) taking as basis the worst case dissipation half life observed in the water phase of the dark water sediment study ($DT_{50\ water}$ = 4.6 d). Same premises were used to calculate initial PEC_{SED}.

The rapporteur Member State also provided PEC_{SW} of metrafenone and its soil photolysis metabolite CL 377160 derived from drainage on cereal crops based on their national scheme. For the active substance the calculation also considered the drainflow of the accumulated substance in soil. The drainflow concentration obtained was of 0.97 µg/ L (70 % of what would be expected form spray drift at 1m). Potential surface water contamination through run-off was not assessed in the DAR. Experts' meeting agreed that due to the high K_{oc} of the active substance runoff and drainage will be of limited significance and that for the purposes of the EU risk assessment no further information was necessary. However, Member States may need to pay special attention to runoff and drain flow in their national risk assessment taking into considerations the particular conditions of their crops.

Potential contamination of ground water by metrafenone and its soil photolysis metabolite was addressed by calculation of PEC_{GW} for the FOCUS Groundwater Scenarios using FOCUS PEARL, v. 1.1.1. The predicted 80th percentile concentrations of metrafenone and metabolite CL 377160 at 1m depth were less than 0.001 µg / L for the spring and winter cereals and vines in all the relevant scenarios.

Metrafenone may be prone to some volatilization from soil or water surfaces. However, it is strongly adsorbed in soil matrices and its atmospheric photochemical oxidative half life was calculated to be 0.63 h and it is not expected to be subject to long-range transport

The risk to birds and mammals was calculated using the nomogram of Hoerger and Kenaga (EPPO 1992) and according to the Guidance Document on Risk Assessment for Birds and mammals Under Council Directive 91/414/EEC (SANCO/4145/2000). The risk to herbivorous and insectivorous birds in cereals and to insectivorous birds in grapevines can be regarded as low according to both risk assessments. Also the risk to herbivorous and insectivorous mammals in cereals and herbivorous mammals in grapevines can be regarded as low according to both risk assessments. The risk to birds and mammals from secondary poisoning is regarded to be low for the representative uses evaluated. As it was noted by EFSA that no risk assessment for birds and mammals from consumption of contaminated drinking water was performed this risk assessment is presented in the addendum by EFSA. The risk to birds and mammals from consumption of contaminated drinking water is considered to be low except for the long term risk to birds in cereals for which the TER value is below the trigger value indicating a high long term risk to birds in cereals from drinking contaminated drinking water. Therefore EFSA proposes a data requirement for the notifier to refine the long term risk to birds in cereals from exposure to contaminated drinking water. This assessment was neither discussed at the EPCO Expert's meeting nor peer reviewed.

The risk to aquatic organisms is regarded to be low without the need for risk mitigation measures. The risk to bees and other arthropod species can be regarded as low based on the available studies. The risk to earthworms and soil micro-organisms can be regarded as low. As the $DT_{90field}$ exceeds 1 year litterbag studies were submitted to address the risk to other soil non-target macro-organisms. The soil concentrations in the study by Krieg *et al* (2004) were calculated to reach 95-97% of the maximum PEC_{soil} in grapevines and cereals. Deviations from control value in loss of mass were small, not statistically significant and the risk posed to soil degradation processes is considered to be low. This study was discussed in the EPCO Expert's meeting. The meeting agreed that this point is addressed.

The risk to non-target plants and biological methods for sewage treatment is considered to be low.

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

- None

Critical areas of concern

- None

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

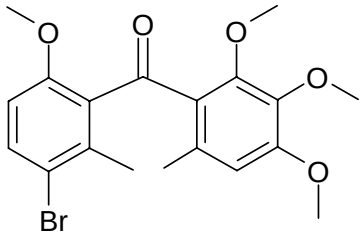
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	Metrafenone
Function (e.g. fungicide)	Fungicide

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

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3'-bromo-2,3,4,6'-tetramethoxy-2',6-dimethylbenzophenone
Chemical name (CA) ‡	Methanone, (3-bromo-6-methoxy-2-methylphenyl)(2,3,4-trimethoxy-6-methylphenyl)
CIPAC No ‡	752
CAS No ‡	220899-03-6
EEC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification ‡ (including year of publication)	None
Minimum purity of the active substance as manufactured ‡ (g/kg)	940 (pilot plant production)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula ‡	$C_{19}H_{21}BrO_5$
Molecular mass ‡	409.27 g/mol
Structural formula ‡	

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

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	99.2 – 100.8 °C (99.5%)
Boiling point (state purity) ‡	The pure a.s. (99.5%) did not show an indication of a boiling point up to a temperature of approx. 310 °C, where the test substance turned to a black tar accompanied by a smell of decomposition
Temperature of decomposition	310 °C
Appearance (state purity) ‡	White crystalline solid (99.5%) Powdery, yellow-white crystalline solid (95.9%)
Relative density (state purity) ‡	1.45 at 20 °C (99.4%)
Surface tension	A 90% saturated solution of the test substance (purity 95.86%) has a surface tension of 67.4 mN/m at 20 °C.
Vapour pressure (in Pa, state temperature) ‡	1.53·10–4 Pa (1.53·10–6 mbar) at 20 °C (99.7%) and: 2.56·10–4 Pa (2.56·10–6 mbar) at 25 °C (99.7%)
Henry's law constant (Pa m^3 mol^{-1}) ‡	Based on the vapour pressure at 20 °C and the water solubility at 20 °C: KH = 0.132 Pa·m³·mol–1.
Solubility in water ‡ (g/L or mg/L, state temperature)	Deionized water (pH unspecified): 0.474 mg/L (20 °C) pH 5: 0.552 mg/L (20 °C) pH 7: 0.492 mg/L (20 °C) pH 9: 0.457 mg/L (20 °C)
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	Acetone 403 g/L (20°C) Acetonitrile 165 g/L (20°C) Dichloromethane 1950 g/L (20°C) Ethyl acetate 261 g/L (20°C) n-Hexane 4.8 g/L (20°C) Methanol 26.1 g/L (20°C) Toluene363 g/L (20°C)
Partition co-efficient (log POW) ‡ (state pH and temperature)	pH of 4.0 at 25 °C: 4.3 The effect of pH on the log KOW was not investigated since the test substance shows no dissociation in water.
Hydrolytic stability (DT50) ‡ (state pH and temperature)	Stable to hydrolysis in the dark after incubation for 5 days at 50 °C in pH 4, pH 7 and pH 9 buffers.
Dissociation constant ‡	No dissociation
UV/VIS absorption (max.) ‡ (if absorption >	(ε [l mol-1 cm-1]): 42443 at 206 nm

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

290 nm state ε at wavelength)	(ε [l mol-1 cm-1]): 8643 at 285 nm Absorption diminishes from 285nm, becoming insignificant above 340 nm.
Photostability (DT50) ‡ (aqueous, sunlight, state pH)	Degraded extensively after irradiation by simulated sunlight for 15 days at pH 7 and 22 °C (first order kinetics, rate constant: 0.225/day; DT_{50} : 3.1 days, DT_{90} : 10.2 days).
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	$2.29 \cdot 10^{-4}$ moles/ einstein (300 – 370nm)
Flammability ‡	Not highly flammable
Explosive properties ‡	Not explosive

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

Appendix 1 – list of endpoints

List of representative uses evaluated*

Crop and/or situation (a)	Member State	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 a.s. (i)	Method, kind (f-h)	Growth stage & season (j)	Number (min max) (k)	interval between applications (min)	kg a.s./ha	water l/ha	kg a.s. /hl		
Cereals (wheat and barley)	Northern & Southern Europe	BAS 560 00 F	F	Powdery mildew *Erysiphe graminis*	SC	300 g/L	over plant spray	30 – 79	1 – 2	21	0.150	100-400	0.05	35	
Cereals[#] (wheat and barley)	Northern & Southern Europe	BAS 560 00 F	F	Eyespot *Pseudocerco-sporella herpotrichoides*	SC	300 g/L	over plant spray	30 – 35	1	-	0.150	100-400	0.05	-	
Grapevines	Northern Europe	BAS 560 02 F	F	Powdery mildew *Uncinula necator*	SC	500 g/L	over plant spray	15 – 81	1 – 8	12	0.1	1000	0.010	28	Water volume applied in function of the crop size and application technique
Grapevines	Southern Europe	BAS 560 02 F	F	Powdery mildew *Uncinula necator*	SC	500 g/L	over plant spray	57 – 81	1 – 8	12	0.1	1000	0.010	28	

[#] It should be noted that the efficacy evaluation made by the RMS concluded that useful reduction of eyespot (*Pseudocercosporella herpotrichoides)* was achieved in winter and spring wheat only

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 the 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)	HPLC with UV detection
Impurities in technical as (principle of method)	HPLC with UV or MS/MS detection Capillary GC with FID or MS detection (solvents) Karl-Fischer titration for water
Plant protection product (principle of method)	HPLC with UV (diode array) detection

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	**Barley grain, grape, wine:** DFG-S19. Solvent extraction, clean-up by solvent partition, GPC and adsorption chromatography. Det. by capillary GC/ECD. Conf by GC/MSD (3 ions). LOQ: 0.02 mg/kg (barley and grape) LOQ: 0.01mg/kg (all other plant commodities). **Citrus, oil seed rape:** DFG-S19. Extraction / clean-up as above with minor variations and omitting the final silica gel clean-up. Det. / conf. by GC/MSD (3 ions) LOQ: 0.02mg/kg (oranges), 0.05mg/kg (OSR)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Analytical methods not required since no residue definition is proposed. **Milk, meat, eggs:** DFG-S19. Extraction / clean-up as above with minor variations and omitting the final silica gel clean-up. Det./ conf. by GC/MSD only (3 ions) LOQ: 0.01mg/kg (milk), 0.05mg/kg (meat and eggs)
Soil (principle of method and LOQ)	Solvent extraction followed by clean-up using adsorption chromatography (silica cartridge). Det. by HPLC / MS (one ion). Conf. by HPLC MS/MS (two ions). LOQ: 0.005mg/kg
Water (principle of method and LOQ)	Extraction by liquid-liquid partition, det. by HPLC with MS detection (full scan / selected ions). Conf. by HPLC-MS/MS. LOQ: 0.05µg/kg (drinking and surface waters)

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

Air (principle of method and LOQ)	Residues absorbed onto an ORBO-43 air sampling tube packed with XAD-2 resin and eluted with acetone. Det, by capillary GC/ECD. Conf. by HPLC-MS (full scan / selected ions). LOQ: 0.03µg/liter air.
Body fluids and tissues (principle of method and LOQ)	No data submitted or required.

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None

‡ Endpoints identified by the 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 ‡	>88% within 72 hours (at 10 mg/kg bw)
Distribution ‡	Widely distributed, with highest levels in gastrointestinal tract and liver
Potential for accumulation ‡	Low
Rate and extent of excretion ‡	67-79% (mainly in faeces via bile) with 24 hours at 10 mg/kg bw.
Metabolism in animals ‡	Extensive, mostly consisting of substitution of ring methoxy groups with hydroxyl groups and subsequent conjugation with glucuronic acid.
Toxicologically significant compounds ‡ (animals, plants and environment)	Metrafenone

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50}oral ‡	> 5000 mg/kg bw
Rat LD_{50}dermal ‡	> 5000 mg/kg bw
Rat LC_{50}inhalation ‡	> 5.0 mg/L
Skin irritation ‡	Non irritant
Eye irritation ‡	Non irritant
Skin sensitization ‡ (test method used and result)	Non-sensitiser (Magnusson and Kligman)

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Increased relative liver weights and histopathological findings in the liver
Lowest relevant oral NOAEL / NOEL ‡	43 mg/kg bw/day
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

‡ Endpoints identified by the 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 ‡	Hepatocellular hypertrophy and hepatocellular adenomas
Lowest relevant NOAEL / NOEL ‡	25 mg/kg bw/day
Carcinogenicity ‡	Hepatocellular adenomas in rats and mice. Non-genotoxic mechanism proposed (chronic induction of cell proliferation/enzyme induction). Not relevant to human exposure

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	No adverse effects on reproductive performance. Reduced pup weights (F1 and F2) and an increased proportion of abnormal sperm (F1 only) in the presence of parental toxicity (reduced bodyweights and food consumption, increased liver and kidney weights, hepatocellular hypertrophy).
Lowest relevant reproductive NOAEL / NOEL ‡	79 mg/kg bw/day
Developmental target / critical effect ‡	Lower foetal bodyweights and premature delivery at maternally toxic dosages, in rabbits only
Lowest relevant developmental NOAEL / NOEL ‡	50 mg/kg bw/day

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

.....	No neurotoxicity studies submitted. No evidence of neurotoxicity in repeat dose studies.

Other toxicological studies ‡ (Annex IIA, point 5.8)

.....	Metrafenone was shown to induce cytochrome P_{450} enzymes in rat liver. Metrafenone did not show tumour initiating potential in rat liver, and cell proliferation in specific zones of the liver (S-phase response) was demonstrated in rats; the effect was reversible.

Medical data ‡ (Annex IIA, point 5.9)

.....	No evidence of adverse effects in personnel exposed to metrafenone during its development.

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

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.25 mg/kg bw/day	Rat, 2 year study	100
AOEL ‡	0.43 mg/kg bw/day	Rat, 13 week study	100
ARfD ‡ (acute reference dose)	Not allocated - Not necessary		

Dermal absorption (Annex IIIA, point 7.3)

BAS 560 02F	2% for concentrate 20% for in-use dilution

Acceptable exposure scenarios (including method of calculation)

Operator	The estimated exposure of the operators applying BAS 560 00F and BAS 560 02F is below the AOEL (from 5% to 53% without PPE, from 4% to 49% with PPE)
Workers	The estimated worker exposure in treated cereal crops or in grapevines is below the AOEL (0.2% and 15% of the AOEL, respectively).
Bystanders	Bystander exposure is below the AOEL either for cereal application (0.14%) or for grapevine application (<3%).

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	No classification proposed for metrafenone. No classification proposed for BAS 560 02F. R43 May cause skin sentisation by skin contact; proposed for BAS 560 00F on the basis of a co-formulant which is a known human skin sensitiser.

‡ Endpoints identified by the 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	Cereals and grapevine
Rotational crops	Lettuce, raddish, canola (replant intervals 30, 60, 90, 365)
Plant residue definition for monitoring	Metrafenone
Plant residue definition for risk assessment	Metrafenone
Conversion factor (monitoring to risk assessment)	Not applicable

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

Animals covered	Goat, hen
Animal residue definition for monitoring	Not proposed by RMS
Animal residue definition for risk assessment	Not proposed by RMS[19]
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Not applicable

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

.....	Not required. Based on rotational crops metabolism data residues in succeeding crops are unlikely if metrafenone is used according to GAP.

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

.....	Residues in grapes and wine are stable for up to 18 months at $\leq$ -20°C. Residues in cereal grain and straw are stable for up to 24 months at $\leq$ -18°C.

[19] should be defined for ruminant liver and kidney (refer to chapter 3.2)

‡ Endpoints identified by the 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	Poultry: yes	Pig: yes
Muscle Liver Kidney Fat Milk Eggs	No ruminant feeding study conducted. Metabolism results indicated that residues will not be of significance at N rate.	No hen feeding study conducted. Metabolism results indicated that residues will not be of significance.	No pig feeding study conducted. Metabolism in rat and ruminant similar, ruminant metabolism indicated that residues will not be of significance.

‡ Endpoints identified by the 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 (a)	Recommendation/comments	MRL	STMR (b)
Wheat	Northern	6 x < 0.01, 2 x 0.01, 2 x 0.03, 3 x 0.04.	grain	0.05	0.01
Wheat	Northern	0.40, 0.58, 2 x 0.61, 0.67, 0.93, 0.98, 1.43, 1.72, 1.80, 1.85, 2.04, 2.32, 3.86.	straw	-	1.43
Wheat	Mediterranean	10 x < 0.01, 3 x 0.01, 0.03.	grain	0.05	0.01
Wheat	Mediterranean	0.67, 0.88, 2 x 1.07, 1.08, 1.09, 1.10, 1.11, 1.25, 1.61, 1.64, 1.69, 1.70, 2.12.	straw	-	1.11
Barley	Northern	0.01, 0.02, 0.03, 0.04, 0.06, 0.07, 0.09, 0.11, 0.14, 2 x 0.15, 0.16, 0.40.	grain	0.50	0.09
Barley	Northern	0.54, 0.64, 0.78, 1.08, 1.10, 1.11, 1.12, 1.15, 1.28, 1.60, 1.70, 2.01.	straw	-	1.11
Barley	Mediterranean	3 x 0.04, 2 x 0.05, 0.06, 0.08, 0.10, 2 x 0.12, 0.13, 0.23.	grain	0.50	0.07
Barley	Mediterranean	0.41, 0.90, 0.96, 1.02, 1.22, 1.34, 1.56, 1.65, 1.94, 2.13, 4.03, 4.25.	straw	-	1.45
Grapevine	Northern	0.11, 0.12, 0.15, 0.18, 0.19, 0.20, 0.31, 0.36.	grape	0.50	0.18
Grapevine	Mediterranean	2 x 0.08, 0.11, 0.17, 0.20, 0.22, 0.23, 0.24, 0.30, 0.34, 0.38.	grape	0.50	0.22

(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 the 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	0.25 mg/kg bw/day
TMDI (European Diet) (% ADI)	<1% (UK) for all consumer groups. <1% based on GEMS/Food European diet
NEDI (% ADI)	Not necessary due to low TMDI
Factors included in NEDI	Not necessary
ARfD	Not necessary
Acute exposure (% ARfD)	Not necessary

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Wheat	Not required due to low residues in grain (< 0.1 mg/kg)	Not applicable	Not applicable
Barley/ Pearl barley	1	0.14	Not allocated
Barley/ Bran	1	2.9	Not allocated
Barley/ Beer	1	0.14	Not allocated
Grape/ wine (young)	8	0.32	No data n/a
Grape/ wine (stored)	8	0.31	No data n/a
Grape/ raisin	2	0.67	No data n/a

* 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)

Wheat grain	0.05 mg/kg
Barley grain	0.50 mg/kg
Grape	0.50 mg/kg

‡ Endpoints identified by the 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 ‡	1.8% after 120 d, [^{14}C-trimethoxyphenyl]-label (n= 1) 1.5 – 5.3% after 120 d, [^{14}C-bromophenyl]-label (n= 4)
Non-extractable residues after 100 days ‡	19.4% after 120 d, [^{14}C- trimethoxyphenyl]-label (n= 1) 17.4 – 24.8% after 120 d, [^{14}C- bromophenyl]-label (n= 4)
*Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	No metabolites ≥ 5% at any time point in aerobic, dark studies

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

Anaerobic degradation ‡	Mineralisation – 0.2 - 1.3% after 120/122 d, (n= 4) Non-extractable residues 29.5 – 38.3% after 120/122 d, (n= 2) Metabolites (>5%) CL 377160 – 5.2 – 5.3% at 7 - 15 d CL 4084564 – 3.7 – 7.3% at 28 d CL 434223 – 2.0 – 8.2% at 8 d Both labels
Soil photolysis ‡	Mineralisation 2.9% after 30 d Non-extractable residues 24.7% after 30 d Metabolites CL 377160 – 18.9% at 14 d Both labels

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

Method of calculation	Laboratory: 1st order kinetics (linear regression, non-linear regression for one anaerobic study, photolysis study by compartment model with ModelMaker v 4.0) Field studies: 1st order and biphasic 1st order (ModelMaker using non-linear regression)

* For ECCO purposes this box requires information on major metabolites (those that occur at > 10% of the applied dose).

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

Laboratory studies ‡ (range or median, with n value, with r^2 value)	parent DT_{50lab} (20°C, aerobic): 182 - 365 d (n= 5, r^2 = 0.86 – 0.98); mean of values corrected to pF 2 used in groundwater modelling = 250.6 days CL 377160: DT_{50lab} (20°C, aerobic): <7 d (n= 3, r^2 = not estimated); DT_{50}7 days for groundwater modelling parent DT_{90lab} (20°C, aerobic):606 – 1212d (n= 5, r^2 = 0.86 – 0.98 according to DT_{50} quoted above; DT_{90} all extrapolated beyond study end) CL 377160: DT_{90lab} (20°C, aerobic): <7 d (n= 3, r^2 = not estimated) [3]DT_{50lab} (10°C, aerobic): 693 d (n= 1, r^2 = 0.94) DT_{50lab} (20°C, anaerobic): 8 – 15 d (n= 4, r^2= 0.95 – 0.99)
	degradation in the saturated zone: no data submitted and no data required.
Field studies ‡ (state location, range or median with n value)	Germany, bare soil, simple 1st order DT_{50} 144 d, DT_{90} 478 d (r^2= 0.89); biphasic 1st order DT_{50} 124 d, DT_{90} 637 days (r^2 = 0.91) UK, bare soil, simple 1st order DT_{50}149 d, DT90 495 d (r^2= 0.42); biphasic calculation not performed Denmark, bare soil, simple 1st order DT_{50} 221 d, DT_{90} 734 d (r^2= 0.55); biphasic 1st order DT_{50} 54 d, DT_{90} >1000 days (r^2 = 0.94) N France , simple 1st order DT_{50} 70 d, DT_{90} 233 d (r^2= 0.74); biphasic 1st order DT_{50} 32 d, DT_{90} 493 days (r^2 = 0.80)
	DT_{90f}: see above

[3] It should clearly be indicated whether the value was obtained by calculation or in a study (e.g. DT_{50lab}/DT_{50calc}). Where the value is calculated Q_{10} and DT_{50} at 20°C used should be stated.

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

Soil accumulation and plateau concentration ‡	Four field accumulation studies (Italy, Spain, 2 x Germany), 4 – 5 years duration. Germany, cereals, 2 x 200 g a.s./ha/year. Peak soil residue in 0-10cm depth first year (1999) 0.024 mg/kg, peak cumulative residue (2003) 0.19 mg/kg. Germany, vines, 8 x 59 – 170 g a.s./ha/year. Peak soil residue in 0-10 cm depth first year (1999) 0.162 mg/kg, peak cumulative residue (2003) 0.32 mg/kg. Spain, bare soil with vines GAP, 8 x 100 g a.s./ha/year. Peak soil residue in 0-10 cm depth first year (1999) 0.09 mg/kg, peak cumulative residue (2002) 0.19 mg/kg. Italy, bare soil with vines GAP, 8 x 100 g a.s./ha/year. Peak soil residue in 0-10 cm depth first year (1999) 0.14 mg/kg, peak cumulative residue (2001) 0.69 mg/kg. Soil photolysis metabolite CL 377160 never found at or above LOQ of 0.02 mg/kg. Field accumulation studies ongoing at April 03. Accumulation modelling with FOCUS-PEARL assuming applications as recommended every year for 26 years, DT_{50}345.4 days, Kom 3223 l/kg, soil bulk density 1.5 g/cm^3, residue remains in top 5 cm: cereals max residue 0.843 mk/kg; vines max residue 1.336 mg/kg; plateau region established at 6-10 years after initial application.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡	K_{oc} parent: 1592 - 5556 cm^3 / g (mean 3105, $^1/_n$= 0.85 – 0.91, mean 0.91, 5 soils)
K_d ‡	K_{oc} CL 377160: 2199 – 21649 cm^3 / g (mean 6499, $^1/_n$= 0.982 – 1.130, mean 1.014, 5 soils) K_f parent: 24.1 - 258 (mean 87.3, 5 soils) K_f CL 377160: 62.1 – 264.1 (mean 105.8, 5 soils)
pH dependence ‡ (yes / no) (if yes type of dependence)	No pH dependence for parent or metabolite

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

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

Column leaching ‡	No studies submitted, none required
Aged residues leaching ‡	No studies submitted, none required
Lysimeter/ field leaching studies ‡	No studies submitted, none required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent (use in cereals)

Method of calculation	DT_{50} (d): 365 days Kinetics: 1st order Field or Lab: representative worst case from lab studies; field values from bare soil application may be unduely affected by soil photolysis.
Application rate	Crop: cereals % plant interception: 50% Number of applications: 2 Interval (d): 21 Application rate(s): 150 g as/ha

PEC(s) (mg/kg)		Multiple application Actual	Multiple application Time weighted average
Initial		0.196	0.196
Short term	4h	0.196	0.196
	2d	0.195	0.196
	4d	0.195	0.195
Long term	7d	0.194	0.195
	28d	0.186	0.191
	50d	0.178	0.187
	100d	0.162	0.179

Maximum accumulated soil concentration calculated by modelling of use in cereals is 0.843 mg as/kg.

Peak PECsoil for CL 377160 following <u>cereal</u> use (molecular weight correction 0.966, 2x 150 g as/ha, 50% interception, no degradation between applications) = 0.037 mg/kg

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

Parent (use in vines)

Method of calculation	DT_{50} (d): 365 days Kinetics: 1st order Field or Lab: representative worst case from lab studies; +field values from bare soil application may be unduely affected by soil photolysis.
Application rate	Crop: vines % plant interception: 60% Number of applications: 8 Interval (d): 12 days Application rate(s): 100 g as/ha

$PEC_{(s)}$ (mg/kg)		Multiple application Actual	Multiple application Time weighted average
Initial		0.394	0.394
Short term	24h	0.394	0.394
	2d	0.393	0.394
	4d	0.392	0.393
Long term	7d	0.389	0.392
	28d	0.374	0.384
	50d	0.359	0.376
	100d	0.326	0.359

Maximum accumulated soil concentration calculated by modelling of use in vines is 1.336 mg as/kg.

Peak PECsoil for CL 377160 following vines use (molecular weight correction 0.966, 8 x 100 g as/ha, 60% interception, no degradation between applications) = 0.078 mg/kg

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)	50°C, pH5, 7 and 9: <10% degradation after 5 days – considered stable to hydrolysis
Photolytic degradation of active substance and relevant metabolites ‡	Xenon arc lamp, equivalent to early autumn sunlight, New jersey USA, 40°N; DT_{50} 6.2 days 12 hour light/dark cycles Highest occurring metabolite, CL 4084564: 8.7%AR (4 d) Estimated DT_{50} at 50°N 13.5 days Summer, 128 days Winter
Readily biodegradable (yes/no)	No

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

Degradation in water/sediment	
- DT_{50} water ‡	3.2 – 4.6 days
- DT_{90} water ‡	10.6 – 15.2 days (1st order, r2= >0.96, n= 2)
- DT_{50} whole system ‡	9.0 – 9.6 days
- DT_{90} whole system ‡	29.8 – 31.8 days (1st order, r2= >0.96, n= 2)
Mineralization	2.6 – 12.4%AR (at 100 d, study end, n= 2)
Non-extractable residues	15.7 – 26.4% AR (at 100 d, study end, n= 2)
Distribution in water / sediment systems (active substance) ‡	Maximum of 56.9% AR in sediment after 3 days. DT_{50}in sediment 4.0 – 4.1 days (DT90 13.2 – 13.7 days, 1st order, r2= >0.92, n= 2)
Distribution in water / sediment systems (metabolites) ‡	Water: Highest individual metabolite: CL 375816, 3.7% AR at 100 d, study end. Sediment: Highest individual metabolites: CL 375816, 6.4% AR at 56 d; CL 377160, 6.2% AT at 7 d.

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

Parent (cereals)

Method of calculation	DT_{50} (d): 4.6 days Kinetics: 1st order Field or Lab: representative worst case from lab sediment water studies
Application rate	Crop: Cereals Number of applications: 2 Interval (d): 21 d Application rate(s): 150 g as/ha Depth of water body: 30 cm
Main routes of entry	Drift at 1 meter: 2.77% drift single application, 2.38% each of two applications

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

PEC(sw) (µg/L)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		1.385	1.385	1.240	1.240
Short term	24h	1.191	1.286	1.067	1.151
	2d	1.025	1.196	0.918	1.071
	4d	0.758	1.040	0.679	0.932
Long term	7d	0.482	0.856	0.432	0.766
	14d	0.168	0.577	0.150	0.517
	21d	0.059	0.419	0.052	0.375
	28d	0.020	0.323	0.018	0.290
	42d	0.002	0.218	0.002	0.196

Parent (vines)

Method of calculation	DT_{50} (d): 4.6 days Kinetics: 1st order Field or Lab: representative worst case from lab sediment water studies
Application rate	Crop: Vines Number of applications: 8 Interval (d): 12 d Application rate(s): 100 g as/ha Depth of water body: 30 cm
Main routes of entry	Drift at 3 meters: 8.02% drift single application, 6.90% each of eight applications

PEC$_{(sw)}$ (µg/L)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		2.673	2.673	2.751	2.751
Short term	24h	2.299	2.482	2.366	2.554
	2d	1.978	2.308	2.035	2.375
	4d	1.463	2.008	1.506	2.066

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

PEC$_{(sw)}$ (µg/L)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Long term	7d	0.931	1.652	0.958	1.700
	14d	0.324	1.114	0.334	1.146
	21d	0.113	0.809	0.116	0.833
	28d	0.039	0.624	0.0.040	0.642
	42d	0.005	0.422	0.005	0.434

Metabolite CL 375816 (Cereals)

Method of calculation	Maximum concentrations calculated only, assumes no dissipation between applications
Application rate	Crop: Cereals Number of applications: 2 Interval (d): 21 d Application rate(s): 150 g as/ha (assumed CL 375816 is formed at a maximum of 3.7% of the applied dose in water, molecular weight correction = 0.599) Depth of water body: 30 cm
Main routes of entry	Drift at 1 meter: 2.38% for each of two applications
PECsw (maximum)	0.053 µg/L

Metabolite CL 375816 (Vines)

Method of calculation	Maximum concentrations calculated only, assumes no dissipation between applications
Application rate	Crop: Vines Number of applications: 8 Interval (d): 12 d Application rate(s): 100 g as/ha (assumed CL 375816 is formed at a maximum of 3.7% of the applied dose in water, molecular weight correction = 0.599) Depth of water body: 30 cm
Main routes of entry	Drift at 3 meter: 6.90% for each of eight applications
PECsw (maximum)	0.408 µg/L

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

PEC (sediment)

Parent (cereals)

Method of calculation	56.9% AR partitioning sediment at 3 d, entry route as for surface water, pattern of decline reflecting that measured in the sediment/water study, 11.6% AR in sediment at study end, 100 d
Application rate	Crop: Cereals Number of applications: 2 Interval (d): 21 d (assumes no degradation between applications) Application rate(s): 150 g as/ha Drift at 1m: 2.38% for each application Sediment depth 5cm, bulk density 1.3 g/cm^3

PEC$_{(sed)}$ (µg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial (3 d)	-	-	peak: 6.250	-
Short term	-	-	-	-
Long term (100 d)	-	-	study end: 1.274	-

Parent (vines)

Method of calculation	56.9% AR partitioning sediment at 3 d, entry route as for surface water, pattern of decline reflecting that measured in the sediment/water study, 11.6% AR in sediment at study end, 100 d
Application rate	Crop: Vines Number of applications: 8 Interval (d): 12 d (assumes no degradation between applications) Application rate(s): 100 g as/ha Drift at 3m: 6.90% for each application Sediment depth 5cm, bulk density 1.3 g/cm^3

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

PEC$_{(sed)}$ (µg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial (3 d)	-	-	peak: 48.321	-
Short term	-	-	-	-
Long term (100 d)	-	-	study end: 9.851	-

Metabolite CL 375816 (Cereals)

Method of calculation	Maximum concentrations calculated only, assumes no dissipation between applications
Application rate	Crop: Cereals Number of applications: 2 Interval (d): 21 d Application rate(s): 150 g as/ha (assumed max 6.4% AR CL 375816 in sediment, molecular weight correction = 0.599) Sediment depth 5 cm, bulk density 1.3 g/cm^3
Main routes of entry	Drift at 1 meter: 2.38% for each of two application
PECsw (maximum)	0.421 µg/kg

Metabolite CL 375816 (Vines)

Method of calculation	Maximum concentrations calculated only, assumes no dissipation between applications
Application rate	Crop: Cereals Number of applications: 8 Interval (d): 12 d Application rate(s): 100 g as/ha (assumed max 6.4% AR CL 375816 in sediment, molecular weight correction = 0.599) Sediment depth 5 cm, bulk density 1.3 g/cm^3
Main routes of entry	Drift at 3 meters: 6.9% for each application
PECsw (maximum)	3.256 µg/kg

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

Metabolite CL 377160 (Cereals)

Method of calculation	Maximum concentrations calculated only, assumes no dissipation between applications
Application rate	Crop: Cereals Number of applications: 2 Interval (d): 21 d Application rate(s): 150 g as/ha (assumed max 6.2% AR CL 377160 in sediment, molecular weight correction = 0.966) Sediment depth 5 cm, bulk density 1.3 g/cm^3
Main routes of entry	Drift at 1 meter: 2.38% for each of two applications
PECsw (maximum)	0.658 µg/kg

Metabolite CL 377160 (vines)

Method of calculation	Maximum concentrations calculated only, assumes no dissipation between applications
Application rate	Crop: Vines Number of applications: 8 Interval (d): 12 d Application rate(s): 100 g as/ha (assumed max 6.2% AR CL 377160 in sediment, molecular weight correction = 0.966) Sediment depth 5 cm, bulk density 1.3 g/cm^3
Main routes of entry	Drift at 3 meters: 6.9% for each application
PECsw (maximum)	5.086 µg/kg

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

Parent

Method of calculation and type of study (e.g. modelling, monitoring, lysimeter)	Modelling using FOCUS PEARL Standard FOCUS scenario 26 year run, cereals and vines
Application rate and pesticide parameters	Cereals: Application regime: two applications/year. Application rate: 150 g as/ha, 50% interception for 1st application, 70% interception 2nd application. Vines: Application regime: eight applications/year. Application rate:100 g as/ha; applications 1-2, 60% interception; applications 3-5 70% interception; applications 6-8 85% interception

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

	Mean DT_{50} 250.6 days (20°C & pF2) – recommended temperature and moisture correction enabled Mean Kom 1801 Mean 1/n 0.91 No volatilisation assumed
$PEC_{(gw)}$	
80th percentile annual average concentrations	All scenarios < 0.001 µg/L

Metabolite CL 377160

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Modelling using FOCUS PEARL Standard FOCUS scenario 26 year run, cereals and vines Metabolite formed in soil photolysis study, thus degradation parameters of parent taken from soil photolysis study
Application rate and pesticide parameters	Cereals: Application regime: two applications/year. Application rate: 150 g as/ha, 50% interception for 1st application, 70% interception 2nd application. Vines: Application regime: eight applications/year. Application rate:100 g as/ha; applications 1-2, 60% interception; applications 3-5 70% interception; applications 6-8 85% interception Mean DT_{50} parent 31 days of 12 hour light/dark cycles from soil photolysis study – recommended temperature and moisture correction enabled Mean parent Kom 1801 Mean parent 1/n 0.91 DT_{50} metabolite 7 days from aerobic degradation study on metabolite Mean metabolite Kom 1573 (excluding hihest value) Mean metabolite 1/n 0.99 (excludes highest value) No volatilisation assumed for parent and metabolite
$PEC_{(gw)}$	
80th percentile annual average concentrations	All scenarios < 0.001 µg/L for both parent and CL 377160

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

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	Not available
Photochemical oxidative degradation in air ‡	DT_{50} of 0.63 hours derived by the Atkinson method of calculation (assumes OH radical concentration of 1.5 x 10^6 molecules/cm^3 over 12 hour day. Software version not reported, but calculation possibly performed manually).
Volatilization ‡	Henry's Law Constant 0.132 Pa.m^3/mol Henry's Law Coefficient (dimentionless) 5.42 x 10^{-5} Vapour pressure 1.53 x 10^{-4} Pa at 20˚C

PEC (air)

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	negligible

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	<u>Soil</u> Definitions for risk assessment: metrafenone and CL 377160[1] Definitions for monitoring: metrafenone <u>Water</u> <u>Ground water</u> Definitions for exposure assessment: metrafenone and CL 377160 Definitions for monitoring: metrafenone <u>Surface water</u> Definitions for risk assessment: metrafenone Definitions for monitoring: metrafenone <u>Sediment</u> Definition for the risk assessment: metrafenone

[1] CL 377160: see Appendix 3

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

	Air Definitions for risk assessment: metrafenone Definitions for monitoring: metrafenone

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

Soil (indicate location and type of study)	No data provided - none expected for a new active substance
Surface water (indicate location and type of study)	No data provided - none expected for a new active substance
Ground water (indicate location and type of study)	No data provided - none expected for a new active substance
Air (indicate location and type of study)	No data provided - none expected for a new active substance

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 (proposed for not being readily biodegradable)

‡ Endpoints identified by the 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} > 5000 mg/kg bw/d (rat)
Acute toxicity to birds ‡	LD_{50} > 2025 mg/kg bw/d (northern bobwhite quail/mallard duck)
Dietary toxicity to birds ‡	NOEC 5314 ppm />948.4 mg/kg bw/d (northern bobwhite quail)
Reproductive toxicity to birds ‡	NOEC 1350 ppm/125.4 mg/kg bw/d (northern bobwhite quail)
Reproductive toxicity to mammals	10000 ppm/811 mg/kg bw/d (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
0.150 x2	cereals	large herbivorous bird	acute	> 250	10
0.150 x2	cereals	small insectivorous bird	acute	> 321	10
0.150 x2	cereals	large herbivorous bird	short term dietary	158	10
0.150 x2	cereals	small insectivorous bird	short term dietary	611	10
0.150 x2	cereals	large herbivorous bird	reproductive	40	5
0.150 x2	cereals	small insectivorous bird	reproductive	155	5
0.8 (from 8 applications	grapevines	small insectivorous bird	acute	> 121.3	10
0.8 (from 8 applications	grapevines	small insectivorous bird	short term dietary	> 229	10
0.8 (from 8 applications	grapevines	small insectivorous bird	reproductive	58	5
150 x2	cereals	small herbivorous mammal	acute	> 206	10
150 x 2	cereals	small insectivorous mammal	acute	> 794	10
150 x 2	cereals	small herbivorous mammal	long term	298	5
150 x 2	cereals	small insectivorous mammal	long term	1149	5
0.8 (from 8 applications)	grapevines	small herbivorous mammal	acute	> 77.5	10

‡ Endpoints identified by the 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
0.8 (from 8 applications)	grapevines	small herbivorous mammal	long term	112	5

According to Guidance Document on Risk Assessment for Birds and Mammals under Council Directive 91/414/EEC 25 September 2002 SANCO/4145/2000

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.150 x2	cereals	large herbivorous bird	acute	188	10
0.150 x2	cereals	small insectivorous bird	acute	250	10
0.150 x2	cereals	large herbivorous bird	short term dietary	153	10
0.150 x2	cereals	small insectivorous bird	short term dietary	210	10
0.150 x2	cereals	large herbivorous bird	reproductive	38	5
0.150 x2	cereals	small insectivorous bird	reproductive	27.9	5
0.8 (from 8 applications	grapevines	small insectivorous bird	acute	> 375	10
0.8 (from 8 applications	grapevines	small insectivorous bird	short term dietary	316	10
0.8 (from 8 applications	grapevines	small insectivorous bird	reproductive	41.8	5
150 x2	cereals	small herbivorous mammal	acute	> 146	10
150 x 2	cereals	small insectivorous mammal	acute	> 3846	10
150 x 2	cereals	small herbivorous mammal	long term	77.9	5
150 x 2	cereals	small insectivorous mammal	long term	1690	5
0.8 (from 8 applications	grapevines	small herbivorous mammal	acute	> 264	10
0.8 (from 8 applications	grapevines	small herbivorous mammal	long term	119	5

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

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Laboratory tests ‡				
Oncorhynchus mykiss	metrafenone	96 h	LC50	> 0.82
Daphnia magna	metrafenone	48 h	EC50	> 0.92
Selenastrum capricornutum	metrafenone	72 h	E_bC50 E_rC50	0.71 >0.87
Oncorhynchus mykiss	BAS 560 00F (300 g metrafenone/L)	96 h	LC50	>94
Daphnia magna	BAS 560 00F (300 g metrafenone/L)	48 h	EC50	20
Selenastrum capricornutum	BAS 560 00F (300 g metrafenone/L)	72 h	E_bC50 E_rC50	2.9 21.0
Oncorhynchus mykiss	BAS 560 02F (550 g metrafenone/L)	96 h	LC50	>104
Daphnia magna	BAS 560 02F (550 g metrafenone/L)	48 h	EC50	>1.979
Selenastrum capricornutum	BAS 560 02F (550 g metrafenone/L)	72 h	E_bC50 E_rC50	>2.248 >2.248
Oncorhynchus mykiss	CL 375816	96 h	LC50	> 99
Daphnia magna	CL 375816	48 h	EC50	>100
Pseudokirchneriella subcapitata	CL 375816	72 h	E_bC50 E_rC50	>100 >100
Oncorhynchus mykiss	CL 4084564	96 h	LC50	16.4
Daphnia magna	CL 4084564	48 h	EC50	46
Pseudokirchneriella subcapitata	CL 4084564	72 h	E_bC50 E_rC50	27.8 38.7
Pimephales promelas	metrafenone	32 days	NOEC	0.228
Daphnia magna	metrafenone	21 days	NOEC	0.225
Chironomus riparius	metrafenone	40 days	NOEC	1.0

Microcosm or mesocosm tests
None submitted. Not required.

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

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
0.150 *	cereals	*Oncorhynchus mykiss*	96 h	1	> 590	100
	cereals	*Daphnia magna*	48 h	1	> 662	100
	cereals	*Selenastrum capricornutum*	72 h	1	511	10
0.300	cereals	*Pimephales promelas*	32 d	1	184	10
	cereals	*Daphnia magna*	21 d	1	182	10
	cereals	*Chironomus riparius*	40	1	719	10
0.800**	grapevines	*Oncorhynchus mykiss*	96 h	3	> 298	100
	grapevines	*Daphnia magna*	48 h	3	> 334	100
	grapevines	*Selenastrum capricornutum*	72 h	3	258	10
0.800	grapevines	*Pimephales promelas*	32 d	3	81	10
	grapevines	*Daphnia magna*	21 d	3	80	10
	grapevines	*Chironomus riparius*	40 d	3	364	
CL 375816 ***						
0.150	cereals	*Oncorhynchus mykiss*	96 h	1	>1867925	100
	cereals	*Daphnia magna*	48 h	1	>1886793	100
	cereals	*Pseudokirchneriella subcapitata*	72 h	1	>1886793	10
0.800	grapevines	*Oncorhynchus mykiss*	96 h	3	>242647	100
	grapevines	*Daphnia magna*	48 h	3	>245098	100
	grapevines	*Pseudokirchneriella subcapitata*	72 h	3	>245098	10

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
CL 4084564***						
0.150	cereals	*Oncorhynchus mykiss*	96 h	1	1171429	100
	cereals	*Daphnia magna*	48 h	1	3285714	100
	cereals	*Pseudokirchneriella subcapitata*	72 h	1	1985714	10
0.800	grapevines	*Oncorhynchus mykiss*	96 h	3	32283	100
	grapevines	*Daphnia magna*	48 h	3	90551	100
	grapevines	*Pseudokirchneriella subcapitata*	72 h	3	54724	10

* Highest PEC is calculated after first application
** Highest PEC is calculated after last of 8 applications
*** Application rate expressed as application of parent compound

Bioconcentration

Bioconcentration factor (BCF) ‡	530
Annex VI Trigger:for the bioconcentration factor	100 for compound not readily biodegradable
Clearance time (CT_{50}) (CT_{90})	0.53 d 2.3 d
Level of residues (%) in organisms after the 14 day depuration phase	< 5%

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

Acute oral toxicity ‡	>114 µg a.s./bee based on active substance >32.7 µg a.s./bee based on 'BAS 560 00F' >58.3 µg a.s./bee based on 'BAS 560 02F'
Acute contact toxicity ‡	>100 µg a.s./bee based on active substance >28.8 µg a.s./bee based on 'BAS 560 00F' >48.9 µg a.s./bee based on 'BAS 560 02F'

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

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
150 g a.s./ha	cereals	acute	< 4.6	50
150 g a.s./ha	cereals	contact	< 5.2	50
100 g a.s./ha	grapevines	acute	< 1.7	50
100 g a.s./ha	grapevines	contact	< 2.0	50

Field or semi-field tests
None reported. Not required

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests						
Typhlodromus pyri	protonymph	'BAS 560 00 F'	0.150	Mortality Reproduction	23.2% 1.8 eggs/female	30%
			0.300	Mortality Reproduction	8.9% 2 eggs/female (control: 4.7 eggs/female)	
Aphidius rhopalosiphi	adult	'BAS 560 00 F'	0.150	Mortality Reproduction	17.6 % 1.1 mummies/ female	30%
			0.300	Mortality Reproduction	0% 2.6 mummies/ female (control: 5.3 eggs/female)	

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Chrysoperla carnea	larva	'BAS 560 00 F'	0.150	Mortality Reproduction Eggs/female hatch rate	0% 29.8 86.4%	30%
			0.300	Mortality Reproduction eggs/female hatch rate	2.1% 31.1 81.9% (control: 30.7 eggs/female; hatch rate: 84.3%)	
Poecilus cupreus	adult	'BAS 560 00 F'	0.300	Mortality Food consumption	0% 4.36 pupae/ beetle (control: 4.26 pupae/beetle)	30%
Typhlodromus pyri	protonymph	'BAS 560 02 F'	0.100	Mortality Reproduction	≤ 1.8% NA	30%
			0.200	Mortality Reproduction	≤ 1.8% NA	
			0.300	Mortality Reproduction	≤ 1.8% NA	
			0.400	Mortality Reproduction	≤ 1.8% 1.4 eggs/female	
			0.500	Mortality Reproduction	≤ 1.8% 2 eggs/female (control: 4.3 eggs/female) LR_{50} > 500 g a.s./ha	

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Aphidius rhopalosiphi	adult	'BAS 560 02 F'	0.010	Mortality Reproduction	0% NA	30%
			0.050	Mortality Reproduction	7.4% NA	
			0.075	Mortality Reproduction	0% NA	
			0.100	Mortality Reproduction	3.3% 3.1 mummies/ female	
			0.150	Mortality Reproduction	46.7% (not treatment related) 5.0 mummies/ female	
			0.300	Mortality Reproduction	0% 1.1 mummies/ female (control: 5.3 mummies/ female) LR_{50} > 300 g a.s./ha	

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Chrysoperla carnea	larva	'BAS 560 02 F'	0.100	Mortality Reproduction eggs/female hatch rate	4.2% 30.3 79.2%	30%
			0.300	Mortality Reproduction eggs/female hatch rate	4.2% 33.8 84.5% (control: 30.7 eggs/female; hatch rate: 84.3%)	
Poecilus cupreus	adult	'BAS 560 02 F'	0.300	Mortality Food consumption	0% 5.84 pupae/beetle (control: 5.97 pupae/beetle)	30%

Hazard quotients for non-target arthropods according to ESCORT II guidance (Guidance Document on Regulatory Testing and Risk Assessment Procedures for Plant Protection Products with Non-Target Arthropods. SETAC August 2001)

Species	Crop	Hazard quotient	Trigger
Typhlodromus pyri	cereals	<0.5	2
Aphidius rhopalosiphi	cereals	<0.85	2
Typhlodromus pyri	grapevines	< 0.7	2
Aphidius rhopalosiphi	grapevines	< 1.16	2

Field or semi-field tests

Four field trials on the predatory mite *Typhlodromus pyri* and one on the predatory mite *Kampinodromus aberrans* in grapevines. When 8 applications were made totalling up to 1020 g a.s./ha there were no long term adverse effects on the population.

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

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

Acute toxicity ‡	LC_{50}** > 500 mg a.s./kg based on active substance NOEC** <500 mg a.s./kg based on active substance LC_{50}** > 150 mg a.s./kg based on 'BAS 560 00F' NOEC** < 150 mg a.s./kg based on 'BAS 560 00F' LC_{50}** > 250 mg a.s./kg based on 'BAS 560 02F' NOEC <250 mg a.s./kg based on 'BAS 560 02F' LC_{50} > 500 mg CL 377 160/kg based on the metabolite NOEC 500 mg CL 377 160/kg base on the metabolite
Reproductive toxicity ‡	LC_{50}** >3 mg a.s./kg based on 'BAS 560 00F' NOEC** 3 mg a.s./kg based on 'BAS 560 00F' LC_{50}** > 10.44 mg a.s./kg based on 'BAS 560 02F' NOEC** 10.44 mg a.s./kg based on 'BAS 560 02F'

** adjusted by 2 to allow for greater amount of organic matter in test soil than in natural soil

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

Application rate (kg as/ha)	Crop	Toxicity endpoint **	Time-scale	TER	Annex VI Trigger
150 g a.s./ha 2x/crop PEC of 0.843 mg *	cereals	LC_{50} >150 mg a.s./kg	acute	> 178	10
150 g a.s./ha 2x/crop PEC of 0.843 mg a.s./kg*	cereal	NOEC 10.44 mg a.s./kg	long term	12.4	5
100 g a.s./ha 2x/crop PEC of 1.336 mg a.s./kg *	grapevines	LC50> 250 mg a.s./kg	acute	> 187	10
100 g a.s./ha 2x/crop PEC of 1.336 mg a.s./kg *	grapevines	NOEC 10.44 mg a.s./kg	long term	7.8	5

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

Application rate (kg as/ha)	Crop	Toxicity endpoint **	Time-scale	TER	Annex VI Trigger
0.037 mg CL 377 160/kg soil (peak concentration of this metabolite)	cereals	LC_{50} > 500 mg CL 377 160/kg	acute	> 13514	10
0.037 mg CL 377 160/kg soil (peak concentration of this metabolite)	cereals	Accounted for in long term study on active substance/products	long term	-	5
0.078 mg CL 377 160/kg soil (peak concentration of this metabolite)	grapevines	LC_{50} > 500 mg CL 377 160/kg	acute	> 6410	10
0.078 mg CL 377 160/kg soil (peak concentration of this metabolite)	grapevines	Accounted for in long term study on active substance/products	long term	-	5

*accounts for accumulation from use in previous years
** adjusted by 2 to allow for greater amount of organic matter in test soil than in natural soil

Effects on other soil macro-organisms

Litter bag study ‡	No effect on organic matter degradation at 0.818 mg as/kg soil and 1.272 mg as/kg soil

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

Nitrogen mineralization ‡	Effects < 25% at 2 mg a.s./kg soil (based on 'BAS 560 00F') Effects < 25% at 0.536 mg a.s./kg soil (based on 'BAS 560 02F') Effects < 25% at 0.31 mg CL377160/kg soil.
Carbon mineralization ‡	Effects < 25% at 2 mg a.s./kg soil (based on 'BAS 560 00F') Effects < 25% at 0.536 mg a.s./kg soil (based on 'BAS 560 02F') Effects < 25% at 0.31 mg CL377160/kg soil.

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

Non target terrestrial plants (Annex IIA point 8.6. Annex IIIA, point 10.8)

Seedling emergence	No effect on 4 monocotyledon spp and 6 dicotyledon spp. at 300 g a.s./ha (based on 'BAS 560 02F')
Seedling growth	No effect on 2 monocotyledon spp. and 4 dicotyledon spp. at 300 g a.s./ha (based on studies with 'BAS 560 00 F') No effect on 4 monocotyledon spp and 6 dicotyledon spp. at 300 g a.s./ha (based on 'BAS 560 02F')

Classification and proposed labelling (Annex IIA, point 10)

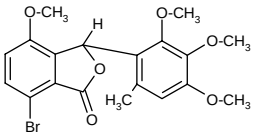
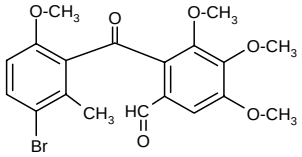
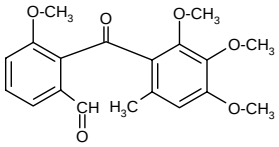
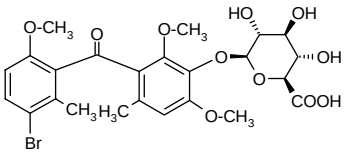
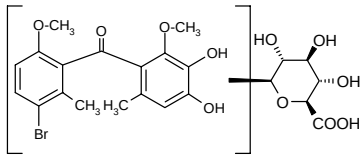
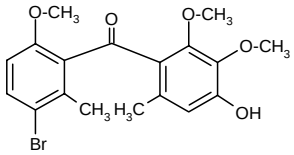
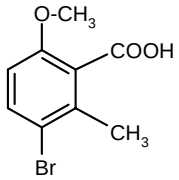
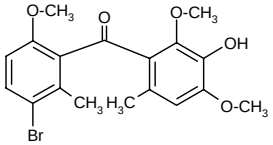
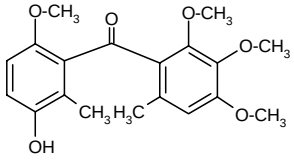
with regard to ecotoxicological data	N	Dangerous for the environment
	R50	Very toxic to aquatic organisms
	R53	May cause long term adverse effects in the aquatic environment
	S60	This material and its container must be disposed of as hazardous waste
	S61	Avoid release to the environment. Refer to special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

‡ Endpoints identified by the 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
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 performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level

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

Code/Trivial name	Chemical name	Structural formula
CL 3000402	1(3H)-isobenzofuranone, 7-bromo-4-methoxy-3-(2,3,4-trimethoxy-6-methylphenyl)-	
CL 379395	benzaldehyde, 2-(3-bromo-6-methoxy-2-methylbenzoyl)-3,4,5-trimethoxy-	
CL 1500836	Benzaldehyde, 3-methoxy-2-(2,3,4-trimethoxy-6-methylbenzoyl)-	
CL 1500698	Methanone, (3-bromo-6-methoxy-2-methylphenyl)[3-(beta-D-glucopyranuronosyloxy)-2,4-dimethoxy-6-methylphenyl]-	
CL 1023363	Mono-O-glucuronide of Methanone, (3-bromo-6-methoxy-2-methylphenyl)(3,4-dihydroxy-2-methoxy-6-methylphenyl)-	
CL 434223	Methanone, (3-bromo-6-methoxy-2-methylphenyl)(4-hydroxy-2,3-dimethoxy-6-methylphenyl)-	
CL 375816	Benzoic acid, 3-bromo-6-methoxy-2-methyl-	
CL 377160	Methanone, (3-bromo-6-methoxy-2-methylphenyl)(3-hydroxy-2,4-dimethoxy-6-methylphenyl)-	
CL 4084564	Methanone, (3-hydroxy-6-methoxy-2-methylphenyl)(2,3,4-trimethoxy-6-methylphenyl)-	

CL 1023424	1(3H)-isobenzofuranone, 4,5,6-trimethoxy-3-(3-bromo-6-methoxy-2-methylphenyl)-