CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance bupirimate[1]

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Bupirimate is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002[3], as amended by Commission Regulation (EC) No 1095/2007[4]. In accordance with the Regulation, at the request of the Commission of the European Communities (hereafter referred to as 'the Commission'), the EFSA organised a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by The Netherlands, being the designated rapporteur Member State (RMS). The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of bupirimate in Annex I to Council Directive 91/414/EEC.

Following the Commission Decision of 5 December 2008 (2008/934/EC)[5] concerning the non-inclusion of bupirimate in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Makhteshim Chemical Works Ltd made a resubmission application for the inclusion of bupirimate in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[6] . The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, The Netherlands, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 26 November 2009.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant for comments on 30 November 2009. The EFSA collated and forwarded all comments received to the Commission on 22 January 2010.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission requested the EFSA to conduct a focused peer review in the areas of mammalian toxicology and fate and behaviour, and to deliver its conclusions on bupirimate.

1 On request from the European Commission, Question No EFSA-Q-2010-00131, issued on 20 September 2010.

2 Correspondence: praper@efsa.europa.eu

3 OJ L224, 21.08.2002, p.25

4 OJ L 246, 21.9.2007, p. 19

5 OJ L 333, 11.12.2008, p.11

6 OJ L 15, 18.01.2008, p.5

Suggested citation: European Food Safety Authority; Conclusion on the peer review of the pesticide risk assessment of the active substance bupirimate. EFSA Journal 2010;8(10):1786. [82 pp.]. doi:10.2903/j.efsa.2010.1786. Available online: www.efsa.europa.eu/efsajournal.htm

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of bupirimate as a fungicide on apple, strawberry, melon and roses, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

No critical areas of concern were identified in the physical chemical properties area. A data gap relating to the specification was identified.

An area of concern was identified in the mammalian toxicology section as it was not possible to demonstrate the compliance of the tested batches with the proposed specification.

Based on the metabolism studies conducted on apple, melon and strawberry, residue definitions for monitoring and risk assessment were defined for the fruit crop group only. MRLs were proposed for bupirimate and for its main metabolite ethirimol. As a worst case, a global chronic risk assessment was performed using the lowest ADI set for ethirimol. No intake concern was identified for the consumer.

Ethirimol and DE-B are major transformation products of bupirimate in soil. Data gaps have been identified for reliable kinetic parameters (DT_{50} values and formation fraction) and reliable adsorption / desorption data for the major metabolite DE-B. In water/sediment systems only ethirimol is found at significant amounts up to 70 d but still at < 10 % AR. Bupirimate dissipates relatively rapidly from the water phase by partition to the sediment, and is moderately persistent in the whole water/sediment system. The groundwater limit of 0.1 µg / L is not exceeded for any of the representative uses modelled for bupirimate. The limit of 0.1 µg / L is exceeded in one scenario for the uses in roses (field and glasshouse) for the metabolite ethirimol. A data gap has been identified to assess the potential groundwater contamination by major soil metabolite DE-B.

A high in-field risk to non-target arthropods from the representative field uses on melon, strawberry, roses, and apple (southern Europe) was not excluded and a data gap was identified. Bupimirate was toxic to aquatic organisms. A data gap was identified to further address the potential risk to aquatic organisms for the metabolite DE-B for the representative field uses. The risk was assessed as low for birds, mammals, aquatic organisms, bees, soil macro- and micro-organisms, non-target plants, and methods for sewage treatment plants.

KEY WORDS

Bupirimate, peer review, risk assessment, pesticide, fungicide

TABLE OF CONTENTS

Summary 1
Table of contents 3
Background 4
The active substance and the formulated product 6
Conclusions of the evaluation 6
1. Identity, physical/chemical/technical properties and methods of analysis 6
2. Mammalian toxicity 6
3. Residues 6
4. Environmental fate and behaviour 7
5. Ecotoxicology 9
6. Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments 10
6.1. Soil 10
6.2. Ground water 10
6.3. Surface water and sediment 11
6.4. Air 11
List of studies to be generated, still ongoing or available but not peer reviewed 12
Particular conditions proposed to be taken into account to manage the risk(s) identified 12
Issues that could not be finalised 12
Critical areas of concern 12
References 13
Appendices 14
Abbreviations 80

BACKGROUND

Legislative framework

Commission Regulation (EC) No 1490/2002[7], as amended by Commission Regulation (EC) No 1095/2007[8] lays down the detailed rules for the implementation of the third stage of the work programme referred to in Article 8(2) of Council Directive 91/414/EEC. This regulates for the European Food Safety Authority (EFSA) the procedure for organising, upon request of the Commission of the European Communities (hereafter referred to as 'the Commission'), a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by the designated rapporteur Member State.

Commission Regulation (EC) No 33/2008[9] lays down the detailed rules for the application of Council Directive 91/414/EEC for a regular and accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 8(2) of Council Directive 91/414/EEC but which were not included in Annex I. This regulates for the EFSA the procedure for organising the consultation of Member States and the applicant(s) for comments on the Additional Report provided by the designated RMS, and upon request of the Commission the organisation of a peer review and/or delivery of its conclusions on the active substance.

Peer review conducted in accordance with Commission Regulation (EC) No 1490/2002

Bupirimate is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007. In accordance with the Regulation, at the request of the Commission, the EFSA organised a peer review of the DAR (The Netherlands, 2007) provided by the designated rapporteur Member State, The Netherlands, which was received by the EFSA on 19 April 2007.

The peer review was initiated on 7 August 2007 by dispatching the DAR to Member States and the applicant Makhteshim Chemical Works Ltd for consultation and comments. In addition, the EFSA conducted a public consultation on the DAR. The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of bupirimate in Annex I to Council Directive 91/414/EEC.

Peer review conducted in accordance with Commission Regulation (EC) No 33/2008

Following the Commission Decision of 5 December 2008 (2008/934/EC)[10] concerning the non-inclusion of bupirimate in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Makhteshim Chemical Works Ltd made a resubmission application for the inclusion of bupirimate in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18, The Netherlands, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report (The Netherlands, 2009). The Additional Report was received by the EFSA on 26 November 2009.

In accordance with Article 19, the EFSA distributed the Additional Report to Member States and the applicant for comments on 30 November 2009. In addition, the EFSA conducted a public consultation on the Additional Report. The EFSA collated and forwarded all comments received to the Commission on 22 January 2010. At the same time, the collated comments were forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the

[7] OJ L224, 21.08.2002, p.25
[8] OJ L246, 21.9.2007, p.19
[9] OJ L 15, 18.01.2008, p.5
[10] OJ L 333, 11.12.2008, p.11

comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 22 February 2010, the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on bupirimate within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were required to be submitted by the applicant in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the Commission on 19 February 2010; the applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant's response to the comments, and the RMS' subsequent evaluation thereof, it was concluded that the EFSA should organise a consultation with Member State experts in the areas of mammalian toxicology and fate and behaviour, and that further information should be requested from the applicant in the areas of physical and chemical properties, mammalian toxicology, and fate and behaviour.

The outcome of the telephone conference, together with EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in consultation with Member State experts, and the additional information to be submitted by the applicant, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in August 2010.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as a fungicide on apple, strawberry, melon and roses, as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2010) comprises the following documents:

- the comments received,
- the Reporting Tables (DAR and AR revision 1-1; 24 February 2010),
- the Evaluation Table (20 September 2010),
- the reports of the scientific consultation with Member State experts (where relevant).

Given the importance of the DAR and the Additional Report including its addendum (compiled version of August 2010 containing all individually submitted addenda (The Netherlands, 2010)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Bupirimate is the ISO common name for 5-butyl-2-ethylamino-6-methylpyrimidine-4-yl dimethylsulfamate (IUPAC).

The representative formulated product for the evaluation was 'Nimrod 25 EC' an emulsifiable concentrate (EC) containing 250 g/l bupirimate.

The representative uses evaluated were on apple as an outdoor foliar spray against fungi, and on indoor and outdoor strawberry, melon, and roses as a foliar spray against fungi. Full details of the GAP can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

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

The minimum purity of bupirimate as manufactured should not be less than 945 g/kg. Ethirimol and toluene were considered to be relevant impurities, however, their maximum level in the technical material has not been agreed (see section 2). The specification must be regarded as provisional as a data gap was identified for evidence to be provided that impurity 6 is <0.1% in production batches, and for information on the peak that elutes just before impurity 3.

The main data regarding the identity of bupirimate and its physical and chemical properties are given in Appendix A.

For plants a HPLC-MS/MS method is available to analyse bupirimate and ethirimol in high water content commodities. For products of animal origin a method is available but has not been assessed since no method is required because MRLs are not proposed. HPLC-MS/MS methods are available for soil and water for both bupirimate and its metabolite ethirimol. A HPLC-MS/MS method is available for air. Methods for body fluids and tissues are not required as the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

Bupirimate was discussed during the PRAPeR meeting 76.

The experts discussed the compliance of batches tested in the mammalian toxicology studies with the proposed specification, however it was not possible to conclude on the issue due to the lack of sufficient data, and therefore a data gap and an area of concern were identified. With regard to the relevance of impurities, toluene appears to have a different toxicological profile and therefore it could be considered relevant. However, in view of the data gap identified concerning the compliance of the batches tested with the proposed specification, it was not possible to conclude on the maximum permitted level in the proposed specification. As for ethirimol, even if its toxicological profile is largely similar to bupirimate, there are still some differences (as reflected in the setting of a different ADI), and therefore ethirimol should be regarded as relevant.

Tested in mammals, bupirimate showed low acute toxicity (oral LD50 about 4000 mg/kg bw, dermal LD50 > 2000 mg/kg bw, LC50 >1.34 mg/L); it is not a skin or eye irritant, but it is a skin sensitiser (R43 "May cause sensitisation by skin contact" was proposed). In short-term toxicity studies in dog the target organ is the thymus, whereas in the rat body weight, liver and thyroid weight are affected. The relevant NOAELs are 15 mg/kg bw/day (dog) and 50 mg/kg bw/day (rat). Bupirimate does not have any genotoxic potential. After repeated administration in long-term studies, target organs are the liver (in dog) and the thyroid (in rat), with relevant NOAELs of 5 mg/kg bw/day and 3 mg/kg bw/day in dog and rat, respectively. In the rat thyroid follicular adenomas occurred at higher doses, but they were considered of no relevance to humans. Bupirimate is not a reproductive toxicant: the relevant parental and offspring NOAEL is 20 mg/kg bw/day, whereas the reproductive NOAEL is 200 mg/kg bw/day (highest dose tested); in developmental toxicity studies the maternal NOAELs are <50 mg/kg

bw/day in rat and 20 mg/kg bw/day in rabbit; the developmental NOAELs are 50 mg/kg bw/day and 80 mg/kg bw/day in rat and rabbit, respectively.

The reference values for bupirimate and its major metabolite ethirimol were discussed. The Acceptable Daily Intake (ADI) of bupirimate is 0.05 mg/kg bw/day based on the 2-year dog study, with a Safety Factor (SF) of 100. The RMS's proposal to set two different AOELs (semi-chronic for operators and chronic for workers in glasshouses for roses) was supported in the meeting. The semi-chronic AOEL is 0.15 mg/kg bw/day based on the 90-day dog study and applying a SF of 100 with 100% oral absorption, whereas the chronic AOEL is 0.05 mg/kg bw/day based on the 2-year dog study, with a SF of 100, and 100% oral absorption. Based on the toxicological profile of bupirimate no ARfD was deemed necessary. As for ethirimol, the ADI is 0.035 mg/kg bw/day, based on the 2-year rat study and applying a SF of 100. The AOEL is 0.05 mg/kg bw/day, based on the developmental toxicity study in rat, with a SF of 100, and 100% oral absorption. No ARfD was needed. The estimated operator exposure to bupirimate for field applications (apple, strawberry, melon and roses) and glasshouse applications (strawberry, melon and rose) was below the AOEL (13-79%) even without the use of personal protective equipment (PPE), as well as for re-entry workers (19-72% of the AOEL, 6-hours exposure). Bystander exposure is ≤7% of the AOEL (70 kg bodyweight).

3. Residues

Metabolism in plants was investigated in the fruit crop group only, on apple, melon and strawberry, using spray or topical applications of ^{14}C-bupirimate, labelled on the pyrimidine ring. Bupirimate is extensively metabolised in plants and only detected in significant proportions shortly after application (27-46% TRR at 3 day PHI). After 14 days, no compound represents more than *c.a.* 10% of TRR, the main identified metabolites being ethirimol and hydroxy-ethirimol. Globally, the metabolism in plant proceeds by hydrolysis of bupirimate to ethirimol, which is further metabolised to hydroxy-ethirimol and de-ethyl-ethirimol. In addition, ethyl guanidine, guanidine and urea were also detected as metabolites resulting from the opening and cleavage of the pyrimidine ring. The metabolism was also seen to be very extensive in rotational crops, with a large number of fractions characterised, the only identified compounds being bupirimate, ethirimol and de-ethyl-ethirimol. Based on these studies, the residue definition for monitoring was limited to bupirimate. However, since ethirimol is also an active substance, a separate residue definition for monitoring was proposed as ethirimol, in order to cover the ethirimol residues resulting from the use of bupirimate. For risk assessment the residue was defined as the sum of bupirimate, ethirimol, hydroxy-ethirimol and de-ethyl-ethirimol expressed as bupirimate. A conversion factor for risk assessment of 3 was derived from the respective proportions at which these compounds were observed at PHI 14 in metabolism studies conducted on strawberry and melon.

A sufficient number of supervised residue trials were provided to derive MRLs for bupirimate. Samples were also analysed for ethirimol and since this compound is also an active substance registered outside the EU, MRLs were proposed for ethirimol in order to cover the use of bupirimate on apple, strawberry and melon. These residue data are supported by the storage stability studies showing that bupirimate and ethirimol are stable in apple matrices up to 24 and 17 months respectively. Bupirimate was slightly degraded under standard hydrolysis to ethirimol (up to 4% TRR). Processing factors were calculated for bupirimate in processed apple, strawberry and melon commodities.

A goat metabolism study was submitted but regarded as not appropriate to propose a residue definition for ruminant products. Nevertheless, and considering the TRRs observed in the different matrices and the animal intake estimated for the representative uses, no significant residues are expected to be present in ruminant matrices. It was therefore concluded that the setting of a residue definition and MRLs for animal matrices is not necessary in view of the representative uses.

Although bupirimate and ethirimol were initially allocated with the same ADI (0.05 mg/kg bw/d), the PRAPeR 76 meeting on toxicology decided to set a separate value of 0.035 mg/kg bw/d for ethirimol, based on slightly different findings in rat (*e.g.* urinary effects) specifically observed with this active substance (see section 2). Considering that bupirimate is nearly completely converted to ethirimol in

rat, and that both compounds denote a number of joint toxicological actions, it was decided as a worst case to perform a combined risk assessment using the lowest ADI value proposed for ethirimol. Based on the EFSA PRIMo model, and using the ethirimol ADI, the proposed MRLs and a conversion factor of 3 for fruit commodities, the highest TMDI is only 29% of the ADI (DE child). No ARfDs were allocated to bupirimate and ethirimol, and therefore an acute risk assessment was not necessary.

4. Environmental fate and behaviour

The route of degradation of bupirimate was investigated in three soils under dark aerobic conditions at 25°C. In two soils degradation was also investigated with a formulated product 25 % EC, and in one of the soils the degradation was investigated at various concentrations. In these experiments ethirimol was a major transformation product of bupirimate. An unidentified metabolite exceeded 5% AR in two subsequent sampling dates in some of the experiments. Further information provided for the resubmission allowed this metabolite to be tentatively identified as DE-B (See Additional Report, November 2009, and Addendum to the Additional Report, May 2010). In a second study DE-B is identified as a major metabolite (>10 % in some of the experiments). Mineralization was negligible or low (max CO_2 0.1 – 17.8 % AR) and unextractable residues amounted to maximum of 57.2 % AR after 329 d. Photolysis is not expected to contribute significantly to the environmental dissipation of bupirimate in soil. Bupirimate exhibits medium to very high persistence in soil under laboratory dark aerobic conditions (11 experiments, 5 soils). Ethirimol (or its hydrochloride salt) exhibits moderate to very high persistence under dark aerobic conditions at 20 °C. The meeting of experts PRAPeR 78 identified a data gap for reliable kinetic parameters (DT_{50} values and formation fraction) and the consequent groundwater assessments for the major soil metabolite DE-B. In an additional study, route and rate of degradation of bupirimate was also investigated under anaerobic conditions. Field trials in France and Spain (bupirimate), and Germany (bupirimate and ethirimol) are available. No modelling kinetic end points may be derived from these studies.

Bupirimate is expected to exhibit low mobility in soil and ethirimol is expected to exhibit low to high mobility in soil based on the batch adsorption / desorption studies. A data gap has been identified for reliable adsorption / desorption data for major metabolite DE-B. Column leaching and aged residue column leaching studies with bupirimate are available as supplementary information. The radioactive fraction in the leachate from the column leaching studies was above 4 and 10 %. This fraction has not been analyzed for metabolites.

Bupirimate is stable to hydrolysis at pH 7 and 9 and is slowly degraded to ethirimol at pH 5 (DT_{50} = 165 d). Ethirimol is stable to hydrolysis at pH 5, 7, and 9. Aqueous photolysis is rapid. In the most recent study, the metabolites (A: max. 32.9 % AR, A2: 13.2 % AR and C: 12.9 % AR) were not identified but in the other studies major metabolites were identified as ethirimol and structural isomers of bupirimate. A worst case surface water exposure assessment was presented by the RMS for the metabolites A, A2 and C (See addendum to the Additional Report, May 2010). Bupirimate is not readily biodegradable according to the available study.

In water sediment systems only ethirmol is found in significant amounts up to 70 d but is still < 10 % AR. Bupirimate dissipates relatively rapidly from the water phase by partition to the sediment and it is moderately persistent in the whole water/sediment system. PEC_{SW} have been calculated by FOCUS SW to step 3 for bupirimate and to step 2 for the metabolite ethirimol. PEC_{SW} for the unknown photolysis metabolites A, A2 and C have been calculated based on parent peak at FOCUS SW step 3 calculations assuming a photo-conversion of 50%. Since no reliable half-life is available for soil metabolite DE-B it is not possible to calculate strictly reliable PEC_{SW} for DE-B as the contribution from run-off cannot be accounted for accurately. PEC_{SW} at FOCUS SW step 1 and 2 levels have been estimated by the RMS in the addendum to the Additional Report (May 2010). The input values used in this calculation only became available to EFSA in August 2010. A DT_{50} for soil of 334 days and the worst case K_{oc} from parent (882 mL/ g) were chosen as default values for soil metabolite DE-B. In the absence of reliable data, a default Koc = 10 mL/g and a DT_{50} = 1000 d should have been used for PEC_{SW}. Therefore, only step 1 calculations have been used by EFSA to finalize the risk assessment, taking into account the worst case assumptions implicit in this calculation. However, the risk to

aquatic organisms due to contamination of surface water by metabolite DE-B is assessed as high at this level (See section 5). Therefore, these calculations will need to be revised once reliable input parameters for metabolite DE-B are available, and a data gap has been identified.

Potential contamination of groundwater by bupirimate and its metabolite ethirimol was estimated by FOCUS GW (PEARL 3.3.3) calculation of the 80th percentile leachate concentration at 1 m depth. The limit of 0.1 µg / L is not exceeded for any of the uses and scenarios simulated for bupirimate. The limit of 0.1 µg / L is exceeded in one scenario for the uses in roses (field and glasshouse) for the metabolite ethirimol. A data gap has been identified to assess the potential groundwater contamination by major soil metabolite DE-B.

5. Ecotoxicology

The studies available were sufficient to address the potential ecotoxicological relevance of the impurities toluene and ethirimol.

Bupirimate is toxic to aquatic organisms. A similar toxicity was observed for both the active substance and the representative formulation 'Nimrod 25 EC'. The metabolite ethirimol was slightly less toxic than the parent. A low risk was identified at the first tier (i.e FOCUS step 3) for all of the representative uses. The aqueous photolysis metabolites A, A2 and C were considered to be of low risk to aquatic organisms since the expected exposure would be negligible. A high acute and chronic risk to fish and aquatic invertebrates for the metabolite DE-B was estimated by EFSA based on FOCUS step1 PECsw provided in the fate section and assuming that it is 10 times more toxic than the parent. Therefore, a data gap was identified to further address the potential risk to aquatic organisms for metabolite DE-B for the field representative field uses.

A potential high in-field risk was assessed at the first tier for the species *Typhlodromus pyri* and *Encarsia formosa*, based on the magnitude of effects in a single rate limit test and the estimated exposure for the representative uses. Extended laboratory tests were provided with the two standard species (i.e. *Typhlodromus pyri* and *Aphidius rhopalosiphi)* and additional species (i.e. *Orius laevigatus* and *Coccinella septempunctata*). Based on the study with *C. septempunctata* a low risk was expected for all representative uses. However, the studies with *A. rhopalosophi*, *T. pyri,* and *O. laevigatus* did not allow to certainly exclude the in-field risk to non-target arthropods because the tested rates that indicated a low risk (i.e. effects <50%) were lower than the estimated in-field exposure for the representative use in apple (southern Europe), and the representative field uses on melon, strawberry and roses. The in-field estimated exposure for these uses ranged from 0.567 to 2 kg a.s./ha. In the study with *O. laevigatus* the highest tested rate was 0.488 kg a.s./ha. In the study with *T. pyri* a percentage of 55% of effects were observed at the highest tested rate of 1.8 kg a.s./ha. In the study with *A. rhopalosiphi* the percentage of effects ranged from 32.6% to 77.5% at tested rates between 0.500 and 0.750 kg a.s./ha. Therefore, due to the uncertainties in the existing dataset, a data gap was identified to further address the in-field risk to non-target arthropods arising from the representative field uses on melon, strawberry, roses, and apple (southern Europe) in order to demonstrate the potential for recovery/re-colonisation within one year. The off-field risk was assessed as low.

The risk was assessed as low for the other non-target organisms (i.e. birds and mammals, bees, non-target soil macro- and micro-organisms, non-target plants and methods for sewage treatments) for all the representative uses. The risk to non-target soil organisms was also assessed as low for the metabolites ethirimol and DE-B.

6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
bupirimate	medium to very high persistence ($DT_{50\ 20\ ^{o}C}$ = 66.5 d– 464 d)	The risk was assessed as low for soil-dwelling organisms.
ethirimol	moderate to very high persistence ($DT_{50\ 20\ ^{o}C}$ = 25.5 d– 3819 d)	The risk was assessed as low for soil-dwelling organisms.
DE-B	No reliable data available. Data gap.	The risk was assessed as low based on the initial highest PECsoil.

6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
bupirimate	Slight to low (K_{Foc} = 882 – 2822 mL/g)	FOCUS GW: No, no scenario exceeds the limit of 0.1 µg / L for any of the representative uses proposed.	yes	yes	yes

ethirimol	Low to high (K_{Foc} = 97 - 950 mL/g)	FOCUS GW: Yes, 1 scenario exceeds the limit of 0.1 µg / L for the representative uses in roses (field and glasshouse).	yes	yes	yes
DE-B	No reliable data available. Data gap.	Data gap	-	no	-

6.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Bupirimate (water and sediment)	Bupirimate is toxic to aquatic organisms. The risk was assessed as low. The lowest endpoint was NOEC =0.10 mg a.s./L (31-days ELS study with *Pimephales promelas*)
Ethirimol (water and sediment)	The risk to aquatic organisms was assessed as low.
DE-B (soil metabolite, water and sediment)	No data available. Potential data gap for effects data, pending on the clarification in the fate section.
Unknown A (aqueous photolysis metabolite)	The risk to aquatic organisms was considered as low.
Unknown A2 (aqueous photolysis metabolite)	The risk to aquatic organisms was considered as low.
Unknown C (aqueous photolysis metabolite)	The risk to aquatic organisms was assessed as low.

6.4. Air

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

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

- Evidence to be provided that impurity 6 is <0.1% in production batches. Information to be provided on the peak that elutes just before impurity 3 (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1).

- Compliance of the batches tested in the mammalian toxicology data package with the proposed specification to be demonstrated (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 2).

- Reliable kinetic parameters (DT_{50} values and formation fraction) and sorption parameters, and the consequent groundwater exposure assessment for soil metabolite DE-B (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 4).

- $PEC_{SW/SED}$ for major soil metabolite DE-B with reliable input parameters (relevant for all field uses evaluated; submission date proposed by the applicant: unknown; see section 4).

- The risk to aquatic organisms for the major soil metabolite DE-B to be addressed (relevant for all representative field uses evaluated; submission date proposed by the applicant: unknown; see section 5).

- The in-field risk to non-target arthropods needs to be further addressed in order to demonstrate the potential for recovery/recolonisation within one year (relevant for the representative use in apple (southern Europe), and the representative field uses on melon, strawberry and roses; submission date proposed by the applicant: unknown; see section 5).

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

None.

ISSUES THAT COULD NOT BE FINALISED

- The specification cannot be finalised as a data gap was identified to address some issues with 2 impurities.

- The surface water and groundwater exposure assessments for the major soil metabolite DE-B cannot be finalised. Following the outcome of the fate assessment the potential risk to aquatic organisms from this metabolite should be assessed.

- The in-field risk assessment for non-target arthropods for the field uses on melon, strawberry, roses and apple (southern Europe) cannot be finalised on the basis of the available data.

CRITICAL AREAS OF CONCERN

- The compliance of the batches tested in the mammalian toxicology data package with the proposed specification was not demonstrated.

- Potential groundwater contamination by major soil metabolite DE-B cannot be excluded.

REFERENCES

EFSA (European Food Safety Authority), 2010. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance bupirimate.

The Netherlands, 2007. Draft Assessment Report (DAR) on the active substance bupirimate prepared by the rapporteur Member State The Netherlands in the framework of Directive 91/414/EEC, April 2007.

The Netherlands, 2009. Additional Report to the Draft Assessment Report on the active substance bupirimate prepared by the rapporteur Member State The Netherlands in the framework of Commission Regulation (EC) No 33/2008, November 2009.

The Netherlands, 2010. Final Addendum to the Additional Report on bupirimate, compiled by EFSA, August 2010.

APPENDICES

APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

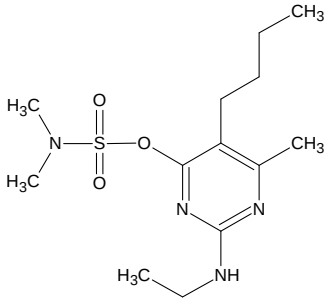
Chapter 2.1 Identity, Physical and Chemical Properties, Details of Uses, Further Information

Identity, Physical and Chemical Properties, Details of Uses, Further Information

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

Rapporteur Member State	The Netherlands
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	5-butyl-2-ethylamino-6-methylpyrimidine-4-yl dimethylsulfamate
Chemical name (CA) ‡	5-butyl-2-(ethylamino)-6-methyl-4-pyrimidinyl dimethylsulfamate
CIPAC No ‡	261
CAS No ‡	41483-43-6
EC No (EINECS or ELINCS) ‡	255-391-2
FAO Specification (including year of publication) ‡	none
Minimum purity of the active substance as manufactured ‡	945 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	ethirimol Max. not agreed by mammalian toxicology. toluene Max. not agreed by mammalian toxicology
Molecular formula ‡	$C_{13}H_{24}N_4O_3S$
Molecular mass ‡	316.42
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	44.5-49.3 °C (98.2%)
Boiling point (state purity) ‡	232 °C (98.2%)
Temperature of decomposition (state purity)	No decomposition before boiling
Appearance (state purity) ‡	fine white powder without specific odour (98.2%) waxy yellow solid with fish odour (93.6%)
Vapour pressure (state temperature, state purity) ‡	at 49.2 °C: 4.58 x 10^{-3} Pa at 39.4 °C: 1.64 x 10^{-3} Pa at 33.5 °C: 4.19 x 10^{-4} Pa at 25 °C: extrapolated to 1.3 x 10^{-4} Pa at 20 °C: extrapolated to 0.57 x 10^{-4} Pa (98.2%)
Henry's law constant ‡	1.35 Pa.m^3/mol (20°C)
Solubility in water (state temperature, state purity and pH) ‡	102.04 mg/L at 20 °C (pH 4) (99.3%) 13.06 mg/L at 20 °C (pH 7) (98.2%) 22.55 mg/L at 20 °C (pH 9) (99.3%)
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20 °C in g/L (93.6%) n-heptane: 23.67 g/L p-xylene: >250 g/L 1,2-dichloroethane: >250 g/L methanol: >250 g/L acetone: >250 g/L ethyl acetate: >250 g/L
Surface tension ‡ (state concentration and temperature, state purity)	35.4 mN/m at 25 °C (90 % saturated solution) (98.2%) 41.3 mN/m at 40 °C (90 % saturated solution) (98.2%)
Partition co-efficient ‡ (state temperature, pH and purity)	log K_{ow} =3.35 at 20 °C (pH 4) (99.3%) log K_{ow} =3.68 at 21 °C (pH 7) (98.2%) log K_{ow} =3.93 at 20 °C (pH 9) (99.3%)
Dissociation constant (state purity) ‡	pK_a = 4.4 is found for the equilibrium: bupirimate-H^+ + H_2O ↔ bupirimate + H_3O^+ (98.2%)

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Ambient temperature: (pure, 99.8% w/w) **acidic (0.11 M HCl - acetonitrile, 9:1, v/v) pH 1.4** λ(max) = 218 nm (shoulder) with ε = 14300 L/mol.cm λ(max) = 235 nm with ε = 21800 L/mol.cm **neutral (water - acetonitrile, 9:1, v/v) pH 7.8** λ(max) = 241 nm with ε = 21400 L/mol.cm **alkaline (0.11 M NaOH - acetonitrile, 9:1, v/v) pH 13.1** λ(max) = 241 nm with ε = 21200 L/mol.cm At 25 °C: (pure, 98.2% w/w) **acidic (1 M HCl - methanol) pH 0.87** λ(max) = 306.4 nm with ε = 5960 L/mol.cm **neutral (water - methanol) pH 8.70** λ(max) = 304.5 nm with ε = 4828 L/mol.cm **alkaline (1 M NaOH - methanol) pH 13.01** λ(max) = 304.1 nm with ε = 4457 L/mol.cm
Flammability ‡ (state purity)	not flammable (93.6%) not auto-flammable, no relative self-ignition temperature (93.6%).
Explosive properties ‡ (state purity)	no explosive properties (93.6%)
Oxidising properties ‡ (state purity)	no oxidising properties expected, based on the molecular structure and mass and the composition of the material.

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS proposal
Active substance	none

Summary of representative uses evaluated (bupirimate)

Crop and / or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min-max (k)	interval between applications (min)	kg as/hl min-max	water l/ha min-max	kg as/ha min-max		
Apple	Southern Europe	Nimrod 25 EC	F	*Sphaerotheca leucotrica*	EC	250 g/L	orchard sprayer	at first signs of disease	4	10-12 days	0.014	1500	0.21	14	[1] [2] [3] [4] [5]
Apple	Northern Europe	Nimrod 25 EC	F	*Sphaerotheca leucotrica*	EC	250 g/L	orchard sprayer	at first signs of disease	4	10-12 days	0.015	1000	0.15	14	[1] [2] [3] [5]
Strawberry	Southern and Northern Europe	Nimrod 25 EC	F G	*Sphaerotheca humuli*	EC	250 g/L	ground sprayer	at first signs of disease	3-4	10 days	0.042	600	0.25	3	[1] [2] [3] [4] [5]
Melon	Southern Europe	Nimrod 25 EC	F G	*Sphaerotheca fulginea*	EC	250 g/L	ground sprayer	at first signs of disease	4	10 days	0.025	1000	0.25	3	[1] [2] [3] [4] [5]
Roses	Northern Europe	Nimrod 25 EC	F	*Sphaerotheca pannosa*	EC	250 g/L	handheld sprayer	at first signs of disease first cycle in spring (April) second cycle in summer (Jul/Aug)	2 cycles of 3 treatments	7-10 days	0.050	750	0.375	-	[1] [2] [3] [4] [5]
Roses	Northern Europe	Nimrod 25 EC	G	*Sphaerotheca pannosa*	EC	250 g/L	handheld sprayer	at first signs of disease	1-4	7-10 days	0.050	1500	0.75	-	[1] [2] [3] [5]

[1] The compliance of the batches tested in the mammalian toxicology data package with the proposed specification was not demonstrated.
[2] The specification cannot be finalised as there is a data gap to address some issues with regard to 2 impurities
[3] The potential groundwater contamination and surface water exposure by major soil metabolite DE-B cannot be excluded due to data gaps that do not allow the exposure assessment to be finalised.
[4] The in-field risk to non-target arthropods from the representative field uses cannot be finalised on the basis of the available data.
[5] For the field uses the surface water assessment needs to be finalized once a refined exposure assessment becomes available. Current low tier assessment shows high acute and chronic risk to fish and aquatic invertebrates.

Remarks:

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) e.g. biting and suckling insects, soil born insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipme uent used must be indicated
(i) g/kg or g/l
(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
(k) The minimum and maximum number of application possible under practical

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(g) All abbreviations used must be explained
conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

Chapter 2.2 – Methods of Analysis

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

Technical as (analytical technique)	GC-FID
Impurities in technical as (analytical technique)	GC-FID for impurities, standard Karl-Fisher for water, heating/weighing for sulphated ash
Plant protection product (analytical technique)	Bupirimate: GC-FID Impurity: GC-FID

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		bupirimate and ethirimol
Food of animal origin		None
Soil		bupirimate
Water	surface	bupirimate
	drinking/ground	ethirimol
Air		bupirimate

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Single method, can be incorporated in multimethod DFG S19 HPLC-MS-MS for bupirimate and ethirimol, LOQ = 0.01 mg/kg for each compound. Valid for high water content matrices.
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not necessary as no MRLs are proposed.
Soil (analytical technique and LOQ)	**bupirimate** Extraction with acetonitrile/water (100:20, v/v). Partitioning/clean-up with SPE (EnviCarb and BondElut LRC-NH_2 placed in series). Elution with dichloromethane/methanol (80:20, v/v). Detection with HPLC-MS/MS Method validated on two soils at spiking levels 0.01 - 1 µg/kg. LOQ 0.01 mg/kg **ethirimol** See above. Method validated on two soils at spiking levels 0.01 – 0.1 µg/kg. LOQ 0.01 mg/kg

Water (analytical technique and LOQ)	**Bupirimate** direct injection into HPLC-MS/MS. LOQ 0.05 µg/L (surface, ground and drinking water) **Ethirimol** See above. LOQ 0.05 µg/L (surface, ground and drinking water)
Air (analytical technique and LOQ)	Determination by HPLC-MS/MS after extraction with acetone. Method validated at spiking levels 1.60 - 404 µg/m^3. LOQ 1.60 µg/m^3.
Body fluids and tissues (analytical technique and LOQ)	Not required. Substance is not classified as toxic (T) or very toxic (T^+)

Chapter 2.3 Impact on Human and Animal Health

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

Rate and extent of absorption:	Oral absorption is rapid and assumed to be 100%
Distribution:	Limited information available; distributes to liver and kidney, but hardly to fat; no information on other organs available.
Potential for accumulation:	Bupirimate or its metabolites do not seem to accumulate in fat upon repeated oral administration, but in kidney and liver, no plateau had yet been reached after 21 days of dosing.
Rate and extent of excretion:	Rapid elimination (75% in 24 h), mainly via urine (65% in 24 h)
Metabolism in animals	Extensively metabolised, no parent detected in excreta. Major pathways for biotransformation include: loss of dimethylsulphamate group, hydroxylation and de-ethylation.
Toxicologically significant compounds (animals and plants)	Bupirimate, ethirimol, de-ethylated ethirimol and hydroxy-de-ethylated ethirimol
Toxicologically relevant compounds (environment)	Bupirimate, ethirimol, de-ethylated bupirimate and an unidentified compound A. Toxicity of de-ethylated bupirimate and the unidentified compound A is not known.

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral	approx. 4000 mg/kg bw	
Rat LD_{50} dermal	> 2000 mg/kg bw	
Rat LC_{50} inhalation	>1.34 (highest attainable)	
Skin irritation	Not irritating	
Eye irritation	Slightly irritating (no classification proposed)	
Skin sensitisation (test method used and result)	Sensitiser (Magnusson & Kligman)	R43

Short-term toxicity (Annex IIA, point 5.3)

Target / critical effect	Thymus (dog), body weight, liver and thyroid weight (rat)	
Lowest relevant oral NOAEL / NOEL	90-day, dog: 15 mg/kg bw/day 90-day, rat: 50 mg/kg bw/day	
Lowest relevant dermal NOAEL / NOEL	No data available – not required	

Lowest relevant inhalation NOAEL / NOEL	No data available – not required	

Genotoxicity (Annex IIA, point 5.4)

Bupirimate is unlikely to be genotoxic	

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

Target/critical effect	liver (dog), thyroid (rat).	
Lowest relevant NOAEL / NOEL	2-year, dog: 5 mg/kg bw/day 2-year, rat: 3 mg/kg bw/day	
Carcinogenicity	In rat: thyroid follicular adenoma (not relevant for human beings).	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect	No effects identified	
Relevant parental NOAEL	20 mg/kg bw/day (decrease in bodyweight)	
Relevant reproductive NOAEL	200 mg/kg bw/day (highest dose tested)	
Relevant offspring NOAEL	20 mg/kg bw/day (decrease in bodyweight, increase in relative liver and kidney weight, delay in physical development)	

Developmental toxicity

Developmental target / critical effect	liver and kidney weight, bodyweight, delay in physical development.	
Relevant maternal NOAEL	Rat: <50 mg/kg bw/day (marginal clinical signs, decrease in bodyweight gain) Rabbit: 20 mg/kg bw/day (decreased body weight gain, and food consumption, increased abortions)	
Relevant developmental NOAEL	Rat: 50 mg/kg bw/day (minor skeletal defects at maternally toxic doses) Rabbit: 80 mg/kg bw/day (increased incidence of unossified skeletal elements and supernumerary ribs)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity	No data - no data required
Repeated neurotoxicity	No data – no data required

Delayed neurotoxicity	No data – no data required

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies	Oral administration of bupirimate induces changes in the thyroid indicative of hypothyroidism, a decrease in thyroxin (T_4) levels and a greater demand for I^{125}. The NOAEL for this effect is < 450 mg/kg bw/day (rat, 28-day)
Studies performed on metabolites or impurities:	Ethirimol

Metabolism of ethirimol

Rate and extent of absorption	Oral absorption of ethirimol is rapid and assumed to be 100%
Distribution	Ethirimol is widely distributed but hardly to fat
Potential for accumulation	Ethirimol or its metabolites do not seem to accumulate in fat upon repeated oral administration, but in other organs, no plateau had yet been reached after 28 days of dosing.
Rate and extent of excretion	Rapid elimination (±90% in 24 h), mainly via urine (±80% in 24 h)
Metabolism in animals	Ethirimol is extensively metabolised. Major pathways for biotransformation include hydroxylation and de-ethylation.

Acute toxicity of ethirimol

Rat LD_{50} oral	approx. 4000 mg/kg bw	
Rat LD_{50} dermal	> 2000 mg/kg bw	
Rat LC_{50} inhalation	> 4.9 mg/L	
Eye irritation	Ethirimol is slightly irritating (no classification proposed)	
Skin sensitisation (test method used and result)	Ethirimol is a non-sensitser (Magnusson & Kligman)	

Short-term toxicity of ethirimol

Target / critical effect	Urinary incontinence, histopathological changes in prostate (rat), decreased body weight gain (dog)	
Lowest relevant oral NOAEL / NOEL	90-day, dog: 50 mg/kg bw/day 90-day, rat: 9 mg/kg bw/day	

Genotoxicity of ethirimol	Ethirimol is unlikely to be genotoxic	

Long-term toxicity and carcinogenicity of ethirimol

Target/critical effect	Urinary incontinence (rat), decrease in body weight gain; increase in relative liver weight, blood urea conc. and thyroiditis (dog).	
Lowest relevant NOAEL / NOEL	2-year, dog: 15 mg/kg bw/day 2-year, rat: 3.5 mg/kg bw/day	
Carcinogenicity	Ethirimol is unlikely to pose a carcinogenic risk to humans	

Reproductive toxicity of ethirimol

Reproduction target / critical effect	Parental: urinary incontinence; Offspring: urinary incontinence, decrease in litter survival	
Relevant parental NOAEL	3 mg/kg bw/day	
Relevant reproductive NOAEL	23 mg/kg bw/day (highest dose tested)	
Relevant offspring NOAEL	3 mg/kg bw/day	

Developmental toxicity of ethirimol

Developmental target / critical effect	Maternal: decrease in bodyweight gain and food consumption Developmental: decrease in litter weight	
Relevant maternal NOAEL	Rat: 5 mg/kg bw/day	
Relevant developmental NOAEL	Rat: 5 mg/kg bw/day	

Neurotoxicity of ethirimol

Acute neurotoxicity	Ethirimol does not inhibit cholinesterase activity in the rat; NOAEL: 500 mg/kg bw/day

Medical data (Annex IIA, point 5.9)

Skin irritation/sensitisation in workers reported; no evidence of adverse effects in consumers.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI	Bupirimate: 0.05 mg/kg bw/day	dog, 2-year oral	100
	Ethirimol 0.035 mg/kg bw/day	2-year rat	100
AOEL semi-chronic	Bupirimate: 0.15 mg/kg bw/day	Dog, 90-day oral	100
AOEL chronic	0.05 mg/kg bw/day	dog, 2-year oral	100
	Ethirimol 0.05 mg/kg bw/day	developmental toxicity study in rat	100
ARfD (acute reference dose)	Not necessary		

Dermal absorption (Annex IIIA, point 7.3)

Formulation (Nimrod 250 EC)	Concentrate: 1.3% Spray dilution: 12% Comparative *in vitro* (human/rat skin)

Acceptable exposure scenarios (including method of calculation)

Operator	The estimated exposure for Nimrod 25 EC was (% of the semichronic AOEL): Apples, field: 23 % (DE, without PPE) 28 % (UK, without PPE) Strawberries, melons, field: 13 % (DE, without PPE) 41 % (UK, without PPE) Strawberries, melons, greenhouse: 60 % (NL, without PPE) Roses, field: 28 % (DE, without PPE) 79 % (UK, without PPE) Roses, greenhouse: 24%; (NL, with PPE)
Workers	Harvesting apples (% semi-chronic AOEL): 19% (EU, without PPE)

	Harvesting strawberries, melons - greenhouse (% chronic AOEL – also covers field re-entry): 49-72% (EU, without PPE) Harvesting roses, field (% semi-chronic AOEL): 39% (EU, without PPE) Harvesting roses, greenhouse (% chronic AOEL): 24% (EU, with PPE) (A 6-hour working day was considered)
Bystanders	Acceptable for proposed uses (EUROPOEM II model: 0.4-7% of semi-chronic AOEL) (70 kg bodyweight considered)

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Substance classified (bupirimate)	Xi: irritant R43 "may cause sensitization by skin contact" S36/S37: Wear suitable protective clothing and gloves

Chapter 2.4 – Residues

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

Plant groups covered	- fruits (apples), by topical application - fruits (strawberries, melons), by spray application
Rotational crops	Cereals (spring wheat), leafy (spinach) and root vegetables (turnip).
Metabolism in rotational crops similar to metabolism in primary crops?	Yes. Bupirimate extensively metabolised in rotational crop and similar metabolites identified (ethirimol, de-ethyl ethirimol)
Processed commodities	Pasteurisation, brewing, baking and boiling and sterilisation: Degradation of bupirimate under all conditions less than 10% (formation of ethirimol <4% and other metabolites <2%)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	yes
Plant residue definition for monitoring	Two separate residue definitions: - bupirimate and - ethirimol (in order to cover the residues of ethirimol resulting from the use of bupirimate)
Plant residue definition for risk assessment	sum of bupirimate, ethirimol, de-ethyl-ethirimol and hydroxy-ethirimol expressed as bupirimate
Conversion factor (monitoring to risk assessment)	Conversion factor 3 for fruit crops derived from the metabolism studies on strawberry and melon at PHI 14-day.

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

Animals covered	Ruminants (goat), but considered not acceptable (Only TRR available, no identification of metabolites)
Time needed to reach a plateau concentration in milk and eggs	-
Animal residue definition for monitoring	Not required according to the supported uses;
Animal residue definition for risk assessment	Not required according to the supported uses;
Conversion factor (monitoring risk assessment	Not relevant
Metabolism in rat and ruminant similar (yes/no)	Not relevant
Fat soluble residue: (yes/no)	Not assessed

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

In confined rotational crop studies, total residues according to the residue definition for enforcement (bupirimate) are <0.01 mg/kg eq for all rotational crops tested at all soil aging periods.

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

Bupirimate: At least 2 years Ethirimol: At least 17 months When stored at -18 °C in high water containing commodities (apples).

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

	Ruminant:	**Poultry:**	**Pig:**
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes 0.15/0.44 mg/kg DM Dairy/Beef cattle	no	no
Potential for accumulation (yes/no):	No	-	-
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No[(1)]	No	No
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	Not required	Not required	Not required
Liver	Not required	Not required	Not required
Kidney	Not required	Not required	Not required
Fat	Not required	Not required	Not required
Milk	Not required		
Eggs		Not required	

[(1)]: Based on the TRRs observed in the goat metabolism study conducted with a dose rate of 4.37 mg/kg DM (*c.a.* 30N/10N for dairy/beef cattle), TRRs in the different matrices are expected to be <0.01 mg/kg when expressed on a 1N rate basis. Given that bupirimate is extensively metabolised in rat, it is assumed that residues would be composed of multiple components, each of them being present at low level, far below 0.01 mg/kg. Therefore residue definition and MRLs for ruminant matrices are not required.

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Bupirimate						
Crop	Northern/ Southern Region, field or glasshouse	Trials results relevant to the representative uses (a)	Recommendation/comments	**MRL** estimated from trials according to representative use	**HR** (c)	**STMR** (b)
Apple	North	<0.01, 0.02, 0.03, 0.04, 0.05, 3x 0.07, 0.11, 0.12	Trials selected within 25% limits of cGAP (4 applications, 0.014-0.017 kg as/hl, intervals 10-12 d and PHI 14 days) MRL, HR and STMR derived from merged data from northern and southern trials (Datasets similar based on Mann-Whitney U-test ($\alpha_{two\text{-}sided}$ = 5%)). Rmax: 0.14 Rber: 0.14	0.2	0.13	0.04
	South	<0.01, 0.01, 0.02, 3x 0.03, 0.04, 0.05, 0.07, 0.13				
	North+ South	2x <0.01, 0.01, 2x 0.02, 4x 0.03, 2x 0.04, 2x 0.05, 4x 0.07, 0.01, 0.12, 0.13				
Strawberry	North (Outdoor)	2x 0.04, 2x 0.05, 0.10, 0.14, 0.24, 0.26, 0.42, 0.49	Trials selected within 25% limits of critical GAP with 4-5 applications of 0.24-0.32 kg as/ha with an interval of 9-13 days and a PHI of 3 days. MRL, HR, STMR derived from glasshouse trials: Rmax: 1.3 Rber: 1.2	2	1.1	0.25
	South (Outdoor)	0.06, 2x0.15, 2x0.16, 2x 0.17, 0.19, 0.41, 0.50				
	North/South (Indoor)	0.09, 0.12, 0.20, 0.21, 0.22, 0.28, 0.51, 2x 0.61, 1.1				
Melon	South Outdoor	3x <0.01, 4 x 0.01, 0.014, 0.016, 2x 0.02, 0.07	Trials selected within 25% limits of cGAP (4 applications, 0.24-0.28 kg as/ha, intervals 9-11 days, PHI 3 days). MRL, HR, STMR derived from glasshouse trials only (residues from indoor dataset significantly higher than field dataset based on Mann-Whitney U-tests ($\alpha_{two\text{-}sided}$ = 5%)). Rmax: 0.13 Rber: 0.15	0.2	0.09	0.04
	Indoor South	<0.01, 0.01, 2x 0.03, 0.032, 0.04, 0.068, 0.07, 0.08, 0.09				

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

(b) Supervised Trials Median Residue i.e. the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

Ethirimol						
Crop	Northern/ Southern Region, Field or Glasshouse	**Trials results relevant to the representative uses** (a)	**Recommendation/comments**	**MRL** estimated from trials according to representative use	**HR** (c)	**STMR** (b)
Apple	field	South: 5x<0.01, 3x 0.01, 2x 0.02 North: 3x <0.01, 2x 0.01, 3x 0.02, 0.03, 0.04	MRL, HR, STMR derived from merged data from northern and southern field residue trials. Rmax: 0.04, Rber: 0.04	0.05	0.04	0.02
Strawberry	North (Outdoor)	3x <0.01, 2x 0.01, 3x 0.03, 0.06	Trials selected within 25% limits of cGAP (4-5 applications, 0.24-0.32 kg as/ha, intervals 9-13 days and PHI 3 days). MRL, HR, STMR derived from indoor and outdoor residue trials.	0.2	0.09	0.01
	South (Outdoor)	2x <0.01, 0.01, 0.02, 0.03, 0.04, 0.05, 2x 0.07, 0.08				
	North/South (Indoor)	5x 0.01, 2x 0.02, 0.03, 0.05, 0.09				
Melon	South (Outdoor)	9x <0.01, 3x 0.01	Trials selected within 25% limits of cGAP (4 applications, 0.24-0.28 kg as/ha,intervals 9-11 days and PHI 3 days) MRL, HR, STMR derived from glasshouse residue trials from Southern Europe.	0.05	0.02	0.01
	South (Indoor)	8x<0.01, 0.01, 0.02				

No risk assessment needed for ethirimol resulting from bupirimate uses for Annex I listing since the risk is covered by that of bupirimate. For MRL harmonisation a conversion factor should be derived for import tolerances of (dim)ethirimol uses from outside EU.

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

ADI	0.05 mg/kg bw/day for bupirimate 0.035 mg/kg bw/day for ethirimol **Chronic assessment based on ADI for ethirimol**
TMDI (% ADI) according to PRIMo rev. 2	Highest TMDI: 29% (DE children)
TMDI (% ADI) according to national (to be specified) diets	-
IEDI (WHO European Diet) (% ADI)	not required
NEDI (specify diet) (% ADI)	not required
Factors included in IEDI and NEDI	TMDI calculations performed using a conversion factor of 3 for fruit crops.
ARfD	Not allocated for bupirimate and ethirimol
IESTI (% ARfD)	Not relevant
NESTI (% ARfD) according to national (to be specified)	Not relevant
Factors included in IESTI and NESTI	Not relevant

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor (values or range)	Yield factor	
apples/ washed apples	1	0.60	-	60%
apples/ wet apple pomace	2	Mean 2.8 (2.2, 3.5)	-	mean 92%
apples/ apple juice	2	Max <0.2 (<0.07, <0.20)	-	max <11%
apples/ apple sauce	2	max <0.2 (<0.07, <0.20)	-	max <11%
strawberries/washed strawberries	2	Mean 1.0 (1.0, 1.0)	-	mean 100%
strawberries/canned strawberries	3	Max 0.80 (0.13, 0.33, 0.80)	-	max 80%
strawberries/strawberry jam	3	Max 0.40 (<0.07, 0.25, 0.4)	-	max 72%
melons/ melon pulp[(a)]	16	max 0.50 (0.10-0.50)	-	-
melons/ melon peel	16	mean 6.2 (4.0-10)	-	-

[(a)]: bupirimate residue levels in melon pulp: 12x <0.01, 4x 0.01 mg/kg

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

bupirimate	
Apples	0.2 mg/kg
Strawberries	2 mg/kg
Melons	0.2 mg/kg
Animal products	Not Required
ethirimol	
Apples	0.05 mg/kg
Strawberries	0.20 mg/kg
Melons	0.05 mg/kg
Animal products	Not Required

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.
MRLs of ethirimol are required for monitoring since it is used as active substance outside the EU

Chapter 2.5 – Fate and Behaviour in the Environment

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

Mineralization after 100 days	0.1 – 17.8% after 84 – 105 d, [pyrimidine-2-^{14}C]-bupirimate (n = 17)
Non-extractable residues after 100 days	8.5-53.1% after 84 – 105 d, [pyrimidine-2-^{14}C]-bupirimate (n = 17)
Metabolites requiring further consideration - name and/or code, % of applied (range and maximum)	**ethirimol** max. 42.2% AR after 182 days **de-ethylated bupirimate (DE-B)** max. 12.9% AR after 84 days; **de-ethylated ethirimol (DE-E)** max 7.7% AR.

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

Anaerobic degradation

Mineralization after 100 days	<0.1-0.1% after 84 days, [pyrimidine-2-^{14}C]-bupirimate (n = 2) flooding after 6 h of aerobic incubation
Non-extractable residues after 100 days	33-42% after 84 days, [pyrimidine-2-^{14}C]-bupirimate (n = 2) flooding after 6 h of aerobic incubation -
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No metabolites different from fully aerobic pathway

Soil photolysis

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	**ethirimol** 8.5 % at 3 d (summer sunlight equivalent at 40 °N)

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

Laboratory studies ‡

Parent	Aerobic conditions - **persistence endpoints**									
Soil	pH	% oc	% MWHC	dose (mg/kg)	temp. (°C)	DT_{50} (d)	DT_{90} (d)	kine-tics	**DT_{50} (20°C, d)**	**DT_{90} (20°C, d)**
Loam	5.1	2.0	40	1.1[(A)]	25	83.0	276	SFO	130	433
	5.1	2.0	40	1.1[(B)]	25	83.3	277	SFO	131	434
								mean	131	434
	5.1	2.0	40	11[(A)(C)]	25	123	410	SFO	193	643
	5.1	2.0	40	11[(B)(C)]	25	468	1553	SFO	734	2436
								mean	464	1540
Sandy loam 1	7.1	3.9	40	5.8	25	54.1	180	SFO	84.8	282
	7.1	3.9	40	5.8	15	86.7	288	SFO	54.4	181
								mean	69.6	232
	7.1	3.9	40	58[(D)]	25	65.3	217	SFO	102	340
Clay loam	7.3	7.1	40	6.6	25	42.4	141	SFO	66.5	221
	7.3	7.1	40	66[(D)]	25	52.2	173	SFO	81.9	272
Sand	5.1	0.5	40	4.8	25	64.4	214	SFO	101	336
Sandy loam 2	6.3	2.7	40	5.6	25	45.8	152	SFO	71.8	238

(A) Non-formulated
(B) Formulated as 25% EC
(C) Dose estimated based on 5 cm soil depth and soil bulk density 1500 kg/m^3; reported dose rate 8.4 kg as/ha.
(D) Reported dose rate 10 kg as/ha.

Laboratory studies ‡								
Parent	Aerobic conditions – **modelling endpoints**							
soil	pH	% oc	% MWHC	dose (mg/kg)	temp. (°C)	DT_{50} (d)	kine-tics	**DT_{50} (20°C, d) pF 2/10 kPa**
Loam	5.1	2.0	40	1.1[(A)]	25	83.0	SFO	130
	5.1	2.0	40	1.1[(B)]	25	83.3	SFO	131
							Mean	131
	5.1	2.0	40	11[(A)(C)]	25	123	SFO	193
	5.1	2.0	40	11[(B)(C)]	25	468	SFO	734
							mean	464
Sandy loam 1	7.1	3.9	40	5.8	25	54.1	SFO	84.8
	7.1	3.9	40	5.8	15	86.7	SFO	54.4
								69.6
	7.1	3.9	40	58[(D)]	25	65.3	SFO	102
Clay loam	7.3	7.1	40	6.6	25	42.4	SFO	66.5
	7.3	7.1	40	66[(D)]	25	52.2	SFO	81.9
Sand	5.1	0.5	40	4.8	25	64.4	SFO	101
Sandy loam 2	6.3	2.7	40	5.6	25	45.8	SFO	71.8
							geometric mean of all values	107
							median of all values	91.5
							geometric mean of low dose results	**84.8**
							median of low dose results	**71.8**

(A) Non-formulated
(B) Formulated as 25% EC
(C) Dose estimated based on 5 cm soil depth and soil bulk density 1500 kg/m^3; reported dose rate 8.4 kg as/ha.
(D) Reported dose rate 10 kg as/ha.

Laboratory studies ‡										
Ethirimol	Aerobic conditions - **persistence endpoints**									
Soil	pH	% oc	% MWHC	dose (mg/kg)	temp. (°C)	DT50 (d)	DT90 (d)	kine-tics	**DT50 (20°C, d)**	**DT90 (20°C, d)**
Sandy loam	5.2	1.0	40	1	22	18.4	298	DFOP	22.1	357
Loamy sand	6.8	2.6	40	1	22	85.6	8555	DFOP	103	10261
Sandy clay loam	7.0	2.3	40	2.97	20	13.5	89.4	FOMC	13.5	89.4
	7.0	2.3	40	2.97	5	84.3	417	DFOP	19.8	98.1[1]
Silt loam	5.4	1.2	pF 2	0.344	20	98.0	374	DFOP	98.0	374

Loamy sand	4.9	1.1	pF 2	0.344	20	76.0	288	DFOP	76.0	288
Loam	6.4	3.3	pF 2	0.344	20	27.9	139	DFOP	27.9	139

[1] normally this study should not be taken into account as the incubation temperature is more than 10 degrees below standard of 20ºC. As the value, after normalisation, is fairly equal to the incubation at 20ºC, in this case the value was not excluded.

Laboratory studies ‡								
Ethirimol	Aerobic conditions - **modelling endpoints**							
soil	pH	% oc	% MWHC	dose (mg/kg)	temp. (°C)	DT50 (d)	kine-tics	**DT50 (20°C, d) pF 2/10 kPa**
Sandy loam	5.2	1.0	40	1	22	203(A)	DFOP	220
Loamy sand	6.8	2.6	40	1	22	3695(A)	DFOP	3819
Sandy clay loam	7.0	2.3	40	2.97	20	26.9(B)	FOMC	26.9
	7.0	2.3	40	2.97	5	102	SFO	24.0[1]
							Mean	25.5
Silt loam	5.4	1.2	pF 2	0.344	20	104	SFO	104
Loamy sand	4.9	1.1	pF 2	0.344	20	81.1	SFO	81.1
Loam	6.4	3.3	pF 2	0.344	20	47.7(A)	DFOP	47.7
							geometric mean	**143**
							median	**92.6**

(A) DT50 derived from the rate constant of the slow phase of DFOP.
(B) DT50 derived from the DT90 (FOMC).
[1] normally this study should not be taken into account as the incubation temperature is more than 10 degrees below standard of 20ºC. As the value, after normalisation, is fairly equal to the incubation at 20ºC, in this case the value was not excluded.

Laboratory studies

DE-B	Aerobic conditions - **modelling endpoints**							
soil	pH	% oc	% MWHC	dose (mg/kg)	temp. (°C)	DT50 (d)	kine-tics	**DT50 (20°C, d) pF 2/10 kPa**
NO RELIABLE STUDY AVAILABLE **DATA GAP**								

Field studies ‡ parent	**persistence endpoints**							
Location	Soil type	% OM	pH	Dose [kg as /ha]	Month of applicatio n	Kinetics	**$DT_{50,field}$ (persis-tence) (d)**	**$DT_{90,field}$ (persis-tence) (d)**
Tarn et Garonne, Fr-S	silty clay loam	1.9	5.5	1.0	August	FOMC	49.9	396
Montanana, E (Sp)	silt loam	2.2	7.6	1.0	August	DFOP	8.4	131
Varendorf, D (Ge)	sandy loam	1.7	5.3	0.75	June	DFOP	4.4	18.7
Offenbach, D (Ge)	sandy loam	1.1	6.2	0.75	June	FOMC	0.8	14.2
Pallhausen, D (Ge)	loam	2.8	6.6	0.75	June	FOMC	0.4	13.3
Haag-Sollern, D (Ge)	silt loam	2.0	6.5	0.75	June	FOMC	1.9	26.0
						Max	**49.9**	**396**

Field studies ‡	
parent	**modelling endpoints:** not available

Field studies ‡ ethirimol	**persistence endpoints**							
Location	Soil type	% OM	pH	Dose [kg as /ha]	Month of app	Kinetics	**$DT_{50,field}$ (persis-tence) (d)**	**$DT_{90,field}$ (persis-tence) (d)**
Offenbach, D (Ge)	sandy loam	1.1	6.2	0.28	August	DFOP	3.4	13.5
Pallhausen, D (Ge)	loam	2.8	6.6	0.28	June	FOMC	0.4	8.1
Haag-Sollern, D (Ge)	silt loam	2.0	6.5	0.28	June	FOMC	0.7	26.9
						Max	**3.4**	**26.9**

Field studies ‡	
ethirimol	**modelling endpoints:** no timestep normalised values available

pH dependence ‡ (yes / no) (if yes type of dependence)	no
Soil accumulation and plateau concentration ‡	-

Laboratory studies ‡

Parent	Anaerobic conditions
In 2 soils, flooded at 6 hours post-treatment, bupirimate degraded with DT50 and DT90 values (persistence, 20°C) of 67.3-81.9 and 362-601 days, respectively. The $DT50_{SFO}$ (lab) values for modelling normalised to 20°C were 109-223 days.	

Soil adsorption/desorption (Annex IIA, point 7.1.2)

bupirimate							
Soil Type	OC (%)	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
clay	3.29	5.7	NA	NA	87	2644	0.9371
silt loam	2.39	7.2	NA	NA	43	1799	0.9417
loam	3.32	5.9	NA	NA	42	1265	0.9395
silt	1.36	6.8	NA	NA	12	882	1.0165
loamy sand	4.43	3.2	NA	NA	125	2822	0.8705
Arithmetic mean/median					46/43	1882/ 1779	0.941/ 0.940
pH dependence, Yes or No			No				

ethirimol							
Soil Type	OC (%)	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
clay loam	3.5	6.3	NA	NA	33	950	0.8736
sandy loam 1	1.3	7.3	NA	NA	2.3	170	0.8078
sandy loam 2	3.1	7.7	NA	NA	3.0	97	0.8828
sand	0.5	5.7	NA	NA	1.8	390	0.8312
Arithmetic mean/median					10/3	402/ 280	0.849/ 0.852
pH dependence (yes or no)			No				

De-ethylated bupirimate (DE-B): Data gap

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

Column leaching ‡	**bupirimate, 25 % EC/WP** Eluation (mm): 190 mm Time period (d): 2 d
	Leachate: 0.24 – 0.56 % bupirimate (measured as ethirimol) in leachate
Aged residues leaching ‡	**1. bupirimate** Aged for (w): 5 w Time period (d): 64 d Elution (mm): 660 mm **2. . bupirimate** Aged for (w): 22 w Time period (d): 64 d Elution (mm): 690 mm **3. bupirimate, 25 % EC** Aged for (w): 22 w Time period (d): 67 d Elution (mm): 690 mm **4. ethirimol** Aged for (d): 60 d Time period (d): 2 d Elution (mm): 200 mm
	1. Analysis of soil residues post ageing (soil residues pre-leaching): 57.4 – 73.2 % bupirimate 4.4 – 13.1 % ethirimol 0.6 – 1.3 %de-ethylated ethirimol 2.7 – 8.7 % de-ethylated bupirimate 66 – 93 % total radioactivity retained in top 10 cm 2. Analysis of soil residues post ageing (soil residues pre-leaching): 46.0 – 66.4 % bupirimate 4.6 – 7.7 % ethirimol 1.1 – 1.5 % de-ethylated ethirimol 2.6 – 7.8 % de-ethylated bupirimate 89.8 – 92.7 % total radioactivity retained in top 5 cm 3. Analysis of soil residues post ageing (soil residues pre-leaching): not available 108 % total radioactivity retained in top 5 cm 4. Analysis of soil residues post ageing (soil residues pre-leaching): 34.4 – 32.8 % ethirimol 2.0 – 2.8 % de-ethylated ethirimol 1.0 – 1.8 % 5-butyl-2,4-dihydroxy-6-methylpyrimidine 1.7 – 2.4 % 2-ethylamino-6-methylpyrimidin-4-ol 70 % total radioactivity retained in top 10 cm

	1. Leachate: 0.8 – 4.4 % total radioactivity in leachate 2. Leachate: 0.7 – 3.0 % total radioactivity in leachate 3. Leachate: 0.3 % total radioactivity in leachate 4. Leachate: 9.8 – 10.2 % total radioactivity in leachate
Lysimeter/ field leaching studies ‡	No studies submitted, none required

Parent	
Method of calculation	The worst case DT50,field value for Europe-N was determined by DFOP kinetics, but the worst case DT90,field value was determined by FOMC kinetics. Therefore PECsoil values were estimated using both kinetic models, and for each individual time point in the analysis, the higher PECsoil value from the two models was chosen. Europe-N: DFOP (worst case DT50) (DT50/DT90 4.4/18.7 d), g = 0.931058, k_1 = 0.176376 d^{-1}, k_2 = 0.00251294 d^{-1}; FOMC (worst case DT90) (DT50/DT90 1.9/26.0 d), α = 0.753816, β = 1.28532. Europe-S: FOMC (DT50/DT90 49.9/396 d), α = 1.12227, β = 58.3988 Plateau concentration (for Europe-S only): Worst-case DT_{90}field: FOMC (DT50/DT90 49.9/396 d), α = 1.12227, β = 58.3988. Incorporation depth 20 cm. Multiple applications in a single season were applied each year as a single dose representing the total seasonal dose.
Application data	Crop: apple, melon, strawberry, roses Depth of soil layer: 5 cm (for plateau conc.: 20 cm) Soil bulk density: 1.5 g/cm^3 % plant interception: 70% (apples), 50% (others) Application rate(s): 4 x 210 g a.s./ha, 10-d interval (apple, Eur-S) 4 x 150 g a.s./ha, 10-d interval (apple, Eur-N) 4 x 250 g a.s./ha, 10-d interval (melon & strawberry) 6 x 375 g a.s./ha, 7-d interval (roses field, 2 blocks of 3 applns, 1st in April, 2nd in July; time in between cycles set to 50 days) 4 x 750 g a.s./ha, 7-d interval (roses greenhouse)

Apple (Northern Europe)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.08431	-
Short term	24h	x	x	0.07237	0.07834
	2d	x	x	0.06320	0.07306

	4d	x	x	0.04905	0.06459
Long term	7d	x	x	0.03526	0.05498
	14d	x	x	0.02466	0.04247
	21d	x	x	0.02025	0.03580
	28d	x	x	0.01742	0.03156
	50d	x	x	0.01407	0.02460
	100d	x	x	0.01240	0.01892

Apple (Southern Europe)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.2675	-
Short term	24h	x	x	0.2632	0.2653
	2d	x	x	0.2591	0.2633
	4d	x	x	0.2513	0.2592
Long term	7d	x	x	0.2403	0.2535
	14d	x	x	0.2180	0.2413
	21d	x	x	0.1994	0.2304
	28d	x	x	0.1836	0.2207
	50d	x	x	0.1466	0.1962
	100d	x	x	0.0996	0.1596
Plateau concentration (before max)		x	x	0.039	x
Plateau concentration (max)		x	x	0.12	x

Melon & strawberry (Southern Europe)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.5307	-
Short term	24h	x	x	0.5223	0.5265
	2d	x	x	0.5141	0.5223
	4d	x	x	0.4985	0.5143
Long term	7d	x	x	0.4768	0.5029
	14d	x	x	0.4325	0.4788
	21d	x	x	0.3956	0.4572
	28d	x	x	0.3642	0.4379
	50d	x	x	0.2908	0.3893
	100d	x	x	0.1975	0.3167
Plateau concentration (before max)		x	x	0.078	x
Plateau concentration (max)		x	x	0.24	x

Strawberry (Northern Europe)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.23418	-
Short term	24h	x	x	0.20103	0.21760
	2d	x	x	0.17555	0.20295

	4d	x	x	0.13624	0.17942
Long term	7d	x	x	0.09795	0.15271
	14d	x	x	0.06851	0.11797
	21d	x	x	0.05625	0.09944
	28d	x	x	0.04839	0.08766
	50d	x	x	0.03908	0.06833
	100d	x	x	0.03444	0.05255

Roses field (Northern Europe)

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.41426	-
Short term	24h	x	x	0.36225	0.38826
	2d	x	x	0.31862	0.36435
	4d	x	x	0.25126	0.32464
Long term	7d	x	x	0.18559	0.27912
	14d	x	x	0.12303	0.21671
	21d	x	x	0.10269	0.18210
	28d	x	x	0.08965	0.16061
	50d	x	x	0.06680	0.12436
	100d	x	x	0.04527	0.09020

Roses protected (Northern Europe)

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.78616	-
Short term	24h	x	x	0.68042	0.73329
	2d	x	x	0.59173	0.68468
	4d	x	x	0.45489	0.60400
Long term	7d	x	x	0.32163	0.51154
	14d	x	x	0.22324	0.39198
	21d	x	x	0.18118	0.32873
	28d	x	x	0.15449	0.28850
	50d	x	x	0.11856	0.22163
	100d	x	x	0.10447	0.16657

Metabolite ethirimol

Method of calculation

Molecular weight relative to the parent: 0.66
Maximum % of occurrence: 42.2%

The dose of ethirimol was calculated by multiplying the dose of parent with the maximum percentage of occurrence of ethirimol and the MW correction factor. Calculations of the PECs values of ethirmol as a function of time were then based on the worst case DT_{50} and DT_{90} field or lab values.

The worst case DT50,field value for Europe-N was determined by DFOP kinetics, but the worst case DT90,field value, was determined by FOMC kinetics. Therefore PECsoil values were estimated using both

kinetic models, and for each individual time point in the analysis, the higher PECsoil value from the two models was chosen.
Europe-N, Field data: DFOP (worst case DT50) (DT50/DT90 3.4/13.5 d), g = 0.939562, k_1 = 0.225565 d^{-1}, k_2 = 0.00633768 d^{-1}; FOMC (worst case DT90); (DT50/DT90 0.7/26.9 d), α = 0.472718
β = 0.207572.
Europe-S, Laboratory data: DFOP, (DT50/DT90 103/10261 d), g = 0.502366, k_1 = 0.0454279 d^{-1}, k_2 = 0.000187566 d^{-1}.
Plateau concentration (for Europe-S only):
Laboratory data: DFOP, (DT50/DT90 103/10261 d), g = 0.502366, k_1 = 0.0454279 d^{-1}, k_2 = 0.000187566 d^{-1}. Incorporation depth 20 cm. Multiple applications in a single season were applied each year as a single dose representing the total seasonal dose. The seasonal dose of ethirimol was calculated by correcting the total seasonal dose of bupirimate by the maximum % of formation and the relative molecular mass.

Apple (Northern Europe)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.02292	-
Short term	24h	x	x	0.01327	0.01809
	2d	x	x	0.01130	0.01519
	4d	x	x	0.00958	0.01281
Long term	7d	x	x	0.00832	0.01116
	14d	x	x	0.00687	0.00937
	21d	x	x	0.00606	0.00840
	28d	x	x	0.00551	0.00775
	50d	x	x	0.00447	0.00653
	100d	x	x	0.00339	0.00523

Apple (Southern Europe)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.07356	-
Short term	24h	x	x	0.07235	0.07296
	2d	x	x	0.07120	0.07236
	4d	x	x	0.06904	0.07124
Long term	7d	x	x	0.06614	0.06967
	14d	x	x	0.06072	0.06655
	21d	x	x	0.05677	0.06395
	28d	x	x	0.05387	0.06179
	50d	x	x	0.04889	0.05721
	100d	x	x	0.04596	0.05232
Plateau concentration (before max)		x	x	0.16	x

Plateau concentration (max)		x	x	0.19	x

Melon & strawberry (Southern Europe)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.14595	-
Short term	24h	x	x	0.14355	0.14475
	2d	x	x	0.14126	0.14358
	4d	x	x	0.13698	0.14135
Long term	7d	x	x	0.13123	0.13824
	14d	x	x	0.12048	0.13205
	21d	x	x	0.11263	0.12688
	28d	x	x	0.10688	0.12260
	50d	x	x	0.09701	0.11351
	100d	x	x	0.09120	0.10381
Plateau concentration (before max)		x	x	0.32	x
Plateau concentration (max)		x	x	0.37	x

Strawberry (Northern Europe)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.06366	-
Short term	24h	x	x	0.03687	0.05026
	2d	x	x	0.03139	0.04220
	4d	x	x	0.02660	0.03559
Long term	7d	x	x	0.02311	0.03099
	14d	x	x	0.01907	0.02604
	21d	x	x	0.01683	0.02334
	28d	x	x	0.01530	0.02152
	50d	x	x	0.01241	0.01815
	100d	x	x	0.00942	0.01453

Roses field (Northern Europe)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.10558	-
Short term	24h	x	x	0.08539	0.09549
	2d	x	x	0.07207	0.08711
	4d	x	x	0.05289	0.07480
Long term	7d	x	x	0.04305	0.06330
	14d	x	x	0.03634	0.05150
	21d	x	x	0.03259	0.04582
	28d	x	x	0.03001	0.04219
	50d	x	x	0.02507	0.03574
	100d	x	x	0.01969	0.02906

Roses protected crops (Northern Europe)

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		x	-	0.20025	-
Short term	24h	x	x	0.16300	0.18162
	2d	x	x	0.13623	0.16562
	4d	x	x	0.09770	0.14129
Long term	7d	x	x	0.07438	0.11761
	14d	x	x	0.06061	0.09255
	21d	x	x	0.05300	0.08064
	28d	x	x	0.04785	0.07308
	50d	x	x	0.03834	0.05989
	100d	x	x	0.02874	0.04671

Metabolite DE-B

Method of calculation	Molecular weight relative to the parent: 0.91 (DE-B) and 0.71 (methylated ethirimol) Maximum % of occurrence: 12.9% (DE-B) and 10.3% (methylated ethirimol) The PEC$_S$ were calculated by correcting the initial PECS of bupirimate after a single application by the maximum formation rate and the relative molar mass of the metabolite. The value thus obtained was multiplied by the number of applications.

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
DE-B				
Apple, Europe-N	x	-	0.02822	-
Apple, Europe-S	x	-	0.03950	-
Melon, strawberry	x	-	0.07838	-
Roses (field)	x	-	0.17635	-
Roses (protected)	x	-	0.14539	-

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	**bupirimate** pH 5: > 30 d at 20 °C ethirimol: 17 % AR (30 d) pH 7 and 9: > 30 d at 20 °C ethirimol: 0.80 and 0.89 % AR (30 d) **ethirimol** pH 5: > 30 d at 22 °C
	bupirimate pH 7: > 30 d at 20 °C ethirimol: 0.80 % AR (30 d) **ethirimol** pH 7: > 30 d at 22 °C

	bupirimate pH 9: > 30 d at 20 °C ethirimol: 0.89 % AR (30 d) **ethirimol** pH 9: > 30 d at 22 °C
Photolytic degradation of active substance and metabolites above 10 % ‡	DT_{50} : 0.02 summer sunlight days at 54 °N ethirimol: 56 % AR (2 d) Unknown A: 32.9 %, unknown A2: 13.2 % AR (2 d) unknown C: 12.9 % AR (4 d)
Quantum yield of direct phototransformation in water at Σ > 290 nm	0.694
Readily biodegradable ‡ (yes/no)	not readily biodegradable according available study

Degradation in water / sediment

Bupiri-mate	Distribution Buprimate: max in water 86.6 % after 0 d. Max. sed 19.7 % after 120 d No metabolites reached levels of > 10 % of AR in the water and/or sediment phase.

Degradation in water / sediment

Parent	**Persistence endpoints**									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (χ^2)	DT_{50}-DT_{90} Water(A)	St. (χ^2)	DT_{50}-DT_{90} sed(A)	St. (χ^2)	Method of calculation
Loam	7.9 – 8.5	7.8	20	37.1-123	5.37	3.6-30.0	9.11	41.4-137	1.37	DFOP/SFO/SFO
Sandy loam	6.6 – 7.0	5.6	20	48.3-160	2.77	6.5-21.7	16.5	51.6-172	2.38	SFO/SFO/SFO
Geometric mean				42.3-140		4.8-25.5		46.2-154		

(A) half-lives for dissipation

Parent	**Modelling endpoints**									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50} whole system	St. (χ^2)	DT_{50} water[3]	St. (χ^2)	DT_{50} sediment[3]	St. (χ^2)	Method of calculation
silt loam[1]	7.9 – 8.5	7.8	20	37.1	5.37	37.1(A)	-	37.1(A)	-	
silt loam[2]	6.6 – 7.0	5.6	20	48.3	2.77	48.3(A)	-	48.3(A)	-	
Geometric mean				42.3		42.3		42.3		

(A) No value was estimated, value for whole system is used.

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

bupirimate Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: 1.1 Molecular weight (g/mol): 316.42 Water solubility (mg/L): 13.06 K_{OC}(L/kg): 1882 $DT50_{20°C,pF2}$ soil (d): 84.8 DT_{50} water/sediment system (d): 42.3 DT_{50} water (d): 42.3 DT_{50} sediment (d): 42.3 Crop interception (%): 70 (apples); 50 (melons/strawberries/roses) Multiple and single application was calculated and the application pattern resulting in the highest PECsw and PECsed values was selected.
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: SWASH 2.1 (9 April 2003), with MACRO 4.4.2, PRZM 1.1.1 and TOXSWA 1.1.1. Vapour pressure: 1.3 x 10^{-4} Pa (25 °C) K_{OC}(L/kg): 1882 1/n: 0.941 Q10 factor 2.58, Arrhenius activation energy 65400 J/mol, alpha factor 0.0948 K^{-1}. Calculations were performed with the combination DT50water = 42.3 days and DT50sediment = 1000 days, as well as with the inverse combination: DT50water = 1000 days and DT50sediment = 42.3 days. Multiple and single application was calculated for each combination. The combination resulting in the highest PECsw and PECsed values was selected.

Application data **Apples, Southern Europe**	**Step 1 & 2** Crop: pome/stone fruit, Southern Europe Crop interception: 70 % Number of applications: 4 Interval (d): 10 Application rate(s): 210 g as/ha Application window: June-September **Step 3** Application window: June-September Crop: pome/stone fruit Scenarios: D3, D4, D5, R1, R2, R3, R4

Application data **Apples, Northern Europe**	**Step 1 & 2** Crop: pome/stone fruit, Northern Europe Crop interception: 70 % Number of applications: 4 Interval (d): 10 Application rate(s): 150 g as/ha Application window: June-September **Step 3** Application window: June-September Crop: pome/stone fruit Scenarios: D3, D4, D5, R1, R2, R3, R4

Application data **Melons and strawberries, field applications, Southern Europe**	**Step 1 & 2** Crop: fruiting vegetables, Southern Europe Crop interception: 50 % Number of applications: 4 Interval (d): 10 Application rate(s): 250 g as/ha Application window: March-May **Step 3** Crop: fruiting vegetables Scenarios: D6, R2, R3, R4

Application data **Melons and strawberries, glasshouse applications**	**Step 2** Crop interception: 0 % Number of applications: 4 Interval (d): 10 Application rate(s): 9.06 g as/ha for single application and 13.4 g as/ha for multiple application (rate corrected to obtain total emission to water body of 0.1 % of original application rate 250 g as/ha) Application window: March-May

Application data **Strawberries, field applications, Northern Europe**	**Step 2** Crop: fruiting vegetables, Northern Europe Crop interception: 50 % Number of applications: 4 Interval (d): 10 Application rate(s): 250 g as/ha Application window: March-May

Application data **Crop: roses, field applications, Northern Europe**	Crop interception: 50 % Number of applications: 2 cycles of 3 Interval (d): 7 d; 2nd cycles starts 50 d after last application of 1st Application rate(s): 375 g as/ha Application window: March-May Peak after 2nd cycle calculated as sum of initial PEC after cycle 2 and actual day 50 PEC after cycle 1 ~~50 d~~ **Step 3** Crop: winter cereals Scenarios: D1, D2, D3, D4, D5, D6, R1, R2, R3, R4 Application window: 1 April to 9 June for first cycle and 1 July to 18 August for second cycle.

Application data	**Crop: roses, glasshouse applications** Crop interception: 0 % Number of applications: 4 Interval (d): 10 Application rate(s): 11.3 g as/ha for single application and 9.34 g as/ha for multiple application (rate corrected to obtain total emission to water body of 0.1 % of original application rate 750 g as/ha) Application window: March-May

FOCUS STEP 1 Scenario **bupirimate**	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
Apple, SE, late appln	0 h	123.8172	-	1.50E+03	-
Apple, NE, late appln	0 h	88.4409	-	1.07E+03	-
Melon/strawberry, SE (F)	0 h	104.1815	-	1.79E+03	-
Strawberry, NE (F)	0 h	104.1815	-	1.79E+03	-
Roses, NE (F)	0 h	273.9258	-	4.02E+03	-

FOCUS STEP 2 Scenario **bupirimate**	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
Apple, SE, late appln	0 h	14.0861	---	225.6863	---
Apple, NE, late appln	0 h	9.1926	---	133.9904	---
Melon/strawberry, SE (F)	0 h	18.0648	---	329.0521	---
Melon & strawberry (G)	0 h	0.151	---	1.1804	---
Strawberry, NE (F)	0 h	9.8986	---	175.5778	---
Roses, NE (F)	0 h	30.9598	---	515.8471	---
Roses, NE (G)	0 h	0.4736	---	3.7881	---

FOCUS STEP 3 Scenario **Apple, SE, late appln bupirimate**	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
D3 ditch	0 h	7.703	-	7.456	-
D4 pond	0 h	0.631	-	4.988	-
D4 stream	0 h	7.456	-	1.366	-
D5 pond	0 h	0.678	-	4.613	-
D5 stream	0 h	8.342	-	2.166	-
R1 pond	0 h	0.826	-	4.603	-
R1 stream	0 h	5.914	-	2.786	-
R2 stream	0 h	7.928	-	1.345	-
R3 stream	0 h	8.336	-	2.922	-

FOCUS STEP 3 Scenario **Melon/strawberry, SE, field appln bupirimate**	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
D6 ditch	0 h	1.57	-	1.293	-
R2 stream	0 h	1.381	-	27.872	-
R3 stream	0 h	3.393	-	8.839	-
R4 stream	0 h	5.017	-	20.422	-

FOCUS STEP 3 Scenario **Roses, NE, field appln bupirimate**	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
D1 ditch	0 h	6.299	-	60.91	-
D1 stream	0 h	2.117	-	30.504	-
D2 ditch	0 h	4.247	-	40.55	-
D2 stream	0 h	3.007	-	25.805	-
D3 ditch	0 h	2.38	-	3.243	-
D4 pond	0 h	0.458	-	5.127	-
D4 stream	0 h	2.05	-	1.72	-
D5 pond	0 h	0.266	-	2.425	-
D5 stream	0 h	2.21	-	0.7998	-
D6 ditch	0 h	2.66	-	11.046	-
R1 pond	0 h	0.665	-	6.682	-
R1 stream	0 h	3.817[(B)]	-	6.681	-
R3 stream	0 h	4.299	-	20.848	-
R4 stream	0 h	7.258	-	23.627	-

ethirimol Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: 1.1 Molecular weight (g/mol): 209.29 Water solubility (mg/L): 233 Soil or water metabolite: soil and photolysis metabolite. K_{OC}(L/kg): 402 $DT50_{20°C,pF2}$ soil (d): 143 DT_{50} water/sediment system (d): 1000~~0~~ DT_{50} water (d): 1000~~0~~ DT_{50} sediment (d): 1000~~0~~ Maximum occurrence observed: 42.~~1~~2 % in soil Maximum % in water-sediment systems 56% AR (representing max % in aqueous photolysis)
Parameters used in FOCUSsw step 3 (if performed)	not performed

Application data **Apples, Southern Europe**	**Step 1 & 2** Crop: pome/stone fruit Number of applications: 4 Interval (d): 10 Application rate(s) parent: 210 g as/ha Application window: June-September
Main route of entry	run-off and drainage and spray drift

Application data **Apples, Northern Europe**	**Step 1 & 2** Crop: pome/stone fruit Number of applications: 4 Interval (d): 10 Application rate(s) parent: 150 g as/ha Application window: June-September
Main route of entry	run-off and drainage and spray drift

Application data **Melons, field applications, Southern Europe**	**Step 1 & 2** Crop: fruiting vegetables Number of applications: 4 Interval (d): 10 Application rate(s) parent: 250 g as/ha Application window: March-May
Main route of entry	run-off and drainage and spray drift

Application data **Strawberries, field applications, Northern and Southern Europe**	**Step 1 & 2** Crop: fruiting vegetables Number of applications: 4 Interval (d): 10 Application rate(s) parent: 250 g as/ha Application window: March-May
Main route of entry	run-off and drainage and spray drift

Application data **Melons and strawberries, glasshouse applications**	**Step 2** Crop interception: 0 % Number of applications: 4 Interval (d): 10 Application rate(s): 2.53 g as/ha for single application and 3.75 g as/ha for multiple application (rate corrected to obtain total emission to water body of 0.1 % of original application rate) Application window: March-May Route of entry: spray drift only

Application data **Roses, field applications, Northern Europe**	**Step 1 & 2** Crop: fruiting vegetables Number of applications: two cycles of 3 Interval (d): 7 Application rate(s) parent: 375 g as/ha Application window: March-May
Main route of entry	run-off and drainage and spray drift

Application data **roses, glasshouse applications**	**Step 2** Crop interception: 0 % Number of applications: 4 Interval (d): 10 Application rate(s): 2.61 g as/ha for single application and 3.16 g as/ha for multiple application (rate corrected to obtain total emission to water body of 0.1 % of original application rate) Application window: March-May Route of entry: spray drift only

FOCUS STEP 1 Scenario **Ethirimol**	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
Apple, SE, late appln	0 h	67.191	-	204.545	-
Apple, NE, late appln	0 h	47.993	-	146.104	-
Melon/strawberry, SE (F)	0 h	63.980	-	243.507	-
Strawberry, NE (F)	0 h	63.980	-	243.507	-
Roses, NE (F)	0 h	158.593	-	547.890	-

FOCUS STEP 2 Scenario **Ethirimol**	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
Apple, SE, late appln	0 h	11.817	---	43.905	---
Apple, NE, late appln	0 h	7.445	---	27.360	---
Melon/strawberry, SE (F)	0 h	12.737	---	50.385	---
Melon and strawberry (G)	0 h	0.098	---	0.2402	---
Strawberry, NE (F)	0 h	7.204	---	28.160	---
Roses, NE (F)	0 h	25.269	---	95.450	---
Roses, NE (G)	0 h	0.4155	---	1.0477	---

Soil metabolite DE-B (de-ethyl-bupirimate)

PECsw (µg/L) and PECsed (µg/kg) for de-ethylated bupirimate(only STEP 1 values) can be considered with some reservations to be adequate for risk assessment due to the lack of adequate input parameters. Reservations are: 1) Koc = 882 mL/g is used for the estimation of the partition between water and sediment (this is the worst case value of parent but does not necessarily represents a worst case for this metabolite); 2) A maximum formation of DE-B of 7.4 % when a maximum of 12.9 % is observed in one of the available experiments. Ecotoloxicological risk assessment is based on these Step 1 FOCUS SW. A data gap has been identified for more refined PEC_{SW} values when measured input parameters for DE-B [soil half life and Koc] become available since risk to aquatic organisms cannot be excluded on basis of these low tier calculations).

DE-B		STEP1
Apples NEU	Initial PECsw	6.2
	Initial PECsed	54.68
Apples SEU	Initial PECsw	8.68
	Initial PECsed	76.38
Strawberries NEU	Initial PECsw	10.33
	Initial PECsed	91.13
Strawberries/melons SEU	Initial PECsw	10.33
	Initial PECsed	91.13

Photolysis metabolites Unk A, Unk A2 and Unk C.

$PIEC_{max}$ for photolysis metabolites Unknown A, Unknown A2 and Unknown C: 2.179 µg/L, 0.874 µg/L and 0.855 µg/L respectively for roses field application NE (2 series of three).

PEC (groundwater) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: PEARL 3.3.3.
Application data	**bupirimate** MW 316.42 g/mole Geomean DT_{50lab} 84.8 d (normalisation to 10kPa or pF2, 20 °C). avg. K_{OC}: 1882, $^1/_n$= 0.941 Vp: 1.3 x 10^{-4} Pa (25 °C) Water solubility : 13.06 mg/L (~~25~~ 20ºC) **ethirimol** MW 209.29 g/mole Max % in soil: 42.2% Geomean $DT50_{20°C,pF2}$ 143 d Avg Koc: 402 L/kg, $^1/_n$= 0.849 Vp: 3.1E-08 Pa at 20°C Water solubility: 150 mg/L at 20°C **DE-B** **Data gap**
Application	**Apples, Southern Europe** Crop: apples Application rate: 210 g/ha.

	No. of applications: 4 Interval: 10 d Time of application (month or season): start 25/5; interception 70% **Apples, Northern Europe** Crop: apples Application rate: 150 g/ha. No. of applications: 4 Interval: 10 d Time of application (month or season): start 1/8; interception 70% **Strawberries, Southern and Northern Europe** **Melons, Southern Europe** Crop: strawberries Application rate: 250 g/ha. No. of applications: 4 Interval: 10 d Time of application (month or season): start 25/5; interception 50% **Roses, field application, Northern Europe** Crop: winter wheat Application rate: 375 g/ha. No. of applications: two cycles of 3 Interval: 7 d Time of application (month or season): 30/4, 7/5, 14/5, and 3/7, 10/7, 17/7; interception 50% **Roses, glasshouse application, Northern Europe** Crop: winter wheat Application rate: 750 g/ha. No. of applications: 4 Interval: 7 d Time of application (month or season): start 25/5; interception 50%

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)

crop	scenario	Bupirimate (µg/L)	ethirimol (µg/L)
Apple (Eur-S) Late application	Chateaudun	<0.001	0.0001
	Hamburg	<0.001	0.0001
	Jokioinen	<0.001	<0.001
	Kremsmuenster	<0.001	<0.001
	Okehampton	<0.001	0.0001
	Piacenza	<0.001	0.0123
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	0.0003
Apple (Eur-N) Late application	Chateaudun	<0.001	0.0003
	Hamburg	<0.001	0.0004
	Jokioinen	<0.001	<0.001
	Kremsmuenster	<0.001	0.0001
	Okehampton	<0.001	0.0002
	Piacenza	<0.001	0.025
	Porto	<0.001	<0.001
	Sevilla	<0.001	0.0001
	Thiva	<0.001	0.0008
strawberry, melon Field/greenhouse	Hamburg	<0.001	0.0009
	Jokioinen	<0.001	<0.001
	Kremsmuenster	<0.001	0.0001
	Sevilla	<0.001	<0.001
Roses Field	Chateaudun	<0.001	<0.001
	Hamburg	<0.001	0.020
	Jokioinen	<0.001	<0.001
	Kremsmuenster	<0.001	0.012
	Okehampton	<0.001	0.031
	Piacenza	<0.001	**0.147**
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	<0.001
Roses Greenhouse Application starts 25 May	Chateaudun	<0.001	0.0001
	Hamburg	<0.001	0.042
	Jokioinen	<0.001	<0.001
	Kremsmuenster	<0.001	0.026
	Okehampton	<0.001	0.057
	Piacenza	<0.001	**0.247**
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	0.0001

A data gap has been identified for the assessment of potential ground water ocnatimation by major soil metabolite DE-B.

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

Application rate	Application rate: 210 – 750 g/ha. No. of applications: 4 Time of application (month or season): spring -

	autumn
Direct photolysis in air	Not studied
Quantum yield of direct phototransformation	bupirimate: 0.694
Photochemical oxidative degradation in air	DT_{50} of < 1 hour derived by the Atkinson model (version 1.90) 12 hr day
Volatilisation	-
Metabolites	-

PEC_A (air)

Method of calculation	Based on the vapour pressure of 1.31 x 10^{-4} Pa (extrapolated value at 25 °C), and a Henry's law constant of 1.35 $Pa \cdot m^3 \cdot mol^{-1}$, it is considered that volatilisation of bupirimate may occur, but concentrations will generally be low. The gas phase oxidation half-life for bupirimate was estimated to be < 1 hour. Should bupirimate volatilise, then the compound will degrade quickly

PEC_A

Maximum concentration	-

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil:	bupirimate, ethirimol, DE-B,
	Surface water:	bupirimate, ethirimol, DE-B (soil metabolite), unknown A, unknown A2, unknown C (photolysis metabolites)
	Sediment:	bupirimate, ethirimol, DE-B (soil metabolite),
	Ground water:	bupirimate, ethirimol, DE-B¸
	Air:	bupirimate

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

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

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Candidate for R53

Chapter 2.6 – Effects on Non-target Species

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

Species	Test substance	Time scale	End point (mg/kg bw.day)	End point (mg/kg feed)
Birds				
Japanese quail	bupirimate	Acute	> 5000	
Pigeon	bupirimate	Acute	> 2747	
Partridge	ethirimol	Acute	> 3000	
Pheasant	ethirimol	Acute	> 3000	
Partridge	Milstem Col	Acute	> 3000 (expressed as ethirimol)	
Pheasant	Milstem Col	Acute	> 3750 (expressed as ethirimol)	
Partridge	ethimirol 80 % JF	Acute	> 2400 (expressed as ethirimol)	
Pheasant	ethimirol 80 % JF	Acute	> 2400 (expressed as ethirimol)	
Mallard duck	bupirimate	Short-term	> 2091	> 10000
Bobwhite quail	bupirimate	Short-term	> 2576	> 10000
Mallard duck	ethirimol	Short-term	> 1960	> 10000
Bobwhite quail	ethirimol	Short-term	> 3385	> 10000
Japanese quail	bupirimate	Long-term	≥ 98	≥ 936
Mallard duck	ethirimol	Long-term	58	425
Mammals				
Rat	bupirimate	Acute	4000	
Rat	ethirimol	Acute	4000	
Rat	Preparation	Acute		
Mice	Metabolite 1	Acute		
Rat	bupirimate	Long-term	400	35
Rat	ethirimol	Long-term	500	23
Additional higher tier studies				

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

Crop and application rate: **apples, Southern EU; 4 x 210 g as/ha (scenario orchard)**

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger[3]
Tier 1 (Birds)				
insectivorous bird	Acute	11.4	> 241	10
	Short-term	6.33	> 330	10
	Long-term	6.33	≥ 15.5	5
Tier 1 (Mammals)				
herbivorous mammal	Acute	20.1	199	10
	Long-term	6.8	5.1	5
Higher tier refinement (Mammals)				
	Acute			10
	Long-term			5

Crop and application rate: **apples, Northern EU; 4 x 150 g as/ha (scenario orchard)**

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger[3]
Tier 1 (Birds)				
insectivorous bird	Acute	8.14	> 338	10
	Short-term	4.52	> 464	10
	Long-term	4.51	≥ 21.7	5
Tier 1 (Mammals)				
herbivorous mammal	Acute	14.3	280	10
	Long-term	4.8	7.3	5
Higher tier refinement (Mammals)				
	Acute			10
	Long-term			5

Crop and application rate: **melons and strawberries, field, 4 x 250 g as/ha (scenario leafy crops)**

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger[3]
Tier 1 (Birds)				
insectivorous bird	Acute	13.5	> 203	10
	Short-term	7.54	> 277	10
	Long-term	7.54	≥ 13.0	5
medium herbivorous bird	Acute	26.4	> 104	10
	Short-term	14.4	> 145	10
	Long-term	7.65	≥ 12.8	5
Tier 1 (Mammals)				
herbivorous mammal	Acute	9.7	412	10
	Long-term	2.8	12.5	5
Higher tier refinement (Mammals)				
	Acute			10
	Long-term			5

Crop and application rate: **roses, field, two cycles of 3 x 375 g as/ha (scenario leafy crops)**

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger[3]
Tier 1 (Birds)				
insectivorous bird	Acute	20.2	> 135	10
	Short-term	11.3	> 185	10
	Long-term	11.3	≥ 8.7	5
medium herbivorous bird	Acute	47.1	> 58.3	10
	Short-term	22.8	> 91.7	10
	Long-term	12.1	≥ 8.1	5
Tier 1 (Mammals)				
herbivorous mammal	Acute	17.4	230	10
	Long-term	4.5	7.8	5
Higher tier refinement (Mammals)				
	Acute			10
	Long-term			5

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

Annex IIIA, point 10.2)

Values in bold are used for risk assessment.

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg as/L)
Laboratory tests ‡				
Fish				
Lepomis macrochirus	bupirimate	96 hr (flow-through)	Mortality, LC_{50}	**1.0** (nominal)[1]
Lepomis macrochirus	bupirimate	96 hr (flow-through)	Mortality, LC_{50}	1.25 (nominal)[1]
Oncorhynchus mykiss	bupirimate	96 hr (flow-through)	Mortality, LC_{50}	1.0 (nominal)[1]
Oncorhynchus mykiss	bupirimate	96 hr (flow-through)	Mortality, LC_{50}	1.1 (actual)[1]
Oncorhynchus mykiss	bupirimate	96 hr (flow-through)	Mortality, LC_{50}	1.25 (actual)[1]
Oncorhynchus mykiss	bupirimate	28 d (flow-through)	Mortality, NOEC	0.30 (actual)
Pimephales promelas	bupirimate	31 d (flow-through) ELS	Mortality, NOEC	**0.10** (nominal)
Lepomis macrochirus	NIMROD 25 EC	96 hr (flow-through)	Mortality, LC_{50}	**1.25** (nominal)[2]
Oncorhynchus mykiss	NIMROD 25 EC	96 hr (flow-through)	Mortality, LC_{50}	1.50 (nominal)[2]
Oncorhynchus mykiss	ethirimol	96 hr (flow-through)	Mortality, LC_{50}	**60.8** (actual)
Oncorhynchus mykiss	ethirimol	96 hr (flow-through)	Mortality, LC_{50}	66 (actual)
Oncorhynchus mykiss	ethirimol	96 hr (flow-through)	Mortality, LC_{50}	73.4 (actual)
Lepomis macrochirus	ethirimol	96 hr (flow-through)	Mortality, LC_{50}	>200 (actual)
Cyprinus caprio	ethirimol	96 hr (flow-through)	Mortality, LC_{50}	100 (actual)
Oncorhynchus mykiss	ethirimol	21 d (semi-static)	Mortality, NOEC	≥ **41.4** (actual)
Aquatic invertebrate				
Daphnia magna	bupirimate	48 h (static)	Immobilisation, EC_{50}	> **3.41** (actual)
Daphnia magna	bupirimate	21 d (semi-static)	Reproduction, NOEC	**0.56** (nominal)
Daphnia magna	NIMROD 25 EC	48 h (static)	Immobilisation, EC_{50}	**3.12** (nominal)

Daphnia magna	ethirimol	48 h (static)	Immobilisation, EC_{50}	**50** (actual)[3]
Daphnia magna	ethirimol	21 d (semi-static)	Reproduction, NOEC	**7.3** (actual)
Sediment dwelling organisms				
No studies submitted, not required				
Algae				
*Pseudokirchne-riella subcapitata**	bupirimate	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**1.6** (nominal)[4] 2.5 (nominal)[4]
Pseudokirchne-riella subcapitata	NIMROD 25 EC	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	1.7 (nominal, expressed as active substance) >2.73 (nominal, expressed as active substance)
*Pseudokirchne-riella subcapitata**	NIMROD 25 EC	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**1.23** (nominal, expressed as active substance)[4] 1.88 (nominal, expressed as active substance)[4]
*Pseudokirchne-riella subcapitata**	ethirimol	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**24** (nominal)[4] 45 (nominal)[4]

Higher plant
Not submitted, not required
Microcosm or mesocosm tests
Not submitted, not required

1: No mortality at 1.0 to 1.25 mg as/L, 100 % mortality at next higher concentration. LC_{50} of 1.0 mg as/L used as *worst-case* estimate.
2: No mortality at 1.25 to 1.5 mg as/L, 100 % mortality at next higher concentration. LC_{50} of 1.25 mg as/L used as *worst-case* estimate.
3: No immobilisation at 50 mg/L, full immobilisation at next higher concentration. EC_{50} 50 mg/L is used as *worst-case* estimate.
4: There were some uncertainties in this study. Therefore, this endpoint is considered as indicative for toxicity. The endpoint was however used in risk assessment.

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

Crop and application rate: **apples, Southern Europe, 4 x 210 g as/ha, late applications, average crop cover**

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	124		**8.1**	100
NIMROD 25 EC	Fish	1.25	Acute	124		**10**	100

bupirimate	Fish	0.1	Chronic	124		**0.81**	10
bupirimate	Aquatic invertebrates	> 3.41	Acute	124		**> 28**	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	124		**25**	100
bupirimate	Aquatic invertebrates	0.56	Chronic	124		**4.5**	10
bupirimate	Algae	1.6	Acute	124		12.9	10
NIMROD 25 EC	Algae	1.23	Acute	124		**9.9**	10
ethirimol	Fish	60.8	Acute	67.2		905	100
ethirimol	Fish	41.4	Chronic	67.2		617	10
ethirimol	Aquatic invertebrates	50.0	Acute	67.2		744	100
ethirimol	Aquatic invertebrates	7.3	Chronic	67.2		109	10
ethirimol	Algae	24	Acute	67.2		357	10
DE-B	Fish	0.1*	Acute	8.68		**12**	100
DE-B	Fish	0.01*	Chronic	8.68		**1**	10
DE-B	Aquatic invertebrates	0.341*	Acute	8.68		**39**	100
DE-B	Aquatic invertebrates	0.056*	Chronic	8.68		**6**	10
DE-B	Algae	0.16*	Acute	8.68		18	10

*toxicity of DE-B assumed to be is 10 time higher than the parent

FOCUS Step 2

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	14.1		**70.9**	100
NIMROD 25 EC	Fish	1.25	Acute	14.1		**88.7**	100
bupirimate	Fish	0.1	Chronic	14.1		**7.1**	10
bupirimate	Aquatic invertebrates	> 3.41	Acute	14.1		> 242	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	14.1		221	100
bupirimate	Aquatic invertebrates	0.56	Chronic	14.1		39.7	10

Refined aquatic risk assessment using higher tier FOCUS modelling. Step 3

Test substance	Scenario	Water body type	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	TER	Annex VI Trigger[1]
bupirimate	R3,	stream	Fish	1.0	Acute	8.37	119	100
NIMROD 25 EC	R3	stream	Fish	1.25	Acute	8.37	149	100
bupirimate	R3,	stream	Fish	0.1	chronic	8.37	11.9	10

Crop and application rate: **apples, Northern Europe, 4 x 150 g as/ha, late applications, average crop cover**

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	88.4		**11**	100
NIMROD 25 EC	Fish	1.25	Acute	88.4		**14**	100
bupirimate	Fish	0.1	Chronic	88.4		**1.1**	10
bupirimate	Aquatic invertebrates	> 3.410	Acute	88.4		**> 39**	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	88.4		**35**	100
bupirimate	Aquatic invertebrates	0.56	Chronic	88.4		**6.3**	10
bupirimate	Algae	1.6	Chronic	88.4		18	10
NIMROD 25 EC	Algae	1.23	Chronic	88.4		14	10
ethirimol	Fish	60.8	Acute	58.0		1048	100
ethirimol	Fish	41.4	Chronic	58.0		714	10
ethirimol	Aquatic invertebrates	50.0	Acute	58.0		862	100
ethirimol	Aquatic invertebrates	7.3	Chronic	58.0		126	10
ethirimol	Algae	24	Chronic	58.0		413	10
DE-B	Fish	0.1*	Acute	6.2		**16**	100
DE-B	Fish	0.01*	Chronic	6.2		**2**	10
DE-B	Aquatic invertebrates	0.341*	Acute	6.2		**55**	100
DE-B	Aquatic invertebrates	0.056*	Chronic	6.2		**9**	10

Crop and application rate: **apples, Northern Europe, 4 x 150 g as/ha, late applications, average crop cover**

DE-B	Algae	0.16*	Acute	6.2		26	10

*toxicity of DE-B assumed to be is 10 time higher than the parent

FOCUS Step 2

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	9.19		109	100
NIMROD 25 EC	Fish	1.25	Acute	9.19		136	100
bupirimate	Fish	0.1	Chronic	9.19		10.9	10
bupirimate	Aquatic invertebrates	> 0.341	Acute	9.19		> 371	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	9.19		339	100
bupirimate	Aquatic invertebrates	0.56	Chronic	9.00		60.9	10

Crop and application rate: **melons and strawberries, Southern Europe, field applications, 4 x 250 g as/ha**

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	104		**9.6**	100
NIMROD 25 EC	Fish	1.25	Acute	104		**12**	100
bupirimate	Fish	0.1	Chronic	104		**0.96**	10
bupirimate	Aquatic invertebrates	> 3.41	Acute	104		**> 33**	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	104		**30**	100
bupirimate	Aquatic invertebrates	0.56	Chronic	104		**5.4**	10
bupirimate	Algae	1.6	Acute	104		15	10
NIMROD 25 EC	Algae	1.23	Acute	104		12	10

ethirimol	Fish	60.8	Acute	64.0		950	100
ethirimol	Fish	41.4	Chronic	64.0		647	10
ethirimol	Aquatic invertebrates	50.0	Acute	64.0		781	100
ethirimol	Aquatic invertebrates	7.3	Chronic	64.0		114	10
ethirimol	Algae	24	Acute	64.0		375	10
DE-B	Fish	0.1*	Acute	10.33		**10**	100
DE-B	Fish	0.01*	Chronic	10.33		**1**	10
DE-B	Aquatic invertebrates	0.341*	Acute	10.33		**33**	100
DE-B	Aquatic invertebrates	0.056*	Chronic	10.33		**5**	10
DE-B	Algae	0.16*	Acute	10.33		15	10

*toxicity of DE-B assumed to be is 10 time higher than the parent

FOCUS Step 2

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	18.1		**55.3**	100
NIMROD 25 EC	Fish	1.25	Acute	18.1		**69.1**	100
bupirimate	Fish	0.1	Chronic	18.1		**5.5**	10
bupirimate	Aquatic invertebrates	> 3.41	Acute	18.1		>188	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	18.1		118	100
bupirimate	Aquatic invertebrates	0.56	Chronic	18.1		30.9	10

Refined aquatic risk assessment using higher tier FOCUS modelling. Step 3

Test substance	Scenario	Water body type	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	TER	Annex VI Trigger[1]
bupirimate	R4	stream	Fish	1.0	Acute	5.02	199	100
NIMROD 25 EC	R4	stream	Fish	1.25	Acute	5.02	249	100
bupirimate	R4	stream	Fish	0.1	Chronic	5.02	19.9	10

Crop and application rate: **melons and strawberries, Northern and Southern Europe, glasshouse applications, 4 x 250 g as/ha**

FOCUS Step 2

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	0.151		6623	100
NIMROD 25 EC	Fish	1.25	Acute	0.151		8278	100
bupirimate	Fish	0.1	Chronic	0.151		662	10
bupirimate	Aquatic invertebrates	> 3.41	Acute	0.151		>22584	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	0.151		14106	100
bupirimate	Aquatic invertebrates	0.56	Chronic	0.151		3709	10
bupirimate	Algae	1.6	Acute	0.151		10596	10
NIMROD 25 EC	Algae	1.23	Acute	0.151		8146	10
ethirimol	Fish	60.8	Acute	0.098		6.2×10^5	100
ethirimol	Fish	41.4	Chronic	0.098		4.2×10^5	10
ethirimol	Aquatic invertebrates	50.0	Acute	0.098		5.1×10^5	100
ethirimol	Aquatic invertebrates	7.3	Chronic	0.098		7.4×10^4	10
ethirimol	Algae	24	Acute	0.098		2.4×10^5	10

Crop and application rate: **strawberries, field application, Northern Europe, 4 x 250 g as/ha**

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	104		**9.6**	100
NIMROD 25 EC	Fish	1.25	Acute	104		**12**	100
bupirimate	Fish	0.1	Chronic	104		**0.96**	10

Crop and application rate: **strawberries, field application, Northern Europe, 4 x 250 g as/ha**

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Aquatic invertebrates	> 3.41	Acute	104		**> 33**	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	104		**30**	100
bupirimate	Aquatic invertebrates	0.56	Chronic	104		**5.4**	10
bupirimate	Algae	1.6	Acute	104		15	10
NIMROD 25 EC	Algae	1.23	Acute	104		12	10
ethirimol	Fish	60.8	Acute	64.0		950	100
ethirimol	Fish	41.4	Chronic	64.0		647	10
ethirimol	Aquatic invertebrates	50.0	Acute	64.0		781	100
ethirimol	Aquatic invertebrates	7.3	Chronic	64.0		114	10
ethirimol	Algae	24	Acute	64.0		375	10
DE-B	Fish	0.1*	Acute	10.33		**10**	100
DE-B	Fish	0.01*	Chronic	10.33		**1**	10
DE-B	Aquatic invertebrates	0.341*	Acute	10.33		**33**	100
DE-B	Aquatic invertebrates	0.056*	Chronic	10.33		**5**	10
DE-B	Algae	0.16*	Acute	10.33		15	10

*toxicity of DE-B assumed to be is 10 time higher than the parent

FOCUS Step 2

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	9.90		101	100
NIMROD 25 EC	Fish	1.25	Acute	9.90		126	100
bupirimate	Fish	0.1	Chronic	9.90		10.1	10

Crop and application rate: **strawberries, field application, Northern Europe, 4 x 250 g as/ha**

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Aquatic invertebrates	>3.41	Acute	9.90		>344	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	9.90		215	100
bupirimate	Aquatic invertebrates	0.56	Chronic	9.90		56.6	10

Crop and application rate: **roses, field application, Northern Europe, 6 x 375 g as/ha**

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	274		**3.7**	100
NIMROD 25 EC	Fish	1.25	Acute	274		**4.6**	100
bupirimate	Fish	0.1	Chronic	274		**0.36**	10
bupirimate	Aquatic invertebrates	> 3.41	Acute	274		**>12.4**	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	274		**7.8**	100
bupirimate	Aquatic invertebrates	0.56	Chronic	274		**2.0**	10
bupirimate	Algae	1.6	Acute	274		**5.84**	10
NIMROD 25 EC	Algae	1.23	Acute	274		**4.5**	10
ethirimol	Fish	60.8	Acute	158		385	100
ethirimol	Fish	41.4	Chronic	158		262	10
ethirimol	Aquatic invertebrates	50.0	Acute	158		316	100
ethirimol	Aquatic invertebrates	7.3	Chronic	158		46	10
ethirimol	Algae	24	Acute	158		152	10

FOCUS Step 2

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	31.0		**32.3**	100
NIMROD 25 EC	Fish	1.25	Acute	31.0		**40.3**	100
bupirimate	Fish	0.1	Chronic	31.0		**3.2**	10
bupirimate	Aquatic invertebrates	> 3.41	Acute	31.0		> 110	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	31.0		101	100
bupirimate	Aquatic invertebrates	0.56	Chronic	31.0		18.1	10
bupirimate	Algae	1.6	Acute	31.0		51.6	10
NIMROD 25 EC	Algae	1.23	Acute	31.0		39.7	10

Refined aquatic risk assessment using higher tier FOCUS modelling. Step 3

Test substance	Scenario	Water body type	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	TER	Annex VI Trigger[1]
bupirimate	R4	stream	Fish	1.0	Acute	7.26	138	100
NIMROD 25 EC	R4	stream	Fish	1.25	Acute	7.26	172	100
bupirimate	R4	stream	Fish	0.1	Chronic	7.26	13.8	10

Crop and application rate: **roses, Northern Europe, glasshouse applications, 4 x 750 g as/ha**

FOCUS Step 2

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Fish	1.0	Acute	0.474		2110	100
NIMROD 25 EC	Fish	1.25	Acute	0.474		2637	100
bupirimate	Fish	0.1	Chronic	0.474		211	10
bupirimate	Aquatic invertebrates	> 3.41	Acute	0.474		>7194	100
NIMROD 25 EC	Aquatic invertebrates	3.12	Acute	0.474		4494	100

Crop and application rate: **roses, Northern Europe, glasshouse applications, 4 x 750 g as/ha**

FOCUS Step 2

Test substance	Organism	Toxicity end point (mg as/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
bupirimate	Aquatic invertebrates	0.56	Chronic	0.474		1181	10
bupirimate	Algae	1.6	Acute	0.474		3376	10
NIMROD 25 EC	Algae	1.23	Acute	0.474		2595	10
ethirimol	Fish	60.8	Acute	0.416		1.5×10^5	100
ethirimol	Fish	41.4	Chronic	0.416		1.0×10^5	10
ethirimol	Aquatic invertebrates	50.0	Acute	0.416		1.2×10^5	100
ethirimol	Aquatic invertebrates	7.3	Chronic	0.416		1.8×10^4	10
ethirimol	Algae	24	Acute	0.416		5.8×10^4	10

Bioconcentration

	Active substance
$logP_{O/W}$	
Bioconcentration factor (BCF)[1] ‡	185 L/kg
Annex VI Trigger for the bioconcentration factor	100
Clearance time (days) (CT_{50})	
(CT_{90})	
Level and nature of residues (%) in organisms after the 14 day depuration phase	

[1] only required if log $P_{O/W}$ >3.
* based on total ^{14}C or on specific compounds

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

Test substance	Acute oral toxicity (LD_{50} µg as/bee)	Acute contact toxicity (LD_{50} µg as/bee)
bupirimate	> 200	> 50

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

Test substance	Acute oral toxicity (LD_{50} µg as/bee)	Acute contact toxicity (LD_{50} µg as/bee)
bupirimate 25 % EC	> 200 (as bupirimate)	> 50 (as bupirimate)
NIMROD 25 EC	105.8 (as bupirimate)	> 100 (as bupirimate)
Field or semi-field tests: not required		

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

Crop and application rate: **roses, field, two cycles of 3 x 375 g as/ha**

Test substance	Route	Hazard quotient	Annex VI Trigger
bupirimate	Contact	< 7.5	50
NIMROD 25 EC	Oral	3.5	50

Crop and application rate: **roses, glasshouse, 4 x 750 g as/ha**

Test substance	Route	Hazard quotient	Annex VI Trigger
bupirimate	Contact	< 15	50
NIMROD 25 EC	Oral	7.1	50

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

Laboratory tests on inert substrates (no LR50 studies submitted)

Species	Test Substance	Dose (kg as/ha)	End point	Adverse Effect (%)	Annex VI Trigger
T. pyri	25 % EL	0.174	mortality	**61**	30 %
			reproduction	**38**	30 %
C. carnea	25 % EC	0.200	mortality	no effects	30 %
			reproduction	no effects	30 %
E. formosa	25 % EC	0.750	mortality	**100**	30 %
P. cupreus	25 % EC	0.750	mortality	0	30 %
			consumption	0	30 %
		1.8	mortality	0	30 %
			consumption	0	30 %

Crop and application rate

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field	Trigger
no LR_{50} studies submitted					

Calculated In-field and off-field exposure (1st tier)

Crop	F/G	Max. single dose (g as/ha)	Number of applications	MAF	Exposure in-field (g as/ha)	Drift	Exposure off-field (g as/ha)[6]
Apples (N-EU)	F	150	4	2.7	405	15.73[3]	64
Apples (S-EU)	F	210	4	2.7	567	15.73[3]	89
Melons	F/G	250	4	2.7	675	2.8[4]	19
Strawberries	F/G	250	4	2.7	675	2.8[4]	19
Roses (N-EU)	F	375	two cycles of 3	2.3[1]	863[2]	8.0[5]	69
Roses (N-EU)	G	750	4	2.7	2025	-	-

1: valid for one series of 3 applications
2: assuming no remaining residue after first series
3: drift value for late application to fruit crops used in accordance with FOCUS Surface water
4: drift value for fruiting vegetables
5. drift value for hand-application, crop height > 50 cm
6: with vegetation distribution factor 10 and uncertainty factor 10

Further laboratory and extended laboratory studies

Species	Life stage	Test substance, substrate and duration	Dose (g as/ha)	Aged (d)	End point	Adverse effect[1,2] (%)	Trigger value
A. rhopalosiphi	mummies	NIMROD 25 % EC; sprayed plants; 48 h	50		mortality	0	50 %
					parasitation	+ 25.1	50 %
			250		mortality	0	50 %
					parasitation	+ 16.7	50 %
			500		mortality	0	50 %
					parasitation	+ 32.6	50 %
			750		mortality	0	50 %
					parasitation	+ 77.5	50 %
			1800		mortality	0	50 %
					parasitation	+ 53.3	50 %

Further laboratory and extended laboratory studies

Species	Life stage	Test substance, substrate and duration	Dose (g as/ha)	Aged (d)	End point	Adverse effect[1,2] (%)	Trigger value
T. pyri	protonymphs	NIMROD 25 EC; leaves from outdoor sprayed trees; 14 d	0	0	mortality	- 6.1	50 %
					reproduction	+ 6.9	50 %
			100	0	mortality	12.2	50 %
					reproduction	0	50 %
			250	0	mortality	0	50 %
					reproduction	+ 13.8	50 %
			750	0	mortality	21.2	50 %
					reproduction	+ 22.4	50 %
			1800	0	mortality	45.1	50 %
					reproduction	+ 55.8	50 %
			50	7	mortality	- 8.1	50 %
					reproduction	+ 17.6	50 %
			100	7	mortality	3.5	50 %
					reproduction	+ 13.2	50 %
			250	7	mortality	- 3.5	50 %
					reproduction	+ 4.4	50 %
			750	7	mortality	1.2	50 %
					reproduction	+ 16.5	50 %
			1800	7	mortality	-2.3	50 %
					reproduction	+ 7.7	50 %
			50	14	mortality	-12.6	50 %
					reproduction	+ 21.4	50 %
			100	14	mortality	-10.3	50 %
					reproduction	+ 28.6	50 %
			250	14	mortality	-12.6	50 %
					reproduction	+ 20.0	50 %
			750	14	mortality	- 8.0	50 %
					reproduction	+ 11.4	50 %
			1800	14	mortality	- 9.2	50 %

					reproduction	+ 4.3	50 %

O. laevigatus	nymphs	NIMROD 25 EC; leaves from outdoor sprayed trees; 11 d	138	0	mortality	9.3	50 %
					egg laying	+ 6.9	50 %
					hatching rate	+ 25.4	50 %
			488	0	mortality	- 4.7	50 %
					egg laying	+ 14.3	50 %
					hatching rate	+ 8.5	50 %
			138	5	mortality	-9.5	50 %
					egg laying	+ 7.7	50 %
					hatching rate	+ 21.9	50 %
			488	5	mortality	-7.1	50 %
					egg laying	+ 28.8	50 %
					hatching rate	+ 2.6	50 %

C. septempunctata	nymphs	NIMROD 25 EC; leaves from outdoor sprayed bean plants; 16 d	750	0	mortality	11.4	50 %
					reproduction	2.8	50 %
			2000	0	mortality	11.4	50 %
					reproduction	25	50 %

1: negative values for mortality indicate decrease in mortality as compared to the control
2: positive values for sublethal parameters indicate increase as compared to control

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point[1]
Earthworms			
Eisenia fetida	bupirimate	Acute 14 days	LC_{50} > 1000 mg /kg d.w.soil ($LC_{50,corr}$ > 500 mg/kg d.w. soil)
	NIMROD 25 EC	Acute 14 days	LC_{50} 187 mg as/kg d.w.soil ($LC_{50,corr}$ 93.5 mg/kg d.w. soil)
	NIMROD 25 EC	Chronic 56 days	2500 g a.s./ha equivalent to 7.3 mg a.s./kg soil (5% o.m.)
	ethirimol	Acute 14 days	>1000 mg a.s./kg soil (5% o.m.)
	ethirimol	Chronic 56 days	81 mg a.s./kg soil (5% o.m.)

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point[1]
	De-ethylated bupirimate (DE-B)	Acute 14 days	606 mg a.s./kg soil (5% o.m.)
Folsomia candida	NIMROD 25 EC	Chronic 28 days	9 mg a.s./kg soil (5% o.m.)
	ethirimol	Chronic 28 days	81 mg a.s./kg soil (5% o.m.)
Other soil macro-organisms: no data available..			
Soil micro-organisms			
Nitrogen mineralisation	bupirimate 25 % EC		soil 1: 17 % effect at day 7 at 0.4 mg as/kg d.w.soil; effects < 25 % after 28 d 23 % effect at day 7 at 8.0 mg as/kg d.w.soil; effects < 25 % after 28 d
Carbon mineralisation	bupirimate 25 % EC		soil 1: 41 % effect at day 6 - 10 at 0.4 mg as/kg d.w.soil; effects < 25 % after 24 d 30 % effect at day 6 - 10 at 8.0 mg as/kg d.w.soil; effects < 25 % after 24 d soil 2: no significant effects
Field studies[2]			
Indicate if not required			

[1] indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

Toxicity/exposure ratios for soil organisms

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
Eisenia fetida	NIMROD 25 EC	Acute	0.79[1]	118	10
	NIMROD 25 EC	Chronic	0.79	9.3	5
	Ethirimol	Acute	0.20	>5000	10
	Ethirimol	Chronic	0.20	405	5
	DE-B	Acute	0.24	2579	10
Folsomia candida	NIMROD 25 EC	Chronic	0.79	11.4	5
	Ethirimol	Chronic	0.20	405	5

Toxicity/exposure ratios for soil organisms

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger

1: highest initial PEC_S after glasshouse application to roses at 4 x 750 g as/ha

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

Preliminary screening data

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g a.s./ha)[2] vegetative vigour	ER_{50} (g/ha)[2] emergence	Exposure[1] (g a.s./ha)[2]	TER	Trigger
Brassica napus, Lupinus angustifolius, Helianthus annuus, Cucumis sativa, Avena sativa, Allium cepa	NIMROD 25 EC	>375		89[3]	**>4.20**[4]	5

[1] explanation of how exposure has been estimated should be provided (e.g. based on Ganzelmeier drift data)
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation
[3]Worst-case exposure for Apples, (S-EU): 210 g a.s./ha, MAF = 2.7, drift = 15.73%.
[4]Risk is considered to be low, since no effects were found at the highest test dose for any of the plant species tested

Additional studies (e.g. semi-field or field studies)

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

Test type/organism	end point
Activated sludge	no significant effects at 625 mg as/L nominal (> 10 times reported water solubility of 18 mg/L)

Ecotoxicologically relevant compounds **(consider parent and all relevant metabolites requiring further assessment from the fate section)**

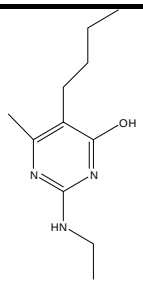
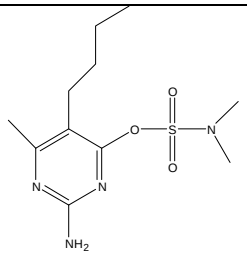
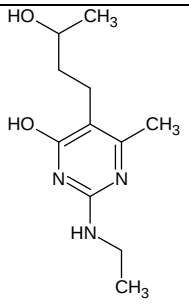
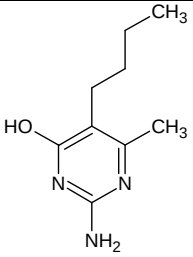
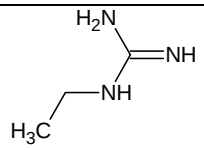
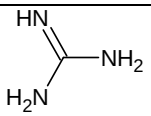
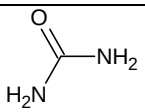
Compartment	
soil	bupirimate, ethirimol
water	bupirimate, ethirimol
sediment	bupirimate
groundwater	bupirimate, ethirimol

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	R51/R53; S60/61

	RMS/peer review proposal
Preparation	

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
ethirimol	5-butyl-2-ethylamino-6-methyl pyrimidin-4-ol	
De-ethyl-bupirimate (DE-B)		
Hydroxyl-ethirimol	2-(ethylamino)-5-(3-hydroxybutyl)-6-methylpyrimidin-4-ol	
de-ethyl-ethirimol	2-amino-5-butyl-6-methylpyrimidin-4-ol	
ethyl guanidine	1-ethylguanidine	
-	guanidine	
-	urea	

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
cGAP	critical good agricultural practice
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography

GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HPLC-MS/MS	high pressure liquid chromatography – mass spectrometry/mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level

OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year