CONCLUSION ON PESTICIDE PEER REVIEW

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

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Buprofezin is one of the 79 substances of the third stage Part A of the review programme covered by Commission Regulation (EC) No 1490/2002[3], as amended by Commission Regulation (EC) No 1095/2007[4]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

Finland being the designated rapporteur Member State submitted the DAR for buprofezin in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 7 July 2005. The peer review was initiated on 2 February 2006 by dispatching the DAR for consultation of the Member States and the sole applicant Nihon Nohyaku Co. Ltd. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed on during a written procedure in October – November 2006. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in May - June 2007 and in December 2007.

A final discussion of the outcome of the consultation of experts took place during a written procedure with Member States in February - March 2008 leading to the conclusions set out in the EFSA Conclusion finalised on 3 March 2008 (EFSA Scientific Report (2008) 128).

Following the Commission Decision of 30 September 2008 (2008/771/EC)[5] concerning the non-inclusion of buprofezin in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Nihon Nohyaku Co. Ltd made a resubmission application for the inclusion of buprofezin 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 conclusions leading to the Decision on non-inclusion, as set out in the Review Report (SANCO/110/08 – rev. final) as follows:

1 On request from the European Commission, Question No EFSA-Q-2009-00913, issued on 21 May 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 263, 02.10.2008, p.18

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 buprofezin. EFSA Journal 2010; 8(6):1624. [77 pp.]. doi:10.2903/j.efsa.2010.1624. Available online: www.efsa.europa.eu

- the information available was insufficient to satisfy the requirements set out in Annex II and Annex III Directive 91/414/EEC, in particular with regard to:
    - the substantial lack of data to assess the consumer exposure, which is regarded as inconclusive
    - the substantial lack of data to assess the risk to soil-dwelling macro-organisms
- and concerns were identified with regard to:
    - the consumer exposure

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, the United Kingdom, being the designated RMS in the resubmission procedure, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 21 August 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 24 August 2009. The EFSA collated and forwarded all comments received to the Commission on 8 October 2009.

In accordance with Article 20, following consideration of the Additional Report and the comments received, the Commission requested the EFSA to deliver its conclusions on buprofezin.

The conclusion from the original review was reached on the basis of the evaluation of the representative uses as an insecticide on tomatoes, lettuce and citrus. The conclusions of the re-submission were reached on the basis of the evaluation of the representative uses of buprofezin as an insecticide and acaricide on tomatoes, lettuce and citrus, with a modification for the use on lettuce only. Full details of the representative uses can be found in Appendix A to this report.

The representative formulated product for the evaluation was „Applaud 25 WP", a wettable powder formulation (WP).

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

Adequate methods are available to monitor buprofezin residues in all matrices.

In mammals, the acute oral, dermal or inhalation toxicity of buprofezin is low (oral and dermal LD_{50} >2000 mg/kg bw, LC_{50} 4.57 mg/L air/4h). Buprofezin is not a skin or eye irritant, nor a skin sensitiser.

Target organs in subchronic and chronic studies are the liver and thyroid, showing increased weight, and histological and clinical chemistry findings. The relevant short-term NOAEL in rats is 13 mg/kg bw/day, while in dogs the relevant NOAEL is 10 mg/kg bw/day. The relevant long-term toxicity NOAEL in rats is 0.9 mg/kg bw/day, while in mice it is 1.82 mg/kg bw/day.

The genotoxicity of buprofezin was discussed in an opinion of the Panel on Plant Protection Products and their Residues (PPR) based on a new micronucleus test in the bone marrow of mouse, showing the induction of micronuclei in the erythrocytes of mouse bone marrow when administered by oral gavage, once daily, for two consecutive days. The Panel considered buprofezin non-genotoxic, and the *in vivo* micronucleus test on bone marrow as not interpretable. The PPR Panel re-evaluated also the long-term toxicity/carcinogenicity studies on buprofezin and concluded that buprofezin is not carcinogenic in rats or mice.

Buprofezin did not show any reproductive toxicity potential: the relevant parental and offspring NOAELs are 6.46 mg/kg bw/day and 9.21 mg/kg bw/day, respectively. The reproductive NOAEL is 66 mg/kg bw/day. As for teratogenicity studies, overall, the NOAEL for both maternal and foetal

effects is 50 mg/kg bw/day (based on decreased food consumption and increased water intake, and decreased foetal weight, skeletal effects and subcutaneous oedema, respectively). It was agreed not to propose any classification.

Buprofezin does not have potential to induce neurotoxicity in mammals.

The Acceptable Daily Intake of 0.01 mg/kg bw/day is based on the relevant NOAEL of 0.9 mg/kg bw/day from the 24-month study in rats, with a safety factor of 100. The Acceptable Operator Exposure Level is 0.04 mg/kg bw/day, based on a NOAEL of 10 mg/kg bw/day, with a safety factor of 100 and a correction for oral absorption of 40 %. The Acute Reference Dose is 0.5 mg/kg bw, based on the NOAEL from the developmental toxicity study and applying a safety factor of 100.

The operator exposure was below the AOEL for tractor-mounted spraying with personal protective equipment (PPE) for tomatoes and citrus, calculated with the German model. For hand-held application, the exposure was below the AOEL with PPE for tomatoes outdoors (UK-POEM). The exposure was below the AOEL with PPE/RPE for hand-held application for tomatoes and lettuce in glasshouse (Dutch model), and for hand-held application in citrus (German model). For bystanders the estimated exposure levels were below the AOEL (< 15%), for both field applications on tomatoes and citrus; bystander exposure for application in greenhouses is unlikely. The worker exposure was estimated to be below the AOEL with gloves when handling tomatoes or lettuce in glasshouse, or tomatoes outdoors. However, the exposure was above the AOEL even with gloves when handling citrus.

The metabolism of buprofezin in plants has been elucidated in three plant groups (fruit crops, leafy crops and oilseed/pulse crops). The parent compound is the major constituent of the final residue, accounting for 47 – 89 % of the TRR for pre-harvest intervals (PHIs) < 27 days. The residues in plants are mainly composed of the parent compound and the sugar conjugates of the metabolite BF4, which are identified as BF9 and BF12 under acidic analysis conditions, or as BF26 when the analytical procedures include neutral or alkaline steps. Therefore, the residues were defined as „buprofezin" only for monitoring, and as „sum of buprofezin and BF4 conjugates analysed as BF9 and BF12 under acidic hydrolysis and expressed as buprofezin" for risk assessment. Maximum residue limits (MRLs) are proposed for tomatoes and citrus, however a complete residue data set is requested for all representative uses in order to derive appropriate conversion factors (CF) for risk assessment, and to propose an MRL for indoor lettuce. Provisionally, and based on the metabolism studies, a CF of 1.5 is proposed for fruit crops.

Based on new studies, processing factors are proposed for citrus and tomato. However, a data gap is identified concerning the possible transfer of the metabolite aniline, especially in processed fractions subject to pasteurisation or sterilisation.

A potential transfer of residues to rotational crops has been noted. Based on the representative uses, no residues are expected in animal commodities, and no residue definitions and MRL are proposed for products of animal origin.

Even if the toxicological profile of some metabolites is not fully addressed, with some of them considered to be of similar or of higher toxicity than the parent compound, the consumer risk assessment gives sufficient margin to conclude on the absence of chronic or acute concerns for the consumer, with the refined calculated intakes being below 10 % of the toxicological reference values. It should be noted that lettuce was not considered in this assessment, since the residue trials were not performed according to the critical GAP and are not appropriate to propose an MRL for this crop. In addition, the assessment for tomatoes and citrus has to be considered provisional, pending the submission of new residue trials on tomatoes and citrus in order to derive sound conversion factors for risk assessment.

In soil under aerobic conditions buprofezin exhibits medium to high persistence. Mineralisation of the phenyl ring to carbon dioxide accounted for 19-51 % applied radioactivity (AR) after 90 - 98 days.

The formation of unextractable residues was a sink, accounting for 23 - 33 % AR after 90 - 98 days. Only minor (< 5% AR) metabolites were formed. Buprofezin exhibits slight mobility in soil. There was no indication that adsorption of buprofezin was pH dependent.

In dark natural sediment water systems buprofezin degraded exhibiting moderate persistence in both water and sediment, forming the metabolite BF10 in water (max. 12 % AR). The terminal metabolite, CO_2, was a sink in the material balance, accounting for a maximum of 18 % AR at 91 days (study end). Unextracted sediment residues were also a sink representing 14 – 15 % AR at study end. The necessary surface water and sediment exposure assessments were appropriately carried out (including some updated calculations for sediment presented in the Additional Report), using the agreed FOCUS scenarios approach for buprofezin at steps 1 - 3 for tomatoes, and steps 1 - 4 for citrus, with spray drift mitigation being applied at step 4. For the metabolite BF10 appropriate FOCUS step 1 and 2 calculations were carried out. These values are the basis for the risk assessment discussed in this conclusion.

The potential for groundwater exposure from the representative uses by buprofezin above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by all pertinent FOCUS groundwater scenarios.

The acute and long-term risk to birds and mammals from the representative uses of buprofezin was assessed as low. The risk assessment for small herbivorous mammals in citrus plantations assumed an interception rate of 70 %, resulting in a TER value that exceeded the Annex VI trigger value. A low risk was also identified for birds and mammals exposed via the ingestion of contaminated earthworms or fish, or via contaminated drinking water.

Buprofezin is very toxic to aquatic organisms. Low risk was identified from the use of buprofezin on tomatoes. However, the application in citrus plantations requires a no-spray-buffer zone of 21 metres when applied adjacent to edge-of-field water courses. The risk to sediment-dwelling organisms was assessed as low from the representative field uses of buprofezin. Buprofezin is not considered to bioaccumulate in fish.

Low risk was identified for all other non-target organisms.

KEY WORDS

Buprofezin, peer review, risk assessment, pesticide, insecticide, acaricide

TABLE OF CONTENTS

BACKGROUND

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. Buprofezin is one of the 79 substances of the third stage, part A of the review programme covered by the Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007 designating Finland as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Finland submitted the report of its initial evaluation of the dossier on buprofezin, hereafter referred to as the DAR (Finland, 2005), to the EFSA on 7 July 2005. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the DAR. In accordance with Article 11(2) of the Regulation (EC) No 1490/2002 the revised version of the DAR was distributed for consultation on 3 February 2006 to the Member States and the applicant Nihon Nohyaku Co., Ltd as identified by the rapporteur Member State.

The comments received on the DAR were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed during a written procedure in October – November 2006 on data requirements to be addressed by the notifier as well as on issues for further detailed discussion at expert level.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings in May - June 2007 and in December 2007. The reports of these meetings were made available to the Member States electronically.

During the initial peer review of the DAR and the consultation of technical experts a concern on genotoxicity and carcinogenicity was identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR). The opinion of the Panel (EFSA, 2007) was adopted on 11 December 2007 and is considered in this conclusion.

A final discussion of the outcome of the consultation of experts took place during a written procedure with Member States in February - March 2008 leading to the conclusions set out in the EFSA Conclusion finalised on 3 March 2008 (EFSA, 2008).

Following the Commission Decision of 30 September 2008 (2008/771/EC)[9] concerning the non-inclusion of buprofezin in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Nihon Nohyaku Co., Ltd made a resubmission application for the inclusion of buprofezin in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[10]. The resubmission dossier included further data in response to the issues identified in the conclusions leading to the Decision on non-inclusion, as set out in the Review Report (European Commission, 2008) as follows:

- the information available was insufficient to satisfy the requirements set out in Annex II and Annex III Directive 91/414/EEC, in particular with regard to:

[7] OJ L224, 21.08.2002, p.25
[8] OJ L246, 21.9.2007, p.19
[9] OJ L 263, 02.10.2008, p.18
[10] OJ L 15, 18.01.2008, p.5

- the substantial lack of data to assess the consumer exposure, which is regarded as inconclusive
- the substantial lack of data to assess the risk to soil-dwelling macro-organisms

and concerns were identified with regard to:

- the consumer exposure

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, the United Kingdom, being the designated RMS in the resubmission procedure, submitted an evaluation of the additional data in the format of an Additional Report (The United Kingdom, 2009). The Additional Report was received by the EFSA on 21 August 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 24 August 2009. The EFSA collated and forwarded all comments received to the Commission on 8 October 2009. The collated comments were also forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the 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 and the comments received, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 6 November 2009, the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on buprofezin 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 11 November 2009; 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 there was no need for EFSA to organise a consultation with Member State experts, however, it was agreed that further information should be requested from the applicant in the area of residues.

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 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 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 March 2010.

The conclusion from the original review was reached on the basis of the evaluation of the representative uses presented in the DAR, i.e. use as an insecticide on tomatoes, lettuce and citrus. The conclusions of the resubmission were reached on the basis of the evaluation of the representative uses of buprofezin as an insecticide and acaricide on tomatoes, lettuce and citrus, with a modification for the use on lettuce only. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A of this conclusion.

The documentation developed during the resubmission peer review was compiled as a Peer Review Report (EFSA, 2010), comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State"s Additional Report:

- the comments received;
- the resulting Reporting Table (rev. 1-1 of 12 November 2009)

as well as the documents summarising the follow-up of the issues identified as not finalised at the end of the commenting period:

- the Evaluation Table (10 May 2010).

Given the importance of the Additional Report including its addendum (compiled version of February 2010 containing all individually submitted addenda) (The United Kingdom, 2010) and the Peer Review Report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion. The documents of the Peer Review Report and the final addendum developed and prepared during the course of the initial review process are made publicly available as part of the background documentation to the original EFSA conclusion finalised on 3 March 2008 (EFSA, 2008).

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Buprofezin is the ISO common name for (*Z*)-2-*tert*-butylimino-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one (IUPAC).

Buprofezin belongs to the class of chitin synthesis inhibitors.

The representative formulated product for the evaluation was „Applaud 25 WP", a wettable powder formulation (WP), containing 250 g/kg buprofezin.

The evaluated representative uses are as an insecticide and acaricide on tomatoes, lettuce and citrus, as proposed by the applicant. For the resubmission the GAP has been modified for the use on lettuce. The pre-harvest interval has been changed from 3 days to 28 days to support the consumer risk assessment. Full details of the representative uses can be found in Appendix A to this report.

CONCLUSIONS OF THE EVALUATION

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

The minimum purity of buprofezin as manufactured should not be less than 985 g/kg. No FAO specification exists.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of buprofezin or the respective formulation. There is one outstanding issue; a sprayability study was requested because of the poor wettability and suspensibility results. A study was provided and was evaluated in the Addendum 4 to Volume 3 of the DAR (Finland, 2008), however the summary of this study did not appear to address the wettability and suspensibility issues. Therefore this issue remains a data gap.

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

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

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

The method for food of plant origin is GC-NPD with an LOQ of 0.01 mg/kg. Buprofezin can be determined by LC-MS/MS with an LOQ of 0.01 mg/kg (lettuce, tomatoes, processed tomato products, citrus, and processed citrus products). The method for soil is GC-NPD with an LOQ of 0.01 mg/kg, with confirmation with a different column with GC-FPD. The water method is HPLC-UV with an LOQ of 0.1 µg/L, and confirmation by LC-MS. Air is analysed by a GC-MSD with an LOQ of 0.27 µg/m^3.
An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see section 3.2). As the active substance is neither toxic nor very toxic, an analytical method for body fluids and tissues is not required.

2. Mammalian toxicity

Buprofezin was discussed in the PRAPeR 24 meeting of experts in June 2007. During the meeting, a concern was raised with regard to genotoxicity and carcinogenicity. It was decided to forward a question to the Panel on Plant Protection Products and their Residues (PPR Panel). In December 2007 the Panel opinion was finalised and the final version adopted (EFSA, 2007). Buprofezin was therefore

discussed for the second time in a meeting of experts (PRAPeR 39, December 2007) to close the remaining open issues where possible.

It was agreed that the batches used in the mammalian toxicity studies are equivalent to the current technical specification.

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

Following oral administration in rats, buprofezin is rapidly absorbed, biotransformed and rather rapidly excreted, predominantly in faeces. Biliary excretion is significant. The oral absorption was discussed in the PRAPeR 24 meeting of experts in June 2007. The value of 50 % proposed by the RMS was probably overestimated: in tests with bile cannulated animals a considerably lower amount of substance was voided via the urine than in non-bile cannulated animals. This is due to a hampered enterohepatic cycle. Thus, based on urinary and bile excretion data, a value of 40 % was considered more appropriate.

Based on the available data, there was no indication for accumulation of buprofezin or its metabolites in the tissues. Buprofezin is extensively metabolised: the main metabolic routes are hydroxylation of the phenyl ring and oxidation of the t-butyl groups, and thiadiazin ring opening.

2.2. Acute toxicity

The acute oral, dermal and inhalation toxicity of buprofezin in rat is low (oral and dermal LD_{50} >2000 mg/kg bw, LC_{50} = 4.57 mg/L air /4h). Clinical signs include decreased locomotor activity, tremor, lacrimation, abnormal gait, and incontinence of urine after high oral doses. Buprofezin is not a skin or eye irritant, nor a skin sensitiser in the guinea pig maximisation test and confirmed by a Local Lymph Node Assay test which was negative.

2.3. Short-term toxicity

The target organs in subchronic studies in both rodents and dogs are the liver and the thyroid, showing increased weight and histological and clinical chemistry findings. The relevant NOAEL in rats is 13 mg/kg bw/day as agreed in the meeting of experts in December 2007; in a 90-day study in dogs, the NOAEL is 10 mg/kg bw/day, while in a 2-year study in dogs the NOAEL is 2 mg/kg bw/day.

2.4. Genotoxicity

The genotoxicity of buprofezin was tested in five different types of *in vitro* assays, and one *in vivo* assay.

Many tests (chromosomal aberration assay, micronucleus test, Rec-assay and Ames test) were considered insufficient by the RMS, and further studies for *in vitro* and *in vivo* chromosomal aberration assays were considered necessary.

In September 2006 the RMS submitted an Addendum (Addendum 1 to Volume 3, Finland, 2008) summarising the additional studies provided by the applicant. In particular, a micronucleus test in the bone marrow of mouse (Addendum 1 to Volume 3, Annex B.6.4.1.6) showed that buprofezin induced micronuclei in the erythrocytes of mouse bone marrow when administered by oral gavage, once daily, for two consecutive days.

The issue was discussed in the PRAPeR 24 meeting in June 2007. This finding was supported by the results of a published *in vivo* study (mouse bone marrow cells). The *in vivo* results were not supported by the presented *in vitro* data that were submitted (Chinese hamster lung cells), but in a published study buprofezin showed aneugenic effects in somatic cells *in vitro* (Syrian hamster embryo cells). Buprofezin did not induce chromosomal aberrations in germ cells *in vivo* (mouse spermatocytes) in a published study. Buprofezin was not mutagenic or genotoxic in the acceptable studies (two point mutation assays and unscheduled DNA synthesis) evaluated previously in the DAR.

A question was forwarded to the PPR Panel on the genotoxic potential of buprofezin. The PPR Panel concluded that the range of studies submitted was adequate and that there was no evidence that buprofezin is genotoxic. The Panel considered the *in vivo* micronucleus test on bone marrow as not interpretable and therefore did not contribute to the evaluation of the genotoxicity of buprofezin. In particular, the results of the study were considered as equivocal and providing only very limited information for the evaluation of the genotoxicity of buprofezin for the following reasons:

- no criteria for micronuclei scoring were reported, except for the fluorescence emission
- it was not possible to establish dose-dependency of the increase in frequency of micronuclei observed in the first experiment, because only the highest dose resulted in a significant response; the second experiment cannot be considered as a confirmatory test, because it was carried out at only a single dose using a different methodology
- the mean frequency of micronucleated immature erythrocytes in concurrent positive controls was higher in the first experiment compared to the second one, evidencing the difference between the two different scoring methods applied
- individual data of micronucleated immature erythrocytes (MNIE)/1000 cells (24.0, 33.5, 6.5, 8.0, 29.0) for buprofezin 2000 mg/kg in the first experiment revealed a large inter-individual variability
- a very large historical positive control range (mitomycin C, 3 mg/kg) calculated from the data of 8 animals in the experimental period 1999-2005 was shown in the original report 10.0-167.2 MNIE/1000 IEs (immature erythrocytes)

The results of the micronucleus test in the bone marrow of mouse cannot exclude an aneuploidogen mechanism, mediated by indirect effects, to explain the increase in the frequency of MNIE induced by high doses of buprofezin, as was suggested by a published *in vitro* study. The mechanism for any induction of micronuclei (MN) by buprofezin was not adequately addressed in the study. Only one experiment including 5 animals was carried out to evaluate the kinetochore positive (KC+) MN, and no historical control values were reported for the % of KC+-MN evaluated by the CREST method (immunofluorescent antikinetochore staining).

The PPR Panel concluded on the basis of an adequate range of suitably conducted tests of genotoxicity, both *in vitro* and *in vivo,* that there is no evidence that buprofezin is genotoxic. The *in vivo* micronucleus test on bone marrow was considered as not interpretable by the Panel and not contributing to the evaluation of the genotoxicity of buprofezin.

2.5. Long-term toxicity

The most prominent effect in chronic toxicity and carcinogenicity studies was the increased liver and thyroid weight, accompanied by histological findings at higher doses.

The relevant NOAEL in rats was 20 ppm (equivalent to 0.9 mg/kg bw/day for males and 1.12 mg/kg bw/day for females) based on slightly increased liver and thyroid weight, and increased incidence of histopathological changes in liver (hypertrophy and foci of cellular alteration) and thyroids (thickening and hyperplasia of follicular epithelial cells; follicular cell hypertrophy).

In mice, the NOAEL was 20 ppm (males, based on increased liver weight), equal to 1.82 mg/kg bw/day.

In the PRAPeR 24 meeting of experts held in June 2007 the carcinogenicity of buprofezin was re-considered, based on the findings in the *in vivo* micronucleus test. According to the evaluation of the RMS the long-term study in rats was supplementary only for evaluation of carcinogenicity. Furthermore, the study showed a mortality of > 50 %, making its acceptability debatable. The experts

agreed that the long-term study in rats had some drawbacks that could have compromised the assessment of the incidence of tumours. It was noted that the JMPR and EPA did not consider the study invalid. Therefore the PPR Panel of EFSA was asked for an opinion also on the carcinogenic potential of buprofezin, in the context of the human risk assessment.

The PPR Panel re-evaluated the long-term toxicity/carcinogenicity studies on buprofezin. The PPR Panel concluded that the differences from the EU guidelines in the protocol for the carcinogenicity study in rats are not such as to prevent its use for the evaluation of the carcinogenic potential of the test compound. In mice and rats, neither the nature nor the incidence of tumours was affected by the administration of buprofezin. The PPR Panel concluded that buprofezin is not carcinogenic in rats or mice. The PRAPeR 39 experts'' meeting (December 2007) agreed with the conclusion.

The PPR Panel concluded that the toxicological database on the carcinogenicity and genotoxicity of buprofezin is sufficient for setting reference values.

2.6. Reproductive toxicity

The reproduction toxicity of buprofezin was investigated in one two-generation reproduction study and in two prenatal toxicity studies in rats. In the two-generation study, parental animals receiving the highest dose of buprofezin (1000 ppm) showed increased liver, kidney and adrenal weight. Increased kidney and liver weight were observed in males, and increased adrenal, pituitary and liver weight in females. Histopathological changes were not observed. Buprofezin did not show effects on reproduction or fertility. The relevant parental and offspring NOAELs were 6.46 mg/kg bw/day and 9.21 mg/kg bw/day, respectively. The reproductive NOAEL was 66 mg/kg bw/day.

As for teratogenicity studies, during the PRAPeR 24 meeting of experts in June 2007, the RMS considered the slight reduction in the degree of ossification of supra-occipital and intra-parietal bone, observed in the developmental toxicity study in rats, as usual findings in such studies and not relevant. The NOAEL for dams and development was set at 200 mg/kg bw/day. However, the JMPR considered the level as a LOAEL, setting a NOAEL at 50 mg/kg bw/day. Historical control data for incomplete ossification of the intra-parietal bone ranged between 7.1 % and 80 %. It was not clear when the studies had been performed. Therefore, they were considered insufficient. Furthermore, subcutaneous oedema was observed: at the mid and high doses the incidence of the effect was outside the range of the historical control data (0 - 17.9 %), showing incidences of 21.5 % and 45.4 %, respectively. The historical background data gave only limited information; the meeting focused therefore on the concurrent controls. The effects were considered as statistically significant, and it was agreed to take them into consideration for setting the NOAELs of the study. Overall, the NOAEL for both maternal and foetal effects would be 50 mg/kg bw/day (decreased food consumption and increased water intake, and decreased foetal weight, skeletal effects and subcutaneous oedema, respectively). It was agreed not to propose any classification.

2.7. Neurotoxicity

Buprofezin does not have structural alerts for delayed neurotoxicity, such as organophosphates. There was no evidence of neurotoxicity in the other toxicity studies that have been conducted with buprofezin. It was therefore considered that buprofezin does not have potential to induce neurotoxicity in mammals.

2.8. Further studies

During the experts'' meetings of the peer review of the initial evaluation, the raw and processed plant metabolites BF4, BF11, BF12, BF25, BF26 and aniline were considered: of these metabolites only BF12 was identified as a rat metabolite during the initial review. BF11 was assumed to be formed in rat metabolism and a precursor for BF12.
BF4 and BF26 showed a higher acute oral toxicity than the parent compound, and were therefore considered relevant (LD_{50} of 300 - 2000 mg/kg bw and 50 - 300 mg/kg bw, respectively; they both

were not mutagenic in the bacterial reverse mutation test). The experts agreed that aniline was also a relevant metabolite.
For BF11 and BF25 no studies were available during the initial review, but the DEREK analysis did not show a concern. Taking into account the very limited information, these metabolites were considered relevant as well.
The experts concluded that for all the metabolites concerned (BF4, BF11, BF12, BF25 and BF26) no reference values could be established on the basis of the available information.

In the Additional Report new data were submitted demonstrating that BF4 is a relatively significant metabolite in rats (*ca* 8 % of the administered dose being found in the liver of rats 3 hours post dose); BF9, BF11 and BF25 were found in rat metabolism at low levels, whereas BF26 and aniline were not detected. For the metabolites BF9, BF11, BF12 and BF25 a toxicity level similar/higher than buprofezin could not be excluded based on the available information.

Based on the results of the residues assessment, a data gap for further toxicological information was maintained for metabolites BF4, BF9, BF12 and BF25.

It is noted that aniline is currently classified for mammalian toxicology (19th Adaptation to Technical Progress updated in the 29th ATP) as R23/24/25 (Toxic by inhalation, in contact with skin, and if swallowed), R40 (Limited evidence of a carcinogenic effect), R41 (Risk of serious damage to eyes), R43 (May cause sensitization by skin contact), R48/23/24/25 (Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin, and if swallowed), and R68 (Possible risk of irreversible effects).

2.9. Medical data

There were no adverse health effects attributable to buprofezin in ten workers who handled the active substance from June 1986 to January 1989. This survey was considered to be rather small and short to reveal any significant effects. According to the applicant, no clinical cases or poisoning cases have been reported. In addition, no epidemiological assessment or observation on experience of the general population has been reported.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

ADI

During the PRAPeR 39 meeting of experts in December 2007, the appropriate NOAEL to derive the ADI was discussed. It was proposed to base the ADI on the relevant NOAEL of 0.9 mg/kg bw/day from the 24-month study in rats. The established ADI is 0.01 mg/kg bw/day, with a safety factor of 100.

AOEL

In the PRAPeR 39 meeting of December 2007, the experts agreed to derive the AOEL from the 90-day dog study (NOAEL 10 mg/kg bw/day, LOAEL 50 mg/kg bw/day), where the findings are in line with the long-term study.

Taking into account a safety factor of 100 and a correction for oral absorption of 40 %, the resulting AOEL is 0.04 mg/kg bw/day.

ARfD

The experts decided to set the ARfD at 0.5 mg/kg bw, based on the NOAEL from the rat developmental toxicity study and applying a safety factor of 100.

2.11. Dermal absorption

In the DAR, the RMS proposed a dermal absorption value of 1% from an *in vitro* study with a WP formulation. It was commented that dermal absorption might be underestimated in this study: the study showed several shortcomings (no individual data provided, the receptor medium used for testing the integrity of membranes was different from the one used in the main study, the amount retained in the skin was not measured). Based on molecular weight and log Pow, a 100 % dermal absorption should be used as a default. However, when looking at the oral absorption, 40 % would be an acceptable value.

The experts agreed to use 40 % as a value for dermal absorption for the concentrate and the dilution.

2.12. Exposure to operators, workers and bystanders

The representative product („Applaud 25 WP“) is formulated as a wettable powder (WP), containing 250 g/kg of buprofezin. It is intended to control whitefly in tomatoes, lettuce and citrus, and also scales in citrus. „Applaud 25 WP“ is applied using tractor-mounted boom sprayer or broadcast air-assisted sprayer for field crops, and a hydraulic hand-held knapsack sprayer for low-level application to small area field crops (outdoors) and in glasshouse. The application rate per treatment varies between 0.2 to 1.0 kg active substance per hectare. The water rate in which the product is diluted varies between 1000 L/ha to 4000 L/ha. The maximum number of applications per season is two for lettuce and three for tomatoes in glasshouse, two for tomatoes in field and one for citrus according to the GAP.

The operator exposure was estimated in different scenarios using the UK POEM or the German model. Greenhouse exposure was estimated by the modified Dutch model.

During the meeting of experts held in December 2007, the RMS was asked to amend the calculations, taking into account the correct treated areas with regard to the method of application.

The RMS submitted recalculations for operator, worker and bystander exposure in the Addendum 5 (Finland, 2008).

Operator exposure

	Application method (crop)	Treated area (ha/day)	Systemic exposure (mg/kg bw/day)	% of systemic AOEL
German model	Tractor-mounted boom sprayer (tomatoes)	20	0.188 0.0173	470 43*
German model	Tractor-mounted broadcast air-assisted sprayer (citrus)	8	0.81 0.038	2025 95°
German model	Hand-held application, high crops; field (citrus, 1 kg/ha)[a]	1	0.53 0.033	1325 82.5[$]
UK POEM	Hand-held application, low crops; field (tomatoes)	1	0.32 0.028	800 70[#]
Dutch	Hand-held sprayer: glasshouse (tomatoes, lettuce)	1	0.29 0.029	725 73^

PPE = Personal protective equipment
* = Gloves during mixing/ loading, coverall and sturdy footwear during application
° = Gloves during mixing/ loading and application, hood, visor, coverall and sturdy footwear during application

$ = Mask with a FFP2SL or P2 filter and gloves during mixing and loading; gloves, coverall and sturdy footwear during application
# = Gloves during mixing/loading and gloves and impermeable coverall during application
^ = Gloves and respiratory protector (with a protection factor of 10) during mixing/loading and application
[a] = It is noted that the calculation for this scenario was performed by the RMS considering an application rate of 0.25 kg/ha instead of 1 kg/ha: with this reduced application rate gloves during mixing/loading and application, coverall and sturdy footwear during application were necessary to reach exposure levels below the AOEL (33%); EFSA recalculated the operator exposure considering the representative application rate of 1 kg/ha: the use of RPE (mask with a FFP2SL or P2 filter) and gloves during mixing and loading, and gloves, coverall and sturdy footwear during application are necessary to reach an estimated exposure below the AOEL (82.5 %).

The operator exposure was below the AOEL for tractor-mounted spraying with personal protective equipment for tomato and citrus, calculated with the German model. For hand-held application on tomatoes outdoors, exposure was below the AOEL with PPE (UK-POEM). The exposure was below the AOEL with PPE/RPE for hand-held application for tomatoes and lettuce in glasshouse (Dutch model), and for hand-held application on citrus in field (German model).

Bystander exposure

The bystander exposure was re-calculated for potential exposure to buprofezin when spraying citrus with tractor-mounted broadcast air-assisted sprayer, and tomatoes with tractor-mounted boom sprayer. The exposure time was considered to be one hour. The selected drift values are reported to be those recommended by the Bystander Working Group (EUROPOEM 2, Bystander Working Group Report, December 2002). EFSA notes that the distance on which the drift is calculated is not reported in the DAR.

Absorption via inhalation was assumed to be 100%, 40% via dermal route and a body weight of 60 kg.

Scenario	Application rate (mg/m^2)	Concentration of active substance in spray (mg/mL)	Drift value (%)	Total exposure (mg/kg bw/day)	% of systemic AOEL
Tomatoes, tractor-mounted boom	20	0.20	0.5	0.0013	3
Citrus, tractor-mounted broadcast air-assisted	100	0.25	5	0.006	15

The bystanders showed estimated exposure levels below the AOEL (< 15%), for both field applications on tomatoes and citrus. Bystander exposure for application in greenhouses is considered unlikely.

Worker exposure

The re-entry exposure was recalculated for tomatoes (in glasshouse and outdoors), and for citrus (tractor-mounted spraying). The scenario assessed for tomatoes is also identical to the one for lettuce. The calculation was made using an algorithm recommended by the Re-entry Working Group (EUROPOEM 2, Re-entry Working Group Report, December 2002).

Dermal exposure of re-entry workers just after the spray has dried on the foliage is calculated with the following equation:

E_{total} = (DFR x TC x T x DA x AR) / Bw

where DFR = Dislodgeable foliar residue, mg/cm2
TC = Transfer coefficient, cm2/h
T = Work rate, h/day
DA = Dermal absorption, %
AR = Application rate, kg a.s./ha
Bw = Body weight, kg

A default value of 0.003 mg/cm^2 for Dislodgeable Foliar Residue (DFR) value was used (EUROPOEM 2; Re-entry Working Group Report, December 2002). A transfer coefficient value of 2500 cm^2/h for bare hands (tomatoes), and 4500 cm^2/h (citrus) were used, respectively. Work rate was assumed 6 h/day. The application rate for tomatoes and lettuce is 0.25 kg a.s./ha, and 1.0 kg a.s./ha for citrus. The worker is assumed to weigh 60 kg and the dermal absorption is 40 %. Inhalation exposure was considered only for the glasshouse application and was estimated according to EUROPOEM 2 (inhalation absorption of 100 %, body weight of 60 kg and time of exposure of 6 hours):

Worker exposure and comparison to the systemic AOEL (0.04 mg/kg/day)

Crop (application method)	PPE	Total systemic exposure (mg/kg bw/day)	% of systemic AOEL
Tomatoes/lettuce	No	0.076	190
(hand-held application, glasshouse)	Yes*	0.0083	21
Tomatoes	No	0.075	188
(tractor-mounted spraying)	Yes*	0.0075	19
Citrus	No	0.54	1350
(tractor-mounted spraying)	Yes*	0.054	135

PPE = Personal protective equipment
Yes* = Gloves

Worker exposure was estimated to be below the AOEL with gloves when handling tomatoes or lettuce in glasshouse, or tomatoes outdoors. However, exposure was over the AOEL even with gloves when handling citrus.

3. Residues

Buprofezin was discussed at the PRAPeR 25 experts‟ meeting for residues in June 2007.

For the resubmission, a new metabolism study on lemon and further information on processing was provided in the Additional Report. The GAP was changed for lettuce, the PHI being increased from 3 to 28 days.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The metabolism of buprofezin was investigated in fruits (lemon), leafy crops (lettuce) and oilseeds (cotton). These studies were conducted in accordance with the representative uses supported by the applicant. A metabolism study on tomato was also submitted but was not considered to provide any information on the metabolic pathway.

For short PHIs (up to 27 days) and for all investigated crops, the parent compound was shown to be the major constituent of the residues, accounting for 47 to 89 % of the TRR, with minor additional metabolites (BF9, BF12 and BF26), essentially identified after hydrolysis. On citrus and for longer PHIs (35 to 70 days), these metabolites were observed at significantly higher levels than the parent compound, but with two different metabolite profiles depicted by the two different metabolism

studies. Metabolite BF26 was major in the original study (Vol.3, B.7.1.2; Finland, 2005), accounting for 34 % TRR after ten weeks, whereas it was minor in the new study (Vol.3, B.7.1.1; The United Kingdom, 2009), where the residues were mainly composed of metabolites BF9 (27% TRR) and BF12 (11% TRR). These differences overall reflect the different ways the samples were processed for analysis. The lemon studies suggest that residues are mainly composed of the parent buprofezin and the sugar conjugates of metabolite BF4. Depending on the analytical procedure employed to release these conjugates, two different profiles are obtained. BF4 was degraded to BF26 in the first study, where an alkaline step was included in the experimental procedure, whereas it was converted to BF9 and BF12 in the new study where the samples were processed under acidic conditions. This assertion is supported by model hydrolysis studies performed with buprofezin and BF4, where it was shown that BF4 is relatively unstable in both acidic and alkaline conditions (half-lives 11-14 h), and significantly degraded to BF26 under alkaline conditions, and to BF9 and BF12 under acidic conditions. In conclusion, the metabolism studies suggest that residues are mainly composed of the parent buprofezin and BF4 sugar conjugates. Depending on the analytical procedures, these BF4 conjugates are identified as BF9 and BF12 under acidic conditions, or as BF26 when the analytical procedure includes a neutral or alkaline step.

Considering that buprofezin was the major part of the residues at PHIs in accordance with the representative uses, the residue definition for monitoring was limited to the parent compound only. For risk assessment, it was questioned whether additional metabolites have to be inserted in the residue definition. Metabolites BF4, BF9 and BF12 are rodent metabolites, whereas BF26 was not identified in rats. However, for most metabolites, the experts on mammalian toxicology concluded that no specific toxicological reference values can be proposed on the basis of the available information, and they have to be considered of similar/higher toxicity than buprofezin (see section 2.8). Having regard to their toxicological relevance, the residue definition for risk assessment was initially proposed as sum of buprofezin and BF4 conjugates analysed as BF9, BF12 and BF26. However, and considering that, depending on the analytical procedures, BF9+BF12 on one hand and BF26 on the other hand, are two different ways to express the residue levels of the BF4 conjugates, it is finally proposed not to include BF26 in the residue definition and to express the residue for risk assessment as:

Sum of buprofezin and BF4 conjugates analysed as BF9+BF12 under acidic hydrolysis conditions and expressed as buprofezin.

This proposal is also supported by the fact that hydrolysis studies in different substrates simulating stomach conditions (40 °C, 1N HCl), have shown buprofezin and BF4 to be mainly degraded to BF9 and/or BF12. However, some inconsistencies were highlighted in these studies and clarification is required concerning the dose rates these experiments were performed with. In addition, BF9 and BF12 are also the main metabolites observed in rotational crops (see point 3.1.2). Unfortunately, the residue trials performed on citrus and tomatoes do not allow the derivation of a conversion factor (CF) according to the residue definitions (see below). Provisionally, EFSA proposes a CF of 1.5, derived from the respective proportions of the parent compound, BF9, and BF12 observed in the new citrus metabolism study, 7 days after application (47 %, 20.3 % and 5.2 % TRR, respectively).

On citrus (mandarin and orange) and tomatoes (outdoor and indoor), a sufficient number of supervised residue trials performed in accordance with the representative uses have been provided to derive MRLs. For tomatoes, the MRL was based on indoor data, since this practice leads to clearly higher levels than in the field (STMR indoor/outdoor: 0.16/0.08 mg/kg). In addition to the parent compound, the samples were analysed also for metabolites BF9 and BF12. The metabolite levels were consistently below or at the LOQ of 0.01 mg/kg in the raw fruits. However, these results have to be considered as not relevant since no hydrolysis was performed during sample analysis, whereas the metabolism studies have shown that these metabolites are resulting from the acidic hydrolysis of the BF4 sugar conjugates. Therefore it was concluded that the studies on citrus and tomatoes are not appropriate to calculate a conversion factor for risk assessment, and a data gap is identified for a full residue data set for citrus and tomatoes, where the samples are analysed according to the residue definition for risk assessment and using an analytical method including an acidic hydrolysis step.

On lettuce, supervised residue trials were conducted under greenhouse conditions. The samples were analysed for buprofezin and metabolites BF9, BF11, BF12, BF25 and BF26, using two separate analytical procedures, including or not an acidic hydrolysis step. Both data sets gave similar results. The metabolite levels were always below the LOQ, except for one trial where BF9 and BF12 were detected at 0.01 mg/kg at PHI 0. Nevertheless, the data set was considered not appropriate to propose a MRL for lettuce, since all trials were performed with a single application instead of two, as specified in the critical GAP. A data gap is therefore identified for a new residue data set for indoor lettuce, the trials being conducted with a total of 2 treatments, as mentioned in the cGAP.

The storage stability studies demonstrate that buprofezin and metabolites BF9 and BF12 are stable under deep freeze storage conditions, in various plant matrices (among which citrus, raw and processed commodities from tomatoes, lettuce…).

Under standard hydrolysis conditions in a buffer solution simulating pasteurisation, boiling and sterilisation, buprofezin was significantly degraded, yielding substantial amounts of a phenyl thiobiuret derivative (BF25, up to 43 % TRR), aniline (up to 19 % TRR), metabolite BF12 (up to 31 % TRR), and to a lesser extent metabolite BF11 (up to 4 % TRR), this degradation being favoured by acidic condition. As mentioned previously for BF9 and BF12, the experts on mammalian toxicity were of the opinion to consider metabolites BF11 and BF25 of similar/higher toxicity than the parent (see section 2.8). However, these two metabolites were generally not detected in the processing studies performed on tomato and citrus or at levels close to the LOQ, where residues were mainly composed of the parent compound buprofezin and to a lesser extent metabolite BF12. Considering the overall results, parent buprofezin appears to be the relevant marker to monitor the residues in raw and processed commodities. No conversion factors were proposed to consider the additional metabolites transferred during processing, especially BF12. However, and as an initial approach, the conversion factor of 1.5 proposed for the raw fruits, seems appropriate to consider the possible transfer of metabolites in processed commodities, since BF12 was always detected in amounts 50 % lower than the buprofezin levels.

Additional processing studies performed on tomato and orange were submitted in the framework of the resubmission in order to assess the transfer of residues to processed commodities under industrial conditions. Each study was conducted using samples collected in plots treated with a 1N and 3N dose rate. The samples were analysed for buprofezin and metabolites BF11, BF12 and BF25. In addition, some fractions were processed under different analytical procedures, including or not an HCl acidic step. Buprofezin, present at significant amounts in the raw commodities, was transferred at significant levels in the processed fractions, and processing factors were derived for tomato (washed fruit, juice, puree, ketchup, canned tomato) and orange (juice, marmalade, pomace). The metabolite levels were usually below the LOQ (0.01 mg/kg), with some positive values close to the LOQ (0.01 - 0.03 mg/kg), except for BF12, which was systematically detected in tomato puree at levels representing about 50 % of the parent levels. In addition, 14 studies showed that residues in citrus pulp resulting from peeling are 5 times lower than in the whole fruit.

No information was provided on the possible levels of aniline in the processed fractions, whereas the standard hydrolysis study has shown this metabolite to be present up to 19 % TRR under boiling conditions. Since aniline is a potential human carcinogen (see section 2.8), and its formation as a degradation product under processing is of toxicological concern, the applicant was asked to submit studies addressing the possible transfer of aniline in processed commodities, especially those usually subject to sterilisation or pasteurisation (juice, puree…). As concluded by the PRAPeR 25 meeting of residues experts (June 2007), a sound risk assessment related to aniline needs to be considered in a much broader context than the framework of the review of buprofezin, however EFSA is of the opinion that information on the possible transfer of aniline in processed commodities is required in order to estimate the contribution of buprofezin to the overall consumer exposure to aniline, and a data gap is identified.

3.1.2. Succeeding and rotational crops

A confined study showed that the metabolic pathway in rotational crops is similar to that observed in primary crops. However the level of the identified metabolites (BF9 and BF12) is similar to that of the parent compound. The information provided indicated that residues of the active substance and its metabolites may occur sporadically in rotational crops at quantifiable levels, ranging from 0.01 to 0.05 mg/kg under practical conditions of use, for plant-back intervals up to 120 days. This may cause a concern, especially considering that rotation in glasshouse crops may occur in rather short time intervals.

Field studies were conducted in the US under field conditions, but were not considered as representative for the use of the compound according to the European representative uses.

The PRAPeR 25 experts'' meeting proposed a waiting period of 1 year between the use of buprofezin in glasshouse before sowing or planting a rotational crop other than lettuce or tomatoes, if measurable residues of buprofezin should not be present in rotational crops. If tolerance levels for residues in rotational crops are considered, field studies reflecting relevant practices in crop rotation should be conducted. In addition to the parent buprofezin, analysis of residues according to the residue definition for risk assessment should be performed, if relevant in the future.

3.2. Nature and magnitude of residues in livestock

Livestock may be exposed to buprofezin residues through consumption of citrus pomace. Considering the STMR for citrus (0.23 mg/kg), the TF in pomace (1.73) and the CF for risk assessment (1.5), the estimated intake by animals is above the trigger value for dairy and beef cattle (0.26 and 0.78 mg/kg DM, respectively).

The metabolism of buprofezin has therefore been investigated in lactating cows at a dose rate of 26.6 mg/kg DM over 7 days (*ca* 100 N and 35 N dose rate for dairy and beef cattle, respectively), and in laying hens. In both species the compound was extensively metabolised and rapidly excreted. The main metabolic pathways proceed through hydroxylation of the phenyl ring, and opening and degradation of the heterocyclic thiadiazin ring. The parent compound was found in trace amounts in poultry products, and only in milk in the lactating cow. Metabolites BF2, BF12, BF13, and BF23 were the only metabolites identified under acid hydrolysis. The nature of the identified metabolites suggests that livestock metabolism is similar to the rat metabolism. However, a large proportion of the extractable radioactivity (reaching 65 % TRR in milk) was only characterized as polar compounds, individually present as small fractions of the TRR. No characterisation or identification of the metabolite pattern was conducted in poultry and ruminant muscle and fat, due to the low level of TRR in these tissues.

Considering the TRRs observed in the different cow matrices, total residues are expected to be very low in milk, fat, and muscle (< 0.001 mg/kg), and in the range of 0.01 to 0.04 mg/kg in liver and kidneys, when expressed on a 1N dose basis. Having regard also to the extensive nature of the metabolism of buprofezin in animals, no single degradation product is expected to be present above 0.01 mg/kg in any tissue. Therefore, the experts concluded that, due to the low estimated exposure level of livestock to buprofezin and its metabolites, there is no need to propose a residue definition for animal commodities, also taking into account that the submitted studies did not show any valid indicator compound.

In the initial review, the PRAPeR 25 meeting of experts on residues were of the opinion that a new metabolism study on lactating goat should be requested, having regard to the possible genotoxicity and carcinogenicity potential of buprofezin. Since this concern was not confirmed in the opinion adopted by the PPR panel (EFSA, 2007), this request is no longer justified. However, if additional uses leading to a significant increase in the animal intake are envisaged, the metabolism in livestock of buprofezin and its main plant metabolite BF4 would have to be reconsidered.

In addition, a particular concern was raised in relation to metabolite BF23, identified as the most abundant compound in milk. This metabolite is paracetamol, used as an analgesic drug, and is known to have mutagenic properties. Nevertheless, it was verified after the experts' meeting that the adverse effects involve dose-thresholds inducing pronounced liver and bone marrow toxicity (Bergman, 1996). These thresholds are considerably higher than possible levels in milk and above medical therapeutic dosage.

A livestock feeding study on lactating cows was performed, and residues of buprofezin and its metabolites BF2, BF12, and BF23 were determined in milk and edible tissues. This study was however of limited relevance, as conjugates were not determined, and also due to the fact that residues of BF23 were found in control samples without explanation. Nevertheless, the parent compound was found in fat tissues at measurable levels, but only at the highest dose group (2 orders of magnitude above the expected critical potential ruminant exposure).

3.3. Consumer risk assessment

The dietary risk assessment performed using the EFSA PRIMo model, using the proposed MRLs for citrus and tomatoes, and the provisional conversion factor of 1.5 for fruit crops, indicates that there are no chronic and acute concerns related to dietary exposure resulting from the representative uses;

- The highest Theoretical Maximum Daily Intake (TMDI) is 83% of the ADI (0.01 mg/kg bw/day) for the DE child. Refined chronic calculation, using STMRs and the processing factor for citrus pulp, leads to a maximum intake representing 9 % of the ADI (WHO Cluster diet B).

- The acute dietary risk assessment shows that the International Estimated Short Term Intake (IESTI) is below the ARfD (0.5 mg/kg bw), with the most critical estimate being for orange fruits (40 % ARfD). Refined acute estimation using HRs and PF is only 9 % of the ARfD (for tomato).

Even if the toxicological profile of several metabolites is not fully addressed, with some of them having to be considered of at least similar or of higher toxicity than the parent compound, the refined consumer risk assessment gives sufficient margin to conclude on the absence of chronic or acute concerns for the consumer, with the refined calculated intakes being below 10 % of the toxicological reference values.

It should be noted that lettuce was not considered in this assessment, since the residue trials were not performed according to the critical GAP and are not appropriate to propose an MRL for this crop. In addition, the assessment for tomatoes and citrus has to be considered provisional, pending the submission of new residue trials on tomatoes and citrus in order to derive sound conversion factors for risk assessment.

3.4. Proposed MRLs

Based on the results of the supervised residue trials and their statistical analysis according to the current guidelines, the following MRLs are needed to accommodate the representative uses:

Commodity	MRL (mg/kg)
Citrus	1
Tomato	1
Lettuce	No MRL was proposed as the submitted residue trials were not performed according to the cGAP (a single application only instead of 2)

4. Environmental fate and behaviour

Buprofezin was discussed at the PRAPeR 22 experts' meeting for environmental fate and behaviour in May 2007. As well as the DAR, the experts considered Addendum 2 to Volume 3 dated April 2007

(Finland, 2008). Moreover, following the PRAPeR 22 meeting, some calculations were updated and subsequently provided in Addendum 4 to Volume 3 dated September 2007 (Finland, 2008).
In the Additional Report only the predicted environmental concentrations (PEC) for groundwater and sediment were updated.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

Soil experiments (5 different soils) were carried out under aerobic conditions in the laboratory (20°C 45 % maximum water holding capacity (MWHC), 25°C 60% MWHC, or 25°C 75% field capacity) in the dark. The formation of residues not extracted by methanol or acetonitrile:water or ethyl acetate were a sink for the applied phenyl ring-^{14}C-radiolabel (accounting for 23 - 33 % of the applied radiolabel (AR) after 90 - 98 days, and 14 - 19 % AR after 150 days). Mineralisation to carbon dioxide of this radiolabel accounted for 19 - 51 % AR after 90 - 98 days in experiments on 3 of these soils (in the remaining 2 soils the study design did not collect carbon dioxide). Only minor (< 5% AR) metabolites were formed.

Under anaerobic laboratory conditions buprofezin was stable. A laboratory soil photolysis study indicated that degradation by photolysis would not be expected to be a process that significantly influences the dissipation of buprofezin in the environment.

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

The rate of degradation of buprofezin was estimated from the results of the studies described in 4.1.1 above. DT_{50} values were 27 - 269 days (single first-order non-linear regression). After normalisation to FOCUS reference conditions (20°C and -10kPa soil moisture content) (FOCUS, 2000), these single first-order DT_{50} values were in the range of 32 - 322 days, with a geometric mean value of 104 days.

Soil dissipation studies (bare soil) were provided from two sites located in Germany in glasshouses, and two field sites in the USA (North Carolina and California). Using the residue levels of buprofezin, determined over the 0 - 7.6 cm soil layer (USA studies) and 0 – 20 cm (German studies), the single first-order DT_{50} values were 37.5 days (California), 38.1 days (North Carolina), 48 and 63 days (Germany) (DT_{90} 124 - 208 days). In the Addendum 2, the DT_{50} values from the USA field trial sites were normalised to a reference temperature of 20°C following the FOCUS kinetics guidance (FOCUS, 2006). The consequent DT_{50} values were 22.6 days (California) and 23.5 days (North Carolina). Normalisation of the German glasshouse dissipation trials or for soil moisture content at the USA trials was not possible due to a lack of daily soil temperature and moisture measurements during the trials.

The experts from the Member States discussed if and how it might be possible to use these dissipation studies to support the representative outdoor uses on tomatoes and citrus. The concern was that in particular for citrus, but also sometimes for field tomatoes, drip irrigation can be used, and that in these situations the soil between the rows of crops may be very dry. Dry inter-row soil strips would be exposed by pesticide applications (particularly for citrus), and therefore the potential for buprofezin to degrade may be reduced compared to the higher soil moisture contents that occurred in the German glasshouse trials, and may have occurred in the USA trials. In an attempt to address this concern, the applicant carried out a soil moisture normalisation to the DT_{50} values calculated from these field studies for the situation, where the soil between the rows might be ¼ field capacity soil moisture, and assuming that the soil moisture at the trial sites had always been at or above field capacity. Using this approach, the soil DT_{50} in dry soils at ¼ field capacity soil moisture would be in the range of 60 - 166.2 days. The experts agreed that, for the outdoor uses in southern Europe, PEC soil including accumulation should be calculated assuming a soil DT_{50} of 166 days. These calculations were carried out by the RMS and are included in Addendum 4. Some experts suggested that the soil between the rows of drip irrigated citrus might be drier than the ¼ field capacity assumed (soil could be as dry as

the wilting point pF 4.2), and therefore they could not agree that this calculation approach could be considered precautionary. Overall, the experts at the meeting considered that calculating a soil PEC including accumulation with the DT_{50} of 166 days was a reasonable approach. They would have preferred to have had field dissipation studies carried out under conditions representative of the southern European conditions for the assessment, since the calculation done introduced some additional uncertainty compared to the more usual situation, where DT_{50} values are derived from reliable field dissipation studies that represent the range of geoclimatic conditions in accordance with the representative uses.

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

The adsorption / desorption of buprofezin was investigated in 7 soils in batch adsorption experiments. It was agreed to take forward the adsorption results from 6 of these soils in the environmental exposure assessment. (The results for 1 soil were excluded from use in further assessment due to the high value for 1/n that was calculated as 1.28). The calculated adsorption K_{Foc} values varied from 2157 to 4854 mL/g (arithmetic mean 3042 mL/g, 1/n 0.75 – 1.18, mean 0.96). There was no evidence of a correlation of adsorption with pH.

The slight mobility of buprofezin and potential soil metabolites were confirmed by the results of laboratory aged column leaching experiments carried out on 2 soils.

The major surface water system metabolite BF10 (see section 4.2.1) does not have an accepted estimated adsorption value (for further discussion see section 4.2.1).

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Buprofezin was stable under sterile aqueous hydrolysis conditions at 25°C at pH 7 and 9. At 25°C at pH 5 buprofezin hydrolysed with an estimated single first-order DT_{50} of 51 days (study duration 30 days), forming the metabolites BF25 (max 19 % AR study end) and BF12 (max 9.9 % AR study end). In a satisfactory aqueous photolysis experiment (see Addendum 2) buprofezin was shown to be essentially stable to aqueous photolysis. A ready biodegradability test (OECD 301B) indicated that buprofezin is „not readily biodegradable", using the criteria defined by the test.

In water-sediment studies (2 systems studied at 20°C in the laboratory, water pH 7.0 - 7.1, a silty clay loam sediment with 5.6 % OC and a sand sediment with 0.7 % OC, and with a higher water:sediment ratio (100:1 w/w) than recommended by study guidelines) buprofezin dissipated from the water partitioning to sediment with single first-order DT_{50} of 13.5 (sandy) and 20 days (silty clay). The degradation in sediment occurred with single first-order whole system DT_{50} being calculated as 47 (sandy) and 51 days (silty clay), with the geometric mean whole system value of 49 days. The metabolite BF10 was identified and present at maxima of 12 % AR at 56 days after treatment in the sandy system (max. 5.2 % AR at 91 days (study end) silty clay) in water, but only accounted for a maximum of 0.7 % AR in sediment. Whilst it is described in the DAR that BF10 was estimated to have single first-order whole system DT_{50} of 57 - 61 days (sandy) and 139 days (silty clay), it should be noted that the value of 139 days is uncertain, as the concentrations were still increasing at the end of the study, and considering that PECsw for metabolite BF10 were calculated at steps 1 & 2, assuming a higher default[11] value of 300 days. These values for DT_{50} for metabolite BF10 were therefore not agreed as appropriate for use in the exposure assessment. The terminal metabolite, CO_2, accounted for 17-18 % of the phenyl ring-14C-radiolabel at study end (91 days). Residues not extracted from sediment by acetone represented 14-15 % AR at study end. The experts concluded that for buprofezin, water and sediment, a DT_{50} of 1000 days (default) and 49 days (geometric mean whole

[11] Default value taken from the aquatic guidance document (European Commission, 2002b).

system value at 20°C), respectively, were acceptable for use as FOCUSsw scenario calculation input at steps 3 and 4. They also confirmed that for the water metabolite BF10 a default whole system DT_{50} value of 300 days and total system formation fraction of 13 % were appropriate for use for FOCUSsw estimates at steps 1 and 2.

FOCUS surface water modelling (in accordance with FOCUS (2001) and FOCUS (2007) guidance) was evaluated up to step 4 for buprofezin (see Addenda 2 and 4), and step 2 for the metabolite BF10 (see DAR). These maximum PEC surface water and sediment values as presented in the DAR for BF10 up to step 1 for tomatoes, and step 2 for citrus, were agreed for use in the risk assessment. It should be noted that the Koc value, used to calculate PEC values for the metabolite BF10 at steps 1 and 2, of 1200 mL/g (QSAR value calculated using EPIWIN (software version used not reported)) does not seem to be a reasonable value, considering the low levels present in sediment during the water sediment study. However, the maximum step 1 PEC in water and sediment for metabolite BF10 can be used for risk assessment, as inputs are only calculated for spray drift (assumption for soil formation was 0.0001%), and this maximum water concentration is independent of the Koc assumed in the calculation, and the use of this Koc likely represents an overestimate of the potential sediment concentrations. The maximum step 2 PEC for BF10 (both water and sediment) from the citrus use (that only has a single application) would also be reliable enough.

The PRAPeR 22 meeting of experts agreed the PEC values provided in Addendum 2 for buprofezin, at step 1 and 2 for citrus, and step 1 for tomatoes. They also agreed the step 3 and step 4 (where just spray drift was mitigated, 21 m no-spray buffer zone, drift reduction *ca.* 90 %) calculations for citrus (also in Addendum 2), but identified that for tomatoes the step 2 calculations could be further refined (with a crop interception factor), and that step 3 calculations were probably triggered. Further tomato step 2 and 3 calculations were subsequently provided in Addendum 4 and were considered as the agreed values that can be used for the risk assessment, as they used standard FOCUS approaches using agreed input parameters, with the exception of the soil DT_{50}, where a longer (more conservative) value than necessary was used (arithmetic mean of 136 days compared to the agreed geometric mean value of 104 days).

Since the risk from buprofezin to sediment-dwelling organisms was calculated to be high using the previously accepted PECsed values for the R2 and R4 scenarios (FOCUS step 3) for tomatoes, in the resubmission procedure updated calculations were submitted for these two scenarios. In these simulations, compared to the original calculations included in the DAR and the addenda, three parameters were changed: the chemical application method as simulated, the soil DT_{50} value, and the application windows (dates of applications were chosen by the model within these defined time windows). These calculations were evaluated in the Additional Report and all these changes were regarded as realistic, therefore the approaches used in the updated calculations were accepted. Since the time of applications used in the original calculations (DAR and addenda) were unrealistic also for the other two pertinent FOCUS scenarios (D6 and R3), similar calculations were performed by the RMS for these scenarios, using realistic application windows (see Evaluation Table, open point 4.1; EFSA, 2010). It is noted that these calculations resulted not only in lower PECsed values, but in lower PECsw values as well, however these PECsw values were not used, since it was not necessary to update the risk assessment for organisms that live in the water phase (see section 5.2). The updated PECsed calculations are included in Appendix A of this conclusion.

4.2.2. Potential for ground water contamination of the active substance and their metabolites, degradation or reaction products

The conclusions of the initial peer review were that with the available database of studies the following input parameters at FOCUS reference conditions were appropriate to be used in FOCUS groundwater scenario modelling. For buprofezin single first-order laboratory DT_{50} of 104 days, a K_{Foc} 3042 mL/g, and 1/n = 0.96.

The representative use of December applications to citrus, and May to August applications to tomatoes outdoors were simulated following FOCUS (2000) guidance using FOCUS PELMO 3.3.2, using

parent buprofezin single first-order laboratory DT_{50} of 136 days (compared to the geometric mean value of 104 days), and adsorption values as agreed during the initial peer review[12]. Buprofezin was calculated to be present in leachate leaving the top 1m soil layer at 80th percentile annual average concentrations of < 0.001 µg/L at all 4 FOCUS groundwater scenarios parameterised for citrus, and all 5 scenarios parameterised for tomatoes (this modelling was reported in the DAR). As a slightly longer (more conservative) DT_{50} value had been used in the simulations, it was concluded that the potential for contamination of groundwater above the 0.1 µg/L parametric drinking water limit by the parent buprofezin from the representative uses (outdoor applications) is low over a broad range of vulnerable groundwater situations across Europe. The available simulations in the DAR did not cover the representative uses in glasshouses (tomatoes and lettuce) that include higher rates and numbers of applications than in the available simulations for the outdoor uses. Although the potential for groundwater exposure was considered also likely to be low from these uses, a data gap was identified in the initial peer review for these uses. To fulfil this data gap simulations were submitted for the resubmission procedure and were evaluated in the Additional Report. Standard FOCUS simulations with three FOCUS models (FOCUS MACRO v. 4.4.2, FOCUS PEARL v. 3.3.3 and FOCUS PELMO v 3.3.2) were run with the agreed input parameters (soil DT_{50} of 104 days, K_{Foc} 3042 mL/g, 1/n = 0.96). Since no lettuce is included in the FOCUS models, cabbage as surrogate crop was used. Two sequences of applications within a year were simulated for the scenarios where two crops of cabbage can be grown. Since buprofezin was calculated to be present in the leachate leaving the top 1m soil layer at 80th percentile annual average concentrations of < 0.001 µg/L at all simulated FOCUS groundwater scenarios, the results of these simulations confirmed that the potential for contamination of groundwater above the 0.1 µg/L parametric drinking water limit is low also from these representative uses (indoor applications), over a broad range of vulnerable groundwater situations across Europe.

4.3. Fate and behaviour in air

The vapour pressure of buprofezin (4.2×10^{-5} Pa at 20°C) means that buprofezin would be classified under the national scheme of The Netherlands as very slightly volatile, indicating that only limited losses due to volatilisation would be expected. Calculations using the method of Atkinson for indirect photo-oxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half-life estimated at about 2.4 hours (assuming an atmospheric hydroxyl radical concentration of 1.5×10^{6} radicals cm^{-3}), indicating that the small proportion of applied buprofezin that does volatilise would be unlikely to be subject to long-range atmospheric transport.

5. Ecotoxicology

Buprofezin was discussed at the PRAPeR 23 experts‟ meeting for ecotoxicology in May 2007.

5.1. Risk to terrestrial vertebrates

Buprofezin is an insect growth regulating insecticide, and acaricide, and the representative uses are on citrus, tomatoes and lettuce. For lettuce only glasshouse use is proposed, and for solid glasshouses no exposure of birds and mammals is expected. For tomatoes, both glasshouse and field use is proposed, with two applications proposed for the field. Only one application, at the stage of maturity, is proposed for citrus.

The available studies indicate low acute toxicity to birds and mammals. For the risk assessment, insectivorous birds and small herbivorous mammals were considered according to SANCO/ 4145/2000 (European Commission, 2002a) for the citrus use, and insectivorous birds, medium herbivorous birds, tomato fruit-eating birds, and large herbivorous mammals were considered for the use on tomatoes. The first-tier acute and short-term TER values for birds, and acute TER values for mammals all exceeded the relevant Annex VI triggers, indicating a low acute risk.

[12] Actual values used 3041mL/g and 1/n = 0.96

A 5.3% reduction in egg shell thickness was observed at 2000 ppm buprofezin (equivalent to 197.70 mg a.s./kg/bw/day) in the avian reproduction study with bobwhite quail. The effect was however not statistically significant. If this effect is taken into account, and a NOEC of 500 ppm (equivalent to 47.96 mg/kg/bw/day) is used in the risk assessment, a TER_{lt} of 1.6 is derived for insectivorous birds from the use on citrus. For the use on tomatoes, the TER_{lt} would be 8.0 for insectivorous birds, and 9.3 for medium herbivorous birds. For tomato fruit-eating birds the TER_{lt} was calculated to be 369, based on maximum mean measured concentration of buprofezin in tomatoes from field trials. The residue data are considered to be a worst case, as buprofezin was applied 3 times instead of twice at the recommended application rate. If the effect seen on egg shell thickness is disregarded, a TER_{lt} of 6.6 is obtained for insectivorous birds in citrus. Since the effect on egg shell thickness was not statistically significant, and no other treatment related signs of toxic effects were observed in the reproduction studies with birds, EFSA agrees with the RMS that the long-term risk to birds is probably low.

For the assessment of the long-term risk to small herbivorous mammals in citrus 70 % interception was taken into account. In the refined risk assessment for mammals all TER_{lt} were above the Annex VI trigger, indicating a low risk. The lowest TER of 6.5 was derived for small herbivorous mammals in citrus.

The risk to earthworm- and fish-eating birds and mammals is considered as low, since the TER values calculated according to SANCO/4145/2000 (European Commission, 2002a) exceed the Annex VI trigger. Corrected calculations, due to amendments of PEC_{soil} and $PEC_{sw,}$ were included in Addendum 2 of April 2007 (Finland, 2008). New calculations were again provided for earthworm-eating birds and mammals in Addendum 4 of September 2007 (Finland, 2008) due to revised PEC_{soil} data.

The risk for acute effects from consumption of contaminated drinking water is considered low for both birds and mammals[13] (calculated by EFSA).

5.2. Risk to aquatic organisms

Based on the available acute toxicity data, the proposed classification of buprofezin is very toxic to aquatic organisms with an EC_{50} of less than 1.0 mg/L (> 0.42 mg/L for *Daphnia magna*; limit of solubility 0.33 mg/L). The formulation „Applaud 25 WP“ was not significantly more toxic than expected based on the content of buprofezin. Since buprofezin is an insect growth regulator, a "spiked water" emergence study with *Chironomus riparius* was submitted. The NOEC from this study was 0.1 mg/L (highest concentration tested). This NOEC, expressed as the maximum measured concentration in sediment in the test (55.3 % seven days after dosing), was calculated by EFSA to be 0.17 mg/kg dry weight sediment[14]. A new study (sediment spiked test) with *C. riparius* resulted in a NOEC of 2.72 mg/kg d.w. sediment.

In the DAR the first-tier acute TER values for aquatic organisms were calculated based on FOCUS steps 1 and 2 PEC_{sw} values for tomatoes, and steps 1, 2 and 3 PEC_{sw} values for citrus. The acute TER values were below the Annex VI trigger, but since no acute toxicity was observed at the limit of solubility, the acute risk from both uses was considered to be low. The long-term TER values for all groups of aquatic organisms were above the Annex VI trigger for the use on tomatoes, using $twaPEC_{sw}$ values from $FOCUS_{sw}$ step 2. As the TER calculation should be based on initial PEC_{sw} values when the time of effect is not known, new TER calculations were provided in Addendum 4 (September 2007), based on new FOCUS calculations including FOCUS step 3. The revised long-term TER values for the use on tomatoes were above the Annex VI trigger for all groups of aquatic organisms, including sediment-dwellers, when calculated on a water and sediment basis. It should be noted that new PEC_{sw} were provided for the use on tomatoes following the resubmission (see section 4.2.1). The

[13] Input parameters for TER calculation. Bird: weight = 10 g, Daily water consumption = 2.7 ml/day, PECdrinking water = 50 mg/L (worst-case tank concentration/5), acute toxicity = 2000 mg/kg bw. Mammal: weight = 10 g, Daily water consumption = 1.6 ml/day, PECdrinking water = 50 mg/L (worst-case tank concentration/5), acute toxicity = 2000 mg/kg bw

[14] 0.553x0.0248mg buprofezin dosed/0.08007kg sediment in test system=0.17 mg/kg dw sediment. Details taken from page 19 of the original study report.

aquatic risk assessment was however not updated, as the risk was addressed at FOCUSsw step 3, based on the previous PEC_{sw} values, which were more conservative.

For the use on citrus a high long-term risk was identified for sediment-dwelling organisms, with TER values of 3.6 for the R4 stream scenario, and 2.7 for the D6 ditch scenario, based on a water concentration with FOCUSsw step 3. TER values expressed on a sediment basis were not calculated. For *Daphnids* a high risk was identified in the D6 ditch scenario, with a TER of 2.2. Risk mitigation measures will be required for the use on citrus, but initially no exposure concentrations incorporating no-spray buffer zones were calculated by the RMS. It should also be noted that 100 day PEC_{twa} values, and the NOEC for growth from an ELS study were used by the RMS in the DAR to calculate the TER_{lt} for fish. Time weight average PEC values were also used to calculate TERs for *Daphnids*. A new risk assessment for aquatic organisms and for the use on citrus was presented in Addendum 2 of April 2007, using initial PEC_{sw} from FOCUS step 4 calculations. With no-spray buffer zones of 21 m all TER values were above the Annex VI trigger, indicating a low risk. The risk assessment was accepted in the PRAPeR 23 meeting of experts.

Buprofezin partitions into sediment, and was found in amounts up to 63% of the applied test material in the sandy water/sediment study at day 3. As outlined above, a high risk for *Chironomus riparius* was identified in the FOCUS step 3 scenarios for the use on citrus. With PEC_{sw} from step 4, using buffer zones of 21 m as presented in Addendum 2, the Annex VI trigger was met when expressing the TER on both a water and sediment basis. For the use on tomatoes, using FOCUS step 3 scenarios (as presented in Addendum 4), the Annex VI trigger was met when expressing the TER on a water basis, but the TER was below the trigger in the R2 and R4 scenarios (two out of four scenarios) when expressed on a sediment basis. However, it should be noted that this NOEC for *C. riparius* is derived from a limit test based on the highest concentration tested, and no effects were observed. A further sediment-dweller study, using spiked sediment was performed. Based on the end point from this new study (NOEC of 2.72 mg/kg d.w. sediment) and new FOCUS Step3 PECsed values, the TER values exceeded the Annex VI triggers for the use on tomatoes.

One metabolite, BF10, was detected above 10 % of the applied dose in the water phase in the water/sediment study. The concentration of this metabolite increased during the study and reached 12 % on day 56. The metabolite is therefore not covered by the 28 d *Chironomus* study using buprofezin. However, as the NOEC for *Chironomus* and *Daphnia* chronic studies are in the same range for buprofezin, and considering that the metabolite is much less acutely toxic to *Daphnia* compared to the parent compound, the risk to aquatic insects is considered to have been addressed.

The bioconcentration factor for whole fish was determined to be 509. However, the clearance time is short (CT_{50} = 0.5 days) and depuration was 98 % after 7 days in clean water.

5.3. Risk to bees

The acute oral and contact toxicity of buprofezin and the representative formulation „Applaud 25 WP" to bees is low. The HQ values are < 10, which is clearly below the Annex VI trigger of 50, and the acute risk is considered to be low. Since buprofezin is an insect growth regulator, effects on honeybee brood should be tested. No malformations of young workers and no dead pupae were found, and the developmental success of the brood treated with the formulation at a dose rate of 4 kg/ha was comparable to the control. Thus, no adverse effects on bee brood would be anticipated.

5.4. Risk to other arthropod species

In accordance with the recommendations for an insect growth regulator in ESCORT II (SETAC, 2001), laboratory studies with *Typhlodromus pyri* (orchard-dwelling predatory mite) and *Chrysoperla carnea* (predacious, foliar-dwelling) were conducted with the representative formulation „Applaud 25 WP". At a dose rate of 3000 g a.s./ha, the corrected mortality was 38 % (< ESCORT II trigger of 50 %) for *T. pyri,* but with a 63 % decrease in egg production. At a dose rate of 1500 g a.s./ha fecundity was decreased to 47 %, and at 750 g a.s./ha to 34 %. Compared to the control, effects on mortality and

fecundity of *C. carnea* did not exceed 50 %. Hence, at the proposed maximum application rate of 1.0 kg a.s./ha in citrus no effects above 50 % would be expected, and the risk is considered to be low.

5.5. Risk to earthworms

The acute toxicity of buprofezin and the representative formulation „Applaud 25 WP" to earthworms is low. However, a reduction in biomass was observed at higher doses in the tests. The NOEC from a reproduction test was set to 500 mg a.s./kg dry soil (250 mg a.s./kg dry soil when corrected for a log P_{ow} > 2), based on a significant reduction in biomass and the number of juveniles produced at 1 kg a.s./kg dry soil.

The TER values were calculated with initial PEC_{soil} derived assuming no crop interception and an application rate of 1 kg a.s./ha. All values were well above the relevant Annex VI trigger, indicating a low risk.

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

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

Studies assessing the toxicity of buprofezin to non-target soil macro-organisms were not provided in the original DAR. Field / glasshouse soil DT_{90} values for buprofezin were in the range of 124 - 208 days, but the PRAPeR 22 fate meeting of experts concluded that a DT_{90} > 1 year was likely under dry soil conditions, that would occur between the rows when a crop such as citrus is drip irrigated (see section 4.1.2). Therefore, in principle, a litterbag study, performed under conditions relevant for citrus, is required. However, the meeting of experts (PRAPeR 23) recommended a reproduction test with *Collembola*, considering the particular conditions for use (e.g. very dry soil), and no risk expected for earthworms and soil micro-organisms. A 28-day *Collembola* reproductive study was submitted, from which a NOEC of 31.25 mg a.s./kg d.w. soil (62.5 mg a.s./kg d.w. soil corrected by a factor of 2) was determined. Using an initial PECsoil of 1.33 mg a.s./kg d.w. soil (based on worse-case scenario in citrus plantations), a TER value of 23.5 was calculated, indicating a low risk to *Collembola* from the use of buprofezin in citrus plantations. The risk to other non-target macro-organisms was considered low for all representative uses evaluated.

5.7. Risk to soil non-target micro-organisms

The effects on soil respiration and nitrification were tested with buprofezin technical. No deviation > 25% from the control was observed after 28 days at dose rates up to 5 kg a.s./ha. Hence, the risk to non-target soil micro-organisms is considered to be low.

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

Results from studies on effects on seedling emergence, seedling growth and seedling development, using a range of plant species (wheat, soy bean, carrots, onions, lettuce, sugar beet and oilseed rape), presented in Addendum 2 of April 2007, did not indicate any phytotoxic effects at application rates up to 10 000 g a.s./ha. Preliminary screening tests indicated the following insect species to be non-susceptible: *Panonychus citri, Tetranychus urticae, Plutella xylostella, Adoxophyes sp, Myzus persicae, Tribolium castaneum*.

5.9. Risk to biological methods of sewage treatment

Buprofezin showed no inhibition of sludge respiration rates in a study reported in Addendum 2 of April 2007. The EC_{50} derived in the study was >1000 mg/L, and therefore no negative effects are expected should the substance reach sewage treatment plants.

6. Residue definitions

6.1. Soil

Definitions for risk assessment: Buprofezin

Definitions for monitoring: Buprofezin

6.2. Water

6.2.1. Ground water

Definitions for exposure assessment: Buprofezin

Definitions for monitoring: Buprofezin

6.2.2. Surface water

Definitions for risk assessment:

water: Buprofezin and buprofezin sulfoxide

sediment: Buprofezin

Definitions for monitoring: Buprofezin

6.3. Air

Definitions for risk assessment: Buprofezin

Definitions for monitoring: Buprofezin

6.4. Food of plant origin

Definitions for risk assessment: Buprofezin + BF4 conjugates analysed as BF9 + BF12 under acidic hydrolysis and expressed as buprofezin

Definitions for monitoring: Buprofezin

6.5. Food of animal origin

Definitions for risk assessment: not necessary

Definitions for monitoring: not necessary

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

7.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Buprofezin	Medium to high persistence Single first-order DT_{50} 32-322 days (20°C, pF2 soil moisture)	Low risk to non-target arthropods, earthworms, and other non-target soil macro-organisms. Low risk to soil non-target micro-organisms, STP, and non-target plants.

7.2. 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 relevance
Buprofezin	Slight mobility K_{Foc} 2157-4854 mL/g	No	Yes	Yes	Yes

7.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Buprofezin	Very toxic to aquatic organisms, the risk assessment indicated a low risk to aquatic organisms for the use on tomatoes. Risk mitigation is required for the use on citrus. The risk for bioaccumulation is considered to be low.
Buprofezin sulfoxide	Low toxicity to fish, daphnids and algae.

7.4. Air

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

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

- A new sprayability study where wettability and suspensibility are addressed (relevant for all uses evaluated, data gap identified by the PRAPeR meeting of experts in May 2007, no submission date proposed by the applicant; refer to chapter 1)

- Further data characterising the toxicological properties of the raw and processed plant metabolites BF4, BF9, BF12 and BF25 are necessary (relevant for all representative uses, data gap identified by the PRAPeR meeting of experts in December 2007 and during the resubmission procedure, no submission date proposed by the applicant; refer to chapter 2.8 and 3.1.1)

- Clarification concerning the dose rates in the model hydrolysis study of buprofezin and its metabolite BF4 (Additional Report, section B.7.8.1) is required (relevant for all uses evaluated, data gap identified during the resubmission procedure, no submission date proposed by the applicant; refer to Evaluation Table open point 3.6 and chapter 3.1.1)

- A complete residue data set for tomatoes and citrus where samples are analysed according to the residue definition for risk assessment, and using an analytical method including an acidic hydrolysis step and validated for parent and BF4 (analysed as BF9 and BF12) (relevant for the representative uses on tomatoes and citrus, data gap identified during the resubmission procedure, no submission date proposed by the applicant; refer to chapter 3.1.1)

- A complete residue database for indoor lettuce where trials are conducted according to the cGAP with a total of 2 applications, and where samples are analysed according to the residue definition for risk assessment, using an analytical method including an acidic hydrolysis step and validated for parent and BF4 (analysed as BF9 and BF12) (relevant for the representative use on lettuce, data gap identified during the resubmission procedure, no submission date proposed by the applicant; refer to chapter 3.1.1)

- New processing studies on tomatoes and citrus taking into account the possible transfer of the metabolite aniline in the processed fractions (relevant for the representative uses on tomatoes and citrus, data gap identified during the resubmission procedure, no submission date proposed by the applicant; refer to chapter 3.1.1)

- Field rotational crop studies relevant to current practices with quantification of residues according to the residue definition for risk assessment (relevant for the representative uses on tomatoes and lettuce if tolerance levels for residues in rotational crops are considered; data gap identified by the PRAPeR meeting of experts in June 2007; no submission date proposed by the applicant; refer to point 3.1.2).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide and acaricide on tomatoes, lettuce and citrus. Full details of the GAP can be found in the list of end points in Appendix A.

The representative formulated product for the evaluation was „Applaud 25 WP", a wettable powder formulation (WP).

Adequate methods are available to monitor buprofezin residues in all matrices.

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

However, the suspensibility and wettability results were poor and a sprayability study is identified as a data gap.

In mammals, the acute oral, dermal or inhalation toxicity of buprofezin is low. Buprofezin is not a skin or eye irritant, nor a skin sensitiser. The relevant short-term NOAEL in rats is 13 mg/kg bw/day, while in dogs the relevant NOAEL is 10 mg/kg bw/day. The relevant long-term toxicity NOAEL in rats is 0.9 mg/kg bw/day, while in mice it is 1.82 mg/kg bw/day. Buprofezin is neither genotoxic nor carcinogenic. Buprofezin did not show any reproductive toxicity potential: the relevant parental and offspring NOAELs are 6.46 mg/kg bw/day and 9.21 mg/kg bw/day, respectively. The reproductive NOAEL is 66 mg/kg bw/day. As for teratogenicity studies, overall, the NOAEL for both maternal and foetal effects is 50 mg/kg bw/day (based on decreased food consumption and increased water intake, and decreased foetal weight, skeletal effects and subcutaneous oedema, respectively). It was agreed not to propose any classification.

Buprofezin does not have potential to induce neurotoxicity in mammals.

The Acceptable Daily Intake is 0.01 mg/kg bw/day, the Acceptable Operator Exposure Level is 0.04 mg/kg bw/day, and the Acute Reference Dose is 0.5 mg/kg bw. The operator exposure was below the AOEL for tractor-mounted spraying with PPE for tomatoes and citrus. For hand-held application, the exposure was below the AOEL with PPE for tomatoes outdoors. The exposure was below the AOEL with PPE/RPE for hand-held applications: for tomatoes and lettuce in glasshouse, and for citrus in field. For bystanders the estimated exposure levels were below the AOEL for both tomatoes and citrus field applications; bystander exposure for application in greenhouses is unlikely. The worker exposure was estimated to be below the AOEL with the use of PPE when handling tomatoes or lettuce in glasshouse, or tomatoes outdoors. The exposure was above the AOEL even with PPE when handling citrus.

The metabolism of buprofezin in plants has been elucidated in three plant groups (fruit crops, leafy crops and oilseed/pulse crops). The parent compound is the major constituent of the final residue, accounting for 47 - 89% of the TRR for PHIs < 27 days. The residues in plants are mainly composed of the parent compound and the sugar conjugates of metabolite BF4, which are identified as BF9 and BF12 under acidic analysis conditions, or as BF26 when the analytical procedures include neutral or alkaline steps. Therefore, the residues were defined as „buprofezin" only for monitoring, and as „sum of buprofezin and BF4 conjugates, analysed as BF9 and BF12 under acidic hydrolysis and expressed as buprofezin" for risk assessment. MRLs are proposed for tomatoes and citrus, however a complete residue data set is requested for all representative uses in order to derive appropriate conversion factors (CF) for risk assessment, and to propose an MRL for indoor lettuce. Provisionally, and based on the metabolism studies, a CF of 1.5 is proposed for fruit crops.

Based on new processing studies, processing factors are proposed for citrus and tomato. However, a data gap is identified concerning the possible transfer of the metabolite aniline, especially in processed fractions subject to pasteurisation or sterilisation.

A potential transfer of residues to rotational crops has been noted. Based on the representative uses, no residues are expected in animal commodities, and no residue definitions and MRL are proposed for products of animal origin.

Even if the toxicological profile of some metabolites is not fully addressed, with some of them considered to be of similar or of higher toxicity than the parent compound, the consumer risk assessment gives sufficient margin to conclude on the absence of chronic or acute concerns for the consumer, with the refined calculated intakes being below 10 % of the toxicological reference values. It should be noted that lettuce was not considered in this assessment, since the residue trials were not performed according to the critical GAP and are not appropriate to propose an MRL for this crop. In addition, the assessment for tomatoes and citrus has to be considered provisional, pending the submission of new residue trials on tomatoes and citrus in order to derive sound conversion factors for risk assessment.

The information available on the fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment at EU level. For the representative uses, the potential for groundwater exposure by buprofezin above the parametric drinking water limit of 0.1 µg/L is low.

The acute and long-term risks to birds and mammals from the representative use of buprofezin were assessed as low. The assessment of risk to small herbivorous mammals in citrus plantations assumed an interception rate of 70 %, resulting in a TER that exceeded the Annex VI trigger value. A low risk was also identified for birds and mammals exposed via the ingestion of contaminated earthworms or fish, or via contaminated drinking water.

Buprofezin is very toxic to aquatic organisms. Low risk was identified from the use of buprofezin on tomatoes. However, application in citrus plantations requires a no-spray buffer zone of 21 metres when applied adjacent to edge-of-field water courses. The risk to sediment-dwelling organisms was assessed as low from the representative field uses of buprofezin. Buprofezin is not considered to bioaccumulate in fish.

Low risk was identified for all other non-target organisms.

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

- Use of PPE/RPE is necessary to reduce exposure levels to below the AOEL for operators. PPE is also necessary to reduce worker exposure to below the AOEL.
- Since residues of the parent compound and metabolites BF9 and BF12 cannot be excluded in rotational crops, a waiting period of 1 year is proposed in glasshouse, between the use of buprofezin and sowing/planting a rotational crop other than lettuce or tomatoes.
- Based on the reviewed aquatic data risk mitigation such as a no-spray buffer zone of 21 m is required to demonstrate TER values above the Annex VI trigger in all FOCUS scenarios for the use on citrus.

ISSUES THAT COULD NOT BE FINALISED

- The consumer risk assessment could not be finalised for lettuce since no MRL has been proposed for this crop, because the residue trials were not performed according to the critical GAP. In addition, the assessment for tomatoes and citrus has to be considered provisional, pending the submission of new residue trials on tomatoes and citrus in order to derive sound conversion factors for risk assessment.

CRITICAL AREAS OF CONCERN

None.

REFERENCES

ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).

Bergman K., Müller L., Weberg Teigen S. (1996). The genotoxicity and carcinogenicity of paracetamol: a regulatory (re)view, Mutation Research, 349, 263-288.

EFSA (European Food Safety Authority), 2007. Opinion on Genotoxic and Carcinogenic Potential of Buprofezin in the Context of the Human Risk Assessment - Scientific Opinion of the Panel on Plant Protection Products and their Residues (PPR). The EFSA Journal (2007), 620, 1-28. http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178680773087.htm.

EFSA (European Food Safety Authority), 2008. Conclusion regarding the peer review of the pesticide risk assessment of the active substance buprofezin. EFSA Scientific Report (2008) 128.

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 buprofezin.

European Commission, 2002a. Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC. SANCO/4145/2000.

European Commission, 2002b. Guidance Document on Aquatic Ecotoxicology Under Council Directive 91/414/EEC. SANCO/3268/2001 rev 4 (final), 17 October 2002.

European Commission, 2008. Review Report for the active substance buprofezin finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 20 May 2008 in support of a decision concerning the non-inclusion of buprofezin in Annex I of Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing this active substance. SANCO/110/08-rev. final, 2 October 2008.

Finland, 2005. Draft Assessment Report (DAR) on the active substance buprofezin prepared by the rapporteur Member State Finland in the framework of Directive 91/414/EEC, May 2005.

Finland, 2008. Final Addendum to Draft Assessment Report on buprofezin, compiled by EFSA, February 2008.

FOCUS (2000). "FOCUS Groundwater Scenarios in the EU review of active substances". Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference SANCO/321/2000-rev.2. 202 pp, as updated by the Generic Guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

FOCUS (2001). "FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC". Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.2. 245 pp.

FOCUS (2006). "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration" Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0, 434 pp.

FOCUS (2007). "Landscape And Mitigation Factors In Aquatic Risk Assessment. Volume 1. Extended Summary and Recommendations". Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment, EC Document Reference SANCO/10422/2005 v2.0. 169 pp.

SETAC (Society of Environmental Toxicology and Chemistry), 2001. Guidance Document on Regulatory Testing and Risk Assessment procedures for Plant Protection Products with Non-Target Arthropods. ESCORT 2.

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

The United Kingdom, 2010. Final Addendum to the Additional Report on buprofezin, compiled by EFSA, February 2010.

APPENDICES

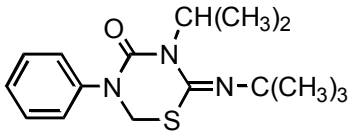
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Active substance (ISO Common Name) ‡	Buprofezin
Function (*e.g.* fungicide)	Insecticide and acaricide

Rapporteur Member State	United Kingdom
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(*Z*)-2-*tert*-butylimino-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one
Chemical name (CA) ‡	2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4-*H*-1,3,5-thiadiazin-4-one
CIPAC No ‡	681
CAS No ‡	69327-76-0
EC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification (including year of publication) ‡	None
Minimum purity of the active substance as manufactured ‡	985 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	$C_{16}H_{23}N_3OS$
Molecular mass ‡	305.44 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	104.6 - 105.6 °C (99.0 %)
Boiling point (state purity) ‡	252 °C (99.6 %)
Temperature of decomposition (state purity)	Not relevant
Appearance (state purity) ‡	White powder (99.0 %)
Vapour pressure (state temperature, state purity) ‡	$4.2 \cdot 10^{-5}$ Pa at 20 °C (99.0 %)
Henry"s law constant ‡	$2.80 \cdot 10^{-2}$ Pa · m^3 · $mole^{-1}$ at 20-25 °C
Solubility in water (state temperature, state purity and pH) ‡	1.75 mg/l at 25 °C, pH 5 (99.7 %) 0.46 mg/l at 25 °C, pH 7 (99.7 %) 0.46 mg/l at 25 °C, pH 9 (99.7 %)
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20-22 °C in g/l (99.0 %) Acetone: 253 Dichloromethane: 587 Ethyl acetate: 241 n-Heptane: 18 Methanol: 87 n-Octanol: 25 Toluene: 336
Surface tension ‡ (state concentration and temperature, state purity)	70.4 mN/m at 20 °C (90 % saturated solution) (99.6 %)
Partition co-efficient ‡ (state temperature, pH and purity)	log P_{ow} = 3.52 pH 4 log P_{ow} = 4.93 pH 7 log P_{ow} = 5.05 pH 9 (Shake flask method) (99.6 %)
Dissociation constant (state purity) ‡	It was not possible to determine a dissociation constant in accordance with OECD 112.
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Neutral λ_{max} = 245 nm, ε= 11515 1 · mol^{-1} · cm^{-1} Acidic λ_{max} = 229 nm, ε= 16463 1 · mol^{-1} · cm^{-1} Basic λ_{max} = 245 nm, ε= 11650 1 · mol^{-1} · cm^{-1} λ_{max} = 220 nm, ε= 9240 1 · mol^{-1} · cm^{-1} (99.6 %)
Flammability ‡ (state purity)	Not flammable (99.6 %)
Explosive properties ‡ (state purity)	Not explosive. (statement)
Oxidising properties ‡ (state purity)	Not oxidising. (statement)

Summary of representative uses evaluated (Buprofezin)

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min–max (l)	Water L/ha min–max	g as/ha min–max (l)		
Tomato	N-EU/ S-EU	Applaud 25 WP	F	Whitefly	WP	250 g/kg	High volume spraying	BBCH 89	2	3 day	20	1000	200	7	[2]
Tomato	N-EU/ S-EU	Applaud 25 WP	G	Whitefly	WP	250 g/kg	High volume spraying	BBCH 87	3	7 day	25	1000	250	3	[2]
Lettuce	N-EU/ S-EU	Applaud 25 WP	G	Whitefly	WP	250 g/kg	High volume spraying	BBCH 49	2	7 day	25	1000	250	28	[1]
Citrus	S-EU	Applaud 25 WP	F	Scales, Whitefly	WP	250 g/kg	High volume spraying	BBCH 89	1		25	4000	1000	7	[2]

[1]: The consumer risk assessment could not be finalised for lettuce, since no MRL could be proposed according to the critical GAP.
[2]: The consumer risk assessment is considered provisional, pending the submission of new residue trials on tomatoes and citrus in order to derive sound conversion factors for risk assessment

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

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)	HPLC-UV
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Buprofezin
Food of animal origin		none
Soil		Buprofezin
Water	surface	Buprofezin
	drinking/ground	Buprofezin
Air		Buprofezin

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	GC-NPD, 0.01 mg/kg buprofezin (cucumber/high water content, lemon/high acid content) LC-MS/MS, 0.01 mg/kg buprofezin (lettuce, tomato, processed tomato products, citrus and processed citrus products)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not relevant
Soil (analytical technique and LOQ)	GC-NPD, 0.01 mg/kg buprofezin
Water (analytical technique and LOQ)	HPLC/UV, 0.1 µg/L buprofezin (surface water)
Air (analytical technique and LOQ)	GC-MSD, 0.27 µg/m^3 buprofezin (36 ^{o}C, 85 % humidity)
Body fluids and tissues (analytical technique and LOQ)	Not relevant, buprofezin is not toxic or very toxic.

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

	RMS/peer review proposal
Active substance	None

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	40% based on urinary excretion within 24 h (2.6% in females and 5.4% in males), and biliary excretion within 24 h (38% in females and 30% in males).
Distribution ‡	Highest levels in urinary bladder, liver and adipose tissues.
Potential for accumulation ‡	No evidence for accumulation;
Rate and extent of excretion ‡	About 90% of total dose eliminated within 48 h. 13-25% of total dose excreted in urine and 60-76% of total dose excreted/eliminated in faeces.
Metabolism in animals ‡	Extensively metabolised, phenyl ring hydroxylation, oxidation of the t-butyl groups and thiadiazin ring opening; conjugation.
Toxicologically relevant compounds ‡ (animals and plants)	Buprofezin and metabolites
Toxicologically relevant compounds ‡ (environment)	Buprofezin

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 2000 mg/kg bw	-
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	-
Rat LC_{50} inhalation ‡	> 4.57 mg/L air /4h (whole body)	-
Skin irritation ‡	Non-irritant	-
Eye irritation ‡	Non-irritant	-
Skin sensitisation ‡	Non-sensitizer (LLNA)	-

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver (hepatotoxicity), thyroid	
Relevant oral NOAEL ‡	90-day, dog: 10 mg/kg bw/day 2-yr dog: 2 mg/kg bw/day 90-day rat: 13 mg/kg bw/day	-
Relevant dermal NOAEL ‡	24-day, rat: 1000 mg/kg bw/day	-
Relevant inhalation NOAEL ‡	No data - not required	-

Genotoxicity ‡ (Annex IIA, point 5.4)

Overall no genotoxic potential	

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

Target/critical effect ‡	Liver (hepatotoxicity), thyroid	
Relevant NOAEL ‡	2-yr rat: 1 mg/kg bw/day (0.9 mg/kg bw/day for males; 1.12 mg/kg bw/day for females) Mouse: 1.82 mg/kg bw/day;	
Carcinogenicity ‡	No carcinogenic potential	-

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No reproduction target found. Decreased body weight gain of pups (up to 12%) at doses where increased organ weights were observed in parents.	-
Relevant parental NOAEL ‡	6.46 mg/kg bw/day	-
Relevant reproductive NOAEL ‡	66 mg/kg bw/day	-
Relevant offspring NOAEL ‡	9.21 mg/kg bw/day	-

Developmental toxicity

Developmental target / critical effect ‡	Maternal: decreased food consumption and increased water intake Foetal: decreased foetal weight, skeletal effects and subcutaneous oedema at maternally toxic dose.	-
Relevant maternal NOAEL ‡	Rat: 50 mg/kg bw/day Rabbit: 50 mg/kg bw/day	-
Relevant developmental NOAEL ‡	Rat: 50 mg/kg bw/day Rabbit: 250 mg/kg bw/day	-

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data-not required	-
Repeated neurotoxicity ‡	No data-not required	-
Delayed neurotoxicity ‡	No data-not required	-

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Lower potency for thyroid inhibition than PTU, likely a different mechanism. Rat was the most sensitive species of those studied (mouse, hamster, guinea pig, rabbit). The NOAEL in rats was 100 mg/kg bw/day for altered serum T3, T4 and protein-binding iodine (PBI) concentration.
Studies performed on metabolites or impurities ‡	Plant metabolite BF4, oral LD_{50}: 300-2000 mg/kg bw Plant metabolite BF26, oral LD_{50}: 50-300 mg/kg bw BF9, oral LD_{50}: 300-2000 mg/kg bw BF11, oral LD_{50}>2000 mg/kg bw BF12, oral LD_{50}: 300-2000 mg/kg bw BF25, oral LD_{50}: 300-2000 mg/kg bw BF4, 28 day gavage dose study: NOAEL 20 mg/kg bw/day BF25, 28 day gavage dose study: NOAEL 2 mg/kg bw/day BF26, 28 day gavage dose study: NOAEL 15 mg/kg bw/day BF9, bacterial reverse mutation assay: negative with and without metabolic activation BF11, bacterial reverse mutation assay: negative with and without metabolic activation BF12, bacterial reverse mutation assay: negative with and without metabolic activation BF25, bacterial reverse mutation assay: negative with and without metabolic activation BF4 and BF26 were not mutagenic in reverse gene mutation tests. Metabolites found in the hydrolysis study, BF11 and BF25 were not structurally alerting using DEREK. The main impurities were not mutagenic in reverse gene mutation tests.

Medical data ‡ (Annex IIA, point 5.9)

No detrimental effects on health in manufacturing personnel

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/d	2-yr rat	100
AOEL ‡	0.04 mg/kg bw/d	90 d dog	100, 40% oral absorption

ARfD ‡	0.5 mg/kg bw	Rat developmental study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation Applaud 25 WP	Concentrate: 40 % (default 100% corrected for limited oral absorption) Spray dilutions: 40 % (default 100% corrected for limited oral absorption)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	German model Tractor-mounted boom sprayer (tomatoes) % AOEL 470 (no PPE) % AOEL 43 Gloves during mixing/ loading, coverall and sturdy footwear during application German model Tractor-mounted broadcast air-assisted sprayer (citrus) % AOEL 2025 (no PPE) % AOEL 95 gloves during mixing/ loading and application, hood, visor, coverall and sturdy footwear during application German model Hand-held application, high crops; field (citrus, 1 kg/ha)[a] % AOEL 1325 (no PPE) % AOEL 82.5 Mask with FFP2SL or P2 filter and gloves during mixing and loading, and gloves, coverall, and sturdy footwear during application UK POEM Hand-held application, low crops; field (tomatoes) % AOEL 800 (no PPE) % AOEL 70 Gloves during mixing/loading and gloves and impermeable coverall during application Dutch, Hand-held sprayer: glasshouse (tomatoes, lettuce) % AOEL 725 (no PPE) % AOEL 73 Gloves and respiratory protector (with a protection factor of 10) during mixing/loading and application
Workers	Worker exposure was estimated to be below the AOEL with gloves when handling tomatoes or lettuce in glasshouse, or tomatoes outdoors (21% and 19 % of the AOEL, respectively). Exposure was above the AOEL even with gloves when handling citrus (135% of the AOEL).

Bystanders	The bystanders showed estimated exposure levels below the AOEL (< 15%) for both field applications on tomatoes and citrus. Bystander exposure after application in greenhouses was considered unlikely.

[a]*It is noted that the calculation for this scenario was performed by the RMS considering an application rate of 0.25 kg/ha instead of 1 kg/ha: with this reduced application rate gloves during mixing/loading and application, coverall and sturdy footwear during application were necessary to reach exposure levels below the AOEL (33%); EFSA recalculated the operator exposure considering the representative application rate of 1 kg/ha: the use of RPE (mask with a FFP2SL or P2 filter) and gloves during mixing and loading, and gloves, coverall and sturdy footwear during application are necessary to reach an estimated exposure below the AOEL (82.5 %).*

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

	RMS/peer review proposal
Substance classified (name)	No classification

Residues

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

Plant groups covered	Fruit crops (Lemon) Leafy crop (Lettuce) Oilseed/Pulses (Cotton) (tomato study informative only)
Rotational crops	Radish (R), lettuce (L) and wheat (C)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes: buprofezin, BF9 and BF12 identified in rotational crops in similar amounts.
Processed commodities	Standard hydrolysis study shows buprofezin to be degraded to BF12, BF25, aniline and at a lower extent to BF11
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No. Hydrolysis study revealed potentially harmful products (aniline), which are not present or at very low amounts in raw commodities (BF11 and BF25 less than 0.3% TRR in citrus).
Plant residue definition for monitoring	Buprofezin
Plant residue definition for risk assessment	Sum buprofezin and BF4 conjugates analysed as BF9 + BF12 under acidic conditions and expressed as buprofezin
Conversion factor (monitoring to risk assessment)	1.5 [Provisional, derived from proportions of parent (47 %), BF9 (20.3 %) and BF12 (5.2 %) observed in the citrus metabolism study at PHI 7 days]

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

Animals covered	Lactating cow and laying hen
Time needed to reach a plateau concentration in milk and eggs	Milk 6 days Eggs 14 days
Animal residue definition for monitoring	Not proposed, since not considered necessary for the representative uses.
Animal residue definition for risk assessment	Not relevant
Conversion factor (monitoring to risk assessment)	Not relevant
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Buprofezin log P_{ow} = 4.80 is fat soluble. Feeding studies reveal that residues are not fat-seeking.

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

A waiting period of 1 year is needed in glasshouse before sowing or planting of a rotational crop other than lettuce or tomatoes.

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

Buprofezin, BF9 and BF12 are stable for at least: - 30 months in lettuce, tomato - 6 months in tomato processed fractions (pomace, juice..) In addition, **buprofezin** is stable at least: - 1 year in citrus, apple, courgette, kiwi and peach Studies on **BF11, BF25 and BF26** stability ongoing. - BF11 and BF26 at least stable for 1-6 months in tomato/tomato processed fractions and lettuce - but BF25 seems not stable more than 1 month in tomato processed fractions and lettuce.

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,** 0.26/0.78 mg/kg DM (dairy/beef cattle)	**No**	**No**
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	No
	Feeding studies (Dairy cows, *ca* 5 mg/kg DM, 20N/6N) Residue levels (buprofezin) in matrices : Max (mg/kg)		
Muscle	<0.05	Not relevant	Not relevant
Liver	<0.05	Not relevant	Not relevant
Kidney	<0.05	Not relevant	Not relevant
Fat	<0.05	Not relevant	Not relevant
Milk	<0.01		
Eggs		Not relevant	

Note: No residue definition and no MRLs were proposed for products of animal origin, based on the cow metabolism study, where it was shown that low TRR are expected in all animal matrices when residues are calculated on a 1N dose rate basis.

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)

Crop	Northern/ Southern field or Indoor,	Trials results relevant to the representative uses (buprofezin residue levels, mg/kg) (a)	Recommendation/ comments	MRL mg/kg	STMR mg/kg (b)	HR mg/kg (c)
Tomato	N+S indoor	0.05, 0.12, 2x 0.13, 0.14, 0.16, 0.24, 0.30, 0.32, 2x 0.52	MRL derived from indoor trial R_{max}: 0.69 R_{ber}: 0.64	1	0.16	0.52
	South, Field	2x 0.01, 0.03, 0.05, 0.06, 2x 0.08, 4x 0.09		-	0.08	0.09
Citrus	South field	**Mandarin:** Whole fruit: 0.11, 0.22, 3x 0.23, 0.41, 0.45, 0.46 Pulp: <0.01, 0.03, 2x 0.04, 0.05, 3x 0.06 **Orange:** Whole fruit: 0.15, 0.17, 0.21, 2x 0.23, 0.25, 0.31, 0.37 Pulp: 0.03, 4x 0.04, 2x 0.05, 0.10	MRL, STMR and HR derived from the merged mandarin and orange data sets R_{max}: 0.53 R_{ber}: 0.71	1	Whole fruit 0.23 Pulp 0.04	Whole fruit 0.46 Pulp 0.10
Lettuce		No MRL proposed, since trials not performed according to the cGAP (all trials conducted with a single application instead of 2 as stated in the cGAP).				

Remark: The supervised residue trials conducted on tomato and citrus are not suitable to calculate the total residue levels (as sum buprofezin+BF9+BF12), since no acidic hydrolysis step was included in the analytical method.

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

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

ADI	0.01 mg/kg bw/d
TMDI (% ADI) according to EFSA PRIMo rev2 model	Maximum TMDI : 83% ADI (DE Child)
TMDI (% ADI) according to national (to be specified) diets	Not calculated
IEDI (% ADI) according to EFSA PRIMo rev2 model)	Maximum IEDI: 9% ADI (WHO Cluster diet B)
NEDI (specify diet) (% ADI)	Not calculated
Factors included in IEDI	STMR, PF whole fruit/pulp for citrus and CF for risk assessment of 1.5
ARfD	0.5 mg/kg bw
IESTI (% ARfD) according to EFSA PRIMo rev2 model	Maximum IESTI (using MRLs values and CF) Orange: 40 % ARfD Grapefruit: 27 % ARfD Tomato: 17 % ARfD
IESTI (% ARfD) according to EFSA PRIMo rev2 model	Maximum refined IESTI (using HR, PF and CF), Tomato: 9 % ARfD Orange: 3 % ARfD
Factors included in IESTI	HR, PF whole fruit/pulp for citrus and CF for risk assessment of 1.5

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

Crop/processed product (**only buprofezin residue levels are taken into account in raw and processed fraction**)	Number of studies	Processing factors		Amount transferred (Optional)
		Transfer factor	Yield factor	
Tomato / Washed tomato	2	1.01	Not calculated	Not calculated
Tomato / Tomato juice after pasteurisation	4	0.34*	Not calculated	Not calculated
Tomato / Puree (concentrate) after sterilisation	4	0.84*	Not calculated	Not calculated
Tomato / Ketchup after sterilisation	4	0.70*	Not calculated	Not calculated
Tomato / Canned tomato after sterilisation	4	0.16*	Not calculated	Not calculated
Orange / Peel	14	3.15	Not calculated	Not calculated
Orange / Pulp	14	0.18	Not calculated	Not calculated
Orange / Orange juice after pasteurisation	4	0.57*	Not calculated	Not calculated
Orange / Marmalade after sterilisation	4	1.28*	Not calculated	Not calculated
Orange / Wet pomace	4	1.73*	Not calculated	Not calculated
Orange / Dry pomace	2	5.26	Not calculated	Not calculated

*: Mean of 8 values (4 studies, each conducted with 2 different RAC collected in a 1N and 3N treated plots)

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

Citrus fruit	1 mg/kg
Tomatoes	1 mg/kg
Lettuce	No MRL proposed (trials not performed according to cGAP)

When the MRL is proposed at the LOQ, this should be annotated by an asterisk (*) after the figure.

Environmental fate and behaviour

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

Mineralization after 100 days ‡	19, 25.4, 50.9 % after 90, 98, 91 d, [^{14}C-phenyl]-label (n=3) Sterile conditions: not studied
Non-extractable residues after 100 days ‡	22.8, 30.6, 33.0 % after 98, 90, 91 d, [^{14}C-phenyl]-label (n=3) Sterile conditions: not studied
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	No metabolites present at > 10% of applied dose, nor > 5% at 2 consecutive time points

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

Anaerobic degradation ‡

Mineralization after 100 days	1.1 % after 364 d, [^{14}C- phenyl]-label (n= 1) Sterile conditions: not studied
Non-extractable residues after 100 days	8 % after 364 d, [^{14}C- phenyl]-label (n=1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No metabolites present at > 10% of applied dose

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No photolysis of buprofezin

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

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	X[1]	pH (KCl)	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50}/DT_{90} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.2	25 °C /75 % of FC	27 / 90	32.3 / 107.1	0.992	SFO
Silty clay loam		6.6	25 °C / 75 % of FC	75 / 209	89.7 / 297.8	0.986	SFO
Sandy loam		6.3	25 °C / 60 %	93 / 308	134 / 447.1	0.986	SFO
Silty clay loam		5.0	25 °C / 60 %	269 / 894	322 /1071	0.990	SFO
Sandy loam soil		6.4	20 °C/ 45 %	99 / 345 99 / 329	99 / 345 99 / 329	0.951	TPEM [1] SFO[2]

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Sandy loam soil		6.4	10 °C/ 45 %	170 / 678			TPEM [1]
Arithmetic mean					135.4		
Geometric mean					104.4		

[1] two phase exponential model
[2] calculated by EFSA according to single first-order kinetics using non-linear regression and the results from Table B.8.1.2.1-6 of the DAR

Field studies ‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Silty sand	Germany (Lu.) [1]		7.1	20	48	160	0.976		SFO [2]
Silty sand	Germany (Ham)[1]		6.7	20	63	208	0.918		SFO [2]
Loamy sand	North Carolina		5.7	90	38.1	128	0.852	23.5 [3]	SFO
Sandy loam	California		7.3	90	37.5	124	0.929	22.6 [3]	SFO
Geometric mean					45.6				

[1]Under glasshouse conditions; temperature still varying according to normal temperature
[2]Timme and Frehse model
[3] Normalised based on soil temperature to a reference temperature of 20°C.

Field studies ‡

Parent	Aerobic conditions (DT_{50} in 1/3 and 1/4 field capacity		
Soil moisture assumption	Studied Site	Field DT_{50}	Field DT_{90}
1/3 of field capacity	Germany (Lustadt)	103.6	344.0
	Germany (Hamburg)	135.9	451.6
	North Carolina	59.8	198.5
	California	48.8	162.0
	Geometric mean	80.0	265.9
1/4 of field capacity	Germany (Lustadt)	126.7	420.8
	Germany (Hamburg)	166.2*	552.3
	North Carolina	73.1	242.8
	California	59.6	198.1
	Geometric mean	97.9	325.2

* This value was chosen for PECsoil calculations

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	Not relevant

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type	X[2]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Loam		4.75	25 °C	1311			
Geometric mean/median							

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Clay loam	3.77	5.2	87.96	2315	85.31	2263	1.0
Sandy loam	3.19	5.0	62.17	1943	68.80	2157	0.95
Loamy sand	1.80	7.9	59.32	3296	69.49	3865	0.92
Sandy loam	1.86	8.1	80.55	4240	90.09	4854	0.93
Silty clay loam[1]	1.45	5.0	318.12	21208	276.82	19091	1.28
Sandy loam	3.07	7.7	114.29	3687	87.42	2844	1.18
Sand	0.46	5.7	4.27	854	10.52	2267	0.75
Arithmetic mean/median				2722		3042	0.96
pH dependence, Yes or No			No				

[1] Not used in risk assessment due to very high 1/n ratio

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

Column leaching ‡	Not relevant
Aged residues leaching ‡	Aged for (d): 30 d Time period (d): 7 d Eluation (mm): 76 mm/day
	Analysis of soil residues post ageing > 95.6-103.4 % total residues/radioactivity retained in top 1-2 cm
	Leachate: 0.9-3.1 % total residues/radioactivity in leachate

[2] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Aged residues leaching ‡	Aged for (d): 60 d Time period (d): 45 d Eluation (mm): 12.7 mm/day
	Analysis of soil residues post ageing > 95.6-103.4 % total residues/radioactivity retained in top 1-2 cm
	Leachate: 0.9-3.1 % total residues/radioactivity in leachate
Lysimeter/ field leaching studies ‡	No lysimeter study; not required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	DT_{50} (d): 166.2 days Kinetics: Field or Lab: representative worst case from field studies calculated towards ¼ of field capacity.
Application data	Crop: Citrus and tomato Depth of soil layer: (e.g. 5 cm). Soil bulk density: 1.5 g/cm^3 % plant interception: - first table: 0 % interception - second table: 70 % for citrus and 25 % for tomato Number of applications: 1 and 2 Interval (d): 0 and 3 days Application rate(s): 1000 and 2 x 200 g as/ha, 300 g as/ha reaching the soil in both cases

PECs (0 % interception)	Tomatoes	Citrus
Maximum for applications in 1 year	0.533	1.33

PEC(s) (70 % interception for citrus and 25 % for tomato) (mg/kg)		Citrus / Tomato DT50 166.2 days (1/4 of field capacity)	
		Actual	twa
Initial	0h	0.400	-
Short term	24h	0.398	0.399
	2d	0.397	0.398
	4d	0.393	0.397
Long term	7d	0.388	0.394
	21d	0.366	**0.383**
	28d	0.356	0.378
	50d	0.325	0.361
	100d	0.264	0.327
Plateau concentration		0.51 mg/kg after 4 yr	-
	21d	0.47	**0.49**

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5: 51 days at 25 °C (1st order) Met BF25: 19 % AR (30 d) Met BF12: 9.9 % (30 d)
	pH 7: 378 days at 25 °C (1st order)
	pH 9: 396 days at 25 °C (1st order)
Photolytic degradation of active substance and metabolites above 10 % ‡	pH 4: no degradation pH 7: DT_{50} 106 days in summer and 446 days in winter pH 9: DT_{50} 140 days in summer and 589 days in winter Artificial light corresponding to sunlight at 40°N in Japan No major metabolites
Quantum yield of direct phototransformation in water at Σ > 290 nm	pH 7: 4.57 x 10^{-4} mol · Einstein $^{-1}$ pH 9: 3.46 x 10^{-4} mol · Einstein $^{-1}$
Readily biodegradable ‡ (yes/no)	No

Degradation in water / sediment

Parent	Distribution, max in water 72.3% after *0.83* d (first sampling). Max. sed 62.9 % after *3* d									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} Water*	St. (r^2)	DT_{50}- DT_{90} sed*	St. (r^2)	Method of calculation
Clay	7.0	ND	20	51 / >90	0.99	20	0.95	61	0.97	SFO

Sand	7.1	ND	20	47	0.92	13.5	0.97	65	0.77	SFO
Geometric mean				49						

*observed decline including partitioning between phases, not degradation

Metabolite: Buprofezin sulfoxide (BF10)	Distribution, max in water 12 % after 56 d. Max. sed 0.7 % after 56 d

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
Clay			18.1 % after 91 d	14.9 % after 91 d	14.9 % after 91 d
Sand			16.9 % after 91 d	13.7 % after 56 d	13.6 % after 91 d

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

Buprofezin

Parameters used in FOCUSsw step 1 and 2	Molecular mass 305 g/mole Water solubility 0.46 mg a.s./L Default DT_{50} for degradation in water phase = 1000 days DT_{50} for degradation in sed. phase = 49 days DT_{50} for degradation in whole system = 49 days DT_{50} for soil 135.6 days (mean lab) K_{Foc}: 3041 mL/g Crop interception: Full canopy (BBCH 89)
Application rate	STEP 1: 400 g ai/ha (tomato), 1000 g a.s./ha (citrus) STEP 2: 2 equal doses of 200 g a.s./ha, 3 days apart (tomato), 1000 g a.s./ha (citrus)
Main routes of entry	Default values from Step 1 and STEP 2 -calculator
Parameters used in FOCUSsw step 3	Vapour pressure: 0.42 x 10^{-4} (the proper value is 0.42 x 10^{-5}) K_{Foc}: 3041 mL/g 1/n: 0.96 (Freundlich exponent for soil) Q10 2.2, Walker equation coefficient 0.7
Application rate	Crop: Citrus Number of applications: 1 Interval (d): 0 Application rate(s): 1000 g as/ha Depth of water body: Default Application window: 26.11-26.12 Crop: Tomato Number of applications: 2 Interval (d): 3 Application rate(s): 200 g as/ha Depth of water body: Default Application window: August-September (note: this application window is regarded as late for the representative use)
Main routes of entry	Default values from STEP 3

FOCUS STEP 1 Tomato N & S, 400 g a.s./ha	PECsw (µg/L)		FOCUS STEP 1 Tomato N & S, 400 g a.s./ha	PECsed (mg/kg)	
	Actual	Time weighted average		Actual	Time weighted average
PEC max, day-0	30.06		PEC max	802.16	
PEC 1 days	26.73	28.39	PEC 1 days	812.72	807.44
PEC 2 days	26.35	27.46	PEC 2 days	801.30	807.22
PEC 4 days	25.61	26.72	PEC 4 days	778.95	798.64
PEC 7 days	24.55	26.02	PEC 7 days	746.58	783.22
PEC 14 days	22.24	24.70	PEC 14 days	676.20	747.01
PEC 21 days	20.14	23.52	PEC 21 days	612.45	712.61
PEC 28 days	18.24	22.43	PEC 28 days	554.71	680.23
PEC 42 days	14.96	20.47	PEC 42 days	455.05	621.23
PEC 50 days	13.36	19.46	PEC 50 days	406.36	590.67
PEC 100 days	6.59	14.52	PEC 100 days	200.33	440.99

FOCUS STEP 2 Tomato N & S, 2 x 200 g a.s./ha	PECsw (µg/L)		FOCUS STEP 2 Tomato N & S, 2 x 200 g a.s./ha	PECsed (mg/kg)	
	Actual	Time weighted average			Actual
PEC max, day-0	3.93	---	PEC max	110.55	---
PEC 1 days	3.68	3.81	PEC 1 days	109.29	109.92
PEC 2 days	3.64	3.73	PEC 2 days	108.04	109.29
PEC 4 days	3.55	3.67	PEC 4 days	105.59	108.05
PEC 7 days	3.44	3.60	PEC 7 days	102.02	106.23
PEC 14 days	3.17	3.45	PEC 14 days	94.15	102.13
PEC 21 days	2.92	3.32	PEC 21 days	86.88	98.24
PEC 28 days	2.70	3.19	PEC 28 days	80.18	94.55
PEC 42 days	2.30	2.96	PEC 42 days	68.29	87.73
PEC 50 days	2.10	2.84	PEC 50 days	62.30	84.13
PEC 100 days	1.18	2.22	PEC 100 days	35.11	65.77

FOCUS STEP 3 Tomato 2 x 200 g a.s./ha	Water body	Application dates	PECSW (µg/L)		PECSED (µg/kg)	
			Actual	TWA	Actual	TWA
Scenario D6	Ditch	16.8 and 19.8	1.920	-	4.299	
Scenario R2	Stream	5.8 and 8.8	0.970	-	59.327	-
Scenario R3	Stream	23.9 and 26.9	1.391*	-	15.025	-
Scenario R4	Stream	23.9 and 26.9	2.254**	-	23.416	-

* Global maximum 4.10.1975 ** Global maximum 4.10.1985

FOCUS STEP 1 Citrus 1000 g a.s./ha	PECsw (µg/L)		FOCUS STEP 1 Citrus 1000 g a.s./ha	PECsed (mg/kg)	
	Actual	Time weighted average		Actual	Time weighted average
PEC max, day-0	118.36		PEC max	2010.00	
PEC 1 days	75.24	96.80	PEC 1 days	2290.00	2150.00
PEC 2 days	74.19	85.76	PEC 2 days	2260.00	2210.00
PEC 4 days	72.12	79.45	PEC 4 days	2190.00	2220.00
PEC 7 days	69.12	75.66	PEC 7 days	2100.00	2190.00
PEC 14 days	62.60	70.74	PEC 14 days	1900.00	2090.00
PEC 21 days	56.70	67.03	PEC 21 days	1720.00	2000.00
PEC 28 days	51.36	63.77	PEC 28 days	1560.00	1910.00
PEC 42 days	42.13	58.04	PEC 42 days	1280.00	1750.00
PEC 50 days	37.62	55.13	PEC 50 days	1140.00	1660.00
PEC 100 days	18.55	41.05	PEC 100 days	564.00	1240.00

FOCUS STEP 2 Citrus 1000 g a.s./ha	PECsw (µg/L)		FOCUS STEP 2 Citrus 1000 g a.s./ha	PECsed (mg/kg)	
	Actual	Time weighted average		Actual	Time weighted average
PEC max, day-0	52.42	---	PEC max	1070.00	---
PEC 1 days	24.37	38.39	PEC 1 days	1060.00	1070.00
PEC 2 days	16.79	29.49	PEC 2 days	1050.00	1060.00
PEC 4 days	39.84	25.49	PEC 4 days	1030.00	1050.00
PEC 7 days	34.99	30.08	PEC 7 days	991.24	1030.00
PEC 14 days	32.29	31.85	PEC 14 days	914.76	992.31
PEC 21 days	29.80	31.58	PEC 21 days	844.19	954.55
PEC 28 days	27.50	30.84	PEC 28 days	779.06	918.71
PEC 42 days	23.42	29.03	PEC 42 days	663.48	852.38
PEC 50 days	21.37	27.96	PEC 50 days	605.31	817.43
PEC 100 days	12.04	22.11	PEC 100 days	341.12	639.05

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
			Actual	TWA	Actual	TWA
R4	Stream	0*	27.65	-	2.792	-
		24	0.003	3.795	2.366	2.614
		2d	0.003	1.899	2.027	2.424
		4d	0.001	0.950	1.562	2.119
		7d	0.001	0.543	1.163	1.797
		14d	<0.001	0.280	0.823	1.385
		21d	<0.001	0.187	0.627	1.163
		28d	<0.001	0.140	0.521	1.016
		42d	<0.001	0.094	0.397	0.829
		50d	<0.001	0.079	0.351	0.771
		100d	2.260	0.051	1.188	0.674
D6	Ditch	0**	36.83	-	78.15	-
		24	33.38	34.99	77.38	78.08
		2d	30.75	33.49	75.49	77.87
		4d	25.55	30.87	70.09	77.05
		7d	15.16	26.37	61.42	75.03
		14d	3.27	17.15	46.43	68.49
		21d	1.343	12.18	37.31	61.92
		28d	0.674	9.370	31.16	56.32

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
			Actual	TWA	Actual	TWA
		42d	0.269	6.389	22.90	47.75
		50d	0.019	5.383	19.62	43.96
		100d	0.006	2.703	10.06	29.63

* Global maximum 10.12.1979 ** Global maximum 6.12.1986

Additional Step 3 FOCUSsw PECsed simulations for applications of buprofezin to tomatoes

Parameters used in FOCUSsw 3	Molecular mass 305.4 g/mole Water solubility 0.46 mg a.s/L at 25°C Vapour pressure: 4.2 x 10^{-5} Pa at 20°C DT_{50} for water phase = 1000 days DT_{50} for sediment phase = 49 days DT_{50} for soil 104 days (geomean lab) Koc: 3041 mL/g 1/n: 0.96 Q10 2.2, Walker equation coefficient 0.7
Application rate	2 x 200 g a.s./ha, 3 days apart to tomatoes (fruiting vegetables) CAM 2 (application to foliage) Plant uptake factor: 0.5 Application window: 1 Aug to 10 Sept (R2); 30 Jun to 25 Aug (R3); 10 Jun to 13 Jul (R4); 30 May to 10 Aug (D6)

PECsediment

R2 stream PECsed (µg a.s./kg d.w.) (date of peak)	**R4 stream PECsed (µg a.s./kg d.w.) (date of peak)**
29.6 (24 Nov)	2.68 (5 July)
R3 stream PECsed (µg a.s./kg d.w.) (date of peak)	**D6 Ditch PECsed (µg a.s./kg d.w.) (date of peak)**
6.68 (28 Jul)	0.841 (7 Jun)

FOCUS sw Step 4 calculations
Use in Citrus with 21m no-spray buffer zones to reduce drift input only, all other modelling inputs as described for Step 3.

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
			Actual	TWA	Actual	TWA
R4	Stream	0*	2.736	-	1.728	-
		24	<0.001	1.863	1.522	1.656
		2d	<0.001	1.011	1.351	1.570
		4d	<0.001	0.507	1.108	1.423
		7d	<0.001	0.290	0.889	1.257
		14d	<0.001	0.145	0.648	1.018
		21d	<0.001	0.097	0.523	0.878
		28d	<0.001	0.125	0.503	0.781
		42d	<0.001	0.087	0.733	0.697
		50d	<0.001	0.073	0.487	0.685
		100d	2.260	0.051	0.187	0.587

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
			Actual	TWA	Actual	TWA
D6	Ditch	0**	3.152	-	6.910	-
		24	2.854	2.993	6.845	6.904
		2d	2.623	2.862	6.683	6.886
		4d	2.168	2.634	6.217	6.815
		7d	1.275	2.243	5.466	6.640
		14d	0.309	1.454	4.156	6.074
		21d	0.118	1.034	3.347	5.503
		28d	0.060	0.797	2.799	5.013
		42d	0.024	0.544	2.188	4.259
		50d	0.010	0.465	1.839	3.942
		100d	0.001	0.235	0.939	2.687

* Global maximum 10.12.1979 ** Global maximum 6.12.1986

Buprofezin sulfoxide

Method of calculation	Molecular mass 321 g/mole Water solubility 0.46 mg a.s/L (active substance) DT_{50} for dissipation from water phase = 300days DT_{50} for dissipation from sed. phase = 300 days DT_{50} for whole system = 300 days Koc 1200 mL/g (Epiwin-program) Formation fraction in water/sediment study 13 % Formation fraction in soil 1.0 x 10^{-3} %
Application rate	STEP 1: 400 g a.s./ha (tomato), 1000 g a.s./ha (citrus) STEP 2: 2 equal doses of 200 g a.s./ha, 3 days apart (tomato), 1000 g a.s./ha (citrus)
Main routes of entry	Default values from Step 1 and STEP 2 -calculator

FOCUS STEP 1 Tomato N & S, 400 g a.s./ha	PECsw (µg/L) Actual	FOCUS STEP 1 Tomato N & S, 400 g a.s./ha	PECsed (µg/kg) Actual
PEC max, day-0	0.504	PEC max, day-1	2.32

FOCUS STEP 1 Citrus 1000 g a.s/ha	PECsw (µg/L) Actual	FOCUS STEP 1 Citrus 1000 g a.s/ha	PECsed (µg/kg) Actual
PEC max, day-0	7.17	PEC max, day-1	33.0

FOCUS STEP 2 Citrus 1000 g a.s/ha	PECsw (µg/L) Actual	FOCUS STEP 2 Citrus 1000 g a.s/ha	PECsed (µg/kg) Actual
PEC max, day-0	7.17	PEC max, day-5	32.7

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Model used: FOCUS-PELMO (version 3.3.2) FOCUS MACRO v. 4.4.2 (for indoor uses only) FOCUS PEARL v. 3.3.3 (for indoor uses only) Crop: Tomato, Citrus Scenarios: Piacenza, Porto, Sevilla, Thiva (citrus) Scenarios: Piacenza, Porto, Sevilla, Thiva, Chateaudûn (Tomato) DT_{50}: mean lab 135.6 days (pF 2 and 20 °C) (field uses) DT_{50}: 104 days (glasshouse uses) K_{Foc}: 3041 mL/g (mean of 6 soils), mean 1/n =0.96 For indoor uses only K_{Foc}: 3042 mL/g, 1/n =0.96 No major metabolites Q10 2.2, Walker equation coefficient 0.7
Application rate	Citrus: 0.3 kg/ha (Maximum application rate of 1 kg a.s./ha 70% interception by the crop) Tomato: 2 x 0.1 kg/ha (3 days interval) (Maximum application rate of 0.2 kg a.s./ha 50% interception by the crop) Tomato (glasshouse): 3 x 0.25 kg/ha 80% interception by the crop Lettuce (glasshouse): 2 x 0.25 kg/ha 70% interception by the crop
$PEC_{(gw)}$	
Maximum concentration	< 0.001 µg/l in all scenarios for all crops (field and glasshouse uses)

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	8.6×10^{-6} mol/Einstein The calculated half-life in natural water bodies at shallow depth was 84 days.
Photochemical oxidative degradation in air ‡	DT_{50} of 2.4 hours derived by the Atkinson model (version AOP v.1.91). (12h day) OH concentration assumed = 1.5×10^{6} OH radicals/cm^3)
Volatilisation ‡	from plant surfaces (BBA guideline): 22 % after 24 hours
	from soil surfaces (BBA guideline): 9 % after 24 hours
Metabolites	No potential volatile metabolites.

PEC (air)

Method of calculation	Not applicable. Low vapour pressure.
$PEC_{(a)}$	
Maximum concentration	Negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: Buprofezin Surface water: Buprofezin, Buprofezin sulfoxide Sediment: Buprofezin Ground water: Buprofezin Air: Buprofezin

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

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water (indicate location and type of study)	Not available
Air (indicate location and type of study)	Not available

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

R53; Not readily biodegradable (BCF 509 measured)

Ecotoxicology

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 ‡				
Bobwhite quail	a.s.	Acute	> 2000	
Mallard duck	a.s.	Acute	> 2000	
Japanese quail	Preparation	Acute	> 2000	
Mallard duck	a.s.	Short-term	> 1306	> 5243
Bobwhite quail	a.s.	Short-term	> 1306	> 5243
Bobwhite quail	a.s.	Long-term	48 [1] 197 [2]	
Mammals ‡				
Rat, Mice	a.s.	Acute	> 2000	
Rat	a.s.	Long-term	66	

[1] NOEC = 48.0 mg kg/bw/d (egg shell thickness; effect not statistically significant)
[2] NOEC = 197.7 mg/kg bw/d (reproductive effects, adult toxicity)

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

Citrus with single application of 1.0 kg a.s./ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous birds	Acute	54.1	> 37	10
Insectivorous birds	Short-term	30.2	> 43	10
Insectivorous birds	Long-term	30.2	1.6 [1]	5
Insectivorous birds	Long-term	30.2	6.6 [2]	5
Earthworm-eating bird	Long-term	6.33	24.4 [2]	5
Fish-eating bird	Long-term	0.11	1797 [2]	5
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	118.15	> 16.9	10
Small herbivorous mammal	Long-term	33.9	**1.95**	5
Earthworm-eating mammal	Long-term	8.05	6.4	5
Fish-eating mammal	Long-term	0.07	971	5
Higher tier refinement (Mammals): 70 % interception taken into account				
Small herbivorous mammal	Long-term	10.16	6.5	5

[1] Based on the NOEC value of 48 mg a.s./kg bw/d (5.3 % decrease in egg shell thickness that was not statistically significantly different)
[2] Based on the NOEC value of 198 mg a.s./kg bw/d for reproductive effects

Tomato with two applications of 0.2 kg a.s./ha with 3 days interval

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous birds	Acute	10.8	> 185	10
Medium herbivorous bird	Acute	18.5	>108	10
Medium herbivorous bird (tomato fruit)	Acute	0.20	>10 000 [1]	10
Insectivorous birds	Short-term	6.03	> 217	10
Medium herbivorous bird	Short-term	9.73	>134	10
Medium herbivorous bird (tomato fruit)	Short-term	0.20	> 6530 [1]	10
Insectivorous birds	Long-term	6.03	8.0 [2]	5
Medium herbivorous bird	Long-term	5.16	9.3 [2]	5
Medium herbivorous bird (tomato fruit)	Long-term	0.13	369 [1, 2]	5
Tier 1 (Mammals)				
Large herbivorous mammal	Acute	6.82	> 293	10
Large herbivorous mammal	Long-term	1.9	34.7	5

[1] Birds eating tomato 'fruits' - scenario has been calculated using the maximum mean measured concentration of buprofezin in tomatoes from field trials

[2] Based on the NOEC value of 48 mg a.s/kg (5.3 % decrease in egg shell thickness that was not statistically significantly different)

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

Group	Test substance	Time-scale	Endpoint	Toxicity[3] (mg/L)
Laboratory tests				
Fish				
Rainbow trout	Technical buprofezin	96 h (flow-through)	LC_{50}	**> 0.33 mg/L** (mm)
Bluegill Sunfish		96 h (flow-through)	LC_{50}	> 0.33 mg/L (mm)
Rainbow trout		28 d (flow-through)	LC_{50} NOEC	0.69 mg/L (mm) 0.15 mg/L (mm)
Rainbow trout		Early life (flow-through)	LOEC NOEC	0.076 mg/L (mm) **0.052 mg/L** (mm)
Rainbow trout	Buprofezin 25 WP	96 h (static)	LC_{50}	> 1.3 mg a.s./L (mm)
Carp	Buprofezin sulfoxide	96 h (static)	LC_{50}	75 mg/L (nom/mm)
Aquatic invertebrates				
Daphnia magna	Technical buprofezin	48 h (static)	EC_{50} [1]	**> 0.42 mg/L** (mm)
Daphnia magna		21 d (semi-static)	EC_{50} [1] NOEC [2]	> 0.36 mg/L (mm) **0.08 mg/L**
Daphnia magna	Buprofezin 25 WP	48 h (static)	EC_{50} [1]	> 1.5 mg a.s./L (mm)
Daphnia magna	Buprofezin sulfoxide	48 h (static)	EC_{50} [1]	> 100 mg/L (nom/mm)

Sediment dwelling organisms				
Chironomus riparius	Technical buprofezin	28 d (static water-spiked study)	NOEC*	0.1 mg/L (nom/mm) 0.17 mg/kg d.w. sediment[4]
Chironomus riparius	Technical buprofezin	28 d (static sediment-spiked study)	NOEC	2.72 mg/kg d.w. sediment (measured)
Algae				
Selenastrum capricornutum	Technical buprofezin	96 h (static)	EbC_{50} ErC_{50}	**> 2.1 mg/L** (mm) > 2.1 mg/L
Selenastrum capricornutum	Buprofezin 25 WP	96 h (static)	EbC_{50} ErC_{50}	> 1.0 mg a.s./L (mm) > 1.0 mg a.s./L
Selenastrum capricornutum	Buprofezin sulfoxide	72 h (static)	EbC_{50} ErC_{50}	49 mg/L (mm) > 740 mg/L (estim.)

Microcosm or mesocosm tests
Not required.

[1] EC_{50} = immobilisation,
[2] = reproduction
[3] based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$) or nominal, but measured concentrations were within ± 80 % (nom/mm)
[4] EFSA calculation based on 0.553x0.0248mg buprofezin dosed/0.08007kg sediment in test system=0.17 mg/kg dw sediment. Details taken from page 19 of the original study report.
*Highest concentration tested had no effect

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

FOCUS STEP 1: Tomato (South and North), 0.4 kg a.s./ha

Test substance	Organism	Toxicity endpoint (mg/L)	Time scale	PECi (µg/L)	TER	Annex VI Trigger
a.s.	Fish	> 0.33	Acute	30.06	>11.0	100
a.s.	Fish	0.052	Chronic	30.06	**1.7**	10
a.s.	Daphnia	> 0.42	Acute	30.06	>14.0	100
a.s.	Daphnia	0.08	Chronic	30.06	**2.7**	10
a.s.	Algae	> 2.1	Acute	30.06	>69.9	10
a.s.	Chironomus[1]	0.10	Chronic	30.06	**3.3**	10
a.s.	Chironomus	2.72 mg/kg d.w. sediment	Chronic	NA[2]	NA	NA
Buprofezin sulfoxide	Fish	75	Acute	0.504	148810	100
Buprofezin sulfoxide	Daphnia	> 100	Acute	0.504	>198413	100
Buprofezin sulfoxide	Algae	49	Acute	0.504	97222	10

[1] PECsw used since buprofezin was spiked in water phase
[2] PECi not calculated for sediment at Focus Step 1

FOCUS STEP 2: Tomato (South and North), 2 x 0.2 kg a.s./ha, Buprofezin

Organism	Toxicity endpoint (mg/L)	Time scale	PECini (µg/L)	TER	Annex VI Trigger
Fish	> 0.33	Acute	3.93	> 84.0	100
Fish	0.052	Chronic	3.93	13.2	10
Daphnia	> 0.42	Acute	3.93	> 106.8	100
Daphnia	0.080	Chronic	3.93	20.4	10
Algae	> 2.1	Acute	3.93	> 534.4	10
Chironomus[1]	0.10	Chronic	3.93	25.4	10
Chironomus riparius	2.72 mg/kg d.w. sediment	Chronic	NA[2]	NA	NA

[1] PECsw used since buprofezin was spiked in water phase
[2] PECini not calculated for sediment at Focus Step 2

FOCUS STEP 3: Tomato (South and North), 2 x 0.2 kg a.s./ha, Buprofezin, Scenario R4 with worst-case PECsw to cover all the other scenarios

Organism	Toxicity endpoint (mg/L)	Time scale	PECini (µg/L)	TER	Annex VI Trigger
Fish	> 0.33	Acute	2.25	> 146.7	100
Fish	0.052	Chronic	2.25	23.1	10
Daphnia	> 0.42	Acute	2.25	> 186.7	100
Daphnia	0.080	Chronic	2.25	35.5	10
Algae	> 2.1	Acute	2.25	> 933.3	10
Chironomus [1]	0.10	Chronic	2.25	44.4	10
Chironomus riparius[2]	2.72 mg/kg d.w. sediment	Chronic	NA	NA	10

[1] PECsw used since buprofezin was spiked in water phase
[2] TER not calculated since buprofezin was spiked in sediment phase

FOCUS STEP 3: Tomato (South and North), 2 x 0.2 kg a.s./ha, Buprofezin, using PEC sediment

Organism	Toxicity endpoint (mg/kg dw sed)	Time scale	PECini (mg/kg dw sed)	TER	Annex VI Trigger
Chironomus	2.72	Chronic	D6 0.000841	3234	10
					10
Chironomus	2.72	Chronic	R3 0.00668	407	10
					10
Chironomus	2.72	Chronic	R2 0.0296	**91**	10
Chironomus	2.72	Chronic	R4 0.00268	**1015**	10

FOCUS STEP 1: Citrus (South), 1.0 kg a.s./ha

Test substance	Organism	Toxicity endpoint (mg/L)	Time scale	PECini (µg/L)	PECtwa (µg/L)	TERini	TERtwa	Annex VI Trigger
a.s.	Fish	> 0.33	Acute	118.4		> 2.8		100
a.s.	Fish	0.052	Chronic	118.4		**0.4**		10
a.s.	Daphnia	> 0.42	Acute	118.4		> 3.5		100
a.s.	Daphnia	0.08	Chronic	118.4		**0.7**		10
a.s.	Algae	> 2.1	Acute	118.4		>17.7		10
a.s.	Chironomus[1]	0.10	Chronic	118.4		**0.80**		10
a.s.	Chironomus	2.72 mg/kg d.w. sediment	Chronic	NA[2]	NA	**NA**	**NA**	NA
Buprofezin sulfoxide	Fish	75	Acute	7.17		10460		100
Buprofezin sulfoxide	Daphnia	> 100	Acute	7.17		>13947		100
Buprofezin sulfoxide	Algae	49	Acute	7.17		6834		10

[1] PEC_{sw} used since buprofezin was spiked in water phase
[2] New PECsed not calculated for citrus plantations

FOCUS STEP 2: Citrus (South), 1.0 kg a.s/ha, Buprofezin

Organism	Toxicity endpoint (mg/L)	Time scale	PECini (µg/L)	PECtwa (µg/L)	TERini	TERtwa	Annex VI Trigger
Fish	> 0.33	Acute	52.42		>6.3		100
Fish	0.052	Chronic	52.42		**1.0**		10
Daphnia	> 0.42	Acute	52.42		>8.0		100
Daphnia	0.08	Chronic	52.42		**1.5**		10
Chironomus [1]	0.10	Chronic	52.42		**1.9**		10
Chironomus	2.72 mg/kg dw sediment	Chronic	NA[2]	NA	NA	NA	10

[1] PECsw used since buprofezin was spiked in water phase
[2] New PECsed not calculated for citrus plantations

FOCUS Step 3: Citrus (South), 1.0 kg a.s./ha

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity endpoint (mg/L)	PECini (µg/L)	TER	Annex VI Trigger
a.s.	D6	Ditch	Fish	Acute	>0.33	36.83	> 9.0	100
a.s.	D6	Ditch	Fish	Chronic	0.052	36.83	**1.4**	10
a.s.	D6	Ditch	Aquatic invertebrates	Acute	> 0.42	36.83	> 11.4	100
a.s.	D6	Ditch	Aquatic invertebrates	Chronic	0.08	36.83	**2.2**	10
a.s.	D6	Ditch	Sediment-dwelling organisms	Chronic	0.10	36.83	**2.7**	10
a.s.	R4	Stream	Fish	Acute	>0.33	27.65	> 12.0	100
a.s.	R4	Stream	Fish	Chronic	0.052	27.65	**1.9**	10
a.s.	R4	Stream	Aquatic invertebrates	Acute	> 0.42	27.65	> 15.2	100

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity endpoint (mg/L)	PECini (µg/L)	TER	Annex VI Trigger
a.s.	R4	Stream	Aquatic invertebrates	Chronic	0.08	27.65	**2.3**	10
a.s.	R4	Stream	Sediment-dwelling organisms	Chronic	0.10	27.65	**3.6**	10
a.s.	R4	Stream	Sediment-dwelling organisms	Chronic	2.72 mg/kg dw sediment	NA[1]	NA	NA

[1] New PECsed not calculated for citrus plantations

FOCUS Step 4: Citrus (South), 1.0 kg a.s./ha

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PECini	TER	Annex VI trigger
D6	Ditch	Fish	Acute	>0.33	21 m	3.15	> 104.8	100
D6	Ditch	Fish	Chronic	0.052	21 m	3.15	16.5	10
D6	Ditch	Aquatic invertebrates	Acute	> 0.42	21 m	3.15	> 133.3	100
D6	Ditch	Aquatic invertebrates	Chronic	0.08	21 m	3.15	25.4	10
D6	Ditch	Sediment-dwelling organisms	Chronic	0.10 0.17 mg/kg dw sediment	21 m	3.15 1.73 µg/kg dw sediment	31.7 99.1	10
R4	Stream	Fish	Acute	>0.33	21 m	2.74	> 120.4	100
R4	Stream	Fish	Chronic	0.052	21 m	2.74	19.0	10
R4	Stream	Aquatic invertebrates	Acute	> 0.42	21 m	2.74	> 153.3	100
R4	Stream	Aquatic invertebrates	Chronic	0.08	21 m	2.74	29.2	10
R4	Stream	Sediment-dwelling organisms	Chronic	0.10 0.17 mg/kg dw sediment	21 m	2.74 6.91 µg/kg dw sediment	36.5 24.8	10
R4	Stream	Sediment-dwelling organisms	Chronic	2.72 mg/kg dw sediment	NA	NA[1]	NA	10

[1] New PECsed not calculated for citrus plantations

Bioconcentration

Bioconcentration factor (BCF)	464 ± 58 (modelled), 509 measured in whole fish tissue
Annex VI Trigger: for the bioconcentration factor	100 for substance which is not readily biodegradable
Clearance time(CT_{50})	0.5 ± 0.04 days Rapidly eliminated from fish tissues during depuration.

(CT_{90})	After 7 days 98 % AR was depurated from the whole fish.
Level of residues (%) in organisms after the 14 day	3.19 mg/kg in edible tissues 23.9 mg/kg in whole fish 30.7 mg/kg in non-edible tissues
Depuration phase	After one day: 77% depuration (edible) 86% depuration (whole) 82% depuration (non-edible) After 7 days: 92% depuration (edible) 98% depuration (whole) 99% depuration (non-edible)

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

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	> 163.5 µg a.s/bee	> 200 µg a.s/bee
Preparation[1]	> 100 µg a.s/bee	> 100 µg a.s/bee
Metabolite 1		
Field or semi-field tests: The development success of the brood was comparable to the control after application of 4 kg Buprofezin 25 WP/ha.		
Field tests are not required because the Q_{HO} and Q_{HC} were less than 50.		

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
1.0	Citrus	Oral	< 10	50
		contact	< 10	50

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

All studies were performed in laboratory, fresh residues on glass plates.

Species	Buprofezin (kg a.s./ha)	Endpoint Mortality (%) (Abbott control corrected)	Endpoint	Endpoint value
Chrysoperla carnea	0.188 0.375 0.750 1.500 3.000 (WP)	0 0 3.5 -3.6 -3.6	Emergence rate in % of control	100 96.3 96.3 100 93.1
Typhlodromus pyri	0.188 0.375 0.750 1.500 3.000 (WP)	12.0 10.0 34.0 34.0 38.0	Decrease in reproduction in % of control	13 32 34 47 63
Chrysoperla carnea	0.188 0.375 0.750 1.500 3.000 (SC)	10 10 20 10 14	Emergence rate in % of control	111 103 97 103 97
Typhlodromus pyri	0.188 0.375 0.750 1.500 3.000 (SC)	0.0 15.4 -11.5 34.6 32.7	Decrease in reproduction in % of control	25 31 6 35 15

Field or semi-field tests
As the laboratory tests indicate a low hazard potential with regard to non-target arthropods, no field testing is required.

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

Acute toxicity	LC_{50} > 500 mg/kg soil* (14-day, buprofezin) LC_{50} > 500 mg a.s./kg soil* (14-day, „Applaud" 25WP)
Reproductive toxicity	NOEC = 250 mg/kg soil*

* The LC_{50} values and NOEC value have been divided by 2, since the log Pow for buprofezin is 4.8.

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
1.0 kg a.s./ha	Citrus	Acute	> 376*	10
1.0 kg a.s./ha	Citrus	Long term	188*	5

* Using a PECsoil of 1.33 mg as/kg, which is worst-case single application to citrus, with no interception.

Effects on soil non-target macro-organisms (Annex IIIA 10.6.2)

Test organism	Test substance	Time scale	NOEC (mg a.s./kg d.w. soil)
Collembola			
Folsomia candida	Technical buprofezin	Chronic 28-day	31.25*

*The NOEC is divided by 2 as the log P_{OW} of the buprofezin is > 2, and the collembolan test was conducted with artificial soil.

Toxicity/exposure ratios for non-target macro-organisms (Annex IIIA, point 10.6.2)

Test organism	Test substance	Time scale	Soil PEC (mg a.s./kg soil)	TER	Trigger
Other soil macro-organisms					
Folsomia candida	Technical buprofezin	28-day	1.33*	23.5	5

* PECsoil of 1.33 mg as/kg, which is worst-case single application to citrus, with no interception.

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

Nitrogen mineralization	No effect up to 5 kg a.s./ha
Carbon mineralization	No effect up to 5 kg a.s./ha

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

Preliminary screening data

Buprofezin had no herbicidal activity on non-target plant species germination, seedling growth, and development, at any of the concentrations from 100 g a.s./ha up to 10000 g a.s./ha of buprofezin.

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

Respiration inhibition test OECD 209	end point
Activated sludge	No effect on specific respiration rate up to 1000 mg/L

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

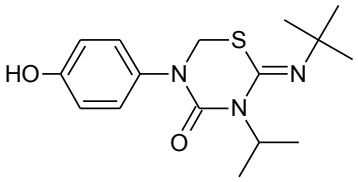
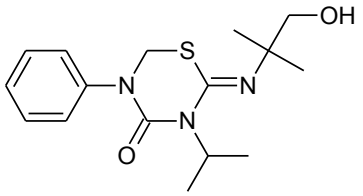
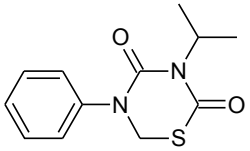
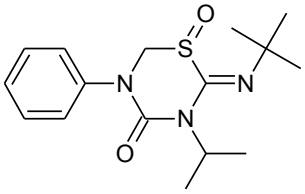
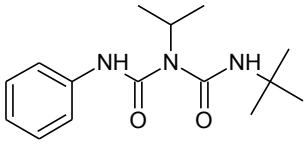
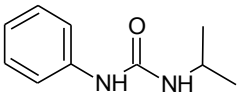
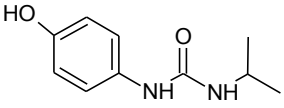
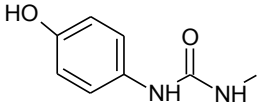
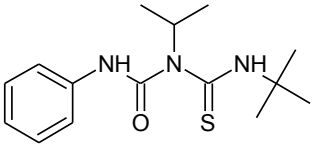
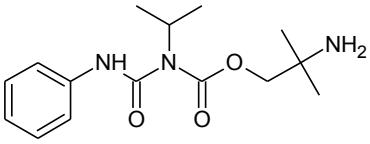
Compartment	
soil	Buprofezin
water	Buprofezin
sediment	Buprofezin
groundwater	Buprofezin

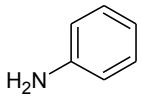
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	R50

	RMS/peer review proposal
Preparation	R51

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name*	Structural formula*
BF2	(2*Z*)-2-(*tert*-butylimino)-5-(4-hydroxyphenyl)-3-(propan-2-yl)-1,3,5-thiadiazinan-4-one	
BF4	(2*Z*)-2-[(1-hydroxy-2-methylpropan-2-yl)imino]-5-phenyl-3-(propan-2-yl)-1,3,5-thiadiazinan-4-one	
BF9	5-phenyl-3-(propan-2-yl)-1,3,5-thiadiazinane-2,4-dione	
BF10 Buprofezin sulfoxide A-12	(2*Z*)-2-(*tert*-butylimino)-5-phenyl-3-(propan-2-yl)-1,3,5-thiadiazinan-4-one 1-oxide	
BF11 biuret A-14	*N*-*tert*-butyl-*N*'-phenyl-*N*-propan-2-yldicarbonimidic diamide	
BF12	1-phenyl-3-propan-2-ylurea	
BF13	1-(4-hydroxyphenyl)-3-propan-2-ylurea	
BF23	1-(4-hydroxyphenyl)-3-methylurea	
BF25 thiobiuret	*N*-*tert*-butyl-*N*'-phenyl-*N*-propan-2-yldicarbonimidothioic diamide	
BF26 (Metabolite A)	2-amino-2-methylpropyl (phenylcarbamoyl)propan-2-ylcarbamate	

Code/Trivial name	Chemical name*	Structural formula*
aniline	aniline	

* ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CF	conversion factor
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DNA	deoxyribonucleic acid
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
ELS	early-life-stage
EMDI	estimated maximum daily intake
EPA	Environmental Protection Agency
ER_{50}	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FC	field capacity
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GC-FPD	gas chromatography with flame photometric detector
GC-MSD	gas chromatography with mass-selective detection
GC-NPD	gas chromatography with nitrogen phosphorous detector
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HR	highest residue
HQ	hazard quotient
IE	immature erythrocytes
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)
KC+	kinetochore positive
K_{oc}	organic carbon adsorption coefficient
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LLNA	Local Lymph Node Assay
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MN	micronuclei
MNIE	micronucleated immature erythrocytes
MRL	maximum residue limit or level
MS	mass spectrometry
MWHC	maximum water holding capacity
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
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
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
PF	processing factor
PHI	pre-harvest interval
pKa	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10-6)
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTU	propyl-thiouracil
QSAR	quantitative structure-activity relationship
r2	coefficient of determination
RMS	rapporteur Member State
RPE	respiratory protective equipment
SFO	single first-order
STMR	supervised trials median residue
STP	sewage treatment plant
T_3	tri-iodothyroxine

T_4	thyroxine
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
TF	transfer factor
TMDI	theoretical maximum daily intake
TPEM	two phase exponential model
TRR	total radioactive residue
UV	ultraviolet
WHO	World Health Organisation
WP	wettable powder
yr	year