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

buprofezin (notified active substance).

(However this ISO name refers to a mix of E and Z isomers. As only the Z isomer exists, the name buprofezin can not be used for this substance. Thus, the manufactures development code (NNI-750) has been used throughout this conclusion)

Finalised: 3 March 2008

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[1]. 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 with the title 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 the Member States in February 2008 leading to the conclusions as laid down in this report.

[1] OJ No L 224, 21.08.2002, p. 25, as last amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide on tomato, lettuce and citrus. Full details of the gap can be found in the attached end points. It should be noted that only the use as an insecticide has been considered during the peer review process, the acaricide use has not been considered.
The representative formulated product for the evaluation was "Applaud 25 WP", a wettable powder formulation (WP). It was concluded during the peer review process that the name buprofezin can not be used for this active substance.

Adequate methods are available to monitor NNI-750 in all matrices.
Only single methods for the determination of residues are available since a multi-residue-methods like the German S19 or the Dutch MM1 are not applicable due to the nature of the residues.
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 was requested.

In mammals, NNI-750 acute oral, dermal or inhalation toxicity is low (oral and dermal LD_{50} >2000 mg/kg bw, LC_{50} 4.57 mg/L air /4h). NNI-750 is not a skin or eye irritant nor a skin sensitiser.
Target organs in subchronic and chronic studies are liver and thyroid, showing increased weights 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 0.90 mg/kg bw/day while in mice, it is 1.82 mg/kg bw/day.
Genotoxicity of NNI-750 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 NNI-750 non genotoxic and the recent in vivo micronucleus test on bone marrow as not interpretable. The PPR Panel re-evaluated also the long-term toxicity/carcinogenicity studies on NNI-750 and concluded that NNI-750 is not carcinogenic in rats or mice.
NNI-750 did not show any reproductive toxicity potential: the relevant parental and offspring NOAELs are 6.46 mg/kg bw/day f 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 (based on decreased food consumption and increased water intake, skeletal effects and subcutaneous oedema, respectively).It was agreed not to propose any classification.
NNI-750 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 an SF 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 an SF 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 an SF 100.
The operator exposure was below the AOEL-value for tractor mounted spraying with personal protective equipment for tomato and citrus calculated with the German model. For hand-held

application exposure was under the AOEL with PPE for tomato outdoors (UK-POEM) and in glasshouse, as for lettuce (Dutch model), and for citrus (German model). The bystanders showed estimated exposure levels below the AOEL (<15%) for both applications on tomato and citrus. Worker exposure was estimated to be below the AOEL with gloves when handling tomato or lettuce in glasshouse or tomato outdoors. Instead, exposure was above the AOEL even with gloves when handling citrus.

The metabolism of NNI-750 in plants has been elucidated. The parent compound is the major constituent of the final residue. Minor plant metabolites were identified. Their structures differ significantly from that of NNI-750 and their toxicological properties have not been sufficiently investigated. Also under processing conditions degradation products are formed with unknown toxicological potential. Therefore, although a residue definition can be proposed for monitoring (NNI-750), the residue definition for risk assessment has not been set. For this reason a consumer risk assessment is currently not possible.
A potential transfer of residues to rotational crops has been noted.
No residues are expected in animal commodities.

In soil under aerobic conditions NNI-750 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. NNI-750 exhibits slight mobility in soil. There was no indication that adsorption of NNI-750 was pH dependant.

In dark natural sediment water systems NNI-750 degraded exhibiting moderate persistence in both water and sediment forming the metabolite NNI-750 sulfoxide (BF-10)[2] in water (max. 12%AR). The terminal metabolite, CO2, 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 using the agreed FOCUS scenarios approach for NNI-750 at steps 1-3 and for citrus steps 1-4, with spray drift mitigation being applied at step 4. For the metabolite NNI-750 sulfoxide (BF-10) 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 applied for intended uses by NNI-750 above the parametric drinking water limit of 0.1 µg/L, was concluded to be low for the outdoor uses assessed in geoclimatic situations that are represented by all pertinent FOCUS groundwater scenarios. An assessment of the potential for groundwater exposure from the applied for intended protected (glasshouse) uses with higher rates and numbers of applications than in outdoor uses is not available, though the potential for groundwater exposure from these uses is also likely to be low.

[2] NNI-750 sulfoxide (BF-10): 2-tert-butylimino-3-isopropyl-5-phenyl-perhydro-1,3,5-thiadiazin-4-one-1-oxide

The acute toxicity of NNI-750 is low to birds and mammals. Following the principles of SANCO/ 4145/2000 the acute and long-term risk to birds and mammals were assessed to below. For the small herbivorous mammal in citrus an interception of 70% was taken in to account to reach a TER-value above the Annex IV trigger. Low risk is foreseen for earthworm- and fish-eating birds and mammals, as the risk to birds and mammals ingesting contaminated drinking water is also considered too be low.

NNI-750 is as very toxic to aquatic organisms. TER values for use in tomatoes indicate low risk without any risk mitigation. Buffer zones of 20 m are required for use in citrus to identify low risk. Further data are needed to address the risk to sediment dwelling organisms from NNI-750. NNI-750 is not considered to bioaccumulate in fish.

Low risk was identified for all other non-target organism groups, except for a data gap on a reproduction test with Collembola, to address the risk of use in citrus.

Key words: NNI-750, buprofezin, peer review, risk assessment, pesticide, insecticide, acaricide.

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000, as amended by Commission Regulation (EC) No 1095/2007 regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Buprofezin is one of the 79 substances of the third stage, part A, covered by the Regulation (EC) No 1490/2002 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 draft assessment report, 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 draft assessment report. In accordance with Article 11(2) of the Regulation (EC) No 1490/2002 the revised version of the draft assessment report was distributed for consultation on 3 February 2006 to the Member States and the main applicant Nihon Nohyaku Co., Ltd as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed during a written procedure in October – November 2006 on data requirements to be addressed by the notifier as well as 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 have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in February 2008 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts a concern on genotoxicity and carcinogenicity was identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR). The opinion[3] of the Panel was adopted on 11 December 2007 and is considered in this conclusion.

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

In accordance with Article 11c (1) of the amended Regulation (EC) No 1490/2002, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received;
- the resulting reporting table (rev. 1-1 of 21 December 2006)

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation;
- the evaluation table (rev. 2-1 of 16 February 2008).

Given the importance of the draft assessment report including its addendum (compiled version of February 2008 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Buprofezin is the ISO common name for (*EZ*)-2-tert-butylimino-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one (IUPAC). However the compound evaluated in the DAR is only the Z isomer and therefore the ISO common can not be used for this compound. It has been demonstrated by the applicant that the E isomer does no exist and therefore it is just that the ISO common name is not correct. The reason for this is unclear but it is probably because when the applicant requested the name they did not know which configuration the molecule was in.

NNI-750 belongs to the class of chitin synthesis inhibitors.

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

The evaluated representative uses are as an insecticide on tomatoes, lettuce and citrus. Full details of the gap can be found in the attached end points.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of NNI-750 as manufactured should not be less than 985 g/kg. At the moment no FAO specification exists. The technical material contains no relevant impurities.
The content of NNI-750 in the representative formulation is 250 g/kg however in volume 4 the value is incorrect.

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 NNI-750 or the respective formulation. There is one outstanding issue in that 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 however the summary of this study does not appear to address the wettability and suspensibility issues and it is also not peer reviewed. Therefore this issue will remain a data gap

The main data regarding the identity of NNI-750 and its physical and chemical properties are given in appendix 1.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of NNI-750 in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. NNI-750 in food of plant origin and in soil, water and air.

A multi-residue method like the Dutch MM1 or the German S19 is not applicable due to the nature of the residues. The method for food of plant origin is GC-NPD with an LOQ of 0.01 mg/kg confirmation is by LC-MS/MS. 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/kg and confirmation by LC-MS. Air is analysed by a GC-MS 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 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 toxicology

NNI-750 was discussed in a 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[4]. NNI-750 was therefore discussed for the second time in a meeting of experts (December 2007) to close left 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 the rat, NNI-750 is rapidly absorbed, biotransformed and rather rapidly excreted predominantly in faeces. Biliary excretion is significant. Oral absorption was discussed in the 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 NNI-750 or its metabolites in the tissues. NNI-750 is extensively metabolised: the main metabolic routes are hydroxylation of phenyl ring and oxidation of t-butyl groups and thiazidin ring opening.

2.2. Acute toxicity

NNI-750 acute oral, dermal and inhalation toxicity 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. NNI-750 is not a skin or eye irritant nor a skin sensitiser in the guinea pig maximisation test and confirmed by a LLNA test which was negative.

2.3. Short term toxicity

Target organs in subchronic studies in both rodents and dogs are liver and thyroid, showing increased weights 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 13-week study in dogs, the NOAEL is 10 mg/kg bw/day while in a 107-week study in dogs, the NOAEL is 2 mg/kg bw/day.

2.4. Genotoxicity

Genotoxicity of NNI-750 was tested in five different types of *in vitro* and one *in vivo* assay.

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

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

In September 2006 the RMS submitted an addendum (addendum 1 to vol 3) summarising new studies provided by the applicant. In particular, a new micronucleus test in the bone marrow of mouse (Inagaki 2006) showed that NNI-750 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 meeting in June 07. 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 NNI-750 showed aneugenic effects in somatic cells *in vitro* (Syrian hamster embryo cells). NNI-750 did not induce chromosomal aberrations in germ cells *in vivo* (mouse spermatocytes) in a published study. NNI-750 was not mutagenic or genotoxic in 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 NNI-750. The PPR Panel concluded that the range of studies submitted was adequate and that there is no evidence that NNI-750 is genotoxic. The Panel considered the recent *in vivo* micronucleus test on bone marrow as not interpretable and not contributing to the evaluation of the genotoxicity of NNI-750. In particular, the results of the study were considered as equivocal and providing only very limited information for the evaluation of the genotoxicity of NNI-750 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 MNIE/1000 cells (24.0, 33.5, 6.5, 8.0, 29.0) for NNI-750 2000 mg/kg in the first experiment, reveal a large interindividual 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

The results of the new *in vivo* study cannot exclude an aneuploidogen mechanism, mediated by indirect effects, to explain the increase in the frequency of MNIE induced by high doses of NNI-750, as was suggested by the published *in vitro* study (Herrera et al 1993). The mechanism for any induction of MN by NNI-750 was not adequately addressed in the study. Only one experiment including 5 animals was carried out to evaluate the kinetochore positive MN and no historical control values were reported for the % of KC+-MN evaluated by the CREST method.

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 NNI-750is genotoxic. The recent *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 NNI-750.

2.5. LONG TERM TOXICITY

The most prominent effect in chronic toxicity and carcinogenicity studies was the increased liver and thyroid weight accompanied with histological findings at higher doses.
The relevant NOAEL in rats was 20 ppm (equivalent to 0.90 mg/kg bw/day for males and 1.12 mg/kg bw/day for females) based on slightly increased liver and thyroid weights 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 meeting of experts held in June 2007 the carcinogenicity of NNI-750 was re-considered, based on the findings in the new *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 meeting 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 carcinogenic potential of NNI-750, in the context of the human risk assessment.
The PPR Panel re-evaluated the long-term toxicity/carcinogenicity studies on NNI-750. 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 NNI-750. The PPR Panel concluded that NNI-750 is not carcinogenic in rats or mice. The PRAPeR experts' meeting (December 2007) agreed with the conclusion.

The PPR Panel concluded that the toxicological database on the carcinogenicity and genotoxicity of NNI-750 is sufficient for setting reference values.

2.6. REPRODUCTIVE TOXICITY

The reproduction toxicity of NNI-750 was investigated in one two-generation reproduction study and in two prenatal toxicity studies. In two-generation study, parental animals receiving the highest dose of NNI-750 (1000 ppm) showed increased liver, kidney and adrenal weights. Increased kidney and liver weights were observed in males and increased adrenal, pituitary and liver weight in females. Histopathological changes were not observed. NNI-750 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 meeting of experts in June 07, 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, JMPR considered the level as a LOAEL, setting a NOAEL at 50 mg/kg bw/day. Historical control data ranged for incomplete ossification of the intra-parietal bone 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 (decreased food consumption and increased water intake, skeletal effects and subcutaneous oedema, respectively). It was agreed not to propose any classification.

2.7. NEUROTOXICITY

NNI-750 does not have structural alerts for delayed neurotoxicity, such as organophosphates. There was no evidence of neurotoxicity in the other toxicity studies that has been conducted with NNI-750. It was therefore considered that NNI-750 does not have potential to induce neurotoxicity in mammals.

2.8. FURTHER STUDIES

In the experts' meetings, the metabolites BF11[5], BF12[6], BF25[7], aniline, BF26[8], BF4[9] were considered: of these metabolites, only BF12 was identified as a rat metabolite. BF11 was assumed to be formed in rat metabolism and a precursor for BF12.

According to the available information BF26 and BF4 are of a higher acute oral toxicity than the parent and therefore considered relevant (LD_{50} of 50-300 mg/kg bw and 300-2000 mg/kg bw, respectively; they both were not mutagenic in the bacterial reverse mutation test).

For BF11 and BF25 no studies were available, but the DEREK analysis did not show a concern. Taking into account the very limited information, these metabolites were considered relevant as well.

The meeting concluded that for all the metabolites concerned (BF4, BF26, BF11, BF12 and BF25) no reference values could be established on the basis of the available information.

[5] BF11: 1-*tert*-butyl-3-isopropyl-5-phenybiuret
[6] BF12 N-Isopropyl-N'-phenylurea
[7] BF25: 1-tert-butyl-3-isopropyl-5-phenyl-2-thiobiuret
[8] BF26: 2-amino-2-methylpropyl-2-methylethyl-4-phenylallophate
[9] BF4: 2-(2-hydroxy-1,1-dimethylethylimino)-3-isopropyl-5-phenyl-perhydro-1,3,5-thiadiazin-4-one

2.9. MEDICAL DATA

There were no adverse health effects attributable to NNI-750 in ten workers who handled NNI-750 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 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 an SF of 100.

AOEL

In the 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 an SF 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 developmental toxicity study and applying an SF 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 MW and log Pow a 100% dermal absorption should be used as a default. But when looking at the oral absorption, 40% would be an acceptable value.

The meeting 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 NNI-750. It is intended to control white fly in tomato, 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 handheld knapsack sprayer for low-level application to small area field crops (outdoors and glasshouse). The application rate per treatment varies between 0.2 to

1.0 kg active ingredient 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 tomato in glasshouse, two for tomato in field and one for citrus according to the notifier.

The operator exposure in different scenarios was estimated 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 (Jan 08).

Operator exposure

	Application method (crop)	Treated area (ha/day)	Systemic exposure (mg/kg bw/day)	% of systemic AOEL
German model	Tractor mounted boom sprayer (tomato)	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)[a]	1	0.13 0.013	325 33§
UK POEM	Hand-held application, low crops; field (tomato)	1	0.32 0.028	800 70#
Dutch	Hand held sprayer: glasshouse (tomato, 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

§ = Gloves during mixing/loading and application, coverall and sturdy footwear during application

#Gloves during mixing/loading and gloves and impermeable coverall during application

^Gloves and respiratory protector during mixing/loading and application

[a]It is noted that the calculation for this scenario has been performed considering an application rate of 0.25 kg/ha instead of 1 kg/ha; however, considering the use of RPE and gloves during mixing and loading and gloves, broad-brimmed headwear, coverall and sturdy footwear during application the estimated exposure is expected to be below the AOEL (about 75%).

The operator exposure was below the AOEL-value for tractor mounted spraying with personal protective equipment for tomato and citrus spraying calculated with the German model. For hand-

held application exposure was under the AOEL with PPE for tomato outdoors (UK-POEM) and in glasshouse, as for lettuce (Dutch model), and for citrus (German model).

Bystander exposure

The bystander exposure was re-calculated for potential exposure to NNI-750 while spraying citrus with tractor mounted broadcast air-assisted sprayer and tomatoes with tractor mounted boom sprayer. Exposure time was considered to be one hour. The selected drift values are reported to be the ones recommended by the Bystander Working Group (EUROPOEM 2, Bystander Working Group Report, December 2002). **EFSA notes** 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 60 kg.

Scenario	Application rate (mg/m^2)	Concentration of active ingredient in spray (mg/mL)	Drift value (%)	Total exposure (mg/kg bw/day)	% of systemic AOEL
Tomato, 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 applications on tomato and citrus.

Worker exposure

The re-entry exposure was recalculated for tomatoes (in glasshouse and outdoors) and citrus (tractor mounted spraying). The scenario assessed for tomatoes is also identical with 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.

Etotal = (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

Default value of 0.003 mg/cm2 for Dislodgeable Foliar Residue (DFR) value was used (EUROPOEM 2; Re-entry Working Group Report, December 2002). Transfer coefficient value of 2500 cm2/h for bare hands (tomato) and 4500 cm2/h (citrus) were used, respectively. Work rate was assumed 6 h/day. The application rate for tomato is 0.25 kg a.i./ha and 1.0 kg a.i./ha for citrus. The worker is assumed to weight 60 kg and the dermal absorption is 40%. Inhalation exposure was considered only for glasshouse application and was estimated in the following equation (EUROPOEM 2, Re-entry Working Group Report, December 2002). The inhalation absorption is 100%, body weight 60 kg and time of exposure 6 hours.:

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

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

PPE = Personal protective equipment
Yes* = Gloves

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

3. Residues

NNI-750 was discussed at the PRAPeR experts' meeting for residues PRAPeR 25 in June 2007
This section deals only with the Z-isomer (NNI-750). Due to steric repulsion of the t-butyl isopropyl moieties, the E-isomer is considered as unstable.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of NNI-750 has been investigated in fruits (citrus), leafy crops (lettuce) and oilseeds (cotton). These studies were conducted in accordance with the representative uses supported by the

applicant. A further metabolism study in tomatoes was also submitted but did not provide any information on the metabolic pathway.

The submitted studies suggest a common metabolism in all plants starting with oxidative cleavage of the dimethylethylimino-side chain and proceeding further through opening, rearrangement and hydrolytic degradation of the thiadiazine ring.

For short term PHI, the metabolic pattern consists in the parent compound, which is the only major constituent of the residue, and in minor metabolites (metabolites BF9[10], BF12 and BF26) essentially identified after acid hydrolysis. Experimental data suggest that these metabolites derive from a main common acid labile conjugated metabolite, postulated to be BF4, which cannot be liberated without further degradation and chemical rearrangements. A further metabolite (metabolite B) was not fully identified, 2 structures being proposed, but is of low stability, present at low level and only produced after acid hydrolysis including dioxane, indicating a low bioavailability. These metabolites are individually present in amounts one order of magnitude lower than the parent compound up to 14 to 28 days after application.

For longer PHIs the citrus study suggests that the ratio of these metabolites to the parent compound is continuously increasing. In particular metabolite BF26 is present in citrus 10 weeks after a single treatment in higher amounts than NNI-750.

Considering the short PHIs proposed for the representative uses the residue definition for monitoring is proposed to be restricted to the parent compound.

For risk assessment, it was questioned whether the metabolites, although present in low amounts, but resulting from important structural modifications could bring additional toxicological concern. Metabolites BF12 and BF9 are mammalian metabolites and their toxicities have been taken into account in the toxicological studies of the active substance. For the other metabolites, as discussed in point 2.8, no toxicological reference value can be established. Using per default the reference values of the parent compound is not considered appropriate considering the fact that part of the plant metabolites were not present in the rat metabolism or/and showed indication of a higher toxicity.

Therefore, despite a proposal (sum of the parent compound and all its metabolites containing the isopropylphenylurea moiety, or alternatively sum of the parent compound, its metabolites BF9, BF12, BF26 and their conjugates expressed as NNI-750) made by the expert meeting on residues prior to the final assessment of the expert meeting on mammalian toxicology, it is the opinion of EFSA that grounds are not sufficient for a residue definition for risk assessment. Further data characterising the toxicological properties of the plant metabolites are necessary.

A sufficient number of supervised residue trials have been submitted in accordance with the representative uses and residues of the parent compound were determined. In oranges and mandarins (8 trials available for each fruit) residue levels are very similar with Supervised Trials Medium Residues (STMR) values of 0.24 and 0.23 mg/kg for oranges and mandarins respectively. The representative uses on tomatoes lead to clearly higher levels in glasshouses (STMR of 0.16 mg/kg) than in field (STMR of 0.08 mg/kg). In lettuce high residue levels (up to 13.5 mg/kg) were found (STMR of 7.07 mg/kg). It must be noted that in many trials free forms of metabolites BF9 and BF12

[10] BF9: 3-isopropyl-5-phenyl-perhydro-1,3,5-thiadiazinan-2,4-dione

were also determined and were consistently found below 0.01 mg/kg. This information must however be considered carefully because no hydrolysis was performed during sample analysis and metabolism studies indicated that metabolites BF9 and BF12 were essentially present in plant as conjugates.

These results can be considered as reliable on the basis of storage stability studies demonstrating that NNI-750 and its metabolites BF9 and BF12 are stable under deep freeze storage conditions, in various plant matrices (among which citrus, tomatoes and processed commodities from tomatoes, lettuce).

In the absence of a residue definition for risk assessment, the relevance of the available residue trials cannot be evaluated.

Under standard hydrolysis conditions in buffer solution simulating pasteurisation, boiling and sterilisation, NNI-750 is significantly degraded yielding substantial amounts of a phenyl thiobiuret derivative (BF25, up to 43 % of the TRR), aniline (up to 19 % of the TRR), metabolite BF12 (up to 31 % of TRR) and in a lesser extent metabolite BF11 (up to 4 % of TRR). This degradation is favoured by acidic condition.

Metabolites BF11 and BF12 were found in the rat metabolism. For the thiobiuret metabolite, similarly as for raw plant commodities, the expert meeting on mammalian toxicology concluded that no toxicological reference value can be set.

Aniline is a potential human carcinogen and mutagen and its formation as degradation product under processing is of toxicological concern. However the opinion of the expert meeting on residues is that a risk assessment related to aniline needs to be considered in a much broader context than the framework of the NNI-750 peer review, and cannot be performed at this stage.

Processing studies were performed in order to assess the transfer of residues to processed commodities under industrial conditions. However, only 1 study reflecting tomato processing to juice, puree, ketchup and canned tomatoes as well as 2 studies reflecting orange processing to juice are available with sufficient amount of residues in the raw commodity for appropriate estimation of transfer factors. In addition only the transfer of the active substance and its free BF12 metabolite were investigated. The results of these studies can therefore only be considered as indicative. Residues of NNI-750 were significantly transferred to tomato and orange juice, ketchup and tomato puree as well as to dry citrus pomace for which a transfer factor of about 5 is suggested. No reliable information is available concerning the degradation products identified in the standard hydrolysis study. Further data could be necessary in the future, depending on the residue definition for risk assessment.

As far as household processing is concerned, 14 studies showed that residues in citrus pulp resulting from peeling are 5 times lower than in the whole fruit.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

A confined study shows 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 indicates 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

legal concern, especially considering that rotation in glasshouse crops may occur in rather short time intervals.

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

The expert meeting proposed a waiting period of 1 year between the use of NNI-750 in glasshouse before sowing or planting a rotational crop other than lettuce or tomatoes if measurable residues of NNI-750 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 parent NNI-750, 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 NNI-750 residues through consumption of citrus pomace. The level of exposure is slightly above the level triggering the performance of metabolism studies.

The metabolism of NNI-750 has therefore been investigated in lactating cows and laying hens. In both species the compound is 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. Parent compound was found in trace amounts in poultry products and only in milk in the lactating goat study. Metabolites BF2[11], BF12, BF13[12], and BF23[13] were the only metabolites identified under acid hydrolysis. The nature of identified metabolites suggests that livestock metabolism is similar to the rat metabolism. A large proportion of the extractable radioactivity (reaching 65 % of 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.

The expert meeting considered that, due to the low exposure level of livestock to NNI-750 and its metabolites total residues are expected to be very low in milk, fat and muscle and in the range of 0.03 to 0.05 mg/kg in liver and kidneys. Considering also the extensive nature of animal metabolism of NNI-750, no single degradation product is expected to be present above 0.01 mg/kg in any tissue. It was however the view of the expert meeting on residues that a new metabolism study in lactating goat should be requested considering in particular the concern related to the genotoxicity and carcinogenicity potential of NNI-750. Based on the opinion adopted by the PPR panel on this issue, it is the opinion of the EFSA that this request for further metabolism data is no longer justified for the time being, but should be reconsidered once information of the toxicological profile of plant metabolites will be available.

Therefore, no residue definition is proposed, taking also in to account that the submitted studies did not show any valid indicator compound.

[11] BF2: 2-tert-butylimino-5-(4-hydroxyphenyl)-3-isopropyl-perhydro-1,3,5-thiadiazinan-4-one
[12] BF13: N-(4-hydroxyphenyl)-N'-isopropylurea
[13] BF23: N-(4-hydroxyphenyl)acetamide

A particular concern was raised by metabolite BF23 identified as the most abundant residual compound in milk. This metabolite is paracetamol, used as analgesic drug, and is known to have mutagenic properties. Nevertheless it was verified after the expert meeting that adverse effects involve dose thresholds inducing pronounced liver and bone marrow toxicity (Bergman, 1996)[14]. 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 NNI-750 and its metabolites BF2, BF12, and BF23 were determined in milk and edible tissues. This study is however of limited relevance as conjugates of metabolites were not determined and also due to the fact that residues of BF23 were found in control samples without explanation. Nevertheless, parent compound was found in fat tissues at measurable levels, but only on the highest dose group (2 orders of magnitude above the expected critical potential ruminant exposure).

3.3. CONSUMER RISK ASSESSMENT

As data to establish a reliable residue definition for risk assessment are lacking, the consumer risk assessment is not performed.

Note : The RMS has provided chronic intake calculations based on the exposure to NNI-750 only. These calculations were performed in accordance with the WHO methodology for the adult European consumer, the German 4-6 year old girl and UK infants, toddlers, children and adults. IEDI/NEDIs (International/National Estimated Daily Intakes) were shown to range from 20 to 90 % of the ADI.

3.4. PROPOSED MRLS

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

NNI-750:

Commodity	***MRL (mg/kg)***
Citrus	1
Tomatoes	1
Lettuce	20

4. Environmental fate and behaviour

NNI-750 was discussed at the PRAPeR experts' meeting for environmental fate and behaviour PRAPeR 22 in May 2007. At that time, the active substance was referred to in the available documentation by the pesticide common name buprofezin. This was subsequently identified as inappropriate. As well as the DAR experts considered addendum 2 to volume 3 dated 10/04/2007.

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

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 NNI-750 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 NNI-750 in the environment.

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

The rate of degradation of NNI-750 was estimated from the results of the studies described in 4.1.1 above. DT_{50} were 27-269 days (single first order non linear regression). After normalisation to FOCUS reference conditions[15] (20°C and -10kPa soil moisture content) these single first order DT_{50} were in the range 32-322 days with a geometric mean value 104 days.

Soil dissipation studies (bare soil) were provided from 2 sites located in Germany in glasshouses and two field sites in the USA (North Carolina and California). Using the residue levels of NNI-750 determined over the 0-7.6cm soil layer (USA studies) and 0-20cm (German studies), single first order DT_{50} 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} from the USA field trial sites were normalised to a reference temperature of 20°C following FOCUS kinetics guidance[16]. The consequent DT_{50} 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 uses these dissipation studies to support the applied for intended 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 soil between the rows of crops may be very dry. Dry inter row soil

[15] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.
[16] "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 Chapter 9.

strips would be exposed from pesticide applications (particularly for citrus) and therefore the potential for NNI-750 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} 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 trials sites had always been at or above field capacity. Using this approach soil DT_{50} in dry soils at ¼ field capacity soil moisture would be in the range 60- 166.2 days. The experts agreed that for the outdoor uses in southern Europe that 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) so could not agree that this calculation approach could be considered precautionary. Overall the experts at the meeting felt 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, as the calculation done introduced some additional uncertainty compared to the more usual situation where DT_{50} are derived from reliable field dissipation studies that represented the range of geoclimatic conditions that represent the applied for intended uses.

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

The adsorption / desorption of NNI-750 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 of 1.28). Calculated adsorption $K_f oc$ 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 low mobility of NNI-750 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 NNI-750 sulfoxide (BF-10)[17] (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

NNI-750 was stable under sterile aqueous hydrolysis conditions at 25°C at pH 7 and 9. At 25°C at pH 5 NNI-750 hydrolysed with an estimated single first order DT_{50} of 51 days (study duration 30 days)

[17] NNI-750 sulfoxide (BF-10): 2-tert-butylimino-3-isopropyl-5-phenyl-perhydro-1,3,5-thiadiazin-4-one-1-oxide

forming the metabolites thiobiuret (BF25) (max 19.9%AR study end) and biuret (BF11) (max 9.9%AR study end). In a satisfactory aqueous photolysis experiment (see addendum 2) NNI-750 was shown to be essentially stable to aqueous photolysis. A ready biodegradability test (OECD 301B) indicated that NNI-750 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) then recommended by study guidelines NNI-750 dissipated from the water partitioning to sediment with single first order DT_{50} of 13.5 (sandy) and 20 days (silty clay). Degradation in sediment occurred with single first order whole system DT_{50} being calculated as 47 (sandy) and 51 days (silty clay) with the geomean whole system value being 49 days. The metabolite NNI-750 sulfoxide (BF-10) 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 NNI-750 sulfoxide (BF-10) 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 concentrations were still increasing at the end of the study and that PECsw for NNI-750 sulfoxide (BF-10) were calculated at steps 1 & 2 assuming a higher default[18] value of 300 days. These values for DT_{50} of NNI-750 sulfoxide (BF-10) 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-^{14}C-radiolabel at study end (91days). Residues not extracted from sediment by acetone represented 14-15 % AR at study end. The meeting of experts concluded that for NNI-750 water and sediment DT_{50} of 1000 days (default) and 49 days (geomean whole system values 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 NNI-750 sulfoxide (BF-10) 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 was evaluated up to step 4 for NNI-750 (see addenda 2 and 4) and step 2 for the metabolite NNI-750 sulfoxide (BF-10) (see DAR). The peer review agreed these maximum PEC surface water and sediment as presented in the DAR for NNI-750 sulfoxide (BF-10) up to step 1 for tomato and step 2 for citrus for use in risk assessment. It should be noted that the Koc value used to calculate NNI-750 sulfoxide (BF-10) PEC values 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 sediment water study. However the maximum step 1 PEC in water and sediment for NNI-750 sulfoxide (BF-10) 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 probably represents an overestimate of potential sediment concentrations. The

[18] Default value taken from the aquatic guidance document Sanco/3268/2001 rev.4.

maximum NNI-750 sulfoxide (BF-10) step 2 PEC (both water and sediment) from the citrus use (that only has a single application) would also be reliable enough.

The meeting of experts agreed the PEC values in the addendum 2 for NNI-750 at step 1 and 2 for citrus and step 1 for tomato. They also agreed the step 3 and step 4 (where just spray drift was mitigated) calculations for citrus (also in the addendum 2) but identified that for tomato 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 are considered agreed values that can be used for the risk assessment, as they use standard FOCUS approaches using input parameters agreed by the peer review with the exceptions of the soil DT_{50} where a longer (more conservative) value than necessary was used (arithmetic mean of 136 days compared to the agreed geomean value of 104 days).

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

The conclusions of the peer review were that with the available database of studies the following chemical substance input parameters at FOCUS reference conditions were appropriate to be used in FOCUS groundwater scenario modelling. For NNI-750 single first order laboratory DT_{50} 104 days and a K_{foc} 3042 mL/g, 1/n=0.96.

The applied for representative use of December applications to citrus and May to August applications to tomatoes outdoors were simulated using FOCUS PELMO 3.3.2 using Parent NNI-750 single first order laboratory DT_{50} 136 days, (compared to 104 days agreed by the peer review) and adsorption values as agreed by the peer review. NNI-750 was calculated to be present in leachate leaving the top 1m soil layer at 80th percentile annual average concentrations of <0.001µg/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} had been used in simulations, it was therefore concluded that the potential for contamination of groundwater above the 0.1µg/L parametric drinking water limit by parent NNI-750 from these applied for representative uses is low over a broad range of vulnerable groundwater situations across Europe. The available simulations do not cover the applied for intended uses in glasshouses (tomatoes and lettuce) that include higher rates and numbers of applications than in the available simulations for the outdoor uses. The potential for groundwater exposure is also likely to be low from these uses but no assessment of this has been provided. A data gap was therefore identified.

4.3. FATE AND BEHAVIOUR IN AIR

The vapour pressure of NNI-750 ($4.2x10^{-5}$ Pa at 20°C) means that NNI-750 would be classified under the national scheme of The Netherlands as very slightly volatile, indicating only limited losses due to volatilisation would be expected. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half life estimated at about 7 hours (assuming an atmospheric hydroxyl radical concentration of

$0.5x10^6$ radicals cm^{-3}) indicating that the small proportion of applied NNI-750 that does volatilise would be unlikely to be subject to long range atmospheric transport.

5. Ecotoxicology

NNI-750 was discussed at the PRAPeR experts' meeting for ecotoxicology (PRAPeR 23) in May 2007. At that time, the active substance was referred to in the available documentation by the pesticide common name buprofezin. This was subsequently identified as inappropriate.

5.1. RISK TO TERRESTRIAL VERTEBRATES

NNI-750 is an insect growth regulating insecticide and the proposed uses are in citrus, tomato 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 for the citrus use, and insectivorous birds, medium herbivorous birds, tomato fruit eating birds and large herbivorous mammals were considered for the use in tomato. First tier acute and short term TER values for birds and acute TER values for mammals are all above the relevant Annex VI triggers indicating a low acute risk.

A 5.3% reduction in egg shell thickness was observed at the highest dose in the reproduction study with bobwhite quail. The effect was however not statistically significant. If this effect is taken into account, a TER_{lt} of 1.6 is derived for insectivorous birds in citrus. For the tomato use the TER_{lt} would be 8.0 for insectivorous birds and 9.3 for herbivorous birds. For tomato fruit eating birds the TER_{lt} was calculated to 369 based on maximum mean measured concentration of NNI-750 in tomato from field trials. The residue data are considered to be a worst case, as NNI-750 was applied 3 times in stead of twice at the recommended application rate. If the effects 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 long-term risk to small herbivorous mammals in citrus 70% interception was taken into account. 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 are above the Annex VI trigger. Corrected calculations,

due to amendments of PEC_{soil} and $PEC_{sw,}$ were included in addendum 2 of April 2007. New calculation were again provide for earthworm eating birds and mammal in addendum 4 (September 2007) 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[19] (calculated by EFSA).

5.2. RISK TO AQUATIC ORGANISMS

Based on the available acute toxicity data, the proposed classification of NNI-750 is as very toxic to aquatic organisms with an EC_{50} of less than 1.0 mg/L (>0.42 for *Daphnia magna*). NNI-750 was however not acutely toxic to fish or daphnids at the limit of solubility in the studies (0.33 mg/L). The formulation 'Buprofezin 25 WP' was not significantly more toxic than expected based on the content of NNI-750. Since NNI-750 is an insect growth regulator "spiked water" reproduction study with *Chironomus riparius* is also available. 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% 7 days after dosing) was calculated by EFSA to be 0.17 mg/kg dry weight sediment[20].

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 tomato and Steps 1, 2 and 3 PEC_{sw} values for citrus. 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. Long-term TER values for all groups of aquatic organisms were above the Annex VI trigger for the use in tomato using $twaPEC_{sw}$ values from $FOCUS_{sw}$ Step 2. As the TER calculation should be based on initial PEC_{sw} values when time to effect is not known, new TER calculations were provide in addendum 4 (September 2007), based on new FOCUS calculations including FOCUS step 3. The revised long-term TER values for use in tomatoes were above the Annex VI trigger for all groups of aquatic organisms, including sediment dwellers when calculated on a water basis.
For the use in 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 in 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 the use in citrus was presented in addendum 2 of April

[19] 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

[20] 0.553x0.0248mg NNI-750dosed/0.08007kg sediment in test system=0.17 mg/kg dw sediment. Details taken from page 19 of the original study report.

2007 using initial PEC_{sw} from FOCUS Step 4 calculations. With no spray buffer zones of 20 m all TER values were above the Annex VI trigger indicating a low risk. The risk assessment was accepted in the meeting of experts (PRAPeR 23).

NNI-750 partitions into sediment, and was found in amounts up to 63% of applied test material in the sandy water/sediment study at day 3. As reported above a high risk for *Chironimus riparius* was identified in the FOCUS Step 3 scenarios for the use in 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. However, for the use on tomatoes with 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 scenarious) when expressed on a sediment basis. However, it should be noticed that the NOEC for *C. riparius* is derived from a limit test based on the highest concentration tested and no effects were observed. Therefore, for the field tomato use the NN-750 risk assessment to sediment dwellers is not finalised. Either a new *Chironomus riparius* chronic study where higher doses are tested and or additional PEC sediment with risk management incorporated would be required to finalise this risk assessment.

One metabolite, NNI-750 sulfoxide (BF-10), above 10% of applied dose was detected in the water phase in the water/sediment study. The concentration of this metabolite was increasing during the study and reached 12% at day 56. The metabolite is therefore not covered by the 28 d *Chironomus* study using NNI-750. However, as the NOEC for Chironimus and Daphnia chronic studies are in the same range for NNI-750 and the metabolite is much less acutely toxic to Daphnia compared to the parent, the risk to aquatic insects is considered to be covered.

The bioconcentration factor for whole fish was determined to 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 NNI-750 and the 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 NNI-750 is an insect growth regulator effects on honey bee brood should be tested. No malformations of young workers and no dead pupae were found and the developmental success of the brood treated with Buprofezin 25 WP 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 insect growth regulator in ESCORT II, laboratory studies with *Typhlodromus pyri* (orchard dwelling predatory mite) and *Chrysoperla carnea* (predacious, foliar dwelling) were conducted with the 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 37%. No significant effects on mortality or fecundity compared to the control were detected for *C. carnea*. 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 NNI-750 and the 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 number of juveniles produced at 1 kg a.s./kg dry soil.

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 NNI-750 were detected in the soil degradation studies.

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

No studies with other non-target soil macro-organisms are available. Field / glasshouse soil DT_{90} values for NNI-750 were in the range of 124-208 days, but the fate meeting of experts concluded that a DT90 > 1 year was likely under dry soil conditions that would occur between tree rows when a crop such as citrus is drip irrigated (see section 4.1.2). Therefore, a litterbag study, performed under conditions relevant for citrus, should be required in principle. However, the meeting of experts (PRAPeR 23) did 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.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects on soil respiration and nitrification were tested with NNI-750 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-suseptible: *Panonychus citri, Tetranychus urticae, Plutella xylostella, Adoxophyes sp, Myzus persicae, Tribolium castaneum.*

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

NNI-750 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

Soil

Definitions for risk assessment: NNI-750

Definitions for monitoring: NNI-750

Water

Ground water

Definitions for exposure assessment: NNI-750

Definitions for monitoring: NNI-750

Surface water

Definitions for risk assessment: water: NNI-750 and NNI-750sulfoxide[21]

sediment: NNI-750

Definitions for monitoring: NNI-750.

Air

Definitions for risk assessment: NNI-750

Definitions for monitoring: NNI-750

Food of plant origin

Definitions for risk assessment: Further data are necessary about the toxicological properties of plant metabolites

Definitions for monitoring: NNI-750

Food of animal origin

Definitions for risk assessment: not necessary

Definitions for monitoring: not necessary

[21] NNI-750sulfoxide (BF-10): 2-tert-butylimino-3-isopropyl-5-phenyl-perhydro-1,3,5-thiadiazin-4-one-1-oxide

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
NNI-750	Medium to high persistence Single first order DT_{50} 32-322 days (20°C, pF2 soil moisture)	Low risk to non-target arthropods and earthworms. No conclusion on risk to other non-target macro organisms due to lack of effect studies. Low risk to soil non-target micro-organisms, STP and non-target plants.

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**
NNI-750	Slight mobility K_{foc} 2157-4854 mL/g	No	Yes	Yes	Yes

Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
NNI-750	Very toxic to aquatic organisms, the risk assessment indicated a low risk to aquatic organisms. Further refinements (larger no-spray buffer zones or additional sediment toxicity test) need to identify low risk for sediment dwelling organisms from the field tomato use. The risk for bioaccumulation is considered to be low.
NNI-750 sulfoxide	Low toxicity to fish, daphnids and algae.

Air

Compound (name and/or code)	**Toxicology**
NNI-750	Not acutely toxic via inhalation

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

- The active substance does not have an ISO common name the name buprofezin is not applicable to the compound evaluated (relevant for all uses evaluated, data gap identified by meeting of experts May 2007, no submission date proposed by the notifier; refer to chapter 1)
- A sprayability study where wettability and suspensibility are addressed (relevant for all uses evaluated, data gap identified by meeting of experts May 2007, no submission date proposed by the notifier; refer to chapter 1)
- Further data characterising the toxicological properties of the raw and processed plant metabolites are necessary (relevant for all uses evaluated, data gap identified by meeting of experts December 2007, no submission date proposed by the notifier; refer to chapter 2.8 and 3.1.1)
- Depending on the residue definition for risk assessment, further supervised field residue trials on primary and rotational crops, processing studies, as well as further consideration of animal exposure and potential transfer of toxicologically relevant residues to animal commodities, might be needed, refer to points 3.1 and 3.2).
- Field rotational crop studies relevant to current practices with quantification of residues according to the residue definitions for monitoring (relevant for uses in tomatoes and lettuce; data gap identified by the expert meeting; no submission date proposed by the notifier; refer to point 3.1.2).
- A further groundwater exposure assessment is required (relevant for the protected (greenhouse) uses on tomatoes and lettuce; data gap identified by EFSA; no submission date proposed by the notifier; refer to point 4.2.2).
- A refined risk assessment for sediment dwellers for NNI-750 is required. Either as a new Chironomus study testing higher sediment concentrations or as FOCUS step 4 calculations with no spray buffer zones (relevant for use in field tomatoes; data gap identified by EFSA; no submission date proposed by the notifier; refer to point 5.2).
- A reproduction test with Collembola exposed to NNI-750 is required (relevant for use in citrus; data gap identified by the meeting of experts; no submission date proposed by the notifier; refer to point 5.6).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide on tomato, lettuce and citrus. Full details of the gap can be found in the attached end points. It should be noted that only the use as an insecticide has been considered during the peer review process, the acaricide use has not been considered.

The representative formulated product for the evaluation was "Applaud 25 WP", a wettable powder formulation (WP). It was concluded during the peer review process that the name buprofezin can not be used for this active substance.

Adequate methods are available to monitor NNI-750 in all matrices.
Only single methods for the determination of residues are available since a multi-residue-methods like the German S19 or the Dutch MM1 are not applicable due to the nature of the residues.
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 was requested.

In mammals, NNI-750 acute oral, dermal or inhalation toxicity is low. NNI-750 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 0.90 mg/kg bw/day while in mice it is 1.82 mg/kg bw/day. NNI-750 is neither genotoxic nor carcinogenic. NNI-750 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 (based on decreased food consumption and increased water intake, skeletal effects and subcutaneous oedema, respectively).It was agreed not to propose any classification.
NNI-750 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 tomato and citrus tractor and hand held spraying and lettuce and tomatoes indoor with the use of PPE. The bystanders showed estimated exposure levels below the AOEL for both tomato and citrus. Worker exposure was estimated to be below the AOEL when handling tomato or lettuce in glasshouse or tomato outdoors. Exposure was above the AOEL even with PPE when handling citrus.

The metabolism of NNI-750 in plants has been elucidated. The parent compound is the major constituent of the final residue. Minor plant metabolites were identified. Their structures differ significantly from that of NNI-750 and their toxicological properties have not been sufficiently investigated. Also under processing conditions degradation products are formed with unknown toxicological potential. Therefore, although a residue definition can be proposed for monitoring (NNI-750), the residue definition for risk assessment has not been set. For this reason a consumer risk assessment is currently not possible.
A potential transfer of residues to rotational crops has been noted.
No residues are expected in animal commodities.

The information available on the fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment at the EU level. For the applied for intended field uses, the potential for groundwater exposure by NNI-750 above the parametric drinking water limit of

0.1 µg/L, is low. A groundwater exposure assessment for the applied for protected (green house) uses that have a more critical dose rate than the field uses is not available, so a data gap was identified, however the potential for groundwater exposure from the protected uses is also likely to be low.

The acute toxicity of NNI-750 is low to birds and mammals. Following the principles of SANCO/ 4145/2000 the acute and long-term risk to birds and mammals were assessed to below. For the small herbivorous mammal in citrus an interception of 70% was taken in to account to reach a TER-value above the Annex IV trigger. Low risk is foreseen for earthworm- and fish-eating birds and mammals, as the risk to birds and mammals ingesting contaminated drinking water is also considered too be low.

NNI-750 is as very toxic to aquatic organisms. TER values for use in tomatoes indicate low risk without any risk mitigation. Buffer zones of 20 m are required for use in citrus to identify low risk. Further data are needed to address the risk to sediment dwelling organisms from NNI-750. NNI-750 is not considered to bioaccumulate in fish.

Low risk was identified for all other non-target organism groups, except for a data gap on a reproduction test with Collembola, to address the risk of use in citrus.

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

- Based on the reviewed aquatic data a risk mitigation e.g. such as no-spray buffer zone of 20 m is required to demonstrate TER values above the Annex VI trigger in all FOCUS scenarios for use in citrus.
- Use of PPE to be considered to reduce exposure for operators and workers.

Critical areas of concern

- There is no ISO common name for this active substance.
- A reliable consumer exposure assessment cannot be performed as data are missing to determine an appropriate residue definition for risk assessment. Aniline has also been identified as a degradation product of concern under processing conditions. Nevertheless it is also recognised that the consumer exposure to aniline may result from many other pesticides or sources and that a meaningful risk assessment should consider all these sources.
- The risk assessment for sediment dwellers can not be finalised for the use in field tomatoes.
- The risk assessment for soil living macro-organisms can not be finalised for the use in citrus.

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

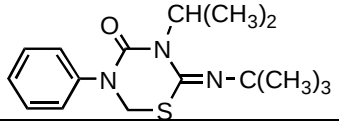
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	The active substance was notified as Buprofezin however this ISO name refers to a mix of E and Z isomers. Only the Z isomer exists therefore the name buprofezin can not be used for this substance. As a result of this the manufacturer's development code (NNI-750) has been used.
Function (e.g. fungicide)	Insecticide and acaricide

Rapporteur Member State	Finland
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 ‡	None for NNI-750
CAS No ‡	69327-76-0
EC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification (including year of publication) ‡	Not allocated
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 ‡	

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

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 l · mol^{-1} · cm^{-1} Acidic λ_{max} = 229 nm, ε= 16463 l · mol^{-1} · cm^{-1} Basic *λ_{max} = 245 nm, ε= 11650 l · mol^{-1} · cm^{-1}* *λ_{max} = 220 nm, ε= 9240 l · 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)

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

Summary of representative uses evaluated *

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			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	[1], [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	[1], [4]
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	3	[1]
Citrus	S-EU	Applaud 25 WP	F	Scales, Whitefly	WP	250 g/kg	High volume spraying	BBCH 89	1		25	4000	1000	7	[1], [3]

1 The risk assessment to consumers is not finalised.
2 The risk assessment to sediment dwellers for NNI-750 is not finalised.
3 The risk assessment to soil dwelling organisms for NNI-750 is not finalised.
4 The exposure assessment to groundwater is not finalised.

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

* 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

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

Appendix 1.2: Methods of Analysis

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

Technical as (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		NNI-750
Food of animal origin		none
Soil		NNI-750
Water	surface	NNI-750
	drinking/ground	NNI-750
Air		NNI-750

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	GC-NPD, 0.01 mg/kg NNI-750 (cucumber/high water content, lemon/high acid content)
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 NNI-750
Water (analytical technique and LOQ)	HPLC/UV, 0.1 µg/l NNI-750 (surface water)
Air (analytical technique and LOQ)	GC/MSD, 0.27 µg/m^3 NNI-750 (36 ^{o}C, 85 % humidity)
Body fluids and tissues (analytical technique and LOQ)	Not relevant, NNI-750 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

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

Appendix 1.3: Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (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)	NNI-750 and metabolites
Toxicologically relevant compounds ‡ (environment)	NNI-750

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 2y dog: 2mg/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	-

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

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 ‡	2y rat: 1mg/kg bw/day Mouse: 1.8 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 ‡	Decreased foetal weights, and increased variations 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	-

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

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 Plant metabolite BF26, oral LD_{50}: 50-300 mg/kg BF4 and BF26 were not mutagenic in reverse gene mutation tests. Metabolites found in hydrolysis study, B11 and 1-tert-butyl-3-isopropyl-5-phenyl-2-thiobiuret, and the plant metabolite B26 were not structurally alerting using DEREK. The four 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	2y rat	100
AOEL ‡	0.04 mg/kg bw	90 d dog	100, 40% oral absorption
ARfD ‡	0.5 mg/kg bw	Rat developmental study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Applaud 25 WP	Concentrate: 40 % (default, based on limited oral absorption) Spray dilutions: 40 % (default, based on limited oral absorption)

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

Exposure scenarios (Annex IIIA, point 7.2)

Operator	German model Tractor mounted boom sprayer (tomato) % 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)[a] % 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) % AOEL 325 (no PPE) % AOEL 33 Gloves during mixing/loading and application, coverall and sturdy footwear during application UK POEM Hand-held application, low crops; field (tomato) % AOEL 800 (no PPE) % AOEL 70 Gloves during mixing/loading and gloves and impermeable coverall during application Dutch, Hand held sprayer: glasshouse (tomato, lettuce) % AOEL 725 (no PPE) % AOEL 73 Gloves and respiratory protector during mixing/loading and application
Workers	Worker exposure was estimated to be below the AOEL with gloves when handling tomato or lettuce in glasshouse or tomato 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 applications on tomato and citrus.

[a]*It is noted that the calculation for this scenario has been performed considering an application rate of 0.25 kg/ha instead of 1 kg/ha; however, considering the use of RPE and gloves during mixing and loading and gloves, broad-brimmed headwear, coverall and sturdy footwear during application the estimated exposure is expected to be below the AOEL (about 75%).*

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

	RMS/peer review proposal
Substance (name)	No classification

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

Appendix 1.4: Residues

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

Plant groups covered	Citrus (F), tomato (F), lettuce (L) and cotton (P/O)
Rotational crops	Radish (R), lettuce (L) and wheat (C)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Standard hydrolysis studies
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No, hydrolysis study revealed potentially harmful products, which are not present in raw commodities.
Plant residue definition for monitoring	NNI-750
Plant residue definition for risk assessment	Data not sufficient
Conversion factor (monitoring to risk assessment)	Not considered.

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 necessary.
Animal residue definition for risk assessment	Not necessary.
Conversion factor (monitoring to risk assessment)	Not necessary
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	The parent, NNI-750 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)

NNI-750 is stable for at least 2.4 years in tomato and 6 month in processed tomato fractions, 2.6 years in lettuce and 12 months in citrus

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

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

	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, 0.12 mg/kg diet (dairy cattle), 0.36 mg/kg diet (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 (Specify the feeding rate in cattle and poultry studies considered as relevant) (dairy cows, 0.4 mg/kg bw/d) Residue levels in matrices : Mean (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	

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

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 or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/ comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Tomato	S-EU, Field	2 x 0.01, 0.03, 0.05, 0.06, 2 x 0.08, 4 x 0.09		0.2	0.09	0.08
Tomato	N-EU + S-EU, Greenhouse	0.05, 0.12, 2 x 0.13, 0.14, 0.16, 0.24, 0.30, 0.32, 2 x 0.52		1.0	0.52	0.16
Lettuce	N-EU + S-EU, Greenhouse	3.81, 4.00, 4.36, 4.58, 4.63, 5.10, 9.00, 11.71, 12.49, 12.61, 13.23, 13.50		20	13.50	7.07
Citrus	S-EU, field	mandarin: 0.11, 0.22, 3 x 0.23, 0.41, 0.45, 0.46 orange: 0.17, 2x 0.21, 0.23, 0.25, 0.31, 0.32, 0.37		1.0	0.46	0.23

(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

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

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

ADI	0.01 mg/kg bw/d
TMDI (% ADI) according to WHO European diet	Inconclusive (residue definition for risk assessment not set)
TMDI (% ADI) according to national (to be specified) diets	Inconclusive (residue definition for risk assessment not set)
IEDI (WHO European Diet) (% ADI)	Inconclusive (residue definition for risk assessment not set)
NEDI (specify diet) (% ADI)	Inconclusive (residue definition for risk assessment not set)
Factors included in IEDI and NEDI	None, data gap relating to processing factors
ARfD	0.5 mg/kg bw
IESTI (% ARfD)	Inconclusive (residue definition for risk assessment not set)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Inconclusive (residue definition for risk assessment not set)
Factors included in IESTI and NESTI	Inconclusive (residue definition for risk assessment not set)

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Tomato/washing/washed tomato	2	1.45[a]	Not calculated	Not calculated
Tomato/ preparation of vegetables juice/tomato juice	2	0.6	Not calculated	Not calculated
Tomato/preparation of other vegetables products/tomato puree (concentrate)	2	1.45	Not calculated	Not calculated
Tomato/ preparation of other vegetables products/ketchup	2	0.75	Not calculated	Not calculated
Tomato/preparation of canned vegetable/canned tomato	2	0.55	Not calculated	Not calculated
Orange/distribution in the edible/non edible portion/peel	14	3.15	Not calculated	Not calculated
Orange/distribution in the edible/non edible portion/pulp	14	0.18	Not calculated	Not calculated
Orange/preparation of fruit juice/orange juice	2	0.57	Not calculated	Not calculated

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Orange/preparation of fruit juice/wet pomace	2	1.78	Not calculated	Not calculated
Orange/preparation of fruit juice/Dry pomace	2	5.26	Not calculated	Not calculated

[a] Residues in raw agricultural commodity at limit of quantification, variable results obtained

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

Citrus fruit	1 mg/kg
Lettuce	20 mg/kg
Tomatoes	1 mg/kg

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

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	25.4, 50.9 % after 98, 91 d, [^{14}C-phenyl]-label (n=2) Sterile conditions: not studied
Non-extractable residues after 100 days ‡	22.8, 33.0 % after 98, 91 d, [^{14}C-phenyl]-label (n=2) 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 NNI-750

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

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[22]	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]
Sandy loam soil		6.4	10 °C/ 45 %	170 / 678			TPEM [1]
Arithmetic mean					135.4		
Geometric mean/median					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[22]	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/median					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.

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

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

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[23]	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							

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

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

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 Elution (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
	Aged for (d): 60 d Time period (d): 45 d Elution (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

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

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 DT_{50} 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**

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

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 BF-25: 19 % AR (30 d) Met BF-12: 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 (eg max in water x after n d. Max. sed x % after n 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/median				49						

*observed decline including partitioning between phases, not degradation

Metabolite: NNI-750 sulfoxide (BF-10)	Distribution (eg max in water 12 % after 91 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

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

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

Parent NNI-750 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) Kfoc: 3041 L/kg Crop interception: Full canopy (BBCH 89)
Parameters used in FOCUSsw step 3 (if performed)	Vapour pressure: 0.42 x 10^{-4} Kfoc: 3041 L/kg 1/n: 0.96 (Freundlich exponent for soil)
Application rate	STEP 1: 400 g ai/ha (tomato), 1000 g ai/ha (citrus) STEP 2: 2 equal doses of 200 g ai/ha, 3 days apart (tomato), 1000 g ai/ha (citrus) 1 dose STEP 3: *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

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

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

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 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	3.93	---	PEC 100 days	110.55	---

FOCUS STEP 3 Tomato 2 x 200 g a.s./ha	Water body	Application dates	PEC_{SW} (µg/L)		PEC_{SED} (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

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

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

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

FOCUS STEP 3 Citrus 1000 g a.s./ha	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (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
		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

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 Citrus 1000 g a.s./ha	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

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

FOCUS STEP 4 Citrus 1000 g a.s./ha	Water body	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
			Actual	TWA	Actual	TWA
		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
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

Metabolite NNI-750 sulfoxide Parameters used in FOCUSsw step 1 and 2	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 L/kg (Epiwin-program) Formation fraction in water/sediment study 13 % Formation fraction in soil 1.0 x 10^{-3} %
Parameters used in FOCUSsw step 3 (if performed)	Not performed
Application rate	STEP 1: 400 g ai/ha (tomato), 1000 ga i/ha (citrus) STEP 2: 2 equal doses of 200 g ai/ha, 3 days apart (tomato), 1000 g ai/ha (citrus) 1 dose
Main routes of entry	Default values from Step 1 and STEP 2 -calculator

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

FOCUS STEP 1 Tomato N&S 400 g a.s./ha	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
PEC max	0h	0.504		-	
	24h	-		2.32	
FOCUS STEP 1 Citrus 1000 g a.s./ha	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
PEC max	0h	7.17		-	
	24h	-		33.00	

FOCUS STEP 2 Citrus 1000 g a.s./ha	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Southern EU PEC max	0 h	7.17		-	
	5 d	-		32.7	

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

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)	Model used: FOCUS-PELMO leaching model (version 3.3.2) 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) Kfoc: 3041 (mean of 6 soils), mean 1/n =0.96 No major metabolites
Application rate	Citrus: 0.3 kg/ha (Maximum application rate of 1 kg ai/ha 70% interception by the crop) Tomato: 2 x 0.1 kg/ha (3 days interval) (Maximum application rate of 0.2 kg ai/ha 50% interception by the crop)

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

Maximum concentration	< 0.001 µg/l in all scenarios for both crops

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

$PEC_{(gw)}$ From lysimeter / field studies

Parent	1st year	2nd year	3rd year
Annual average (µg/L)	Not available, not required	Not available, not required	Not available, not required

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 x 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 x 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 residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: NNI-750 Surface Water: NNI-750, NNI-750sulfoxide Sediment: NNI-750 Ground water: NNI-750 Air: NNI-750

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

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

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)

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

Appendix 1.6: Effects on non-target Species

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

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	
Additional higher tier studies ‡				

[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
Higher tier refinement (Birds)				
Not required	Acute			
	Short-term			
	Long-term			

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

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
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 bird 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 NNI-750 in tomato 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)

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

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[3] (mg/L)
Laboratory tests ‡				
Fish				
Rainbow trout	Technical NNI-750	96 hr (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	NNI-750sulfoxide	96 h (static)	LC_{50}	75 mg/L (nom/mm)
Aquatic invertebrates				
Daphnia magna	Technical NNI-750	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	NNI-750 sulfoxide	48 h (static)	EC_{50} [1]	> 100 mg/L (nom/mm)
Sediment dwelling organisms				
Chironomous riparius	Technical NNI-750	28 d (static)	NOEC	0.1 mg/L (nom/mm) 0.17mg/kgdw sediment[4]
Algae				
Selenastrum capricornutum	Technical NNI-750	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

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[3] (mg/L)
Selenastrum capricornutum	NNI-750 sulfoxide	72 h (static)	EbC_{50} ErC_{50}	49 mg/L (mm) > 740 mg/L (estim.)
Microcosm or mesocosm tests Not required.				

[1] EC50 = 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 NNI-750dosed/0.08007kg sediment in test system=0.17 mg/kg dw sediment. Details taken from page 19 of the original study report

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

FOCUS Step1

Tomato (South and North), 0.4 kg a.s/ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	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
NNI-750 sulfoxide	Fish	75	Acute	0.504		148810	100
NNI-750 sulfoxide	Daphnia	> 100	Acute	0.504		>198413	100
NNI-750 sulfoxide	Algae	49	Acute	0.504		97222	10

[1] PECsw used since NNI-750 was spiked in water phase

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

FOCUS Step 2

Tomato (South and North), 2 x 0.2 kg a.s/ha, NNI-750

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PECi (µg/L)	TER	Annex VI Trigger
a.s.	N & S	Fish	> 0.33	Acute	3.93	> 84.0	100
a.s.	N & S	Fish	0.052	Chronic	3.93	13.2	10
a.s.	N & S	Daphnia	> 0.42	Acute	3.93	> 106.8	100
a.s.	N & S	Daphnia	0.080	Chronic	3.93	20.4	10
a.s.	N & S	Algae	> 2.1	Acute	3.93	> 534.4	10
a.s.	N & S	Chrinonomus[1]	0.10	Chronic	3.93	25.4	10

[1] PECsw used since NNI-750 was spiked in water phase

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Tomato (South and North), 2 x 0.2 kg a.s/ha, NNI-750, Scenario R4 with worst case PECsw to cover all the other scenarios

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECi (µg/L)	TER	Annex VI trigger
a.s.	R4	Stream	Fish	Acute	> 0.33	2.25	> 146.7	100
a.s.	R4	Stream	Fish	Chronic	0.052	2.25	23.1	10
a.s.	R4	Stream	Daphnia	Acute	> 0.42	2.25	> 186.7	100
a.s.	R4	Stream	Daphnia	Chronic	0.080	2.25	35.5	10
a.s.	R4	Stream	Algae	Acute	> 2.1	2.25	> 933.3	10
a.s.	R4	Stream	Chrinonomus[1]	Chronic	0.10	2.25	44.4	10

[1] PECsw used since NNI-750 was spiked in water phase

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

FOCUS Step 3

Tomato (South and North), 2 x 0.2 kg a.s/ha, NNI-750, using PEC sediment

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point[1] (mg/kg sed)	PECi (mg/kg sed)	TER	Annex VI trigger
a.s.	D6	Ditch	Chrinonomus	Chronic	0.17	0.0043	39.8	10
a.s.	R2	Stream	Chrinonomus	Chronic	0.17	0.0593	**2.8**	10
a.s.	R3	Stream	Chrinonomus	Chronic	0.17	0.0150	11.4	10
a.s.	R4	Stream	Chrinonomus	Chronic	0.17	0.0234	**7.3**	10

[1] EFSA calculation based on 0.553x0.0248mg NNI-750dosed/0.08007kg sediment in test system=0.17 mg/kg dw sediment. Details taken from page 19 of the original study report

FOCUS Step1

Citrus (South), 1.0 kg a.s/ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	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
NNI-750 sulfoxide	Fish	75	Acute	7.17	-	10460	100
NNI-750 sulfoxide	Daphnia	> 100	Acute	7.17	-	>13947	100
NNI-750 sulfoxide	Algae	49	Acute	7.17	-	6834	10

[1] PEC_{sw} used since NNI-750 was spiked in water phase

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

FOCUS Step 2

Citrus (South), 1.0 kg a.s/ha, NNI-750

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC i (µg/L)	TER	Annex VI Trigger
a.s.	South	Fish	> 0.33	Acute	52.42	>6.3	100
a.s.	South	Fish	0.052	Chronic	52.42	**1.0**	10
a.s.	South	Daphnia	> 0.42	Acute	52.42	>8.0	100
a.s.	South	Daphnia	0.08	Chronic	52.42	**1.5**	10
a.s.	South	Chrinonomus[1]	0.10	Chronic	52.42	**1.9**	10

[1] PECsw used since NNI-750 was spiked in water phase

FOCUS Step 3

Citrus (South), 1.0 kg a.s./ha, NNI 750

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECi (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
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

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

FOCUS Step 4

Citrus (South), 1.0 kg a.s./ha, NNI 750

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PEC i (µg/L)	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

Bioconcentration				
	Active substance	Metab. 1	Metab. 2	Metab . 3
$logP_{O/W}$		Not required		
Bioconcentration factor (BCF) ‡	464 ± 58 (modelled), 509 measured in whole fish tissue	Not required		
Annex VI Trigger for the bioconcentration factor	100 for substance which is not readily biodegradable	Not required		
Clearance time (days) (CT_{50})	0.5 ± 0.04 days	Not required		

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

Bioconcentration		
(CT_{90})	Rapidly eliminated from fish tissues during depuration. After 7 days 98 % AR was depurated from the whole fish.	Not required
Level and nature of residues (%) in organisms after the 14 day depuration phase	3.19 mg/kg in edible tissues 23.9 mg/kg in whole fish 30.7 mg/kg in non-edible tissues	Not required
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)	Not required

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	> 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 control after application of 4 kg NNI-750 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: 1 kg as/ha

Test substance	Route	Hazard quotient	Annex VI Trigger
Citrus	Oral	< 10	50
	contact	< 10	50

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

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha)
Typhlodromus pyri ‡	a.s	Mortality	> 3000
Aphidius rhopalosiphi ‡		Mortality	*

Not required for insect growth regulators (Escort II).

HQ is not relevant for insect growth regulators (Escort II).

Further laboratory and extended laboratory studies ‡

Species	**NNI-750[1] (kg a.s./ha)**	**Endpoint Mortality (%) (Abbott control corrected)**	**Endpoint**	**Endpoint value**	**Trigger 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	50 %
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***	50 %
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	50 %
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	50 %

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

*Trigger is not exceeded at the highest intended application rate of 1 kg as/ha.

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

Field or semi-field tests As the laboratory tests indicate a low hazard potential with regard to non-target arthropods at the highest intended application rate of 1 kg as/ha, no field testing is required.

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

Test organism	Test substance	Time scale	End point
Earthworms			
Eisenia foetida	a.s. ‡	Acute 14 days	LC50 > 500 mg/kg soil*
Eisenia foetida	a.s. ‡	Chronic 8 weeks	NOEC = 250 mg/kg soil*
Eisenia foetida	Applaud 25 WP	Acute	LC_{50} > 500 mg a.s./kg soil*
Other soil macro-organisms			
Not required			
Collembola			
Not required			
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡	28 days	No effect up to 5 kg as/ha
Carbon mineralisation	a.s. ‡	28 days	No effect up to 5 kg as/ha
Field studies			
Not required			

***** The LC_{50} values and NOEC value have been divided by 2, since the log Pow for NNI-750 is 4.8.

Toxicity/exposure ratios for soil organisms

Application rate: 1 kg as/ha

Test organism	Test substance	Time scale	Soil PEC* mg as/kg	TER	Trigger
Earthworms					
Eisenia foetida	a.s. ‡	Acute	1.33	376	10
Eisenia foetida	a.s. ‡	Chronic	1.33	188	5
Eisenia foetida	Preparation	Acute	1.33	376	10

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

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

Preliminary screening data

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

NNI-750 had no herbicidal activity on non target plant species germination, seedling growth and development at any of the concentrations from 100 g ai/ha up to 10000 g ai/ha of NNI-750.

Laboratory dose response tests or any additional studies (e.g. semi-field or field studies)

Not required

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

Respiration inhibition test OECD 209	Endpoint
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	NNI-750
water	NNI-750
sediment	NNI-750
groundwater	NNI-750

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	R50/53 Very toxic to aquatic organisms, may cause long term adverse effects in the aquatic environment

	RMS/peer review proposal
Preparation	R51/53 Toxic to aquatic organisms, may cause long term adverse effects in the aquatic environment

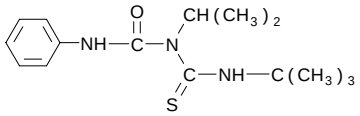
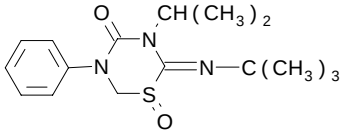
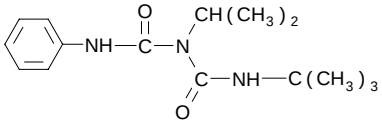
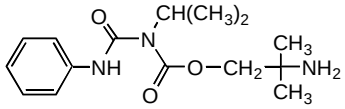
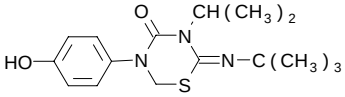
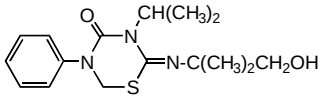
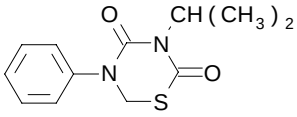
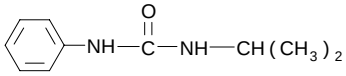
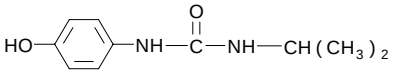
‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

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

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

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
thiobiuret BF25	1-*tert*-butyl-3-isopropyl-5-pheny-2-thio-biuret	
NNI-750 sulfoxide BF10 A-12	2-*tert*-butylimino-3-isopropyl-5-phenyl-perhydro-1,3,5-thiadiazin-4-one-1-oxide	
biuret BF11 A-14	1-*tert*-butyl-3-isopropyl-5-phenybiuret	
BF26 (MetaboliteA)	2-amino-2-methylpropyl-2-methylethyl-4-phenylallophate	
BF2	2-tert-butylimino-3-isopropyl-5-(4-hydroxyphenyl)-perhydro-1,3,5-thiadiazin-4-one	
BF4	2-(2-hydroxy-1,1-dimethylethylimino)-3-isopropyl-5-phenyl-perhydro-1,3,5-thiadiazin-4-one	
BF9	3-isopropyl-5-phenyl-perhydro-1,3,5-thiadiazin-2,4-dione	
BF12	N-Isopropyl-N'-phenylurea	
BF13	N-(4-hydroxyphenyl)-N'-isopropylurea	
BF23	N-(4-hydroxyphenyl)acetamide