CONCLUSION ON PESTICIDE PEER REVIEW

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

Issued on 30 September 2008

SUMMARY

Lufenuron is one of the 84 substances of the third stage Part B 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 six months a conclusion on the risk assessment to the EU-Commission.

Portugal being the designated rapporteur Member State submitted the DAR on lufenuron in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 20 September 2006. The peer review was initiated on 20 April 2007 by dispatching the DAR for consultation of the Member States and the sole applicant Syngenta Ltd. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in May - June 2008.

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

This conclusion was reached on the basis of the evaluation of the representative uses as an insecticide on grapes and tomatoes as proposed by the notifier. Full details of the GAP can be found in the attached list of endpoints.

The representative formulated product for the evaluation was "Match 050 EC", an emulsifiable concentrate (EC).

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

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a modified multi-method (The German S19 method). The extraction procedure was as detailed in S19 however, the analysis was performed by LC-MS/MS which is a detection method not used in the multi-method.
For the other matrices only single methods are available to determine residues of lufenuron.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. The outstanding issue is that the specification is not agreed.

With regard to its toxicological properties, lufenuron has shown a potential of bioaccumulation in fat, and a systemic bioavailability of 70%, with a very low metabolism. During the acute toxicity testing, lufenuron showed skin sensitisation properties and the classification as **R43 "May cause sensitisation by skin contact"** was proposed. In oral short term studies with different species, clinical signs of neurotoxicity (tonic-clonic seizures or convulsions) and liver changes were observed, as well as some deaths in one dog study resulting in the proposed classification **Xn, R48/22 "Harmful: danger of serious damage to health by prolonged exposure if swallowed"**. No mutagenic or carcinogenic potential was detected in the available studies. In the long term studies, the incidence and severity of the convulsions in both species were also taken into account for the setting of the NOAELs. No specific adverse effect on fertility or embryofoetal development was observed in the studies for reproductive toxicity, with low maternal toxicity (reduced body weight) and minimal offspring toxicity (delayed righting reflex). In a 4-month neurotoxicity study with rats, convulsions or fasciculations were induced at the high dose without any impairment of motor/cognitive functions or histopathological changes in the nervous system.
The agreed **acceptable daily intake** (**ADI**) was **0.015 mg/kg bw/day** based on the second 1-year dog study (Altman, 1995), and the agreed systemic **acceptable operator exposure level** (**AOEL**) was **0.01 mg/kg bw/day** using the same dog study but applying a correction factor for bioavailability (70%). Both reference values were derived with the use of a safety factor of 100. The setting of an acute reference dose (ARfD) was not considered necessary. The agreed dermal absorption values for humans were 13% for the dilution and 2% for the concentrate. The operator exposure estimates with the German model for use in field or in greenhouse didn't show exposure levels above the AOEL even without the use of personal protective equipment.

The metabolism of lufenuron has been tested in three crop categories namely tomato (fruits), cabbage (leafy crop) and cotton (pulses and oilseeds). Lufenuron is always the major component of the residue, no significant metabolites were found. It was concluded that the residue definition for risk assessment and monitoring is lufenuron. A full set of residue trials were supplied for grapes in the north and south of Europe. A full set of residues trials data were available for protected tomatoes; a reduced data set was accepted for outdoor tomatoes in the south as the use is much less critical.

The stability of residues in freezer storage was demonstrated for a period of two years. Sufficient processing data were submitted for tomatoes and grapes which showed an overall reduction of the residues in processed commodities. The rotational crop studies demonstrated that residues of lufenuron are unlikely to occur in crops planted after the treated crop is harvested. Given that lufenuron is lipophilic it is unlikely to be taken up by plants. The only possible issue would be soil contamination but this will easily be removed during preparation of food before consumption.
From the representative uses in grape and tomato evaluated there is no animal intake according to the current guidance. However, metabolism studies in hens and goats were provided that demonstrated that the only significant residue that will be present is lufenuron. Feeding studies were also provided but it can not be concluded if the dose levels were appropriate, because there is no animal consumption expected for the representative crops. Lufenuron is a pair of enantiomers and it is currently not addressed if the ratio remains the same in the plant metabolism. Potentially the consumer risk assessment could under estimate the risk by a factor of 2 (assuming the residue is only 1 isomer and all the toxicity comes from it). For the UK consumer model intakes were highest for the vegetarian population subgroup at 10 % of the ADI using the STMR and 80% of the ADI when using the proposed MRLs. For the WHO European diet the TMDI was 3.42 % and IEDI was 0.62 %. For the Portuguese diet the TMDI was 20.22% and the NEDI was 2.63%. An acute risk assessment has not been conducted as an ARfD has not been set.

In soil under aerobic conditions lufenuron exhibits high to very high persistence forming the major soil metabolites CGA 238277[2] (max. 32% applied radioactivity (AR)) which exhibits low to moderate persistence and CGA 224443[3] (max. 33% AR) which exhibits moderate to medium persistence. Under sunlight the major metabolite CGA 149772[4] can be formed (max. 11%AR) which exhibits low persistence. Mineralisation of the dichlorophenyl ring to carbon dioxide was relatively limited accounting for 1-7 % AR after 91-100 days; this value for the difluorophenyl ring was 34% AR at 90 days. The formation of unextractable residues was a sink, accounting for 17-59% AR (range for both rings) after 90-100 days. Lufenuron is immobile in soil. CGA 238277 exhibits slight mobility, CGA 224443 is immobile or exhibits slight mobility and CGA 149772 exhibits very high mobility in soil. There was no indication that adsorption of either lufenuron or these metabolites were pH dependent.

In dark natural sediment water systems lufenuron partitioned rapidly to sediment where it degraded, exhibiting moderate to high persistence in sediment, to the metabolites CGA 238277 and CGA 224443 which exhibited moderate and high persistence respectively. The terminal metabolite, CO_2, accounted for only 0.2 % AR of the dichlorophenyl ring by 90 days but 11.8-36% AR for the difluorophenyl ring at 90 days. Unextracted sediment residues were a sink representing 6-15% AR and 12-37% AR for each radiolabel respectively at 90 days). The necessary surface water and sediment exposure assessments were appropriately carried out using the agreed FOCUS scenarios

[2] CGA 238277: [2,5-dichloro-4-(1,1,2,3,3,3-hexafluoro-propoxy)-phenyl]-urea
[3] CGA 224443: 2,5-dichloro-4-(1,1,2,3,3,3-hexafluoro-propoxy)-phenylamine
[4] CGA 149772: 2,6-difluorobenzamide

approach for lufenuron at steps 1-4, with spray drift mitigation being applied at step 4. For the metabolites CGA 238277 and CGA 224443 and CGA 149772 that may leach from soil to surface water appropriate FOCUS step 1 and 2 calculations were carried out. These values are the basis for the risk assessment discussed in this conclusion. Information on the fate and behaviour in soil and water of the individual enantiomers of lufenuron is not available. The potential for groundwater exposure from the applied for intended uses by lufenuron, CGA 238277, CGA 224443 and CGA 149772 above the parametric drinking water limit of 0.1 µg/L, was concluded to be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios.

The acute toxicity to birds and mammals and the short-term toxicity to birds were considered to be low from exposure to lufenuron. Long-term reproductive endpoints of 19.7 and 8.7 mg a.s./kg bw/d were agreed by Member State experts for birds and mammals respectively. TERs from the standard tier 1 risk assessment indicated a low risk for all intended outdoor uses, except for the risk to small herbivorous mammals from the use in vine. A refined risk assessment provided after the peer-review and agreed by EFSA indicated a low risk, based on a vine foliar interception factor of 70%. The risk from consumption of contaminated drinking water from puddle was assessed as low. The risk from secondary poisoning for the worst-case vine use was assessed as low, based on a no-spray buffer zone of 5 m and 10 m respectively for fish eating birds and mammals. The potential for biomagnification was assessed as high for birds and mammals. Food-chain modelling indicated a low risk for all steps of the food chain for the worst case use in vine, based on appropriate mitigation measures (e.g. no-spray buffer zones). No mitigation measures were required for the tomato use. The risk to birds and mammals from the metabolite CGA 224443 was assessed as low by the RMS after the peer-review.
The toxicity of lufenuron suggested a classification as very toxic to aquatic organisms. The lowest acute end point value for *Daphnia magna* was an EC_{50} of 0.4 µg a.s./L, based on a formulation study. The lowest chronic toxicity to fish (NOEC=20 µg a.s./L) was identified from a fish full life cycle study. A lower NOEC of 2 µg a.s./L could potentially be derived from a chronic toxicity study with fish, pending further statistical analysis. The chronic study to daphnia was not accepted by member state experts. No new study was required as chronic toxicity to invertebrates was covered by a microcosm study. A NOAEC of 0.1 µg a.s./L from the microcosm study was agreed by member state experts with an assessment factor of 2-3. The aquatic risk assessment for the tomato use indicated a low risk, based on the microcosm endpoint and no-spray buffer zones of 5 m. For use in vine a low risk was identified, based on a no-spray buffer zone of approximately 25 m. The latter assessment would be based on an assessment factor of 2. Application of an assessment factor of 3 would require further refinement of the risk characterisation for potentially more susceptible FOCUS surface water scenarios. The risk to sediment dwellers from lufenuron exposure was assessed as low in case of a no spray buffer zone of 5 m, as well as the risk from the relevant metabolites. Bioaccumulation and bio-magnification was assessed, resulting in a BCF of 28.000 and a slow elimination rate. Risk assessment based on food-chain modelling suggested a low risk to fish, also considering the potential lower toxicity of 2 µg a.s./L from the chronic fish toxicity study.

First tier risk assessment indicated a risk to bees. As the higher tier field studies were not accepted by member state experts, lufenuron should not be applied during the flowering season of the GAP crops. Further data were required to address the risk to bees from treated flowering weeds. The initial risk assessment to non-target arthropods from lufenuron (IGR) indicated a potential high risk. The higher tier field study was not accepted by member state experts. Further data were required to address the risk to non-target arthropods. The assessment of soil non-target macro-organisms indicated a potential high risk to collembola. The higher tier litter bag study provided to address the risk was not accepted by member state experts, as the exposure did not cover the expected plateau PEC_{soil}. Further data were required to address the risk.
The risk to earthworms, soil non-target micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

Key words: lufenuron, peer review, risk assessment, pesticide, insecticide

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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. Lufenuron is one of the 84 substances of the third stage, part B, covered by the Regulation (EC) No 1490/2002 designating Portugal as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Portugal submitted the report of its initial evaluation of the dossier on lufenuron, hereafter referred to as the draft assessment report, received by EFSA on 20 September 2006. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1490/2002 on 20 April 2007 to the Member States and the main applicant Syngenta 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, EFSA identified and agreed on lacking information to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the notifier, a scientific discussion took place in expert meetings in May – June 2008. 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 September 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 no critical issues were identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR).

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 7 March 2008)

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 29 September 2008).

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

Lufenuron is the ISO common name for (*RS*)-1-[2,5-dichloro-4-(1,1,2,3,3,3-hexafluoro-propoxy)-phenyl]-3-(2,6-difluorobenzoyl)-urea (IUPAC).

Lufenuron, belongs to the class of chitin synthesis inhibitors, other examples of this group are novaluron and diflubenzuron. It acts mostly by ingestion; larvae are unable to moult, and also cease feeding.

The representative formulated product for the evaluation was "Match 050 EC", an emulsifiable concentrate (EC).
The evaluated representative use was as an insecticide on grapes and tomatoes. Full details of the GAP can be found in the attached list of endpoints.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

Currently (September 2008), no minimum purity for lufenuron as manufactured can be given, because further clarification is needed. The PRAPeR meeting of experts concluded that the available data did not support the specification given in the addendum to vol. 4. For this reason there is no agreed specification. The technical material contains no relevant impurities.

The content of lufenuron in the representative formulation is 50 g/L (pure).

Besides the specification, 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 lufenuron or the respective formulations.

The main data regarding the identity of lufenuron 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 lufenuron 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. lufenuron in food of plant origin (high acid, high water and dry matrices), lufenuron in soil, water and air.

Residues in food can be determined with a modified multi-method (the German S19 method). The extraction procedure was in accordance with S19 however, HPLC with MS/MS detection was used which is not part of the S19 method. The limit of quantification was 0.02 mg/kg. Soil was analysed by HPLC-MS/MS with a LOQ of 0.01 mg/kg. The water method was also HPLC-MS/MS with an LOQ of 0.05 µg/L. Air was analysed by HPLC-UV with a LOQ of 1.0 µg/m^3. The soil and water methods can be used as confirmatory methods for air.
Methods are not required for products of animal origin as no MRLs will be set. A method for body fluids and tissues is also not required as lufenuron is not classified as toxic or very toxic.

2. Mammalian toxicology

Lufenuron was discussed by the experts in mammalian toxicology in June 2008 (PRAPeR meeting 49, round 10).
It was stated that lufenuron is an equimolar mixture of R and S-enantiomer, and that a conversion between both isomers is not expected in the technical specification. Therefore it is assumed that the equimolar mixture of enantiomers has been tested within the toxicological batches.
Considering the proposed technical specification (Addendum to Vol. 4, May 2008), five impurities were found in lower levels in the toxicological batches. Based on the available information, the experts agreed that none of the impurities was relevant and that the maximum levels proposed in the technical specification were acceptable. It was also noted during the meeting that the proposed technical specification had not been agreed by Section 1.

2.1. ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Lufenuron is only partially absorbed from the gastro-intestinal tract (peak blood concentration after 8h) after oral administration. The highest residue level was found in fat where a marked accumulation was observed after repeated administration. Significantly lower amounts were measured in other tissues, including the brain. It is very slowly excreted predominantly in faeces via a non-biliary process (33% within 24h, still measurable after 21 days). The metabolism of lufenuron is minimal (around 1%) and consists of deacylation followed by cleavage of the ureido group. Based on the blood concentration time curves following oral and intravenous administration, the systemic bioavailability of lufenuron was estimated to be 70%.

2.2. ACUTE TOXICITY

Lufenuron was shown to be of low acute toxicity to rats when administered orally, dermally or by inhalation (oral and dermal LD_{50} >2000 mg/kg bw, LC_{50} by inhalation >2.3 mg/L/4h, highest achievable concentration of the aerosol). Slightly irritant to the eyes (but not triggering classification), the compound was not irritant to the skin but showed skin sensitisation properties in a Magnusson and Kligman maximization test. Therefore the proposed classification was **R43 "May cause sensitisation by skin contact"**.

2.3. SHORT TERM TOXICITY

Oral short term studies were performed in rats (range-finding 28-day, and 90-day), dogs (28-day, 90-day and 1-year) and mice (90-day, additional information).

In **rats**, lufenuron induced functional effects on the nervous system (tonic-clonic seizures), body weight changes, and hepato- and adrenotropic effects resulting in a NOAEL of 10 mg/kg bw/day (90-day study). In **mice**, clinical signs of neurotoxicity were also observed (tonic-clonic seizures) with mortality at high dose (≥ 150 mg/kg bw/day) as well as dose-dependent tissues concentrations of lufenuron with accumulation in fat but not in brain. No NOAEL was derived for the mice because the available studies were considered as additional information, being performed with limited investigations.

In **dogs**, convulsions and deaths were observed at doses ≥30 mg/kg bw/day in the 1-year studies but no clinical signs were shown in the 90-day study up to 2000 mg/kg bw/day. The equivocal thyroid changes in the first 1-year study (Briffaux, 1992) at the low dose (4 mg/kg bw/day) were considered adverse by the experts, even if not supported by any functional investigations. Based on liver changes (increased weight and incidence of cell hypertrophy) in the second 1-year study (Altman, 1995) at 7 mg/kg bw/day, the agreed overall NOAEL was 1.5 mg/kg bw/day.

In the 28-day dermal study in rats, no systemic toxic effects or local irritation were observed up to the highest dose tested of 1000 mg/kg bw/day.

With regard to classification and labelling, the experts agreed that **Xn, R48/22** "**Harmful: danger of serious damage to health by prolonged exposure if swallowed"** should be considered by EChA, based on mortality and clinical signs in the second 1-year dog study (at 30 mg/kg bw/day).

2.4. GENOTOXICITY

No potential for mutagenicity was observed with lufenuron tested *in vitro* in bacteria (Ames test), in mammalian cells systems (clastogenicity in Chinese hamster ovary cells, gene mutation in Chinese hamster cells V79, and unscheduled DNA synthesis in rat hepatocytes, human fibroblasts and MRC-9 human cells), and *in vivo* in a mouse micronucleus test and unscheduled DNA synthesis test with rat liver cells.

2.5. LONG TERM TOXICITY

Long term toxicity and carcinogenicity of lufenuron were tested in rats (2-year) and mice (18-month). In both species, convulsions were observed at all dose levels including the control group.

For the **rat** study, historical control data for convulsions were provided in the addendum 1 to B.6 (May 2008). Taking also into account the absence of dose-response relationship, the experts agreed that these convulsions were only relevant at dose levels ≥ 20 mg/kg bw/day, when a clear increase in incidence and severity was observed. Therefore the meeting confirmed a NOAEL of 2 mg/kg bw/day based on convulsions and histological effects in gastrointestinal tract, lungs and urinary tract.

In the **mouse** study, the convulsions observed at doses ≤ 2 mg/kg bw/day (including the control group) were not considered relevant because they were within the historical control range or without dose-response relationship. Therefore, based on the adverse findings at 22 mg/kg bw/day (increased incidence and severity of convulsions, decreased survival and histological changes in the liver and the prostate), the experts agreed on the proposed NOAEL of 2 mg/kg bw/day.

With regard to the carcinogenic potential, the incidence of benign tumours in rats (testis and meninges) was not considered relevant by the experts, occurring within the historical control range and with a concomitant increased survival. Similarly, the increased incidence of lung adenomas in male mice at 22 mg/kg bw/day was not considered treatment-related. Even occurring above the historical control range, it was without dose-response relationship and at a dose producing a high systemic toxicity (increased mortality). In conclusion it was agreed that, based on the available information, lufenuron had no carcinogenic potential.

2.6. REPRODUCTIVE TOXICITY

The adverse effects on fertility and offspring were investigated in one rat multigeneration study, whereas the potential for developmental toxicity of lufenuron was studied in rats and rabbits.

Considering that the increased number of pairs not mating was not adverse in the absence of effects on fertility, the experts agreed on a reproductive NOAEL of 20 mg/kg bw/day. Based on a minimal delay in the emergence of the surface righting reflex, the agreed offspring NOAEL was 8 mg/kg

bw/day. Since the increased body weight in parental animals was not considered adverse, the parental NOAEL was agreed to be 20 mg/kg bw/day.

In both teratology studies, there were no effects on embryofoetal development, and maternal toxicity was only observed in the study with rats. Consequently both developmental NOAELs as well as the maternal NOAEL in rabbits were 1000 mg/kg bw/day; whereas the maternal NOAEL in rats was 500 mg/kg bw/day based on reduced body weight and food consumption.

2.7. NEUROTOXICITY

Convulsions were observed in short term and long term studies in different species, but were not accompanied by histopathological changes in the nervous system.

In a 4-month rat neurotoxicity study, single episodes of clonic-tonic convulsions or fasciculations were induced at the high dose. In addition, the animals were shown to be more susceptible to the convulsive effect of pentylenetetrazole, but partially recovered over a 2-month period without exposure. There were no indications for impaired motor or cognitive functions or for permanent lesions in the peripheral or central nervous system. The resulting NOAEL was 5.4 mg/kg bw/day.

In the addendum 1 (May 2008), mechanistic explanations were provided to clarify neurotoxicity. The proposal considered that the saturation of fat compartments with lufenuron and the subsequent increase of the brain levels would trigger the onset of convulsions. It was noted that this might explain how lufenuron reaches brain but not the way it exerts neurotoxicity. However, the experts agreed that this would not affect the overall assessment since only very high and prolonged exposure (≥ 20 mg/kg bw/day) can lead to convulsive effects.

The meeting also agreed that a developmental neurotoxicity study was not necessary according to the dataset and considering that approved test protocols are not adapted to assess a long term neurotoxic effect.

2.8. FURTHER STUDIES

2.8.1. Metabolites

Several studies were performed with the metabolites CGA 149772[5] and CGA 224443[6] (also known as CA 944A). After acute oral administration, CGA 149772 showed a low toxicity (LD_{50} 2065 mg/kg bw) whereas the metabolite CGA 224443 was more toxic (LD_{50} 1273 mg/kg bw). In addition, CGA 224443 was negative in an Ames test.

Results of a one-generation rat study with CGA 224443 were also presented in the DAR. Taking into account a decreased number of implantation sites at the high dose, the reproductive NOAEL was 63.3 mg/kg bw/day. The maternal and offspring NOAELs were 9.7 mg/kg bw/day based on borderline effects on body weights in females and in pups at 63.3 mg/kg bw/day, as well as liver changes in females.

5 CGA 149772: 2,6-difluoro-benzamide
6 CGA 224443: 2,5-dichloro-4-(1,1,2,3,3,3-hexafluoro-propoxy)-phenyl amine

2.8.2. Supplementary studies with lufenuron

In an investigative study with rats, no effects were observed on the endocrine system (pituitary, adrenal and genital organs) thereby confirming the absence of reproductive effect in the multigeneration study.

Further information on the potential transfer of lufenuron into human milk has been provided in the addendum 1 (May 2008) and presented during the meeting by the RMS. Based on a study with dairy cows (Tribolet, 1995), it is presumed that the milk level of lufenuron (in mg/L) is 5 times higher than the dietary intake (in mg/kg bw/day). Assuming the same transfer into human milk, resulting from the highest theoretical maternal intake from the consumption of treated crops, the exposure level of infants (body weight 10kg, milk consumption 1L/day) is expected to be 5300 times lower than the offspring NOAEL in the rat 2-generation study.

EFSA notes (post PRAPeR meeting): even considering that the transfer into human milk would be up to 13 (instead of 5), a margin of safety of 2000 would still be obtained with regard to the offspring NOAEL.

2.9. MEDICAL DATA

In manufacturing plant personnel, no adverse health effect has been reported. Similarly no significant toxicity has been reported during accidental ingestion by humans of the veterinary product containing lufenuron.

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

Acceptable daily intake (**ADI**)

The agreed **ADI** was **0.015** mg/kg bw/day, derived from the second 1-year dog study (Altman, 1995, see further details in 2.3) with the use of a safety factor of 100.

Acceptable operator exposure level (**AOEL**)

Using the same 1-year dog study (Altman, 1995, see further details in 2.3) and a safety factor of 100, as well as a correction for systemic bioavailability of 70%, the agreed **AOEL** was **0.01** mg/kg bw/day.

Acute reference dose (**ARfD**)

The meeting agreed with the RMS that an ARfD was not necessary.

2.11. DERMAL ABSORPTION

The dermal absorption studies were performed with the formulation Match 050 EC (A-7814 A containing naphthalene), whereas the representative formulation A-7814 K contains a naphthalene-depleted solvent. They were considered as equivalent for the dermal absorption results.

With regard to the results of the *in vivo* study, the meeting agreed to include the amount in the treated skin and to exclude the tape strips (corresponding to stratum corneum), resulting in dermal absorption values of 13% for the dilution and 11% for the concentrate. Based on the *in vitro* results and the derived correction factors for the ratio rat/human skin (6.5 for the concentrate and 1 for the dilution), the agreed dermal absorption values for human were 13% for the dilution and 2% for the concentrate.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Match 050 EC is an emulsifiable concentrate formulation containing 50 g lufenuron/L for use as insecticide in grapes (field use) or tomatoes (field and greenhouse use). The maximum application rate in tomatoes is 30 g a.s./ha (field use) diluted in a minimum volume of 200 L water/ha, whereas for grapes it is 50 g a.s./ha diluted in a minimum volume of 500 L water/ha.

Operator exposure

The estimates for outdoor cultures were calculated using both the German model[7] and the UK POEM[8] model. For indoor applications, the results of a surrogate greenhouse exposure study were taken as a basis for the exposure estimates during spraying. To represent the worst case, exposure during mixing/loading for greenhouse applications is calculated with the German model for hand-held applications. Revised calculations were provided in the Addendum 2 (July 2008). The different scenarios and results are presented in the table below.

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

UK POEM (field use)	**No PPE**	**With PPE[1]**
Tractor boom sprayer, tomatoes (50 ha/day)	147	24
Tractor air-sprayers, grapes (15 ha/day)	273	190
Hand-held sprayer, tomatoes (1 ha/day)	190	71
GERMAN MODEL (field use)	**No PPE**	**With PPE[2]**
Tractor boom sprayer, tomatoes (20 ha/day)	27	6
Tractor airblast sprayers, grapes (8 ha/day)	89	14
Hand-held sprayer, grapes (1 ha/day)	69	16
GREENHOUSE APPLICATION (tomatoes)	**No PPE**	**With PPE[3]**
Gun application, high crop on ground model (1 ha/day)	58	2

PPE[1] (personal protective equipment): gloves during mixing and loading and application, PPE[2]: gloves during mixing/loading only, broad-brimmed headwear, coverall and sturdy footwear during application, PPE[3]: gloves.

[7] Lundehn J. R. et al.; Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products; Mitteilungen aus der Biologischen Bundesanstalt, Heft 277, Berlin 1992
[8] Predictive operator exposure model (POEM; UK MAFF, 2003).

Worker exposure

Re-entry exposure of workers has been estimated using an exposure model proposed by Krebs et al. (1996), with a revised transfer coefficient from Europoem II (4,500 cm²/person/hour for both uses instead of 30,000 for grapes and 8,000 for tomatoes), a dislodgeable foliar residue value of 1 µg a.s./cm²/kg a.i. and a workday of 8h. The predicted exposure is 39% of the AOEL without protective equipment, and 2% of the AOEL when impermeable gloves and long sleeved shirt are used.

Bystander exposure

Dermal exposure for bystanders is directly correlated to the amount of active substance applied per area, the size of the uncovered body surface contaminated and the drift distance (between the bystander and the application machinery). Based on drift values from Rautmann et al. (2001), the predicted exposure of bystanders is 1% of the AOEL (see addendum 2, July 2008).

3. Residues

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of lufenuron has been investigated in representatives of three crop categories, i.e. tomato (fruits), cabbage (leafy crops) and cotton (pulses and oilseeds). Lufenuron was always the major compound found in all three crops, showing no significant degradation even when the compound is injected into plants. Only one minor metabolite CGA 238277[9] was identified in cabbage, (0.6% TRR in cabbage head (0.012 mg/kg) and 3.3% TRR in wrapper leaves (0.023 mg/kg)) and tomato (0.2%TRR in the spray application (0.002 mg/kg) and 2% TRR in the injection of fruit experiment). In tomato, the crop representative of the intended uses (grapes and tomatoes), the metabolism study was performed with an application rate identical to that proposed for field tomatoes, but lower than the intended for indoor conditions (100 g a.s/ha). The PHIs used in the tomato metabolism study cover these intended uses. Therefore, in spite of this low dosing, the metabolic picture is clear. Lufenuron is a stable and persistent compound and it is the only significant residue that will be found in plant commodities.

A full set of residue trials in grapes for both the north and the south of Europe were provided (12 in the north and 9 in the south). The resultant Highest Residue (HR) was 0.67 mg/kg and the STMR was 0.12 mg/kg. For protected tomato a full data set was provided; 13 trials with a HR of 0.25 mg/kg and a STMR of 0.07 mg/kg. For outdoor tomatoes in the south of Europe the gap is much less critical; three trials were provided that supported this. The HR was 0.05 mg/kg.

[9] CGA 238277: [2,5-dichloro-4-(1,1,2,3,3,3-hexafluoro-propoxy)-phenyl]-urea

It was noted that lufenuron has a pair of enantiomers and potentially if there is a change in the ratio of these during metabolism the changed ratio may not be covered by the toxicological end point. The meeting agreed the ratio can be presumed to be stable as there is nearly no metabolism occurring. After the meeting and on consultation within EFSA, it was considered that this is an incorrect assumption as, although it is not degrading, we have no data to demonstrate that the isomer ratio is the same as it was when the material was applied. It is well known that for some substances, light energy can cause photolytic conversion of one isomer to another. Lufenuron absorbs light at wavelengths at which this possibility is not excluded. Potentially the consumer risk assessment could under estimate the risk by a factor of 2 (assuming the residue is only 1 isomer and all the toxicity comes from it).

The stability of residues was demonstrated in a freezer storage test with cotton seed, cabbage and oranges. Lufenuron was seen to be stable for a period of 2 years. Stability in products of animal origin was also considered and the data demonstrated that lufenuron is stable for at least 9 months. Given this information and the fact that lufenuron has high to very high persistence in the environment, lufenuron can be considered stable in frozen samples.

In the nature of the residue on processing study it was noted that some of the recoveries were high but the meeting of experts PRAPeR 50 considered that they were within analytical variation. The data showed that lufenuron is stable under the conditions of the test. It is therefore unlikely that break down products will be formed during industrial or domestic processing.

Processing studies of grapes and tomatoes treated with lufenuron have been conducted and processing factors have been calculated. Lufenuron residues in pasteurised juice and wine, from grapes, were at or below the limit of determination. No transference of residues occurred into wine. From grapes into juice a transfer factor of 0.17 was calculated.
A good balance of lufenuron residues during processing of tomatoes into juice, puree and preserves was achieved. The majority of the residue remained in the pomace and peel. No transference of residue into juice and preserves was observed. The transfer factor into puree was 0.85.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

In a confined rotational crop study lufenuron labelled in the difluorophenyl ring was applied at a rate of 150 g a.s./ha 0.5 N (for the total dose) to bare soil. Lettuce, wheat, maize and carrots were planted 63 days after treatment. The crops were harvested 99, 126 and 197 days later. As expected from such an environmentally persistent compound the only significant residue identified was lufenuron. The main residues were less than 0.01 mg/kg except for lettuce where 0.025 mg/kg lufenuron was detected and carrot where the TRR was 0.023 mg/kg in small carrots but lufenuron was not specifically analysed for.

In the second study lufenuron labelled in the dichlorophenyl ring was applied at a rate of 130 g a.s./ha circa 0.5 N (for total dose). Lettuce was transplanted, and winter wheat , maize and sugar beet were sown at typical intervals of 76, 126, 331 and 306 days after treatment respectively. Lettuce was harvested 106 and 138 days after treatment wheat 307, 363 and 418 days, sugar beet 363, 418 and 519 days and maize 363, 418 and 495 days. TRR in all crops at all time points was <0.005 mg/kg parent equivalents.

The meeting of experts heard that the active substance can accumulate in soil for 6 years and it was concluded that these studies were not worst case. The meeting agreed that the compound will not be taken up by plants as log Kow is high and that it will be adsorbed to the soil. It was therefore considered that the positive residues seen were due to soil contamination which will be easily removed during house hold preparation. Therefore from a consumer point of view there is no concern.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

From the representative uses in grape and tomato evaluated there is no animal intake according to current guidance. However, metabolism studies in hens and goats were provided that demonstrated that the only significant residue that will be present is lufenuron. Feeding studies in dairy cattle and steers were also provided, but it can not be concluded if the dose levels are appropriate because there are no animal intakes from the representative crops.

3.3. CONSUMER RISK ASSESSMENT

For the UK consumer model intakes were highest for the vegetarian population subgroup at 10 % of the ADI using the STMR and 80% of the ADI when using the proposed MRLs. For the WHO European diet the TMDI was 3.42 % and IEDI was 0.62 %. For the Portuguese diet the TMDI was 20.22% and the NEDI was 2.63%. An acute risk assessment has not been conducted as an ARfD has not been set. However, potentially the consumer risk assessment could under estimate the risk by a factor of 2 (assuming the residue is only 1 isomer and all the toxicity comes from it).

3.4. PROPOSED MRLS

A MRL of 1 mg/kg is proposed for grapes and 0.3 mg/kg for tomatoes.

4. Environmental fate and behaviour

Lufenuron was discussed at the PRAPeR experts' meeting for environmental fate and behaviour PRAPeR 47 in May 2008. It should also be noted that the methods of analysis used in all the fate and behaviour studies were not stereoselective. Therefore the regulatory dossier provides no information on the behaviour of each individual lufenuron enantiomer in the environment. Therefore all residues

reported as lufenuron in this conclusion are for the sum of the 2 enantiomers. It is not known if either isomer is degraded more quickly than the other in the environmental matrices studied.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Soil experiments (4 different soils) were carried out under aerobic conditions in the laboratory (20°C and either 75% 1/3 bar water holding capacity (WHC) or 40% maximum water holding capacity (MWHC)) in the dark. The formation of residues not extracted by acetone was a sink for the applied dichlorophenyl ring radiolabel (17-59% of the applied radiolabel (AR) after 91 to 100 days). Mineralisation to carbon dioxide of this radiolabel accounted for only 1 to 7.4 % AR after 91 to 100 days. These values for the difluorophenyl ring radiolabel (only 1 soil studied) were 34 % AR and 53% AR at 90 days respectively. The major (>10 AR) extractable breakdown products present were CGA 238277 (max. 10.1 to 32% AR at 14, 30 and 82days) and CGA 224443 (max. 22 to 33% AR at 59, 61 and 149 days).

Data on anaerobic degradation in soil indicated that breakdown was slower than under aerobic conditions and no novel metabolites compared to those formed under aerobic conditions were identified. In laboratory soil photolysis studies, the novel photodegradation product CGA 149772 was identified accounting for a maximum of 11.2% AR, though photolytic degradation of lufenuron was relatively slow (calculated first order DT_{50} 119-165 days in dry soils with light energy estimated as being equivalent to sunlight at 40°N).

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

The rate of degradation of lufenuron was estimated from the results of the dark aerobic soil degradation studies described in 4.1.1 above and an additional experiment in a silt loam soil (20°C 50% MWHC) in the dark. DT_{50} values were 13.6 to 83 days (single first order non linear regression). After normalisation to FOCUS reference conditions[10] (20°C and -10kPa soil moisture content) this range of single first order DT_{50} becomes 11.2 to 76 days (geometric mean 20.8 days).

From these 5 experiments kinetic fitting was also carried out to estimate rates of degradation for the 2 major metabolites. For CGA 238277 single first order DT_{50} were 8.1 to 42.1 days, (associated kinetic formation fractions from lufenuron fitted with either a single first order or a first order multi compartment (FOMC) model 0.373 to 0.989). For CGA 224443 single first order DT_{50} were 24.8 to 103.4 days, (associated kinetic formation fractions from CGA 238277 (single first order) 0.489 to 0.994, except for 1 soil where the formation fraction of 0.84 was calculated directly from lufenuron (single first order)). After normalisation to FOCUS reference conditions (20°C and -10kPa soil

[10] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002, Q10 2.2, Walker equation coefficient 0.7.

moisture content) this range of CGA 238277 single first order DT_{50} becomes 6.6 to 38.4 days (geometric mean 12.2 days, arithmetic mean kinetic formation fraction from lufenuron 0.77). This range for CGA 224443 becomes 16.9 to 94.2 days (geometric mean 37.6 days, arithmetic mean kinetic formation fraction from CGA 238277, 0.74). See addendum 1 section B.8 to the DAR and the report of the meeting of experts for full details on these DT_{50} and kinetic formation fraction estimates for CGA 238277 and CGA 224443. There are also summary tables B.8.79 to B.8.81 outlining this information on pages 237-238 addendum 2 to B.8.

The major (> 10 % AR) photodegradation product, CGA 149772 was applied as test substance to 3 soils and incubated in the laboratory (aerobic dark 20°C 45%MWHC). Single first-order DT_{50} values from these studies were calculated to be 2.7 to 4.8 days. After normalisation to FOCUS reference conditions[11] (20°C and -10kPa soil moisture content) this range of single first order DT_{50} becomes 2.7 to 4 days (geometric mean 3.3 days).

The Member State experts agreed that satisfactory field soil dissipation studies (bare soil) were provided from 3 sites in southern Europe (Huesca Spain, Buzignargues southern France, Thermi Greece) and a site in Switzerland (Klus) where applications were made between June and September. (Note residue levels determined at the Thermi trial site for days 451 to 707 are reported in addendum 1 section B.8 to the DAR and in Table B.8.54a on page 208 of addendum 2 section B.8 to the DAR). Using the residue levels of parent lufenuron determined over the 0-20 cm soil layer (residues in deeper soil layers were not detected and generally were only present in the 0-10cm soil layer), single first order DT_{50} agreed as appropriate by the Member State experts were 151, 198, 334 and 434 days. The Member State experts concluded that it was not possible to obtain satisfactory DT_{50} estimates from the field studies carried out in California, Mississippi and New York (USA). The results of the 4 satisfactory European field dissipation studies were normalised to FOCUS reference conditions (20°C and -10kPa soil moisture content) using a time step normalisation, following the recommendations described in Chapter 9 of FOCUS kinetics guidance[12]. This range of single first order DT_{50} is 94 to 372 days (geomean value 185 days) (see pages 227 to 235 and Table B.8.83 page 240 addendum 2 section B.8 to the DAR).
When analysed for (Huesca, Thermi and Klus trial sites) the 3 metabolites CGA 238277, CGA 224443 and CGA 149772 were generally not detected (>0.01 mg/kg) with the exception of CGA 238277 which was found at 0.01 mg/kg in a single sample at the Huesca site and CGA 224443 that was found at up to 0.03 mg/kg in 3 samples at the Tierce site (lufenuron applied at 250 to 282 g/ha, Klus site excluded). At the Klus trial site where radiolabelled test substance had been applied at 130

[11] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.
[12] "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, Normalisation assumptions Q10 2.2, Walker equation coefficient 0.7.

g/ha, CGA 238277 residues were in the range of 0.002 to 0.015 mg/kg. At this site, when detected (>0.0005 mg/kg), CGA 224443 was present at up to 0.008 mg/kg.

The longest available not normalised lufenuron single first order soil DT_{50} of 434 days was agreed by the experts from the Member States for use in PEC soil calculations for lufenuron (including calculations of accumulation). The resulting PEC for lufenuron and its 3 metabolites (calculated using the maximum observed formation fractions observed in laboratory studies) can be found in appendix 1.

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

The adsorption / desorption of lufenuron was investigated in 5 soils in satisfactory batch adsorption experiments. Calculated adsorption $K_f oc$ values varied from 11888 to 74833 mL/g, (arithmetic mean 41182 mL/g) (1/n 0.81 – 1.06, arithmetic mean 0.98). There was no evidence of a correlation of adsorption with pH.

The adsorption / desorption of CGA 238277 was investigated in three soils in satisfactory batch adsorptions experiments. Calculated adsorption $K_f oc$ values were 2156-2441 mL/g (arithmetic mean 2263 mL/g) (1/n 0.87 – 1.02, arithmetic mean 0.95). There was no evidence of a correlation of adsorption with pH.

The adsorption / desorption of CGA 224443 was investigated in three soils in satisfactory batch adsorptions experiments. Calculated adsorption $K_f oc$ values were 4388-5684 mL/g (arithmetic mean 4930 mL/g) (1/n 0.89 – 0.94, arithmetic mean 0.91). There was no evidence of a correlation of adsorption with pH.

The adsorption / desorption of CGA 149772 was investigated in three soils in satisfactory batch adsorptions experiments. CGA 149772 remained almost entirely in the soil solution. The amount adsorbed was negligible, such that it was not possible to estimate soil adsorption values.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Lufenuron was essentially stable under sterile hydrolysis conditions at 25°C at pH 5, 7 and 9. In a range of laboratory studies where the direct aqueous photolysis of lufenuron was investigated under sterile conditions, rates of degradation (single first order DT_{50}) of 18-34 days equated to summer sunlight at 30 to 40°N were determined. Lufenuron degraded to CGA 149772, CGA 224443 and an unidentified photodegradation product 'M2B' (containing the difluorophenyl radiolabel), which accounted for maxima of 62 % AR, 21% AR and 14.6 % AR respectively. In a laboratory sterile aqueous photolysis study with a natural pond water where indirect photolysis may occur, a single first

order DT_{50} of 11 days equated to summer sunlight at 30 to 40°N was determined. No single degradate containing the dichlorophenyl radiolabel used accounted for > 10% AR.

In water-sediment studies (2 systems studied at 20°C in the laboratory in the dark) lufenuron partitioned rapidly from the water to the sediment (taking less than 1 day), it subsequently degraded with whole system single first order DT_{50} estimated to be 34 to 188 days (geomean value 112 days). The metabolites formed remained in the sediment phase of the systems with CGA 238277 (max. 20 - 47 % AR at 59 -120 days after treatment) and CGA 224443 (max. 13 - 26 % AR at 120 -269 days after treatment) being the only major (>10% AR) metabolites present. Single first order degradation DT_{50} of 45 and 54 days (associated kinetic formation fractions from lufenuron 0.91 and 0.95) and 101 and 117 days (associated kinetic formation fractions from CGA 238277 0.52 and 0.61) respectively were estimated. The terminal metabolite, CO_2, accounted for only 0.2 % AR of the dichlorophenyl ring radiolabel by 90 days but 11.8 to 36% AR for the difluorophenyl ring label at 90 days. Residues not extracted from sediment by acetone were a sink representing 6-15% AR and 12-37% AR for each radiolabel respectively at 90 days. The experts agreed that for lufenuron the geomean DT_{50} of 112 days (whole system values) was appropriate for use as FOCUSsw scenario calculation input for the sediment compartment with a default value of 1000 days being utilised for the water compartment at steps 3 and 4.

FOCUS surface water modelling was evaluated up to step 4 for lufenuron and step 2 for the metabolites CGA 238277, CGA 224443 (originating from soil and formed in the water body) and CGA 149772 (originating just from soil, as the expected rapid adsorption to sediment of lufenuron was expected to limit the potential for this metabolite to be formed by aqueous photolysis in aquatic systems). The peer review agreed that these PEC surface water and sediment as presented in the DAR up to step 2 for the metabolites were appropriate for use in risk assessment and the values on pages 284 to 293 of addendum 2 section B.8 to the DAR would be appropriate at steps 3 and 4 for lufenuron. At step 4 the only mitigation considered a was no spray drift buffer zone of 5, 10, 15, 20 and 30 m for vines and 5, 10 and 15 m for tomatoes that were implemented following the methods prescribed by $FOCUS_{sw}$ guidance. These PEC are included in appendix 1 to this conclusion as agreed EU endpoints with the exception of the vine 30 m buffer zone values that do not comply with EU guidance[13] as 30 m no spray zones mitigate spray drift (excepting the pond water body) by more than 95%, which is the upper limit for spray drift mitigation recommended by this agreed guidance. A buffer zone of 25 m would respect the 95% drift reduction limit, but calculations for this distance were not available to the peer review. A data gap to provide simulations for this buffer distance for the use on vines was therefore identified.

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

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

The applied for representative use of summer applications to grape vines and outdoor tomatoes was simulated using FOCUS PELMO 3.3.2 using the following input parameters: lufenuron single first order DT_{50} 128 days, K_{foc} 41182 mL/g, 1/n=0.98; CGA 238277 single first order DT_{50} 15.2 days, formation fraction from lufenuron 0.77, K_{foc} 2263 mL/g 1/n=0.94; CGA 224443 single first order DT_{50} 44.2 days, formation fraction from CGA 238277 0.76, K_{foc} 4930 mL/g 1/n=0.91; CGA 149772 single first order DT_{50} 3.4 days, formation fraction from lufenuron 0.1, K_{foc} 0 mL/g 1/n=0.9 (default).

The parent lufenuron, CGA 238277 and CGA 224443 were calculated to be present in leachate leaving the top 1m soil layer at 80th percentile annual average concentrations of <0.001µg/L. For CGA 149772 this range was <0.001 to 0.003µg/L.

The Member State experts agreed that, based on this modelling, the potential for groundwater contamination above the parametric drinking water limit of 0.1µg/L from the applied for intended uses was low for lufenuron and its metabolites CGA 238277, CGA 224443 and CGA 149772, even if the substance input parameters used were not exactly as had been concluded as most appropriate by the peer review.

For completeness and to support future assessments the substance parameters that should have been used are: lufenuron single first order DT_{50} 185 days, K_{foc} 41182 mL/g, 1/n=0.98; CGA 238277 single first order DT_{50} 12.2 days, formation fraction from lufenuron 0.77, K_{foc} 2263 mL/g 1/n=0.95; CGA 224443 single first order DT_{50} 37.6 days, formation fraction from CGA 238277 0.74, K_{foc} 4930 mL/g 1/n=0.91; CGA 149772 single first order DT_{50} 3.3 days, formation fraction from lufenuron 0.11, K_{foc} 0 mL/g 1/n=0.9 (default).

4.3. FATE AND BEHAVIOUR IN AIR

The vapour pressure of lufenuron ($<4.74 \times 10^{-6}$ Pa at 25°C) means that lufenuron would be classified under the national scheme of The Netherlands as very slightly volatile, indicating significant losses due to volatilisation would not 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 1.03 days (assuming an atmospheric hydroxyl radical concentration of 1.5×10^6 radicals cm^{-3}) indicating the small proportion of applied lufenuron that will volatilise would be unlikely to be subject to long range atmospheric transport.

5. Ecotoxicology

Lufenuron was discussed in the meeting of ecotoxicology experts PRAPeR 48 (subgroup 1) in May 2008, on the basis of the Draft Assessment Report (2006), Corrigendum 1 (May 2008) and

Addendum 1 (May 2008). Subsequent to PRAPeR 48 the DAR was updated (Addendum 2, September 2008) to include all corrections from corrigendum 1 (May 2008), addendum 1 (May 2008) and the amendments agreed during the meeting of experts. The updated version also included a new statistical assessment of the long-term toxicity study to fish (Vial, 1992), which was not peer-reviewed. Furthermore, the DAR was amended with additional information added to some of the study summaries and the RMS has added further risk assessments in response to the outcome of the expert meeting. EFSA notes that none of these assessments were peer-reviewed.

Lufenuron is the active substance in the formulated product Match 050 EC (50 g/L). The representative field uses were in vine (1-2 x 50 g a.s./ha at minimum 14 days interval) for North Europe (NEU) and South Europe (SEU) and tomato (1-3 x 30 g a.s./ha at minimum 7 days interval) in SEU. The representative uses also included glasshouse use on tomato (1-3 x 100 g a.s./ha at minimum 7 days interval).
Several formulation studies (e.g. section on bees, non-target arthropods and non-target plants) were provided with the formulation A-7814 A. The data for this formulation were deemed to be valid for assessing the risk from application of the 'K' variant, as the formulation differs only in the depletion of naphthalene from the solvent used.
It was highlighted during the peer-review that lufenuron consist of 2 enantiomers and potentially if there was a change in the ratio of these during degradation the changed ratio would not have been covered by the ecotoxicological endpoint. It was agreed in the meeting of member state experts that there was no agreed specification and no conclusion could be drawn on the ecotoxicological relevance of the specification. EFSA noted while drafting the conclusion, that potentially the ecotoxicological risk assessment could under estimate the risk by a factor of 2 (assuming the residue was only 1 isomer and all the toxicity came from this isomer).

The risk assessment was conducted according to the following guidance documents: Risk Assessment for Birds and Mammals. SANCO/4145/2000, September 2002: Aquatic Ecotoxicology. SANCO/3268/2001 rev.4 final, October 2002; Terrestrial Ecotoxicology. SANCO/10329/2002 rev.2 final, October 2002; Risk Assessment for non-target arthropods. ESCORT 2, March 2000, SETAC.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The glasshouse use of lufenuron on tomatoes was not considered to pose a risk to birds and mammals as exposure would be negligible. A risk assessment was provided for the outdoor uses in vine and tomatoes.

The acute toxicity (LD_{50} > 2000 mg a.s./kg bw) and short-term toxicity (LC_{50} > 966 mg a.s./kg bw/d) to birds was considered to be low based on available studies for both Mallard duck (*Anas platyrhynchos*) and Bobwhite quail (*Colinus virginianus*). The lowest reproductive endpoint of 19.7 mg/kg bw/d was identified from a study with Bobwhite quail. First tier TER calculations indicated a

low risk to birds for all intended outdoor uses. The acute toxicity (LD_{50} > 2000) study with rats indicated a low mammalian toxicity. The NOAEC endpoint from the 2-generation reproductive study was discussed in the meeting of experts. The RMS suggested using 17 mg as/kg bw/d (corrected to 20.9 mg a.s./kg bw/d during expert meeting) for the risk assessment. It was, however, agreed by the experts to use the lower value of 8.3 mg as/kg bw/d from the rat multi-generation study in the risk assessment given the uncertainty regarding the ecotoxicological relevance of effects (clonic-tonic convulsions and histological changes) seen at 20.4 mg/kg bw/d in this study. Whereas the first tier TERs from the acute risk assessment ($TER_{a\ tomato}$ = 1600 and $TER_{a\ vine}$ = 280) and the long-term risk assessment for the tomato use ($TER_{lt\ tomato}$ = 48) were above the Annex VI trigger levels., a potential high long-term risk was identified to small herbivorous mammals from use in vine ($TER_{lt\ vine}$ = 3.5). The exposure was refined by taking a vine canopy interception factor of 70% into account. A calculated TER value of 7.2 indicated a low risk to mammals. The latter refinement was not peer-reviewed as it was provided in the revised DAR after the expert meeting. EFSA, however, confirmed the refined risk assessment.

The risk for consumption of contaminated drinking water was only assessed for birds in the DAR. The TER value indicated a low risk to birds. EFSA provided an acute risk assessment for both birds and mammals when drafting the conclusion, based on the revision of the guidance document on risk assessment for bird and mammals[14]. The leave scenario was not considered relevant for the intended uses in vine and tomato. TERs for both wine and tomato in the puddle scenario were several orders of magnitude above the trigger for birds and mammals, indicating a low risk.

Bioaccumulation and food chain behaviour

A log P_{ow} of 5.12 triggered the assessment of risk from secondary poisoning and biomagnification. The TER calculations provided in the DAR indicated a low risk to earthworm-eating birds and mammals, based on both an estimated and a measured BCF in earthworms. The TERs indicated a high risk to fish-eating birds and mammals also after a revision (Addendum 1, May 2008), based on the higher BCF value of 28000 recommended during the review process. All TERs related to secondary poisoning were updated in the revised DAR following the expert meeting, based on new PEC calculations for soil and water. As these PEC_{soil} values were again updated by EFSA while drafting the conclusion, the TERs were consequently recalculated by EFSA. The final TERs were well above the Annex VI trigger for earthworm-eating birds (TERs in the range of 130-4519) and mammals (TERs in the range 43-1520), based on $PEC_{soil,\ 21\ d\ twa}$ of 0.03 and 0.086 mg a.s./kg respectively for use in tomato and vine. The TERs for fish-eating birds and mammals were above the Annex VI trigger for uses in tomato, based on FOCUS Step 3 $PEC_{sw,\ 21\ d\ twa}$ calculations of 0.00017 mg a.s./L. For uses in vine a refined risk assessment was required to retrieve TER values above the Annex VI trigger for both fish-eating birds and mammals. Application of a no-spray buffer zone of 5

[14] Scientific Opinion of the Panel on Plant protection products and their Residues (PPR) on the Science behind the Guidance Document on Risk Assessment for birds and mammals (Question No EFSA-Q-2006-064) Adopted on 17 June 2008

m ($PEC_{sw, 21\ d\ twa}$ = 0.0006 mg a.s./L) and 10 m ($PEC_{sw, 21\ d\ twa}$ = 0.0002 mg a.s./L) respectively for fish eating birds and mammals, gave TERs indicating a low risk. In conclusion a low risk was identified by EFSA from secondary poisoning of birds and mammals, based on appropriate mitigation measures.

The potential for biomagnification was assessed in the DAR by calculation of BAF values, i.e. where the whole-body residue in an animal at steady state would be higher than the residue in its food (BAF > 1). The adsorption, distribution and excretion (ADME) of lufenuron was provided in a study with Bobwhite quail. The study provided an adsorption efficiency coefficient of 0.73 (corrected in addendum 1 and agreed by Member State experts) and a depuration half-life of 5 days. Based on these values and default food intake rate relative to bodyweight (FIR/bw) from the *Guidance Document*, BAF values in the range of 1.6-5.5 for herbivorous, insectivorous, granivorous and carnivorous birds indicated a clear potential for biomagnification in birds.
It was agreed by Member State experts to use the measured adsorption efficiency of 70% from the rat study instead of the default value of 60% to derive BAF values for mammals. Also the depuration rate in rats was based on the mean measured excretion half-life of 12 days. BAF values in the range of 2.8-17 for herbivorous, insectivorous, granivorous and carnivorous mammals also indicated a clear potential for biomagnification in mammals.

The risk from food chain accumulation was assessed following the approach recommended in Appendix III of the *Guidance Document*. The toxic endpoint used in the assessment of the biomagnification in food chains was discussed in the meeting of experts. In the DAR the endpoint derived from a 90-day dietary toxicity study with bobwhite quail was used in the risk assessment. The derivation of a NOEC expressed as a body burden of 600 mg as/kg body weight was based on the maximum residues of lufenuron found in fat tissues. Experts agreed that this endpoint should not be used. As only male birds were used in the study, a plateau concentration was not fully reached during the 90 day study and reproductive effects were not considered. The experts agreed that the concentration in the food of 200 mg/kg from the Bobwhite quail reproduction study should be used as the NOEC (corresponds to 19.7 mg/kg bw/day) in the food chain modelling. In the DAR the following four avian food chain scenarios were considered in the risk assessment:

Example Taxa		
Primary Producer / Consumer	Secondary Consumer	Tertiary Consumer
Short grass	Pigeon	Falcon
Insect	Warbler	Hawk
Small fish	Kingfisher	Hawk
Macrophytes	Duck	Falcon

The predicted environmental concentration in an organism due to consumption of contaminated food was calculated for each step of the food chain based on adsorption efficiency multiplied by weight specific food intake rate (FIR/bw) and concentration in the food and divided by depuration rate. I.e.

the concentration in falcon would be based on the residue concentration in pigeon, which would again be based on the residue concentration in short grass. The adsorption efficiency coefficient and depuration rate used for birds was derived from the 90 day dietary study with Bobwhite quail mentioned above. Species specific FIR/bw values were derived from literature.

The initial residue concentration in *short grass* and *small insects* was calculated in accordance with the *Guidance Document*, i.e. based on application rate and appropriate RUD and MAF values. The initial PEC in small fish was estimated using a dynamic food web model, which was fitted to measured residue values in fish from a mesocosm study (see section 5.2). As the concentration modelled for herbivorous fish was higher than for omnivorous fish, based on the worst-case FOCUS Step 4 PEC_{sw} values for vine use in the R3 stream including a no-spray buffer zone of 5 m, this value ($PEC_{fish,food\ web\ model}$) was used in the food chain modelling. In addition member state experts agreed also to use a PEC for fish ($PEC_{fish,secondary\ poisoning}$) estimated as for the assessment of secondary poisoning for the food chain 'small fish-kingfisher-hawk' risk assessment. $PEC_{fish,secondary\ poisoning}$ was based on the higher FOCUS Step 4 $PEC_{sw,\ 5\ m\ no\text{-}spray\ buffer\ zone}$. The initial PEC in macrophytes was estimated from measured residues in macrophytes from an outdoor microcosm study and the highest predicted FOCUS Step 4 $PEC_{sw,\ 5\ m\ no\text{-}spray\ buffer\ zone}$ values, assuming a linear relationship between exposure and macrophyte concentration. The initial PEC calculations were agreed by the member state experts. The initial PEC for *short grass* was recalculated in the revised DAR (addendum 2) as it was based on an incorrect RUD value (the correct long-term $RUD_{short\ grass}$ for insecticide application in vine should be 46). EFSA agrees to the corrections provided by the RMS after the peer-review. Recalculated TER values were provided in the revised DAR (addendum 2) in accordance with conclusions of the member state experts, i.e. using the reproductive endpoint of 200 mg a.s./kg and the additional assessment based on $PEC_{fish,secondary\ poisoning}$[15]. TERs for all food chain steps were above the Annex VI trigger of 5.

TERs provided by the RMS in the revised DAR for the use in tomato indicated a low risk to hawks without any need for risk mitigation. EFSA agreed with the TER values presented in the revised DAR, but it should be noted that the calculations were not peer-reviewed.

In the DAR the following mammalian food chain scenarios (consisting of two or three trophic levels) were considered in the risk assessment:

Example Taxa		
Primary Producer / Consumer	**Secondary Consumer**	**Tertiary Consumer**
Short grass	Rabbit	Fox
Large insects	Mouse	Weasel
Fish	Otter	-

The $PEC_{organism,food}$ was calculated for each trophic level, based on measured values of adsorption efficiency and depuration rate of 70% (originally 60% in the DAR) and 12 days respectively (as

[15] Please note that the $PEC_{fish,\ secondary\ poisoning}$ value was updated by EFSA after submission of the conclusion to the Commission, based on a correction of the 21 day TWA PEC_{SW} value used in the calculation.

mentioned above), in addition to FIR/bw values from the literature. Like for the assessment of biomagnification in birds, the initial residue concentration in *short grass* (corrected as for birds; see above) and *large insects* were calculated in accordance with the Bird and Mammals Guidance Document. Also the PECs in fish was identical to the values used for birds. TERs in the DAR were recalculated in the revised DAR (addendum 2) in accordance with conclusions of the member state experts, i.e. using the revised mammalian reproductive endpoint of 100 mg a.s./kg and the additional assessment based on $PEC_{fish,secondary\ poisoning}$[15]. TERs for all food chain steps were above the Annex VI trigger of 5. TERs provided by the RMS in the revised DAR for the use in tomato indicated a low risk to hawks without any need for risk mitigation. EFSA agreed with the TER values presented in the revised DAR, but it should be noted that the calculations were not be peer-reviewed.

Metabolites

It was agreed in the meeting of experts that the risk for secondary poisoning to birds and mammals from exposure to the metabolite CGA 224443 should be addressed. The RMS provided an assessment in the update DAR (non peer-reviewed). Avian tests have not been carried out with any lufenuron metabolites. Mammalian toxicity studies indicated that the metabolite was slightly more toxic than lufenuron. However, it was still considered to be of low toxicity to vertebrates (LD_{50} = 1273 mg/kg bw/day). The BCF for the metabolite was expected to be much lower than the BCF for lufenuron as indicated by the lower log P_{ow} value of 3.7. As the risk for bioaccumulation was considered to be low for lufenuron, it was expected that the metabolite CGA 224443 would also pose a low risk to both birds and mammals. Furthermore, exposure to the metabolites of lufenuron through the consumption of residues on food items was considered to be minimal. Since exposure to lufenuron from the intended uses was considered to pose a low risk to birds and mammals, the risk from the metabolites was also expected to be low. The risk from secondary poisoning was assessed, based on PEC_{soil} values provided in the revised DAR (addendum 2) and considering a similar long-term toxicity of CGA 224443 as for the active substance. As EFSA revised the PEC_{soil} values for CGA 224443 while drafting the DAR ($PEC_{soil\ 21\ d\ twa\ tomato}$ = 0.0056 mg a.s./kg, $PEC_{soil\ 21\ d\ twa\ vine}$ = 0.0167 mg a.s./kg), the TER calculation for earthworm eating birds and mammals was additionally updated by EFSA. The calculated TERs for all intended outdoor uses (TERs in the range of 533-4519) clearly exceed the Annex VI trigger of 5, indicating a low risk. For the risk to fish-eating mammals, residue measurement in fish from outdoor microcosm studies indicated that the metabolite could not be detected in fish tissue during the study, despite it was present in the surrounding environment (water and sediment). This indicates that the metabolite poses a negligible risk of bioaccumulation in fish, and therefore long-term effects from secondary poisoning or biomagnification in food chains was not expected. It was concluded overall by the RMS that the intended use of lufenuron would pose negligible secondary poisoning risk of metabolite CGA 224443 to fish eating mammals. The risk assessment for metabolite CGA 224443 was not included in the list of endpoints as the assessment was not peer-reviewed.

Overall the risk to birds and mammals consuming food and drinking water, which have been directly exposed to lufenuron, was assessed as low. The risk to birds and mammals following food chain exposure indicated a low risk at all steps of the food chain model for the use in vine, based on appropriate mitigation measures (e.g. no-spray buffer zones). No mitigation measures were needed for the use in tomato. The risk of the metabolite CGA 224443 was assessed as low after the peer-review.

5.2. RISK TO AQUATIC ORGANISMS

Based on the available acute toxicity data, lufenuron was proposed to be classified as very toxic to aquatic organisms. The lowest acute end point value for technical lufenuron was for *Daphnia magna*, with an EC_{50} of 1.3 µg a.s./L. An acute daphnia toxicity study including sediment was presented in the DAR (EC_{50} = 4 µg a.s./L). The member state experts agreed to base the initial risk assessment on the endpoint from the study without sediment. Based on the content of the active substance, the acute toxicity of the formulation (A-7814 A) was found to be slightly lower (0.4 µg a.s./L) than technical lufenuron. The chronic daphnia study was considered not valid as the tested material did not match the technical specification. The meeting of experts agreed that no new study should be required, as enough data were available for invertebrates to address the risk to aquatic invertebrates, i.e. a *Chironomus riparius* long-term study and the microcosm study. Two chronic toxicity studies on fish, covering a prolonged toxicity study and a full life cycle study (FFLC) were available for technical lufenuron. In addition a 33 days fish flow through study was provided with the formulation. The endpoint in the prolonged toxicity study with the active substance (Vial, 1992) was discussed by member state experts. Potentially, a NOEC of 2 µg a.s./L could be derived if effects on growth rate (length and weight) were statistically significant. Such effects were deemed to be ecologically relevant by the experts, and this endpoint would drive the risk assessment for fish. No statistical information on the significance was available in the study and experts agreed that the applicant should provide such information. The applicant did submit a statistical assessment of the study after the expert meeting, concluding that effects on growth rate and length were not significant. The applicant suggested a NOEC of 69 µg a.s./L from this study. The RMS included this assessment in the revised DAR (addendum 2, August 2008). EFSA noted that the statistical assessment had not been peer-reviewed and based on an initial assessment EFSA disagree to the statistical analysis, as it did not follow the draft OECD guidance on statistical analyse of ecotoxicity data[16] (the blank control was applied as control instead of the vehicle control). A data gap remains to derive the statistical significant endpoint from this study.

The algae toxicity endpoint agreed during the peer-review was an E_bC_{50} of 8.8 mg a.s./L for *Selenastrum capricoruntum*. A microcosm study without fish was available for higher tier aquatic risk assessment. A NOAEC of 0.3 µg a.s./L was suggested in the DAR. The member state experts, however, agreed on a NOAEC of 0.1 µg a.s./L, as no recovery was evident at the end of the study for some of the effects detected at the 0.3 µg a.s./L exposure level. No NOEC could be derived from the

[16] (OECD Guidance, draft, 2003)

study. The meeting suggested an assessment factor in the range of 2 to 3 to be used in the risk assessment.

TERs for the aquatic risk assessment were updated in the revised DAR (addendum 2) to reflect the microcosm endpoint agreed by experts and agreed FOCUS PEC values. The RMS did provide FOCUS Step 1 to 3 TERs for all intended uses in the list of endpoint revised after the expert meeting. In addition TERs for FOCUS Step 4 vine scenarios with no-spray buffer zones of 20 and 30 m were included. EFSA agrees to all the revised TER values. EFSA, however, noted that the TERs based on no-spray buffer zones of 30 m in vine would exceed the maximum agreed mitigations limit (see fate section 4.2.1) and were not included in Appendix 1. For vine and tomato uses the TERs of a FOCUS Step 3 (R1 pond scenario) did not meet the Annex VI trigger for the acute risk assessment to daphnia or for the chronic risk assessment to *C. riparius*. Acute toxicity data for 16 different aquatic invertebrate species were presented in the DAR and used for SSD analysis. The RMS was of the opinion that the SSD should be considered only as 'additional information' and the risk assessment should be refined by use of microcosm data. This was supported by the member state experts. FOCUS step 4 PEC_{sw} calculations for use in vine indicated TER values above the recommended assessment factor of 2-3 in the pond part of the R1 scenario with a no-spray buffer zone of 5 m, based on the microcosm NOAEC of 0.1 µg a.s./L. For the additional 5 scenarios TERs were still below the assessment factor of 2-3 with no-spray buffer zones of 20 m (TER: 1.3-1.8). EFSA noted that PEC_{sw} based on a no-spray buffer zone of 25 m (not provided in the DAR) would respect the maximum limitations on mitigation, and the resulting TERs for all scenarios might respect the lower value of two of the agreed assessment factors. However, if the higher assessment factor of 3 has to be respected for potentially more susceptible FOCUS surface water scenarios, further refinements would be required to address the risk. For tomato use, TERs for all scenarios were above 2 applying a no-spray buffer zone of 5 m.

The applicant presented landscape level risk assessment (GIS) for use in vineyards in France. The RMS considers this information useful to be used at Member States level, but not relevant at EU level. This opinion was shared by the meeting of experts. It was noted in the meeting, that the landscape modelling represents only one area and extrapolation would be difficult to other EU areas/conditions.

The toxicity to sediment dwellers was addressed by a long-term study on *C. riparius* including both water-spiked and sediment-spiked test systems. TERs were provided in the DAR, based on both PEC_{sed} and PEC_{sw}. For the sediment based risk assessment TER values above the Annex VI trigger were derived at FOCUS Step 4, based on a 5 m no-spray buffer zone for both intended outdoor uses.

The major metabolites considered to be pertinent for surface water evaluation were CGA 238277 and CGA 224443, which were formed in aquatic sediment at 48 % and 26 % respectively, and CGA 149772, which was formed at 35 % in a hydrolysis study. It was evident from acute toxicity studies that the metabolite CGA 149772 was of lower toxicity to aquatic organisms than the parent. The metabolites CGA 238277 and CGA 224443 were significantly less toxic to daphnia than lufenuron,

but more toxic to fish and algae. Acute TER values were calculated for three metabolites CGA 238277, CGA 224443 and CGA 149772. Long-term TER values were only calculated for CGA 224443 since this metabolite was the most acutely toxic and therefore the long-term risk assessment for this metabolite covers the potential risks of the other two. All TERs (based on FOCUS Step 1) were above the Annex VI trigger, indicating a low risk to aquatic organisms from lufenuron related metabolites for all intended outdoor uses. In accordance with the aquatic guidance document, no assessment of the risk to sediment dwellers from the major metabolites was provided, as the exposure to daphnia from the major metabolites indicated a low risk.

Bioaccumulation

Lufenuron has a log P_{ow} of 5.12 and therefore its potential to bioaccumulate in aquatic organisms needed to be evaluated. In bio-concentration studies with bluegill sunfish and fathead minnow, the BCF values were calculated to be 5,300 and 28,000 respectively. Bioaccumulation of lufenuron was also assessed in a higher tier microcosm study with bluegill sunfish (*Lepomis macrochirus*), based on exposure both via the food chain and via the water. The study provided a maximum BCF of 360 and data on maximum residues in whole fish of 1.8 and 0.147 µg a.s./L, based on initial exposure concentrations of 0.5 and 5 µg a.s./L respectively (Volz, 2003). Lufenuron fulfilled the criteria for the assessment of biomagnification. For lufenuron, the maximum BCF was 28,000, more than 27 % of radioactivity was eliminated in a 29 day depuration phase and it had a half-life in water of 1 day and 63 - 112 days in sediment, indicating that although very quickly dissipated from the water phase it was persistent in sediment. Several assessments of bio-accumulation and bio-magnification were provided in the DAR.

An assessment of the risk to aquatic invertebrates from bioaccumulation was provided in the DAR, based on estimation of critical body burden. This risk assessment was not accepted as the bioaccumulation study for invertebrates was considered not valid by the member state experts (EFSA noted that the risk assessment was still present in the revised DAR (addendum 2)). Member state experts agreed that the risk to invertebrates was addressed in the microcosm study, since the duration of the study was long enough for biomagnification to occur. A risk assessment based on critical body burden in fish was provided in the DAR, based on the fish full life cycle endpoint of 20 µg a.s./L and a BCF of 28,000. It was estimated that the critical body burden of 420 mg a.s./kg would be 2900 times higher than the body burdens measured in fish under field conditions (0.147 µg a.s./kg) at an exposure rate of 0.5 µg a.s./L. The latter exposure would be higher than the maximum exposures foreseen with the no-spray buffer zones and thus addressing the risk in the higher tier for all the intended uses is required (see above). It was noted by member state experts that a lower chronic endpoint of 2 µg a.s./L may be agreed for fish, pending statistical assessment. EFSA noted, however, that the critical body burden would still be 380 times higher than the measured body burden, indicating a low risk to fish from bio-concentration.

In addition, the potential for biomagnification in piscivorous fish (tertiary consumers) was considered by use of food chain modelling according to Carbonell et al, 2000[17] as recommended in the Aquatic Guidance Document. The assimilation efficiency (α) and feeding rate was assumed to be 0.3 and 15 % of the wet body weight per day respectively for a tertiary consumer (Carbonell et al, 2000). The depuration rate (k) was measured in the field study with fish (Volz, 2003), indicating a half-life up to 45 days.

The predicted environmental concentration in the food item, i.e. the secondary consumer fish was based on the maximum FOCUS PECsw calculations with a 5 m no-spray buffer zone for a pond (R1) as it was considered unlikely that the stream or ditch habitat would be capable of supporting a large tertiary consumer fish. It was assumed that the body burden in fish would vary linearly with the exposure, and a body burden of 0.018 mg/kg in the secondary consumer fish was extrapolated from a field exposure study with fish. The maximum predicted environmental concentration in the tertiary fish consumer due to food was thus a $PEC_{organism,\ food}$ of 0.053 mg/kg. The total body burden in the tertiary consumer was considered to be the sum of the body burden due to food and the body burden due to water. If it was assumed that the concentration in the tertiary consumer fish due to the water phase was the same as that in the secondary consumer fish, i.e. 0.018 mg/kg, the maximum total predicted body burden in the tertiary consumer fish following use of lufenuron at recommended label rates would be 0.071 mg/kg (i.e., 0.053 mg/kg + 0.018 mg/kg). This would be an overestimate of the contribution to the body burden from the water phase, as the measured body burden in the fish field study includes the contribution from both food and water. The resulting value of 0.071 mg/kg was approximately 6000 times lower than the critical body burden of 420 mg/kg corresponding to the NOEC from the fish full life cycle study. This indicates that bioaccumulation of lufenuron in tertiary consumers would cause a low risk following the use of lufenuron at all label rates. EFSA notes that even the potentially lower chronic fish endpoint of 2 µg a.s./L, i.e. critical body burden of 56 mg/kg (see above), would not change this conclusion.

In addition to the food chain modelling recommended in the Aquatic Guidance Document, the applicant provided a risk assessment also considering exposure through consumption of macrophytes. The outdoor field study with fish (Volz, 2003) indicated that removal of lufenuron from the water phase by macrophytes was considerable. The risk assessment was presented in the DAR, on the basis of a dynamic food web model (including primary producer to top predator in a model pond ecosystem) fitted to the actual field data by Volz (2003). It was assumed that the fish were exposed to lufenuron at the maximum FOCUS Step 4 PEC_{sw} in a pond at 5m from the application site following application to vines, i.e. 0.04 µg as/L. The maximum predicted concentration was 0.053 mg/kg in the herbivorous fish, 0.015 mg/kg in the omnivorous fish and 0.026 mg/kg in the top predator. These maximum predicted body burdens were approximately 7900, 28000 and 16000 times lower respectively than the body burden of 420 mg/kg corresponding to the NOEC from the fish full life cycle study of 20 µg/L. EFSA notes that even the potentially lower chronic fish endpoint of 2 µg a.s./L, i.e. critical body

[17] Carbonell G, Ramos C, Pablos MV, Ortiz JA and Tarazona JV (2000). A system dynamic model for the assessment of different exposure routes in aquatic ecosystems. The Science of the Total Environment 247: 107-118

burden of 56 mg/kg (see above), would not change this conclusion. This conclusion would respect the outcome of the meeting of member state experts, as the potential lower chronic fish endpoint of 2 µg a.s./L was assessed, and exposure was based on initial FOCUS PEC_{sw} values to avoid 'double counting' of dissipation into sediment.

The risk of bioaccumulation of the metabolites of lufenuron was also considered in the DAR. The major metabolite CGA 149772 has a log P_{ow} of 0.26 and it broke down rapidly in metabolism studies, and therefore it was not expected to pose a high risk of bioaccumulation. The major metabolites CGA 224443 and CGA 238277 have a log P_{ow} of 3.7 and 4.3 respectively, and therefore an evaluation of their potential to bio-accumulate was triggered. The BCF for the metabolites were expected to be much lower than the BCF for lufenuron as indicated by the lower log P_{ow} values. On this basis, since the parent lufenuron was considered to pose a negligible bioaccumulation risk for aquatic organisms, it was concluded that the metabolites CGA 224443 and CGA 238277 would also pose a negligible risk. Furthermore, the metabolites were never found at any significant level in fish from the outdoor field study with bluegill sunfish (Volz 2003), although the metabolites were present in the surrounding environment.

Overall, the assessment for aquatic organisms (including food chain modelling) and sediment dwellers suggested a low risk from the intended outdoor uses of lufenuron and its metabolites, in case appropriate risk mitigation measures were applied, e.g. a no-spray buffer zone of 5 m for tomato use and no-spray buffer zone of approximately 25 m for vine uses. The latter risk assessment would be based on an assessment factor of 2. If an assessment factor of 3 was to be applied, further refinement of the risk would be required for the more susceptible FOCUS surface water scenarios. EFSA noted that no assessment of the risk to aquatic organisms from glasshouse use of lufenuron was provided in the DAR. However, considering an exposure equivalent to 0.1% emission (Dutch glasshouse assumption) was used, the exposure from glasshouse use would be lower than the exposure from field use for tomatoes (including a 5 m no-spray buffer zone).

5.3. RISK TO BEES

The effects of technical lufenuron were investigated in both an oral and a contact test and, as lufenuron acts as an insect growth regulator (IGR), a bee brood study was also provided with the formulation A-7814 A. No laboratory acute study was carried out with the lufenuron formulation, as it had been tested in higher tier field studies which were triggered by the effects observed in the brood test. Hazard quotients of 0.25 indicated a low risk to bees from lufenuron. The brood test, however, indicated detrimental effects on the brood at worst case exposure rates similar to the spray concentration for tomatoes. Higher tier field studies were provided in orchard sprayed at 75 g as/ha after flowering and in flowering melon crop sprayed at doses up to 50 g a.s./ha. Although there was only one application in the orchard field study, it was considered acceptable by the RMS since the dose was higher (75 g/ha) than the expected GAP use (50 g/ha) and because application was after flowering (GAP = end of flowering). In addition there was interception by the orchards and bees were only exposed to flowers

on the ground, but there were no observations of foraging activity (results of foraging activity were not reported). No effects were seen on brood and colony development. In the melon field study, the application (30 or 50 g a.s./ha) made during flowering was followed by foraging activity. The study showed the same results. The risk assessment to bees was discussed by member state experts. The meeting criticised the relevance and acceptability of the studies due to the lack of information in the study (i.e. foraging activity, no toxic standard, year 2003 was hot and that might have impacted the behaviour of the bees) and because there was only one application while the GAP indicated 1-3 application. Member state experts concluded that available data were not sufficient to assess the risk to bees exposed to the substance. Consequently, the exposure of the bees should be avoided by application after flowering of the crop or in the absence of flowering weeds. After the peer-review, EFSA considered that further data should be required to address the risk from flowering weeds. EFSA noted that the risk to bees was not assessed in the DAR for the glass-house tomato use. In case of Annex I inclusion member states may require data to address the risk to glass-house pollinators.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Studies with non-target arthropods have been conducted with the formulation A-7814 A. The testing strategy used for the studies provided in the DAR followed the approach recommended in the ESCORT 2 guidance document (Candolfi *et al.* 2001)[18] but focussing on the insect growth stages that are likely to be most sensitive to the effects of a growth regulator. In extended laboratory studies LR_{50} and reproductive endpoints were provided for *Typhlodromus pyri* (LR_{50} > 100 g a.s./ha, no significant reproductive effects at highest test rate of 100 g a.s./ha), *Coccinella septempunctata* (LR_{50} = 20-21 g a.s./ha, no effects on hatching at highest test rate of 45 g a.s./ha and no unacceptable effects on fecundity at the only test rate of 5 g a.s./ha), *Chrysoperla carnea* (LR_{50} = 0.4 g a.s./ha, no effects on hatching at highest test rate of 2.5 g a.s./ha and no unacceptable effects on reproduction at the only test rate of 0.025 g a.s./ha) and *Orius laevigatus* (LR_{50}, egg = 0.66 g a.s./ha and LR_{50}, nymphs = 5.3 g a.s./ha, no significant effects on hatching at highest test rate). For the in-field risk assessment no Hazard Quotient (HQ) was provided as no Tier 1 effect studies were available. LR_{50} endpoints from tier 2 studies were compared to the worst case in-field and off-field exposure rate, indicating effects greater than 50% were to be expected for some species both in-field and off-field. A higher tier field test was designed and carried out in order to address the risk from lufenuron as an IGR to sensitive stages of representative arthropods. An apple orchard was exposed to levels equivalent to in-crop exposure (2 x 50 g a.s./ha) and off-crop exposure (2 x 3.5 g a.s./ha). Member state experts discussed if the species in orchards were representative for tomatoes/vines. Experts noted that the exposure did not cover the intended GAP, recovery of all the affected species was not complete (in some cases at drift rate), the reference substance dimethoate displayed low effects and there were uncertainties about the

[18] Candolfi MP, Barrett KL, Campbell PJ, Forster R, Grandy N, Huet M-C, Lewis G, Oomen PA, Schmuck R & Vogt H (2001). Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. SETAC, Pensacola, USA. ISBN 1-8806110520x. Results of the ESCORT 2 Workshop, Wageningen 21-23 March 2000.

application rate if it corresponded to the full application rate or % of the "nominal" concentration. It was noted by experts that effects on some taxa were more extensive than was reported in the DAR. Based on the uncertainties expressed by experts it was concluded that the study should not be considered reliable for assessment of the intended uses. No conclusion could be drawn on the risk to non-target arthropods for any of the intended outdoor uses and further higher tier data were required to address the risk to non-target arthropods. EFSA notes that a response from the applicant to the conclusion of member state experts was provided in the DAR (addendum 2). The response was not included in this conclusion as it was provided after the peer-review. Furthermore, EFSA notes that the risk to non-target arthropods from glass-house tomato use has not been addressed in the DAR. In case of Annex 1 inclusion, member states may require data to address the risk to non-target arthropods used for biological pest control.

5.5. RISK TO EARTHWORMS

Studies on acute and long-term toxicity of lufenuron (LC_{50} > 1000 mg a.s./kg, $NOEC_{56\ d}$ = 1.2 mg a.s./kg) and its major metabolites CGA 224443 (LC_{50} = 530 mg a.s./kg, $NOEC_{56\ d}$ = 3.0 mg CGA 224443/kg), CGA 149772 (LC_{50} > 1000 mg a.s./kg) and CGA 238277 (LC_{50} = 610 mg a.s./kg), to earthworms were provided. No acute toxicity study was available with the formulation A-7814 A, since the formulation only contains a single active ingredient (lufenuron) and it was considered that the toxicity data obtained with the active substance could be used to predict reliably the toxicity of the formulation. The metabolite CGA 224443 had the highest acute toxicity to earthworms of the three major soil metabolites. In addition it was the most persistent, with a mean laboratory DT_{90} of 133 days, compared to 60.1 days and approximately 28 days for CGA 238277 and CGA 149772 respectively. A long-term earthworm reproduction study was therefore carried out with CGA 224443. All toxic endpoints were corrected, to take into account the log P_{ow} > 2. TER calculations for field uses were recalculated by EFSA during drafting of the conclusion and provided in Appendix 1, based on a new plateau PECsoil value also calculated by EFSA while drafting the conclusion. All calculated TER values were orders of magnitudes above the Annex VI trigger, indicating a low acute and long-term risk to earthworms from lufenuron and the relevant metabolites for all intended outdoor uses. The meeting of member state experts discussed if exposure from glasshouses was expected. For permanent glasshouses the risk was considered low by member state experts but for temporary glasshouses/tunnels member states might wish to ask for further data to clarify the risk to earthworms. No field test on earthworms was required since the risk assessment indicated low acute and chronic risk to earthworms. In addition, during a 21-days exposure in artificial soil at 0.026 mg/kg dw soil and 0.26 mg/kg dw soil dose rates, lufenuron did not accumulate in worms (*Eisenia fetida*). In conclusion the risk for earthworms was considered to be low for the intended uses of lufenuron.

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

The toxicity of the lufenuron formulation A-7814 A and the major metabolite of lufenuron, CGA 224443, to Collembola were determined. The NOEC for A-7814 A and CGA 224443 were 0.2 mg

as/kg and 6.4 mg CGA 224443/kg respectively. In addition, a litter bag test was carried out in which exposure to A-7814 A at 0.05 mg as/kg soil followed (after 13 days) by an application of 100 g as/ha, had no significant effect on organic material decomposition under field conditions. The risk assessment for Collembola provided in the revised DAR (addendum 2) was subsequently updated by EFSA while drafting the conclusion, based on new plateau PEC_{soil} values. The toxic endpoints were reduced by a factor two, due to log $P_{ow} > 2$. New TERs were calculated based on recalculation of the plateau PEC_{soil} values. Whereas a TER value of 178 indicated a low risk to Collembola from the metabolite CGA 224443, TER values of 0.82 and 2.3 for vine and tomato respectively, indicated that further refinements were required to identify a low risk. The potential risk was addressed in the DAR by the litterbag study. Member state experts, however, noted that the application rate in the litter bag study did not cover the intended uses (plateau PECsoil level was higher than the initial exposure in the litter bag study). Additionally, no monitoring of the fauna was performed and the study did not address the structural aspects. Member state experts agreed that no conclusion could be drawn on risk assessment to soil non-target macro-organisms or organic matter breakdown, and the applicant would need to submit appropriate information to address the risk to soil non-target macro-organisms and organic matter breakdown for all intended field uses. The RMS provided further assessment of the litter bag study in the revised DAR (addendum 2) after the peer-review. The RMS argued that the litter bag test addressed the risk to soil non-target macro-organisms, based on new calculations of plateau PEC_{soil} values provided by the RMS after the expert meeting. EFSA, however, calculated new plateau PEC_{soil} values of 0.087 mg a.s./kg in vine when drafting the conclusion, which still indicated that the exposure of 0.05 mg a.s./kg in the litterbag test would not cover the estimated plateau PEC_{soil}. The plateau PEC_{soil} of 0.031 mg a.s./kg calculated by EFSA for tomato may be covered by the level of exposure in the litter bag study. However, as there were further concerns regarding the limitations of the litter bag study and the latter assessments by the RMS and EFSA were provided after the peer-review, EFSA recommends keeping the data gap for further information to address the risk to soil non-target macro-organisms for the intended outdoor uses.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

Lufenuron had no significant effects, in terms of metabolic activity of the microbial biomass, in short-term respiration or nitrogen conversion tested in two soils at concentrations of 0.2 and 2 mg. In similar studies with the metabolites CGA 149772, CGA 224443 and CGA 23877 with concentrations up to 0.123, 0.15 and 0.155 mg/kg respectively, no deviations from the control > 25% were observed in terms of metabolic activity of the microbial biomass in nitrogen conversion or dehydrogenase activity tests. The tested exposure level was 23 times higher for lufenuron than the plateau PEC_{soil} estimated for the worst case use in vine. The tested effect levels for the metabolites were 8-40 times higher than the plateau PEC_{soil} concentrations expected for the metabolites at the worst case use. It was concluded that the risk to soil non-target micro-organisms was considered to be low for all intended uses.

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

A tier I screening of the effects of the formulation A-7814 A on pre- and post-emergence non-target higher plants was provided, showing no observable effects on 6 species (2 monocotyledons and 4 dicotyledons) at rates up to 1000 mL formulation/ha (nominally 50 g a.s./ha). TERs were all above the Annex VI trigger, based on the worst-case vine applications (maximum off-field predicted environmental rate ($PER_{off\text{-}field}$) of 4.01 g as/ha). The risk to non-target plants was assessed to be low.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

In a test for inhibition of oxygen consumption by activated sludge from a sewage treatment system a 3 hour EC_{50} > 100 mg a.s./L was determined for lufenuron and the two metabolites CGA 149772 and CGA 224443. It could be assumed that no undue effects to sewage treatment would occur, when lufenuron was applied according to the intended uses.

6. Residue definitions

Soil

Definition for risk assessment: constituent enantiomers of lufenuron, CGA 238277, CGA 224443 and CGA 149772

Definition for monitoring: constituent isomers of lufenuron

Water

Ground water

Definition for exposure assessment: constituent enantiomers of lufenuron, CGA 238277, CGA 224443 and CGA 149772

Definition for monitoring: constituent isomers of lufenuron

Surface water

Definition for risk assessment:

surface water: constituent enantiomers of lufenuron, CGA 238277, CGA 224443 and CGA 149772

sediment: constituent enantiomers of lufenuron, CGA 238277, CGA 224443 and CGA 149772

Definition for monitoring: constituent isomers of lufenuron

Air

Definition for risk assessment: constituent enantiomers of lufenuron

Definitions for monitoring: constituent isomers of lufenuron

Food of plant origin

Definition for risk assessment: constituent isomers of lufenuron

Definition for monitoring: constituent isomers of lufenuron

Food of animal origin

Definition for risk assessment: constituent isomers of lufenuron

Definition for monitoring: constituent isomers of lufenuron

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
Constituent enantiomers of lufenuron	High to very high persistence Single first order DT_{50} 151-434 days (European field studies)	Low risk to earthworms. Further data required to address the risk to soil non-target macro-organisms, as initial TER indicated a potential high risk to collembola from use of lufenuron
CGA 238277	Low to moderate persistence Single first order DT_{50} 6.6-38.4 days (20°C, -10kPa soil moisture)	Risk to soil organisms assessed to be low.
CGA 224443	Moderate to medium persistence Single first order DT_{50} 16.9-94.2 days (20°C, -10kPa soil moisture)	Risk to soil organisms assessed to be low.
CGA 149772	Low persistence Single first order DT_{50} 2.7-4 days (20°C, -10kPa soil moisture)	Risk to soil organisms assessed to be low.

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
Constituent enantiomers of lufenuron	Immobile K_{foc} 11888-74833 mL/g	No	Yes	Yes	Very toxic to aquatic organisms
CGA 238277	slight mobility K_{foc} 2156-2441 mL/g	No	No	No data available. Assessment not required.	Very toxic to aquatic organisms
CGA 224443	slight mobility to immobile K_{foc} 4388-5684 mL/g	No	No	Data available: oral LD_{50} 1273 mg/kg bw Ames test negative no reproductive toxicity Assessment not required.	Very toxic to aquatic organisms
CGA 149772	Very high mobility K_{foc} 0 mL/g	No	No	Acute data available. Assessment not required.	Harmless to aquatic organisms

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Constituent enantiomers of lufenuron	Risk to aquatic organisms assessed to be low, based on a no-spray buffer zone of 5 m for tomato use and a no-spray buffer zone of approximately 25 m for vine use.
CGA 238277	Risk to aquatic organisms assessed to be low
CGA 224443	Risk to aquatic organisms assessed to be low
CGA 149772	Risk to aquatic organisms assessed to be low

Air

Compound (name and/or code)	Toxicology
Constituent enantiomers of lufenuron	LC_{50} by inhalation >2.3 mg/L/4h (highest achievable concentration of the aerosol) – no classification

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

- A specification which is supported by the batch data (relevant for all uses evaluated, data gap identified by PRAPeR meeting of experts May 2008, proposed submission date unknown, refer to chapter 1)
- Impact of different isomer ratios on the consumer risk assessment of lufenuron needs to be addressed (relevant for all applied for intended uses; data gap identified by EFSA after the experts' meeting; no submission date proposed; refer to point 3.1.1).
- Lufenuron consists of 2 enantiomers. This needs to be taken into account in the environmental risk assessment. Information on the toxicity and/or on the degradation of the 2 enantiomers in the environment is needed. (relevant for all representative uses evaluated; no submission date proposed by the applicant; refer to sections 4 and 5).
- FOCUS surface water PEC calculations at step 4 for a no spray buffer distance of 25 m (relevant for use in vines, data gap identified by EFSA when finalising the conclusion; submission date proposed by the notifier: unknown; refer to points 4.2.1 and 5.2)
- An analysis to derive a statistical significant endpoint from the prolonged toxicity study with fish (Vial, 1992) is required (relevant for field uses in vine and tomatoes; submission date proposed by the notifier: no date suggested; data gap agreed in the meeting of experts; refer to point 5.2)
- A higher tier field study is required to address the risk to non-target arthropods (relevant for field uses in vine and tomatoes; submission date proposed by the notifier: no date suggested; data gap agreed in the meeting of experts; refer to point 5.4)
- A higher tier study to address the risk to soil non-target macro-organisms is required (relevant for field uses in vine and tomatoes; submission date proposed by the notifier: no date suggested; data gap agreed in the meeting of experts; refer to point 5.6)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

This conclusion was reached on the basis of the evaluation of the representative uses as an insecticide on grapes and tomatoes. Full details of the GAP can be found in the attached list of end points.
The representative formulated product for the evaluation was "Match 050 EC", an emulsifiable concentrate (EC).

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a modified multi-method (The German S19

method). The extraction procedure was as detailed in S19 however, the analysis was performed by LC-MS/MS which is a detection method not used in the multi-method.
For the other matrices only single methods are available to determine residues of lufenuron.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. The outstanding issue is that the specification is not agreed.

With regard to its toxicological properties, lufenuron has shown a potential of bioaccumulation in fat, and a systemic bioavailability of 70%, with a very low metabolism. During the acute toxicity testing, lufenuron showed skin sensitisation properties and the classification as **R43 "May cause sensitisation by skin contact"** was proposed. In oral short term studies with different species, clinical signs of neurotoxicity (tonic-clonic seizures or convulsions) and liver changes were observed, as well as some deaths in one dog study resulting in the proposed classification **Xn, R48/22 "Harmful: danger of serious damage to health by prolonged exposure if swallowed"**. No mutagenic or carcinogenic potential was detected in the available studies. In the long term studies, the incidence and severity of the convulsions in both species were also taken into account for the setting of the NOAELs. No specific adverse effect on fertility or embryofoetal development was observed in the studies for reproductive toxicity, with low maternal toxicity (reduced body weight) and minimal offspring toxicity (delayed righting reflex). In a 4-month neurotoxicity with rats, convulsions or fasciculations were induced at the high dose without any impairment of motor/cognitive functions or histopathological changes in the nervous system.
The agreed **acceptable daily intake** (**ADI**) was **0.015 mg/kg bw/day**, the agreed **acceptable operator exposure level** (**AOEL**) was 0.01 mg/kg bw/day, and the acute reference dose (ARfD) was considered not necessary. The agreed dermal absorption values for humans were 13% for the dilution and 2% for the concentrate. The operator exposure estimates with the German model for use in field or in greenhouse didn't show exposure levels above the AOEL even without the use of personal protective equipment.

The metabolism of lufenuron has been tested in three crop categories namely tomato (fruits), cabbage (leafy crop) and cotton (pulses and oilseeds). Lufenuron is always the major component of the residue, no significant metabolites were found. It was concluded that the residue definition for risk assessment and monitoring is lufenuron. A full set of residue trials were supplied for grapes in the north and south of Europe. A full set of residue data was available for protected tomatoes a reduced data set was accepted for outdoor tomatoes in the south as the use is much less critical.
The stability of residues in freezer storage was demonstrated for a period of two years. Sufficient processing data were submitted for tomatoes and grapes which showed an overall reduction of the residues in processed commodities. The rotational crop studies demonstrated that residues of lufenuron are unlikely to occur. Certainly, given that lufenuron is lipophilic, it is unlikely to be taken

up by plants. The only possible issue would be soil contamination but this will easily be removed during preparation.
From the representative uses in grape and tomato evaluated there is no animal intake according to the current guidance. However, metabolism studies in hens and goats were provided that demonstrated that the only significant residue that will be present is lufenuron. Feeding studies were also provided but it can not be concluded if the dose levels are appropriate because there are no animal intakes from the representative crops. Lufenuron is a pair of enantiomers and it is currently not addressed if the ratio remains the same in the plant metabolism. Potentially the consumer risk assessment could under estimate the risk by a factor of 2 (assuming the residue is only 1 isomer and all the toxicity comes from it). For the UK consumer model intakes were highest for the vegetarian population subgroup at 10 % of the ADI using the STMR and 80% of the ADI when using the proposed MRLs. For the WHO European diet the TMDI was 3.42 % and IEDI was 0.62 %. For the Portuguese diet the TMDI was 20.22% and the NEDI was 2.63%. An acute risk assessment has not been conducted as an ARfD has not been set.

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, though information on the behaviour of the individual enantiomers is not available. Also the provision of FOCUS surface water step 4 calculations for the use on vines with a no spray buffer distance of 25 m would enable a confirmation of the number of FOCUS surface water scenarios that respect the agreed peer reviewed TER triggers for the requested use on vines. For the applied for intended uses, the potential for groundwater exposure by lufenuron and its soil metabolites CGA 238277, CGA 224443 and CGA 149772 above the parametric drinking water limit of 0.1 µg/L, is low.

The acute toxicity to birds and mammals and the short-term toxicity to birds were considered to be low from exposure to lufenuron. Long-term reproductive endpoints of 19.7 and 8.7 mg a.s./kg bw/d were agreed by member state experts for birds and mammals respectively. TERs from the standard tier 1 risk assessment indicated a low risk for all intended outdoor uses, except for the risk to small herbivorous mammals from the use in vine. A refined risk assessment provided after the peer-review and agreed by EFSA indicated a low risk, based on an vine foliage interception factor of 70%. The risk from consumption of contaminated drinking water from puddles was assessed as low. The risk from secondary poisoning for the worst-case vine use was assessed as low, based on a no-spray buffer zone of 5 m and 10 m respectively for fish eating birds and mammals. The potential for biomagnification was assessed as high for birds and mammals. Food-chain modelling indicated a low risk for all steps of the food chain for the worst case use in vine, based on appropriate mitigation measures (e.g. no-spray buffer zones). No mitigation measures were required for the tomato use. The risk to birds and mammals from the metabolite CGA 224443 was assessed as low by the RMS after the peer-review.

The toxicity of lufenuron suggested a classification as very toxic to aquatic organisms. The lowest acute end point value for *Daphnia magna* was an EC_{50} of 0.4 µg a.s./L, based on a formulation study. The lowest chronic toxicity to fish (NOEC=20 µg a.s./L) was identified from a fish full life cycle study. A lower NOEC of 2 µg a.s./L could potentially be derived from a chronic toxicity study with fish, pending further statistical analysis. The chronic study to daphnia was not accepted by member state experts. No new study was required as chronic toxicity to invertebrates was covered by a microcosm study. A NOAEC of 0.1 µg a.s./L was agreed by member state experts with an assessment factor of 2-3. The aquatic risk assessment for the tomato use indicated a low risk, based on the microcosm endpoint and no-spray buffer zones of 5 m. For use in vine a low risk was identified, based on a no-spray buffer zone of approximately 25 m. The latter assessment would be based on an assessment factor of 2. Application of an assessment factor of 3 would require further refinement of the risk characterisation for potentially more susceptible FOCUS surface water scenarios. The risk to sediment dwellers from lufenuron exposure was assessed as low in case of a no spray buffer zone of 5 m, as well as the risk from the relevant metabolites. Bioaccumulation and bio-magnification was assessed, resulting in a BCF of 28.000 and a slow elimination rate. Risk assessment based on food-chain modelling suggested a low risk to fish, also considering the potential lower toxicity of 2 µg a.s./L from the chronic fish toxicity study.

Firs tier risk assessment indicated a risk to bees. As the higher tier field studies were not accepted by member state experts, lufenuron should not be applied during the flowering season of the GAP crops. Further data were required to address the risk to bees from treated flowering weeds. The initial risk assessment to non-target arthropods from lufenuron (IGR) indicated a potential high risk. The higher tier field study was not accepted by member state experts. Further data was required to address the risk to non-target arthropods. The assessment of soil non-target macro-organisms indicated a potential high risk to collembola. The higher tier litter bag study provided to address the risk was not accepted by member state experts, as the exposure did not cover the expected plateau PEC_{soil}. Further data were required to address the risk.

The risk to earthworms, soil non-target micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

Persistent bioaccumulating and toxic (PBT) hazard assessment criteria (chemical safety assessment under REACH[19])

During the written commenting period on the final draft of this conclusion, 2 member states commented that lufenuron fulfilled the criteria to be considered a PBT substance under the hazard assessment criteria that have been defined under REACH Annex XIII.

[19] REACH Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006. Guidance on information requirements and chemical safety assessment Annex XIII. Chapter R.11: PBT Assessment, May 2008 Guidance on the implementation of REACH

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

- A no-spray buffer zone of 5 m was required for use in vine to address the risk for fish-eating birds and the risk to predatory birds as indicted by the hawk assessment based on the food chain modelling.
- A no-spray buffer zone of up to 10 m was required for use in vine to address the risk for fish-eating mammals and the risk to predatory mammals as indicted by the otter assessment based on the food chain modelling.
- For the aquatic risk assessment a no-spray buffer zone of 5 m for the tomato use and a no-spray buffer zone of approximately 25 m for vine uses were required. The latter mitigation proposal would be based on an assessment factor of 2. If an assessment factor of 3 was to be applied, than for the more susceptible FOCUS surface water scenarios, further information to refine the risk characterisation would be required.
- The exposure of bees during flowering or in the presence of flowering weeds should be avoided. Member States may also consider the risk to glasshouse pollinators and non target arthropods used for biological pest control

Critical areas of concern

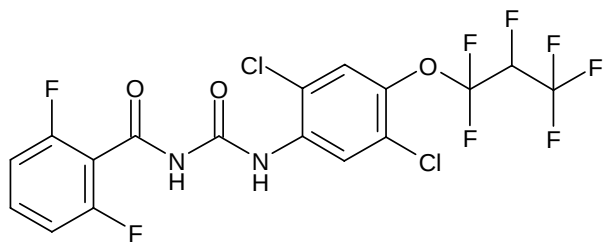
- An agreed specification is not available
- The risk assessment for non-target arthropods was not finalised.
- The risk assessment for soil non-target macro-organisms was not finalised

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

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

Active substance (ISO Common Name) ‡	Lufenuron
Function (*e.g.* fungicide)	Insecticide
Rapporteur Member State	Portugal
Co-rapporteur Member State	

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(*RS*)-1-[2,5-dichloro-4-(1,1,2,3,3,3-hexafluoro-propoxy)-phenyl]-3-(2,6-difluorobenzoyl)-urea
Chemical name (CA) ‡	N-[[[2,5-dichloro-4-(1,1,2,3,3,3-hexafluoro-propoxy)-phenyl]amino]carbonyl]-2,6-difluoro-benzamide
CIPAC No ‡	704
CAS No ‡	103055-07-8
EC No (EINECS or ELINCS) ‡	not available
FAO Specification (including year of publication) ‡	not available
Minimum purity of the active substance as manufactured ‡	Open
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	none
Molecular formula ‡	$C_{17}H_8Cl_2F_8N_2O_3$
Molecular mass ‡	511.2 g/mol
Structural formula ‡	

Appendix 1 – list of endpoints

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	168.7°C to 169.4°C (997 g/kg)
Boiling point (state purity) ‡	thermal decomposition starts at about 242°C before the boiling point is reached (997 g/kg)
Temperature of decomposition (state purity)	242°C (997 g/kg)
Appearance (state purity) ‡	white fine powder (997 g/kg)
	white fine free-flowing powder (961 g/kg)
Vapour pressure (state temperature, state purity) ‡	$< 4 \cdot 10^{-6}$ Pa at 25°C (995 g/kg)
Henry's law constant ‡	$< 3.4 \cdot 10^{-2}$ Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	pH 5: 54 µg / L (25 °C) pH 7: 46 µg / L (25 °C) pH 9: 64 µg / L (25 °C) (997 g/kg)
Solubility in organic solvents ‡ (state temperature, state purity)	All in g/L at 25ºC: acetone 460 dichloromethane 84 ethyl acetate 330 hexane 0.10 methanol 52 octanol 8.2 toluene 66 (995 g/kg)
Surface tension ‡ (state concentration and temperature, state purity)	68.3 - 72.8 mN/m (filtrates of 10.0 g/L suspension, at 20ºC) (961 g/kg)
Partition co-efficient ‡ (state temperature, pH and purity)	log P_{OW} = 5.12 (25 ºC) (pH: no dependence on pH expected) (995 g/kg)

Appendix 1 – list of endpoints

Dissociation constant (state purity) ‡	pKa_1 = 10.18 at 20ºC in methanol:water mixtures (997 g/kg)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	ε_{max} = 37293 $L.cm^{-1}.mol^{-1}$ at λ = 210 nm in neutral solution (methanol) ε = 30588 $L.cm^{-1}.mol^{-1}$ at λ = 210 nm in acidic solution (methanol + 1N HCl) ε = 4871 $L.cm^{-1}.mol^{-1}$ at λ = 295 nm in basic solution (methanol + 1N NaOH) No absorption maximum between 295 and 750 nm. (997 g/kg)
Flammability ‡ (state purity)	Not highly flammable (961 g/kg)
Explosive properties ‡ (state purity)	Not explosive (961 g/kg)
Oxidising properties ‡ (state purity)	Not oxidising (961 g/kg)

Appendix 1 – list of endpoints

Summary of representative uses evaluated (*Lufenuron*)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
Grape	N EU	Match 050 EC	F	Biting and sucking insects	EC	50 g/l	High volume spraying	End flowering to ripening	1 - 2	14	5	1000	50	21	[1]
Grape	S EU	Match 050 EC	F	Biting and sucking insects	EC	50 g/l	High volume spraying	End flowering to ripening	1 - 2	14	5	1000	50	21	[1]
Tomato	S EU	Match 050 EC	F	Biting and sucking insects	EC	50 g/l	High volume spraying	Fruiting to PHI	1 - 3	7	3	1000	30	7	[1]
Tomato	EU	Match 050 EC	G	Biting and sucking insects	EC	50 g/l	High volume spraying	3 leaves to PHI	1 - 3	7	10	1000	100	7	[1]

* 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

Appendix 1 – list of endpoints

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV
Impurities in technical as (analytical technique)	organic by-products by HPLC, residual solvents by GC
Plant protection product (analytical technique)	HPLC-UV No CIPAC method is available.

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		constituent isomers of lufenuron
Food of animal origin		constituent isomers of lufenuron however no MRL is proposed
Soil		constituent isomers of lufenuron
Water	surface	constituent isomers of lufenuron
	drinking/ground	constituent isomers of lufenuron
Air		constituent isomers of lufenuron

Appendix 1 – list of endpoints

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	High water, high acid content and dry matrices: Extraction and cleanup based on multi-residue method DFG S19 followed by HPLC-MS/MS – 0.02 mg/kg (Primary method Anspach and ILV Schulz)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not required (no MRL proposed)
Soil (analytical technique and LOQ)	HPLC-MS/MS – 0.01 mg/kg
Water (analytical technique and LOQ)	HPLC-MS/MS – 0.05 µg/L (Surface water and drinking water)
Air (analytical technique and LOQ)	HPLC-UV - 1.0 µg/m^3
Body fluids and tissues (analytical technique and LOQ)	Not required (a.s. is not classified as toxic or highly toxic).

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

	RMS/peer review proposal
Active substance	Not classified

Appendix 1 – list of endpoints

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Systemic bioavailability of ca 70%.
Distribution ‡	Initially widely distributed; highest residues in fat at 168 hours.
Potential for accumulation ‡	Potential for accumulation in fat, terminal half life of up to 37 days.
Rate and extent of excretion ‡	Slow: 33% within 24h, still measurable after 21 days Mainly in faeces by a non biliary process
Metabolism in animals ‡	Metabolism is minimal (app. 1%) by deacylation followed by cleavage of the ureido group.
Toxicologically relevant compounds ‡ (animals and plants)	Lufenuron.
Toxicologically relevant compounds ‡ (environment)	Lufenuron.

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 ‡	> 2.35 mg/L 4h, nose only, aerosol (maximum achievable concentration)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	Sensitiser (Magnusson & Kligman)	R43

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Tonic-clonic convulsions (rats, mice, dogs) Liver changes (rats, dogs), thyroid changes (dogs) Mortality at higher doses (LOAEL 30 mg/kg bw/d in dogs)	
Relevant oral NOAEL ‡	1.5 mg/kg bw/d (1-yr, dog) 10 mg/kg bw/d (90-d, rat)	Xn; R48/22

Appendix 1 – list of endpoints

Relevant dermal NOAEL ‡	1000 mg/kg bw/d (highest dose tested, 28-day rat)	
Relevant inhalation NOAEL ‡	No data available – not required.	

Genotoxicity ‡ (Annex IIA, point 5.4)

No genotoxic potential.	

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

Target/critical effect ‡	Tonic-clonic convulsions (rat, mouse: LOAEL 20/22 mg/kg bw/d), deaths (mouse) Lungs, liver and urinary tract (rats) Liver and prostate (mice)	
Relevant NOAEL ‡	2.0 mg/kg bw/d (2-year, rat) 2.1 mg/kg bw/d (18-month, mouse)	
Carcinogenicity ‡	No carcinogenic potential.	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Offspring: minimal delay in the emergence of righting reflex Parental/Reproductive: no adverse effect	
Relevant parental NOAEL ‡	20 mg/kg bw/d (highest dose tested)	
Relevant reproductive NOAEL ‡	20 mg/kg bw/d (highest dose tested)	
Relevant offspring NOAEL ‡	8 mg/kg bw/d	

Developmental toxicity

Developmental target / critical effect ‡	Minimal maternal toxicity (reduction in body weight gain and food consumption) in rats. No embryofoetal toxicity.	
Relevant maternal NOAEL ‡	Rats: 500 mg/kg bw/d Rabbits: 1000 mg/kg bw/d (highest dose tested)	

Appendix 1 – list of endpoints

Relevant developmental NOAEL ‡	Rats and rabbits: 1000 mg/kg bw/d (highest dose tested)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data – not required	
Repeated neurotoxicity ‡	4-month rat neurotoxicity study: Single episodes of clonic-tonic convulsions or fasciculations and facilitated pentylenetetrazol-induced generalised convulsions. NOAEL: 5.4 mg/kg bw/d	
Delayed neurotoxicity ‡	No data – not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data – not required.
Studies performed on metabolites or impurities ‡	Metabolite CGA 224433 LD_{50}, oral in rats: 1273 mg/kg bw Ames test negative One-generation study in rats: mean number of implantations sites and average litter size were significantly lower at maternally toxic levels (reduced body weight and liver changes). Maternal and offspring NOAEL: 9.7 mg/kg bw/d Reproductive NOAEL: 63.3 mg/kg bw/d Metabolite CGA 149772 LD_{50}, oral in rats: 2065 mg/kg bw

Medical data ‡ (Annex IIA, point 5.9)

No detrimental effects on health in manufacturing personnel.

Appendix 1 – list of endpoints

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.015 mg/kg bw/d	Dog, 1-y study	100
AOEL ‡	0.010 mg/kg bw/d	Dog, 1-y study	100 and 70% of systemic bioavailability
ARfD ‡	Not allocated – not necessary		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation MATCH® 050 EC (50 g/L)	Rat *in vivo* and comparative *in vitro* (human/rat skin). Concentrate: 2% Spray dilution: 13%

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Estimated exposures (in % AOEL) without/with PPE		
		UK POEM	German model
	tractor appl., low crops high crops	147 / 24 273 / 190	27 / 6 89 / 14
	hand-held appl., low crops high crops	190 / 71 -	- 69 / 16
	greenhouse appl.	-	58 / 2 (German study)
Workers	Estimated exposures (in % of AOEL): 39% without PPE 2% with PPE		
Bystanders	Exposure considered to be negligible: 1% of AOEL		

Appendix 1 – list of endpoints

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

	RMS/peer review proposal
Substance classified (lufenuron)	Xn Harmful R43 May cause sensitization by skin contact R48/22 Harmful: danger of serious damage to health by prolonged exposure if swallowed

Appendix 1 – list of endpoints

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

Plant groups covered	Fruits (tomato), Leafy vegetable (cabbage), Oilseeds and pulses (cotton)
Rotational crops	Lettuce, wheat, maize, carrot, sugar beet
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Grapes (raisin, juice and wine); tomato (juice, perserve and puree)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	constituent isomers of lufenuron
Plant residue definition for risk assessment	constituent isomers of lufenuron
Conversion factor (monitoring to risk assessment)	none

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

Animals covered	Goats and hens
Time needed to reach a plateau concentration in milk and eggs	8-10 days in milk 10-11 days in eggs
Animal residue definition for monitoring	constituent isomers of lufenuron
Animal residue definition for risk assessment	constituent isomers of lufenuron
Conversion factor (monitoring to risk assessment)	not applicable
Metabolism in rat and ruminant similar (yes/no)	yes
Fat soluble residue: (yes/no)	yes

Appendix 1 – list of endpoints

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

In a confined field plot treated with radiolabelled lufenuron at a rate equivalent to 130 g as/ha residues in food and feed commodities were <0.01 mg/kg. In a indoor study (150 g as/ha) the residues were generally below 0.01 mg/kg except for lettuce and carrot root (126 d) where the TRR was 0.047 and 0.023 mg/kg respectively.

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

Lufenuron is stable in cottonseed, cabbage and oranges for at least 24 months at –180C. Lufenuron residues are stable for at least 9 months in animal tissues, milk and blood at –180C.

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)	No	No	No
Potential for accumulation (yes/no):	Yes	Yes	-
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Yes	Yes	-
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	-	-	-
Liver	-	-	-
Kidney	-	-	-
Fat	-	-	-
Milk	-		
Eggs		-	

Appendix 1 – list of endpoints

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)
Grapes	N and S	N: 2x 0.05, 2x 0.06, 0.08, 0.10, 3x0.12, 0.19, 0.34 S: 2 x 0.11, 0.14, 0.15, 0.19, 0.22, 0.35, 0.55, 0.67		1	0.67	0.12
Tomato	N and S	Indoor: 0.02, 2x 0.04, 2x 0.05, 2x 0.07, 2x 0.08, 0.09, 0.10, 0.11, 0.25		0.3	0.25	0.07
	S	Field: 2x <0.02, 0.03; 0.05	Not used for MRL calculation			-

(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

Appendix 1 – list of endpoints

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

ADI	0.015 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	3.42%
TMDI (% ADI) according to national (to be specified) diets	20.22% (portuguese diet), 80% (UK diet)
IEDI (WHO European Diet) (% ADI)	0.62 %
NEDI (specify diet) (% ADI)	2.63 % (portuguese diet), 10 % (UK diet)
Factors included in IEDI and NEDI	-
ARfD	Not proposed as there are no acute concerns
IESTI (% ARfD)	Not applicable
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not applicable
Factors included in IESTI and NESTI	Not applicable

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	
Grape/raisin	1	6.2 (mean)	-	134
Grape/wine	4	0 (residue found <0.02 mg/kg)	-	0%
Tomato/juice	1	0 (residue found <0.005 mg/kg)	-	0%
Tomato/preserve	1	0 (residue found <0.005 mg/kg)	-	0%
Tomato/puree	1	0.85	-	96

Appendix 1 – list of endpoints

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

Grapes	1 mg/kg
Tomatoes	0.3 mg/kg

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

Appendix 1 – list of endpoints

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

Mineralization after 100 days ‡	2-15 % after 149/360 d, [^{14}C-dichlorophenyl]-label (n^{20}= 4) 58 % after 360 d, [^{14}C-difluorophenyl]-label (n= 1) Sterile conditions: 0.05% after 91 days (n= 1)
Non-extractable residues after 100 days ‡	24.6-74.9 % after 149/360 d, [^{14}C- dichlorophenyl]-label (n= 4) 28.3 % after 360 d, [^{14}C- difluorophenyl]-label (n= 1) Sterile conditions: 0.77% after 91 days (n= 1)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	CGA 238277 - 10-31.8% at 82-30 d (n= 4) [^{14}C-dichloropheny] label CGA 224443 – 21.6-32.8 % at 59-149 d (n= 4) [^{14}C-dichloropheny] label

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

Anaerobic degradation ‡

Mineralization after 100 days	2.7 % after 90 d, [^{14}C- dichloropheny]-label (n= 1) 39.6 % after 90 d, [^{14}C- difluorophenyl]-label (n= 1) Sterile conditions: not studied
Non-extractable residues after 100 days	32.4 % after 90 d, [^{14}C- dichloropheny]-label (n= 1) 34.4 % after 90 d, [^{14}C- difluorophenyl]-label (n= 1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	none

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	CGA 149772 – 11.1 % at 16 d (n= 1) [^{14}C- difluorophenyl] label

[20] n corresponds to the number of soils.

Appendix 1 – list of endpoints

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

Laboratory studies ‡

lufenuron	Aerobic conditions						
Soil type	X[21]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam	a	7.2	20ºC / 75% 0.33 bar	29.6/98.3	24.2	0.992	SFO (k=0.013)
Loam	a	6.8	20ºC / 75% 0.33 bar	21.2/70.6	17.3	0.990	SFO (k=0.033)
Loam	b	6.8	20ºC / 75% 0.33 bar	13.6/45.2	11.1	0.997	SFO (k=0.051)
Loamy sand	a	5.0	20ºC / 40% MWHC	83.1/276.1	75.7	0.992	SFO (k=0.008)
Sandy loam	a	7.3	20ºC / 40% MWHC	17.4/57.6	11.8	0.974	SFO (k=0.04)
Silt loam	a	7.2	20ºC / 60 FC	16.3/54.0	13.0	0.979	SFO (k=0.043)
Geometric mean/median					**20.8***		

a – [^{14}C- dichlorophenyl]-label
b - [^{14}C- difluorophenyl]-label
* the overall geomean was calculated using the 5 values, with 2 experiments in the loam soil considered as replicates (single value for the loam soil of 13.9 days)

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

Appendix 1 – list of endpoints

CGA238277	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam	a	7.2	20ºC / 75% 0.33 bar	13.6/45.1	k1=0.05 ff=0.88 parent	11.1	0.989	SFO-parentFOMC
Loam	a	6.8	20ºC / 75% 0.33 bar	8.1/26.8	k1=0.086 ff=0.989 parent	6.6	0.987	SFO-parentFOMC
Sandy loam	a	5.0	20ºC / 40% MWHC	42.1/139.8	k1=0.016 ff=0.373 parent	38.4	0.990	SFO-SFO
Loamy sand	a	7.3	20ºC / 40% MWHC	14.0/46.4	k1=0.049 ff=0.776 parent	9.5	0.986	SFO-SFO
Silt loam	a	7.2	20ºC / 60 FC	12.8/42.5	k1=0.054 ff=0.863 parent	10.2	0.972	SFO-SFO
Geometric mean/median				15.8/52.1		**12.2**		

a – [^{14}C- dichloropheny]-label

Appendix 1 – list of endpoints

CGA224443	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam	a	7.2	20ºC / 75% 0.33 bar	51.6/171.3	k2=0.013 ff=0.724 CGA238277	42.2	0.989	SFO-SFO
Loam	a	6.8	20ºC / 75% 0.33 bar	48.1/159.8	k2=0.014 ff=0.489 CGA238277	39.3	0.987	SFO-SFO
Sandy loam	a	5.0	20ºC / 40% MWHC	103.4/344	k2=0.028 ff=0.994 CGA238277	94.2	0.990	SFO-SFO
Loamy sand	a	7.3	20ºC / 40% MWHC	24.8/82.5	k1=0.048 ff=0.84 parent	16.9	0.986	SFO-SFO
Silt loam	a	7.2	20ºC / 60 FC	35.8/118.8	k2=0.019 ff=0.748 CGA238277	28.5	0.972	SFO-SFO
Geometric mean/median				50.2/155.9		**37.6**		

a – [^{14}C- dichloropheny]-label

CGA 149772	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Silt loam		7.2	20ºC / 45%	2.7/8.8	-	2.7	0.990	SFO
Silt loam		7.6	20ºC / 45%	4.0/13.4	-	4.0	0.987	SFO
Sandy loam		5.1	20ºC / 45%	4.8/15.9	-	3.3	0.993	SFO
Geometric mean/median				3.7/12.3		**3.3**		

Appendix 1 – list of endpoints

Field studies ‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X [1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Clay loam/cropped	Huesca/Spain		7.4	0-20	151	503	0.88	94	SFO (χ2=18.9)
Clay loam/cropped	Klus/Switzerland		7.3	0-30	198	659	0.85	115	SFO (χ2=29.3)
Sandy loam/crooped	Termi/Greece		7.5	0-20	334	1141	0.74	291	SFO (χ2=16.3)
Loam/crooped	Buzignargues/France		7.9	0-10	434	1444	0.75	372	SFO (χ2=5.3)
Geometric mean/median					256			**185**	

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	Plateau concentration of 0.056 mg/kg reached after 6 years application of 100 g/ha per annum in field studies in vine. Plateau concentration of 0.034 mg/kg reached after 5 years application of 90 g/ha per annum in field studies in tomato

Laboratory studies ‡

Parent	Anaerobic conditions - not estimated

Appendix 1 – list of endpoints

Soil adsorption/desorption (Annex IIA, point 7.1.2)

lufenuron ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sand	0.43	7.0	210	-	321	74833	1.06
Loamy sand	0.77	5.7	395	-	481	62357	1.04
Silt loam	1.39	5.7	577	-	166	11888	0.81
Silt loam	4.39	7.1	2225	-	1963	44714	1.00
Humic soil	19.4	6.6	2309	-	2350	12117	1.00
Arithmetic mean/median					1056	41182	
pH dependence, Yes or No			No				

CGA 238277 ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	1.1	7.6	23.4	-	23.7	2156	1.02
Silt loam	2.1	7.3	55.6	-	50.8	2441	0.95
Silt loam	4.7	7.2	131	-	103	2191	0.87
Arithmetic mean/median					59.2	2263	
pH dependence (yes or no)			No				

CGA 224443 ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	0.78	7.4	44.9	-	44.3	5684	0.94
Loam	2.0	7.1	93.7	-	87.8	4388	0.90
Silt loam	4.7	7.2	241	-	222	4718	0.89
Arithmetic mean/median					118	4930	
pH dependence (yes or no)			No				

CGA 149772 ‡ No measurable adsorption

Appendix 1 – list of endpoints

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

Column leaching ‡	Not studied
Aged residues leaching ‡	Not studied
Lysimeter/ field leaching studies ‡	Not studied

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	DT_{50} (d): 434 days Kinetics: SFO Field or Lab: representative worst case from field studies.
Application data	Crop: vine Depth of soil layer: 5cm Soil bulk density: 1.5g/cm^3 % plant interception: 70% Number of applications: 2 Interval (d): 14 Application rate(s): 50 g as/ha

$PEC_{(s)}$ (mg/kg)	**Single application Actual**	**Single application Time weighted average**	**Multiple application Actual**	**Multiple application Time weighted average**
Initial	0.020		0.087	
Short term				
24h	0.020	0.020	0.087	0.087
2d	0.020	0.020	0.087	0.087
4d	0.020	0.020	0.087	0.087
Long term				
7d	0.020	0.020	0.086	0.087
28d	0.019	0.020	0.083	0.085
50d	0.018	0.019	0.081	0.084
100d	0.017	0.018	0.074	0.081
Plateau concentration	0.049 mg/kg after 10 yr			

Appendix 1 – list of endpoints

CGA 238277 Method of calculation	Molecular weight relative to the parent: 371/511 DT_{50} (d): 38.4 days Kinetics: SFO Field or Lab: representative worst case from lab studies.
Application data	Assumed Met is formed at a maximum of 31.8 % of the max PEC for lufenuron

PEC(s) (mg/kg)	**Single application Actual**	**Single application Time weighted average**	**Multiple application Actual**	**Multiple application Time weighted average**
Initial			0.020	
Short term				
24h			0.020	0.020
2d			0.019	0.020
4d			0.019	0.019
Long term				
7d			0.018	0.019
28d			0.012	0.016
50d			0.008	0.013
100d			0.003	0.009
Plateau concentration	Not relevant			

Appendix 1 – list of endpoints

CGA 224443 Method of calculation	Molecular weight relative to the parent: 328/511 DT_{50} (d): 94.2 days Kinetics: SFO Field or Lab: representative worst case from lab studies.
Application data	Assumed Met is formed at a maximum of 32.8 % of the max PEC for lufenuron

PEC(s) (mg/kg)	**Single application Actual**	**Single application Time weighted average**	**Multiple application Actual**	**Multiple application Time weighted average**
Initial			0.018	
Short term				
24h			0.018	0.018
2d			0.018	0.018
4d			0.017	0.018
Long term				
7d			0.017	0.018
28d			0.015	0.016
50d			0.012	0.015
100d			0.009	0.013
Plateau concentration	Not relevant			

Appendix 1 – list of endpoints

CGA149772 Method of calculation	Molecular weight relative to the parent: 157/511 DT_{50} (d): 4.4 days Kinetics: SFO Field or Lab: representative worst case from lab studies.
Application data	Assumed Met is formed at a maximum of 10.1 % of the max PEC for lufenuron

PEC(s) (mg/kg)	**Single application Actual**	**Single application Time weighted average**	**Multiple application Actual**	**Multiple application Time weighted average**
Initial			0.003	
Short term				
24h			0.002	0.002
2d			0.002	0.002
4d			0.001	0.002
Long term				
7d			0.001	0.002
28d			0.000	0.001
50d				
100d				
Plateau concentration	Not relevant			

Appendix 1 – list of endpoints

Parent Method of calculation	DT_{50} (d): 434 days Kinetics: SFO Field or Lab: representative worst case from field studies.
Application data	Crop: Tomato Depth of soil layer: 20cm to calculate the plateau then 5cm in final year or for the single application just 5cm Soil bulk density: 1.5g/cm^3 % plant interception: 80% Number of applications: 3 Interval (d): 7 Application rate(s): 30 g as/ha

$PEC_{(s)}$ (mg/kg)	**Single application Actual**	**Single application Time weighted average**	**Multiple application Actual**	**Multiple application Time weighted average**
Initial	0.024		0.031	
Short term				
24h	0.024	0.024	0.031	0.031
2d	0.024	0.024	0.031	0.031
4d	0.024	0.024	0.031	0.031
Long term				
7d	0.023	0.023	0.031	0.031
28d	0.023	0.023	0.030	0.030
50d	0.022	0.022	0.029	0.030
100d	0.020	0.020	0.026	0.029
Plateau concentration	0.00725 mg/kg after 7 yr (calculated over 20cm)			

Appendix 1 – list of endpoints

CGA 238277 Method of calculation	Molecular weight relative to the parent: 371/511 DT_{50} (d): 38.4 days Kinetics: SFO Field or Lab: representative worst case from lab studies.
Application data	Assumed Met is formed at a maximum of 31.8 % of the max PEC for lufenuron

PEC(s) (mg/kg)	**Single application Actual**	**Single application Time weighted average**	**Multiple application Actual**	**Multiple application Time weighted average**
Initial			0.007	
Short term			0.007	0.007
24h				
2d			0.007	0.007
4d			0.007	0.007
Long term			0.006	0.007
7d				
28d			0.004	0.006
50d			0.003	0.005
100d			0.001	0.003
Plateau concentration	Not relevant			

Appendix 1 – list of endpoints

CGA 224443 Method of calculation	Molecular weight relative to the parent: 328/511 DT_{50} (d): 94.2 days Kinetics: SFO Field or Lab: representative worst case from lab studies.
Application data	Assumed Met is formed at a maximum of 32.8 % of the max PEC for lufenuron

PEC(s) (mg/kg)	**Single application Actual**	**Single application Time weighted average**	**Multiple application Actual**	**Multiple application Time weighted average**
Initial			0.006	
Short term				
24h			0.006	0.006
2d			0.006	0.006
4d			0.006	0.006
Long term				
7d			0.006	0.006
28d			0.005	0.006
50d			0.004	0.005
100d			0.003	0.005
Plateau concentration	Not relevant			

Appendix 1 – list of endpoints

CGA149772 Method of calculation	Molecular weight relative to the parent: 157/511 DT_{50} (d): 4.4 days Kinetics: SFO Field or Lab: representative worst case from lab studies.
Application data	Assumed Met is formed at a maximum of 10.1 % of the max PEC for lufenuron

PEC(s) (mg/kg)	**Single application Actual**	**Single application Time weighted average**	**Multiple application Actual**	**Multiple application Time weighted average**
Initial			0.001	
Short term				
24h			0.0007	0.0007
2d			0.0007	0.0007
4d			0.0003	0.0007
Long term				
7d			0.0003	0.0007
28d			0	0.0004
50d				
100d				
Plateau concentration	Not relevant			

Appendix 1 – list of endpoints

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5: stable
	pH 7: stable
	pH 9:stable
Photolytic degradation of active substance and metabolites above 10 % ‡	DT_{50} : 17-18.6 h test system days Values for test system days above equated to 30-40°N using the quantum yield; DT_{50} 111 - 1781days from summer to winter for lufenuron for shallow water. In a second sterile experiment, results Equated to 30- 40°N summer sunlight for the test system light path length; DT50 18 – 34 days. Major metabolites: CGA 149772 (max 62%AR), CGA 224443 (max 21%AR) and unidentified 'M2B' (max 14.6%AR).
Quantum yield of direct phototransformation in water at Σ > 290 nm	Φ = 0.0026
Readily biodegradable ‡ (yes/no)	No data submitted, substance considered not ready biodegradable.

Degradation in water / sediment

Parent	Distribution (eg max in water *33.6* after *0* d. Max. sed 101.7 % after *7* d)									
Water / sediment system	pH water phase	pH sed	t. oC	DT50-DT90 whole sys.	St. (r2)	DT50-DT90 water	St. (r2)	DT50-DT90 sed	St. (r2)	Method of calculation
Rhine	8.5	7.4	20	159.7[a] 187.6[b]	0.99 0.98		-		_	SFO
Pond	8.4	7.1	20	33.6[a] 67.2[b]	0.93 0.96		-		-	SFO
Geometric mean/median				112						

a – [^{14}C- dichloropheny]-label
b - [^{14}C- difluorophenyl]-label

Appendix 1 – list of endpoints

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Rhine	8.5	7.4	4.0% [a] after 360 d 40.0%[b] after 360 d	40.3% [a] after 360 d 20.7%[b] after 360 d	40.3% [a] after 360 d 20.7%[b] after 360 d
Pond	8.4	7.1	1.5% [a] after 360 d 49.4%[b] after 360 d	43.9 % [a] after 360 d 38.0%[b] after 182 d	43.9 % [a] after 360 d 32.0%[b] after 182 d

a – [^{14}C- dichlorophenyl]-label
b - [^{14}C- difluorophenyl]-label

CGA 238277	Distribution (eg Max. sed 47.5 % after *59*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	r^2	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Rhine	8.5	7.4	20	45.4 a	0.99		-		-	SFO
Pond	8.4	7.1	20	53.9 a	0.93		-		-	SFO
Geometric mean/median				49.7						

CGA 224443	Distribution (eg Max. sed 26 % after *120*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	r^2	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Rhine	8.5	7.4	20	101.4[a]	0.99		-		-	SFO
Pond	8.4	7.1	20	116.9 [a]	0.93		-		-	SFO
Geometric mean/median				109.2						

a – [^{14}C- dichlorophenyl]-label

Appendix 1 – list of endpoints

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

Parent Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: version 1.1 Molecular weight (g/mol): 511.1 Water solubility (mg/L): 0.046 K_{OC}/K_{OM} (L/kg): 41182 DT_{50} soil (d): 185 days DT_{50} water/sediment system (d):112 (representative worst case from sediment water studies) DT_{50} water (d): 1000 DT_{50} sediment (d): 122 Crop interception (%): average crop cover
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: Vapour pressure: $1x10^{-12}$ Kom/Koc:41182 1/n: 0.984 (mean)
Application rate	Crop: vine Crop interception: full canopy (70%, step2) Number of applications: 2 Interval (d): 14 Application rate(s): 50 g as/ha Application window: 1st June – 15th July

FOCUS STEP 1 Scenario	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	**3.27**		245.53	
	24 h	0.64	1.96	**263.60**	254.57
	7 d	0.62	0.82	253.99	258.17
	28 d	0.54	0.64	223.04	243.18
	42 d	0.50	0.60	204.53	233.34

Appendix 1 – list of endpoints

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	**1.22**		**30.37**	
	24 h	0.44	0.83	30.18	30.27
	7 d	0.07	0.23	29.09	29.72
	28 d	0.06	0.11	25.61	27.92
	42 d	0.06	0.09	23.51	26.79
Southern EU	0 h	**1.21**		**37.39**	
	24 h	0.44	0.83	37.17	37.28
	7 d	0.09	0.24	35.83	36.61
	28 d	0.08	0.12	31.53	34.38
	42 d	0.07	0.11	28.95	32.99

Appendix 1 – list of endpoints

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
D6	Ditch	0	0.828		**6.225**	
		24	0.477	0.567	6.204	6.223
		7d	0.226	0.358	5.595	6.131
		28d	0.034	0.159	3.475	5.205
		42d	0.016	0.114	2.687	4.640
R1	Pond	0	0.029		0.673	
		24	0.024	0.026	0.673	0.673
		7d	0.018	0.021	0.670	0.672
		28d	0.011	0.016	0.644	0.669
		42d	0.009	0.014	0.621	0.664
R1	Stream	0	0.605		1.322	
		24	0.002	0.116	1.251	1.280
		7d	0.000	0.017	1.160	1.211
		28d	0.000	0.005	1.018	1.126
		42d	0.000	0.003	0.934	1.076
R2	Stream	0 h	0.814		1.547	
		24 h	0.001	0.089	1.532	1.538
		7 d	0.000	0.013	1.493	1.516
		28 d	0.000	0.003	1.470	1.477
		42 d	0.000	0.002	1.385	1.461
R3	Stream	0 h	**0.852**		2.496	
		24 h	0.018	0.257	2.441	2.468
		7 d	0.011	0.039	2.326	2.394
		28 d	0.000	0.010	2.107	2.256
		42 d	0.000	0.007	2.011	2.193
R4	Stream	0 h	0.607		1.148	
		24 h	0.003	0.126	1.109	1.128
		7 d	0.000	0.018	1.064	1.092
		28 d	0.000	0.005	0.988	1.047
		42 d	0.000	0.003	0.940	1.025

Appendix 1 – list of endpoints

FOCUS STEP 4 Scenario 5 meters	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
D6	Ditch	0	0.500		**3.756**	
		24	0.288	0.342	3.744	3.755
		7d	0.136	0.216	3.377	3.700
		28d	1.316	0.096	2.100	3.143
		42d	1.008	0.069	1.624	2.801
R1	Pond	0	0.034		0.747	
		24	0.028	0.03	0.746	0.747
		7d	0.021	0.025	0.744	0.746
		28d	0.013	0.018	0.715	0.742
		42d	0.011	0.016	0.690	0.737
R1	Stream	0	0.441		0.693	
		24	0.002	0.084	0.654	0.670
		7d	0.000	0.012	0.602	0.631
		28d	0.000	0.003	0.524	0.583
		42d	0.000	0.002	0.479	0.556
R2	Stream	0 h	0.593		0.777	
		24 h	0.001	0.065	0.769	0.773
		7 d	0.000	0.009	0.750	0.761
		28 d	0.000	0.002	0.738	0.742
		42 d	0.000	0.001	0.695	0.734
R3	Stream	0 h	**0.621**		1.266	
		24 h	0.013	0.187	1.236	1.251
		7 d	0.006	0.029	1.176	1.212
		28 d	0.000	0.007	1.065	1.141
		42 d	0.000	0.005	1.016	1.108
R4	Stream	0 h	0.442		0.699	
		24 h	0.002	0.092	0.257	0.572
		7 d	0.000	0.013	0.118	0.553
		28 d	0.000	0.003	0.059	0.530
		42 d	0.000	0.002	0.044	0.518

Appendix 1 – list of endpoints

FOCUS STEP 4 Scenario 10 meters	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
D6	Ditch	0	0.181		**1.355**	
		24	0.104	0.123	1.351	1.355
		7d	0.049	0.078	1.220	1.335
		28d	0.008	0.035	0.760	1.135
		42d	0.004	0.025	0.588	1.012
R1	Pond	0	0.019		0.409	
		24	0.016	0.017	0.409	0.409
		7d	0.011	0.014	0.408	0.409
		28d	0.007	0.010	0.392	0.407
		42d	0.006	0.009	0.379	0.404
R1	Stream	0	0.160		0.248	
		24	0.001	0.031	0.101	0.227
		7d	0.000	0.004	0.055	0.205
		28d	0.000	0.001	0.177	0.186
		42d	0.000	0.001	0.160	0.176
R2	Stream	0 h	0.215		0.241	
		24 h	0.000	0.024	0.236	0.238
		7 d	0.000	0.003	0.229	0.233
		28 d	0.000	0.001	0.255	0.226
		42 d	0.000	0.001	0.212	0.224
R3	Stream	0 h	**0.225**		0.420	
		24 h	0.005	0.068	0.229	0.407
		7 d	0.005	0.011	0.123	0.385
		28 d	0.000	0.003	0.071	0.357
		42 d	0.000	0.002	0.057	0.345
R4	Stream	0 h	0.160		0.242	
		24 h	0.001	0.033	0.093	0.201
		7 d	0.000	0.005	0.043	0.187
		28 d	0.000	0.001	0.021	0.175
		42 d	0.000	0.001	0.016	0.170

Appendix 1 – list of endpoints

FOCUS STEP 4 Scenario 15 meters	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
D6	Ditch	0	0.098		**0.735**	
		24	0.056	0.067	0.732	0.734
		7d	0.027	0.042	0.661	0.724
		28d	0.004	0.019	0.413	0.616
		42d	0.002	0.014	0.319	0.549
R1	Pond	0	0.013		0.272	
		24	0.011	0.011	0.272	0.272
		7d	0.008	0.009	0.271	0.272
		28d	0.005	0.007	0.261	0.270
		42d	0.004	0.006	0.252	0.268
R1	Stream	0	0.087		0.131	
		24	0.000	0.017	0.051	0.088
		7d	0.000	0.002	0.027	0.077
		28d	0.000	0.001	0.065	0.069
		42d	0.000	0.001	0.058	0.065
R2	Stream	0 h	0.116		0.116	
		24 h	0.000	0.013	0.034	0.082
		7 d	0.000	0.002	0.016	0.080
		28 d	0.000	0.000	0.008	0.077
		42 d	0.000	0.000	0.007	0.076
R3	Stream	0 h	**0.122**		0.221	
		24 h	0.003	0.037	0.117	0.173
		7 d	0.003	0.006	0.060	0.137
		28 d	0.000	0.002	0.033	0.125
		42 d	0.000	0.001	0.026	0.121
R4	Stream	0 h	0.087		0.132	
		24 h	0.000	0.018	0.051	0.083
		7 d	0.000	0.003	0.023	0.070
		28 d	0.000	0.001	0.012	0.064
		42 d	0.000	0.000	0.009	0.062

Appendix 1 – list of endpoints

FOCUS STEP 4 Scenario 20 meters	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
D6	Ditch	0	0.064		**0.474**	
		24	0.036	0.043	0.473	0.474
		7d	0.017	0.027	0.427	0.467
		28d	0.003	0.012	0.267	0.398
		42d	0.001	0.009	0.206	0.354
R1	Pond	0	0.009		0.205	
		24	0.008	0.008	0.205	0.205
		7d	0.006	0.007	0.204	0.204
		28d	0.004	0.005	0.196	0.196
		42d	0.003	0.004	0.189	0.189
R1	Stream	0	0.056		0.090	
		24	0.000	0.011	0.076	0.082
		7d	0.000	0.002	0.066	0.072
		28d	0.000	0.000	0.056	0.064
		42d	0.000	0.000	0.051	0.061
R2	Stream	0 h	0.075		0.083	
		24 h	0.000	0.008	0.080	0.081
		7 d	0.000	0.001	0.077	0.079
		28 d	0.000	0.000	0.076	0.077
		42 d	0.000	0.000	0.071	0.077
R3	Stream	0 h	**0.079**		0.149	
		24 h	0.002	0.024	0.139	0.145
		7 d	0.003	0.004	0.127	0.135
		28 d	0.000	0.001	0.112	0.123
		42 d	0.000	0.001	0.107	0.119
R4	Stream	0 h	0.056		0.085	
		24 h	0.000	0.012	0.033	0.076
		7 d	0.000	0.002	0.015	0.069
		28 d	0.000	0.000	0.007	0.063
		42 d	0.000	0.000	0.006	0.061

Appendix 1 – list of endpoints

FOCUS STEP 4 Scenario 30 meters	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
R1	Pond	0	0.006		0.133	
		24	0.005	0.005	0.133	0.133
		7d	0.004	0.004	0.132	0.132
		28d	0.002	0.003	0.127	0.132
		42d	0.002	0.003	0.123	0.131

Application rate

Crop: field tomato
Crop interception: full canopy (70%, step 2)
Number of applications: 3
Interval (d): 7
Application rate(s): 30 g as/ha
Application window: 1st May – 30th September

FOCUS STEP 1 Scenario	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	**1.36**		220.98	
	24 h	0.55	0.96	**225.67**	223.32
	7 d	0.53	0.60	217.45	221.79
	28 d	0.46	0.52	190.94	208.38
	42 d	0.43	0.50	175.10	199.89

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Southern EU	0 h	**0.21**		**29.59**	
	24 h	0.08	0.15	29.47	29.53
	7 d	0.07	0.07	28.41	29.02
	28 d	0.06	0.07	24.99	27.26
	42 d	0.06	0.07	22.96	26.16

Appendix 1 – list of endpoints

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
D6	Ditch	0	**0.181**		0.382	
		24	0.009	0.064	0.287	0.359
		7d	0.000	0.010	0.150	0.228
		28d	0.000	0.003	0.078	0.159
		42d	0.000	0.002	0.059	0.136
R2	Stream	0 h	0.032		3.635	
		24 h	0.000	0.003	3.619	3.628
		7 d	0.000	0.001	3.507	3.558
		28 d	0.000	0.000	2.659	2.935
		42 d	0.000	0.000	1.810	2.745
R3	Stream	0 h	0.034		2.389	
		24 h	0.001	0.010	2.370	2.378
		7 d	0.000	0.002	2.331	2.358
		28 d	0.000	0.000	2.220	2.295
		42 d	0.000	0.000	2.163	2.264
R4	Stream	0 h	0.024		**4.115**	
		24 h	0.000	0.003	4.086	4.099
		7 d	0.000	0.002	3.997	4.049
		28 d	0.000	0.001	3.879	3.987
		42 d	0.000	0.000	3.737	3.928

Appendix 1 – list of endpoints

FOCUS STEP 4 Scenario 5 meters	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
D6	Ditch	0	**0.049**		0.102	
		24	0.002	0.017	0.077	0.096
		7d	0.000	0.003	0.040	0.061
		28d	0.000	0.001	0.021	0.043
		42d	0.000	0.000	0.016	0.037
R2	Stream	0 h	0.012		1.819	
		24 h	0.000	0.001	1.811	1.815
		7 d	0.000	0.000	1.755	1.781
		28 d	0.000	0.000	1.395	1.469
		42 d	0.000	0.000	1.265	1.374
R3	Stream	0 h	0.013		1.196	
		24 h	0.000	0.004	1.186	1.191
		7 d	0.000	0.001	1.167	1.181
		28 d	0.000	0.000	1.112	1.149
		42 d	0.000	0.000	1.083	1.133
R4	Stream	0 h	0.009		**2.061**	
		24 h	0.000	0.002	2.046	2.052
		7 d	0.000	0.001	2.000	2.027
		28 d	0.000	0.000	1.942	1.996
		42 d	0.000	0.000	1.871	1.966

Appendix 1 – list of endpoints

FOCUS STEP 4 Scenario 10 meters	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
D6	Ditch	0	**0.026**		0.053	
		24	0.001	0.009	0.040	0.050
		7d	0.000	0.003	0.021	0.032
		28d	0.000	0.000	0.011	0.022
		42d	0.000	0.000	0.008	0.019
R2	Stream	0 h	0.006		0.548	
		24 h	0.000	0.001	0.545	0.547
		7 d	0.000	0.000	0.524	0.536
		28 d	0.000	0.000	0.424	0.442
		42 d	0.000	0.000	0.392	0.414
R3	Stream	0 h	0.007		0.368	
		24 h	0.000	0.002	0.362	0.365
		7 d	0.000	0.000	0.355	0.360
		28 d	0.000	0.000	0.338	0.350
		42 d	0.000	0.000	0.329	0.345
R4	Stream	0 h	0.005		**0.631**	
		24 h	0.000	0.001	0.623	0.626
		7 d	0.000	0.000	0.606	0.616
		28 d	0.000	0.000	0.588	0.605
		42 d	0.000	0.000	0.566	0.596

Appendix 1 – list of endpoints

FOCUS STEP 4 Scenario 15 meters	Water body	Day after overall maximum	PEC_{SW} (µg/L) single		PEC_{Sed} (µg/kg) multiple	
			Actual	TWA	Actual	TWA
D6	Ditch	0	**0.018**		0.037	
		24	0.000	0.006	0.028	0.035
		7d	0.000	0.001	0.015	0.022
		28d	0.000	0.000	0.008	0.015
		42d	0.000	0.000	0.006	0.013
R2	Stream	0 h	0.004		0.184	
		24 h	0.000	0.000	0.183	0.183
		7 d	0.000	0.000	0.177	0.180
		28 d	0.000	0.000	0.142	0.148
		42 d	0.000	0.000	0.124	0.139
R3	Stream	0 h	0.005		0.125	
		24 h	0.000	0.001	0.123	0.124
		7 d	0.000	0.000	0.120	0.122
		28 d	0.000	0.000	0.114	0.118
		42 d	0.000	0.000	0.111	0.117
R4	Stream	0 h	0.003		**0.214**	
		24 h	0.000	0.001	0.210	0.212
		7 d	0.000	0.000	0.204	0.208
		28 d	0.000	0.000	0.197	0.204
		42 d	0.000	0.000	0.190	0.200

Appendix 1 – list of endpoints

Metabolite CGA 238277 Parameters used in FOCUSsw step 1 and 2	Molecular weight: 371.1 Water solubility (mg/L): 3.9 Soil or water metabolite: soil and water Koc/Kom (L/kg): 2263 DT_{50} soil (d): 15.2 days (geometric mean from lab studies) DT_{50} water/sediment system (d):53.9 (representative worst case from sediment water studies) DT_{50} water (d): 53.9 DT_{50} sediment (d): 53.9 Crop interception (%): average crop cover (50%) Maximum occurrence observed (% molar basis with respect to the parent) Water: 47% Sediment: 53.9%
Parameters used in FOCUSsw step 3 (if performed)	Not performed
Application rate	Crop: vine Number of applications: 2 Interval (d): 14 Application rate(s): 50 g as/ha Depth of water body: 30 cm Application window: 1st June – 15th July
Main routes of entry	

FOCUS STEP 1 CGA 238277	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	1.05		55.26	
	24 h	0.15	0.60	61.60	58.43
	7 d	0.14	0.21	59.36	60.18
	28 d	0.13	0.15	52.12	50.21
	42 d	0.12	0.14	47.80	48.19

Appendix 1 – list of endpoints

FOCUS STEP 2 CGA 238277	Day after overall maximum	PEC_{SW} (µg/L) multiple		PEC_{SED} (µg/kg) multiple	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.46		10.79	
	24 h	0.16	0.31	10.73	10.76
	7 d	0.01	0.08	10.33	10.56
	28 d	0.01	0.03	9.07	9.91
	42 d	0.01	0.02	8.32	9.50
Southern EU	0 h	0.46		13.42	
	24 h	0.16	0.31	13.42	13.32
	7 d	0.04	0.08	12.93	13.21
	28 d	0.03	0.03	11.35	12.39
	42 d	0.02	0.02	10.41	11.87

Application rate

Crop: tomato
Number of applications: 3
Interval (d): 7
Application rate(s): 30 g as/ha
Depth of water body: 30 cm
Application window: 1st May – 30th September

FOCUS STEP 1 CGA 238772	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	**0.40**		49.73	
	24 h	0.13	0.26	51.50	**50.62**
	7 d	0.12	0.14	49.62	50.56
	28 d	0.11	0.12	43.57	47.54
	42 d	0.10	0.11	39.95	45.60

FOCUS STEP 2 CGA 238772	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Southern EU	0 h	0.07		8.54	
	24 h	0.03	0.06	8.50	8.52
	7 d	0.01	0.02	8.19	8.37
	28 d	0.01	0.01	7.19	7.86
	42 d	0.01	0.01	6.20	7.53

Appendix 1 – list of endpoints

Metabolite CGA 224443 Parameters used in FOCUSsw step 1 and 2	Molecular weight: 328.0 Water solubility (mg/L): 40 Soil or water metabolite: soil and water Koc/Kom (L/kg): 4930 DT_{50} soil (d): 44.2 days (geometric mean from lab studies) DT_{50} water/sediment system (d):117 (representative worst case from sediment water studies) DT_{50} water (d): 117 DT_{50} sediment (d): 117 Crop interception (%): average crop cover (50%) Maximum occurrence observed Water: 0% Sediment: 26.0% Soil: 32.8%
Parameters used in FOCUSsw step 3 (if performed)	Not performed
Application rate	Crop: vine Number of applications: 2 Interval (d): 14 Application rate(s): 50 g as/ha Depth of water body: 30 cm Application window: 1st June – 15th July
Main routes of entry	

FOCUS STEP1 CGA 224443	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	0.57		50.42	
	24 h	0.13	0.35	53.39	51.91
	7 d	0.12	0.16	51.44	52.34
	28 d	0.11	0.13	45.17	49.27
	42 d	0.10	0.12	41.42	47.29

Appendix 1 – list of endpoints

FOCUS STEP 2 CGA 224443	Day after overall maximum	PEC_{SW} (µg/L) multiple		PEC_{SED} (µg/kg) multiple	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.22		7.51	
	24 h	0.08	0.15	7.50	7.50
	7 d	0.01	0.04	7.23	7.38
	28 d	0.01	0.02	6.35	6.93
	42 d	0.01	0.02	5.82	6.65
Southern EU	0 h	0.22		9.92	
	24 h	0.08	0.15	9.90	9.91
	7 d	0.01	0.04	9.54	9.74
	28 d	0.01	0.02	8.37	9.14
	42 d	0.01	0.02	7.68	8.77

Application rate

Crop: field tomato
Number of applications: 3
Interval (d): 7
Application rate(s): 30 g as/ha
Depth of water body: 30 cm
Application window: 1st May – 30th September

FOCUS STEP 1 CGA 224443	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	0.24		43.97	
	4 d	0.11	0.18	44.71	44.34
	7 d	0.10	0.12	43.08	43.95
	28 d	0.09	0.10	37.83	41.29
	42 d	0.08	0.10	34.69	39.60

FOCUS STEP 2 CGA 224443	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Southern EU	0 h	0.05		6.99	
	24 h	0.02	0.03	6.96	6.97
	7 d	0.01	0.02	6.70	6.85
	14 d	0.01	0.01	5.89	6.43
	42 d	0.01	0.01	5.40	6.16

Appendix 1 – list of endpoints

Metabolite CGA 149772 Parameters used in FOCUSsw step 1 and 2	Molecular weight: 157.1 Water solubility (mg/L): $1x10^{-12}$ Soil or water metabolite: soil and water Koc/Kom (L/kg): 0 DT_{50} soil (d): 3.4 days (geometric mean from lab studies) DT_{50} water/sediment system (d):1000 (default in absence of measured data) DT_{50} water (d): 1000 DT_{50} sediment (d): 1000 Crop interception (%): average crop cover (50%) Maximum occurrence observed Water: 0% Sediment: 0% Soil: 10.1%
Parameters used in FOCUSsw step 3 (if performed)	Not performed
Application rate	Crop: vine Number of applications: 2 Interval (d): 14 Application rate(s): 50 g as/ha Depth of water body: 30 cm Application window: 1st June – 15th July
Main routes of entry	

FOCUS STEP 1 CGA 149772	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	0.03		7.54	
	24 h	0.02	0.02	7.56	**7.55**
	7 d	0.02	0.02	7.28	7.44
	28 d	0.02	0.02	6.39	6.98
	42 d	0.01	0.02	5.86	6.70

Appendix 1 – list of endpoints

FOCUS STEP 2 CGA 149772	Day after overall maximum	PEC_{SW} (µg/L) multiple		PEC_{SED} (µg/kg) multiple	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.00		0.77	
	24 h	0.00	0.00	0.77	0.77
	7 d	0.00	0.00	0.74	0.75
	28 d	0.00	0.00	0.65	0.62
	42 d	0.00	0.00	0.59	0.61
Southern EU	0 h	0.02		1.33	
	24 h	0.01	0.00	1.32	1.33
	7 d	0.00	0.00	1.28	1.30
	28 d	0.00	0.00	1.12	1.22
	42 d	0.00	0.00	1.03	1.17

Application rate

Crop:field tomato
Number of applications: 3
Interval (d): 7
Application rate(s): 30 g as/ha
Depth of water body: 30 cm
Application window: 1st May – 30th September

FOCUS STEP 1 CGA 149772	Day after overall maximum	PECSW (µg/L)		PECSED (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	0.03		6.79	
	24 h	0.02	0.02	6.84	6.81
	7 d	0.02	0.02	6.59	6.82
	28 d	0.01	0.02	5.79	6.32
	42 d	0.01	0.01	5.31	6.06

FOCUS STEP 2 CGA 149772	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Southern EU	0 h	0.00		0.99	
	24 h	0.00	0.00	0.98	0.98
	7 d	0.00	0.00	0.95	0.97
	28 d	0.00	0.00	0.83	0.91
	42 d	0.00	0.00	0.76	0.87

Appendix 1 – list of endpoints

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: PELMO (version 3.3.2) Scenarios: Chateaudun, Hamburg, Kremsmunster, Piacenza, Porto, Sevilla, Thiva Geometric mean or median parent $DT_{50lab/field}$ 128 d* (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.2). K_{OC}: 41182, arithmetic mean or median x, $^1/_n$= 0.98. Metabolites: CGA 238277 Geometric mean or median parent $DT_{50lab/field}$ 15.2 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.2). Kinetic formation fraction from parent 0.77 K_{OC}:2263, arithmetic mean x, $^1/_n$= 0.94. Metabolites: CGA 224443 Geometric mean or median parent $DT_{50lab/field}$ 44.2d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.2). Kinetic formation fraction from CGA 238277, 0.76 K_{OC}: 4930, arithmetic mean or median x, $^1/_n$= 0.94. Metabolites: CGA 149772 Geometric mean or median parent $DT_{50lab/field}$ 3.4 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.2). Kinetic formation fraction from parent 0.10 K_{OC}: 0, arithmetic mean or median x, $^1/_n$= n.a.
Application rate	Application rate: 50 g/ha. Vines No. of applications: 2 Time of application (month or season): 1st June – 15th July
Application rate	Application rate: 30 g/ha. Field tomatoes No. of applications: 3 Time of application (month or season): 1st May – 30th September

Appendix 1 – list of endpoints

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

	Scenario	lufenuron (µg/L)	Metabolite (µg/L)		
			CGA 238277	CGA 224443	CGA 149772
Model /Vine	Chateaudun	< 0.001	< 0.001	< 0.001	< 0.001
	Hamburg	< 0.001	< 0.001	< 0.001	0.003
	Jokioinen	-	-	-	-
	Kremsmunster	< 0.001	< 0.001	< 0.001	0.001
	Okehampton	-	-	-	-
	Piacenza	< 0.001	< 0.001	< 0.001	0.001
	Porto	< 0.001	< 0.001	< 0.001	0.001
	Sevilla	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva	< 0.001	< 0.001	< 0.001	< 0.001

	Scenario	lufenuron (µg/L)	Metabolite (µg/L)		
			CGA 238277	CGA 224443	CGA 149772
Model /tomato	Chateaudun	< 0.001	< 0.001	< 0.001	< 0.001
	Hamburg	-	-	-	-
	Jokioinen	-	-	-	-
	Kremsmunster	-	-	-	-
	Okehampton	-	-	-	-
	Piacenza	< 0.001	< 0.001	< 0.001	0.001
	Porto	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva	< 0.001	< 0.001	< 0.001	< 0.001

*note that the PECgw values were estimated based on a soil **DT50 of 128 days**. The currect **DT50 soil is 184** days (geo mean). At PRAPeR 47 it was agreed that the use of the DT50 of 128 days instead of DT50 of 184 dyas in soil will not, in principle, affect the PECgw for the active substance and a worst case (shorter parent DT50) has been already considered for the metabolites.

PEC$_{(gw)}$ From lysimeter / field studies – not studied

Appendix 1 – list of endpoints

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

Direct photolysis in air ‡	Not studied
Quantum yield of direct phototransformation	Not studied except as already indicated in aqueous soln
Photochemical oxidative degradation in air ‡	DT50 of 1.03 days OH radical: 1.5 x 10^6 OH-radical per cm^3 Rate constant: 10.368 x 10^{-12} cm^3 sec^{-1}
Volatilisation ‡	Not studied
	Not studied
Metabolites	Not studied

PEC (air)

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant

$PEC_{(a)}$

Maximum concentration	negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: lufenuron, CGA238277, CGA 224443, CGA 149772 Surface Water: lufenuron, CGA238277, CGA 224443, CGA 149772 Sediment: lufenuron, CGA238277, CGA 224443, CGA 149772 Ground water: lufenuron CGA238277, CGA 224443, CGA 149772 Air: lufenuron

Appendix 1 – list of endpoints

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

Soil (indicate location and type of study)	No data submitted – not requested
Surface water (indicate location and type of study)	No data submitted – not requested
Ground water (indicate location and type of study)	No data submitted – not requested
Air (indicate location and type of study)	No data submitted – not requested

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

Candidate to R53

Appendix 1 – list of endpoints

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 ‡				
C.virginianus.	a.s.	Acute	-	2000
A. platyrhynchos	a.s.	Acute	-	2000
	Preparation	Acute	-	-
	Metabolite 1	Acute	-	-
C.virginianus	a.s.	Short-term	966	-
C.virginianus	a.s.	Long-term	19.7	200
C.virginianus	a.s.	Long-term (90-day dietary)	-	20,000.00
Mammals ‡				
Rat and mouse	a.s.	Acute	> 2000	
Rat	CGA 149772	Acute	2065	
Rat	CGA 224443	Acute	1273	
Rat	a.s.	Long-term	8.3 males 10.9 females	100
Rat	CGA 224443	Long-term	7.1 (males) 29.4 (females)	150
Additional higher tier studies ‡				

Appendix 1 – list of endpoints

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

Crop and application rate

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Leafy crops – Medium herb.	Acute	3.4	590	10
Leafy crops – insectivorous		1.6	1230	10
Orchard/vine - insectivorous		2.7	740	10
Leafy crops – Medium herb.	Short-term	1.8	530	10
Leafy crops – insectivorous		0.9	1100	10
Orchard/vine - insectivorous		1.5	640	10
Leafy crops – Medium herb.	Long-term	1.0	21	5
Leafy crops – insectivorous		0.9	22	5
Orchard/vine - insectivorous		1.5	13	5
Tomato – earthwor eating bird	Long-term	0.054[4,5] 0.0044[6]	367 4519	5
Vine – earthworm eating bird	Long-term	0.151[4,5] 0.012[6]	130 1610	5
Ttomato – fish eating bird	Long-term	0.998[4]	19.7	5
Vine –fish eating bird	Long-term	4.7[4] 3.4[7]	**4.2** 5.75	5
Tomato – drinking wate puddle scenario	Acute	0.001	2013351[9]	10
Vine – drinking wate puddle scenario	Acute	0.001	1811808[9]	10
Higher tier refinement (Birds)				
	Acute			10
	Short-term			10
	Long-term			5

Appendix 1 – list of endpoints

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Mammals)				
Leafy crops – medium herbivorous	Acute	1.24	> 1600	10
Orchard/vine - small herbivorous		7.1	> 280	10
Leafy crops – medium herbivorous	Long-term	0.35	48	5
Orchard/vine - small herbivorous		2.34	3.5	5
Leafy crops – earthwor eating mammals	Long-term	0.067[4,5] 0.0055[6]	123 1520	5
Orchard/vine – earthworm eating mammals	Long-term	0.192[4,5] 0.016[6]	43 533	5
Leafy crops – fish eating mammals	Long-term	0.998[4]	13.4	5
Orchard/vine –fish eating mammals	Long-term	2.91[4] 0.77[8]	**2.9** 10.8	5
Tomato – drinking wate puddle scenario	Acute	0.0007	2763423[9]	10
Vine – drinking wate puddle scenario	Acute	0.0008	2486796[9]	10
Higher tier refinement (Mammals)				
	Acute			10
	Long-term	1.15[10]	7.2	5

[1] in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)
[2] for cereals indicate if it is early or late crop stage
[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.
[4] Daily dose (mg/kg bw/day)
[5] Calculated BCF
[6] Experimental BCF
[7] Based on PECsw with a 5 m non-spray buffer zone
[8] Based on PECsw with a 10 m non-spray buffer zone
[9] Drinking warter RA based on the revised guidance document on risk assessesment for birds and mammals (Question No EFSA-Q-2006-064, adopted on 17 June 2008) (soil DT_{50} = 185 days, K_{oc} = 41182 kg/L, $PEC_{puddle, vine}$ = 0.16 µg a.s./L, $PEC_{puddle, tomato}$ = 0.14 µg a.s./L, drinking water rate of 7 and 5.1 mL/d for a small granivorous bird and mammal respectively)
[10] RUD calculations refined with 70% interception i.e. 30% deposition onto ground foliage

Appendix 1 – list of endpoints

Toxicity/exposure ratios for vine* use for terrestrial vertebrates exposed through the food chain

Primary Producer/Consumer		Secondary Consumer			Tertiary Consumer		
Taxon	**PEC (mg as/kg bw)**	**Taxon**	**PEC (mg as/kg bw)**	**TER**	**Taxon**	**PEC (mg as/kg bw)**	**TER**
Birds							
Short grass	3.22	Pigeon	12.85	15.6	Falcon	12.49	16.0
Insect	1.45	Warbler	6.93	28.9	Hawk	13.47	14.9
Small fish	0.83[2]	Kingfisher	3.23	62.0	Hawk	6.27	31.9
Small fish	4.7[3]	Kingfisher	18.3	10.9	Hawk	35.5	5.6
Mammals							
Short grass	3.22	Rabbit	11.6197586	8.61	Fox	13.0421773	7.67
Large insects	0.26	Mouse	1.60034483	62.49	Weasel	6.43173068	15.55
Fish	0.83[2]	Otter	1.01174138	98.84	-	-	-
Fish	4.7[3]	Otter	5.7	17	-	-	-

* TERs presented for the worst-case use in vine. All TERs exceeds the Annex VI trigger for tomato use, without any mitigation measures.

[1] PEC from fish used for secondary poisoning modelling

[2] PEC_{fish} based on dynamic food web model and FOCUS Step 4 R3 stream scenario including 5 m non-spray buffer zone for vine use (= worst case exposure scenario)

[3] PEC_{fish} based on calculation as for birds and mammals secondary poisoning and FOCUS Step 4 R3 stream scenario including 5 m non-spray buffer zone for vine use (= worst case exposure scenario). Please note that the PEC_{fish} value was updated by EFSA after submission of the conclusion to the Commission, based on a correction of the 21 day TWA PEC_{SW} value used in the calculation (i.e. PEC_{fish} = 0.000168 mg/L x 28000).

Appendix 1 – list of endpoints

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* (mg m.a./L)
Laboratory tests ‡				
Fish				
L. macrochirus	a.s.	96 hr (static)	Mortality, EC_{50}	>29
O. mykiss.	a.s.	21 d (flow-through)	Growth NOEC	**
P. promelas	a.s.	359d (full life cycle)	F1 NOEC	0.020
O. mykiss.	A-7814 A	96 hr (static)	Mortality, EC_{50}	0.994 mg as/L (18 mg A-7814 A/L)
	A-7814 A	33 d (flow-through)	Early Life cycle, NOEC	0.08 mg a.s./L 1.7 mg A-7814 A /L)
O. mykiss.	CGA 224443	96 hr (static)	Mortality, EC_{50}	0.37
O. mykiss.	CGA 224443	28 d (flow-through)	Growth NOEC	0.11
S. gairdneri	CGA 149772	96 hr (static)	Mortality, EC_{50}	> 100
O. mykiss.	CGA 238277	96 hr (static)	Mortality, EC_{50}	1.1

Appendix 1 – list of endpoints

Group	Test substance	Time-scale (Test type)	End point	Toxicity* (mg m.a./L)
Aquatic invertebrate				
D. magna	a.s.	48 h (static)	Mortality, EC_{50}	0.0013
D. magna	A-7814 A	48 h (static)	Mortality, EC_{50}	0.00041 (0.0072 mg A-7814 A/L
	Preparation	21 d (static)	Reproduction, NOEC	-
D. magna	CGA 224443	48 h (static)	Mortality, EC_{50}	0.95
D. magna	CGA 224443	21 d (semi-static)	Reproduction, NOEC	0.09
D. magna	CGA 149772	48 h (static)	Mortality, EC_{50}	> 100
D. magna	CGA 238277	48 h (static)	Mortality, EC_{50}	2.6
Sediment dwelling organisms				
C. riparius.	a.s.	28 d (static)	NOEC	0.002 (spk water) 0.04 (spk sediment)
	Metabolite 2	28 d (static)	NOEC	
Algae				
S. capricornutum	a.s.	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	- 8.8
S subspicatus	CGA 224443	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	- 0.017
S subspicatus	CGA 149772	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	- > 100
S. capricornutum	CGA 238277	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.176 0.509
Higher plant				
Indicate species.	a.s.	14 d (static)	Fronds, EC_{50}	Not relevant
	Preparation	14 d (static)	Fronds, EC_{50}	Not relevant
	Metabolite 1	14 d (static)	Fronds, EC_{50}	Not relevant

Appendix 1 – list of endpoints

Group	Test substance	Time-scale (Test type)	End point	Toxicity* (mg m.a./L)
Microcosm or mesocosm tests Two applications of lufenuron at **0.1 µg as/L** had no direct significant treatment-related effects ($p < 0.05$) on any of the physico-chemical parameters, on phytoplankton and macroinvertebrate communitiy structure (PRC) or population dynamics (univariate statistics) measured in the study. Phytoplankton community structure, pH and turbidity each showed a single significant alteration ≥ 55 days following the last application. Isolated and not dose-dependent significant effects were seen in Oscillaforia spec., Clamydomonas spec, Anabaena spec., *Chromulina minima* cf., Total phytoplankton, Cyclopidae, Daphnia spec., *Keratella quadrata*, Synchaeta spec., *Asellus aquaticus* and Gerris spec. from ESAS samples, Lymnea spec. and Corixidae from nets samples, emergence PRC and total emergence. However, all these effects were either single effects and isolated or a result of very low overall abundance leading to arbitrary non-systematic significances because of peak control densities. They are thus not considered significant adverse effects. Zooplankton community structure was altered in the 0.1 µg as/L treatment, but recovered rapidly within 27 days following the last application. Recovery within 34 days following the second application was also seen in copepod taxa, such as Copepodites and Nauplia, which had the highest significant positive weight in the zooplankton PRC. It is concluded that **no ecologically unacceptable effects were present following two lufenuron applications at the 0.1 µg as/L treatment rate**. **NOAEC = 0.1 µg L**				

* indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.
** Study is available but an agreed endpoint is pending statistical analysis.

Appendix 1 – list of endpoints

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

FOCUS Step1

Vines and 2 x 50 g as/ha

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
a.s.	Fish	994	Acute	3.27		300	100
a.s.	Fish	20	Chronic	3.27		**6.11**	10
a.s.	Aquatic invertebrates	1.3	Acute	3.27		**0.39**	100
a.s.	Algae	8.8	Chronic	3.27		**2.69**	10
a.s.	Higher plants[2]		Chronic				10
a.s.	Sediment-dwelling[3] organisms	2.0 (spk water)	Chronic	3.27 (PECsw)		**0.6**	10
a.s.	Sediment-dwelling[3] organisms	40.0 (spk sed)	Chronic	263.6 (PECsed)		**0.152**	10
CGA 224443	Fish	370	Acute	0.57		649	100
CGA 224443	Algae	17	Chronic	0.57		29.8	10
A-7814 A	Aquatic invertebrates	0.41		3.27		**0.13**	100

[1]If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[2] only required for herbicides
[3]consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

Appendix 1 – list of endpoints

Tomatoes 3 x 30 g/ha

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC_i (µg/L)	PEC_{twa}	TER	Annex VI Trigger[1]
a.s.	Fish	994	Acute	1.36		731	100
a.s.	Fish	20	Chronic	1.36		14.7	10
a.s.	Aquatic invertebrates	1.3	Acute	1.36		**0.96**	100
a.s.	Algae	8.8	Chronic	1.36		**6.47**	10
a.s.	Higher plants[2]		Chronic				10
a.s.	Sediment-dwelling[3] organisms	2.0 (spk water)	Chronic	1.36 (PECsw)		**1.47**	10
a.s.	Sediment-dwelling[3] organisms	40.0 (spk sed)	Chronic	225.67 (PECsed)		**0.177**	10
CGA 224443	Fish	370	Acute	0.24		1542	100
CGA 224443	Algae	17	Chronic	0.24		70.8	10
A-7814 A	Aquatic invertebrates	0.41	Acute	1.36		**0.30**	100

[1]If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[2] only required for herbicides
[3]consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

Appendix 1 – list of endpoints

FOCUS Step 2

Vine, late stage crop, 2 x 50 g/ha, 14d interval between applications

Test substance	N/S[1]	Organism[2]	Toxicity end point (µg/L)	Time scale	PEC[3] (µg/L)	TER	Annex VI Trigger[4]
a.s.	N/S	Fish	994	Acute	1.22	815	100
a.s.	N/S	Fish	20	Chronic	1.22	16.4	10
a.s.	N/S	Aquatic invertebrates	1.3	Acute	1.22	**1.07**	100
a.s.	N/S	Algae	8.8	Chronic	1.22	**7.2**	10
a.s.		Higher plants[5]		Chronic			10
a.s.	N/S	Sediment-dwelling organisms[6]	2.0 (spk water)	Chronic	1.22 (PECsw)	**1.64**	10
a.s.	N/S	Sediment-dwelling[6] organisms	40.0 (spk sed)	Chronic	37.39 (PECsed)	**1.07**	10
Metabolites		Relevant organisms					
A-7814 A	N/S	Aquatic invertebrates	0.41	Acute	1.22	**0.34**	100

[1] indicate whether Northern of Southern
[2] include critical groups which fail at Step 1.
[3] indicate whether maximum or twa values have been used.
[4] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[5] only required for herbicides
[6] consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

Appendix 1 – list of endpoints

Tomatoes, 3 x 30g/ha with 7d interval between applications, growth stage: vegetable and fruiting

Test substance	N/S[1]	Organism[2]	Toxicity end point (µg/L)	Time scale	PEC[3] (µg/L)	TER	Annex VI Trigger[4]
a.s.	N/S	Fish	994	Acute	0.21	4733	100
a.s.	N/S	Fish	20	Chronic	0.21	95.2	10
a.s.	N/S	Aquatic invertebrates	1.3	Acute	0.21	**6.2**	100
a.s.	N/S	Algae	8.8	Chronic	0.21	41.9	10
a.s.		Higher plants[5]		Chronic			10
a.s.	N/S	Sediment-dwelling organisms[6]	2.0 (spk water)	Chronic	0.21 (PECsw)	**9.52**	10
a.s.	N/S	Sediment-dwelling[6] organisms	40.0 (spk sed)	Chronic	29.59 (PECsed)	**1.35**	10
Metabolites		Relevant organisms					
A-7814 A	N/S	Relevant organisms	0.41	Acute	0.21	**1.95**	100

[1] indicate whether Northern of Southern
[2] include critical groups which fail at Step 1.
[3] indicate whether maximum or twa values have been used.
[4] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[5] only required for herbicides
[6] consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

Appendix 1 – list of endpoints

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Vine, 2 x 50 g/ha, 14d interval between applications; R3-stream was the worst case exposure scenario

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (µg/L)	PEC[4] (µg/L)	TER	Annex VI trigger[5]
a.s.	R3	Stream	*D. magna*	Acute	1.3	0.853	**1.52**	100
a.s	R3	Stream	alga	Chronic	8.8	0.853	10.3	10
a.s.	R3	Stream	Sediment-dwelling organisms	Chronic	2.0 (spk water)	0.853 (PECsw)	**2.34**	10
a.s.	D6	Ditch	Sediment-dwelling organisms	Chronic	40.0 (spk sed)	6.225 (PECsed)	**6.43**	10
A-7814 A	R3	Stream	*D. magna*	Acute	0.41	0.853	**0.48**	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 2.
[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

Tomatoes, 3 x 30 g/ha, 7d interval between applications; D6-ditch was the worst case exposure scenario

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (µg/L)	PEC[4] (µg/L)	TER	Annex VI trigger[5]
a.s.	D6	Ditch	*D. magna*	Acute	1.3	0.181	**7.18**	100
a.s	D6	Ditch	alga	Chronic	8.8	0.181	48.6	10
a.s.	D6	Ditch	Sediment-dwelling organisms	Chronic	2.0 (spk water)	0.181 (PECsw)	11	10
a.s.	R4	Strem	Sediment-dwelling organisms	Chronic	40.0 (spk sed)	4.115 (PECsed)	9.72	10
A-7814 A	D6	Ditch	*D. magna*	Acute	0.41	0.181	**2.27**	100

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 2.

Appendix 1 – list of endpoints

[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

FOCUS Step 4

Vine, 2 x 50 g/ha, 14d interval between applications; R3-stream was: This was the worst case exposure scenario. *D. magna* was the most sensitive species of aquatic invertebrates.

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point	Buffer zone distance	PEC[4]	TER	Annex VI trigger[5]
R3	stream	Aquatic invertebrates	acute	1.3	5m	0.622	**2.09**	100
R3	stream	Aquatic invertebrates	acute	1.3	10m	0.225	**5.78**	100
R3	stream	Aquatic invertebrates	acute	1.3	15m	0.122	**10.66**	100
R3	stream	Aquatic invertebrates	acute	1.3	20m	0.079	**16.46**	100

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 3.
[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

Higher Tier refinement – Mesocosm (Step 4 PECsw values application to vines – 5m)

Scenario	Water body Type	Toxicity EndPoint	PEC (µg/L)	TER	Annex VI trigger
D6	Ditch	NOEAEC = 0.1 µg/L	0.500	**0.2**	2-3*
R1	Pond		0.034	2.9	2-3*
R1	Strem		0.441	**0.23**	2-3*
R2	Strem		0.593	**0.17**	2-3*
R3	Strem		**0.622**	**0.16**	2-3*
R4	Strem		0.442	**0.23**	2-3*

* Safety factor of 2 to three agreed at PRAPeR 48

Appendix 1 – list of endpoints

Higher Tier refinement – Mesocosm (Step 4 PECsw values application to vines – 10 m)

Scenario	Water body Type	Toxicity EndPoint	PEC (µg/L)	TER	Annex VI trigger
D6	Ditch	NOEAEC = 0.1 µg/L	0.181	**0.55**	2-3*
R1	Pond		0.019	5.26	2-3*
R1	Strem		0.160	**0.625**	2-3*
R2	Strem		0.215	**0.465**	2-3*
R3	Strem		**0.225**	**0.444**	2-3*
R4	Strem		0.160	**0.625**	2-3*

* Safety factor of 2 to three agreed at PRAPeR 48

Higher Tier refinement – Mesocosm (Step 4 PECsw values application to vines – 15m)

Scenario	Water body Type	Toxicity EndPoint	PEC (µg/L)	TER	Annex VI trigger
D6	Ditch	NOEAEC = 0.1 µg/L	0.098	**1.0**	2-3*
R1	Pond		0.013	7.7	2-3*
R1	Strem		0.087	**1.15**	2-3*
R2	Strem		0.116	**0.86**	2-3*
R3	Strem		**0.122**	**0.82**	2-3*
R4	Strem		0.087	**1.15**	2-3*

* Safety factor of 2 to three agreed at PRAPeR 48

Higher Tier refinement – Mesocosm (Step 4 PECsw values application to vines – 20m)

Scenario	Water body Type	Toxicity EndPoint	PEC (µg/L)	TER	Annex VI trigger
D6	Ditch	NOEAEC = 0.1 µg/L	0.064	1.6	2-3*
R1	Pond		0.009	11	2-3*
R1	Strem		0.056	1.8	2-3*
R2	Strem		0.075	**1.3**	2-3*
R3	Strem		**0.079**	**1.3**	2-3*
R4	Strem		0.056	1.8	2-3*

* Safety factor of 2 to three agreed at PRAPeR 48

Appendix 1 – list of endpoints

Higher Tier refinement – Mesocosm (Step 4 PECsw values application to vines – 30m)

Scenario	Water body Type	Toxicity EndPoint	PEC (µg/L)	TER	Annex VI trigger
R1	Pond	NOEAEC = 0.1 µg/L	0.006	17	2-3*

* Safety factor of 2 to three agreed at PRAPeR 48

Higher Tier refinement – Mesocosm (Step 4 PECsw values application to tomato – 5m)

Scenario	Water body Type	Toxicity EndPoint	PEC (µg/L)	TER	Annex VI trigger
D6	Ditch	NOEAEC = 0.1 µg/L	0.049	2.0	2-3*
R2	Pond		0.012	8.3	2-3*
R3	Strem		0.013	7.7	2-3*
R4	Strem		0.009	11	2-3*

* Safety factor of 2 to three agreed at PRAPeR 48

Risk Assessment for Sediment Dwellers based on Step 4 PECsed values application to vines – 5m)

Scenario	Water body Type	Toxicity EndPoint	PECsed (mg/L)	TER	Annex VI trigger
D6	Ditch	28-day NOEC = 40.0 µg/L	3.756	10.65	10
R1	Pond		0.747	53.55	10
R1	Stream		0.693	57.72	10
R2	Stream		0.777	51.48	10
R3	Stream		1.266	31.60	10
R4	Stream		0.699	57.22	10

Appendix 1 – list of endpoints

Risk Assessment for Sediment Dwellers based on Step 4 PECsed values application to tomatoes – 5m)

Scenario	Water body Type	Toxicity EndPoint	PECsed (mg/L)	TER	Annex VI trigger
D6	Ditch	28-day NOEC = 40.0 µg/L	0.102	392.16	10
R2	Strem		1.819	22.0	10
R3	Strem		1.196	33.44	10
R4	Strem		2.061	19.41	10

Bioconcentration				
	Active substance	CGA 238277	CGA 224443	CGA 149772
log$P_{O/W}$	5.12	4.3	3.7	0.26
Bioconcentration factor (BCF)[1] ‡	28000*			
Annex VI Trigger for the bioconcentration factor				
Clearance time (days) (CT_{50})	36 days**			
(CT_{90})	120 days**			
Level and nature of residues (%) in organisms after the 14 day depuration phase	90%**	2.2%**	1.3%**	

[1] only required if log $P_{O/W}$ >3.
* based on total ^{14}C (from study of Maynard *et al*, 2004)
** from Forbis, 1987 (Uptake, Depuration and Bioconcentration Study with bluegill sunfish)

Appendix 1 – list of endpoints

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. ‡	> 197	> 200
Preparation[1]		
Metabolite 1		
Field or semi-field tests 28d field test with A-7814 A, in an apple orchard after flowering (with flowering weeds present) – No adverse effects at application rate of 75g as/ha; 15d field test with A-7814 A in flowering melon - No adverse effects at application rate of 50g as/ha.		
Indicate if not required		

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

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

Crop and application rate

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	< 0.25	50
a.s.	oral	< 0.25	50
Preparation	Contact		50
Preparation	oral		50
Preparation	Higher tier risk assessment Based on the available field studies the exposure of the bees should be avoided by application after flowering of the crop or in the absence of flowering weeds.		

Appendix 1 – list of endpoints

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[1])
Typhlodromus pyri ‡ Lab Tier 2 2-D (eggs/nymphus)	A-7814 A	Mortality	> 100 g as/ha
Typhlodromus pyri ‡ Lab Tier 2 2-D (nymphus – residue exp.)‡	A-7814 A	Mortality	> 100 g as/ha
Coccinella septempunctata‡ Lab Tier 2 2-D(eggs) plus 3-D(larvae)	A-7814 A	Mortality	21 g as/ha
Coccinella septempunctata‡ Lab Tier 2 3-D (larvae - residue exp.)	A-7814 A	Mortality	20 g as/ha
Chrysoperla carnea‡ Lab Tier 2 2-D(eggs) plus 3-D(larvae)	A-7814 A	Mortality	0.4 g as/ha
Chrysoperla carnea‡ Lab Tier 2 2-D (larvae – residue exp.)	A-7814 A	Mortality	0.4 g as/ha
Orius laevigatus‡ Lab Tier 2 2-D (eggs/nymphus)	A-7814 A	Mortality	0.66 g as/ha
Orius laevigatus‡ Lab Tier 2 2-D (nymphus - residue exp.)	A-7814 A	Mortality	5.3 g as/ha

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Appendix 1 – list of endpoints

Lufenuron: Worst-case in-field PER values for use in non-target arthropod risk assessment, based on an application rate of 100 g as/ha and 100% deposition

Exposure scenario	Study type being considered in risk assessment	Relevant PER for comparison with study data	Calculation method
In-field foliar	All	100 g as/ha	Application rate x no. applications
In-field soil	All	100 g as/ha	Application rate x no. applications x crop interception (assumed 0%)

Lufenuron: Worst-case off-field PER values for use in non-target arthropod risk assessment, based on an application rate of 100 g as/ha (drift% = 7.23%)

Exposure scenario	Study type being considered in risk assessment	Relevant PER for comparison with study data	Calculation method
Off-field	Higher tier laboratory, 2-D	3.6 g as/ha	(In-field foliar PER x drift% / distribution factor 10) x safety factor 5
Off-field	Higher tier laboratory, 3-D	36 g as/ha	In-field foliar PER x drift% x safety factor 5
Off-field	Field study	7.2 g as/ha	In-field foliar PER x drift%

Appendix 1 – list of endpoints

Vine, 2 x 50 g as/ha (Comment to RMS from EFSA while drafting the conclusion: The HQ approach should only be considered for Tier 1 effect data, which is not the case here. Plese convert the table below (HQ) to the format in the next table below.

Test substance	Species	Effect (LR_{50} g/ha)	PER in-field	PER off-field	HQ in-field	HQ off-field[1]	Trigger
A-7814 A	*T. pyri*	100	100	3.6	1	0.036	2
A-7814 A	*T. pyri*	100	100	3.6	1	0.036	2
A-7814 A	*C. septempunctata*	21	100	3.6(eggs) 36(larvae)	**4.76**	0.17(eggs) 1.7(larvae)	2
A-7814 A	*C. septempunctata*	20	100	36	**5**	1.8	2
A-7814 A	*C. carnea*	0.4	100	3.6(eggs) 36(larvae)	**250**	**9(eggs) 90(larvae)**	2
A-7814 A	*C. carnea*	0.4	100	36	**250**	**90**	2
A-7814 A	*O. laevigatus*	0.66	100	3.6	**151.5**	**5.45**	2
A-7814 A	*O. laevigatus*	5.3	100	3.6	**18.87**	0.68	2

[1] indicate distance assumed to calculate the drift rate

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)[1,2]	End point	% effect[3]	Trigger value
Correct format for NTA RA						50%

[1] indicate whether initial or aged residues
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation
[3] indicate if positive percentages relate to adverse effects or not

Field or semi-field tests. A fiels study submitted by the applicant was considered not reliable by member state experts (PRAPeR 48).

Appendix 1 – list of endpoints

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

Test organism	Test substance	Time scale	End point[1]
Earthworms			
	a.s. ‡	Acute 14 days	LC_{50} (corr.) > 500 mg a.s./kg d.w.soil
	a.s. ‡	Chronic 8 weeks	-
	Preparation	Acute	-
	Preparation	Chronic	NOEC (56d, corr.) = 0.6 mg a.s./kg d.w.soil
	CGA 224443	Acute	LC_{50} (corr.) = 265 mg a.s./kg d.w.soil
	CGA 224443	Chronic	NOEC (56d, corr.) = 1.5 mg a.s./kg d.w.soil
	CGA 149772	Acute	LC_{50} > 1000 mg a.s./kg d.w.soil
	CGA 238277	Acute	LC_{50} (corr.)= 305 mg a.s./kg d.w.soil
Other soil macro-organisms			
Litterbag	a.s. ‡		
	Preparation		No effect on organic matter at 100 g as/ha
	Metabolite 1		
Collembola			
	a.s. ‡	Chronic	NOEC mg a.s./kg d.w.soil (mg a.s/ha)
	Preparation	Chronic	NOEC = 0.2 mg a.s./kg d.w.soil NOEC (corr.) = 0.1 mg a.s./kg d.w.soil
	CGA 224443	Chronic	NOEC = 6.4 mg a.s./kg d.w.soil NOEC (corr.) = 3.2 mg a.s./kg d.w.soil

Appendix 1 – list of endpoints

Test organism	Test substance	Time scale	End point[1]
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡		5.1 to 21.3% effect at day 28 at 2mg a.s./kg d.w.soil (1500 g a.s/ha)
	CGA 149772		-3.6% effect at day 28 at 0.123 mg/kg d.w.soil
	CGA 224443		3% effect at day 28 at 0.15 mg/kg d.w.soil
	CGA 238277		-5.2% effect at day 28 at 0.155 mg/kg d.w.soil
Carbon mineralisation	a.s. ‡		2 to 5% effect at day 28 at 2mg a.s./kg d.w.soil (1500 g a.s/ha)
	CGA 149772		9.1% effect at day 28 at 0.123 mg/kg d.w.soil
	CGA 224443		3% effect at day 28 at 0.15 mg/kg d.w.soil
	CGA 238277		-4.5% effect at day 28 at 0.155 mg/kg d.w.soil
Field studies[2]			
Indicate if not required			

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

Appendix 1 – list of endpoints

Toxicity/exposure ratios for soil organisms

Vines 2 x 50 g/ha; Tomatoes 3 x 30 g/ha – field and 3 x 100 g/ha

Test organism	Test substance	Time scale	Soil PEC[2, 3]	TER	Trigger
Earthworms					
	a.s. ‡	Acute	0.087 - Vine	5757	10
			0.031 – tomato field	16129	10
	a.s. ‡	Chronic	-		5
	Preparation	Acute	-		10
	Preparation	Chronic	0.122 – vine plateau	4.9	5
			0.0434 – tomato field plateau	13.8	5
	CGA 224443	Acute	0.018 - vine	14722	10
			0.006 – tomato field	44167	10
	CGA 224443	Chronic	0.018 - vine	83	5
			0.006 – tomato field	250	5
	CGA 149772	Acute	0.003 - vine	333,333.3	10
			0.001 – tomato field	100,000	10
	CGA 238277		0.020 – vine	15250	10
			0.007 – tomato field	43571	10

Appendix 1 – list of endpoints

Test organism	Test substance	Time scale	Soil PEC[2, 3]	TER	Trigger
Other soil macro-organisms					
Soil mite	a.s. ‡				
	Preparation				
	Metabolite 1				
Collembola	a.s. ‡				
	Preparation	Chronic	0.122 – vine plateau	**0.82**	5
			0.0434 – tomato field plateau	**2.3**	5
	CGA 224443	Chronic	0.018 – vine	178	5

[1] to be completed where first Tier triggers are breached
[2] indicate which PEC soil was used (e.g. plateau PEC)
[3] The PECsoil values were recalculated by EFSA when writing the conclusion

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

Preliminary screening data

Not required for herbicides as ER_{50} tests should be provided

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour	ER_{50} (g/ha)[2] emergence	Exposure[1] (g/ha)[2]	TER	Trigger
	A-7814 K	50 g as/ha		4.01 g as/ha (Ganzelmeier & Rautmann 2000)	12	5

[1] explanation of how exposure has been estimated should be provided (e.g. based on Ganzelmeier drift data)
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation

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

Appendix 1 – list of endpoints

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

Test type/organism	end point
Activated sludge	
lufenuron	3-hour EC_{80} > 100 mg as/L
CGA 149772	3-hour IC_{80} > 100 mg/L
CGA 224443	3-hour EC_{80} > 100 mg/L (EC_{20} = 17.2 mg/L)
Pseudomonas sp	

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

Compartment	
soil	Parent (lufenuron), Metabolite (CGA 224443)
water	Parent (lufenuron)
sediment	-
groundwater	-

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

	RMS/peer review proposal
Preparation	R50/53

APPENDIX 2 – ABBREVIATIONS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
a.s.	active substance
AV	avoidance factor
BAF	bioaccumulation factor
BCF	bioconcentration factor
BOD	biological oxygen demand
bp	boiling point
bw	body weight
c	centi- (x 10^{-2})
°C	degree Celsius (centigrade)
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
cm	centimetre
cv	coefficient of variation
d	day
DAR	draft assessment report
DFR	dislodgeable foliar residue
DM	dry matter
DO	dissolved oxygen
DOC	dissolved organic carbon
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
dw	dry weight
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
ECD	electron capture detector
EDI	estimated daily intake
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

Appendix 2 – abbreviations

EU	European Union
F	field
F_0	parental generation
F_1	filial generation, first
F_2	filial generation, second
FAO	Food and Agriculture Organisation of the United Nations
FIA	fluorescence immuno assay
FID	flame ionisation detector
FIR	food intake rate
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FPD	flame photometric detector
f(twa)	time weighted average factor
g	gram
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GIS	geographic information system
GLP	good laboratory practice
GS	growth stage
h	hour(s)
H	Henry's Law constant (calculated as a unitless value) (see also K)
ha	hectare
HDT	highest dose tested
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
HR	highest residue
IGR	insect growth regulator
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K	Kelvin or Henry's Law constant (in atmospheres per cubic meter per mole) (see also H)13

Appendix 2 – abbreviations

K_{ads}	adsorption constant
K_{des}	apparent desorption coefficient
K_{oc}	organic carbon adsorption coefficient
K_{om}	organic matter adsorption coefficient
kg	kilogram
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)
LR_{50}	lethal rate, median
LT	lethal threshold
m	metre
M	molar
MAF	multiple application factor
µm	micrometer (micron)
MC	moisture content
µg	microgram
mg	milligram
MHC	moisture holding capacity
min	minute(s)
mL	millilitre
mm	millimetre
mN	milli-Newton
mo	month(s)
mol	Mol
MOS	margin of safety
mp	melting point
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
n	normal (defining isomeric configuration)
NAEL	no adverse effect level
nd	not detected

Appendix 2 – abbreviations

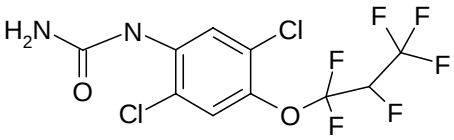
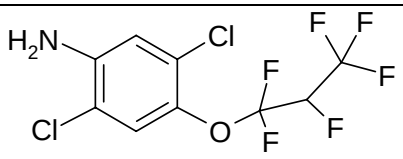
NEDI	no effect daily intake (mg/kg body wt/day)
NESTI	national estimated short term intake
NEU	Northern Europe
ng	nanogram
NIR	near-infrared-(spectroscopy)
nm	nanometer
NMR	nuclear magnetic resonance
no	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
OC	organic carbon content
OM	organic matter content
Pa	Pascal
PBT	persistent bioaccumulating and toxic
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
pH	pH-value
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PNEC	predicted no effect concentration
P_{ow}	partition coefficient between n-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
r^2	coefficient of determination
RfD	reference dose
RH	relative humidity
RPE	respiratory protective equipment
RUD	residue per unit dose
s	second

Appendix 2 – abbreviations

SD	standard deviation
SEU	Southern Europe
SF	safety factor
sp	species (only after a generic name)
spp	subspecies
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TC	technical material
TER	toxicity exposure ratio
TER_I	toxicity exposure ratio for initial exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TK	technical concentrate
TMDI	theoretical maximum daily intake
TWA	time weighted average
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
wk	week
yr	year

Appendix 3 – used compound code(s)

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
CGA 238277	[2,5-dichloro-4-(1,1,2,3,3,3-hexafluoro-propoxy)-phenyl]-urea	
CGA 224443	2,5-dichloro-4-(1,1,2,3,3,3-hexafluoro-propoxy)-phenylamine	
CGA 149772	2,6-difluorobenzamide