CONCLUSION ON PESTICIDE PEER REVIEW

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

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This scientific output, published on 29 April 2010, replaces the earlier version published on 15 April 2010[*]

SUMMARY

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

Denmark being the designated rapporteur Member State submitted the DAR on napropamide in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 6 September 2005. The peer review was initiated on 17 February 2006 by dispatching the DAR for consultation of the Member States and the sole applicant United Phosphorus. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed on during a written procedure in April - May 2007. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in October 2007.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in February - March 2008 leading to the conclusions set out in the EFSA Conclusion finalised on 26 March 2008 (EFSA Scientific Report (2008) 140).

Following the Commission Decision of 7 November 2008 (2008/902/EC)[5] concerning the non-inclusion of napropamide in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant United Phosphorus made a resubmission application for the inclusion of napropamide in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[6]. The resubmission dossier included further data in response to the issues identified in the conclusions leading to the Decision on non-inclusion, as set out in the Review Report (SANCO/112/08) as follows:

1 On request from the European Commission, Question No EFSA-Q-2009-00857, issued on 26 March 2010.
2 Correspondence: praper@efsa.europa.eu
[*] The list of end points in Appendix A (page 38) has been updated to include the EINECS number and to correct the chemical name of the active substance.
[3] OJ L224, 21.08.2002, p.25
[4] OJ L 246, 21.9.2007, p. 19
[5] OJ L 326, 04.12.2008, p.35
[6] OJ L 15, 18.01.2008, p.5
For citation purposes: European Food Safety Authority; Conclusion on the peer review of the pesticide risk assessment of the active substance napropamide. EFSA Journal 2010; 8(4):1565. [73 pp.]. doi:10.2903/j.efsa.2010.1565. Available online: www.efsa.europa.eu

- Leaching of metabolites to groundwater
- The minimum purity can not be concluded
- The impurity specification can not be concluded

and concerns were identified with regard to:

- Groundwater contamination of the active substance in the Southern EU
- No risk assessment for aquatic organisms available
- A potential risk to soil functioning (organic matter breakdown)

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, Denmark, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 29 June 2009.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant for comments on 30 June 2009. The EFSA collated and forwarded all comments received to the Commission on 13 August 2009.

In accordance with Article 20, following consideration of the Additional Report and the comments received, the Commission requested the EFSA to conduct a focused peer review in the areas of environmental fate and behaviour and ecotoxicology, and deliver its conclusions on napropamide.

The conclusion from the original review was reached on the basis of the evaluation of the representative uses of napropamide as a pre-planting herbicide on head cabbage, Brussels sprouts, cauliflower, broccoli, calabrese, tomatoes and oilseed rape. The conclusion of the peer review of the resubmission was reached on the basis of the evaluation of the same representative uses. Full details of the representative uses can be found in Appendix A to this report.

The representative formulated product for the evaluation was ‘Devrinol SC 450’, a suspension concentrate (SC), registered under different trade names in Europe.

Residues in food of plant origin can be determined with a multi-method (the German S19 method). For the other matrices only single methods are available to determine residues of napropamide. It should be noted that the residue definition for water is not finalised, and therefore further methods could be required in the future.

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.

In the mammalian metabolism studies, napropamide was rapidly and extensively absorbed (> 90 %), and widely distributed. Extensive metabolism and enterohepatic circulation were observed as biliary excretion was a major pathway, and then excretion was rapid through urine and faeces. Fifteen metabolites were identified, and only < 0.5 % of the dose was recovered as the parent compound.

Napropamide has low acute toxicity, and no classification is proposed related to acute toxicity testing including irritancy and sensitisation. The critical effect observed in short-term and long-term studies was decreased body weight. Two out of six *in vitro* gene mutation assays showed positive effects, as well as one weak positive effect was observed for DNA damage and repair in mammalian cells out of five chromosomal tests, but the three *in vivo* tests were all negative. Overall, no genotoxic potential is attributed to napropamide. No potential for carcinogenicity or neurotoxicity was observed. No adverse effects on fertility or on reproductive parameters were observed, except for a higher abortion rate at maternally toxic doses in rabbits, which could not be ruled out as being a substance-related effect. No foetotoxicity or teratogenicity was evidenced. The relevant short-term NOAEL was the dose level of 50 mg/kg bw/day from the 1-year oral toxicity study in dogs and the 90-day oral study in rats, and the

overall relevant long-term NOAEL was set at 30 mg/kg bw/day derived from both 2-year rat studies. The toxicological hazard assessment of the metabolite NOPA according to the guidance document on the relevance of metabolites in groundwater, using the available data, indicates that this metabolite is not relevant, and that the ADI of the parent compound is applicable to this metabolite if groundwater concentrations would exceed the trigger value of 0.75 µg/L.

The acceptable daily intake (**ADI**) of napropamide is set at 0.3 mg/kg bw/day, based on the long-term rat studies and applying a safety factor of 100; the acceptable operator exposure level (**AOEL**) is 0.5 mg/kg bw/day, based on the 1-year dog study and a safety factor of 100. No acute reference dose (**ARfD**) is allocated.

The estimated operator exposure is below the AOEL when no personal protective equipment (PPE) is used according to the German model estimates; according to the UK POEM model, operator exposure is below the AOEL when gloves are worn during mixing/loading and application. No risk is anticipated for workers or bystanders.

Napropamide is extensively metabolised in plants. More than 10 metabolites have been identified, but their individual concentration levels are not expected to exceed 0.01 mg/kg. Considering the low consumer exposure and the toxicological profile of the compound, the residue definition for risk assessment and monitoring is proposed to be restricted to the parent compound only. Supervised residue trials confirmed that maximum residue limits (MRLs) can be set at the analytical limit of quantification (0.01* mg/kg) for all representative uses. Investigation of the effect of processing on residues is not needed. Livestock exposure is minimal, and a residue definition for animal commodities is not necessary. A potential transfer of soil residues of napropamide above 0.01 mg/kg is present for root crops for plant back intervals up to 180 days. No risk for the consumer resulting from the presence of napropamide residues in plant commodities has been identified. However, the consumer exposure to the metabolite NOPA present in drinking water could not be finalised, as the assessment of the levels that might be present in groundwater is not finalised.

In soil under aerobic conditions napropamide exhibits moderate to very high persistence, forming the minor non-transient soil metabolite NOPA (accounting for a maximum of 5.78% of the applied radioactivity (AR) in 30°C incubations and 1.1% AR in 20°C incubations), which exhibits low persistence. It should be noted that the database is limited, and further data are necessary to further clarify the persistence of napropamide (southern European field studies). Mineralisation of the 1-naphthyl radiolabel to carbon dioxide accounted for only 5% AR after 90 days. The formation of unextractable residues was a sink, accounting for 12.7-14.7 % AR after 90 days. Napropamide exhibits medium to low mobility in soil, while metabolite NOPA exhibits high mobility in soil. The adsorption behaviour of NOPA was pH dependant (lower adsorption as soil pH increased).

In dark natural sediment water systems napropamide partitioned relatively slowly from water to sediment where it degraded, exhibiting high to very high persistence. The terminal metabolite, CO_2, was a small sink in the material balance, accounting for a maximum of 3.6 % AR at 100 days (study end). Unextracted sediment residues were the major sink, representing 11-19 % AR at study end. In a laboratory aqueous photolysis study napropamide was photolysed to 4 major metabolites (all identified). The necessary surface water and sediment exposure assessments (including the potential for accumulation in sediment) using the agreed FOCUS scenarios approach are available.

The potential for groundwater exposure from the representative uses by napropamide above the parametric drinking water limit of 0.1 µg/L was concluded to be low under the geoclimatic situations that are represented by all the FOCUS groundwater scenarios. For the metabolite NOPA further assessment is required to finalise the groundwater exposure assessment. However, based on the available simulations, that use too favourable input parameters, it is clear that a groundwater non-

* MRL is set at the limit of quantification (LOQ)

relevance assessment is triggered, and NOPA concentrations will be > 0.75 µg/L. From the mammalian toxicological point of view, sufficient information is available to conclude on the non-relevance of NOPA. However, a consumer risk assessment would be required before a conclusion on groundwater non-relevance of NOPA could be finalised, and this requires the estimates of potential levels in groundwater to be finalised.

The risk to birds was assessed as low for all representative uses. The first-tier long-term TER value of 4.5 was below the trigger of 5 for the use on tomatoes. It was agreed that the risk to insectivorous birds is likely to be low, because the end point (NOEC reproduction) is based on the highest tested dose, and that a certain proportion of the insect prey would consist of large insects (lower residues compared to small insects). The risk to earthworm-eating and fish-eating birds from secondary poisoning was assessed as low.

The risk to mammals is considered to be low for the representative uses. The long-term TERs for insectivorous mammals and earthworm-eating mammals were below the trigger of 5 for the use in southern Europe (tomatoes). The submitted information gave some indication that the proportion of time spent feeding in the treated area (PT) is likely to be considerably lower than assumed in the first-tier risk assessment. In a weight of evidence approach it was agreed that the risk to insectivorous and earthworm-eating mammals is low. The risk from plant metabolites was considered to be addressed by the risk assessment for the parent napropamide.

Napropamide is very toxic to aquatic organisms. The risk assessment for aquatic organisms is driven by the toxicity to *Lemna gibba*. The refinement based on a study containing sediment in the test system was not accepted by the experts in the PRAPeR 33 meeting. The end points to be used in the risk assessment were discussed, since several studies with Lemna species and different aquatic invertebrate species were available. The experts suggested using in the aquatic risk assessment the end point of 0.067 mg a.s./L, and a geometric mean value of 5.4 mg a.s./L, for macrophytes and invertebrates, respectively. The risk to aquatic organisms (excluding rooted aquatic macrophytes) was assessed as low based on FOCUS step 3 PECsw values for the representative use on brassicas. Two full FOCUS scenarios out of 6 resulted in TER values above the trigger of 10 for Lemna (D4 and R1) for the use on winter oilseed rape, and no full FOCUS scenario resulted in a TER exceeding the trigger of 10 for the use on tomatoes. No major metabolites in surface water were identified in the water/sediment study. However, the experts on environmental fate and behaviour agreed that the parent compound, as well as 5 different photolysis metabolites and NOPA (where groundwater becomes surface water) should be considered for risk assessment. The risk assessment from the metabolite NOPA remains open since the PECgw is not finalised. In addition, data gaps were identified to address the risk to macrophytes rooted in the sediment, and to refine the risk to aquatic organisms for the use in southern Europe (tomatoes), with e.g. FOCUS step 4 calculations.

The risk of bioconcentration in fish was assessed as low. The risk to earthworms and soil non-target micro-organisms was assessed as low for the uses in northern Europe, but is not finalised for the use in southern Europe. The risk to soil functioning (organic matter breakdown) was assessed as low for northern European uses (brassicas and oilseed rape), but cannot be excluded for the higher application rates for the southern European use on tomatoes.

The risk to bees, non-target arthropods and biological methods of sewage treatment is considered to be low.

KEY WORDS

Napropamide, peer review, risk assessment, pesticide, herbicide

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BACKGROUND

Commission Regulation (EC) No 1490/2002[7], as amended by Commission Regulation (EC) No 1095/2007[8] lays down the detailed rules for the implementation of the third stage of the work programme referred to in Article 8(2) of Council Directive 91/414/EEC. This regulates for the European Food Safety Authority (EFSA) the procedure for organising, upon request of the Commission of the European Communities (hereafter referred to as 'the Commission'), a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by the designated rapporteur Member State. Napropamide is one of the 79 substances of the third stage, part A of the review programme, covered by the Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007, designating Denmark as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Denmark submitted the DAR on napropamide (Denmark, 2005) to the EFSA on 6 September 2005. Following an administrative evaluation, the DAR was distributed for consultation on 17 February 2006 to the Member States and the main applicant United Phosphorus as identified by the rapporteur Member State.

The comments received on the DAR were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed during a written procedure in April – May 2007 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in experts' meetings in October 2007. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in February - March 2008 leading to the conclusions set out in the EFSA Conclusion finalised on 26 March 2008 (EFSA, 2008a).

Following the Commission Decision of 7 November 2008 (2008/902/EC)[9] concerning the non-inclusion of napropamide in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant United Phosphorus made a resubmission application for the inclusion of napropamide in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[10]. The resubmission dossier included further data in response to the issues identified in the conclusions leading to the Decision on non-inclusion, as set out in the Review Report (European Commission, 2008) as follows:

- Leaching of metabolites to groundwater
- The minimum purity can not be concluded
- The impurity specification can not be concluded

and concerns were indentified with regard to:

- Groundwater contamination of the active substance in the Southern EU
- No risk assessment for aquatic organisms available
- A potential risk to soil functioning (organic matter breakdown)

[7] OJ L224, 21.08.2002, p.25
[8] OJ L246, 21.9.2007, p.19
[9] OJ L 326, 04.12.2008, p.35
[10] OJ L 15, 18.01.2008, p.5

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, Denmark, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report (Denmark, 2009). The Additional Report was received by the EFSA on 29 June 2009.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant for comments on 30 June 2009. The EFSA collated and forwarded all comments received to the Commission on 13 August 2009. The collated comments were also forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report and the comments received, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 29 September 2009, the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on napropamide within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were required to be submitted by the applicant in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the Commission on 9 September 2009; the applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant's response to the comments, and the RMS' subsequent evaluation thereof, it was concluded that the EFSA should organise a consultation with Member State experts in the areas of environmental fate and behaviour and ecotoxicology, and that there was no need to request further information from the applicant.

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

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

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

During the peer review of the DAR and the Additional 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).

The conclusion from the original review was reached on the basis of the evaluation of the representative uses as presented in the DAR, i.e. use as a herbicide on head cabbage, Brussels sprouts, cauliflower, broccoli, calabrese, tomatoes and oilseed rape. The conclusion of the peer review of the resubmission was reached on the basis of the evaluation of the same representative uses. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A.

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

- the comments received;

- the resulting reporting table (rev. 1-1 of 10 September 2009)

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

- the reports of the scientific expert consultation;
- the evaluation table (1 March 2010).

Given the importance of the Additional Report including its addendum (compiled version of January 2010 containing all individually submitted addenda) (Denmark, 2010) and the Peer Review Report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion. The documents of the Peer Review Report and the final addendum developed and prepared during the course of the initial review process are made publicly available as part of the background documentation to the original conclusion, finalised on 26 March 2008 (EFSA, 2008a).

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the draft assessment report (Volume 3, B8, B9, Volume 4), which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can be found in the original draft assessment report together with the Peer Review Report, both of which are publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Napropamide is the ISO common name for (*RS*)-*N*,*N*-diethyl-2-(1-naphthyloxy)propionamide (IUPAC). Napropamide is a racemic mixture.

Napropamide belongs to the class of amide herbicides such as isoxaben and fomesafen. It is a selective systemic herbicide, absorbed by the roots, with translocation acropetally. It inhibits root development and growth.

The representative formulated product for the evaluation was 'Devrinol SC 450', a suspension concentrate (SC), containing 450 g/L napropamide (pure), registered under different trade names in Europe.

The evaluated representative uses are as a pre-planting herbicide to head cabbage, Brussels sprouts, cauliflower, broccoli, calabrese, tomatoes and oilseed rape. Full details of the GAP can be found in the list of end points in Appendix A of this conclusion.

CONCLUSIONS OF THE EVALUATION

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

The minimum purity of napropamide as manufactured should not be less than 930 g/kg. No FAO specifications exist.

The five-batch data and the technical material specification presented in the Additional Report were considered acceptable. The biological activity of the two isomers has also been addressed. Toluene was considered as an impurity of toxicological relevance based on its hazards, however the level proposed in the technical specification (maximum 0.14%) does not give rise to significant toxicological concern.

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 napropamide or the respective formulation.

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

Adequate analytical methods are available for the determination of napropamide in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.

Residues of napropamide in food/feed of plant origin can be determined with a multi-method (the German S19 method) with LOQs of 0.01 mg/kg in tomatoes, cauliflower and oilseed rape. Residues in soil are analysed by GC-MS with a LOQ of 0.01 mg/kg. Monitoring of residues of napropamide in groundwater and drinking water can be done by GC-MS with LOQs of 0.05 µg/L, and in surface water by GC-MS with a LOQ of 1 µg/L. It should be noted however, that the residue definition for water in general is not finalised and therefore further methods could be required in the future. Air is analysed for napropamide by HPLC-UV with a LOQ of 3.3 µg/m^3. An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see section 3.2). A method for body fluids and tissues is not required as the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

Napropamide was discussed at the PRAPeR experts' meeting on mammalian toxicology (PRAPeR 34) in October 2007, based on the DAR and the addendum to Volume 3 B6 of the DAR provided by the Rapporteur Member State in September 2007 (Denmark, 2008). After the experts' meeting, the RMS

provided a further addendum to Volume 3 B6 of the DAR in January 2008 (Denmark, 2008) to address the open points set by the experts. Upon resubmission of the substance no further expert consultation was considered necessary related to mammalian toxicology.

The PRAPeR 34 meeting of experts could not conclude on the comparability of the batches used in the toxicological studies and on the relative toxicity between the two isomers due to lack of data, however data on the relative toxicity of the isomers were not considered necessary. Toluene was considered a relevant impurity in the technical specification, and its level should be kept below 0.14%. The impurity profile of the batches used in the toxicological studies is no longer available due to the age of the studies. Napropamide has been manufactured at different plant facilities, however, the manufacturing process has not changed over the years. Overall, the batches used in the toxicological studies are less pure than the technical specification, indicating that the impurities would have been sufficiently tested. Therefore it can be considered that the technical specification is represented by the toxicological studies.

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

Napropamide is rapidly and extensively absorbed (> 90 %) after oral administration, based on urinary (15%) and biliary (78%) excretion after 24 hours. The highest levels of radioactivity were found in the tissues six hours after administration, mainly in the gastrointestinal tract and blood-rich organs, such as the liver, spleen and kidneys; an extensive enterohepatic circulation was observed. The elimination of napropamide was rapid, 42-52 % was excreted in urine, and 23-34 % in faeces during the first 24 hours. Seven days after dosing, the tissues contained less than 0.3 % of the administered dose, mostly associated with the cellular fraction of the blood. There was no potential for accumulation.

Napropamide was extensively metabolised. 15 metabolites were identified in urine or faeces, while only < 0.5% of the dose administered was recovered as the parent compound. The metabolites identified included various permutations of mono- and di- de-ethylation of the alkyl side chain, hydrolysis of the propionamide to the carboxylic acid, hydroxylation of the naphthyl ring, primarily at the position 4, and subsequent glucuronidation. The metabolite profile was similar in faeces and urine; the major metabolites were glucuronide conjugates, 4-OGlu-NPAM, 4-OGlu-DE-NPAM, 4-OGlu-NOPAM and 4-OGlu-NOPA. It is not known whether the metabolic pathway is the same for both isomers.

2.2. Acute toxicity

The acute toxicity of napropamide is low. The acute eye irritation was discussed at the PRAPeR 34 meeting, focusing on the generally poor quality of the studies presented; however, considering the most severe scores for eye irritation, the experts agreed that no classification is required for napropamide. Three studies were presented to assess the sensitizing properties of napropamide; two modified Buehler tests with shortcomings, and an open epicutaneous test in guinea pig that was not accepted by the rapporteur Member State. A maximization test of Magnusson & Kligman conducted with a formulation containing 45% napropamide was also considered, and the experts agreed with the conclusion that napropamide is not a skin sensitizer. **No classification is proposed related to the acute toxicity testing of napropamide.**

2.3. Short-term toxicity

Oral short-term effects of napropamide were studied in 28-day and 90-day studies in rat and dog species, in two 6-week studies in mice, and in two 1-year dog studies; a 30-day dermal study in rats was also presented. Although shortcomings were identified mainly in the subacute studies (range-finding and/or older studies), only one 6-week study in mice was not accepted by the rapporteur Member State due to the few parameters recorded.

The target organ of napropamide in rats, mice and dogs was the liver, characterised with increased liver weight and occasional liver enzyme changes; decreased body weight and food consumption were also common findings in rats and dogs, and additionally mild anaemia was observed in rats. The

rapporteur Member State provided more detailed information on the second 1-year dog study (Volume 3, B.6.3.2-4, Denmark, 2005) in the addendum of September 2007. Based on the increased incidence of liquid faeces at the dose level of 250 mg/kg bw/day, a NOAEL of 50 mg/kg bw/day was agreed by the experts, vomiting and reduced body weight gain were also noted at 1000 mg/kg bw/day.

The relevant oral short-term NOAEL was the same dose level of 50 mg/kg bw/day for the 1-year dog study and the 90-day rat study (the highest dose tested in this latter study).

In a 30-day dermal study in rats, no treatment-related effects were observed, either systemic or local irritation, up to the highest dose level of 1000 mg/kg bw/day.

2.4. Genotoxicity

The mutagenic and DNA damaging potential of napropamide was studied in several *in vitro* test systems using bacteria and mammalian cells, and in *in vivo* test systems. Most studies were performed prior to the adoption of GLP, but Quality Statements were available and the deviations were not considered to affect the outcome of the overall conclusion.

Napropamide presented negative results when tested in two bacterial reverse mutation assays in *Salmonella typhimurium* and *Escherichia coli*, one host-mediated assay, and a gene mutation assay in Chinese hamster ovary cells; however the latter was not considered fully acceptable by the rapporteur Member State. Two mammalian gene mutation tests presented positive results in mouse lymphoma L5178Y cells (with and without metabolic activation) and in Chinese hamster V79 lung cells (in the presence of metabolic activation system only).

No clastogenic effects were seen in an *in vitro* cytogenetic assay in mouse lymphoma L5178Y cells. No evidence of DNA damage and repair was noted in a UDS assay *in vitro*, and in a rec-assay in *Bacillus subtilis.* One of two DNA assays in human fibroblasts was considered weakly positive with metabolic activation only.

When tested *in vivo* (in two micronucleus tests and one GLP compliant *in vivo* UDS assay), negative results were obtained.

Based on the weight of evidence, napropamide is not considered to possess genotoxic potential.

2.5. Long-term toxicity

The long-term toxicity of napropamide was studied in two 2-year oral studies in rats, and in two 18-month studies in mice; one of the mouse studies was not accepted by the rapporteur Member State due to scarce data presented that were not reliable.

The main effect observed in rats upon long-term exposure to napropamide was the decreased body weight. Detailed statistical information was given in the addendum (Denmark, 2008), and the experts agreed to set the NOAEL at the dose level of 10.5 mg/kg bw/day from the first study from 1991 (Volume 3, B.6.5.1, Denmark, 2005), based on decreased body weight at the next higher dose level of 48 mg/kg bw/day; the higher doses produced signs of mild anaemia and liver enzyme changes indicative of liver toxicity.

In the earlier rat study from 1978 (Volume 3, B.6.5.5, Denmark, 2005), **the NOAEL was set at 30 mg/kg bw/day**, based also on decreased body weight and food consumption at the next higher dose level of 100 mg/kg bw/day. Although the latter study is quite old, the body weight data were generally well reported, and the experts considered that no concern would arise in using this NOAEL as the relevant NOAEL for long-term exposure to napropamide.

In mice, **the NOAEL was set at the dose level of 55 mg/kg bw/day**, based on reduced body weight, and increased liver and kidney weights at the dose level of 455 mg/kg bw/day.

No carcinogenic potential was observed in either rats or mice upon long-term exposure to napropamide.

2.6. Reproductive toxicity

A three-generation reproductive study was performed prior to GLP and OECD Guideline adoption, but the deviations were not considered relevant for the outcome of the study. Further information including statistical significance of body weight and body weight gain obtained in the three generations was evaluated by the rapporteur Member State in the addendum of September 2007.

The experts agreed with the rapporteur Member State on **the NOAEL of 30 mg/kg bw/day for both parental and offspring toxicity**, based on reduced body weight at the next dose level of 100 mg/kg bw/day. No effects on reproductive parameters or on fertility were observed, therefore **the NOAEL for reproductive toxicity was set at 100 mg/kg bw/day, the highest dose tested**.

The effects of napropamide on the development were examined in several studies in rats and rabbits. One study in each species was not accepted by the rapporteur Member State due to the scarce number of test animals, and generally poor reporting. However, there were two acceptable studies performed in rats and one in rabbits, which could be used for the evaluation, and two range-finding studies in each species as additional information.

In rats, evidence of maternal toxicity comprising of clinical signs of toxicity, decreased body weight gain during gestation, and decreased food consumption were observed at 400 mg/kg bw/day. Neither foetal nor developmental toxicity was apparent at this dose level and higher, as observed in a supplementary study. **The NOAEL for maternal toxicity was established at the dose level of 110 mg/kg bw/day**, based on the findings described above, and **the NOAEL for developmental toxicity was set at 1000 mg/kg bw/day, the highest dose tested**.

In rabbits, decreased body weight gain and increased abortions were observed in pregnant does treated with napropamide at the highest dose level of 1000 mg/kg bw/day. Further information on whether the abortions could be linked to a few unproductive males used in the study was included in the addendum. The experts agreed with the rapporteur's opinion that it had not been demonstrated that the abortions were only due to the lower fertility of the males, and an effect of napropamide treatment on abortion rates could not be excluded. **The NOAEL for both maternal and developmental toxicity was set at the next lower dose level of 300 mg/kg bw/day**. Neither embryofoetal toxicity nor teratogenicity was observed at any dose level.

2.7. Neurotoxicity

No studies were conducted. Napropamide does not belong to a chemical group known to induce neurotoxicity; no concern was raised from the other general studies, and therefore no study is required.

2.8. Further studies

Three studies were submitted in the DAR on **NOPA**, a minor metabolite found in rat's urine, which is also potentially present as a plant metabolite, and in the environment. The results showed an oral LD_{50} of NOPA in male rats of 2710 mg/kg bw, a dermal LD_{50} in male rats > 4640 mg/kg bw, and that NOPA is not an eye irritant. In the resubmission application, four genotoxicity studies – three *in vitro* and one *in vivo* - were submitted and assessed by the rapporteur Member State in the Additional Report. Positive results were found in an *in vitro* chromosome aberration test in human lymphocytes at cytotoxic dose levels, in the absence of metabolic activation. Negative results were obtained in a reverse mutation test using *Salmonella typhimurium* and *Escherichia coli*, in a mouse lymphoma test in mammalian cells *in vitro*, and in a mouse micronucleus assay *in vivo*. Overall, no genotoxic potential was attributed to the metabolite NOPA. Therefore the toxicological hazard assessment of NOPA according to the guidance document on the relevance of metabolites in groundwater (European Commission, 2003) indicates that this metabolite is not relevant in groundwater.

When revising the conclusion, some scenarios were highlighted in the environmental fate and behaviour section where concentrations of NOPA in groundwater might be expected to exceed the trigger value of 0.75 µg/L (see section 4.2.2). Although NOPA was found to be only a minor rat metabolite (about 2% in female rat urine), conjugation products of NOPA such as 4-OGlu-NOPA were present in higher amount (about 12 % in male rat urine), indicating that the sufficient presence of NOPA in rat metabolism would allow the adoption of the reference values (ADI) of the parent substance napropamide also for the metabolite NOPA. Although this information has not been peer-reviewed, it can be considered that additional toxicological data on the metabolite NOPA is not required.

Most of the **plant metabolites** were identified as being also rat metabolites, except three metabolites: **HNQ, PA and 1-naphthol**. No toxicological information was available to the PRAPeR 34 meeting of experts on these metabolites, except on the classification of 1-naphthol from the European Chemical Bureau (ECB) website. The experts agreed that the reference values of napropamide could be applied to the common metabolites derived from plant and rat, but the data requirement for toxicological information on the three metabolites remained open. After the experts' meeting, the applicant provided to the rapporteur Member State information on the toxicity profile of HNQ, PA and 1-naphthol, which was evaluated by the rapporteur Member State in the addendum dated January 2008 and in the Additional Report. Although these metabolites appear to be more toxic than the parent compound, it was concluded in the Reporting Table (point 2(4); EFSA, 2010) that they do not pose an undue risk to the consumers, considering the low levels found as residues in plants (refer to point 3.1.1).

2.9. Medical data

PRAPeR 34 identified a data gap for medical data on occupational health surveillance. This information was provided in the follow-up addendum to the experts' meeting and in the Additional Report. No abnormalities were found among manufacturing personnel based on two reports on medical surveillance from two different manufacturing sites. However, no information on observations on exposure of the general population and epidemiological studies were submitted, this has therefore been identified as a data gap.

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

ADI

Initially in the DAR, the rapporteur Member State proposed an ADI of 0.11 mg/kg bw/day, based on the first long-term rat study presenting a NOAEL of 10.5 mg/kg bw/day.

In the addendum of September 2007, the rapporteur Member State made a new ADI proposal, considering also the NOAEL from the older 2-year rat study, resulting in an overall NOAEL of 30 mg/kg bw/day for both rat studies (see point 2.5).

The experts at the PRAPeR 34 meeting agreed with this approach, and **the ADI for napropamide was established at 0.3 mg/kg bw/day,** based on this overall long-term NOAEL in rats and an assessment factor of 100. The ADI is supported by the 3-generation rat study.

AOEL

The rapporteur Member State proposed in the DAR an AOEL of 0.3 mg/kg bw/day based on the NOAEL of 30 mg/kg bw/day from the 3-generation rat study.

In the addendum of September 2007, this value was revised, considering the same type of critical effects observed in the short-term studies, as well as dose spacing. The new proposal was based on the 1-year dog study with a NOAEL of 50 mg/kg bw/day, a safety factor of 100, and no correction factor for oral absorption (> 90%). The experts agreed with this approach and **the AOEL was set at 0.5 mg/kg bw/day.**

ARfD

The rapporteur Member State proposed an ARfD of 0.3 mg/kg bw in the DAR, and an ARfD of 0.5 mg/kg bw in the addendum of September 2007, based on the same data as referred to above for setting the AOEL.

Considering the critical effects observed in the short-term studies, the experts did not consider that they were relevant for an acute exposure. Taking into account the entire toxicological profile of the substance, the experts agreed not to set an ARfD.

No ARfD was allocated.

2.11. Dermal absorption

For the PRAPeR 34 experts' meeting, only one *in vivo* study in rats was available, which was conducted with a wettable powder (WP) formulation containing 53% napropamide, instead of the representative 450 g napropamide/L suspension concentrate (SC) formulation, 'Devrinol SC 450'. The study was not considered acceptable for the evaluation of the dermal absorption from the concentrate formulation, however, the 1:100 dilution was considered to be comparable to the in-use field dilution of the representative formulation. The experts agreed with the proposal of the rapporteur Member State to consider as a worst case a 26% dermal absorption value, which includes the skin depot after 96 hours, for the risk assessment of handling both the dilution and the concentrate formulation. The experts noted however, that a strong recommendation should be made to Member States to require new data during national registration procedures.

In the resubmission application, an *in vitro* dermal absorption study using human skin was conducted with 'Devrinol 45 FL', a formulation identical to the representative formulation ('Devrinol SC 450'). In this study a dermal absorption of 0.7%, 6.5%, and 13.4% was observed for the high dose (corresponding to the concentrate formulation), an intermediate dose (22.5 g/L aqueous dilution of the formulation concentrate), and a low dose (0.9 g/L aqueous dilution of the formulation concentrate), respectively. Accordingly, it was concluded to use **0.7 % dermal absorption** when handling the concentrated formulation (during mixing and loading), and **13.4 %** when handling the in-use spray dilution.

2.12. Exposure to operators, workers and bystanders

The representative formulation 'Devrinol SC 450' is a suspension concentrate formulation, containing 450 g napropamide/L.

The exposure data were recalculated in the addendum of January 2008 based on the parameters agreed at the PRAPeR 34 experts' meeting. During the resubmission procedure new calculations were provided, considering the revised values for dermal absorption.

Operator exposure

'Devrinol SC 450' is intended to be applied to the ground, pre-crop drilling, followed by incorporation into the soil, as a selective herbicide on oilseed rape, tomatoes, cabbage, cauliflower, Brussels sprouts and broccoli/calabrese. Application to the soil surface is achieved with a conventional tractor-mounted boom with hydraulic nozzles or a downward placed air-assisted sprayer. No indoor uses are permitted.

According to the representative uses, the maximum applied dose is 2.25 kg a.s./ha, corresponding to 5 L product/ha (for tomatoes). An application volume of 500 L spray/ha was considered for the calculations.

Further estimates were performed for oilseed rape (for which the applied dose is 1.2 kg a.s./ha, corresponding to 2.67 L product/ha with an application volume of 200 L spray/ha), as well as for cabbage, cauliflower, Brussels sprouts, and broccoli/calabrese.

For the UK POEM, a container size of 10 L (63 mm neck opening) was used; default value for work rate is 50 ha/day and for operator body weight is 60 kg; according to the German model, default value for work rate is 20 ha/day and for operator body weight is 70 kg.

According to the UK POEM model calculations, the exposure of operators is below the AOEL only if PPE (gloves during mixing/loading and application) are worn (as shown for the worst-case oilseed rape applications). According to the German model, the exposure is below the AOEL when no PPE is used.

Estimated operator exposure presented as % of AOEL (0.5 mg/kg bw/day) for **tomatoes** (application rate of 2.25 kg a.s./ha – 500 L spray/ha)

Tractor-mounted (field crop)	No PPE	With PPE during M/L	With PPE during M/L & application
UK POEM	98	86 (a)	15 (a)
German model	37	-	2.7 (b)

(a) PPE: gloves
(b) PPE: gloves (M/L & application), protective garment and sturdy footwear (application)

Estimated operator exposure presented as % of AOEL (0.5 mg/kg bw/day) for **oilseed rape** (application rate of 1.2 kg a.s./ha – 200 L spray/ha)

Tractor-mounted (field crop)	No PPE	With PPE during M/L	With PPE during M/L & application
UK POEM	121	115 (a)	19 (a)
German model	20	-	1.5 (b)

(a) PPE: gloves
(b) PPE: gloves (M/L & application), protective garment and sturdy footwear (application)

Estimated operator exposure presented as % of AOEL (0.5 mg/kg bw/day) for **cabbage, cauliflower, Brussels sprouts and broccoli/calabrese** (application rate of 1.0 kg a.s./ha – 200 L spray/ha)

Tractor-mounted (field crop)	No PPE	With PPE during M/L	With PPE during M/L & application
UK POEM	99	93 (a)	16 (a)
German model	17	-	1.2 (b)

(a) PPE: gloves
(b) PPE: gloves (M/L & application), protective garment and sturdy footwear (application)

Worker exposure

Napropamide is applied directly to the soil before crop drilling and if appropriate, incorporated into the soil. The potential for subsequent worker exposure following this method of application was therefore considered negligible, and a worker re-entry risk assessment was not considered necessary.

Bystander exposure

According to the EUROPOEM II, the following assumptions were considered: worst-case application rate of 2.25 kg a.s./ha, 500 L spray/ha, 0.03 mL/m^3 surrogate inhalation exposure value, 0.005 % of application rate for surrogate dermal contamination, and a body weight of 70 kg.

Adding the potential dermal and inhalation exposures, bystander exposure represents about 1 % of the AOEL.

3. Residues

Napropamide was discussed at the PRAPeR experts' meeting for residues (PRAPER 35) in October 2007. Upon resubmission, additional information was provided by the Rapporteur Member State in June 2009 (Denmark, 2009) on the toxicity of some plant metabolites (see point 2.8). No further expert consultation was considered necessary related to the residues section.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The metabolism of napropamide has been investigated in cabbage (leafy crop), tomatoes and apples (fruiting vegetables), oilseed rape (oilseeds), and potatoes (root/tuber crops). The studies were conducted in accordance with the representative use pattern of the product. The compound was labelled in the naphthalene moiety.

At harvest all plants showed a similar metabolic pattern, although due to the limited amount of radioactive material present, metabolites could only be identified in cabbage, tomatoes and potatoes. The plant metabolism of napropamide involves desethylation, ring hydroxylation, hydrolysis, as well as oxidative processes, leading to the main metabolites NQ, PA and 1-naphthol. In addition, radioactivity was present in plant sugars, indicating a natural incorporation of $^{14}CO_2$ produced by degradation of napropamide in soil. Organosoluble residues at harvest amounted from 36% (tomatoes) to 74% (oilseed rape forage and potato foliage). Napropamide was found in trace amounts, representing about 1% of the Total Radioactive Residues (TRR). Metabolites were present in both free and conjugated forms, and were individually present in amounts comparable to or higher than the parent compound, but none of them appeared to be major (all below 10% of TRR). At normal application rate, individual metabolites are not expected to exceed 0.01 mg/kg.

The plant metabolic pathways are qualitatively similar to those observed in rats. Considering that the rat metabolism is as extensive as the plant metabolism, the PRAPeR 34 experts' meeting on mammalian toxicology estimated that the toxicological end points characterising the active substance should also be applied to metabolites. Three plant end-metabolites (HNQ, PA and 1-naphthol), found in the metabolism studies in cabbage, tomatoes and potatoes, are however not covered by the rat studies. Although the toxicological data submitted in the Additional Report indicated that these metabolites are probably more toxic than the parent compound (see section 2.8), it was concluded in the Reporting Table (points 2(4) and 3(1); EFSA, 2010) not to consider these metabolites for the consumer risk assessment, having regard to the absolute low levels of these compounds that are expected in plants at harvest (<0.003 mg/kg).

The RMS proposed to restrict the residue definition to napropamide for monitoring and risk assessment. This was agreed by the PRAPeR 35 meeting of experts. It was however noted that the definition for risk assessment may underestimate by 1 to 2 orders of magnitude the global toxicological burden, considering the ratio between the parent compound and all metabolites produced by plant metabolism. This was however considered of no consequence in the final outcome of the risk assessment, given the very low portion of the ADI used. The possible change in the ratio of constituting isomers by plant metabolism or due to environmental conditions was also considered by the meeting of experts. It was considered that the impact on consumer safety would not be an issue in this case, as the exposure is minimal.

A sufficient number of residue trials have been conducted in accordance with the supported representative uses. These trials (8 trials on head cabbage, 8 trials on Brussels sprouts, 7 trials on cauliflower and broccoli/calabrese, and 10 trials on oilseed rape for Northern Europe, as well as 8 trials in tomatoes for Southern Europe) were carried out with soil application of the compound before

planting or sowing, and resulted in all cases in residues at harvest below the LOQ. The LOQ used in these trials ranged from 0.01 to 0.10 mg/kg. These results confirmed the expectations from plant metabolism studies. The results of these supervised trials can be considered as reliable on the basis of storage stability studies in brassicas and oilseed rape, demonstrating that napropamide residues are stable up to one year when stored under deep freeze conditions. As no residues are present in raw commodities, the effect of processing and household preparation does not need to be investigated.

3.1.2. Succeeding and rotational crops

The cultivation of certain crops within one year after the use of napropamide may cause problems due to phytotoxic effects. A confined rotational crop study was carried out using carrots, lettuce, and wheat as succeeding crops, planted 60, 180 and 360 days after soil treatment at 4800 g a.s./ha. This application rate is 5N in case of brassicas, 4N in case of oilseed rape, and 2N in case of tomatoes. Under these circumstances the TRR were ranging from 0.08 (lettuce) to 0.41 mg/kg (wheat forage) for the 60 days interval, and decreased to 0.04 (lettuce and carrot roots) to 0.11 mg/kg (wheat grain) for the 360 days interval. Unchanged napropamide was found in mature commodities at levels generally below 0.01 mg/kg, except in carrot roots, where the levels were 0.05 and 0.02 mg/kg for the 60 days and 180 days intervals, respectively. Two metabolites were identified, suggesting that the metabolism in rotational crops is similar to that in primary crops. In a field study, where wheat was cultivated as a rotational crop to oilseed rape, residues in straw and grains were below the LOQ of 0.01 mg/kg.

The information available suggests a potential for low but measurable napropamide residues in rotational crops, particularly in root crops. The RMS proposed a waiting period of 180 days from the use of napropamide before planting or sowing rotational crops. This should be considered at Member State level.

3.2. Nature and magnitude of residues in livestock

The expected residue intakes by livestock are largely below 0.1 mg/kg, since no detectable residues are present in plant commodities. Therefore metabolism studies in animals and a residue definition for animal commodities are not necessary. Metabolism studies have however been conducted in lactating goats and laying hens. In both animals napropamide is rapidly excreted and extensively metabolised. No feeding studies were conducted given that the animal exposure is minimal.

3.3. Consumer risk assessment

No risk for the consumer has been identified resulting from the representative uses of napropamide.

Chronic exposure

The chronic dietary exposure assessment has been carried out according to the WHO guidelines for calculating Theoretical Maximum Daily Intakes (TMDI). Three consumption patterns were considered: the WHO European typical diet for adult consumers, the diets in UK for infants, schoolchildren and adults, which take into consideration high individual consumption levels (at the 97.5th percentile of the distribution of consumptions in the respective populations), as well as the German national diet for 4-6 year old girls. Residues in tomatoes, oilseed rape and brassicas were considered to be at the LOQ level of 0.01 mg/kg. For all these diets it was calculated that the consumer exposure is largely below the ADI (less than 0.01 %). As mentioned under point 3.1.1, the non-inclusion of metabolites in the residue definition for risk assessment does not alter the overall conclusion regarding consumer health. A consumer risk assessment for the metabolite NOPA in drinking water is considered necessary as a consequence of its expected concentrations in groundwater (see section 4.2.2), in accordance with the guidance document on the relevance of metabolites in groundwater (European Commission, 2003). However, the groundwater exposure assessment for this metabolite is not finalised. Consequently, the consumer exposure to the metabolite NOPA present in drinking water could not be finalised.

Acute exposure

The potential consumer acute exposure does not need to be assessed as no ARfD was allocated to the compound.

3.4. Proposed MRLs

Based on the results of the supervised residue trials, it is proposed to set the MRL at the LOQ of 0.01* mg/kg in oilseed rape, tomatoes, head cabbage, Brussels sprouts, cauliflower and broccoli/calabrese.

4. Environmental fate and behaviour

4.1. Fate and behaviour in soil

Napropamide was discussed at the PRAPeR experts' meetings for environmental fate and behaviour (PRAPeR 32 in November/December 2007 and PRAPeR 72 in October 2009). It should 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 napropamide enantiomer in the environment. Therefore all residues reported as napropamide in section 4 of 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.

4.1.1. Route of degradation in soil

Soil experiments (2 different soils) were carried out under aerobic conditions in the laboratory (20°C or 30°C at field capacity (FC), defined as pF2), or 75% of FC (defined as 1/3 bar) moisture content in the dark. In the 20°C pF2 study (sandy loam, pH 6, 3.4% organic carbon (OC)) the formation of residues not extracted by acetonitrile, acetonitrile/water and acidified dioxane were a sink for the applied 1-naphthyl-^{14}C-radiolabel (12.7-14.7% of the applied radiolabel (AR) after 90 days). Mineralisation to carbon dioxide in this experiment accounted for 5.0% AR after 90 days. Most of the applied radioactivity remained as the test substance napropamide. The only identified metabolite was NOPA, which only accounted for a maximum 1.1% AR at 90 days. In the 30°C 75% FC study (sandy loam, pH 7.6, 0.6% OC) the formation of residues not extracted by acetone and acidified methanol were a sink for the applied 1-naphthyl-^{14}C-radiolabel (7.9% of the applied radiolabel (AR) after 90 days). Mineralisation to carbon dioxide in this experiment accounted for 3.5 % AR after 90 days. Again, most of the applied radioactivity remained as the test substance napropamide. However, in this experiment the metabolite NOPA accounted for a maximum of 5.78% AR at 90 days, and also accounted for 5.2% AR at 60 days. The PRAPeR 32 meeting of experts discussed whether a groundwater exposure assessment was necessary for this minor metabolite NOPA. The applicant's position reflected in addendum to Vol. 3 B.8 of September 2007 (Denmark, 2008) was that although the metabolite was present at > 5% AR at 2 sampling points in one of the available route of degradation studies, considering the fact that the pertinent study did not follow guidelines (pertinent deviations identified were the temperature of 30°C and low OC content of 0.35 %), a groundwater exposure assessment for NOPA was not triggered. The consensus of the PRAPeR 32 meeting of experts was that a groundwater exposure assessment for NOPA was appropriate and necessary, as the OC content of the soil was not too low to be considered representative of agricultural soils. Also, because in field dissipation studies the degradation rates were higher than in the available laboratory studies (see point 4.1.2), a faster rate of transformation of the active substance was expected under field conditions, and this would mean that greater NOPA formation potential under actual field conditions would be expected than seen in the 20°C laboratory incubations, where limited breakdown of napropamide had occurred at the end of the experiments.

Data on anaerobic degradation in soil (25°C dark laboratory) resulted in no mineralisation to CO_2, with napropamide accounting for nearly all the extractable radioactivity, with the balance being

* The MRL is set at the limit of quantification (LOQ) of the analytical method

radioactivity not extracted by acetonitrile, acetonitrile/water and acidified dioxane (9.4% AR at study end 365 days). In a laboratory soil photolysis study, no novel photodegradation products were identified, though the degradation of parent napropamide did appear to be facilitated by light energy. However, for the reperesentative uses that involve soil incorporation immediately following the spray application, there is limited potential for photolysis to contribute to the loss of the napropamide applied to soil.

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

The rate of degradation of napropamide was estimated from the results of the studies described in 4.1.1 above and experiments on an additional 3 soils incubated at 20°C and pF2, with 1 of these soils additionally being incubated at 10°C and pF2. Napropamide exhibits persistence such that DT_{50} estimates from laboratory studies of 120 day durations are quite uncertain (often extrapolated beyond the study durations). DT_{50} values were: 120, 380, 380 and 400 days (single first-order non-linear regression, 20°C pF2, 4 different soils), 446 days (single first-order non-linear regression, 30°C, 75% FC, 1 soil), and 463 days (DT_{90} > 1000 days, double first-order in parallel model (DFOP), 10°C, pF2, 1 soil). As the 20°C experiments were carried out at FOCUS reference conditions (20°C and pF2 soil moisture content), no normalisation of these DT_{50} values would be required for use in FOCUS modelling. The geometric mean laboratory value that could be appropriate for use in FOCUS modelling is therefore 289 days (calculated from just the 20ºC pF2 incubations). However, because of the extrapolated nature of these DT_{50} values, the PRAPeR 32 meeting of experts agreed that it was most appropriate to use the results of field studies to obtain the DT_{50} for use in leaching models.

An uncertain single first-order degradation DT_{50} of 19.5 days for NOPA (possible but needs to be clarified associated kinetic formation fraction of 0.286 or 28.6%) was estimated from the 30°C laboratory study dosed with napropamide. This value when normalised to FOCUS reference conditions[11] (20°C and pF2) was reported to be 40.5 days, using a compartment model that included a ghost compartment as well as a sink (see addendum to Vol. 3 B.8 of September 2007). The Member State experts at PRAPeR 32 agreed that a data gap should be set for the applicant to provide reliable soil degradation rates for NOPA in a minimum of 3 different soils. Data to address this data gap (laboratory soil incubations in the dark at 20ºC and 45% maximum water holding capacity (MWHC) where NOPA was applied as test substance) were provided in the resubmission application, and were evaluated in the Additional Report. The DT_{50} estimates from these incubations were: 4.5, 5.8 and 6.8 days (single first-order non-linear regression, 3 different soils). As the 20°C experiments were carried out at soil moisture contents above FOCUS reference conditions (pF2 soil moisture content), no normalisation of these DT_{50} values would be required for use in FOCUS modelling. The consequent geometric mean laboratory value that is appropriate for use in FOCUS modelling was therefore agreed as 5.62 days.

Field soil dissipation studies considered appropriate for use in an EU exposure assessment reflecting conditions in northern Europe were available from 4 sites in Germany and 2 sites in Canada (both in Ontario). The study designs incorporated the applied napropamide into the soil in line with the representative uses, there was no crop present. Weather data from the North American field trials over the study durations were compared to the EU climatic conditions and this comparison is reported in the addendum to Vol. 3 B.8 of September 2007. The PRAPeR 32 meeting of experts discussed this comparison and agreed with the conclusion set out in the addendum by the RMS that the 2 Canadian trials could be considered representative of northern EU conditions, but the available USA trials considered reliable in the DAR (California and Mississippi sites) were not representative of EU conditions. Kinetic fits applying single first-order degradation kinetics utilising non-linear regression to the EU representative field dissipation trial sites were presented in the addendum to Vol. 3 B.8 of September 2007. Using the residue levels of the parent napropamide after applications were made in

[11] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002 (FOCUS, 2000) and a Q10 of 2.2.

the autumn (September and October) determined over the whole core sample where residues were detected (either 0-10cm (Germany) or 0-15cm (Canada) soil layer) resulted in single-first order DT_{50} of 31-127 days (German trials) and 14-90 days (Canadian trials). NOPA was not analysed for in the German and Canadian experiments. The Member State experts agreed that these were the appropriate end points to use in the northern EU exposure assessment, and that these DT_{50} values could be considered to represent degradation rates, so be used in leaching modelling for more northern EU scenarios. However, they agreed that as it was clear that the Mississippi and California trials could not be considered representative of southern EU conditions, a data gap for field dissipation trials representative of southern EU conditions was necessary. They also wished to advise the applicant that if they decided to carry out further field dissipation studies, it would be appropriate to analyse samples for NOPA as well as napropamide.

The experts at PRAPeR 32 agreed that when the field trials database was not normalised to FOCUS reference conditions, a geomean single first-order DT_{50} of 50 days might be used in FOCUS leaching modelling, but only to cover uses in the North of the EU. The issue here is that under drier southern EU conditions a DT_{50} longer than 50 days may well be pertinent.

In the resubmission application the applicant used FOCUS kinetics guidance (FOCUS, 2006) to normalise these four German and two Canadian field dissipation studies to a reference temperature of 20ºC (using the rate constant normalisation approach). They were unable to normalise the field trials to FOCUS soil moisture reference conditions (pF2), as the weather data available were from local weather stations and it was not possible to have any confidence that the precipitation obtained from the weather stations would have been representative for the trial sites. This normalisation assumed single first-order kinetics, and used an appropriate Q10 value of 2.58 as recommended by EFSA (EFSA, 2007). The approach taken was evaluated by the rapporteur Member State in the Additional Report. The resulting single first-order DT_{50} values equated to 20ºC for the five trial sites considered to give satisfactory visual fits were 5.3 to 50.8 days, with a geometric mean value of 19 days. (The Rodney Ontario site was excluded, as the normalised fit significantly underestimated the measured residue at both the beginning and end of the time series).

The longest available field napropamide single first-order soil DT_{50} of 127 days was agreed by the PRAPeR 32 meeting of experts for use in PEC soil calculations (that includes calculation of an accumulated plateau), but only for uses in the North of the EU. The resulting PEC values can be found in Appendix A. A data gap was identified for PEC soil calculations to be calculated for the South of the EU when the results of pertinent field studies become available.

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

The adsorption/desorption of napropamide was investigated in 10 soils in batch adsorption experiments (5 experiments evaluated in the DAR and 5 in the Additional Report). The calculated adsorption K_{Foc} values varied from 208 to 1593 mL/g (arithmetic mean 649 mL/g, median 545 mL/g). There was no evidence of a correlation of adsorption with pH. The values of the Freundlich slopes associated with these K_{Foc} were 0.72 - 1.08 (arithmetic mean 0.915, median 0.966 mL/g). Though for 4 of the soils the exact numerical 1/n values were not reported (neither in the original study report nor the GLP archive of the applicant, as the study is older than the archiving period used by the laboratory), it was clear from the graphs of the Freundlich slope determinations that are available, that the 1/n for these 4 soils was essentially 1. This value of 1 has been used for these 4 soils when calculating the average 1/n indicated above for all 10 soils. The PRAPeR 72 meeting of experts agreed that the arithmetic mean values, indicated above for napropamide, were the appropriate values for use in FOCUS exposure calculations.

The adsorption/desorption of NOPA was investigated in 4 soils in appropriate guideline batch adsorptions experiments. The calculated adsorption K_{Foc} values were 28 - 81 mL/g (1/n 0.96 – 1.03, mean 0.84). There was a clear correlation between adsorption and pH (lower adsorption as soil pH increased), as demonstrated by the regression presented in addendum to Vol. 3 B.8 of September

2007. Scenario-specific K_{Foc} and 1/n for each FOCUS groundwater scenario were calculated by the applicant based on this regression as indicated in Appendix A. These values were agreed as appropriate by the PRAPeR 32 meeting of experts to be used for the FOCUS scenario modelling at EU level.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Napropamide was essentially stable under sterile hydrolysis conditions at 40°C at pH 5 and 7 and 9.

In laboratory studies where the aqueous photolysis of napropamide was investigated under sterile pH 7 conditions, rates of degradation (single first-order DT_{50}) of 2-70 hours were estimated from the quantum yield calculated to be 0.5 for a 30 cm depth of water from spring to winter, respectively, for mid European conditions. Napropamide was converted to 2 different hydroxy napropamide isomers (Isomer 1, 20% AR max; Isomer 2, 27% AR max), diethylamine (26% AR max), dimer (9% AR max), and MNF (15% AR max). A ready biodegradability test (OECD 301E) indicated that napropamide is 'not readily biodegradable' using the criteria defined by the test.

In dark water-sediment studies (2 systems studied at 20°C in the laboratory, sediment pH 6.2 & 7.4, water pH 7.2-7.6) napropamide degraded slowly, and partitioned relatively slowly from water to the sediment (first-order water dissipation DT_{50} values 24-32 days; first-order whole system DT_{50} 250-400 days, extrapolated beyond the study duration of 100 days). The terminal metabolite, CO_2, accounted for only 1.7-3.6 % AR of the 1-naphthyl-^{14}C-radiolabel at study end. Residues not extracted from sediment by acetonitrile:water followed by acidified dioxin were a sink, representing 11-19% AR at study end. The experts at PRAPeR 32 confirmed that for napropamide, geomean water/sediment whole system DT_{50} values of 316 days were acceptable for use as FOCUSsw scenario TOXSWA calculation input for the sediment compartment, and that for water either a default of 1000 days, or scenario (latitude and water body depth/season) specific photolysis DT_{50} (appropriately calculated from quantum yield) would be appropriate. It was noted that in the simulations provided in the Additional Report the default value of 1000 days had been utilised.

The experts at PRAPeR 32 were unable to accept the PEC surface water and sediment calculations that were made available before that meeting (addendum to Vol. 3 B.8 of September 2007), as the applicant had parameterised the models to exclude spray drift as a route of entry to surface water, which was not appropriate for a herbicide that is applied using ground spraying equipment (before subsequently being incorporated into soil). The experts therefore identified a data gap for new FOCUS surface water calculations. New calculations to address this data gap were provided in the Additional Report. As requested by the PRAPeR 32 meeting of experts, these new calculations were FOCUS step 4 calculations, as they included both spray drift inputs to TOXSWA and soil incorporation when parameterising PRZM and MACRO[12] which was done outside the SWASH shell. These calculations utilised routines to adjust degradation rates for the climates at the different scenarios, using a Q10 of 2.58 (EFSA, 2007), and Walker equation coefficient of 0.7. Also as requested, accumulation in sediment was assessed by these calculations for the FOCUS scenario that gave the highest sediment concentrations (D2 ditch for winter oilseed rape, R1 pond for brassicas and R2 stream for tomatoes). PECs in surface water were also calculated for the potential photolysis metabolites hydroxy napropamide isomers 1 and 2, diethylamine, dimmer, and MNF, on the basis of the highest PEC surface water calculated for the parent napropamide. Mitigation measures were not incorporated in any of the calculations. These PEC values can be found in Appendix A.

[12] For PRZM an even incorporation depth over the top 8cm soil layer was appropriately defined. An appropriate parameterisation for MACRO in relation to soil incorporation was also used. The approaches used followed the procedures outlined in PPR Opinion EFSA (2004a).

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

The representative use of spring applications to brassicas, summer applications to winter oilseed rape and March to May applications to field tomatoes were simulated (in line with EFSA, 2004b; EFSA, 2007; and with the exception of some substance property values; FOCUS, 2000) using FOCUS PEARL 3.3.3 and FOCUS PELMO 3.3.2. The following input parameters were used for napropamide: single first-order DT_{50} of 19 days (from field studies normalised to a reference temperature of 20 ºC but normalised to field capacity soil moisture, see section 4.1.2), K_{Foc} of 839 mL/g (K_{Fom} 487 mL/g), 1/n=0.81. The evaluation of these simulations that were carried out for all the pertinent FOCUS groundwater scenarios is presented in the Additional Report. Napropamide was calculated to be present in the leachate leaving the top 1m soil layer at 80th percentile annual average concentrations in the range < 0.0005 µg/L. The PRAPeR 72 meeting of experts considered that these simulations and results were sufficient to conclude that for the representative uses napropamide would not be expected to be found in vulnerable groundwater at concentrations exceeding the parametric drinking water limit of 0.1µg/L. It should be noted that following the conclusions of the peer review, the input parameters that are appropriate for use for napropamide in any future simulations are as follows: K_{Foc} 649 mL/g (K_{Fom} 376 mL/g), 1/n=0.915, and in the absence of any other field dissipation trials becoming available, a single first-order DT_{50} of 19 days.

For the soil metabolite NOPA groundwater modelling was evaluated in the addendum to Vol. 3 B.8 of September 2007 and discussed at the PRAPeR 32 meeting of Member State experts. The experts considered that the modelling could not be accepted, as the combination of napropamide degradation rate, NOPA formation fraction and NOPA degradation rates that had been selected were expected to have resulted in leachate concentration estimates that were too favourable (lower than would have resulted from assessment practice that complied better with the relevant EU guidance).

Although the NOPA modelling available to the PRAPeR 32 meeting was considered to give too favourable a picture in relation to the potential for the leaching of NOPA, these simulations indicated that there could be a high potential for NOPA to leach to groundwater at concentrations higher than the parametric drinking water limit of 0.1 µg/L. It was also noted that concentrations were likely to be > 0.75 µg/L, a level pertinent to the metabolite non-relevance assessment.

In the resubmission application better quality degradation data were available for the metabolite NOPA (new laboratory incubations where NOPA was the test substance) that indicated that it is less persistent than previously estimated (see 4.1.2, a geomean single first-order value at FOCUS reference conditions of 5.62 days is now agreed as appropriate). New NOPA groundwater simulations using these new NOPA degradation data were provided and presented in the Additional Report. The Member State experts at PRAPeR 72 discussed the groundwater leaching assessment for NOPA. This assessment for the metabolite NOPA used the same simulation approach that is described for the parent napropamide noted in the first paragraph of this section above, a kinetic formation fraction for NOPA from napropamide of 1, and the appropriate NOPA DT_{50} from the new laboratory incubations. The adsorption input values for NOPA were the pH dependent FOCUS scenario specific values, outlined in section 4.1.3 and Appendix A, as had been agreed as appropriate by the experts at PRAPeR 32. The PRAPeR 72 meeting of experts agreed that these simulations were insufficient to conclude on the potential of NOPA to leach to groundwater due to the fact that the use of the precursor napropamide field DT_{50} (that had not been normalised to FOCUS reference conditions for soil moisture) would mean that the simulations would underestimate the mass formation of the metabolite NOPA in the soil column in the simulations. The napropamide K_{Foc} value used (slightly higher than the value that should have been used) would also mean that some proportion of the metabolite NOPA formed would have been predicted to be formed in soil layers nearer to the soil surface than would have been expected. Consequently, these simulations were agreed to have underestimated the annual average leachate concentrations of the metabolite NOPA. The experts therefore agreed that there was a need for updated simulations. Consequently, the experts identified a data gap for the applicant to further address the PEC groundwater for the metabolite NOPA.

To inform risk managers following the PRAPeR 72 experts' meeting, EFSA completed groundwater simulations for the representative use on winter oilseed rape (1.2 kg/ha incorporated over the top 8 cm, no crop interception, application date being the emergence date defined for the scenario). All simulations used PEARL 3.3.3, and as had been done by the applicant, used a Q10 of 2.58 and Walker equation coefficient of 0.7. Napropamide input parameters were: K_{Foc} 649 mL/g (K_{Fom} 376 mL/g), 1/n=0.915, and the DT_{50} of 19 days [a DT_{50} which will result in underestimated NOPA formation / underestimated NOPA groundwater exposure]; NOPA kinetic formation fraction from napropamide 1; NOPA DT_{50} of 5.62 days. When a NOPA K_{Foc} of 40mL/g (K_{Fom} 23.2 mL/g), and 1/n of 0.98 value from a soil of pH 6.5 was used, 2 out of the 6 scenarios had a 80th percentile annual average recharge concentrations < 0.1µg/L (Porto and Chateaudun), 3 out of the 6 scenarios had these concentrations in the range 0.1 to 0.75 µg/L, and the Piacenza scenario had a concentration > 0.75 µg/L (0.98 µg/L). When a NOPA K_{Foc} of 81 mL/g (K_{Fom} 47 mL/g), and 1/n of 0.96 value from a soil of pH 5.4 was used, all 6 scenarios had these concentrations < 0.1µg/L. For groundwater aquifers that are overlaid by predominantly alkaline soils [from a soil of pH 7.6, NOPA K_{Foc} of 35mL/g (K_{Fom} 20.3 mL/g), and 1/n of 1.03], these concentrations were < 0.1µg/L at just the Porto scenario (concentration 0.088 µg/L), 3 out of the 6 scenarios had these concentrations in the range 0.1 to 0.75 µg/L, and 2 (Hamburg and Piacenza) had a concentration > 0.75 µg/L (0.88 and 1.86 µg/L).

In conclusion, the groundwater exposure assessment for the soil metabolite NOPA is not finalised and there is a data gap for this to be addressed. However, taking what is considered a somewhat 'best-case' approach in estimating groundwater exposure using the available data, there are clear indications that for the representative use that is expected to give the highest groundwater concentrations (winter oilseed rape), the groundwater exposure concentrations for the metabolite NOPA would be predicted to be > 0.75 µg/L. Therefore it was necessary for the groundwater metabolite's non-relevance assessment, that is pertinent for substances above this 0.75 µg/L trigger, to be completed for the metabolite NOPA. The groundwater concentrations of NOPA have the potential to be greatest where groundwater aquifers are overlaid by predominantly alkaline soils.

4.3. Fate and behaviour in air

The vapour pressure of napropamide ($2.2x10^{-5}$Pa at 25°C) means that napropamide would be classified under the national scheme of The Netherlands as very slightly volatile, indicating that 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 0.522 hours (assuming an atmospheric hydroxyl radical concentration of $1.5x10^{6}$ radicals cm^{-3}), indicating that the small proportion of applied napropamide that will volatilise would be unlikely to be subject to long-range atmospheric transport.

5. Ecotoxicology

Napropamide was discussed at the PRAPeR experts' meetings for ecotoxicology (PRAPeR 33 in November/December 2007 and PRAPeR expert teleconference TC 26 in November 2009). It should be noted that the available risk assessment did not consider that napropamide consists of 2 enantiomers. This adds additional uncertainty to the outcome of the risk assessment and needs to be addressed. Following a comment from the section on physical-chemical properties, in the original review a data gap was identified for the applicant to provide an assessment whether the new technical specification is covered by the batches tested in the ecotox studies. Upon resubmission of napropamide an Additional Report was provided in June 2009, and an addendum to Volume 3 B9 of the Additional Report (Denmark, 2010) was submitted in December 2009 after the experts' teleconference in November 2009. The applicant argued that the technical material used in the ecotoxicological studies consisted of the 2 enantiomers at a ratio of 1:1, and that potential changes in the ratios due to differences in degradation in the environment would also have occurred in the test systems. It is acknowledged that this may be true, however no further information was provided whether there are differences in toxicity or differences in the degradation of the 2 enantiomers. Therefore uncertainty remains with regard to this point.

The impurity profile of the batches used in the toxicological studies is no longer available due to the age of the studies. Napropamide has been manufactured at different plant facilities, however the manufacturing process has not changed over the years. Overall, the batches used in the ecotoxicological studies have a purity comparable to the technical specification, indicating that the impurities would have been sufficiently tested. Therefore it can be considered that the technical specification is represented by the ecotoxicological studies.

5.1. Risk to terrestrial vertebrates

The risk to birds and mammals was calculated according to the Guidance Document on Birds and Mammals (European Commission, 2002). All the representative uses are leafy crops. Therefore the risk was calculated for an insectivorous and a medium herbivorous bird, and for a medium herbivorous mammal.

The acute and short-term risk to birds can be regarded as low for all the representative uses. Also the long-term risk was assessed as low for all uses except for the use on tomatoes. The application rate for the use on tomatoes is higher than for the other uses, resulting in a long-term TER of 4.5. The RMS suggested a refined risk assessment based on the assumption that about half of the insects (carrying lower residues) are taken from the off-field area, considering that tomato plants would not be an attractive feeding ground for insectivorous birds. However, this approach was questioned by the PRAPeR 33 meeting of experts, and a quantification of the percentage of insects taken from the off-field area was considered as scientifically not justified on the basis of the available data. The experts suggested using a weight of evidence approach instead. It was agreed that the risk to insectivorous birds is likely to be low, because the end point (NOEC reproduction) is based on the highest tested dose and a certain proportion of the insect prey would consist of large insects.

The risk to birds from secondary poisoning is considered to be low. The preliminary TER values were in the range of 46 -103, indicating some margin of safety. The final TER values for earthworm- and fish-eating birds were calculated as 52 (with a 21 d twa PECsoil of 3.095 mg a.s./kg), and 4754 (with a 21 d twa PECsw of 3.156 µg a.s./L from worst-case FOCUS step 3 scenario D2), confirming the low risk from secondary poisoning.

The risk to mammals is considered to be low for most representative uses and exposures evaluated, except for insectivorous mammals and secondary poisoning of earthworm-eating mammals for the use in Southern EU (tomatoes). For northern EU the TER is acceptable (7.8 and 6.6, respectively). In the original review a data gap for a refined risk assessment for insectivorous mammals and earthworm-eating mammals based on realistic PEC_{soil} was identified in the PRAPeR 33 experts' meeting, for the use in southern Europe (tomatoes). A risk assessment for fish-eating mammals was also required to be conducted after establishing reliable PECsw values.

In the resubmission application, a new risk assessment was provided based on a refined PT value of 0.5 for insectivorous mammals. The information provided did not allow a quantification of the PT value. However, the new information provided indications that the PT values are likely to be significantly lower than 1 in most cases for fields with low vegetation cover. Since the TER values would exceed the trigger of 5 with PT values of less than 0.83, it was considered that the long-term risk for small insectivorous mammals is likely to be low. The risk assessment for earthworm-eating and fish-eating mammals, based on the PECsoil of 3.095 mg a.s./kg and PECsw of 3.156 µg a.s./L (as for birds), resulted in TERs of 3.98 (earthworm-eating mammals) and 750 (fish-eating mammals). The applicant proposed a refined PT of 0.5. The refinement was based on the information provided for insectivorous mammals. The information does not allow a quantification of the PT, but it gives an indication that the PT values are likely to be significantly lower than 1. PT values of less than 0.72 would result in TERs of > 5. In a weight of evidence approach it was considered that the risk to earthworm-eating mammals is likely to be low.

A long-term risk assessment for birds and mammals from exposure via contaminated drinking water was conducted by the RMS. The TERs based on PECsw values were above the trigger of 5. In the

addendum of January 2008 (Denmark, 2008) a long-term risk assessment based on the 5-fold dilution of the sprayed solution resulted in TERs of 4.8 (birds) and 0.28 (mammals). Long-term exposure from contaminated drinking water accumulated in leaf puddles was considered as not relevant by previous expert meetings, and it was decided that an acute risk assessment should be conducted. No acute risk assessment was presented in the DAR or in the addendum. However, the acute TERs for birds and mammals would be above 10 if calculated according to SANCO/4145/2000 (European Commission, 2002), suggesting a low risk to birds and mammals from uptake of contaminated drinking water. In addition, a risk assessment was conducted for exposure from puddles formed on the soil surface according to the PPR opinion (EFSA, 2008b). The TERs were well above the trigger of 5 confirming the low risk from exposure via contaminated drinking water.

The risk from plant metabolites was considered to be addressed by the risk assessment for the parent napropamide.

Overall, it can be concluded that the risk to birds and mammals is likely to be low for all representative uses.

5.2. Risk to aquatic organisms

The aquatic risk assessment is driven by the toxicity to *Lemna gibba*. As a refinement step it was suggested in the DAR to use the end point for *Lemna gibba* from a study with sediment present in the test system. The refinement was not accepted by the experts in the PRAPeR 33 meeting. The experts discussed which end point from the available studies with *Lemna* should be used for the risk assessment, since several studies were available. The study with the formulation was considered valid, and the end point of 0.067 mg a.s./L should be considered in the risk assessment. The toxicity of the active substance was lower, and the end point of 0.237 mg a.s./L was agreed for technical napropamide.

In the Additional Report a new risk assessment for *Lemna* was presented according to the PPR opinion on dimoxystrobin (EFSA, 2005). This approach was discussed in the PRAPeR TC 26 expert teleconference. The majority of the experts agreed that in a test with sediment, where the active substance partitions quickly to the sediment, initial effects on *Lemna* would be masked by rapid recovery, as soon as concentrations in the water phase drop below a critical level. This was a general concern for using the dimoxystrobin approach with very fast growing taxa like *Lemna* or algae. Furthermore, there was uncertainty regarding the dissipation curve in the test system, since the modelling was based on only 2 time points where concentrations were measured. It was decided that the risk assessment should be based on the lowest observed end point for *Lemna* tested with the formulation in a semi-static test (E_bC_{50} = 0.067 mg a.s./L). The risk to aquatic organisms was assessed as low based on FOCUS step3 PECsw values for the representative use on brassicas. Two full FOCUS scenarios out of 6 resulted in TERs above the trigger of 10 for Lemna (D4 and R1) for the use on winter oilseed rape, and no full FOCUS scenario resulted in a TER exceeding the trigger of 10 for the use on tomatoes. It was suggested by the experts to refine the risk assessment further by using FOCUS step 4 calculations, since such a refinement was not applied in the available risk assessment (data gap). The experts discussed the consequences of napropamide partitioning to sediment. It was considered uncertain whether the risk to rooted macrophytes would be covered by the assessment for *Lemna*. It was proposed that further information on the risk to rooted macrophytes should be required to complete the risk assessment for aquatic organisms (data gap). The experts suggested that this information could be provided at Member State level.

The geometric mean value of the available studies with aquatic invertebrates was used in combination with the standard Annex VI trigger. It was noted in the PRAPeR 33 meeting that different groups of organisms with different sensitivities should not be combined in the geomean calculation. The experts suggested a consolidation of the end points with daphnids and *Crassostrea virginia*. The end points of *D. magna* (8 mg a.s./L), *C. virginica* (1.4 mg/L), *P. duorarum* (18 mg a.s./L) and *M. bahia* (4.2 mg a.s./L) were combined to a geometric mean value of 5.4 mg a.s./L, which should be used in the risk assessment.

No major metabolites in surface water were identified in the water/sediment study. However, the fate experts agreed that the parent compound, as well as 5 different photolysis metabolites and NOPA (where groundwater becomes surface water) should be considered in the risk assessment. A risk assessment for the metabolite NOPA was provided in the Additional Report. The risk to aquatic organisms was assessed as low for situations where groundwater becomes surface water (assuming a 10 times higher toxicity compared to the parent compound) by the rapporteur Member State. However, the PECgw values for the metabolite NOPA were assessed as not reliable by the experts on environmental fate and behaviour (see section 4.2.2). Therefore the risk to aquatic organisms can only be finalised after reliable PECgw values for NOPA are established (data gap). No risk assessment was conducted for the photolysis metabolites. In the resubmission the applicant made a case that the photolysis metabolites would have been formed also in the test systems. However, information on the irradiated spectrum, maximum, and light intensity were not reported in the tests. No conclusion could be drawn whether the metabolites were formed, and if so, at what concentrations they were present in the test systems. Therefore a data gap was identified to address the risk from photolytic metabolites to *Lemna*.

A study on bioconcentration in fish is available as the LogPow is 3.3. The resulting BCF is 98, which is below the Annex VI trigger value of 100. Furthermore, less than 5% of residues (measured as ^{14}C) remained in the fish after the 14-day depuration phase. The risk of bioconcentration in fish is considered to be low.

In conclusion, the risk to aquatic organisms (excluding rooted aquatic macrophytes) from exposure to napropamide was assessed as low for the use on brassicas. Two full FOCUS scenarios out of 6 resulted in TERs above the trigger of 10 for *Lemna* (D4 and R1) for the use on winter oilseed rape. No full FOCUS scenario resulted in a TER greater than the trigger of 10 for the use on tomatoes. In order to draw a final conclusion on the risk to aquatic organisms, the risk from exposure to photolysis metabolites and NOPA needs to be addressed.

5.3. Risk to bees

An acute contact and oral toxicity study on bees with the lead formulation ‘Devrinol SC 450’ is available. All resulting HQ values (10 - 22.5) do not breach the appropriate Annex VI trigger value, indicating a low risk to bees.

5.4. Risk to other arthropod species

A standard laboratory study with the indicator species is available. No statistically significant effects were observed in the tests with the indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri*, at an application rate of 4.5 kg a.s./ha (about 4 times and 2 times the application rates of the representative uses). The validity of the study with *A. rhopalosiphi* was questioned in the peer-review and the RMS presented a re-analysis in the updated addendum from January 2008. The observed effects (8% mortality and 31% reduction in reproduction) were assessed as statistically not significant. Furthermore, also a laboratory study with *Lycosid spiders* and *Pterostichus melanarius* is available. No effects were observed at 1240 g a.s./ha. This study confirmed the low toxicity to non-target arthropods. Although it is noted that the tested dose rate in this study does not cover the application rate in tomatoes, no repetition of this study at a higher dose rate is considered necessary, as the risk to non-target arthropods can be regarded as low based on the studies with the indicator species (see above). Overall, it is concluded that the risk to non-target arthropods is low for the representative uses.

5.5. Risk to earthworms

A study on the acute toxicity to earthworms with the active substance napropamide, and a study on the reproductive toxicity with the lead formulation ‘Devrinol SC 450’ were available. The end point for napropamide and the lead formulation ‘Devrinol SC 450’ were corrected for the organic matter content of the test soil, as the logPow exceeds 2 for napropamide. The acute and long-term TERs for the northern European uses were above the Annex VI trigger values, indicating a low risk. A new risk assessment based on a PECsoil of 3.118 mg a.s./kg (maximum plateau concentration plus initial

PECsoil) resulted in TERs above the trigger of 5. However, this PECsoil was considered as not reliable by the experts on environmental fate and behaviour. The risk assessment for the southern European use (tomatoes) can only be finalised once reliable PECsoil values are established (data gap).

No major metabolites in soil were identified.

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

A litterbag study (triggered by the DT_{90} of 410 days) with the lead formulation 'Devrinol SC 450' is available to address this Annex point. The lead formulation 'Devrinol SC 450' was applied the first time at a rate of 1858 g formulation/ha, and incorporated into the soil to a depth of 10 cm to mimic a plateau concentration of 0.509 mg a.s./kg soil in the upper 10 cm soil layer. One week later the test item was applied again at 5475 g formulation/ha, corresponding to the highest application rate of the representative uses evaluated (tomatoes, 2.25 kg a.s./ha equivalent to 1.5 mg a.s./kg soil in the upper 10 cm), resulting in a concentration of 3.509 mg a.s./kg dry soil. Decomposition of organic matter was reduced by 7.1%, 12.4%, 18.3% and 11.2% compared to the control after 28, 96, 174 and 360 days, respectively. The observed effects were >10% after 1 year, indicating a potential high risk to soil functioning at the tested concentration of 3.509 mg a.s./kg dry soil. Considering that the soil concentrations are about 1/3 lower than the tested concentration and that the trigger of 10% reduction in decomposition of organic matter was only slightly exceeded in the test, the risk to organic matter breakdown was assumed to be low for the uses in northern Europe (brassicas and oilseed rape). However, a high risk to organic matter breakdown cannot be excluded for the higher application rates in southern Europe (data gap). The risk assessment for the southern European use (tomatoes) can only be finalised once reliable PECsoil values for southern European conditions are established.

5.7. Risk to soil non-target micro-organisms

The effects of napropamide were tested on soil microbial respiration and nitrogen transformation. No deviations of more than 25 % after 28 days at 15.92 mg a.s./kg soil on soil microbial respiration and on nitrogen transformation were observed (i.e. no breaching of the Annex VI trigger value). The dose rate of 15.92 mg a.s./kg soil is well above the maximum PEC_{soil} for the northern European uses. The risk assessment for southern European uses (use on tomatoes) can only be finalised after reliable PECsoil values for southern European conditions have been established (data gap).

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

Three studies on the effects of formulations containing napropamide on non-target plants were submitted. At least 6 different species were tested in each study. In the first two studies the products were sprayed on the soil, and in the third study the product was mixed in the soil. During this third study the lowest ER_{50} (= 132 g a.s./ha for *Beta vulgaris*) was observed. This value was not taken into account in the risk assessment, as mixing into the soil is considered as not relevant for the off-field area. Therefore the lowest ER_{50} (= 310 g as/ha for *Avena fatua*) from the study by Farmer & Canning (Volume 3 B.9.9.1, Denmark, 2005) was used in the risk assessment. Based on this end point the risk to non-target plants can be considered as low without the need for risk mitigation measures. A new study with the metabolite NOPA and *Poa annua* and *Stellaria media* indicated no pesticidal activity of the metabolite NOPA.

5.9. Risk to biological methods of sewage treatment

The 3 hour EC_{50} for inhibition of respiration of sewage sludge micro-organisms exceeds 1000 mg a.s./L. Based on this study the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

6.1. Soil

Definitions for risk assessment:	napropamide
Definitions for monitoring:	napropamide

6.2. Water

6.2.1. Ground water

Definitions for exposure assessment:	napropamide and NOPA
Definitions for monitoring:	at least napropamide but data gaps need to be addressed before this definition can be finalised.

6.2.2. Surface water

Definitions for risk assessment:	
Water:	napropamide, hydroxy napropamide isomers 1 and 2, diethylamine, dimer, MNF and NOPA in situations where groundwater becomes surface water.
Sediment:	napropamide
Definitions for monitoring:	napropamide, data gaps need to be addressed before it can be concluded whether NOPA, isomers 1 and 2, diethylamine, dimer, or MNF would need to be monitored or not.

6.3. Air

Definitions for risk assessment:	napropamide
Definitions for monitoring:	napropamide

6.4. Food of plant origin

Definitions for risk assessment:	napropamide
Definitions for monitoring:	napropamide

6.5. Food of animal origin

Definitions for risk assessment:	no residue definition necessary (as livestock exposure < 0.1 mg/kg DM).
Definitions for monitoring:	no residue definition necessary (as livestock exposure < 0.1 mg/kg DM)

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

7.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
napropamide	moderate to very high persistence Single first-order DT_{50} 120-400 days (20°C, pF2 soil moisture) Single first-order DT_{50} 14-127 days (field studies)	The risk to earthworms, soil micro-organsims and soil functioning (organic matter breakdown) was assessed as low for the exposure predicted under northern European conditions, but for the higher application rates in southern Europe (tomatoes) the risk assessment is not finalised as the soil exposure assessment is not finalised.

7.2. Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
napropamide	Medium to low mobility K_{Foc} 208-1593 mL/g	No	Yes	Yes	Yes
NOPA	high mobility K_{Foc} 28-81 mL/g (pH dependent)	Yes, though there is a data gap, concentrations > 0.75µg/L will be expected	No	No Low acute toxicity; no genotoxic potential Reference values of parent are applicable to NOPA	Data gap identified. (Risk assessment not finalised as the exposure assessment is not finalised).

7.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
napropamide	Very toxic to aquatic organisms. The lowest end point was observed for *Lemna gibba* (E_bC_{50} = 0.067 mg/L).
hydroxy napropamide isomer 1	No information provided (data gap)
hydroxy napropamide isomer 2	No information provided (data gap)
diethylamine	No information provided (data gap)
dimer	No information provided (data gap)
MNF	No information provided (data gap)

7.4. Air

Compound (name and/or code)	**Toxicology**
napropamide	LC_{50} inhalation, 4-hour exposure, in rat > 4.8 mg/L air (no classification required)

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

- Observation on exposure of the general population and epidemiological studies (relevant for all representative uses; identified by EFSA when revising the conclusion, refer to point 2.9).
- A consumer risk assessment from exposure to NOPA via the consumption of drinking water using the ADI for napropamide is required for geoclimatic situations where groundwater concentrations > 0.75 µg/L might be expected. This assessment cannot be completed until the groundwater exposure assessment for NOPA is finalised (relevant for at least the representative use evaluated on oilseed rape; identified by EFSA when revising the conclusion, refer to points 3.3 and 4.2.2).
- Field dissipation studies dosed with napropamide and incorporated in accordance with the intended use under southern EU conditions, analysing for residues of at least napropamide but recommended to also analyse for NOPA residues, at 4 different trial sites (relevant for the representative uses in the South of the EU; identified by the PRAPeR 32 meeting of fate and behaviour experts in 2007, date of submission unknown; refer to point 4.1.2).
- PEC in soil for napropamide to be calculated (including accumulation if pertinent) using the results from the required south EU field dissipation studies (relevant for the representative uses in the South of the EU; identified by the PRAPeR 32 meeting of fate and behaviour experts in 2007, date of submission unknown; refer to point 4.1.2).
- Applicant to further address the PEC groundwater for the metabolite NOPA accounting for the formation from napropamide in situations where degradation of napropamide is faster than assumed in the current assessment (related to the non-normalization to moisture reference conditions for the parent napropamide). A kinetic formation fraction of 1 for NOPA should be used in groundwater simulations, unless appropriate experimental evidence is provided to support another value. A sensitivity analysis by using lower parent DT_{50} to reflect the effect of moisture correction on the mass formation simulated for NOPA, and consequently on the PEC GW of NOPA, is an approach that could be considered. The napropamide K_{Foc} that should be used in any simulations is 649 mL/g, and the 1/n is 0.915. NOPA DT_{50} that should be used is 5.6 days with K_{Foc} and 1/n as listed in Appendix A for each FOCUS groundwater scenario (relevant for all representative uses; identified by the PRAPeR 72 meeting of fate and behaviour experts in 2009, date of submission unknown; refer to point 4.2.2).
- Napropamide consists of two enantiomers. This needs to be considered in the environmental risk assessment (relevant for all representative uses; data gap identified in the EFSA conclusion of March 2008 (EFSA, 2008a); no submission date proposed; refer to chapter 5).
- The risk to aquatic organisms needs refinement (e.g. with FOCUS step 4 calculations) (relevant for the southern European use on tomatoes; data gap identified in the PRAPeR expert Teleconference (TC 26) on ecotoxicology in November 2009; no submission date proposed; refer to point 5.2).
- The risk to macrophytes rooted in the sediment needs to be addressed in order to finalise the aquatic risk assessment (data gap identified in the PRAPeR expert Teleconference (TC 26) on ecotoxicology in November 2009; no submission date proposed; refer to point 5.2).
- The risk from the groundwater metabolite NOPA to aquatic organisms needs to be addressed further since no reliable PECgw values were available for the assessment of ecotoxicological relevance (relevant for all representative uses, data requirement identified during the first peer review; the risk assessment provided in the Additional Report was not based on reliable PECgw values; no submission date proposed; refer to point 5.2).
- The photolysis metabolites need to be considered in the aquatic risk assessment (relevant for all representative uses, data requirement identified during the peer review and confirmed in the PRAPeR 32 experts' meeting on fate and behaviour (in November/December 2007); the information in the Additional Report was not sufficient to address the risk and a data gap was identified in the PRAPeR expert Teleconference (TC 26) on ecotoxicology in November 2009; no submission date proposed; refer to point 5.2).

- A risk assessment for earthworms (relevant for the southern European use on tomatoes; data gap identified by EFSA after the PRAPeR 33 experts' meeting; no submission date proposed; refer to point 5.5).
- The risk to soil functioning (organic matter breakdown) needs to be addressed (relevant for the southern European use on tomatoes; the original data gap was identified by EFSA after the PRAPeR 33 experts' meeting in the first peer review; data gap partly closed after receipt of the Additional Report (for the northern European uses); a litterbag study based on a dose-response design is underway; refer to point 5.6).
- A risk assessment for soil non-target micro-organisms (relevant for the southern European use on tomatoes; data gap identified after the PRAPeR 33 experts' meeting; no submission date proposed; refer to point 5.7).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as a pre-planting herbicide on head cabbage, Brussels sprouts, cauliflower, broccoli, calabrese, tomatoes and oilseed rape. Full details of the GAP can be found in the list of end points at Appendix A.

The representative formulated product for the evaluation was 'Devrinol SC 450', a suspension concentrate (SC), registered under different trade names in Europe.

Residues in food of plant origin can be determined with a multi-method (the German S19 method). For the other matrices only single methods are available to determine residues of napropamide. It should be noted however that the residue definition for water is not finalised, and therefore further methods could be required in the future.

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.

In mammalian metabolism studies, napropamide was rapidly and extensively absorbed, and widely distributed. Extensive metabolism and enterohepatic circulation were observed, and then excretion was rapid through urine and faeces.

Napropamide has low acute toxicity, and no classification is proposed related to acute toxicity testing, including irritancy and sensitisation. The critical effect observed in short-term and long-term studies was decreased body weight. Two out of six *in vitro* gene mutation assays showed positive effects, as well as one weak positive effect for DNA damage and repair in mammalian cells was observed out of five chromosomal tests, but three *in vivo* tests were all negative. Overall, no genotoxic potential is attributed to napropamide. No potential for carcinogenicity or neurotoxicity was observed. No adverse effects on fertility or on reproductive parameters were observed, except for a higher abortion rate at maternally toxic doses in rabbits, which could not be ruled out as being a substance-related effect. No foetotoxicity or teratogenicity was evidenced. The toxicological hazard assessment of the metabolite NOPA according to the guidance document on the relevance of metabolites in groundwater, using the available data, indicates that this metabolite is not relevant, and that the ADI of the parent compound is applicable to this metabolite if groundwater concentrations would exceed the trigger value of 0.75 µg/L.

The ADI of napropamide is set at 0.3 mg/kg bw/day; the AOEL is 0.5 mg/kg bw/day considering an assessment factor of 100. No acute reference dose is allocated.

The estimated operator exposure is below the AOEL when no PPE is used according to the German model; according to the UK POEM model, operator exposure is below the AOEL when gloves are worn during mixing/loading and application. No risk is anticipated for workers or bystanders.

Napropamide is extensively metabolised in plants. More than 10 metabolites have been identified, but their individual concentration levels are not expected to exceed 0.01 mg/kg. Considering the low consumer exposure and the toxicological profile of the compound, the residue definition for risk assessment and monitoring is proposed to be restricted to the parent compound only. Supervised residue trials confirmed that MRLs can be set at the analytical limit of quantification (0.01 mg/kg) for all representative uses. Investigation of the effect of processing on residues is not needed. Livestock exposure is minimal, and a residue definition for animal commodities is not necessary. A potential transfer of soil residues of napropamide above 0.01 mg/kg is present for root crops for plant back intervals up to 180 days. No risk for the consumer resulting from the presence of napropamide residues in plant commodities has been identified. However, the consumer exposure to the metabolite NOPA present in drinking water (where groundwater is the source of the drinking water) could not be finalised.

The available data were sufficient to complete the environmental exposure assessment at EU level, with the notable exceptions that the groundwater exposure assessment for the soil metabolite NOPA, and the soil exposure assessment under southern European conditions could not be finalised. For the representative uses, the potential for groundwater exposure by the active substance napropamide above the parametric drinking water limit of 0.1 µg/L was assessed as low. For the soil metabolite NOPA there is an identified potential for contamination of groundwater above the parametric drinking water limit of 0.1 µg/L, and concentrations above the relevance assessment trigger of 0.75 µg/L are also expected. A groundwater metabolite relevance assessment is triggered for NOPA.

The risk to birds was assessed as low for all representative uses. The risk to mammals is considered to be low for the representative uses evaluated. The long-term TERs for insectivorous mammals and earthworm-eating mammals were below the trigger of 5 for the use in southern Europe (tomatoes). The submitted information gave some indication that the proportion of time spent feeding in the treated area (PT) is likely to be considerably lower than assumed in the first-tier risk assessment. In a weight of evidence approach it was agreed that the risk to insectivorous and earthworm-eating mammals is low. Napropamide is very toxic to aquatic organisms. The risk to aquatic organisms (excluding rooted aquatic macrophytes) was assessed as low based on FOCUS step 3 PECsw values for the representative use on brassicas. Two full FOCUS scenarios out of 6 resulted in TERs above the trigger of 10 for Lemna (D4 and R1) for the use on winter oilseed rape, and no full FOCUS scenario resulted in a TER exceeding the trigger of 10 for the use on tomatoes. No major metabolites in surface water were identified in the water/sediment study. However, the experts on environmental fate and behaviour agreed that the parent compound, as well as 5 different photolysis metabolites and NOPA (where groundwater becomes surface water) should be considered for risk assessment. The risk assessment from the metabolite NOPA remains open since the PECgw is not finalised. In addition, data gaps were identified to address the risk to macrophytes rooted in the sediment, and to refine the risk to aquatic organisms for the use in southern Europe (tomatoes), with e.g. FOCUS step 4 calculations. The risk of bioconcentration in fish was assessed as low. The risk to earthworms and soil non-target micro-organisms was assessed as low for the uses in northern Europe, but is not finalised for the use in southern Europe. The risk to soil functioning (organic matter breakdown) was assessed as low for nothern European uses (brassicas and oilseed rape), but cannot be excluded for the higher application rates in the southern European use on tomatoes. The risk to bees, non-target arthropods and biological methods of sewage treatment is considered to be low.

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

Although not related to consumer safety issues, a plant back interval of 180 days should be observed before using a root crop as rotational crop (refer to point 3.1.2).

ISSUES THAT COULD NOT BE FINALISED

Overall, the risk assessment could not be finalised for any of the representative uses. See summary of the representative uses in Appendix A as well as the list below for further details of the issues that are not finalised for the individual uses.

- A consideration of the impact on the environmental fate and behaviour and/or environmental effects in relation to the enantiomers of napropamide is not finalised.
- The groundwater exposure assessment for the metabolite NOPA is not finalised.
- The consumer risk assessment from exposure to NOPA via drinking water that is obtained from groundwater is not finalised.
- The aquatic risk assessment for the photolysis metabolites and the metabolite NOPA is not finalised.
- The aquatic risk assessment for the use on tomatoes (southern Europe) needs to be refined further with FOCUS step 4 calculations.
- A risk assessment to rooted aquatic macrophytes is not available therefore the risk assessment for aquatic plants is not finalised.
- The soil exposure assessment, risk to earthworms and soil non-target macro- and micro-organisms is not finalised for the southern European uses.

CRITICAL AREAS OF CONCERN

None.

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APPENDICES

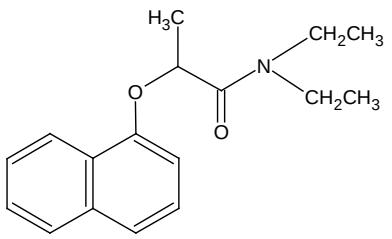
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Active substance (ISO Common Name) ‡	Napropamide
Function (*e.g.* fungicide)	Herbicide

Rapporteur Member State	Denmark
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(*RS*)-*N*,*N*-diethyl-2-(1-naphthyloxy)propionamide
Chemical name (CA) ‡	*N*,*N*-diethyl-2-(1-naphthalenyloxy)propanamide
CIPAC No ‡	271
CAS No ‡	15299-99-7
EC No (EINECS or ELINCS) ‡	239-333-3
FAO Specification (including year of publication) ‡	none
Minimum purity of the active substance as manufactured ‡	930 g/kg napropamide (racemic mixture)
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Toluene maximum 0.14 %
Molecular formula ‡	$C_{17}H_{21}NO_2$
Molecular mass ‡	271.36 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	74.5-77.5°C (99.9%)
Boiling point (state purity) ‡	316.7°C (99.9%)
Temperature of decomposition (state purity)	not relevant
Appearance (state purity) ‡	Pure material: white odourless solid (99.8%)
	Technical material: light brown solid with mouldy or camphor-like odour (98.9 %)
Vapour pressure (state temperature, state purity) ‡	$2.2 \cdot 10^{-5}$ Pa at 25°C (extrapolated) (99.7 %)
Henry's law constant ‡	$8.1 \cdot 10^{-5}$ Pa · m³ / mol
Solubility in water (state temperature, state purity and pH) ‡	74 mg/L (25°C) (99.7 %)
	The solubility has not been carried out at different pHs as the molecule does not dissociate within the range pH 2 to pH 12.
Solubility in organic solvents ‡ (state temperature, state purity)	The solubility in different organic solvents at 20°C was determined to be (purity: technical. Exact purity not stated): n Heptane 11.1 g/L Acetone 440 g/L Ethyl acetate 290 g/L Propan-2-ol 230 g/L Toluene 361 g/L Dichloromethane 692 g/L
Surface tension ‡ (state concentration and temperature, state purity)	σ = 64.1 mN/m (66 mg/L aqueous solution at 20°C) (purity: technical. Exact purity not stated)
Partition co-efficient ‡ (state temperature, pH and purity)	LogPow = 3.3 at 25°C, independent of pH, pH not stated. (99.8 %)
	Effect of pH was not investigated, since there is no dissociation in water in the environmentally relevant pH-range
Dissociation constant (state purity) ‡	None (purity 93.9%).

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	(Purity: 99.9%) solution — wavelength [nm] — molar extinction coefficient [L / mol · cm] neutral — 215 — 58800 neutral — 282 — 10500 acidic — 215 — 58600 acidic — 282 — 10900 Maximum unreliable under alkaline conditions No λ_{max} for absorbancy > 290 nm, but absorbancy to 350 nm.
Flammability ‡ (state purity)	Not highly flammable (94.1 %)
Explosive properties ‡ (state purity)	Not explosive (94.1 %)
Oxidising properties ‡ (state purity)	Not oxidising (technical material. Exact purity not stated)

Summary of intended uses

Crop and/ or situation	Member State, Country or Region	Product name	F G or I	Pests or Group of pests controlled	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days)	Remarks
(a)			(b)	(c)	Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL (l) min – max	water L/ha min – max	kg as/ha (l) min – max	(m)	
Head cabbage	EU, North	Devrinol SC, 450	F	Annual grasses and broad-leaved weeds	SC	450g/l	Application to soil surface, followed by soil incorporation into the top 5-8 cm preplanting and cultivation over 20 cm following harvest	Before sowing/ planting	1	Not applicable	0.5	200	1.0	Not applicable.	[I] [II]
Brussels sprouts	EU, North	Devrinol SC, 450	F	Annual grasses and broad-leaved weeds	SC	450g/l	Application to soil surface, followed by soil incorporation into the top 5-8 cm preplanting and cultivation over 20 cm following harvest	Before sowing/ Planting	1	Not applicable	0.5	200	1.0	Not applicable	[I] [II]
Cauliflower	EU, North	Devrinol SC, 450	F	Annual grasses and broad-leaved weeds	SC	450g/l	Application to soil surface, followed by soil incorporation into the top 5-8 cm preplanting and cultivation over 20 cm following harvest	Before sowing/ Planting	1	Not applicable	0.5	200	1.0	Not applicable	[I] [II]
Broccoli/ calabrese	EU, North	Devrinol SC, 450	F	Annual grasses and broad-leaved weeds	SC	450g/l	Application to soil surface, followed by soil incorporation into the top 5-8 cm preplanting and cultivation over 20 cm following harvest	Before sowing/ Planting	1	Not applicable	0.5	200	1.0	Not applicable	[I] [II]
Tomatoes	EU, South	Devrinol SC, 450	F	Annual grasses and broad-	SC	450g/l	Application to soil surface, followed by soil incorporation into	Before sowing/ Planting	1	Not applicable	0.45	500	2.25	Not applicable	[I] [II]

Crop and/ or situation (a)	Member State, Country or Region	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)	kg as/hL (l) min – max	water L/ha min – max	kg as/ha (l) min – max		
				leaved weeds			the top 5-8 cm preplanting and cultivation over 20 cm following harvest								[III]
Oilseed rape	EU	Devrinol SC, 450	F	Annual grasses and broad-leaved weeds	SC	450g/l	Application to soil surface, followed by soil incorporation into the top 5-8 cm preplanting and cultivation over 20 cm following harvest	Before sowing/ planting	1	Not applicable	0.6	200	1.2	Not applicable	[I] [II]

* 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 of the technical substance. 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

[I] The groundwater exposure assessment, consequent consumer risk assessment, and consequent aquatic risk assessment for the metabolite NOPA are not finalised.
[II] The aquatic risk assessment from exposure to photolysis metabolites, and risk assessment for the active substance for rooted aquatic macrophytes are not finalised (note appropriate exposure assessments are available).
[III] The risk to soil non-target macro and micro-organisms and the risk to aquatic organisms are not finalised (note both the exposure and risk assessments are not finalised).

Methods of Analysis

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

Technical as (analytical technique)	GC-MS
Impurities in technical as (analytical technique)	GC-MS
Plant protection product (analytical technique)	GC-MS

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Napropamide
Food of animal origin		None
Soil		Napropamide
Water	surface	Not finalised, at least napropamide
	drinking/ground	Not finalised, at least napropamide
Air		Napropamide

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Method DFG-S19 (multi-residue method): Extraction performed with acetone/water followed by partition with dichloromethane. Extracts were cleaned-up using gel permeation chromatography. Determination performed by GC/MSD. Napropamide LOQ: 0.01 mg/kg, fruiting vegetables, brassica and oilseed (i.e. tomatoes, cauliflower and oilseed rape).
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	No method for animal products is necessary, since no MRL was set.
Soil (analytical technique and LOQ)	Napropamide: GC-MS LOQ: 0.01 mg/kg
Water (analytical technique and LOQ)	Napropamide: GC-MS LOQ: 0.05 µg/L for drinking and ground water LOQ: 1 µg/L for surface water
Air (analytical technique and LOQ)	Napropamide: HPLC-UV LOQ: 3.3 µg/m³
Body fluids and tissues (analytical technique and LOQ)	Not required [substance is not classified as toxic (T) or very toxic (T^+)]

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

	RMS/peer review proposal :
Active substance	None

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	> 90 % based on urinary (15 %) and biliary (78 %) excretion within 24 h. Highest blood concentration after 6 hours.
Distribution ‡	Uniformly distributed
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	Rapid and extensive (approx. 90 %) within 72 h. Majority excreted within 24 hours mainly via urine (42-52 %) and 23-34 % via faeces, 78 % of dose via bile within 24 h indicating extensive enterohepatic circulation.
Metabolism in animals ‡	Extensively metabolised (> 99 %); 15 metabolites in urine and faeces; Metabolic pathway: dealkylation, hydroxylation, hydrolysis followed by conjugation
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 4.8 mg/L/4h (nose-only)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitization (test method used and result) ‡	Non-sensitiser (Modified Buehler tests)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver; rat, dog (increased weight, hepatotoxicity) Body weight change; dog	
Relevant oral NOAEL ‡	1-year, dog: 50 mg/kg bw/day 90-day, rat: 50 mg/kg bw/day	
Relevant dermal NOAEL ‡	30-day, rat: > 1000 mg/kg bw/day	
Relevant inhalation NOAEL ‡	No data available - not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

Overall negative in *in vitro* tests, but positive response in *in-vitro (mammalian cell gene mutation test)*. No evidence for genotoxicity *in-vivo*.	

Overall no genotoxic potential.	

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

Target/critical effect ‡	Liver; mice only (increased weight) Kidney; mice only (increased weight) Body weight changes; mice, rat	
Relevant NOAEL ‡	2-year, rat: 30 mg/kg bw/day 18-month, mouse: 55 mg/kg bw/day	
Carcinogenicity ‡	Napropamide is unlikely to pose a carcinogenic risk to humans.	

Reproductive toxicity (Annex IIA, point 5.6)

Multigeneration study

Reproduction target / critical effect ‡	Decreased bodyweight parental and pups. No reproductive effects	
Relevant parental NOAEL ‡	30 mg/kg bw/day (conc. in food adjusted in relation to food consumption)	
Relevant reproductive NOAEL ‡	100 mg/kg bw/day	
Relevant offspring NOAEL ‡	30 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Reduced bodyweight gain in dams (rat and rabbit). Abortions (rabbit)	
Relevant maternal NOAEL ‡	Rat: 110 mg/kg bw/day Rabbit: 300 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 1000 mg/kg bw/day Rabbit: 300 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data, no concern from other studies	
Repeated neurotoxicity ‡	No data, no concern from other studies	
Delayed neurotoxicity ‡	No data, no concern from other studies	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data.

Studies performed on metabolites or impurities ‡	Metabolites NOPA was tested for acute oral and dermal toxicity, eye irritation and genotoxicity *in vitro* and *in vivo*. Rat, oral LD_{50} = 2710 mg/kg bw Rat, dermal LD_{50} >4640 mg/kg bw No eye irritation. Negative bacterial tests and gene mutation test *in vitro*. Weak clastogenic effect in chromosome aberration *in vitro*. No genotoxic effect in a micronucleus test *in vivo*. Overall no genotoxic potential.

Medical data ‡ (Annex IIA, point 5.9)

No abnormalities from health surveillance of manufacturing personnel. No reported poisoning incidents. No epidemiological studies available.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.3 mg/kg bw/day	Rat, 2-year studies	100
AOEL ‡	0.5 mg/kg bw/day	Dog, 1-year	100
ARfD ‡	Not allocated - not necessary		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Devrinol 450 SC	Concentrate: 0.7% (450 g/L) Spray dilutions: 6.5% (22.5 g/L) and 13.4% (0.9 g/L) Based on an *in vitro* human skin study with the identical product 'Devrinol 45 FL'

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Pre-crop drilling application to soil surface followed by incorporation into soil, SC formulation: Tractor mounted equipment — % of AOEL **Oilseed rape** (application rate 1.2 kg ai/ha) German model with PPE (gloves during M/L & application; protective garment & sturdy footwear during application) 1.5 % without PPE 20 % UK POEM model with PPE (gloves during M/L & application) 19 % without PPE 121 % **Tomatoes** (application rate 2.25 kg ai/ha) German model with PPE (gloves during M/L & application; protective

	garment & sturdy footwear during application) 2.7 % without PPE 37 % UK POEM model with PPE (gloves during M/L and application) 15 % without PPE 98 % **Brassica vegetables** – Cabbage, Brussels sprouts, Cauliflower, calabrese, broccoli (application rat 1.0 kg ai/ha) German model with PPE (gloves during M/L & application; protective garment & sturdy footwear during application) 1.2 % without PPE 17 % UK POEM model with PPE (gloves during M/L & application) 16 % without PPE 99 % According to the German model, the estimated operator exposure is below the AOEL when no PPE is used; according to the UK POEM model, operator exposure is below the AOEL when gloves during mixing/loading (M/L) and application are worn.
Workers	The potential for worker exposure in these cases is negligible, as re-entry is not considered necessary shortly after spraying. Only one application is allowed per year. Devrinol is applied directly to the soil before crop drilling and immediately incorporated into the soil.
Bystanders	Bystander exposures were estimated using surrogate exposure values at the 90th percentile proposed by the EUROPOEM II Bystander Working Group (BWG)[13]. Results showed that total exposure from both dermal and inhalation is very low being only 1 % of the AOEL.

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

	RMS/peer review proposal:
Substance classified (napropamide)	No classification

[13] Gilbert, A. et al (2002) EUROPOEM II: Report of the Bystander Working Group. FAIR3 CT96-1406

Residues

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

Plant groups covered	Leafy crops (cabbage), root vegetables (potato), fruit crops (tomato, apple), oilseeds (oilseed rape)
Rotational crops	Leafy crops (lettuce), root vegetables (carrot) and cereals (wheat)
Plant residue definition for monitoring	Napropamide
Plant residue definition for risk assessment	Napropamide
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	Ruminants and Hens
Animal residue definition for monitoring	Not discussed and no proposal necessary (as intakes by livestock ≤0.1 mg/kg diet/day)
Animal residue definition for risk assessment	Not discussed and no proposal necessary (intakes by livestock ≤0.1 mg/kg diet/day).
Conversion factor (monitoring to risk assessment)	Not discussed
Metabolism in rat and ruminant similar (yes/no)	Not discussed
Fat soluble residue: (yes/no)	Not discussed

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

.....	Lettuce, carrot (top and root) and wheat. residues <0.01 mg/kg for 180 DAT.
Pot studies: Wheat, Carrots, Lettuce	Only trace levels of napropamide detected
Field trials: Winter wheat	No residues detected

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

.....	Napropamide residues stable for up to 11 months in cabbage (high water content matrices), and at least one year in oilseed rape (oil-containing crops) when stored at approximately -18°C

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:

Ruminant: No	**Poultry:** No	**Pig:** No
No study required	No study required	No study required

Summary of critical residues data (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern / Southern Region	Trials results relevant to the critical GAP (a)	Recommendation/ comments	**MRL** (mg/kg)	**HR** (mg/kg)	**STMR** (mg/kg) (b)
Head cabbage	North	8x <0.01 mg/kg		0.01*	0.01	0.01
Brussels sprouts	North	8x <0.01 mg/kg		0.01*	0.01	0.01
Cauliflower	North	7x <0.01 mg/kg		0.01*	0.01	0.01
Broccoli/calabrese	North	7x <0.01 mg/kg		0.01*	0.01	0.01
Tomato	South	8x <0.01 mg/kg		0.01*	0.01	0.01
Rapeseed	North	10x <0.01 mg/kg		0.01*	0.01	0.01

(a) Numbers of trials in which particular residue levels were reported
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP

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

ADI	0.3 mg/kg bw (proposed by RMS).
TMDI (% ADI)	PSD UK Consumer Model 0.000025 mg/kg bw/day (<0.1% ADI), for Adults 0.000026 mg/kg bw/day (<0.1% ADI), for children 0.000051 mg/kg bw/day (<0.1% ADI), for toddlers 0.000063 mg/kg bw/day (0.1% ADI), for infants BBA German model 0.000028 mg/kg bw/day (<0.1% ADI), for female children WHO/GEMS European regional diet 0.000020 mg/kg bw/day (<0.1% ADI), for Adults
IEDI (European Diet) (% ADI)	Not required.
Factors included in IEDI	Not required.
ARfD	Not necessary
Acute exposure (% ARfD)	Not relevant.

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

Crop/processed crop	Number of studies	Transfer factor	% Transference
Not required, since no significant residues (all residues <0.01 mg/kg) occur in the plant or plant product for further processing, and TMDI <10% of ADI.			

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

Crop or Crop Group	**Proposed MRLs** (mg/kg)
Head cabbage	0.01*
Brussels sprouts	0.01*
Cauliflower	0.01*
Broccoli/calabrese	0.01*
Tomato	0.01*
Rapeseed	0.01*

* MRL set at the limit of quantification of the analytical method.

Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	20°C ^{14}C-1-naphthyl labelling 4.9-5.2% AR after 90 days (n=1, duplicate samples but one soil) 30°C ^{14}C-1-naphthyl labelling 3.5% AR after 90 days (n=1)
Non-extractable residues after 100 days ‡	20°C ^{14}C-1-naphthyl labelling 12.7-14.7% AR after 90 days (n=1, duplicate samples) 30°C ^{14}C-1-naphthyl labelling 7.9% AR after 90 days (n=1)
Relevant metabolites - name and/or code, % of applied (range and maximum) ‡	20°C: NOPA; range: D[14]-1.1% AR, max 1.1% AR Polar metabolites; range: D[15]-1.5% AR; max. 1.5% AR Unknown metabolites; range: 0.2-2.9% AR max. 2.9% AR 30°C: NOPA; range: 0.03-5.78% AR, max 5.78% AR

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

Anaerobic degradation ‡	25°C ^{14}C-1-naphthyl labelling Mineralisation: 0% AR after 90 days (n=1; water/soil system) Non-extractable residues: 12.7 % AR after 90 days (n=1) (9.4% AR at 365 days) Metabolites: NOPA, 0.6-0.8% AR (n=1)
Soil photolysis ‡	25°C ^{14}C-1-naphthyl labelling Mineralisation: 55.6% AR after irradiation for 28 equivalent solar days at latitude 37° 56'N (n=1) Miscellaneous (not identified): range 0.7-4.1% AR (n=1)

[14] D = minimum cannot be defined, because the substance was not recorded as a discrete peak
[15] D = minimum cannot be defined, because the substance was not recorded as a discrete peak

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

Method of calculation	Laboratory: mainly 1. order but also biexp. kinetics Field studies: 1. order
Laboratory studies	**Napropamide** DT_{50lab} (20°C, aerobic): 120, 380, 380 and 400 d; average 308 d (n=4) 1st order; pF2 DT_{90lab} (20°C, aerobic): 410, >1000, >1000 and >1000 d; (n=4) 1st order; pF2
	DT_{50lab} (10°C, aerobic): 463 d (biexp.; n=1); pF2 DT_{90lab} (10°C, aerobic): >1000 d (biexp.; n=1); pF2
	DT_{50lab} (30°C, aerobic): 446 d (1. Order; n=1); 75% moisture
	DT_{50lab} (25°C, anaerobic): > 365 d (n=1)
	Degradation in the saturated zone: No data submitted and no data required
	NOPA DT_{50lab} (3 soils, 20°C), 4.5; 5.8 and 6.8 days, geometric mean = 5.62 days
Field studies (state location, range or median with n value) ‡	**Napropamide** DT_{50f}: Germany, bare soil, 31; 34; 96; 127 d (n=4); 1. Order. DT_{50f}: Canada, bare soil, 14; 90 d (n=2); 1. Order N Europe:Longest field single first order DT_{50f} = 127 days (non-normalised) S Europe: (No field dissipation data for S- EU). Normalised (temperature[16]) 1 order field DT_{50} 5.3, 13.9, 18, 36.9, 50.8 days, geometric mean = 19.0 days[17].
	DT_{90f}: Germany, bare soil, 180; 290; 400 d (n=3); 1-order.
Soil accumulation and plateau concentration ‡	$PEC_{plateau}$ for three dose rates: 1.0 kg a.s./ha: $PEC_{plateau}$ = 0.053 mg/kg soil 1.2 kg a.s./ha: $PEC_{plateau}$ = 0.063 mg/kg soil 2.25 kg a.s./ha: $PEC_{plateau}$ = 0.118 mg/kg soil (Values represent concentrations before the last seasons applications are made, distributed over a mixing depth of 20cm).

[16] Normalisation assumed a Q10 of 2.58 in line with EFSA (2007)
[17] Should be used for FOCUS calculations for the active substance

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence (yes / no) (if yes type of dependence) ‡	**Napropamide** Adsorption: K_{foc}: 208; 465; 480; 674, 1170, 409, 610, 647,1164 and 1593 mL/g (arithmetic mean = 649 mL/g; 10 soils) K_f: 3.4; 5.1; 6.4;8.6, 14.8, 8.1, 16.2, 18.3, 20.7 and 44.5 mL/g (arithmetic mean = 14.6 mL/g; 10 soils) 1/n: 1, 1, 1, 1, 1.08, 0.7196, 0.7414, 0.8116, 0.8688, 0.9326 (arithmetic mean = 0.915) Desorption: K_{des}: 10.98, 28.6, 30.25, 31.17, 50.63, 60.59 (average = 40.25 mL/g, 6soils) No pH dependence For FOCUS gw modelling K_{foc}: 649L/kg, 1/n=0.915
	NOPA Adsorption: K_{foc}: 28; 35; 40 and 81 mL/g (average= 46 mL/g; 4 soils) $K_{f:}$ 0.14; 0.28; 0.44 and 2.1 mL/g (average= 0.74 mL/g; 1/n= 0.96-1.03; 4 soils) FOCUS groundwater scenario specific adsorption values Kfoc 1/n Châteaudun 33.4 1.01 Hamburg 82.1 0.952 Jokioinen 85.2 0.95 Kremsmünster 48.6 0.985 Okehampton 68.1 0.964 Piacenza 60.8 0.971 Porto 119.4 0.929 Sevilla 41.8 0.995 Thiva 38.8 1.00 Regression equations relating pH to adsorption $LogK_{Foc}$ = -0.1627x + 2.744 Log1/n = 0.0106x - 0.0753 where x=pH Desorption: K_{foc}: 81; 110; 120 and 130 mL/g (average= 110 mL/g; 4 soils) $K_{f:}$ 0.52; 0.89; 1.2 and 3.0 mL/g (average= 1.4 mL/g; 4 soils) 1/n = 1.0 Yes, pH dependence. Adsorption increases as pH decreases.

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

Column leaching ‡	Guideline: Precipitation: Presented study not acceptable, none required.
Aged residues leaching ‡	No reliable information is available.
Lysimeter/ field leaching studies ‡	No reliable information is available.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	N. Europe: Max $DT_{50field}$ (d): 127 days (moisture: pF2) Kinetics: 1st order Field study representing worst case (for 1st order kinetics). Assumption: Plateau reached at even distribution in the top 20 cm layer, subsequent application to the top 5 cm. Both: Bulk soil density of 1.5 g/cm^3. Spray deposition is assumed to be 100%. No interception, no losses to surface runoff, leaching and volatilisation. S. Europe: Data gap.
Application rate	N. Europe: Crops: Brassicas, oilseed rape S. Europe: Crop: tomatoes 0 % plant interception: Pre-emergence therefore no plant interception Application rate: N. Europe: One time 1,200 kg as/ha, S. Europe: One time 2,250 g as/ha

Northern Europe:

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average
	$DT_{50field}$ = 127 d	

Initial	**0 d**	**2.063**	**2.063**
Short term	**1d**	**2.052**	**2.057**
	2d	**2.041**	**2.052**
	4d	**2.018**	**2.041**
Long term	**7d**	**1.986**	**2.024**
	21d	**1.840**	**1.949**
	28d	**1.771**	**1.913**
	50d	**1.570**	**1.805**
	100d	**1.195**	**1.590**
	365d	**0.281**	**0.894**

Southern Europe: Data gap as no DT_{50} for southern European conditions is available. If the DT_{50} of 127 days was assumed (note DT_{50} in S Europe under dry conditions could be longer than in N Europe so this is not necessarily a conservative assumption), assuming even incorporation over 5cm annual applications of 2.25 kg a.s. /ha, an accumulated value would be higher than for N Europe at 3.47 mg/kg. The consequent 21 day TWA value would be 3.095mg/kg.

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

	Napropamide
Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature) ‡	pH_5_: Stable (25° and 40°C)
	pH_7_: Stable (25° and 40°C)
	pH_9_: Stable (25° and 40°C)
Photolytic degradation of active substance and relevant metabolites ‡	DT_{50} = 2-70 hr. in Mid-European conditions depending on season Hydroxy napropamide Isomer 1 (up to 20%), hydroxy napropamide Isomer 2 (up to 27%), diethylamine (up to 26%) dimer (up to 9%), MNF (up to 15%)
Readily biodegradable (yes/no) ‡	No
Quantum yield of direct phototransformation in water at Σ > 290 nm	Φ=0.5
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡	DT_{50} water : 24; 32 d (n=2; 1. Order) DT_{90} water : Not stated in the study report DT_{50} whole system: 400 d (ext[18].); 250 d (ext) (n=2; 1 order) Geometric mean = 316 days DT_{90} whole system: not calculated
Mineralization	1.7% AR; 3.6% AR after 100 d (n=2) (Other volatiles than CO_2 <0.3%)
Non-extractable residues	11% AR; 19% AR after 100 d (n=2)

[18] Ext = extrapolated value

Distribution in water / sediment systems (active substance) ‡	Water/sediment ratios at 0 d and 100 d: Ratio (0 d): 1.9; 2.3 (n=2) Ratio (100 d): 0.15; 0.07 (n=2)
Distribution in water / sediment systems (metabolites) ‡	No major metabolites (<3% AR)

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

Parent:

Method of calculation	FOCUS step 3, TOXSWA model Molecular mass (g/mol) 271 K_{oc} (mL/g) 838.74 (average K_{oc} value from five soils [Pandey, 2007]) Freundlich Constant 0.81 (average value from five soils [Pandey, 2007]) DT_{50} in sediment-water system (days) 316 (geometric mean of two systems [Long *et al*., 1995]) DT_{50} in water (days) 1000 (worst-case default) DT_{50} in sediment (days) 316 (geometric mean of two systems) DT_{50} in soil (days) 19.0 (geometric mean first-order normalised $DT_{50field}$ value from six field trials) Solubility (mg/L) 74 Vapour pressure (Pa) 0 (set to 0 since field dissipation data would include losses by volatilisation) Plant uptake coefficient 0.5 (FOCUS default) Kinetics: 1st order Water body:Ditch (D6) Depth of water body: 30 cm Q10= 2.58, Walker equation coefficient 0.7
Application rate	Crop: tomato 2250 g/ha Number of applications 1
Main routes of entry	spray drift runoff/drainage

PEC$_{(sw)}$ (µg / l)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		14.105	-		
Short term	1d	0.672	6.917		
	2d	0.0416	3.550		
	4d	0.026	1.791		
Long term	7d	0.0168	1.033		
	14d	0.00244	0.521		
	21d	0.000861	0.348		
	28d	0.0016	0.261		
	42d	0.00078	0.174		
	50d	0.000505	0.147		
	100 d	0.000216	0.0735		

Method of calculation	FOCUS step 3, TOXSWA model Molecular mass (g/mol) 271 K_{oc} (mL/g) 838.74 (average K_{oc} value from five soils [Pandey, 2007]) Freundlich Constant 0.81 (average value from five soils [Pandey, 2007]) DT_{50} in sediment-water system (days) 316 (geometric mean of two systems [Long *et al*., 1995]) DT_{50} in water (days) 1000 (worst-case default) DT_{50} in sediment (days) 316 (geometric mean of two systems) DT_{50} in soil (days) 19.0 (geometric mean first-order normalised $DT_{50field}$ value from six field trials) Solubility (mg/L) 74 Vapour pressure (Pa) 0 (set to 0 since field dissipation data would include losses by volatilisation) Plant uptake coefficient 0.5 (FOCUS default) Kinetics: 1st order Water body:Ditch (D2) Depth of water body: 30 cm Q10= 2.58, Walker equation coefficient 0.7
Application rate	Crop: winter oilseed rape 1200 g/ha Number of applications 1
Main routes of entry	1.9275% areic mean deposition runoff/drainage

PEC$_{(sw)}$ (µg / l)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		7.739	-		
Short term	1d	7.050	7.367		
	2d	6.575	7.080		
	4d	5.980	6.663		
Long term	7d	5.453	6.248		
	14d	0.662	4.341		
	21d	0.850	3.156		
	28d	0.864	2.583		
	42d	0.814	2.003		
	50d	0.0807	1.751		
	100 d	0.0495	0.901		

Photolysis metabolites:

Method of calculation

FOCUS step 3, TOXSWA model

	Isomer1	Isomer2	Dimer	Diethyl-amine	MNF
Mw (g/mol)	271	271	540	73	198
Max % formation (molar yield)	20	27	9	26	15
Max % formation (mass yield)	20	27	9.0	7.0	11.0

Water body: Ditch (D6), Streams R2, R3 and R4

Application rate

Crop: tomato
2250 g/ha
Number of applications 1

Scenario	Maximum initial PEC$_{sw}$ (µg/L) following single annual application					
	Napropamide	Isomer 1	Isomer 2	Dimer	Diethylamine	MNF
D6 (ditch)	14.105	2.821	3.808	1.269	0.988	1.546
R2 (stream)	12.436	2.487	3.358	1.119	0.871	1.363
R3 (stream)	13.283	2.657	3.586	1.195	0.930	1.456
R4 (stream)	9.397	1.879	2.537	0.846	0.658	1.030

PEC (sediment)

Parent:

Method of calculation	FOCUS step 3, TOXSWA model Molecular mass (g/mol) 271 Koc (mL/g) 838.74 Freundlich Constant 0.81 DT_{50} in sediment-water system (days) 316 DT_{50} in water (days) 1000 (worst-case default) DT_{50} in sediment (days) 316 DT_{50} in soil (days) 19.0 Solubility (mg/L) 74 Vapour pressure (Pa)V 0 Plant uptake coefficient 0.5 (FOCUS default) Kinetics: 1st order Water body: Ditch (D6) and stream (R2) Depth of water body: 30 cm
Application rate	Crop: Brassicas, oilseed rape and tomato 1000, 1200 and 2250 g/ha Number of applications 1 and 9

Focus Step 3, Ditch (D6) and Stream (R2), single application

PEC$_{(sed)}$ (µg / kg)		Actual		Time weighted average	
		Ditch (D6)	Stream (R2)	Ditch (D6)	Stream (R2)
Initial		4.613	43.307	-	-
Short term	**1d**	3.936	42.305	4.445	42.828
	2	3.329	42.026	4.150	42.446
	4	2.601	40.723	3.635	41.919
Long term	**7d**	2.048	40.242	3.109	41.396
	14	1.492	37.814	2.445	40.173
	21	1.232	35.98	2.089	39.089
	28	1.078	36.700	1.858	38.476
	42	0.882	33.667	1.566	37.361
	50	0.806	32.307	1.451	36.669
	100	0.526	26.071	1.051	32.883

PEC_{sed} – potential for accumulation in worst-case scenario of all three crops

Year	D2 ditch (Winter oilseed rape)		R1 pond (Brassicas – 1st crop in season)		R2 stream (Tomatoes)	
	Peak (µg/kg)	% of Yr 1	Peak (µg/kg)	% of Yr 1	Peak (µg/kg)	% of Yr 1
1	20.213	100.00	2.532	100.00	43.307	100.00
2	22.822	112.91	3.923	154.94	55.313	127.72
3	24.058	119.02	4.716	186.26	60.519	139.74
4	24.745	122.42	5.168	204.11	63.128	145.77
5	25.137	124.36	5.448	215.17	64.508	148.96
6	25.380	125.56	5.622	222.04	65.290	150.76
7	25.546	126.38	5.757	227.37	65.743	151.81
8	25.609	126.70	5.817	229.74	66.017	152.44
9	25.680	127.05	5.847	230.92	66.152	152.75

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

Parent:

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Modelling using FOCUS model (PEARL and PELMO) Scenarios: Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva Molecular mass (g/mol) 271 Koc (mL/g) 838.74 Freundlich Constant, 1/n 0.81 DT50 in soil (days) 19.0 Solubility (mg/L) 74 Vapour pressure (Pa)V 0 Plant uptake coefficient 0.5 (FOCUS default) Q10= 2.58, Walker equation coefficient 0.7

Application rate

Crop	Time of appl. Dates relative to emergence of the crops	Application rate (g as/ha)
Cabbage	Feb, May, Aug	1000
Oilseed rape	Jul, Aug, Sep	1200
Tomato	Mar, Apr, May	2250

PEC$_{(gw)}$

Maximum concentration	Value not provided by FOCUS model shells, not required.
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Annual average concentration (80th percentile) according to FOCUS guidance: active substance < 0.0005 µg/L

Metabolite, NOPA:

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Data gap

Application rate

Crop	Time of appl. Dates relative to emergence of the crops	Application rate (g as/ha)

PEC$_{(gw)}$

Maximum concentration	Data gap
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Data gap

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	Φ=0.5
Photochemical oxidative degradation in air ‡	DT_{50} of 0.552 hours derived by Atkinson method of calculation
Volatilization ‡	from soil surfaces: Not studied – not expected to volatilise
	from soil surfaces: Not studied – not expected to volatilise

PEC (air)

Method of calculation	Not calculated - negligible

$PEC_{(a)}$

Maximum concentration	Not calculated - negligible

Definition of the Residue (Annex IIA, point 7.3)

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: napropamide Surface Water: napropamide, photolysis metabolites (5; hydroxy napropamide isomers 1 and 2, diethylamine, dimer and MNF) and NOPA (where groundwater becomes surface water) Sediment: napropamide Ground water: napropamide and NOPA Air: napropamide

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

Soil (indicate location and type of study)	No available data
Surface water (indicate location and type of study)	No available data
Ground water (indicate location and type of study)	No available data
Air (indicate location and type of study)	No available data

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Candidate for R53. May cause long term adverse effects.

Effects on non-target Species

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

Acute toxicity to mammals	LD_{50}	4680	mg/kg bw (rats)
Acute toxicity to birds	LD_{50}	> 2250	mg/kg bw (bobwhite quail)
Dietary toxicity to birds	LC_{50}	> 7200	ppm ≈ 1572 mg/kg bw/day (mallard duck)
Reproductive toxicity to birds	NOEL	3000	ppm ≈ 309 mg/kg bw /day (mallard duck)
Reproductive toxicity to mammals	NOEL	30	mg/kg bw/day (rats)

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
2.25	Tomato	Herbivorous bird	Acute	15	10
2.25	Tomato	Insectivorous bird	Acute	18	10
2.25	Tomato	Herbivorous bird	Short-term	23	10
2.25	Tomato	Insectivorous bird	Short-term	23	10
2.25	Tomato	Herbivorous bird	Long term	8.5	5
2.25	Tomato	Insectivorous bird	Long term	**4.5**	5
1.2	Oilseed rape	Herbivorous bird	Long term	8.5	5
1.2	Oilseed rape	Insectivorous bird	Long term	8.6	5
2.25	Tomato	Vermivorous bird	Secondary poisoning	52[a]	5
1.2	Oilseed rape	Vermivorous bird	Long term	86	5
1	Brassicas	Vermivorous bird	Long term	103	5
1.2	Oilseed rape	Fish-eating bird	Secondary poisoning	4754[b]	5
2.25	Tomato	Vermivorous mammal	Long term	3.98[c]	5
1.2	Oilseed rape	Vermivorous mammal	Long term	6.6	5
1	Brassicas	Vermivorous mammal	Long term	7.9	5
2.25	Tomato	Insectivorous mammal	Acute	236	10
2.25	Tomato	Insectivorous mammal	Long term	8.3	5
1.2	Oilseed rape	Insectivorous mammal	Long term	7.8	5
1	Brassicas	Insectivorous mammal	Long term	9.3	5
1.2	Oilseed rape	Fish-eating mammal	Long term	750[b]	5

[a]TER calculated with a worst-case 21-d twa PECs of 3.095
[b]TER calculated with a worst-case 21-d twa PECsw of 3.156
[c]TER calculated with a 21-d twa PECs of 3.095, the long-term risk to earthworm-eating mammals was assessed as likely to be low in a weight of evidence approach.

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

Group	Test substance	Time-scale	Endpoint	Toxicity[1] (mg/l)
Laboratory tests				
Salmo gairdneri	Napropamide	96 h	Mortality, EC_{50}	**6.6 (m)**
Salmo gairdneri	Napropamide	28 d	Growth NOEC	**1.1 (m)**
Daphnia magna	Napropamide	21 d	Reproduction, NOEC	4.3 (m)
Daphnia magna	Napropamide	21 d	Length of P_0, NOEC	1.1 (m)
Invertebrates	Napropamide	48-96 h	Geometric mean of L/EC_{50} values	**5.4**
Lemna minor	Napropamide	14 d	E_bC_{50}	**0.237 (m)**
Lemna gibba	Devrinol 450SC	7 d	E_bC_{50}	**0.067 (m)**
Lemna gibba	Devrinol 450SC	7 d	E_bC_{50}	0.136 (m)
Anabaena sp.	Napropamide	72 h	E_bC_{50}	14.2 (m)
Selenastrum capricornutum	45% FL formulation	72 h	Biomass, EC_{50}	1.71 (m)
Selenastrum capricornutum	45% FL formulation	72 h	Growth rate, EC_{50}	~ 4.95 (m)
Selenastrum capricornutum	45% FL formulation	72 h	Biomass, NOEC	0.54
Selenastrum capricornutum	45% FL formulation	72 h	Growth rate, NOEC	0.54
Daphnia magna	Devrinol 45 Flow	48 h	Mortality, EC_{50}	**8.0 (n)**
Microcosm or mesocosm tests				
Not required				

1: n = nominal, m = measured

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

Tomatoes (fruiting vegetables)							
Scenario	Water body type	Max initial PEC (µg/L) [1]	Acute TER		Chronic TER		
			Fish (96 h)	*Daphnia* (48 h)	Fish (28 d)	*Daphnia* (21 d)	*Lemna* (7 d)
D6	Ditch	14.105	468	383	78.0	78.0	**4.75**
R2	Stream	12.436	531	434	88.5	88.5	**5.39**
R3	Stream	13.283	497	407	82.8	82.8	**5.04**
R4	Stream	9.397	702	575	117	117	**7.13**

Winter oilseed rape					
Scenario	Water body type	Max initial PEC (µg/L) [1]	Acute TER		Chronic TER
			Fish (96 h)	*Daphnia* (48 h)	*Lemna* (7 day)
D2	Ditch	7.739	853	698	**8.66**
	Steam	6.859	962	787	**9.77**
D3	Ditch	7.665	861	705	**8.74**
D4	Pond	0.262	25191	20611	256
	Stream	6.570	1005	822	10.2
D5	Pond	0.263	25095	20532	254.8
	Stream	7.088	931	762	**9.45**
R1	Pond	0.262	25191	20611	256
	Stream	5.023	1314	1075	13.3
R3	Stream	7.057	935	765	**9.49**

Brassicas (leafy vegetables)			
Scenario	Water body type	Max initial PEC (µg/L) [1]	*Lemna* (7 day) TER
D3	Ditch	6.343	10.6
D4	Pond	0.218	307
	Stream	5.032	13.3
D6	Ditch	6.383	10.5
R1	Pond	0.237	283
	Stream	4.172	16.1
R2	Stream	5.611	11.9
R3	Stream	5.900	11.4
R4	Stream	4.147	16.2

[1] See addendum to AR, Annex B.8 (December 2009), Section B.8.6.2, for details of PEC_{sw} values.
Applicant's PEC_{sw} calculations accepted by RMS.
Note: TERs >100 for acute exposure and > 10 for chronic exposure are all acceptable
Values in bold indicate unacceptable risk. For refinement, see addendum to AR, Annex B.9 (Dec 2009)

Bioconcentration

Bioconcentration factor (BCF) ‡	98
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	Not reported ~ 7 days
Level of residues (%) in organisms after the 14 day depuration phase	< 5% (measured as ^{14}C)

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

Acute oral toxicity (study with the "lead formulation")	LD 50 ~ > 100 µg/bee
Acute contact toxicity (study with the "lead formulation")	LD50 ~ > 100 µg/bee

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
2.25	Tomato	Oral	22.5	50
2.25	Tomato	Contact	22.5	50
1.2	Oil seed rape	Oral	12	50
1.2	Oil seed rape	Contact	12	50
1.0	Brassicas	Oral	10	50
1.0	Brassicas	Contact	10	50

Field or semi-field tests
No data submitted

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

Species	Stage	Test Substance	Dose (kg as • ha^{-1})	Endpoint	Effect (%)	Annex VI Trigger (%)
Laboratory tests						
Typhlodromus pyri	Nymph	Napropamide	4.5	Mortality Fertility	~ 0 24.7	50
Aphidius rhopalosiphi	Adult	Napropamide	4.5	Mortality Fertility	n.s. (8) n.s. (31)	50
Lycosid spiders.	Adult	Napropamide	1.24	Mortality Food uptake	0 0	50
Pterostichus melanarius	Adult	Napropamide	1.24	Mortality Food uptake	0 0	50

n.s. = not significant

Field or semi-field tests No data submitted

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

Acute toxicity ‡, LC_{50}	564 mg/kg soil dry weight (* /2 = 282)
Reproductive toxicity ‡, NOEC	60 mg/kg soil dry weight (* / 2 = 30) (highest conc. tested, lead formulation)

*Because the logKow for napropamide is 3.3, the effect concentrations should be divided by 2.

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

A worst-case PECsoil for southern EU could be estimated from the conditions and application rate in combination with the DT_{50} of northern EU soils (Even distribution in top 5 cm soil of 2.25 kg as/ha. Bulk soil density of 1.5 g/cm3. Spray deposition is assumed to be 100%. No interception, no losses to surface runoff, leaching and volatilisation.).

This calculation results in a peak concentration of 3.118 mg as/kg soil

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
2.25	Tomato	Acute	90	10
2.25	Tomato	Chronic	9.6	5

Effects on other soil non-target macro-organisms

In a litter bag study, napropamide was applied twice at seven days interval, resulting in a total dose of approx. 2.9 kg as/ha. Overall, there were biological effects on the test system that cannot be disregarded. Therefore, the results are not conclusive for tomatoes (2.25 kg a.s/ha). A new study should be in preparation, which may be used for national registration.

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

Nitrogen mineralization	< 25 % effect at day 28 at 15.92 mg a.s./kg d.w. soil (mg a.s/ha).**11.250** g as/ha
Carbon mineralization	0 % effect at day 28 at 15.92 mg a.s./kg d.w. soil (mg a.s/ha).**11.250** g as/ha

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 – spray application (not soil incorporation)

Most sensitive species	Test substance	ER_{50} (g as/ha)[2] vegetative vigour	ER_{50} (g as/ha)[2] emergence	Exposure[1] (g as/ha)[2]	TER	Trigger
Avena fatua	Devrinol 50 DF (not lead)	310	>4500	62.3	5.0	5.0
Beta vulgaris	Devrinol 50 DF (not lead)	430	>4500	62.3	6.9	5.0

[1] exposure at 1 m distance from crop = 2.77% of 2250 g as/ha.

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

None provided.

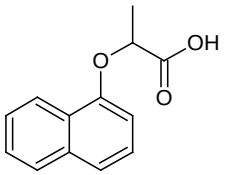
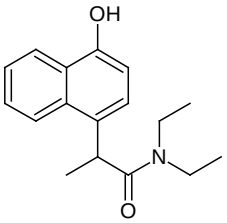
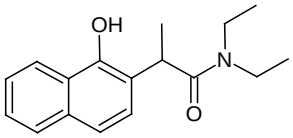
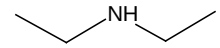
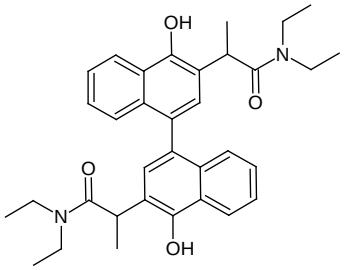
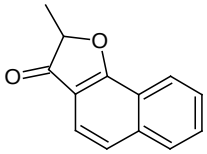
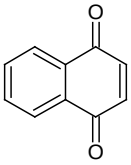
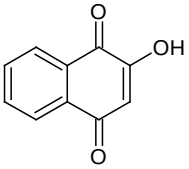
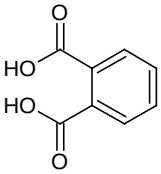
Effects on biological methods for sewage treatment (Annex IIA 8.7)

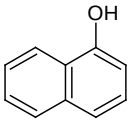
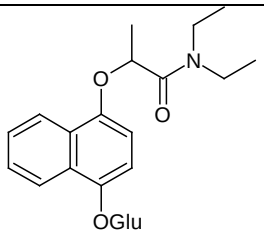
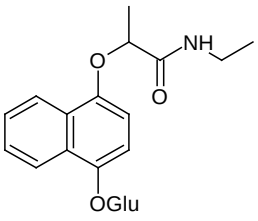
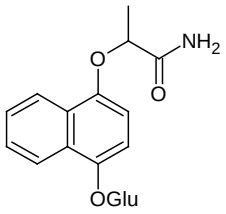
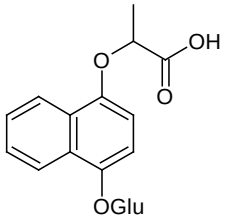
Test type/organism	end point
Activated sludge	Respiration inhibition, 3 hours, EC50 >1000 mg as/L
Pseudomonas sp	Growth inhibition, 6 hours. EC50 > 65.7 mg as/L

Classification and proposed labelling (Annex IIA, point 10) Napropamide

with regard to ecotoxicological data	N; R50/53, Dangerous to the environment, very toxic, may cause long term adverse effects

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name**	Structural formula**
NOPA (U12) (also referred to as α-naphthoxy propionic acid in the dossier)	2-(naphthalen-1-yloxy)propanoic acid	
hydroxy napropamide isomer 1	*N*,*N*-diethyl-2-(4-hydroxynaphthalen-1-yl)propanamide	
hydroxy napropamide isomer 2	*N*,*N*-diethyl-2-(1-hydroxynaphthalen-2-yl)propanamide	
diethylamine	*N*-ethylethanamine	
dimer	2,2'-(4,4'-dihydroxy-1,1'-binaphthalene-3,3'-diyl)bis(*N*,*N*-diethylpropanamide)	
MNF	2-methylnaphtho[1,2-*b*]furan-3(2*H*)-one	
NQ	naphthalene-1,4-dione	
HNQ	2-hydroxynaphthalene-1,4-dione	
PA	benzene-1,2-dicarboxylic acid	

Code/Trivial name*	Chemical name**	Structural formula**
1-naphthol	naphthalen-1-ol	
4-OGlu-NPAM	*N*-[(4-{[1-(diethylamino)-1-oxopropan-2-yl]oxy}naphthalen-1-yl)oxy]glutamic acid [4-glucuronyl-(*N*,*N*-diethyl-2-(1-naphthoxy)) propionamide]	
4-OGlu-DE-NPAM	*N*-[(4-{[1-(ethylamino)-1-oxopropan-2-yl]oxy}naphthalen-1-yl)oxy]glutamic acid [4-glucuronyl-(*N*-ethyl-2-(1-naphthoxy)) propionamide]	
4-OGlu-NOPAM	*N*-({4-[(1-amino-1-oxopropan-2-yl)oxy]naphthalen-1-yl}oxy)glutamic acid [glucuronyl-(1-naphthoxy) propionamide (position of hydroxylation unconfirmed)]	
4-OGlu-NOPA	*N*-{[4-(1-carboxyethoxy)naphthalen-1-yl]oxy}glutamic acid [4-glucuronyl-(1-naphthoxy) propionic acid]	

* The metabolite name in bold is the name used in the conclusion.
** ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

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ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
ADI	acceptable daily intake
ai	active ingredient
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DFOP	double first-order in parallel model
DM	dry matter
DNA	deoxyribonucleic acid
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FC	field capacity
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GLP	good laboratory practice
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HQ	hazard quotient
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median

LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mg	milligram
M/L	mixing and loading
mm	millimetre
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
MWHC	maximum water holding capacity
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OC	organic carbon
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
POEM	Predictive Operator Exposure Model
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PRAPeR	Pesticide Risk Assessment Peer Review
PT	proportion of time spent feeding in the treated area
r^2	coefficient of determination
RMS	rapporteur Member State
RPE	respiratory protective equipment
SC	suspension concentrate
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
TRR	total radioactive residues
UDS	unscheduled DNA synthesis
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
WP	wettable powder
yr	year