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

napropamide.

Finalised: 26 March 2008

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[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

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 as laid down in this report.

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 attached end points.
The representative formulated product for the evaluation was "Devrinol SC 450", a suspension concentrate formulation (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 has been validated). For the other matrices only single methods are available to determine residues of napropamide. For surface water the supplied method does not have a LOQ that is low enough and

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

therefore a new data gap has been identified. In addition to this it should be noted that the residue definition for water is not finalised and therefore further methods could be required in the future.
Due to various reasons the minimum purity of the active substance and the impurity specification can not be concluded on.
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 (> 90 %), and widely distributed. Extensive metabolism and enterohepatic circulation were observed, as biliary excretion was a major pathway, and then excretion was rapid trough urine and faeces. Fifteen metabolites were identified and only < 0.5 % of the dose was recovered as parent compound.
Napropamide has low acute toxicity and no classification is proposed related to acute toxicity testing including irritancy and sensitisation. Critical effect observed through 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 out of five chromosomal tests, but three *in vivo* tests were all negative. So, overall, no genotoxic potential is attributed to napropamide. No potential for carcinogenicity or neurotoxicity was observed; no adverse effect on fertility or on reproductive parameters was observed either, except for a higher abortion rate at maternally toxic doses in the rabbit which could not be ruled out from being a substance related effect. No foetotoxicity or teratogenicity was evidenced. Relevant short term NOAEL was the dose level of 50 mg/kg bw/day from the 1-year oral toxicity study in dog and 90-day oral study in rat, and the overall relevant long term NOAEL was 30 mg/kg bw/day derived from both 2-year, rat studies.
The acceptable daily intake (ADI) is set at 0.3 mg/kg bw/day; the acceptable operator exposure level (AOEL) is 0.5 mg/kg bw/day considering an assessment factor of 100 and no acute reference dose is allocated.
The estimated operator exposure is below the AOEL if personal protective equipment (PPE) is used. No risk is anticipated for workers or bystanders derived from napropamide applications.

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 on a provisional basis. Further information is needed to conclude on the toxicological relevance of 3 metabolites which are not covered by the toxicological studies performed with the parent compound.
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.

Provisionally, no risk for the consumer has been identified.

In soil under aerobic conditions napropamide exhibits moderate to very high persistence forming the minor non transient soil metabolite NOPA[2] (accounting for a maximum of 5.8% of applied radioactivity (AR) in 30°C incubations and 1.1%AR in 20°C incubations) which exhibits moderate persistence. Note the database is limited and further data are necessary to further clarify the persistence of both napropamide (southern European field studies) and NOPA. Mineralisation of 1-naphthyl radiolabel to carbon dioxide accounted for only 5% AR after 90 days. The formation of unextractable residues was a sink, accounting for 13.2 % AR after 90 days. Napropamide exhibits medium to low mobility in soil, 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 using the agreed FOCUS scenarios approach are not available so the risk assessment to aquatic organisms is not finalised.

The potential for groundwater exposure from the applied for intended uses by napropamide above the parametric drinking water limit of 0.1 µg/L, was concluded to be low under the more northern European geoclimatic situations that are represented by the FOCUS groundwater scenarios. However further field DT_{50} reflecting southern European conditions are required before the groundwater exposure assessment for parent napropamide can be finalised. For the metabolite NOPA further soil DT_{50} and kinetic formation fraction data are 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 relevance assessment is triggered and NOPA concentrations will be > 0.75µg/L. From the mammalian toxicological point of view NOPA is not relevant, but biological screening data against target plants and a consumer risk assessment would be required before a conclusion on groundwater non relevance of NOPA could be finalised.

The risk to birds was assessed as low for all representative uses evaluated. The first-tier long-term TER value of 4.6 was below the trigger of 5 for the use in tomato. It was agreed that the risk to insectivorous birds is likely to be low because the endpoint (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 birds from secondary poisoning for earthworm-eating birds was assessed as low. The TER values were in the range of 46 -103 indicating some margin of safety. The risk assessment the Southern European use (tomato) can be finalised once

[2] NOPA: 2-(1-naphthyloxy)propionic acid.

updated PEC_{soil} values are available. The risk to fish-eating birds and mammals needs to be assessed after reliable PECsw values are established.
The risk to mammals is considered to be low for the representative uses evaluated, except the risk to insectivorous mammals and earthworm-eating mammals for the use in Southern Europe (tomato). The risk from plant metabolites was considered to be addressed by the risk assessment for the parent napropamide. 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 meeting. The endpoints 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 endpoints of 0.067 mg a.s./L and a geometric mean value of 5.4 mg a.s./L for macrophytes and invertebrates, respectively. No conclusion can be drawn on the risk to aquatic organisms since no reliable PECsw values were established. A high risk to aquatic organisms cannot be excluded for the representative uses of napropamide. No major metabolites in surface water were identified in the water/sediment study. However, the fate experts agreed that the parent as well as 5 different photolysis metabolites and NOPA (where groundwater becomes surface water) should be considered for risk assessment
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. A high risk to soil functioning (organic matter breakdown) was indicated by the available litter-bag study since effects of >10% were observed until one year after application of napropamide and further refinement of the risk assessment is necessary.
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 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000, as amended by Commission Regulation (EC) No 1095/2007 regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Napropamide is one of the 79 substances of the third stage, part A, covered by the Regulation (EC) No 1490/2002 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 report of its initial evaluation of the dossier on napropamide, hereafter referred to as the draft assessment report, to the EFSA on 6 September 2005. Following an administrative evaluation, the draft assessment report 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 draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed during a written procedure in 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 as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR).

In accordance with Article 11(4) of the Regulation (EC) No 1490/2002, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

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

- the comments received;
- the resulting reporting table (rev. 1-1 of 13 June 2007)

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

- the reports of the scientific expert consultation;
- the evaluation table (rev. 2-1 of 11 March 2008).

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

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 racemic.

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 formulation (SC) 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 attached end points.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

At the moment no minimum purity of napropamide as manufactured can be given, because further clarification is needed. Originally two manufacturing sites were proposed however, one of these has stopped production and the previous requirement for an equivalence check is now redundant. In the January 2008 addendum to Volume 4 a new specification for the now single source was proposed but this was not considered in the peer review process. Some additional quality control data were supplied in the January 2008 addendum to volume 4 but they were not summarised in enough detail. No comparison has been made between the technical specification and the batches tested in the mammalian and ecotoxicology studies. In addition to this the biological activity of the two isomers has not been addressed.

From the manufacturing process toluene may be present in the technical material. The meeting of experts on mammalian toxicology considered this and concluded that if present it is relevant and that the level should not exceed 0.1%. Therefore toluene is a relevant impurity. Given the nature of this relevant impurity the usual requirements can be waived so that spectral data and storage stability data are not required. Also a method of analysis for toluene in the formulation is not required at this stage but may be required at Member State level.

The content of napropamide in the representative formulation is 450 g/L (pure). However, in Volume 4 it is clear that the nominal content given for the formulation is not correct and this needs to be amended.

Beside the specification, the assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of napropamide or the respective formulation. However, the following data gaps were identified:

- Surface tension of the Plant Protection Product.

The original surface tension study was questioned by the meeting of experts as the result was very low. The applicant now has preliminary results of a new study that shows that the original study is incorrect. This therefore confirms the data gap.

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

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of napropamide in the technical

material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Methods are available to monitor napropamide in food of plant origin (excluding dry matrices); soil, water and air.

Residues in food can be determined with a multi-method (the German S19 method has been validated) with an LOQ of 0.01 mg/kg. Residues in soil are analysed by GC-MS with an LOQ of 0.01 mg/kg. For ground water and drinking water the method of analysis is by GC-MS with an LOQ of 0.05 µg/L. The method of analysis for surface water is not acceptable as the LOQ is too high. From the ecotoxicological assessment the LOQ would have to be < 6.7 µg/L. In addition to this it should be noted 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 GC-UV with an 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 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 toxicology

Napropamide was discussed at the PRAPeR Expert's Meeting on mammalian toxicology (PRAPeR 34) in October 2007.

The meeting could not conclude on the comparability of the batches used in the toxicological studies (see point 1) and on the relative toxicity between the two isomers due to lack of data, however data on relative toxicity of isomers was not considered necessary. Toluene was considered a relevant impurity in the technical specification, and its level should be kept below 0.1 %.

EFSA note: Further information on the comparability of the toxicological batches with (non-peer reviewed) specifications was provided in an addendum to volume 3, dated January 2008, a follow up to PRAPeR 34 meeting of October 2007; this addendum was not peer-reviewed.

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. 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. Elimination of napropamide was rapid, 52-62 % was excreted in urine, and 37-52 % in faeces during the first 72

hours. Seven days after dosing, tissues contained less than 0.3 % of the administered dose, mostly associated to 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 parent compound. 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. Metabolite profile was similar in faeces and urine; the major metabolites were glucuronide conjugates, 4-OGlu-NPAM[3], 4-OGlu-DE-NPAM[4], 4-OGlu-NOPAM[5] and 4-OGlu-NOPA[6]. It is not known whether the metabolic pathway is the same for both isomers.

2.2. ACUTE TOXICITY

Acute toxicity of napropamide is low. The acute eye irritation was discussed at the meeting focusing on the generally poor quality of the studies presented; however, considering the most severe scores for eye irritation, the meeting 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 % of 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 each rat and dog species, two 6-week studies in mice, and two 1-year dog studies; a 30-day dermal study in rat 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; additionally mild anaemia was observed in rats. The rapporteur Member State provided more detailed information on the second 1-year dog study (Smith, 1995) in an addendum to volume 3, B.6, dated 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).

[3] 4-OGlu-NPAM: 4-glucuronyl-(N,N-diethyl-2-(1-naphthoxy)) propionamide
[4] 4-OGlu-DE-NPAM: 4-glucuronyl-(N-ethyl-2-(1-naphthoxy)) propionamide
[5] 4-OGlu-NOPAM: glucuronyl-(1-naphthoxy) propionamide (position of hydroxylation unconfirmed)
[6] 4-OGlu-NOPA: 4-glucuronyl-(1-naphthoxy) propionic acid

In a dermal 30-day, study in rats, no treatment-related effect was 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 vivo* test systems. Most studies were performed prior to the adoption of GLP, but Quality Statements were available and 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 fully acceptable to the rapporteur Member State. Two mammalian gene mutation tests presented positive results in mouse lymphoma L5178Y cells (with and without metabolic activation) and 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 assays) negative results were obtained.

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

2.5. LONG TERM TOXICITY

Long term toxicity was studied in two 2-year oral studies in the rat and two 18-month studies in the mouse; one of the mouse study was not accepted by the rapporteur Member State due to scarce data presented that were not reliable.

Main effects observed in the rat upon long term exposure to napropamide were decreased body weight. Detailed statistical information was given in the addendum dated September 2007 and the experts agreed to set the NOAEL at the dose level of 10.5 mg/kg bw/day in the first study (Pettersen & Wahlberg, 1991a) based on decreased body weight at the next higher dose level of 48 mg/kg bw/day; higher doses produced signs of mild anaemia and liver enzyme changes indicative of liver toxicity.

In the earlier rat study (Trutter & Lemen, 1978) **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, body weights data were generally well reported and the meeting 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 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 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 September 2007 addendum.
The experts agreed with the rapporteur on **the NOAEL of 30 mg/kg bw/day for both parental and offspring's toxicity**, based on reduced body weights at the next dose level of 100 mg/kg bw/day. No effect on reproductive parameters or on fertility was observed, so **the NOAEL for reproductive toxicity was 100 mg/kg bw/day, the highest dose tested**.

The effects of napropamide on the development were examined in several studies in rat and rabbit. One study in each species were not accepted by the rapporteur Member State due to scarce number of test animals, and generally poor reporting, however there were two acceptable studies performed in rat and one in rabbit which could be used for the evaluation and two range-finding studies in each species as additional information.
In the rat, evidence of maternal toxicity comprising 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 the dose level of 110 mg/kg bw/day**, based on the findings described above, and **the NOAEL for developmental toxicity was 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 with a few unproductive males used in the study was included in the addendum (September 2007). The experts agreed with the rapporteur's opinion that it had not been demonstrated that the abortions were only due to 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 do 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**[7], a minor metabolite found in rat's urine, which is also potentially present in plant's metabolites and in the environment. The results were that the oral

[7] NOPA or U12: 2-(1-naphthyloxy)propionic acid, (also referred to as α-naphthoxy propionic acid in the dossier)

LD_{50} of NOPA in male rat is 2710 mg/kg bw, the dermal LD_{50} in male rat is > 4640 mg/kg bw and that NOPA is not an eye irritant.

Further information on the toxicological relevance of the **plant's metabolites** was included in the addendum of September 2008, in which, based on a statement from the applicant, no concern was raised. Most of the plant metabolites were identified as being as well rat's metabolites, except three metabolites: **NQ[8], PA[9] and 1-naphthol**. No toxicological information was available on these metabolites, except on the classification of 1-naphthol from the European Chemical Bureau (ECB) site. The meeting agreed that the reference values of napropamide could be applied to the common metabolites from the plants and the rat, but **the data requirement for toxicological information on the three metabolites remained open**.

EFSA note: After the experts meeting, the applicant provided to the rapporteur Member State exhaustive available information on the toxicological relevance of the three metabolites of concern (NQ, PA and 1-naphthol) and these information were evaluated by the rapporteur Member State in the addendum to volume 3, dated January 2008 (follow up to PRAPeR 34 meeting), but not peer-reviewed.

2.9. MEDICAL DATA

A data gap was identified at the PRAPeR 34 meeting on medical data on occupational health surveillance.

EFSA note: After the experts meeting, the applicant provided to the rapporteur Member State supplementary information on medical surveillance at the two production sites; these data were summarized in the addendum of January 2008 but not peer-reviewed.

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

The experts at the PRAPeR 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 the rat and an assessment factor of 100. The ADI is supported by the 3-generation, rat study.

[8] NQ: 1,4-naphthoxyquinone
[9] PA: o-phthalic acid

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 meeting 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 referred 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 meeting agreed not to set an ARfD.

No ARfD was allocated.

2.11. DERMAL ABSORPTION

Only one *in vivo* study in rats is 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 45 SC. 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 meeting 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.

It was noted however that a strong recommendation should be made to Member States to require new data during national registration procedures.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Devrinol 45 SC is a suspension concentrate formulation containing 450 g napropamide/L.

Exposure data were recalculated in the addendum from January 2008 based on the parameters agreed at the PRAPeR expert meeting.

Operator exposure

Devrinol 45 SC is intended to be applied to the ground, pre-crop drilling, followed by incorporation into the soil, as a selective herbicide in winter 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. No indoor uses are permitted.

According to the representative uses, the maximum applied dose is 2.25 kg a.i./ha, corresponding to 5 L product/ha (for tomatoes); an application volume of 500 L spray/ha was considered for the calculations.
A further estimates was performed for oilseed rape, for which the applied dose is 1.2 kg a.i./ha, corresponding to 2.67 L product/ha with an application volume of 200 L spray/ha. Exposure is expected to be lower for cabbage, cauliflower, Brussels sprouts and broccoli/calabrese due to lower application rates.

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) is used. According to the German model, the exposure is below the AOEL when PPE is worn (gloves during mixing/loading and application, plus coverall and boots during application).

Estimated operator exposure presented as % of AOEL (0.5 mg/kg bw/day) for tomatoes (application rate of 2.25 kg a.i./ha

Tractor-mounted (field crop)	**No PPE**	**With PPE during M/L**	**With PPE during M/L & application**
UK POEM	651	187 (a)	50.4 (a)
German model	148.4	-	5.8 (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.i./ha

Tractor-mounted (field crop)	**No PPE**	**With PPE during M/L**	**With PPE during M/L & application**
UK POEM	493	234 (a)	48.8 (a)
German model	79.2	-	3.0 (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

New calculations for the bystander exposure risk assessment were presented in the addendum of January 2008 considering the parameters agreed at the expert meeting.

According to the EUROPOEM II, the following assumptions were considered: worst-case application rate of 2.25 kg a.i./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 2.2% of the AOEL.

3. Residues

Napropamide was discussed at the PRAPeR experts meeting for residues (PRAPER 35) in October 2007.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of napropamide has been investigated in cabbages (leafy crop), tomatoes (fruiting vegetables), oilseed rape (oilseeds), potatoes and apples. 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 plant 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 1,4-naphthoxyquinone (NQ), phthalic acid (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 amount 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 or higher than the parent compounds 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 in addition that the rat metabolism is as extensive as the plant metabolism, the expert meeting on mammalian toxicology estimated that the toxicological end points characterising the active substance should also be applied to metabolites. The three plant end-metabolites (NQ, PA and 1-Naphthol) are however not covered by the rat metabolism. Information in order to assess the toxicological relevance of these metabolites needs to be submitted.

The RMS has proposed to restrict the residue definition to napropamide for monitoring and risk assessment. This was agreed by the meeting of experts. It was however noted that the definition for

risk assessment may under estimate by 1 to 2 orders of magnitude the global toxicological burden considering the ratio between parent and all metabolites produced by plant metabolism. This was however considered of no consequence on the final outcome of the risk assessment given the very low portion of the ADI used. The residue definition for risk assessment must however be considered as provisional as the toxicological relevance of 3 plant metabolites still need to be investigated.

The possible change in the ratio of constituting isomers by plant metabolism or due to environmental conditions has also been considered by the expert meeting. It was however 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 20 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 Limit of Quantification (LOQ). The LOQ used in these trials ranged from 0.01 to 0.1 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

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 4.8 kg/ha. This application rate is 5N in case of brassicas, 4N in case of oilseed rape and 2N in case of tomatoes. In these circumstance 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 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 proposes a waiting period of 180 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. This must however be considered as provisional as the toxicological relevance of 3 plant metabolites still need to be investigated.

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 the 4-6 year old girl. 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 % of the ADI).

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.

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 supervised residue trials, it is proposed to set the MRL below 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' meeting for environmental fate and behaviour PRAPeR 32 in November/December 2007. 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 (13.2% 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 5.8%AR at 90 days and also accounted for 5.2%AR at 60 days. The member state experts discussed if a groundwater exposure assessment was necessary for this minor metabolite NOPA. The applicant's position presented in the reporting table and addendum to Vol. 3 B.8 of September 2007 was that though the metabolite was present at > 5%AR at 2 sampling points in one of the available route of degradation studies that fact that the pertinent study did not follow guidelines (pertinent deviations identified were the temperature of 30°C and low oc content 0.35 %) a groundwater exposure assessment for NOPA was not triggered. The consensus of the 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 degradation rates were higher than in the available laboratory studies (see section 4.1.2), a faster rate of transformation of the active substance was expected under field conditions and this would mean 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 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 applied for intended 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} 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} 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. However because of the extrapolated nature of these DT_{50}, experts from the member state agreed 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[10] (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 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. This available single DT_{50} and associated kinetic formation fraction cannot currently be considered an agreed EU endpoint.

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 applied for intended uses, there was no crop present. Weather data from North American field trials over the study durations were compared to EU climatic conditions and this comparison is reported in the addendum to Vol. 3 B.8 of September 2007. The member state 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 parent napropamide after applications were made in the autumn (September and October) determined over the whole core sample where residues were detected

[10] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

(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. Member state experts agreed that these were the appropriate endpoints to use in the northern EU exposure assessment and that these DT_{50} could be considered to represent degradation rates, so be used in leaching modelling for more northern EU scenarios. They however 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 agreed that with the current field trials database that had not been 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.
The longest available field napropamide single first order soil DT_{50} of 127 days was agreed by the experts from the member states 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 can be found in appendix 1. 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 are 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 4 soils in batch adsorption experiments. Calculated adsorption $K_f oc$ values varied from 465 to 11700 mL/g, (mean 599 mL/g). There was no evidence of a correlation of adsorption with pH. The values of the Freundlich slopes associated with these $K_f oc$ were not available 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). The applicant indicated that they would be able to provide a newer study. However the RMS felt these results from the available study could be taken forward in the risk assessment if a 1/n value of 1 was used as input to leaching modelling, in combination with the value of 599mL/g. They had therefore not requested the applicant to provide the newer study. The experts from the member states agreed that this was an appropriate way forward and that the new data were not essential to finalise the EU risk assessment. These values noted here are therefore those reported in appendix 1 as the agreed EU endpoints.

The adsorption / desorption of NOPA was investigated in 4 soils in appropriate guideline batch adsorptions experiments. Calculated adsorption $K_f oc$ 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 the addendum to Vol. 3 B.8 of September 2007. Scenario specific Kfoc and 1/n for each FOCUS groundwater scenario were calculated by the

applicant based on this regression as indicated in appendix 1. These values were agreed as appropriate by the member state experts to use for the FOCUS scenario modelling at the 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 a 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 30cm depth of water from spring to winter respectively for mid European conditions. Napropamide was converted to 2 different hydroxy napropamide isomers (1[11], 20% AR max; 2[12] 27%AR max), diethylamine (26%AR max) dimer[13] (9%AR max) and MNF[14] (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 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 to the meeting of experts the default of 1000 days had been utilised.

As a consequence of the comments made on the DAR, new FOCUS surface water and sediment predicted environmental concentration calculations were provided by the applicant for napropamide. These were evaluated in the addendum to Vol. 3 B.8 of September 2007. Unfortunately the experts were unable to accept the new calculations 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. These new calculations would need to incorporate the results of the southern EU field dissipation trials that the experts also identified as a data gap (see section 4.1.2). To clarify the required new calculations will

[11] Isomer 1: N,N-diethyl-2-(4-hydroxy-2-naphtyl)propionamide
[12] Isomer 2: N,N-diethyl-2-(1-hydroxy-2-naphtyl)propionamide
[13] dimer: 3,3'bis(1-(N,N-diethyl-carbamoyl)ethyl)-1,1'binaphtalene-4,4'-diol
[14] MNF: α-naphthol, 2-methyl-naphtho(1,2-b)-2H-furan-3-one

be FOCUS step 4 calculations because they need to include both spray drift inputs to TOXSWA and also include soil incorporation when parameterising PRZM and MACRO[15] which will need to be done outside the SWASH shell. Also it is expected that (at least for the scenarios with ponds defined) accumulation in sediment will need to be estimated by running TOXSWA for more than one 18 month period and adding sediment residues from the end of the previous run to the subsequent 18 month simulation until a plateau is reached[16], again by FOCUS definition's this is considered step 4 as it will need to be done outside the SWASH shell. The napropamide properties agreed by the meeting of experts (in addition to those already discussed above regarding water and sediment) that should be used as input are: Single first order soil DT_{50} for northern Europe 50 days with PRZM and MACRO corrections for temperature and soil moisture disabled, for southern Europe soil DT_{50} is dependant on the results of a data gap; Kfoc 599mL/g, 1/n=1. If necessary to conclude the risk assessment, further step 4 calculations incorporating risk mitigation measures may need to be considered. Once these new PEC for napropamide have been calculated consequent PEC in surface water also need to be calculated for the potential photolysis metabolites hydroxy napropamide isomers 1 and 2, diethylamine, dimer and MNF. The meeting of experts agreed the values in Table 1, page 37 in the addendum to Vol. 3 B.8 of September 2007 as the appropriate factors (mass yields) to use for these calculations.

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

The applied for intended use of Spring applications to brassicas, summer applications to winter oilseed rape and May application to field tomatoes were simulated using FOCUS PEARL 3.3.3 and FOCUS PELMO 3.3.2 using the following input parameters: napropamide single first order DT_{50} 50 days (from field studies), K_{foc} 599 mL/g (K_{fom} 347 mL/g), 1/n=1. As not normalised field studies were the source of the soil DT_{50} the simulation routines for correcting soil temperature and moisture were disabled. As the field trials were only considered representative of northern EU geoclimatic conditions, the simulation results for the Sevilla and Thiva scenarios (southern EU scenarios most easily differentiated as unlikely to represent North EU conditions) are not considered to be agreed EU endpoints. The evaluation of these simulations can be found in the addendum to Vol. 3 B.8 of September 2007. Napropamide was calculated to be present in leachate leaving the top 1m soil layer at 80th percentile annual average concentrations in the range <0.001 to 0.0655 µg/L. The member state experts considered that these simulations and results were appropriate to conclude on the groundwater contamination potential of the applied for intended uses covering more northern EU geoclimatic conditions.

For the soil metabolite NOPA groundwater modelling was provided in the addendum to Vol. 3 B.8 of September 2007 and discussed at the meeting of member state experts. They considered that the

[15] For PRZM an even incorporation depth over the top 8cm soil layer should be appropriately defined, note the PPR Opinion on FOCUSsw (The EFSA Journal (2004) 145, 1-31, discusses approaches to appropriately parameterise MACRO and PRZM for soil incorporation.
[16] see FOCUSsw scenario guidance (SANCO/4802/2001-rev.2 final (May 2003) section 8.7.3 page 217

modelling could not be accepted as the DT_{50} input parameter used originated from only a single soil and resulted in too favourable an assessment, as the combination of formation fractions (1.1% and 5.76% maximum observed values) and DT_{50} used (41 days, that represents a true degradation rate) were inappropriate. Therefore there is a data gap for a groundwater exposure assessment for NOPA ideally using a kinetic formation fraction from napropamide and a true NOPA degradation rate from a larger database (see section 4.1.2 where a data gap for further NOPA degradation rates is already identified). The experts noted that if a maximum observed value is used for formation in a modelling approach that simulates an application rate for the metabolite as if it was a parent compound (as had been done in addendum to Vol. 3 B.8 of September 2007), then the DT_{50} for NOPA should have been derived by fitting an observed decline from the NOPA peak in the available study where parent napropamide was dosed and NOPA was formed. This would be a significantly longer DT_{50} value than 41 days that the applicant had used.

Although the available NOPA modelling is considered to give too favourable a picture in relation to the potential for the leaching of NOPA, it is already clear that there is a high potential for NOPA to leach to groundwater at concentrations higher than the parametric drinking water limit of 0.1µg/L, that a groundwater non relevance assessment is triggered and concentrations will be > 0.75µg/L. (NOPA was calculated to be present in leachate leaving the top 1m soil layer at 80th percentile annual average concentrations up to 1.6µg/L).

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 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 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' meeting for ecotoxicology PRAPeR 33 in November/December 2007. It should be noted that the available risk assessment did not consider that napropamid consists of 2 enantiomeres. 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 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.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk to birds and mammals was calculated according to the Guidance Document on Birds and Mammals (SANCO/4145/2000). 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 evaluated. Also the long term risk was assessed as low for all uses except for the use in tomato. The application rate for the use in tomato 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 in the expert-meeting and a quantification of the percentage of insects taken in 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 endpoint (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 can be calculated once updated PEC_{sw} (fish-eating birds) for all uses and PEC_{soil} (earthworm-eating birds) values for Southern EU are available.

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 (tomato). For Northern EU the TER is acceptable (6.6 and 7.8, respectively). A data gap for a refined risk assessment for insectivorous mammals and earthworm eating mammals based on realistic PEC_{soil} was identified in the expert meeting for the use in Southern Europe (tomato). A risk assessment for fish-eating mammals needs to be conducted after establishing reliable PECsw values.
A long-term risk assessment for birds and mammals from exposure to 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 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 contaminaded 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 suggesting a low risk to birds and mammals from uptake of contaminated drinking water.
The risk from plant metabolites was considered to be addressed by the risk assessment for the parent napropamide.

Overall it is concluded that the risk to birds and mammals is low for the uses in Northern Europe. Some uncertainty remains with regard to the long-term risk to insectivorous birds for the use in tomatoes. The long-term risk to insectivorous and vermivorous mammals needs further refinement for

the use in Southern Europe (tomato) depending on the outcome of a new risk assessment based on realistic PECsoil values.

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 endpoint for *Lemna gibba* from a study with sediment present in the test system. The refinement was not accepted by the experts in the PRAPeR meeting. The experts discussed which endpoint 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 endpoint of 0.067 mg a.s./L should be considered in the risk assessment. The toxicity of the active substance was lower and the endpoint of 0.237 mg a.s./L was agreed for technical napropamide.

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 meeting that different groups of organisms with different sensitivities should not be combined in the geomean calculation. The experts suggested a consolidation of the endpoints with daphnids and *Crassostrea virginia*. The endpoints 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 as well as 5 different photolysis metabolites and NOPA (where groundwater becomes surface water) should be considered in the risk risk assessment

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.

No conclusion can be drawn on the risk to aquatic organisms since no reliable PECsw values were established. A high risk to aquatic organisms cannot be excluded for the representative uses of napropamide.

5.3. RISK TO BEES

An acute contact and oral toxicity study on bees with the lead formulation Devrinol 450 SC 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 in the suggested 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 (not peer-reviewed). 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 confirms 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 evaluated.

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 45 SC was available. The endpoint for napropamide and the lead formulation Devrinol 45 SC 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. The risk assessment for the Southern European use (tomatoes) can only be finalised once reliable PECsoil values are established.

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 450 SC is available to address this annex point. The lead formulation Devrinol 450 SC 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 (tomato, 2.25 kg a.s./ha equivalent to 1.5 mg a.s./kg soil in the upper 10 cm).. 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 concentrations. It is not possible from the available study to conclude on a low risk for uses with lower application rates since only one concentration in soil was tested. The risk to soil functioning needs to be addressed further for all representative uses.

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 Europena uses (use in tomatoes) can only be finalised after reliable PECsoil values have been established.

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 (1990) was used in the risk assessment. Based on this endpoint the risk to non-target plants can be considered as low without the need for risk mitigation measures.

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

Soil

Definitions for risk assessment: napropamide

Definitions for monitoring: napropamide

Water

Ground water

Definitions for exposure assessment: napropamide and NOPA[17]

Definitions for monitoring: At least napropamide but data gaps need to be addressed before this definition can be finalised.

[17] NOPA: 2-(1-naphthyloxy)propionic acid.

Surface water

Definitions for risk assessment:

water: napropamide. hydroxy napropamide isomers 1[18] and 2[19], diethylamine, dimer[20], MNF[21] 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 if isomers 1 and 2, diethylamine, dimer, MNF or NOPA would need to be monitored or not.

Air

Definitions for risk assessment: napropamide

Definitions for monitoring: napropamide

Food of plant origin

Definitions for risk assessment: napropamide (provisional)

Definitions for monitoring: napropamide

Food of animal origin

Definitions for risk assessment: no residue definition necessary as the livestock exposure is minimal

Definitions for monitoring: no residue definition necessary as the livestock exposure is minimal

[18] isomer1: N,N-diethyl-2-(4-hydroxy-2-naphtyl)propionamideme

[19] isomer2: N,N-diethyl-2-(1-hydroxy-2-naphtyl)propionamide

[20] dimer: 3,3'bis(1-(N,N-diethyl-carbamoyl)ethyl)-1,1'binaphtalene-4,4'-diol

[21] MNF: α-naphthol, 2-methyl-naphtho(1,2-b)-2H-furan-3-one

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

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 was assessed as low but a high risk to soil functioning (organic matter breakdown) was indicated by the available litter-bag study.

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} 208-1170 mL/g	No	Yes	Yes	Yes
NOPA	high mobility K_{foc} 28-81 mL/g (pH dependant)	Yes, though there is a data gap concentrations > 0.75µg/L expected	No data were made available. Data are necessary.	No	No data were made available. Data are necessary.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
napropamide	See point 5.2.
hydroxy napropamide isomer 1	No information provided
hydroxy napropamide isomer 2	No information provided
diethylamine	No information provided
dimer	No information provided
MNF	No information provided

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

- A revised specification for the now single source where the relevant impurity toluene is included (relevant for all uses evaluated, data gap identified by EFSA February 2008 for the toluene issue and for the single source issue by the meeting of experts October 2007, date of submission unknown, refer to chapter 1).
- Information on the biological activity of the isomers (relevant for all uses evaluated, data gap identified by the meeting of experts October 2007, date of submission unknown, refer to chapter 1).
- Further data to justify the minimum purity of the active substance (relevant for all uses evaluated, data gap identified by the meeting of experts October 2007, some QC data were supplied and evaluated in the January 2008 addendum to Volume 4 but insufficient detail was given, refer to chapter 1).
- Comparison of the new technical specification with the material tested in the ecotoxicology and mammalian toxicology studies (relevant for all uses evaluated, data gap identified by the meeting of experts October 2007, submitted and evaluated by rapporteur Member State in addendum to volume 3, follow-up to PRAPeR meeting, dated January 2008, but not peer-reviewed, refer to chapters 1 and 2).
- Surface tension of the plant protection product (relevant for all uses evaluated, data gap identified by the meeting of experts October 2007, date of submission unknown, refer to chapter 1).
- Method of analysis for surface water with an LOQ of < 6.7 µg/L (relevant for all uses evaluated, data gap identified by EFSA February 2008 as a result of the outcome of the meeting of experts ecotoxicology, date of submission unknown, refer to chapter 1).
- Information allowing to assess the toxicological relevance of 1,4-naphthoxyquinone (NQ), o-phthalic acid (PA) and 1-naphthol (relevant for all representative uses evaluated; identified by the experts meetings on mammalian toxicology and residues, submitted and evaluated by rapporteur Member State in addendum to volume 3, follow-up to PRAPeR meeting, dated January 2008, but not peer reviewed; refer to point 2.8 and 3.1.1).
- Medical data on occupational health surveillance (relevant for all representative uses evaluated; identified by the experts meeting on mammalian toxicology, submitted and summarized in addendum to volume 3, follow-up to PRAPeR meeting, dated January 2008, but not peer-reviewed; refer to point 2.9).
- Reliable soil degradation rates for NOPA in a minimum of 3 different soils (relevant for all representative uses evaluated; identified by the meeting of fate and behaviour experts, date of submission unknown: refer to point 4.1.2).
- 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 all

representative uses in the south of the EU; identified by the meeting of fate and behaviour experts, 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 all representative uses in the south of the EU; identified by the meeting of fate and behaviour experts, date of submission unknown; refer to point 4.1.2).
- PEC in surface water and sediment for napropamide to be calculated using FOCUS surface water scenarios to include spray drift, appropriately parameterise PRZM and MACRO to include soil incorporation and cover the potential for accumulation in sediment from use in consecutive seasons; required for north Europe but also needs to incorporate the results of southern EU field dissipation trials (data gap above) (relevant for all representative uses evaluated; identified by the meeting of fate and behaviour experts, date of submission unknown; refer to point 4.2.1).
- PEC in surface water for photolysis metabolites hydroxy napropamide isomers 1 and 2, diethylamine, dimer and MNF to be calculated using the results from the napropamide PEC in surface water (relevant for all representative uses evaluated; identified by the meeting of fate and behaviour experts, date of submission unknown; refer to point 4.2.1).
- PEC in groundwater for napropamide to be calculated to incorporate the results of southern EU field dissipation trials (data gap above) (relevant for all representative uses in the south of the EU; identified by the meeting of fate and behaviour experts, date of submission unknown; refer to point 4.2.2).
- PEC in groundwater for NOPA to be calculated to incorporate the results of NOPA soil DT50 (data gap above) and using an appropriate formation fraction from napropamide (relevant for all representative uses evaluated; identified by the meeting of fate and behaviour experts, date of submission unknown;: refer to point 4.2.2).
- Napropamide consists of two enantiomeres. This needs to be considered in the environmental risk assessment. (relevant for all uses; data gap identified after the expert meeting (PRAPeR 33); no submission date proposed; refer to chapter 5).
- The risk to fish-eating birds and mammals needs to be calculated when reliable PECsw values for napropamide are available. (relevant for all uses evaluated; data gap identified by EFSA after the experts meeting on ecotoxicology since PECsw values were not calculated according to the recommendations of the experts on fate and behaviour; no submission date proposed; see point 5.1).
- The long-term risk to insectivorous and vermivorous mammals needs to be refined (relevant for the use in Southern Europe (tomato); data gap identified in the expert meeting on ecotoxicology (PRAPeR 33 in November/December 2007; no submission date proposed; refer to point 5.1.)
- An aquatic risk assessment for napropamide needs to be conducted with correct PECsw values (relevant for all representative uses; data gap identified in the expert meeting (PRAPeR 33 in November/December 2007; no submission date proposed; refer to point 5.2).
- The photolysis metabolites and the groundwater metabolite NOPA need to be considered in the aquatic risk assessment. (relevant for all uses, data requirement identified during the peer-

review and confirmed in the expert meeting on fate and behaviour (PRAPeR 32 in November/December 2007); no submission date proposed; refer to point 5.2).

- A risk assessment for earthworms (relevant for the Southern European use (tomato); data gap identified by EFSA after the experts meeting; no submission date proposed; see point 5.5).
- The risk to soil functioning (organic matter breakdown) needs to be addressed (relevant for all representative uses; data gap identified by EFSA after the experts meeting; no submission date proposed; refer to point 5.6).
- A risk assessment for soil non-target micro-organisms. (relevant for the Southern European use (tomato); data gap identified after the meeting of experts; no submission date proposed; see 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 attached end points.

The representative formulated product for the evaluation was "Devrinol SC 450", a suspension concentrate formulation (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 has been validated). For the other matrices only single methods are available to determine residues of napropamide. For surface water the supplied method does not have a LOQ that is low enough and therefore a new data gap has been identified. In addition to this it should be noted that the residue definition for water is not finalised and therefore further methods could be required in the future.

Due to various reasons the minimum purity of the active substance and the impurity specification can not be concluded on.

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 trough urine and faeces.

Napropamide has low acute toxicity and no classification is proposed related to acute toxicity testing including irritancy and sensitisation. Critical effect observed through 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 out of five chromosomal tests, but three *in vivo* tests were all negative. So, overall, no genotoxic potential is attributed to napropamide. No potential for carcinogenicity or neurotoxicity was observed; no adverse

effect on fertility or on reproductive parameters was observed either, except for a higher abortion rate at maternally toxic doses in the rabbit which could not be ruled out from being a substance related effect. No foetotoxicity or teratogenicity was evidenced.
The acceptable daily intake (ADI) is set at 0.3 mg/kg bw/day; the acceptable operator exposure level (AOEL) is 0.5 mg/kg bw/day considering an assessment factor of 100 and no acute reference dose is allocated.
The estimated operator exposure is below the AOEL if personal protective equipment (PPE) is used. No risk is anticipated for workers or bystanders derived from napropamide applications.

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 on a provisional basis. Further information is needed to conclude on the toxicological relevance of 3 metabolites which are not covered by the toxicological studies performed with the parent compound.
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.
Provisionally, no risk for the consumer has been identified.

A large number of data gaps need to be addressed before the EU level environmental exposure assessment can be finalised (for details refer to the list of studies to be generated, where 7 data gaps in the area of environmental fate and behaviour are identified). The only exposure assessment that could be finalised for the whole EU was the air assessment. In relation to the applied for intended uses in the north of the EU, the exposure assessments of the predicted environmental concentration in soil and groundwater (but just for the active substance napropamide in groundwater) could be finalised. For the applied for intended uses in the north of the EU, the potential for groundwater exposure by the active substance napropamide above the parametric drinking water limit of 0.1 µg/L, is 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, though this exposure assessment could not be finalised with the data that were available to the peer review. A groundwater metabolite relevance assessment is triggered for NOPA.

The risk to birds was assessed as low for all representative uses evaluated except for the use in tomato where the first-tier long-term TER value of 4.6 was below the trigger of 5. It was agreed that the risk to insectivorous birds is likely to be low because the endpoint (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 earthworm-eating birds from secondary poisoning was assessed as low. The risk assessment for the Southern European use (tomato) can only be finalised once updated PEC_{soil} values are available. The risk to fish-eating birds and mammals needs to be assessed after reliable PECsw values are established.

The risk to mammals is considered to be low for the representative uses evaluated, except the risk to insectivorous mammals and earthworm-eating mammals for the use in Southern Europe (tomato). 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 meeting. The endpoints 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 endpoints of 0.067 mg a.s./L and a geometric mean value of 5.4 mg a.s./L for macrophytes and invertebrates, respectively. No conclusion can be drawn on the risk to aquatic organisms since no reliable PECsw values were established. A high risk to aquatic organisms cannot be excluded for the representative uses of napropamide. No major metabolites in surface water were identified in the water/sediment study. However, the fate experts agreed that the parent as well as 5 different photolysis metabolites and NOPA (where groundwater becomes surface water) should be considered for risk assessment

The risk of bioconcentration in fish was assessed as low. The risk to earthworms and soil non-target micro-organsisms was assessed as low for the uses in Northern Europe but is not finalised for the use in Southerne Europe. A high risk to soil functioning (organic matter breakdown) was indicated by the available litter-bag study since effects of >10% were observed until one year after application of napropamide and further refinement of the risk assessment is necessary.

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

- The estimated operator exposure was below the AOEL only if PPE as gloves during mixing/loading and application is used (refer to point 2.12).
- 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).

Critical areas of concern

- The minimum purity for the active substance is not agreed or the maximum levels for the impurities. There is no comparison between the technical specification and the materials tested the ecotoxicology and mammalian toxicology studies.
- The potential for groundwater contamination of the active substance napropamide cannot be finalised for the evaluated intended uses in the southern EU.

- A groundwater non relevance assessment is triggered for the metabolite NOPA, however this cannot be finalised as the groundwater exposure assessment is not finalised and data gaps are identified in the areas of ecotoxicology and biological screening for activity against target plants. In addition a consumer risk assessment from consumption of NOPA via drinking water would appear necessary if it is confirmed concentrations of NOPA are > 0.75µg/L as expected.
- Napropamide is very toxic to aquatic organisms. No risk assessment is currently available.
- A potential high risk to soil functioning (organic matter breakdown) was indicated in the litter-bag study.
- The risk to earthworms and soil non-target micro-organisms is not finalised for the Southern European use (tomato).

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

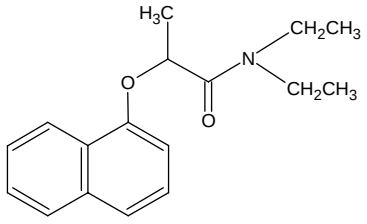
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	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)propionamide
CIPAC No ‡	271
CAS No ‡	15299-99-7
EC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification (including year of publication) ‡	none
Minimum purity of the active substance as manufactured ‡	Open (racemic mixture)
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Toluene maximum content <0.1 %
Molecular formula ‡	$C_{17}H_{21}NO_2$
Molecular mass ‡	271.36 g/mol
Structural formula ‡	

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

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	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)	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.*

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

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)

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

Summary of representative uses evaluated *

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL min – max (l)	water L/ha min – max	kg as/ha min – max (l)		
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		1.0	Not applicable.	[1] [2] [3]
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	Before sowing/ Planting	1	Not applicable	0.5		1.0	Not applicable	[1] [2] [3]

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

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL min – max (l)	water L/ha min – max	kg as/ha min – max (l)		
							top 5-8 cm preplanting and cultivation over 20 cm following harvest								
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		1.0	Not applicable	[1] [2] [3]
Broccoli/	EU,	Devrinol	F	Annual grasses and	SC	450g/l	Application to soil	Before	1	Not	0.5		1.0	Not appli	[1]

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

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL min – max (l)	water L/ha min – max	kg as/ha min – max (l)		
calabrese	North	SC, 450		broad-leaved weeds			surface, followed by soil incorporation into the top 5-8 cm preplanting and cultivation over 20 cm following harvest	sowing/ Planting		applicable				cable	[2] [3]
Tomatoes	EU, South	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	Before sowing/ Planting	1	Not applicable	0.45		2.25	Not applicable	[1] [2] [3]

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

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL min – max (l)	water L/ha min – max	kg as/ha min – max (l)		
							over 20 cm following harvest								
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		1.2		[1] [2] [3]

Reasons for greying out:
[1] There is no technical specification for the active substance.
[2] Napropamide is very toxic to aquatic organisms. No risk assessment is currently available.
[3] Groundwater exposure assessment for the metabolite NOPA and the non relevance assessment for NOPA need to be finalised.

* 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
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give**

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

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	**the rate for the variant (e.g. benthiavalicarb-isopropyl).** (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application (k) Indicate the minimum and maximum number of application possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

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

Appendix 1.2: Methods of Analysis

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

Technical as (analytical technique)	GC-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	Open
	drinking/ground	Open
Air		None

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 with partition with dichloromethane. Extracts were cleaned-up using gel permeation chromatography. Determination performed by GC/MSD. Napropamide LOQ: 0.01 mg/kg (cauliflower, tomatoes and rapeseed).
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	The method proposed by notifier was not sufficiently validated. No method for animal products is necessary, since no residues in animal products will occur above 0.01 mg/kg.
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 Open 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^+)]

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

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

	RMS/peer review proposal
Active substance	None

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	> 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 1-naphtol, o-phthalic acid, 1,4-naphtoxyquinone [22]
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 air/4 h (nose-only)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	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; rat, 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, rabbit: > 1000 mg/kg bw/day	

[22] Non peer reviewed information from the applicant after PRAPeR meeting shows no genotoxicity or classification as toxic or very toxic of any of the 3 impurities. RMS considers the 3 metabolites not toxicologically relevant.

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

Relevant inhalation NOAEL ‡	No data available - not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

Some positive responses *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 & kidneys: 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)

Reproduction toxicity

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 & 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	

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

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**[23] was tested for acute oral and dermal toxicity and eye irritation: Rat, oral LD_{50} = 2170 mg/kg bw Rat, dermal LD_{50} > 4640 mg/kg bw No eye irritation

Medical data ‡ (Annex IIA, point 5.9)

……..	No reports on occupational health surveillance[24] are available. No cases of poisoning are reported. No epidemiological studies are available

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.30 mg/kg bw/day	rat, 2-year studies.	100
AOEL ‡	0.50 mg/kg bw/day	dog, 1-year study	100
ARfD ‡	Not allocated - not necessary		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Devrinol 45 SC	Concentrate: 26% Spray dilutions: 26% Based on a rat *in vivo* dermal absorption study with dilutions of Devrinol 50 WP

[23] NOPA or U12: (1-naphthoxy) propionic acid or α-naphthoxy propionic acid
[24] A data gap was set for medical data on occupational health surveillance. Non peer reviewed information was submitted from the applicant after PRAPeR meeting.

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

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Acceptable for proposed uses. The estimated exposure for Devrinol 45 SC according to the German model and UK model (application rate 2.25 kg a.i./ha in tomatoes) was below AOEL only if PPE is worn. Tractor mounted equipment % of AOEL German model Without PPE: up to 148% PPE (gloves, coverall and sturdy footwear): up to 5.8% UK model Without PPE: up to 651% PPE (gloves mix/load and application): up to 50.4%
Workers	Not relevant since re-entry is not considered necessary shortly after spraying.
Bystanders	Bystander exposures were up to 2.2%) of AOEL (EUROPOEM II Bystander Working Group)

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

	RMS/peer review proposal
Substance (napropamide)	No classification

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

Appendix 1.4: Residues

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

Plant groups covered	Leafy crops (cabbage), root vegetables (potatoes), fruit (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. Provisional due to the outstanding toxicology requirements for the metabolites naphtoxyquinone, 1-naphthol and phtalic acid.
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
Time needed to reach a plateau concentration in milk and eggs	No data available.
Animal residue definition for monitoring	None. Not necessary as intakes by livestock ≤0.1 mg/kg diet/day since no detectable residues are expected.
Animal residue definition for risk assessment	None. Not necessary as intakes by livestock ≤0.1 mg/kg diet/day.
Conversion factor (monitoring to risk assessment)	None.
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes

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 planted 180 DAT.

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

Storage stability of napropamide residues was examined in brassicas (high water content) and oilseed (oil-containing crops). Napropamide residues were found to be stable in crops stored at approximately -18°C for up to 11 month for cabbage and at least one year for oilseed rape.

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

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

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

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

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

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

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Head cabbage	North	7 x <0.01 mg/kg	-	0.01* mg/kg	0.01 mg/kg	0.01 mg/kg
Brussels sprouts	North	7 x <0.01 mg/kg	-	0.01* mg/kg	0.01 mg/kg	0.01 mg/kg
Cauliflower	North	7 x <0.01 mg/kg	-	0.01* mg/kg	0.01 mg/kg	0.01 mg/kg
Broccoli/calabrese	North	7 x <0.01 mg/kg	-	0.01* mg/kg	0.01 mg/kg	0.01 mg/kg
Tomato	South	8 x <0.01 mg/kg	-	0.01* mg/kg	0.01 mg/kg	0.01 mg/kg
Rapeseed	North	8 x <0.01 mg/kg	-	0.01* mg/kg	0.01 mg/kg	0.01 mg/kg

(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 representative use
(c) Highest residue

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

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

ADI	0.3 mg/kg bw (proposed by RMS).
TMDI (% ADI) according to WHO European diet	< 1 % (WHO).
TMDI (% ADI) according to national (to be specified) diets	< 1 % (UK and German model).
IEDI (WHO European Diet) (% ADI)	Not required.
NEDI (specify diet) (% ADI)	Not required.
Factors included in IEDI and NEDI	Not required.
ARfD	Evaluated not necessary by RMS
IESTI (% ARfD)	Not applicable.
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not applicable.
Factors included in IESTI and NESTI	Not applicable.

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
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.

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralisation 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)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	20°C: NOPA; range: D[25]-1.1% AR, max 1.1% AR Polar metabolites; range: D[26]-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 ‡

Mineralisation after 90 days	25°C 14C-1-naphthyl labelling 0% AR after 90 days (n=1; water/soil system)
Non-extractable residues after 90 days	25°C 14C-1-naphthyl labelling 12.7 % AR after 90 days (n=1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	25°C 14C-1-naphthyl labelling NOPA, 0.6-0.8% AR (n=1)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	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)

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

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

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

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
	Metabolite NOPA Data gap for reliable DT50.
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 S Europe: Data gap.
	DT_{90f}: Germany, bare soil, 180; 290; 400 d (n=3); 1-order.
	For FOCUS scenario modelling DT_{50} – 50 d (geomean based on field data not normalised to reference conditions and only pertinent for northern EU assessment).
	Metabolite NOPA Data gap for reliable DT50.

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

Soil accumulation and plateau concentration ‡	No data submitted. Justification required since one DT90f > 1 year (Germany), which triggers soil accumulation test or model calculation. However an accumulated soil PEC is presented under PEC soil.

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 and1170 mL/g (average= 599 mL/g; 5 soils) K_f: 3.4; 5.1; 6.4;8.6 and 14.8 mL/g (average= 7.67 mL/g; 1/n= ~1 ; 5 soils) Desorption: K_f: 10.98 mL/g (1 soil) Estimated coefficients for other soils not reported. No pH dependence For FOCUS gw modelling K_{foc}: 599 mL/g, 1/n=1
	NOPA Adsorption: K_{foc}: 28; 35; 40 and81 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

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)

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

	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 ‡	Available study not acceptable, none required.
Aged residues leaching ‡	Guideline: None (The study did not follow the recommendation of SETAC (1995) Aged for: 30 d Precipitation: 13 mm/d Time period (d): 45 d Leachate: 0.83-0.93% radioactivity in leachate with NOPA identified as a component of the leachate 97% total radioactivity remained in the top 13 cm
Lysimeter/ field leaching studies ‡	Location: West Virginia, USA Study type: Field leaching (commercial field) with monitoring Number of applications: 3 - 4 years Application rate: 6.7-14.6 kg/ha in total (>3N). The concentration of residues in ground water samples at 90 cm depth were up to 0.2 µg napropamide/L.

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

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	N. Europe: Max $DT_{50field}$ (d): 127 days 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. 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 data	N. Europe: Crops: Brassicas, oilseed rape S. Europe: Crop: tomatoes % plant interception: Pre-emergence therefore no plant interception Application rate: N. Europe: One time 1,200 g 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
		$DT50_{field}$ = 127 d	
Initial	0 d	2.063	2.063
Short term	1 d	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		

Southern Europe: Data gap.as no DT50 for southern European conditions is available. If the DT50 of 127 days was assumed (note DT50 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.

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

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5: 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 metabolites above 10 % ‡	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%)
Quantum yield of direct phototransformation in water at Σ > 290 nm	Φ=0.5
Readily biodegradable ‡ (yes/no)	No

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[27].); 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)
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) and PEC sediment (Annex IIIA, point 9.2.3)

Napropamide: Data gap

[27] Ext = extrapolated value

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

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

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)	Modelling using FOCUS model (PELMO & PEARL) Scenarios: Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva DT50 Soil: 50 d (Field study) Not normalised. Temperature and moisture correction switched off K_{OC}: 599 L/kg 1/n=1

Application rate

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

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

PEARL (PELMO concentrations were lower)	Scenario	Parent (µg/l)			NOPA Metabolite (µg/l) Data gap		
		Cabbage	Rape	Tomatoes	Cabbage	Rape	Tomatoes
	Châteaudun	<0.001	<0.001	0.0001			
	Hamburg	<0.001	0.0001	-			
	Jokioinen	<0.001	-	-			
	Kremsmünster	<0.001	0.0001	-			
	Okehampton	-	0.0002	-			
	Piacenza	-	0.0056	0.0655			
	Porto	<0.001	<0.001	<0.001			
	Sevilla						
	Thiva						

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

Direct photolysis in air ‡	Not studied, not required
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
Volatilisation ‡	from soil surfaces: Not studied – not expected to volatilise
	from plant surfaces: Not studied – not expected to volatilise

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

PEC (air)

Method of calculation	Not calculated - negligible

$PEC_{(a)}$

Maximum concentration	Not calculated - negligible

Residues requiring further assessment

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: 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

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

Candidate for R53. May cause long term adverse effects.

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

Appendix 1.6: Effects on non-target Species

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Bobwhite quail	a.s.	Acute	> 2250	-
	Preparation	Acute	-	-
	Metabolite 1	Acute	-	-
	a.s.	Short-term	1572	> 7200
	a.s.	Long-term	309	3000
Mammals ‡				
rats	a.s.	Acute	4680	-
	Preparation	Acute	-	-
	Metabolite 1	Acute	-	-
	a.s.	Long-term	30	-
Additional higher tier studies ‡ No data available.				

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

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	Subchronic	8.5	5
2.25	Tomato	Insectivorous bird	Subchronic	**4.5**	5
1.2	Oil seed rape	Herbivorous bird	Subchronic	8.5	5
1.2	Oil seed rape	Insectivorous bird	Subchronic	8.6	5
2.25	Tomato	Vermivorous bird	Long term	46	5
1.2	Oil seed rape	Vermivorous bird	Long term	86	5
1	Brassicas	Vermivorous bird	Long term	103	5
2.25	Tomato	Vermivorous mammal	Long term	3.5	5
1.2	Oil seed 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	4.1	5
1.2	Oil seed rape	Insectivorous mammal	Long term	7.8	5
1	Brassicas	Insectivorous mammal	Long term	9.3	5

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

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
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 the most sensitive aquatic organisms (Annex IIIA, point 10.2)

No reliable PECsw values were established and hence no aquatic risk assessment is available.

Bioconcentration	
Bioconcentration factor (BCF) ‡	98

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

Bioconcentration	
Annex VI Trigger for the bioconcentration factor	100
Clearance time (days) (CT_{50})	Not reported
(CT_{90})	~ 7 days
Level and nature 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)

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	-	-
Preparation	~ > 100	~ > 100
Metabolite 1	-	-
Field or semi-field tests: No data required.		

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

Application rate (kg as/ha)	Test substance	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

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

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

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

Test organism	Test substance	Time scale	End point
Earthworms			
	a.s. ‡	Acute 14 days	564 mg/kg soil dry weigth (* /2 = 282)
	a.s. ‡	Chronic 8 weeks	-
	Preparation	Acute	-
	Preparation	Chronic	60 mg/kg soil dry weight (* / 2 = 30) (highest conc. tested, lead formulation)
	Metabolite 1	Acute	-
	Metabolite 1	Chronic	-

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

Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡	28 days	< 25 % effect at 15.92 mg a.s./kg d.w. soil (mg a.s/ha). **11.250** g as/ha
	Metabolite 1	-	-

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

Carbon mineralisation	a.s. ‡	28 days	0 % effect at 15.92 mg a.s./kg d.w. soil (mg a.s/ha) **11.250** g as/ha
	Metabolite 1	-	-
Field studies 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 indicating a potential high risk to organic matter breakdown.			

Toxicity/exposure ratios for soil organisms

Oilseed rape, 1.2 kg as/ha

Test organism	Test substance	Time scale	Soil PEC	TER	Annex VI Trigger
Earthworms					
	a.s. ‡	Acute	-	136	10
	a.s. ‡	Chronic	-	-	5
	Preparation	Acute	-	-	10
	Preparation	Chronic	-	14.5	5
	Metabolite 1	Acute	-	-	10
	Metabolite 1	Chronic	-	-	5

The risk assessment for tomato use (Southern Europe) cannot be finalised (data gap in fate and behaviour)

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/ha) vegetative vigour	ER_{50} (g/ha) emergence	Exposure (g/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.

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

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	Endpoint
Activated sludge	Respiration inhibition, 3 hours, EC50 >1000 mg as/L
Pseudomonas sp	Growth inhibition, 6 hours. EC50 > 65.7 mg as/L

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

Compartment	
soil	napropamide
water	napropamide. hydroxyl napropamide isomers 1[28] and 2[29], diethylamine, dimmer[30], MNF[31] and NOPA in situations where groundwater becomes surface water.
sediment	napropamide
groundwater	napropamide, NOPA

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

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

[28] isomer1: N,N-diethyl-2-(4-hydroxy-2-naphtyl)propionamideme

[29] isomer2: N,N-diethyl-2-(1-hydroxy-2-naphtyl)propionamide

[30] dimer: 3,3'bis(1-(N,N-diethyl-carbamoyl)ethyl)-1,1'binaphtalene-4,4'-diol

[31] MNF: ά-naphthol, 2-methyl-naphtho(1,2-b)-2H-furan-3-one

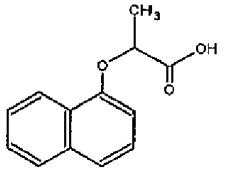
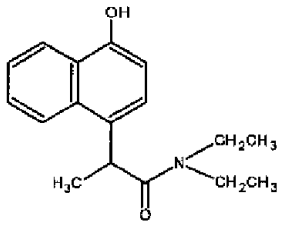
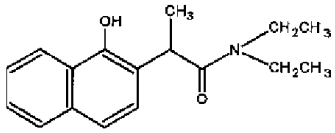
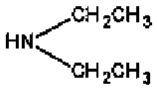
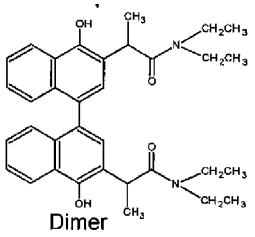
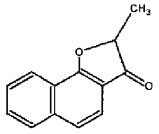
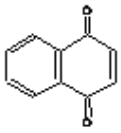
‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

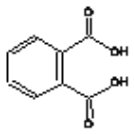
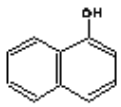
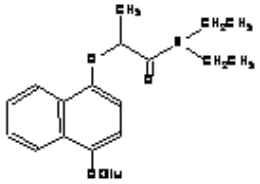
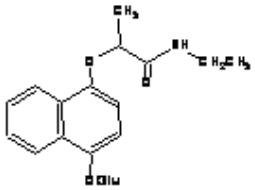
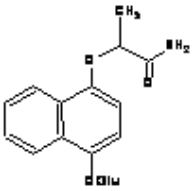
APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
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
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry

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

APPENDIX 3 - USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
NOPA (U12)	2-(1-naphthyloxy)propionic acid	
Hydroxy napropamide isomer 1	N,N-diethyl-2-(4-hydroxy-2-naphtyl)propionamide	
Hydroxy napropamide isomer 2	N,N-diethyl-2-(1-hydroxy-2-naphtyl)propionamide	
diethylamine	diethylamine	
dimer	3,3'bis(1-(N,N-diethyl-carbamoyl)ethyl)-1,1'binaphtalene-4,4'-diol	
MNF	α-naphthol, 2-methyl-naphtho(1,2-b)-2H-furan-3-one	
NQ	1,4-naphthoxyquinone	

Code/Trivial name	Chemical name	Structural formula
PA	o-phthalic acid	
	1-naphthol	
4-OGlu-NPAM	4-glucuronyl-(N,N-diethyl-2-(1-naphthoxy)) propionamide	
4-OGlu-DE-NPAM	4-glucuronyl-(N-ethyl-2-(1-naphthoxy)) propionamide	
4-OGlu-NOPAM	glucuronyl-(1-naphthoxy) propionamide (position of hydroxylation unconfirmed)	
4-OGlu-NOPA	4-glucuronyl-(1-naphthoxy) propionic acid